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Quantum Medicine

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Abstract: Quantum medicine **(**Quantum healing) is a pseudo-scientific mixture of ideas which purportedly draw on quantum mechanics, psychology, philosophy, and neurophysiology. Advocates of quantum healing assert that quantum phenomena govern health and wellbeing. There are a number of different versions, which allude to various quantum ideas including wave particle duality and virtual particles, and more generally to "energy" and to vibrations. Quantum healing is a form of alternative medicine.
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Key words: Quantum; Medicine; cell; life; research; literature

Introduction

Quantum medicine **(**Quantum healing) is a pseudo-scientific mixture of ideas which purportedly draw on quantum mechanics, psychology, philosophy, and neurophysiology. Advocates of quantum healing assert that quantum phenomena govern health and wellbeing. There are a number of different versions, which allude to various quantum ideas including wave particle duality and virtual particles, and more generally to "energy" and to vibrations.[1] Quantum healing is a form of alternative medicine.

Deepak Chopra coined the term "quantum healing" when he published the first edition of his book with that title in 1989.[2][3] His discussions of quantum healing have been characterised as technobabble - "incoherent babbling strewn with scientific terms"[4] which drives those who actually understand physics "crazy"[5] and as "redefining Wrong".[6]

Quantum healing has a number of vocal followers, but the scientific community widely regards it as nonsensical.[7] The main criticism revolves around its systematic misinterpretations of modern physics,[8] especially of the fact that macroscopic objects (such as the human body or individual cells) are much too large to exhibit inherently quantum properties like interference and wave function collapse. Most literature on quantum healing is almost entirely philosophical, omitting any physics.[9]

Physicist Brian Cox argues that misuse of the word "quantum", such as its use in the phrase *quantum healing*, has a negative effect on society as it undermines genuine science and discourages people from engaging with conventional medicine. He states that "for some scientists, the unfortunate distortion and misappropriation of scientific ideas that often accompanies their integration into popular culture is an unacceptable price to pay."[8]

This article introduces recent research reports as references in the related studies.

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PubMed Literatures

Abbey, C. K. and H. H. Barrett (2001). "Human- and model-observer performance in ramp-spectrum noise: effects of regularization and object variability." J Opt Soc Am A Opt Image Sci Vis **18**(3): 473-488.

We consider detection of a nodule signal profile in noisy images meant to roughly simulate the statistical properties of tomographic image reconstructions in nuclear medicine. The images have two sources of variability arising from quantum noise from the imaging process and anatomical variability in the ensemble of objects being imaged. Both of these sources of variability are simulated by a stationary Gaussian random process. Sample images from this process are generated by filtering white-noise images. Human-observer performance in several signal-known-exactly detection tasks is evaluated through psychophysical studies by using the two-alternative forced-choice method. The tasks considered investigate parameters of the images that influence both the signal profile and pixel-to-pixel correlations in the images. The effect of low-pass filtering is investigated as an approximation to regularization implemented by image-reconstruction algorithms. The relative magnitudes of the quantum and the anatomical variability are investigated as an approximation to the effects of exposure time. Finally, we study the effect of the anatomical correlations in the form of an anatomical slope as an approximation to the effects of

different tissue types. Human-observer performance is compared with the performance of a number of model observers computed directly from the ensemble statistics of the images used in the experiments for the purpose of finding predictive models. The model observers investigated include a number of nonprewhitening observers, the Hotelling observer (which is equivalent to the ideal observer for these studies), and six implementations of channelized-Hotelling observers. The human observers demonstrate large effects across the experimental parameters investigated. In the regularization study, performance exhibits a mild peak at intermediate levels of regularization before degrading at higher levels. The exposure-time study shows that human observers are able to detect ever more subtle lesions at increased exposure times. The anatomical slope study shows that human-observer performance degrades as anatomical variability extends into higher spatial frequencies. Of the observers tested, the channelized-Hotelling observers best capture the features of the human data.

Abdolmaleki, A., et al. (2017). "Computer-aided drug design to explore cyclodextrin therapeutics and biomedical applications." Chem Biol Drug Des **89**(2): 257-268.

Cyclodextrin (CD) is a subset of the macrocyclic structural class, which is an important class of small organic agents that are useful functional excipients. They have wide range application possibilities in different fields of sciences such as material preparation, medicine, analytical chemistry, and separation processes. They are used widely in pharmaceutical formulations and drug delivery for increasing the water solubility of low soluble drugs and drug candidates. Due to the ring structure, they behave differently than smaller molecules and may be capable of hitting new classes of targets. A macrocyclic molecule presents varied functionality and stereochemical complexity in a pre-organized conformation of the ring structure. This can result in high selectivity and affinity for protein targets while conserving enough bioavailability to arrive at intracellular locations. Regardless of these valuable features, and the verified success of several marketed macrocycle drugs isolated from natural compounds, this class has been little explored in drug development. This study describes some of the key features of the CDs therapeutic discovery. Also, the application of computational chemistry approaches such as QSAR/QSPR, molecular docking, and molecular/quantum mechanics for modeling of CD-drug system is reviewed briefly.

Abedini-Nassab, R. (2017). "Nanotechnology and Nanopore Sequencing." Recent Pat Nanotechnol **11**(1): 34-41.

DNA sequencing is one of the crucially important tasks in the fields of genetics and cellular biology, which is benefiting from nanotechnology. DNA carries genetic information and sequencing it in a quick way helps researchers in achieving essential goals, including personalized medicine. Solid state nanopores potentially can offer more durability, in sequencing biomolecules, over the proteinbased nanopores. In recent years, various ideas are introduced towards the goal of fast and low cost sequencing. In this review article recent advances presented in journal articles as well as patents in this field, including sequencing methods, membrane materials and their fabrication techniques, drilling methods, and biomolecule translocation speed control ideas are investigated.

Abramovits, W., et al. (2010). "Applications of nanomedicine in dermatology: use of nanoparticles in various therapies and imaging." J Cosmet Dermatol **9**(2): 154-159.

BACKGROUND: Nanoscale technology is rapidly being incorporated into medicine. Nanodermatology concentrates on the use of nanomaterials (sized less than 1000 nm) on the skin. This article gives basic descriptions of various nanomaterials currently used in dermatology. METHODS: Studies retrievable through PubMed and other relevant literature from the nanotechnology industry pertaining to the use of nanoparticles in dermatology are reviewed. The authors provide their insight into potential applications for skin conditions. RESULTS: Nanotechnology-based products and technology have a promising, inevitable future in medicine particularly in dermatology, such as prevention of disease, treatment, and imaging with less invasiveness. CONCLUSIONS: The advent of nanoparticles including nanostructured lipid particles and solid lipid nanoparticles, dendrimers, and quantum dots have already many cosmetic applications as well as great potential in dermatologic applications.

Adeola, H. A., et al. (2020). "Prospects of nanodentistry for the diagnosis and treatment of maxillofacial pathologies and cancers." Heliyon **6**(9): e04890.

Despite the commendable milestones achieved in molecular maxillofacial pathology in the last decade, there remains a paucity of utilization of ancillary nanomolecular tools that complement the omics-based approaches. As the advent of omics science transforms our understanding of tumour biology from a phenomenological to a complex network (systems-oriented) paradigm, several ancillary tools have emerged to improve the scope of individualized medicine. Targeted nano drug delivery systems have significantly reduced toxicity of chemotherapeutic agents in a precise manner. Many conventional cancer

therapies are limited in efficacy and this has led to the emergence of nanomedical innovations. Despite the success of nanomedicine, a major challenge that persists is tumour heterogeneity and biological complexity. A good understanding of the interaction between inorganic nanoparticles and the biological systems has led to the development of better tools for individualized medicine. Tools such as the composite organic-inorganic nanoparticles (COINs) and the quantum dots (QD) have significantly improved the identification and quantification of disease biomarkers, histopathological detection methods, as well as improving the clinical translation and utility of these nanomaterials. Nanomedicine has lent credence to several multipronged theranostic applications in medicine, and this has improved the medical practice tremendously. Despite the palpable influence of nanomedicine on the delivery of individualized medical therapies, the term "nanodentistry" remains in the background without much hype, albeit some progress has been made in this area. Hence, this review discusses the potential and challenges of nanodentistry in the diagnosis and treatment of maxillofacial pathologies, particularly cancer in resource-limited settings.

Agoramoorthy, G. and C. Chakraborty (2007). "Re: introduction to nanotechnology: potential applications in physical medicine and rehabilitation." Am J Phys Med Rehabil **86**(12): 1031-1032; author reply 1032.

Ahmed, L., et al. (2018). "Molecular mechanism of activation of human musk receptors OR5AN1 and OR1A1 by (R)-muscone and diverse other musk-smelling compounds." Proc Natl Acad Sci U S A **115**(17): E3950-E3958.

Understanding olfaction at the molecular level is challenging due to the lack of crystallographic models of odorant receptors (ORs). To better understand the molecular mechanism of OR activation, we focused on chiral (R)-muscone and other musk-smelling odorants due to their great importance and widespread use in perfumery and traditional medicine, as well as environmental concerns associated with bioaccumulation of musks with estrogenic/antiestrogenic properties. We experimentally and computationally examined the activation of human receptors OR5AN1 and OR1A1, recently identified as specifically responding to musk compounds. OR5AN1 responds at nanomolar concentrations to musk ketone and robustly to macrocyclic sulfoxides and fluorine-substituted macrocyclic ketones; OR1A1 responds only to nitromusks. Structural models of OR5AN1 and OR1A1 based on quantum mechanics/molecular mechanics (QM/MM) hybrid methods were validated through direct comparisons with activation profiles from site-directed mutagenesis experiments and analysis of binding energies for 35 musk-related odorants. The experimentally found chiral selectivity of OR5AN1 to (R)- over (S)-muscone was also computationally confirmed for muscone and fluorinated (R)-muscone analogs. Structural models show that OR5AN1, highly responsive to nitromusks over macrocyclic musks, stabilizes odorants by hydrogen bonding to Tyr260 of transmembrane alpha-helix 6 and hydrophobic interactions with surrounding aromatic residues Phe105, Phe194, and Phe207. The binding of OR1A1 to nitromusks is stabilized by hydrogen bonding to Tyr258 along with hydrophobic interactions with surrounding aromatic residues Tyr251 and Phe206. Hydrophobic/nonpolar and hydrogen bonding interactions contribute, respectively, 77% and 13% to the odorant binding affinities, as shown by an atom-based quantitative structure-activity relationship model.

Ailioaie, L. M. and G. Litscher (2020). "Molecular and Cellular Mechanisms of Arthritis in Children and Adults: New Perspectives on Applied Photobiomodulation." Int J Mol Sci **21**(18).

Juvenile idiopathic arthritis and adult rheumatoid arthritis are two major groups with chronic joint pain and inflammation, extra-articular manifestations, and high risk of comorbidities, which can cause physical and ocular disability, as well as create great socio-economic pressure worldwide. The pathogenesis of arthritis manifested in childhood and adulthood is multifactorial, unclear, and overly complex, in which immunity plays an important role. Although there are more and more biological agents with different mechanisms of action for the treatment of arthritis, the results are not as expected, because there are partial responses or non-responsive patients to these compounds, high therapeutic costs, side effects, and so on; therefore, we must turn our attention to other therapeutic modalities. Updating knowledge on molecular and cellular mechanisms in the comparative pathogenesis of chronic arthritis in both children and adults is necessary in the early and correct approach to treatment. Photobiomodulation (PBM) represents a good option, offering cost-effective advantages over drug therapy, with a quicker, more positive response to treatment and no side effects. The successful management of PBM in arthritis is based on the clinician's ability to evaluate correctly the inflammatory status of the patient, to seek the optimal solution, to choose the best technology with the best physical parameters, and to select the mode of action to target very precisely the immune system and the molecular signaling pathways at the molecular level with the exact amount of quantum light energy in order to obtain the desired immune modulation and the remission of the disease. Light is a very powerful tool in medicine because it can simultaneously target many

cascades of immune system activation in comparison with drugs, so PBM can perform very delicate tasks inside our cells to modulate cellular dysfunctions, helping to initiate self-organization phenomena and finally, healing the disease. Interdisciplinary teams should work diligently to meet these needs by also using single-cell imaging devices for multispectral laser photobiomodulation on immune cells.

Akerman, M. E., et al. (2002). "Nanocrystal targeting in vivo." Proc Natl Acad Sci U S A **99**(20): 12617-12621.

Inorganic nanostructures that interface with biological systems have recently attracted widespread interest in biology and medicine. Nanoparticles are thought to have potential as novel intravascular probes for both diagnostic (e.g., imaging) and therapeutic purposes (e.g., drug delivery). Critical issues for successful nanoparticle delivery include the ability to target specific tissues and cell types and escape from the biological particulate filter known as the reticuloendothelial system. We set out to explore the feasibility of in vivo targeting by using semiconductor quantum dots (qdots). Qdots are small (<10 nm) inorganic nanocrystals that possess unique luminescent properties; their fluorescence emission is stable and tuned by varying the particle size or composition. We show that ZnS-capped CdSe qdots coated with a lung-targeting peptide accumulate in the lungs of mice after i.v. injection, whereas two other peptides specifically direct qdots to blood vessels or lymphatic vessels in tumors. We also show that adding polyethylene glycol to the qdot coating prevents nonselective accumulation of qdots in reticuloendothelial tissues. These results encourage the construction of more complex nanostructures with capabilities such as disease sensing and drug delivery.

Alam, F., et al. (2015). "Unique roles of nanotechnology in medicine and cancer-II." Indian J Cancer **52**(1): 1-9.

Applications of nanotechnology in medicine and cancer are becoming increasingly popular. Common nanomaterials and devices applicable in cancer medicine are classifiable as liposomes, polymeric-micelles, dendrimers, nano-cantilevers, carbon nanotubes, quantum dots, magnetic-nanoparticles, gold nanoparticles (AuNPs) and certain miscellaneous nanoparticles. Here, we present review of the structure, function and utilities of the various approved, under trial and pretrial nanodevices applicable in the cancer care and medicine. The liposomes are phospholipid-vesicles made use in carrying drugs to the target site minimizing the bio-distribution toxicity and a number of such theranostics have been approved for clinical practice. Newly worked out liposomes and polymeric micelles are under the trail phases for nano-therapeutic utility. A multifunctional dendrimer conjugate with imaging, targeting and drug molecules of paclitaxel has been recently synthesized for cancer theranostic applications. Nano-cantilever based assays are likely going to replace the conventions methods of chemical pathological investigations. Carbon nanotubes are emerging for utility in regenerative and cancer medicine. Quantum dots hold great promise for the micro-metastasis and intra-operative tumor imaging. Important applications of magnetic nanoparticles are in the cardiac stents, photodynamic therapy and liver metastasis imaging. The AuNPs have been employed for cell imaging, computed tomography and cancer therapy. Besides these categories, miscellaneous other nanoparticles are being discovered for utility in the cancer diagnosis and disease management. However, the use of nanoparticles should be cautious since the toxic effects of nanoparticles are not well-known. The use of nanoparticles in the clinical practice and their toxicity profile require further extensive research.

Albaqami, M., et al. (2020). "Arabidopsis cryptochrome is responsive to Radiofrequency (RF) electromagnetic fields." Sci Rep **10**(1): 11260.

How living systems respond to weak electromagnetic fields represents one of the major unsolved challenges in sensory biology. Recent evidence has implicated cryptochrome, an evolutionarily conserved flavoprotein receptor, in magnetic field responses of organisms ranging from plants to migratory birds. However, whether cryptochromes fulfill the criteria to function as biological magnetosensors remains to be established. Currently, theoretical predictions on the underlying mechanism of chemical magnetoreception have been supported by experimental observations that exposure to radiofrequency (RF) in the MHz range disrupt bird orientation and mammalian cellular respiration. Here we show that, in keeping with certain quantum physical hypotheses, a weak 7 MHz radiofrequency magnetic field significantly reduces the biological responsivity to blue light of the cryptochrome receptor cry1 in Arabidopsis seedlings. Using an in vivo phosphorylation assay that specifically detects activated cryptochrome, we demonstrate that RF exposure reduces conformational changes associated with biological activity. RF exposure furthermore alters cryptochrome-dependent plant growth responses and gene expression to a degree consistent with theoretical predictions. To our knowledge this represents the first demonstration of a biological receptor responding to RF exposure, providing important new implications for magnetosensing as well as possible future applications in biotechnology and medicine.

Ashley, C. E., et al. (2011). "The targeted delivery of multicomponent cargos to cancer cells by nanoporous

particle-supported lipid bilayers." Nat Mater **10**(5): 389-397.

Encapsulation of drugs within nanocarriers that selectively target malignant cells promises to mitigate side effects of conventional chemotherapy and to enable delivery of the unique drug combinations needed for personalized medicine. To realize this potential, however, targeted nanocarriers must simultaneously overcome multiple challenges, including specificity, stability and a high capacity for disparate cargos. Here we report porous nanoparticle-supported lipid bilayers (protocells) that synergistically combine properties of liposomes and nanoporous particles. Protocells modified with a targeting peptide that binds to human hepatocellular carcinoma exhibit a 10,000-fold greater affinity for human hepatocellular carcinoma than for hepatocytes, endothelial cells or immune cells. Furthermore, protocells can be loaded with combinations of therapeutic (drugs, small interfering RNA and toxins) and diagnostic (quantum dots) agents and modified to promote endosomal escape and nuclear accumulation of selected cargos. The enormous capacity of the high-surface-area nanoporous core combined with the enhanced targeting efficacy enabled by the fluid supported lipid bilayer enable a single protocell loaded with a drug cocktail to kill a drug-resistant human hepatocellular carcinoma cell, representing a 10(6)-fold improvement over comparable liposomes.

Baimuratov, A. S., et al. (2015). "Dislocation-induced chirality of semiconductor nanocrystals." Nano Lett **15**(3): 1710-1715.

Optical activity is a common natural phenomenon, which occurs in individual molecules, biomolecules, biological species, crystalline solids, liquid crystals, and various nanosized objects, leading to numerous important applications in almost every field of modern science and technology. Because this activity can hardly be altered, creation of artificial active media with controllable optical properties is of paramount importance. Here, for the first time to the best of our knowledge, we theoretically demonstrate that optical activity can be inherent to many semiconductor nanowires, as it is induced by chiral dislocations naturally developing during their growth. By assembling such nanowires in two- or three-dimensional periodic lattices, one can create optically active quantum supercrystals whose activity can be varied in many ways owing to the size quantization of the nanowires' energy spectra. We believe that this research is of particular importance for the future development of semiconducting nanomaterials and their applications in nanotechnology, chemistry, biology, and medicine.

Baimuratov, A. S., et al. (2015). "Giant Optical Activity of Quantum Dots, Rods, and Disks with Screw Dislocations." Sci Rep **5**: 14712.

For centuries mankind has been modifying the optical properties of materials: first, by elaborating the geometry and composition of structures made of materials found in nature, later by structuring the existing materials at a scale smaller than the operating wavelength. Here we suggest an original approach to introduce optical activity in nanostructured materials, by theoretically demonstrating that conventional achiral semiconducting nanocrystals become optically active in the presence of screw dislocations, which can naturally develop during the nanocrystal growth. We show the new properties to emerge due to the dislocation-induced distortion of the crystal lattice and the associated alteration of the nanocrystal's electronic subsystem, which essentially modifies its interaction with external optical fields. The g-factors of intraband transitions in our nanocrystals are found comparable with dissymmetry factors of chiral plasmonic complexes, and exceeding the typical g-factors of chiral molecules by a factor of 1000. Optically active semiconducting nanocrystals-with chiral properties controllable by the nanocrystal dimensions, morphology, composition and blending ratio-will greatly benefit chemistry, biology and medicine by advancing enantiomeric recognition, sensing and resolution of chiral molecules.

Bell, I. R. and G. E. Schwartz (2013). "Adaptive network nanomedicine: an integrated model for homeopathic medicine." Front Biosci (Schol Ed) **5**: 685-708.

This paper presents an evidence-based model for the nature and mode of action of homeopathic remedies. Recent studies reveal that homeopathic remedies contain nanoparticles (NPs) of source materials formed by "top-down" mechanical grinding in lactose and/or succussion (forceful agitation) in ethanolic solutions. Silica nanostructures formed during succussions in glass and/or biosynthesized by specific plant extract tinctures also may acquire and convey epitaxial information from remedy source materials into higher potencies. NPs have enhanced bioavailability, adsorptive capabilities, adjuvant reactivity, electromagnetic and quantum properties compared with their bulk forms. NPs induce adaptive changes in the organism at nontoxic doses (hormesis), serving as salient, low level danger signals to the biological stress response network. Activation of stress response effectors, including heat shock proteins, inflammasomes, cytokines and neuroendocrine pathways, initiate beneficial compensatory reactions across the interconnected networks of the organism as a complex adaptive system. Homeopathic remedies act by stimulating hormetic adaptive rather than

conventional pharmacological effects. Updating terminology from "homeopathy" to "adaptive network nanomedicine" reflects the integration of this historical but controversial medical system with modern scientific findings.

Bell, I. R., et al. (2013). "Advances in Integrative Nanomedicine for Improving Infectious Disease Treatment in Public Health." Eur J Integr Med **5**(2): 126-140.

INTRODUCTION: Infectious diseases present public health challenges worldwide. An emerging integrative approach to treating infectious diseases is using nanoparticle (NP) forms of traditional and alternative medicines. Advantages of nanomedicine delivery methods include better disease targeting, especially for intracellular pathogens, ability to cross membranes and enter cells, longer duration drug action, reduced side effects, and cost savings from lower doses. METHODS: We searched Pubmed articles in English with keywords related to nanoparticles and nanomedicine. Nanotechnology terms were also combined with keywords for drug delivery, infectious diseases, herbs, antioxidants, homeopathy, and adaptation. RESULTS: NPs are very small forms of material substances, measuring 1-100 nanometers along at least one dimension. Compared with bulk forms, NPs' large ratio of surface-area-to-volume confers increased reactivity and adsorptive capacity, with unique electromagnetic, chemical, biological, and quantum properties. Nanotechnology uses natural botanical agents for green manufacturing of less toxic NPs. DISCUSSION: Nanoparticle herbs and nutriceuticals can treat infections via improved bioavailability and antiinflammatory, antioxidant, and immunomodulatory effects. Recent studies demonstrate that homeopathic medicines may contain source and/or silica nanoparticles because of their traditional manufacturing processes. Homeopathy, as a form of nanomedicine, has a promising history of treating epidemic infectious diseases, including malaria, leptospirosis and HIV/AIDS, in addition to acute upper respiratory infections. Adaptive changes in the host's complex networks underlie effects. CONCLUSIONS: Nanomedicine is integrative, blending modern technology with natural products to reduce toxicity and support immune function. Nanomedicine using traditional agents from alternative systems of medicine can facilitate progress in integrative public health approaches to infectious diseases.

Bretheau, L., et al. (2013). "Exciting Andreev pairs in a superconducting atomic contact." Nature **499**(7458): 312-315.

The Josephson effect describes the flow of supercurrent in a weak link-such as a tunnel junction, nanowire or molecule-between two superconductors. It is the basis for a variety of circuits and devices, with applications ranging from medicine to quantum information. Experiments using Josephson circuits that behave like artificial atoms are now revolutionizing the way we probe and exploit the laws of quantum physics. Microscopically, the supercurrent is carried by Andreev pair states, which are localized at the weak link. These states come in doublets and have energies inside the superconducting gap. Existing Josephson circuits are based on properties of just the ground state of each doublet, and so far the excited states have not been directly detected. Here we establish their existence through spectroscopic measurements of superconducting atomic contacts. The spectra, which depend on the atomic configuration and on the phase difference between the superconductors, are in complete agreement with theory. Andreev doublets could be exploited to encode information in novel types of superconducting qubits.

Chinnasamy, S., et al. (2020). "Combining in silico and in vitro approaches to identification of potent inhibitor against phospholipase A2 (PLA2)." Int J Biol Macromol **144**: 53-66.

Phospholipase A2 (PLA2) is the main constituent of snake venom. PLA2 enzymes catalyze the Ca(2+) dependent hydrolysis of 2-acyl ester bonds of 3-sn-phospholipids, releasing fatty acids and lysophospholipids. Inside the body of the victim, PLA2 from snake venom induces either direct or indirect pathophysiological effects, including anticoagulant, inflammatory, neurotoxic, cardiotoxic, edematogenic, and myotoxic activities. Therefore, there is a need to find the potential inhibitors against PLA2 responsible for snakebite. In this study, we employed in silico and in vitro methods to identify the potential inhibitor against PLA2. Virtual screening and molecular docking studies were performed to find potent inhibitor against PLA2 using Traditional Chinese Medicine Database (TCM). Based on these studies, Scutellarin (TCM3290) was selected and calculated by density functional theory calculation at B3LYP/6-31G**(++) level to explore the stereo-electronic features of the molecule. Further, molecular docking and DFT of Minocycline was carried out. Quantum polarized ligand docking was performed to optimize the geometry of the protein-ligand complexes. The protein-ligand complexes were subjected to molecular dynamics simulation and binding free energy calculations. The residence time of a protein-ligand complex is a critical parameter affecting natural influences in vitro. It is nonetheless a challenging errand to expect, regardless of the accessibility of incredible PC assets and a large variety of computing procedures. In this metadynamics situation, we used the conformational flooding technique to deal with rank inhibitors constructions. The systematic free energy perturbation (FEP) protocol and calculate the energy of both complexes. Finally,

the selected compound of TCM3290 was studied in vitro analysis such as inhibition of PLA2 activity, hyaluronidase activity and fibrinogenolytic activity. The TCM3290 had a more binding affinity compare to Minocycline, and interacted with the key residues of TYR63 and GLY31. DFT represented the highest HOMO and LUMO energy of 0.15146 eV. MD simulation with 100 ns proved that an inhibitor binding mode is more stable inside the binding site of PLA2. In vitro analysis shows that TCM3290 significantly neutralized by PLA2. The above observations confirmed that Scutellarin (TCM3290) had a potent snake venom neutralizing capacity and could hypothetically be used for therapeutic drives of snakebite envenomation.

Denis, P. A. (2013). "Alzheimer's disease: a gas model. The NADPH oxidase-Nitric Oxide system as an antibubble biomachinery." Med Hypotheses **81**(6): 976-987.

Alzheimer's disease (AD) is a neurodegenerative disease of unknown origin. The pathological lesions that define AD would be linked to the insidious accumulation of nitrogen, having invaded the brain interstitial fluid (ISF) from the blood via the physiological cycling pool of vascular glucose transporters (GLUT-1). According to this hypothesis, the nitrogen nanobubbles, being chemically inert and actually indestructible for human beings, can not escape from the ISF anymore. They would exert a huge and deleterious pressure against cellular components, especially in microglia and in astrocytes. They could enhance the existing cell oxygen anisotropy, which might enhance the natural bubble nucleation of O2-2O2 in cells or in mitochondria. Indeed, with the help of a new symbolic representation for gas nuclei in chemical reactions, the NADPH oxidase-NO system is identified for the first time, as an antibubble biomachinery, able to break O2-2O2 bubbles up as it releases superoxide O2-. Superoxide is considered as a quantum bubble, which collapses through the reactivity of the gaseous NO radical. Their combination in soluble peroxinitrite provides the change from one state of matter to another, avoiding any risk of a bubble enlargement, and finally avoiding the risk of enzyme crowding or of a bulk pressure variation. However, a bubble is expected to entrap Nitric Oxide (NO), which leads theoretically to a decrease in its bioavailability, and is expected to trigger a guanylyl-cyclase-mediated inflammatory cascade, that could explain the inflammation in AD. In vitro, any increase in the hydrostatic pressure has already been linked to the microtubule disorganization. The amyloid deposits, also known as senile plaques, would behave as a sponge toward ISF nitrogen; Abeta is considered as a foam-stabilizing agent. By taking the shape of cerebral amyloid angiopathy, the amyloid could confine the nitrogen leak from the blood, and progressively insulate the Blood-Brain Barrier against the pollutant. All these theoretical features finally lead to the death of the neurons. The comprehensive statement of the theoretical pro-inflammatory action of inert gases is a real upheaval for the whole medicine.

Dzobo, K., et al. (2019). "Targeting the Versatile Wnt/beta-Catenin Pathway in Cancer Biology and Therapeutics: From Concept to Actionable Strategy." OMICS **23**(11): 517-538.

This expert review offers a critical synthesis of the latest insights and approaches at targeting the Wnt/beta-catenin pathway in various cancers such as colorectal cancer, melanoma, leukemia, and breast and lung cancers. Notably, from organogenesis to cancer, the Wnt/beta-catenin signaling displays varied and highly versatile biological functions in animals, with virtually all tissues requiring the Wnt/beta-catenin signaling in one way or the other. Aberrant expression of the members of the Wnt/beta-catenin has been implicated in many pathological conditions, particularly in human cancers. Mutations in the Wnt/beta-catenin pathway genes have been noted in diverse cancers. Biochemical and genetic data support the idea that inhibition of Wnt/beta-catenin signaling is beneficial in cancer therapeutics. The interaction of this important pathway with other signaling systems is also noteworthy, but remains as an area for further research and discovery. In addition, formation of different complexes by components of the Wnt/beta-catenin pathway and the precise roles of these complexes in the cytoplasmic milieu are yet to be fully elucidated. This article highlights the latest medical technologies in imaging, single-cell omics, use of artificial intelligence (e.g., machine learning techniques), genome sequencing, quantum computing, molecular docking, and computational softwares in modeling interactions between molecules and predicting protein-protein and compound-protein interactions pertinent to the biology and therapeutic value of the Wnt/beta-catenin signaling pathway. We discuss these emerging technologies in relationship to what is currently needed to move from concept to actionable strategies in translating the Wnt/beta-catenin laboratory discoveries to Wnt-targeted cancer therapies and diagnostics in the clinic.

Ekins, R. (1994). "Immunoassay: recent developments and future directions." Nucl Med Biol **21**(3): 495-521.

All analytical techniques employed in the biological sciences rely on recognition of the shape and structure of molecules of the substance of interest (the analyte). Such molecular recognition and sensing usually relies on the use other molecules possessing a complementary structure, implying a specific lock and key relationship between the two. Antibodies comprise a class of recognition molecules evolved by nature for the purpose of bodily defence, and are clearly of

particular utility in this context. However techniques of increasing sophistication (including the techniques of molecular biology) are currently being developed which enable the artificial construction of antibody-like molecules possessing improved molecular recognition properties which can be harnessed for microanalytical purposes. Oligonucleotide probes likewise exhibit the property of binding to complementary nucleotide sequences, and the techniques of, for example, in situ hybridisation therefore share many features with immunoassay techniques. Microanalytical techniques relying on binding reactions between substances possessing complementary lock and key molecular structures are unlikely to be superseded within the foreseeable future, only the labels used to monitor such reactions, and the means of production of "recognition molecules", being subject to further development. Such techniques already enter into all areas of life, including medicine, agriculture, etc, and are likely to increase further in importance with increasing concern regarding chemically complex contaminants in food, the environment, etc. Developments in this field are clearly directed to slightly differing objectives as indicated in this presentation. These include methodological simplification (making the techniques cheaper and more widely available), improvements in sensitivity (to enable the detection and measurement of substances beyond the reach of current methods) and the construction of transducer-based sensor methods (permitting, inter alia, the monitoring of changing analyte concentrations). However the combination of the "ultrasensitivity" of current single analyte assay methods with the ability simultaneously to determine multiple analytes in the same sample represents, in my view, the next major methodological challenge in this field, and--if successfully addressed--will constitute a quantum advance on present analytical methods. Indeed the development of miniaturised multianalyte binding assay techniques may ultimately comes to be seen as analagous to, for example, the introduction of the word processor, and other similar major technological advances of the past decade.

El-Ansary, A., et al. (2013). "Toxicity of novel nanosized formulations used in medicine." Methods Mol Biol **1028**: 47-74.

Nanotechnology involves the creation and manipulation of materials at nanoscale levels (1-100 nm) to create products that exhibit novel properties. While this motivation has driven nanoscience and technology in physics and engineering, it is not the main reason that nanoparticles are useful for systemic applications in the human body. The application of nanotechnology to medicine, known as nanomedicine, concerns the use of precisely engineered materials at this length scale to develop novel therapeutic and diagnostic modalities. A number of nanotherapeutic formulations are already approved for medical use and more are in the approval pipeline currently. This chapter is intended to provide an overview of the toxicity of these therapeutic nanoparticles and to summarize the current state of the field. We begin with background on the sources of exposure to nanoparticles, followed by reviewing different forms of nanosized therapeutic tools as quantum dots, nanoshells, nanocapsules, echogenic bubble, and "nanoshuttles." Moreover, cytotoxic effects of nanoparticles on cell membrane, mitochondrial function, prooxidant/antioxidant status, enzyme leakage, DNA, and other biochemical endpoints were elucidated. We highlight the need for caution during the use and disposal of such manufactured nanomaterials to prevent unintended environmental impacts. Moreover, different strategies which could be used to minimize or eliminate nanotoxicity were also discussed in detail. Understanding of how to tune size and surface properties to provide safety will permit the creation of new, more effective nanomedicines for systemic use.

El-Nassan, H. B. (2014). "Recent progress in the identification of BRAF inhibitors as anti-cancer agents." Eur J Med Chem **72**: 170-205.

The "RAS/BRAF/MEK/ERK" pathway has been associated with human cancers due to the frequent oncogenic mutations identified in its members. In particular, BRAF is mutated at high frequency in many cancers especially melanoma. This mutation leads to activation of the MAPK signaling pathway, inducing uncontrolled cell proliferation, and facilitating malignant transformation. All these facts make BRAF an ideal target for antitumor therapeutic development. Many BRAF inhibitors have been discovered during the last decade and most of them exhibit potent antitumor activity especially on tumors that harbor BRAF(V600E) mutations. Some of these compounds have entered clinical trials and displayed encouraged results. The present review highlights the progress in identification and development of BRAF inhibitors especially during the last five years.

El-Sadik, A. O., et al. (2010). "Nanoparticle-labeled stem cells: a novel therapeutic vehicle." Clin Pharmacol **2**: 9-16.

Nanotechnology has been described as a general purpose technology. It has already generated a range of inventions and innovations. Development of nanotechnology will provide clinical medicine with a range of new diagnostic and therapeutic opportunities such as medical imaging, medical diagnosis, drug delivery, and cancer detection and management. Nanoparticles such as manganese, polystyrene, silica, titanium oxide, gold, silver, carbon, quantum dots, and iron oxide have received enormous attention in the creation of new types of analytical tools for

biotechnology and life sciences. Labeling of stem cells with nanoparticles overcame the problems in homing and fixing stem cells to their desired site and guiding extension of stem cells to specific directions. Although the biologic effects of some nanoparticles have already been assessed, information on toxicity and possible mechanisms of various particle types remains inadequate. The aim of this review is to give an overview of the mechanisms of internalization and distribution of nanoparticles inside stem cells, as well as the influence of different types of nanoparticles on stem cell viability, proliferation, differentiation, and cytotoxicity, and to assess the role of nanoparticles in tracking the fate of stem cells used in tissue regeneration.

Estrich, N. A., et al. (2017). "Engineered Diblock Polypeptides Improve DNA and Gold Solubility during Molecular Assembly." ACS Nano **11**(1): 831-842.

Programmed molecular recognition is being developed for the bionanofabrication of mixed organic/inorganic supramolecular assemblies for applications in electronics, photonics, and medicine. For example, DNA-based nanotechnology seeks to exploit the easily programmed complementary base-pairing of DNA to direct assembly of complex, designed nanostructures. Optimal solution conditions for bionanofabrication, mimicking those of biological systems, may involve high concentrations of biomacromolecules (proteins, nucleic acids, etc.) and significant concentrations of various ions (Mg(2+), Na(+), Cl(-), etc.). Given a desire to assemble diverse inorganic components (metallic nanoparticles, quantum dots, carbon nanostructures, etc.), it will be increasingly difficult to find solution conditions simultaneously compatible with all components. Frequently, the use of chemical surfactants is undesirable, leaving a need for the development of alternative strategies. Herein, we discuss the use of artificial, diblock polypeptides in the role of solution compatibilizing agents for molecular assembly. We describe the use of two distinct diblock polypeptides with affinity for DNA in the stabilization of DNA origami and DNA-functionalized gold nanoparticles (spheres and rods) in solution, protection of DNA from enzymatic degradation, as well as two 3D tetrahedral DNA origamis. We present initial data showing that the diblock polypeptides promote the formation in the solution of desired organic/inorganic assemblies.

Etgar, L., et al. (2010). "Trajectory control of PbSe-gamma-Fe2O3 nanoplatforms under viscous flow and an external magnetic field." Nanotechnology **21**(17): 175702.

The flow behavior of nanostructure clusters, consisting of chemically bonded PbSe quantum dots and magnetic gamma-Fe(2)O(3) nanoparticles, has been investigated. The clusters are regarded as model nanoplatforms with multiple functionalities, where the gamma-Fe(2)O(3) magnets serve as transport vehicles, manipulated by an external magnetic field gradient, and the quantum dots act as fluorescence tags within an optical window in the near-infrared regime. The clusters' flow was characterized by visualizing their trajectories within a viscous fluid (mimicking a blood stream), using an optical imaging method, while the trajectory pictures were analyzed by a specially developed processing package. The trajectories were examined under various flow rates, viscosities and applied magnetic field strengths. The results revealed a control of the trajectories even at low magnetic fields (<1 T), validating the use of similar nanoplatforms as active targeting constituents in personalized medicine.

Evangelatos, N. and I. Eliadi (2016). "Are Allopathic and Holistic Medicine Incommensurable?" Forsch Komplementmed **23**(1): 37-42.

The shift from the Aristotelian to the Newtonian scientific paradigm gave birth to progresses in the natural, hard sciences and contributed to the emergence of modernity. Allopathic medicine gradually implemented those progresses, transforming itself into contemporary biomedicine. In the early 20th century, replacement of Newtonian physics by quantum mechanics and Einstein's theory of relativity resulted in a new paradigm shift in the natural, hard sciences. This shift gave birth to post-modern perceptions, which attempt to put those changes in context. Within this new context, holistic therapeutic approaches are considered more compatible with the new paradigm. Different paradigms in the natural, hard sciences are considered to be incommensurable (in the Kuhnian sense). This incommensurability is also transferred to the different societal contexts, the different <<Weltanschauungen>> that rely on different scientific paradigms. However, drawing on arguments that range from historical and philosophical to practical and sociological ones, we argue that, although based on different scientific paradigms, allopathic and holistic medicine are not incommensurable, but rather complementary. This may be related to the inherent attributes of medicine, a fact that reinforces the debate on its epistemological status.

Fahey, F. H., et al. (1987). "Detection efficiency of a high-pressure gas scintillation proportional chamber." Med Phys **14**(1): 115-123.

The detection efficiency of a high-pressure, gas scintillation proportional chamber (GSPC), designed for medical imaging in the 30-150 keV energy range, has been investigated through measurement and Monte Carlo simulation. Measurements were conducted on a GSPC containing 4 atm of pure xenon separated from a hexagonal array of seven ultraviolet-sensitive photomultiplier tubes by 1.27-cm-thick fused-silica windows. Experimental

measurements of the photopeak efficiency, fluorescence escape efficiency, and the energy collection efficiency were obtained. Results were also obtained for different photon energies and different values of temporal resolution. The measurements were compared with the results obtained from a Monte Carlo simulation designed specifically for investigating the imaging of low-energy photons (below 150 keV) with a gas-filled detector. The simulation was used to estimate photopeak efficiency, fluorescence escape efficiency, photopeak-to-fluorescence escape peak ratio, quantum interaction efficiency, energy collection efficiency, and local energy collection efficiency. The photopeak efficiency of the GSPC relative to that of a 3-in. (7.62-cm)-thick sodium iodide crystal was measured to be 0.284 +/- 0.001 at 60 keV and 0.057 +/- 0.001 at 140 keV. Of the 60-keV photons incident upon the detector, 70% +/- 4% interacted in the detector, with 28% +/- 1% being in the photopeak, as estimated both by experimentation and through the simulation. The maximum energy collection efficiency was found to be 65% at 60 keV, with 46% being deposited within 0.2 cm of the initial photon interaction. The information gained from this study is being used to design an optimized detector for use in specialized nuclear medicine studies.

Faria, H. A. and A. A. de Queiroz (2015). "A novel drug delivery of 5-fluorouracil device based on TiO2/ZnS nanotubes." Mater Sci Eng C Mater Biol Appl **56**: 260-268.

The structural and electronic properties of titanium oxide nanotubes (TiO2) have attracted considerable attention for the development of therapeutic devices and imaging probes for nanomedicine. However, the fluorescence response of TiO2 has typically been within ultraviolet spectrum. In this study, the surface modification of TiO2 nanotubes with ZnS quantum dots was found to produce a red shift in the ultra violet emission band. The TiO2 nanotubes used in this work were obtained by sol-gel template synthesis. The ZnS quantum dots were deposited onto TiO2 nanotube surface by a micelle-template inducing reaction. The structure and morphology of the resulting hybrid TiO2/ZnS nanotubes were investigated by scanning electron microscopy, transmission electron microscopy and X-ray diffraction techniques. According to the results of fluorescence spectroscopy, pure TiO2 nanotubes exhibited a high emission at 380nm (3.26eV), whereas TiO2/ZnS exhibited an emission at 410nm (3.02eV). The TiO2/ZnS nanotubes demonstrated good bio-imaging ability on sycamore cultured plant cells. The biocompatibility against mammalian cells (Chinese Hamster Ovarian Cells-CHO) suggesting that TiO2/ZnS may also have suitable optical properties for use as biological markers in diagnostic medicine. The drug release characteristic of TiO2/ZnS nanotubes was explored using 5-fluorouracil (5-FU), an anticancer drug used in photodynamic therapy. The results show that the TiO2/ZnS nanotubes are a promising candidate for anticancer drug delivery systems.

Farrer, N. J., et al. (2009). "Photoactivated chemotherapy (PACT): the potential of excited-state d-block metals in medicine." Dalton Trans(48): 10690-10701.

The fields of phototherapy and of inorganic chemotherapy both have long histories. Inorganic photoactivated chemotherapy (PACT) offers both temporal and spatial control over drug activation and has remarkable potential for the treatment of cancer. Following photoexcitation, a number of different decay pathways (both photophysical and photochemical) are available to a metal complex. These pathways can result in radiative energy release, loss of ligands or transfer of energy to another species, such as triplet oxygen. We discuss the features which need to be considered when developing a metal-based anticancer drug, and the common mechanisms by which the current complexes are believed to operate. We then provide a comprehensive overview of PACT developments for complexes of the different d-block metals for the treatment of cancer, detailing the more established areas concerning Ti, V, Cr, Mn, Re, Fe, Ru, Os, Co, Rh, Pt, and Cu and also highlighting areas where there is potential for greater exploration. Nanoparticles (Ag, Au) and quantum dots (Cd) are also discussed for their photothermal destructive potential. We also discuss the potential held in particular by mixed-metal systems and Ru complexes.

Farzamfar, S., et al. (2018). "Will Nanotechnology Bring New Hope for Stem Cell Therapy?" Cells Tissues Organs **206**(4-5): 229-241.

The potential of stem cell therapy has been shown in preclinical trials for the treatment of damage and replacement of organs and degenerative diseases. After many years of research, its clinical application is limited. Currently there is not a single stem cell therapy product or procedure. Nanotechnology is an emerging field in medicine and has huge potential due to its unique characteristics such as its size, surface effects, tunnel effects, and quantum size effect. The importance of application of nanotechnology in stem cell technology and cell-based therapies has been recognized. In particular, the effects of nanotopography on stem cell differentiation, proliferation, and adhesion have become an area of intense research in tissue engineering and regenerative medicine. Despite the many opportunities that nanotechnology can create to change the fate of stem cell technology and cell therapies, it poses several risks since some nanomaterials are cytotoxic and can affect the differentiation program of stem cells and their viability.

Here we review some of the advances and the prospects of nanotechnology in stem cell research and cell-based therapies and discuss the issues, obstacles, applications, and approaches with the aim of opening new avenues for further research.

Fishman, J. M., et al. (2012). "Decellularized rabbit cricoarytenoid dorsalis muscle for laryngeal regeneration." Ann Otol Rhinol Laryngol **121**(2): 129-138.

OBJECTIVES: Although considerable progress has been made in regenerative medicine, a quantum step would be the replacement and/or regeneration of functional muscle tissue. For example, although patients' airways can now be successfully replaced with stem cell-based techniques, a much greater patient need would be addressed by regeneration of the muscles required for engineering a functional larynx, in which active movement is critical. The rabbit cricoarytenoid dorsalis muscle was chosen for the present study because it is equivalent to the posterior cricoarytenoid muscle, the only significant abductor muscle in human larynges. METHODS: Rabbit cricoarytenoid dorsalis muscles were harvested, and different decellularization methods were compared by use of a combination of histologic, immunohistochemical, and molecular techniques. Decellularized scaffolds were implanted into Sprague-Dawley rats as part of a 2-week biocompatibility study to assess immunogenicity. RESULTS: Decellularization with a combination of latrunculin B, potassium iodide, potassium chloride, and deoxyribonuclease resulted in total DNA clearance and reduced levels of major histocompatibility complex class II expression, with relative preservation of the scaffold's structural integrity (collagen, elastin, and glycosaminoglycan content). The scaffolds showed minimal signs of rejection at 2 weeks in a cross-species (xenotransplantation) study. CONCLUSIONS: Decellularized laryngeal muscles, which are nonimmunogenic, may provide the optimal scaffold source for the generation of a fully functional tissue-engineered larynx.

Fitzgerald, R., et al. (2020). "The next generation of current measurement for ionization chambers." Appl Radiat Isot **163**: 109216.

Re-entrant ionization chambers (ICs) are essential to radionuclide metrology and nuclear medicine for maintaining standards and measuring half-lives. The requirements of top-level metrology demand that systems must be precise and stable to 0.1 % over many years, and linear from 10(-14) A to 10(-8) A. Thus, laboratories depend on bespoke current measurement systems and often rely on sealed sources to generate reference currents. To maintain and improve present capabilities, metrologists need to overcome two looming challenges: ageing electronics and decreasing availability of sealed sources. Possible solutions using Ultrastable Low-Noise Current Amplifiers (ULCAs), resistive-feedback electrometers, and (quantum) single-electron pumps are reviewed. Broader discussions of IC design and methodology are discussed. ULCAs show promise and resistive-feedback systems which take advantage of standard resistor calibrations offer an alternative.

Fleischer, C. C. and C. K. Payne (2014). "Nanoparticle-cell interactions: molecular structure of the protein corona and cellular outcomes." Acc Chem Res **47**(8): 2651-2659.

The use of nanoparticles (NPs) in biology and medicine requires a molecular-level understanding of how NPs interact with cells in a physiological environment. A critical difference between well-controlled in vitro experiments and in vivo applications is the presence of a complex mixture of extracellular proteins. It has been established that extracellular serum proteins present in blood will adsorb onto the surface of NPs, forming a "protein corona". Our goal was to understand how this protein layer affected cellular-level events, including NP binding, internalization, and transport. A combination of microscopy, which provides spatial resolution, and spectroscopy, which provides molecular information, is necessary to probe protein-NP-cell interactions. Initial experiments used a model system composed of polystyrene NPs functionalized with either amine or carboxylate groups to provide a cationic or anionic surface, respectively. Serum proteins adsorb onto the surface of both cationic and anionic NPs, forming a net anionic protein-NP complex. Although these protein-NP complexes have similar diameters and effective surface charges, they show the exact opposite behavior in terms of cellular binding. In the presence of bovine serum albumin (BSA), the cellular binding of BSA-NP complexes formed from cationic NPs is enhanced, whereas the cellular binding of BSA-NP complexes formed from anionic NPs is inhibited. These trends are independent of NP diameter or cell type. Similar results were obtained for anionic quantum dots and colloidal gold nanospheres. Using competition assays, we determined that BSA-NP complexes formed from anionic NPs bind to albumin receptors on the cell surface. BSA-NP complexes formed from cationic NPs are redirected to scavenger receptors. The observation that similar NPs with identical protein corona compositions bind to different cellular receptors suggested that a difference in the structure of the adsorbed protein may be responsible for the differences in cellular binding of the protein-NP complexes. Circular dichroism spectroscopy, isothermal titration calorimetry, and fluorescence spectroscopy show that the structure of BSA is altered following incubation with cationic NPs, but not anionic NPs. Single-particle-

tracking fluorescence microscopy was used to follow the cellular internalization and transport of protein-NP complexes. The single particle-tracking experiments show that the protein corona remains bound to the NP throughout endocytic uptake and transport. The interaction of protein-NP complexes with cells is a challenging question, as the adsorbed protein corona controls the interaction of the NP with the cell; however, the NP itself alters the structure of the adsorbed protein. A combination of microscopy and spectroscopy is necessary to understand this complex interaction, enabling the rational design of NPs for biological and medical applications.

Foletti, A., et al. (2009). "Cellular ELF signals as a possible tool in informative medicine." Electromagn Biol Med **28**(1): 71-79.

According to Quantum Electro-Dynamical Theory by G. Preparata, liquid water can be viewed as an equilibrium between of two components: coherent and incoherent ones. The coherent component is contained within spherical so called "coherence domains" (CDs) where all molecules synchronously oscillate with the same phase. CDs are surrounded by the incoherent component where molecules oscillate with casual phases regarding each other. The existence of coherent domain in water has been demonstrated in a set of experiments on pure water exposed to high voltage, under this condition the electric field concentrates inside the water, arranging the water molecules to form high ordered structure. Recently has been studied the influence of combined static and alternating parallel magnetic fields on the current through the aqueous solution of glutamic acid; outlining the relevance of low frequency electro-magnetic field in interacting with biological target. Additional results demonstrate that at combined static and alternating parallel, magnetic fields matching the ion cyclotron energy resonance of a particular charged molecule into biological tissue an intrinsic weak magnetic field is generated by ion currents in the cell. These results should increase the reliability and the clinical feasibility of the use of electromagnetic field, tuned at ion cyclotron resonance of charged molecules, as a biophysical approach to interfere with biological mechanisms. We demonstrate that Exposure of human epithelial cell to ion cyclotron energy resonance generated by a commercial electromedical device (Vega select 719) tuned to calcium ion at 7 Hz act as a differentiation factor, thus opening up the possibility to use particular extremely low frequency electro magnetic field protocols, in informative medicine.

Foletti, A. and J. Pokorny (2015). "Biophysical approach to low back pain: a pilot report." Electromagn Biol Med **34**(2): 156-159.

Since biophysical treatment has been reported to be effective in the general management of pain, we decided to assess the specific effect and treatment duration of this therapeutic strategy in low back pain. We were interested in verifying the possibility that a single clinical procedure could reduce pain and improve patients' quality of life within a period of three months. An Electromagnetic Information Transfer Through Aqueous System was employed to record endogenous therapeutic signals from each individual using an electromagnetic recording device (Med Select 729). A highly significant reduction in the Roland Morris low back pain and disability questionnaire score was observed after 3 months following a single biophysical intervention (11.83 +/- 6 at baseline versus 2.3 +/- 3.25 at 3 months, $p < 0.0001$). This preliminary report provides further evidence of the theoretical implications and clinical applications of Quantum Electro Dynamic concepts in biology and medicine.

Fonin, A. V., et al. (2014). "Fluorescence of dyes in solutions with high absorbance. Inner filter effect correction." PLoS One **9**(7): e103878.

Fluorescence is a proven tool in all fields of knowledge, including biology and medicine. A significant obstacle in its use is the nonlinearity of the dependence of the fluorescence intensity on fluorophore concentration that is caused by the so-called primary inner filter effect. The existing methods for correcting the fluorescence intensity are hard to implement in practice; thus, it is generally considered best to use dilute solutions. We showed that correction must be performed always. Furthermore, high-concentration solutions (high absorbance) are inherent condition in studying of the photophysical properties of fluorescent dyes and the functionally significant interactions of biological macromolecules. We proposed an easy to use method to correct the experimentally recorded total fluorescence intensity and showed that informative component of fluorescence intensity numerically equals to the product of the absorbance and the fluorescence quantum yield of the object. It is shown that if dye molecules do not interact with each other and there is no reabsorption (as for NATA) and spectrofluorimeter provides the proportionality of the detected fluorescence intensity to the part of the absorbed light (that is possible for spectrofluorimeter with horizontal slits) then the dependence of experimentally detected total fluorescence intensity of the dye on its absorbance coincides with the calculated dependence and the correction factor for eliminating the primary inner filter effect can be calculated on the basis of solution absorbance. It was experimentally shown for NATA fluorescence in the wide range of absorbance (at least up to 60). For ATTO-425, which fluorescence and absorption spectra overlap, the elimination of the primary and secondary filter effects and additional spectral analysis allow to conclude that the most

probable reason of the deviation of experimentally detected fluorescence intensity dependence on solution absorbance from the calculated dependence is the dye molecules self-quenching, which accompanies resonance radiationless excitation energy transfer.

Ford, M. C. and P. S. Ho (2016). "Computational Tools To Model Halogen Bonds in Medicinal Chemistry." J Med Chem **59**(5): 1655-1670.

The use of halogens in therapeutics dates back to the earliest days of medicine when seaweed was used as a source of iodine to treat goiters. The incorporation of halogens to improve the potency of drugs is now fairly standard in medicinal chemistry. In the past decade, halogens have been recognized as direct participants in defining the affinity of inhibitors through a noncovalent interaction called the halogen bond or X-bond. Incorporating X-bonding into structure-based drug design requires computational models for the anisotropic distribution of charge and the nonspherical shape of halogens, which lead to their highly directional geometries and stabilizing energies. We review here current successes and challenges in developing computational methods to introduce X-bonding into lead compound discovery and optimization during drug development. This fast-growing field will push further development of more accurate and efficient computational tools to accelerate the exploitation of halogens in medicinal chemistry.

Frank, N. D., et al. (2019). "Evaluation of reagents used to coat the hollow-fiber bioreactor membrane of the Quantum(R) Cell Expansion System for the culture of human mesenchymal stem cells." Mater Sci Eng C Mater Biol Appl **96**: 77-85.

The addition of a coating reagent to promote cell adherence is necessary to prepare the membrane surface of the Quantum(R) Cell Expansion System hollow-fiber bioreactor for the culture of mesenchymal stem cells. In this study, the efficacy of 8 potential coating reagents has been compared in terms of the doubling times of their cell populations, cell morphology, characterization via flow cytometry, and capacity for trilineage differentiation. Human fibronectin (FN), pooled human cryoprecipitate (CPPT), and recombinant human vitronectin (VN) were successful as coating reagents, and each product has advantages in different cell culture contexts. Mesenchymal stem cells harvested from Quantum cultured with each of these 3 compounds as coating reagents all met International Society for Cellular Therapy standards for plastic adherence, surface marker expression, and successful trilineage differentiation. No significant differences were observed among the doubling times from Quantum harvests using FN, CPPT, or VN as coating reagents (P=0.31). Coating with gelatin, human serum albumin, collagen I, polyllysine, and polydlysine resulted in significantly lower harvest yield; these agents are not recommended for use as coating reagents in the Quantum system.

Frolov, S. M., et al. (2009). "Ballistic spin resonance." Nature **458**(7240): 868-871.

The phenomenon of spin resonance has had far-reaching influence since its discovery 70 years ago. Electron spin resonance driven by high-frequency magnetic fields has enhanced our understanding of quantum mechanics, and finds application in fields as diverse as medicine and quantum information. Spin resonance can also be induced by high-frequency electric fields in materials with a spin-orbit interaction; the oscillation of the electrons creates a momentum-dependent effective magnetic field acting on the electron spin. Here we report electron spin resonance due to a spin-orbit interaction that does not require external driving fields. The effect, which we term ballistic spin resonance, is driven by the free motion of electrons that bounce at frequencies of tens of gigahertz in micrometre-scale channels of a two-dimensional electron gas. This is a frequency range that is experimentally challenging to access in spin resonance, and especially difficult on a chip. The resonance is manifest in electrical measurements of pure spin currents-we see a strong suppression of spin relaxation length when the oscillating spin-orbit field is in resonance with spin precession in a static magnetic field. These findings illustrate how the spin-orbit interaction can be harnessed for spin manipulation in a spintronic circuit, and point the way to gate-tunable coherent spin rotations in ballistic nanostructures without external alternating current fields.

Fugard, A. J., et al. (2019). "Hydrogen-Bond-Enabled Dynamic Kinetic Resolution of Axially Chiral Amides Mediated by a Chiral Counterion." Angew Chem Int Ed Engl **58**(9): 2795-2798.

Non-biaryl atropisomers are valuable in medicine, materials, and catalysis, but their enantioselective synthesis remains a challenge. Herein, a counterion-mediated O-alkylation method for the generation of atropisomeric amides with an er up to 99:1 is outlined. This dynamic kinetic resolution is enabled by the observation that the rate of racemization of atropisomeric naphthamides is significantly increased by the presence of an intramolecular O-HNCO hydrogen bond. Upon O-alkylation of the H-bond donor, the barrier to rotation is significantly increased. Quantum calculations demonstrate that the intramolecular H-bond reduces the rotational barrier about the aryl-amide bond, stabilizing the planar transition state for racemization by approximately 40 kJ mol(-1) , thereby facilitating the observed dynamic kinetic resolution.

Fujita, H., et al. (2018). "Bright Dots and Smart Optical Microscopy to Probe Intracellular Events in Single Cells." Front Bioeng Biotechnol **6**: 204.

Probing intracellular events is a key step in developing new biomedical methodologies. Optical microscopy has been one of the best options to observe biological samples at single cell and sub-cellular resolutions. Morphological changes are readily detectable in brightfield images. When stained with fluorescent molecules, distributions of intracellular organelles, and biological molecules are made visible using fluorescence microscopes. In addition to these morphological views of cells, optical microscopy can reveal the chemical and physical status of defined intracellular spaces. This review begins with a brief overview of genetically encoded fluorescent probes and small fluorescent chemical dyes. Although these are the most common approaches, probing is also made possible by using tiny materials that are incorporated into cells. When these tiny materials emit enough photons, it is possible to draw conclusions about the environment in which the tiny material resides. Recent advances in these tiny but sufficiently bright fluorescent materials are nextly reviewed to show their applications in tracking target molecules and in temperature imaging of intracellular spots. The last section of this review addresses purely optical methods for reading intracellular status without staining with probes. These non-labeling methods are especially essential when biospecimens are thereafter required for in vivo uses, such as in regenerative medicine.

Funk, R. H., et al. (2009). "Electromagnetic effects - From cell biology to medicine." Prog Histochem Cytochem **43**(4): 177-264.

In this review we compile and discuss the published plethora of cell biological effects which are ascribed to electric fields (EF), magnetic fields (MF) and electromagnetic fields (EMF). In recent years, a change in paradigm took place concerning the endogenously produced static EF of cells and tissues. Here, modern molecular biology could link the action of ion transporters and ion channels to the "electric" action of cells and tissues. Also, sensing of these mainly EF could be demonstrated in studies of cell migration and wound healing. The triggers exerted by ion concentrations and concomitant electric field gradients have been traced along signaling cascades till gene expression changes in the nucleus. Far more enigmatic is the way of action of static MF which come in most cases from outside (e.g. earth magnetic field). All systems in an organism from the molecular to the organ level are more or less in motion. Thus, in living tissue we mostly find alternating fields as well as combination of EF and MF normally in the range of extremely low-frequency EMF. Because a bewildering array of model systems and clinical devices exits in the EMF field we concentrate on cell biological findings and look for basic principles in the EF, MF and EMF action. As an outlook for future research topics, this review tries to link areas of EF, MF and EMF research to thermodynamics and quantum physics, approaches that will produce novel insights into cell biology.

Gagnon, D., et al. (1989). "Introduction to holospectral imaging in nuclear medicine for scatter subtraction." IEEE Trans Med Imaging **8**(3): 245-250.

An approach to image analysis and processing, called holospectral imaging, is proposed for dealing with Compton scattering contamination in nuclear medicine imaging. The method requires that energy information be available for all detected photons. A set of frames (typically 16) representing the spatial distribution at different energies is then formed. The relationship between these energy frames is analyzed, and the original data is transformed into a series of eigenimages and eigenvalues. In this space it is possible to distinguish the specific contribution to the image of both primary and scattered photons and, in addition, noise. Under the hypothesis that the contribution of the primary photons dominates the image structure, a filtering process can be performed to reduce the scattered contamination. The proportion of scattered information removed by the filtering process is evaluated for all images and depends on the level of residual quantum noise, which is estimated from the size of the smaller eigenvalues. Results indicate a slight increase in the statistical noise but also an increase in contrast and greatly improved ability to quantitate the image.

Galan, S. R. G., et al. (2018). "Post-translational site-selective protein backbone alpha-deuteration." Nat Chem Biol **14**(10): 955-963.

Isotopic replacement has long-proven applications in small molecules. However, applications in proteins are largely limited to biosynthetic strategies or exchangeable (for example, N-H/D) labile sites only. The development of postbiosynthetic, C-(1)H --> C-(2)H/D replacement in proteins could enable probing of mechanisms, among other uses. Here we describe a chemical method for selective protein alpha-carbon deuteration (proceeding from Cys to dehydroalanine (Dha) to deutero-Cys) allowing overall (1)H-->(2)H/D exchange at a nonexchangeable backbone site. It is used here to probe mechanisms of reactions used in protein bioconjugation. This analysis suggests, together with quantum mechanical calculations, stepwise deprotonations via on-protein carbanions and unexpected sulfonium ylides in the conversion of Cys to Dha, consistent with a 'carba-Swern' mechanism. The ready application on existing, intact protein constructs (without specialized culture or genetic methods) suggests this C-D labeling strategy as a

possible tool in protein mechanism, structure, biotechnology and medicine.

Gambardella, A., et al. (2016). "Magnetic hydroxyapatite coatings as a new tool in medicine: A scanning probe investigation." Mater Sci Eng C Mater Biol Appl **62**: 444-449.

Hydroxyapatite films enriched with magnetite have been fabricated via a Pulsed Plasma Deposition (PPD) system with the final aim of representing a new platform able to disincentivate bacterial adhesion and biofilm formation. The chemical composition and magnetic properties of films were respectively examined by X-ray photoelectron spectroscopy (XPS) and Superconducting Quantum Interference Device (SQUID) measurements. The morphology and conductive properties of the magnetic films were investigated via a combination of scanning probe technologies including atomic force microscopy (AFM), electrostatic force microscopy (EFM), and scanning tunneling microscopy (STM). Interestingly, the range of adopted techniques allowed determining the preservation of the chemical composition and magnetic properties of the deposition target material while STM analysis provided new insights on the presence of surface inhomogeneities, revealing the presence of magnetite-rich islands over length scales compatible with the applications. Finally, preliminary results of bacterial adhesion tests, indicated a higher ability of magnetic hydroxyapatite films to reduce Escherichia coli adhesion at 4h from seeding compared to control hydroxyapatite films.

Georgieva, I., et al. (2014). "Lanthanide and transition metal complexes of bioactive coumarins: molecular modeling and spectroscopic studies." J Inorg Biochem **135**: 100-112.

The present paper summarizes theoretical and spectroscopic investigations on a series of active coumarins and their lanthanide and transition metal complexes with application in medicine and pharmacy. Molecular modeling as well as IR, Raman, NMR and electronic spectral simulations at different levels of theory were performed to obtain important molecular descriptors: total energy, formation energy, binding energy, stability, conformations, structural parameters, electron density distribution, molecular electrostatic potential, Fukui functions, atomic charges, and reactive indexes. The computations are performed both in gas phase and in solution with consideration of the solvent effect on the molecular structural and energetic parameters. The investigations have shown that the advanced computational methods are reliable for prediction of the metal-coumarin binding mode, electron density distribution, thermodynamic properties as well as the strength and nature of the metal-coumarin interaction (not experimentally accessible) and correctly interpret the experimental spectroscopic data. Known results from biological tests for cytotoxic, antimicrobial, anti-fungal, spasmolytic and anti-HIV activities on the studied metal complexes are reported and discussed.

Gerigk, M., et al. (2015). "Nanoparticle shape anisotropy and photoluminescence properties: Europium containing ZnO as a Model Case." Nanoscale **7**(40): 16969-16982.

The precise control over electronic and optical properties of semiconductor (SC) materials is pivotal for a number of important applications like in optoelectronics, photocatalysis or in medicine. It is well known that the incorporation of heteroelements (doping as a classical case) is a powerful method for adjusting and enhancing the functionality of semiconductors. Independent from that, there already has been a tremendous progress regarding the synthesis of differently sized and shaped SC nanoparticles, and quantum-size effects are well documented experimentally and theoretically. Whereas size and shape control of nanoparticles work fairly well for the pure compounds, the presence of a heteroelement is problematic because the impurities interfere strongly with bottom up approaches applied for the synthesis of such particles, and effects are even stronger, when the heteroelement is aimed to be incorporated into the target lattice for chemical doping. Therefore, realizing coincident shape control of nanoparticle colloids and their doping still pose major difficulties. Due to a special mechanism of the emulsion based synthesis method presented here, involving a gelation of emulsion droplets prior to crystallization of shape-anisotropic ZnO nanoparticles, heteroelements can be effectively entrapped inside the lattice. Different nanocrystal shapes such as nanorods, -prisms, -plates, and -spheres can be obtained, determined by the use of certain emulsification agents. The degree of morphologic alterations depends on the type of incorporated heteroelement M(n+), concentration, and it seems that some shapes are more tolerant against doping than others. Focus was then set on the incorporation of Eu(3+) inside the ZnO particles, and it was shown that nanocrystal shape and aspect ratios could be adjusted while maintaining a fixed dopant level. Special PL properties could be observed implying energy transfer from ZnO excited near its band-gap (3.3 eV) to the Eu(3+) states mediated by defect luminescence of the nanoparticles. Indications for an influence of shape on photoluminescence (PL) properties were found. Finally, rod-like Eu@ZnO colloids were used as tracers to investigate their uptake into biological samples like HeLa cells. The PL was sufficient for identifying green and red emission under visible light excitation.

Geszke-Moritz, M. and M. Moritz (2013). "Quantum dots as versatile probes in medical sciences: synthesis, modification and properties." Mater Sci Eng C Mater Biol Appl **33**(3): 1008-1021.

Quantum dots (QDs) are semiconductor inorganic fluorescent nanocrystals in the size range between 1 and 20 nm. Due to their very small size, they possess unique properties and behave in different way than crystals in macro scale. The specificity of QDs makes them widespread in many branches of human life. The disciplines that took recently huge advantage from the development of nanotechnology are medicine and pharmacy. The creation of particles of very tiny sizes allowed these two sciences to develop or revolutionize the techniques of diagnosis or drug delivery. The most important feature for application of fluorescent nanocrystals in medical and pharmaceutical sciences is their high surface to volume ratio enabling QDs' conjugation to multiple ligands. Other properties of great importance are dispersibility and water stability, high and not easy quenched fluorescence, biocompatibility, and small and uniform sizes. In this review with ca. 200 references the recent developments in QD synthesis, surface modification, QD-based bioimaging, biotracking of drug molecules, biosensing and photodynamic therapy are summarized.

Ghaderi, S., et al. (2011). "Fluorescence nanoparticles "quantum dots" as drug delivery system and their toxicity: a review." J Drug Target **19**(7): 475-486.

Fluorescence nanocrystals or quantum dots (QDs) are engineered nanoparticles (NP) that have shown great promise with potential for many biological and biomedical applications, especially in drug delivery/activation and cellular imaging. The use of nanotechnology in medicine directed to drug delivery is set to expand in the coming years. However, it is unclear whether QDs, which are defined as NPs rather than small molecules, can specifically and effectively deliver drugs to molecular targets at subcellular levels. When QDs are linked to suitable ligands that are site specific, it has been shown to be brighter and photostable when compared with organic dyes. Interestingly, pharmaceutical sciences are exploiting NPs to minimize toxicity and undesirable side effects of drugs. The unforeseen hazardous properties of the carrier NPs themselves have given rise to some concern in a clinical setting. The kind of hazards encountered with this new nanotechnology materials are complex compared with conventional limitations created by traditional delivery systems. The development of cadmium-derived QDs shows great potential for treatment and diagnosis of cancer and site-directed delivery by virtue of their size-tunable fluorescence and with highly customizable surface for directing their bioactivity and targeting. However, data regarding the pharmacokinetic and toxicology studies require further investigation and development, and it poses great difficulties to ascertain the risks associated with this new technology. Additionally, nanotechnology also displays yet another inherent risk for toxic cadmium, which will enter as a new form of hazard in the biomedical field. This review will look at cadmium-derived QDs and discuss their future and their possible toxicities in a disease situation.

Ghafary, S. M., et al. (2017). "Simultaneous Gene Delivery and Tracking through Preparation of Photo-Luminescent Nanoparticles Based on Graphene Quantum Dots and Chimeric Peptides." Sci Rep **7**(1): 9552.

Designing suitable nano-carriers for simultaneous gene delivery and tracking is in the research priorities of the molecular medicine. Non-toxic graphene quantum dots (GQDs) with two different (green and red) emission colors are synthesized by Hummer's method and characterized by UV-Vis, Photoluminescence (PL), Fourier Transform Infrared (FTIR) and Raman spectroscopies, Atomic Force Microscopy (AFM), Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM). The GQDs are conjugated with MPG-2H1 chimeric peptide and plasmid DNA (pDNA) by non-covalent interactions. Following conjugation, the average diameter of the prepared GQDs increased from 80 nm to 280 nm in complex structure, and the zeta-potential of the complex increased (from -36.87 to -2.56 mV). High transfection efficiency of the nano-carrier and results of confocal microscopy demonstrated that our construct can be considered as a nontoxic carrier with dual functions for gene delivery and nuclear targeting.

Ghanbari, H., et al. (2011). "A nanocage for nanomedicine: polyhedral oligomeric silsesquioxane (POSS)." Macromol Rapid Commun **32**(14): 1032-1046.

Ground-breaking advances in nanomedicine (defined as the application of nanotechnology in medicine) have proposed novel therapeutics and diagnostics, which can potentially revolutionize current medical practice. Polyhedral oligomeric silsesquioxane (POSS) with a distinctive nanocage structure consisting of an inner inorganic framework of silicon and oxygen atoms, and an outer shell of organic functional groups is one of the most promising nanomaterials for medical applications. Enhanced biocompatibility and physicochemical (material bulk and surface) properties have resulted in the development of a wide range of nanocomposite POSS copolymers for biomedical applications, such as the development of biomedical devices, tissue engineering scaffolds, drug delivery systems, dental applications, and biological sensors. The application of POSS nanocomposites in combination with other nanostructures has also been

investigated including silver nanoparticles and quantum dot nanocrystals. Chemical functionalization confers antimicrobial efficacy to POSS, and the use of polymer nanocomposites provides a biocompatible surface coating for quantum dot nanocrystals to enhance the efficacy of the materials for different biomedical and biotechnological applications. Interestingly, a family of POSS-containing nanocomposite materials can be engineered either as completely non-biodegradable materials or as biodegradable materials with tuneable degradation rates required for tissue engineering applications. These highly versatile POSS derivatives have created new horizons for the field of biomaterials research and beyond. Currently, the application of POSS-containing polymers in various fields of nanomedicine is under intensive investigation with expectedly encouraging outcomes.

Ghoran, S. H., et al. (2016). "Isolation, spectroscopic characterization, X-ray, theoretical studies as well as in vitro cytotoxicity of Samarcandin." Bioorg Chem **66**: 27-32.

Samarcandin 1, a natural sesquiterpene-coumarin, was isolated as well as elucidated from F. assa-foetida which has significant effect in Iranian traditional medicine because of its medicinal attitudes. The crystal structure of samarcandin was determined by single-crystal X-ray structure analysis. It is orthorhombic, with unit cell parameters a=10.8204 (5)A, b=12.9894 (7)A, c=15.2467 (9)A, V=2142.9 (2)A(3), space group P212121 and four symmetry equivalent molecules in the unit cell. Samarcandin was isolated in order to study for its theoretical studies as well as its cellular toxicity as anti-cancer drug against two cancerous cells. In comparison with controls, our microscopic and MTT assay data showed that samarcandin suppresses cancer cell proliferation in a dose-dependent manner with IC50=11muM and 13 for AGS and WEHI-164 cell lines, respectively. Density functional theory (DFT) and time-dependent density functional theory (TD-DFT) of the structure was computed by three functional methods and 6-311++G(* *) standard basis set. The optimized molecular geometry and theoretical analysis agree closely to that obtained from the single crystal X-ray crystallography. To sum up, the good correlations between experimental and theoretical studies by UV, NMR, and IR spectra were found.

Ghoroghchian, P. P., et al. (2007). "Controlling Bulk Optical Properties of Emissive Polymersomes Through Intramembranous Polymer-Fluorophore Interactions." Chem Mater **19**(6): 1309-1318.

Interdisciplinary investigation at the interface of chemistry, engineering, and medicine has enabled the development of self-assembled nanomaterials with novel biochemical and electro-optical properties. We have recently shown that emissive polymersomes, polymer vesicles incorporating porphyrin-based fluorophores, feature large integrated-emission oscillator strengths and narrow emission bands; these nanoscale assemblies can be further engineered to fluoresce at discrete wavelengths throughout the visible and near-infrared (NIR) spectral domains. As such, emissive polymersomes effectively define an organic-based family of soft-matter quantum-dot analogs that possess not only impressive optical properties, but also tunable physical and biomaterial characteristics relative to inorganic fluorescent nanoparticles.Here, we expand upon our initial studies on poly(ethyleneoxide)-block-poly(butadiene)-based vesicles to examine fluorophore membrane-loading in other polymersome systems. Through modulation of fluorophore ancilliary group substituents and choice of polymer chain chemistries, we are able to predictably control intramembranous polymer-fluorophore interactions; these phenomena, in turn, influence the nature of fluorophore solvation, local dielectric environment, and emission quantum yield within emissive polymersome assemblies. By utilizing different classes of vesicle-generating diblock copolymers, including bioresorbable poly(ethyleneoxide)-block-poly(epsilon-caprolactone) (PEO-b-PCL) and poly(ethyleneoxide)-block-poly(gamma-methyl-epsilon-caprolactone) (PEO-b-PMCL), we ascertain general principles important for engineering nanoscale optical vesicles. Further, this work heralds the first generation of fully-biodegradable fluorescent nanoparticles suitable for deep-tissue in vivo imaging.

Gibbons, M. C. (2008). "Populomics." Stud Health Technol Inform **137**: 265-268.

Increasing evidence suggests that socio-behavioral factors are more important determinants of healthcare outcomes than historically recognized. In addition, the US healthcare system is primarily oriented to acute, hospital based, disease treatment. As such, responding adequately to the health and healthcare needs of both non-hospitalized and hospitalized patients with chronic diseases is proving difficult. Improving population level health problems like healthcare disparities is also challenging, in part because of this complex interplay of socio-behavioral, community and biologic factors within the context of the current healthcare system. Recent advances in the computer sciences and information technologies have spawned several methodologic advances in the biological, molecular and clinical sciences (eg, DNA chip technology and microarray analysis), enabled quantum leaps in molecular and submolecular medicine, and catalyzed the emergence of whole new fields of study such as proteomics, and genomics. With the emergence of Populomics, the behavioral and population sciences are on the verge of a similar

information technology-based scientific revolution. Integrating knowledge from the molecular sciences to the population sciences has the potential to propel health and disease inquiry, treatments and interventions well beyond current limitations, to yield insights and advances not currently possible. This paper briefly discusses the conceptual origins, theoretic basis and the future potential of this field.

Gibson, K. D. and S. J. Sibener (2021). "A new method of isotope enrichment and separation: preferential embedding of heavier isotopes of Xe into amorphous solid water." Phys Chem Chem Phys **23**(13): 7902-7907.

In this paper, we examine a new method for isotope separation involving the embedding of atoms and molecules into ice. This method is based upon isotope dependent embedding, i.e. capture, in a cryogenic matrix which exhibits excellent single-pass enrichment as demonstrated successfully for selected isotopes of Xe. This is a totally new method that holds significant promise as a quite general method for enrichment and purification. It is based upon exploiting the energetic and momentum barriers that need to be overcome in order to embed a given isotope or isotopologue into the capture matrix, initially amorphous ice. From our previous experiments, we know that there is a strong dependence of the embedding probability with incident momentum. Using supersonic molecular beam techniques, we generated Xe atomic beams of controlled velocities, relatively narrow velocity distributions due to supersonic expansion, and with all of the entrained isotopes having identical velocities arising from the seeded molecular beam expansion. As we had postulated, the heavier isotope becomes preferentially absorbed, i.e., embedded, in the ice matrix. Herein we demonstrate the efficacy of this method by comparing the capture of (134)Xe and (136)Xe to the reference isotope, (129)Xe. Enrichment of the heavier isotopes in the capture matrix was 1.2 for (134)Xe and 1.3 for (136)Xe greater than that expected for natural abundance. Note that enriched isotopic fractions can be collected from either the condensate or the reflected fraction depending on interest in either the heavier or lighter isotope, respectively. Cycling of these single-step enrichment events for all methods can lead to significantly higher levels of purification, and routes to scale-up can be realistically envisioned. This method holds significant promise to be quite general in applicability, including both atomic isotopes or molecular isotopologues across a wide range of particle masses spanning, essentially, the periodic table. This topic has profound implications and significant potential impact for a wide-variety of isotope-based technologies in the physical and biological sciences, medicine, advanced energy and energetic systems, including isotopically-purified materials that exhibit high-performance electronic and thermal characteristics, as well as isotopically purified spin-free materials for use in quantum information science platforms.

Giehm, G. (1959). "[Did quantum physics shake the fundamentals of modern medicine]." Hippokrates **30**(1): 63-67.

Gold, J. (1985). "Quantum physics and the philosophy of medicine." J R Soc Med **78**(1): 85-86.

Goodman, G. and M. E. Gershwin (2011). "Physics, biology and the origin of life: the physicians' view." Isr Med Assoc J **13**(12): 719-724.

Physicians have a great interest in discussions of life and its origin, including life's persistence through successive cycles of self-replication under extreme climatic and man-made trials and tribulations. We review here the fundamental processes that, contrary to human intuition, life may be seen heuristically as an ab initio, fundamental process at the interface between the complementary forces of gravitation and quantum mechanics. Analogies can predict applications of quantum mechanics to human physiology in addition to that already being applied, in particular to aspects of brain activity and pathology. This potential will also extend eventually to, for example, autoimmunity, genetic selection and aging. We present these thoughts in perspective against a background of changes in some physical fundamentals of science, from the earlier times of the natural philosophers of medicine to the technological medical gurus of today. Despite the enormous advances in medical science, including integration of technological changes that have led to the newer clinical applications of magnetic resonance imaging and PET scans and of computerized drug design, there is an intellectual vacuum as to how the physics of matter became translated to the biology of life. The essence and future of medicine continue to lie in cautious, systematic and ethically bound practice and scientific research based on fundamental physical laws accepted as true until proven false.

Graudenz, K. and C. Raulin (2003). "[From Einstein's Quantum Theory to modern laser therapy. The history of lasers in dermatology and aesthetic medicine]." Hautarzt **54**(7): 575-582.

Laser technology has considerably expanded therapeutic modalities in dermatology and aesthetic medicine. In addition, lasers have broadened the spectrum of diagnostic and therapeutic options in many other medical fields. Dermatologists, especially Dr. Leon Goldman, played an important role in the evolution and use of medical lasers. There was a long way from the concept of stimulated emission as the fundamental idea of laser technology by Albert Einstein in 1917 to the practical use of the laser today.

We review the development of laser technology from the early days through the latest advances.

Greenan, T. J. (1993). "Diagnostic imaging of sports-related spinal disorders." Clin Sports Med **12**(3): 487-505.

Diagnostic imaging is a dynamic field that has taken a quantum leap over the past several years with the advent of MRI. Accordingly, it is integral that the sports medicine clinician be well acquainted with the sundry imaging modalities at his or her disposal, and be able to choose the appropriate study or studies that will provide the most useful and accurate information. Conventional radiography should be the first study performed in every athlete with sports-related injury to the spine. If radiography reveals evidence of spondylolysis with or without spondylolisthesis, MRI would be an extremely helpful adjunct for evaluation of the disc spaces, nerve roots, and neural foramina. Osseous fragments in the vicinity of the pars defect are well seen on CT but not MRI. These fragments can migrate and become symptomatic. Therefore, in the work-up of this subset of patients, CT does offer important supplementary data to the MRI. When conventional radiographs of the cervical spine corrected for magnification render the diagnosis of congenital cervical spinal stenosis, MRI should invariably be the next procedure of choice for evaluation of the spinal cord and to assess the functional reserve of the spinal canal. MRI is also the modality of choice now for evaluation of the athlete with degenerative disc disease and for the identification of degenerative disc disease associated with lumbar Scheuermann's disease. In the athlete with an acute cervical spine injury, following conventional radiography, the patient should be evaluated with CT to better characterize and define the extent of the fracture and to search for additional fractures. MRI should be performed in these patients after CT as it provides extremely valuable information regarding the status of the spinal cord. MRI because of its unparalleled soft-tissue contrast, noninvasive nature, ability to image in three orthogonal planes, and myelographic effect with certain pulses sequences has become the ideal imaging modality for spinal disease, and sports-related spinal disorders are certainly no exception.

Grigsby, C. L., et al. (2012). "Understanding nonviral nucleic acid delivery with quantum dot-FRET nanosensors." Nanomedicine (Lond) **7**(4): 565-577.

Nonviral delivery of nucleic acids is a potentially safe and viable therapeutic modality for inherited and acquired diseases. However, current systems have proven too inefficient for widespread clinical translation. The rational design of improved carriers depends on a quantitative, mechanistic understanding of the rate-limiting barriers to efficient intracellular delivery. Separation of the nucleic acid from the carrier is one of the barriers, which may be analyzed by Forster resonance energy transfer (FRET), a mechanism used to detect interactions between fluorescently labeled molecules. When applied to the molecular components of polymer or lipid-based nanocomplexes, FRET provides information on their complexation status, uptake, release and degradation. Recently, the design of FRET systems incorporating quantum dots as energy donors has led to improved signal stability, allowing prolonged measurements, as well as increased sensitivity, enabling direct detection and the potential for multiplexing. The union of quantum dots and FRET is providing new insights into the mechanisms of nonviral nucleic acid delivery through convergent characterization of delivery barriers, and has the potential to accelerate the design of improved carriers to realize the potential of nucleic acid therapeutics and gene medicine.

Grim, P. (2007). "Free will in context: a contemporary philosophical perspective." Behav Sci Law **25**(2): 183-201.

Philosophical work on free will is inevitably framed by the problem of free will and determinism. This paper offers an overview of the current state of the philosophical art. Early sections focus on quantum indeterminism, an outline of the most influential logical argument for incompatibilism between free will and determinism, and telling problems that face incompatibilism. A major portion of the paper focuses on the compatiblist alternative, favored by many working philosophers. The conditional account of free will offered by classical compatibilism can be shown to be inadequate. A number of compatibilist options remain open, however, and seem promising for future research. These include "hierarchical" or "mesh" accounts of free will, normative perspectives and an approach to free will in terms of an emphasis on context. Final sections draw out the implications of contemporary compatibilism for the brain and behavioral sciences and for the law.

Grzesiuk, M., et al. (2016). "Photosynthetic sensitivity of phytoplankton to commonly used pharmaceuticals and its dependence on cellular phosphorus status." Ecotoxicology **25**(4): 697-707.

Recently pharmaceuticals have become significant environmental pollutants in aquatic ecosystems, that could affect primary producers such as microalgae. Here we analyzed the effect of pharmaceuticals on the photosynthesis of microalgae commonly found in freshwater-two species of Chlorophyceae and a member of the Eustigmatophyceae, via PAM fluorometry. As pharmaceuticals, three medicines often consumed in households were chosen: (i) fluoxetine, an antidepressant, (ii) propranolol, a beta-blocker and (iii) ibuprofen, an anti-inflammatory and analgesic

medicine. The EC50 for the quantum yield of photosystem II in phytoplankton acclimated to inorganic phosphorus (Pi)-replete and Pi-limited conditions was estimated. Acute toxicity experiments over a 5 h exposure revealed that Nannochloropsis limnetica was the least sensitive to pharmaceuticals in its photosynthetic yield out of all species tested. Although the estimation of sub-lethal effects can be vital in contrast to that of LC50s, the EC50 values in all species and for all medicines were orders of magnitude higher than concentrations found in polluted surface water. Chlamydomonas reinhardtii was the most sensitive to fluoxetine (EC50 of 1.6 mg L(-1)), and propranolol (EC50 of 3 mg L(-1)). Acutodesmus obliquus was most sensitive to ibuprofen (EC50 of 288 mg L(-1)). Additionally, the sensitivity to the pharmaceuticals changed under a Pi-limitation; the green algae became less sensitive to fluoxetine and propranolol. In contrast, Pi-limited algal species were more sensitive to ibuprofen. Our results suggest that the sensitivity of algae to pharmaceuticals is (i) highly compound- and species-specific and (ii) dependent on the cellular P status.

Guerard, F., et al. (2016). "Unexpected Behavior of the Heaviest Halogen Astatine in the Nucleophilic Substitution of Aryliodonium Salts." Chemistry **22**(35): 12332-12339.

Aryliodonium salts have become precursors of choice for the synthesis of (18) F-labeled tracers for nuclear imaging. However, little is known on the reactivity of these compounds with heavy halides, that is, radioiodide and astatide, at the radiotracer scale. In the first comparative study of radiohalogenation of aryliodonium salts with (125) I(-) and (211) At(-) , initial experiments on a model compound highlight the higher reactivity of astatide compared to iodide, which could not be anticipated from the trends previously observed within the halogen series. Kinetic studies indicate a significant difference in activation energy (Ea =23.5 and 17.1 kcal mol(-1) with (125) I(-) and (211) At(-) , respectively). Quantum chemical calculations suggest that astatination occurs via the monomeric form of an iodonium complex whereas iodination occurs via a heterodimeric iodonium intermediate. The good to excellent regioselectivity of halogenation and high yields achieved with diversely substituted aryliodonium salts indicate that this class of compounds is a promising alternative to the stannane chemistry currently used for heavy radiohalogen labeling of tracers in nuclear medicine.

Guerard, F., et al. (2014). "Rational design, synthesis, and evaluation of tetrahydroxamic acid chelators for stable complexation of zirconium(IV)." Chemistry **20**(19): 5584-5591.

Metals of interest for biomedical applications often need to be complexed and associated in a stable manner with a targeting agent before use. Whereas the fundamentals of most transition-metal complexation processes have been thoroughly studied, the complexation of Zr(IV) has been somewhat neglected. This metal has received growing attention in recent years, especially in nuclear medicine, with the use of (89) Zr, which a beta(+) -emitter with near ideal characteristics for cancer imaging. However, the best chelating agent known for this radionuclide is the trishydroxamate desferrioxamine B (DFB), the Zr(IV) complex of which exhibits suboptimal stability, resulting in the progressive release of (89) Zr in vivo. Based on a recent report demonstrating the higher thermodynamic stability of the tetrahydroxamate complexes of Zr(IV) compared with the trishydroxamate complexes analogues to DFB, we designed a series of tetrahydroxamic acids of varying geometries for improved complexation of this metal. Three macrocycles differing in their cavity size (28 to 36-membered rings) were synthesized by using a ring-closing metathesis strategy, as well as their acyclic analogues. A solution study with (89) Zr showed the complexation to be more effective with increasing cavity size. Evaluation of the kinetic inertness of these new complexes in ethylenediaminetetraacetic acid (EDTA) solution showed significantly improved stabilities of the larger chelates compared with (89) Zr-DFB, whereas the smaller complexes suffered from insufficient stabilities. These results were rationalized by a quantum chemical study. The lower stability of the smaller chelates was attributed to ring strain, whereas the better stability of the larger cyclic complexes was explained by the macrocyclic effect and by the structural rigidity. Overall, these new chelating agents open new perspectives for the safe and efficient use of (89) Zr in nuclear imaging, with the best chelators providing dramatically improved stabilities compared with the reference DFB.

Hardman, R. (2006). "A toxicologic review of quantum dots: toxicity depends on physicochemical and environmental factors." Environ Health Perspect **114**(2): 165-172.

As a growing applied science, nanotechnology has considerable global socioeconomic value, and the benefits afforded by nanoscale materials and processes are expected to have significant impacts on almost all industries and all areas of society. A diverse array of engineered nanoscale products and processes have emerged [e.g., carbon nanotubes, fullerene derivatives, and quantum dots (QDs)], with widespread applications in fields such as medicine, plastics, energy, electronics, and aerospace. With the nanotechnology economy estimated to be valued at dollar 1 trillion by 2012, the prevalence of these materials in society will be increasing, as will the likelihood of exposures. Importantly, the vastness and

novelty of the nanotechnology frontier leave many areas unexplored, or underexplored, such as the potential adverse human health effects resulting from exposure to novel nanomaterials. It is within this context that the need for understanding the potentially harmful side effects of these materials becomes clear. The reviewed literature suggests several key points: Not all QDs are alike; engineered QDs cannot be considered a uniform group of substances. QD absorption, distribution, metabolism, excretion, and toxicity depend on multiple factors derived from both inherent physicochemical properties and environmental conditions; QD size, charge, concentration, outer coating bioactivity (capping material and functional groups), and oxidative, photolytic, and mechanical stability have each been implicated as determining factors in QD toxicity. Although they offer potentially invaluable societal benefits such as drug targeting and in vivo biomedical imaging, QDs may also pose risks to human health and the environment under certain conditions. Key words: environment, human health, nanomaterials, nanosized particles, nanotechnology, nanotoxicology, quantum dots, toxicology.

Harmon, B. J., et al. (2003). "The Military Health System Computer-based Patient Record." AMIA Annu Symp Proc: 1068.

The Composite Health Care System II (CHCS II) is the Military's electronic Computer-based Patient Record, a clinical information system that will generate, maintain, and provide secure online access to a comprehensive and legible health record. In moving to CHCS II, the Department of Defense (DoD) is making the quantum leap from paper based medical records to computer based patient record (CPR). The CPR will enable DoD health care to meet its strategic goals for the 21st century and is paramount to providing comprehensive patient-focused information.

Harris, A. D., et al. (2017). "Edited (1) H magnetic resonance spectroscopy in vivo: Methods and metabolites." Magn Reson Med **77**(4): 1377-1389.

The Proton magnetic resonance ((1) H-MRS) spectrum contains information about the concentration of tissue metabolites within a predefined region of interest (a voxel). The conventional spectrum in some cases obscures information about less abundant metabolites due to limited separation and complex splitting of the metabolite peaks. One method to detect these metabolites is to reduce the complexity of the spectrum using editing. This review provides an overview of the one-dimensional editing methods available to interrogate these obscured metabolite peaks. These methods include sequence optimizations, echo-time averaging, J-difference editing methods (single BASING, dual BASING, and MEGA-PRESS), constant-time PRESS, and multiple quantum filtering. It then provides an overview of the brain metabolites whose detection can benefit from one or more of these editing approaches, including ascorbic acid, gamma-aminobutyric acid, lactate, aspartate, N-acetyl aspartyl glutamate, 2-hydroxyglutarate, glutathione, glutamate, glycine, and serine. Magn Reson Med 77:1377-1389, 2017. (c) 2017 International Society for Magnetic Resonance in Medicine.

Hartman, K. B., et al. (2008). "Detecting and treating cancer with nanotechnology." Mol Diagn Ther **12**(1): 1-14.

Nanotechnology offers many opportunities for enhanced diagnostic and therapeutic medicine against cancer and other diseases. In this review, the special properties that result from the nanoscale size of quantum dots, metal colloids, superparamagnetic iron oxide, and carbon-based nanostructures are reviewed and interpreted against a background of the structural and electronic detail that gives rise to their nanotechnologic behavior. The detection and treatment of cancer is emphasized, with special attention paid to the biologic targeting of the disease. The future of nanotechnology in cancer research and clinical practice is projected to focus on 'theranostic' nanoparticles that are both diagnostic and therapeutic by design.

Hatami, M., et al. (2016). "Engineered nanomaterial-mediated changes in the metabolism of terrestrial plants." Sci Total Environ **571**: 275-291.

Engineered nanomaterials (ENMs) possess remarkable physicochemical characteristics suitable for different applications in medicine, pharmaceuticals, biotechnology, energy, cosmetics and electronics. Because of their ultrafine size and high surface reactivity, ENMs can enter plant cells and interact with intracellular structures and metabolic pathways which may produce toxicity or promote plant growth and development by diverse mechanisms. Depending on their type and concentration, ENMs can have positive or negative effects on photosynthesis, photochemical fluorescence and quantum yield as well as photosynthetic pigments status of the plants. Some studies have shown that ENMs can improve photosynthetic efficiency via increasing chlorophyll content and light absorption and also broadening the spectrum of captured light, suggesting that photosynthesis can be nano-engineered for harnessing more solar energy. Both up- and down-regulation of primary metabolites such as proteins and carbohydrates have been observed following exposure of plants to various ENMs. The potential capacity of ENMs for changing the rate of primary metabolites lies in their close relationship with activation and biosynthesis of the key enzymes. Several classes of secondary metabolites such as phenolics, flavonoids, and alkaloids have been shown to be induced (mostly accompanied by stress-related factors) in plants exposed to different ENMs, highlighting their great

potential as elicitors to enhance both quantity and quality of biologically active secondary metabolites. Considering reports on both positive and negative effects of ENMs on plant metabolism, in-depth studies are warranted to figure out the most appropriate ENMs (type, size and optimal concentration) in order to achieve the desirable effect on specific metabolites in a given plant species. In this review, we summarize the studies performed on the impacts of ENMs on biosynthesis of plant primary and secondary metabolites and mention the research gaps that currently exist in this field.

Hausen, B. M., et al. (2003). "Structure-activity relationships in allergic contact dermatitis. Part III. The sensitizing capacity of substituted phenanthrenequinones: a quantum-mechanical approach." Am J Contact Dermat **14**(2): 82-89.

BACKGROUND: Nonterpenoid and diterpenoid phenanthrenequinones (PACs) have been found in the plant kingdom. Some of them occur in plants used in traditional Chinese medicine like Tan-Shen whereas others are constituents of orchids that are popular as ornamental plants. OBJECTIVE: Case reports and our own observations in orchid nurseries suggest that some or even all of these PACs possess a distinct sensitizing potency. Occasional exposure (particularly of botanists) to field-grown orchids, as well as occupational contact with sawdust of PAC-containing tropical timbers, caused allergic contact dermatitis. However, experimental studies in guinea pigs to determine the sensitizing capacity of PACs have not been performed so far. METHODS: Guinea pigs were sensitizied by a modified Freund's complete adjuvant method with four naturally occurring and 22 synthetic PACs in order to find out which and how many substituents at the carbons of the three rings of the PAC will influence the sensitizing power of the molecule. Subsequently, the lowest unoccupied molecular orbital (LUMO) coefficients were calculated to show whether a correlation exists between chemical reactivity and sensitizing capacity. RESULTS: Sensitizing capacity was found to be strong in two PACs, moderate in eight PACs, and weak in ten PACs. Five PACs were extremely weak in sensitizing capacity, and one PAC was completely negative. Two substituents on the left-hand carbons C-7 and C-8 of ring C were shown to be responsible for a strong sensitizing capacity. One methoxy group alone or three of them, especially when localized at C-5, decreased the sensitizing capacity to moderate. Substitution with a methoxy group at C-3 and/or at C-2 of the quinonoid ring itself (ring A) led to a weak sensitizing capacity. The ortho-quinones 1,2-PAC and 9,10-PAC were also weakly sensitizing. In fact, LUMO coefficient calculations corroborated a good correlation between chemical reactivity and sensitizing capacity. CONCLUSION: Substitution with methoxy groups at C-7 and/or at C-8 of ring C of 1,4-phenanthrenequinone increases the LUMO coefficients at the 2,3 double bond of ring A and thus facilitates nucleophilic substitution of protein nitrogen or sulfur nucleophiles at this electron-deficient double bond. The four naturally occurring PACs that were investigated--cypripedin, denbinobin, annoquinone-A, and latinone--do not fulfill these criteria and are thus only weak sensitizers. However, as-yet-unstudied phenanthrenequinones occurring in plants or trees and having no substituents at C-2 or C-3 of the quinonoid ring must be considered potentially strong allergens.

Havanur, S., et al. (2019). "Poly(N,N-diethyl acrylamide)/functionalized graphene quantum dots hydrogels loaded with doxorubicin as a nano-drug carrier for metastatic lung cancer in mice." Mater Sci Eng C Mater Biol Appl **105**: 110094.

Cancer has emanated as a daunting menace to human-kind even though medicine, science, and technology has reached its zenith. Subsequent scarcity in the revelation of new drugs, the exigency of salvaging formerly discovered toxic drugs such as doxorubicin has emerged. The invention of drug carrier has made drug delivery imminent which is ascribable to its characteristic traits of specific targeting, effective response to stimuli and biocompatibility. In this paper, the nanoscale polymeric drug carrier poly(N,N-diethyl acrylamide) nanohydrogel has been synthesized by inverse emulsion polymerization. Lower critical solution temperature of the polymeric carrier has been modified using graphene quantum. The particle size of pure nanohydrogel was in the range of 47 to 59.5nm, and graphene quantum dots incorporated nanohydrogels was in the range of 68.1 to 87.5nm. Doxorubicin (hydroxyl derivative of anthracycline) release behavior as a function of time and temperature was analyzed, and the Lower critical solution temperature of the synthesized nanohydrogels has been found to be in the range of 28-42 degrees C. Doxorubicin release characteristics have improved significantly as the surrounding temperature of the release media was increased near to physiological temperature. Further, the cumulative release profile was fitted in the different kinetic model and found to follow a Fickian diffusion release mechanism. The hydrogel was assessed for its cytotoxicity in B16F10 cells by MTT assay. In-vivo studies were done to study the lung metastasis by melanoma cancer and the results showed a rational favorable prognosis which was confirmed by evaluating hematological parameters and the non-immunogenic nature of nanohydrogel by cytokine assay. Comprehensively, the results suggested that poly(N,N-diethyl acrylamide) nanohydrogels have potential application as an intelligent drug carrier for melanoma cancer.

He, F., et al. (2011). "[Study of population pharmacokinetic model and parameter analyses for multiple components in Chinese matria medica formula]." Zhongguo Zhong Yao Za Zhi **36**(20): 2866-2870.

OBJECTIVE: To eluciate and establish a new population pharmacokinetic mathematical models and parameter calculation for the multiple components in the Chinese Matria Medica Formula (CMMF) through analyses of population pharmacokinetic parameter calculation for single compounds. METHOD: The model was been set up by statistic moment principle to form a new population pharmacokinetics for the mutiple components in CMMF according to the single compound population pharmacokinetic parameter calculation principle. RESULT: It have been established the mathematical model for the population pharmacokinetic model for CMMF that consisted of a series of parameters: 1) total quantum zero moment as AUC(T), 2) first moment as MRT(T), mean residence time of metabolism, 3) second moment as VRT(T), variance of mean residence time of metabolism, 4) total body clearance CL(T), 5) total apparent volum V(T), 6) 95% of total ingredient metabolic time interval PI(T)(0.95), 7) 95% of total ingredient accumulation metabolic time interval Pa(T)(0.95) etc that were correlated with single population pharmacokinetic parameters. CONCLUSION: The population pharmacokinetic model and parameter calculation for CMMF can be established on the bases of single compound population pharmacokinetics by way of total quantum statistic moment principle to be expansived taylor expression at point of population parameter typical values to divide population pharmacokinetic total quantum statistical moment parameters into the four term of typical value, fixed effect, biologic variation and experiment error.

He, F. Y., et al. (2013). "[Experimental studies on pharmacokinetics of three components in Buyanghuanwu injection on base of total quantum statistical moment]." Zhongguo Zhong Yao Za Zhi **38**(2): 253-262.

OBJECTIVE: To verify established the total quantum statistic moments model with astragaloside IV, paeoniflorin, tetramethylpyrazine in Buyanghuanwu injection, in order to establish a pharmacokinetic experimental method with multi-component traditional Chinese medicine (TCM) compound system. METHOD: The RP-HPLC was adopted, with the chromatographic column of C18, 4.6 mm x 250 mm, 5 microm. As for astragaloside IV, the ELSD detector was adopted with acetonitrile-water (35: 65) as the mobile phase at 1 mL x min(-1); the pressure of column was (15.0 +/- 0.408) MPa, the column temperature was 30 degrees C. Regarding paeoniflorin and tetramethylpyrazine, the detection of wavelengths was 254 nm, with acetonitrile-water (35:65) as the mobile phase at 1 mL x min(-1), the column pressure of (15.17 +/- 0.41) MPa. The pharmacokinetic parameters for single component were dealt with DAS and the total quantum statistical moment (TQSM) parameters were calculated using formulations. RESULT: All of the three components followed the two compartmental pharkacokinetic model ($P < 0.01$) in rats. Compared with the superimposed total concentration, each single component showed difference in parameters up to 10 000 times at most, whereas the RSD of TQSM parameters was 3.510%. The TQSM pharmacokinetic parameters of the three components in Buyanghuanwu injection showed that AUC(t), MRT(t), VRT(t), CL(t), V(t), were (119.8 +/- 27.20) g x min x L(-1), (210.0 +/- 54.49) min, (5.608 +/- 2.723) x 10(4) min2, (0.319 6 +/- 0.068 8) mL x min(-1) x kg(-1) and (64.12 +/- 8.243) mL x kg(-1), respectively, suggesting that the half-life time for the three components were (145.5 +/- 37.76) min and 95% of them were metabolized within 0-674. 2 min. CONCLUSION: The TQSM can be used to study pharmacokinetic parameters of multi-component TCM compound, because the method can characterize the pharmacokinetic regularity of quantum-time change in a multi-component system.

Husak, A., et al. (2016). "Photochemical formation of quinone methides from peptides containing modified tyrosine." Org Biomol Chem **14**(46): 10894-10905.

We have demonstrated that quinone methide (QM) precursors can be introduced in the peptide structure and used as photoswitchable units for peptide modifications. QM precursor 1 was prepared from protected tyrosine in the Mannich reaction, and further used as a building block in peptide synthesis. Moreover, peptides containing tyrosine can be transformed into a photoactivable QM precursor by the Mannich reaction which can afford monosubstituted derivatives 2 or bis-substituted derivatives 3. Photochemical reactivity of modified tyrosine 1 and dipeptides 2 and 3 was studied by preparative irradiation in CH3OH where photodeamination and photomethanolysis occur. QM precursors incorporated in peptides undergo photomethanolysis with quantum efficiency PhiR = 0.1-0.2, wherein the peptide backbone does not affect their photochemical reactivity. QMs formed from dipeptides were detected by laser flash photolysis (lambdamax approximately 400 nm, tau = 100 mus-20 ms) and their reactivity with nucleophiles was studied. Consequently, QM precursors derived from tyrosine can be a part of the peptide backbone which can be transformed into QMs upon electronic excitation, leading to the reactions of peptides with different reagents. This proof of principle showing the ability to photochemically trigger peptide modifications and interactions with other molecules

can have numerous applications in organic synthesis, materials science, biology and medicine.

Hyland, G. J. (2008). "Physical basis of adverse and therapeutic effects of low intensity microwave radiation." Indian J Exp Biol **46**(5): 403-419.

A physical basis of adverse and therapeutic effects of low intensity microwave radiation is presented based on the concept of oscillatory similitude between the frequency of an external microwave field (together with any lower frequency modulations thereof) and those of certain endogenous dipolar coherent excitations allied to aliveness, which play the role of 'tuned circuits' via which a living organism is electromagnetically sensitised in a non-linear way to external fields too weak to be able to cause heating. From this perspective, an external electromagnetic field affects a living system not as a toxin but rather by perturbing its endogenous electromagnetic activity. The possibility of adverse perturbation is illustrated by reference to the microwave fields used in mobile telecommunications whose signals interfere in a non-thermal way with biofunctionality--in particular, undermining the efficacy of processes that would otherwise afford natural protection against the development of pathology. Therapeutic modalities of microwave exposure, on the other hand, are illustrated using the example of microwave resonance therapy--which can be considered as an electromagnetic version of acupuncture, and as an example of 'quantum medicine'--whose normalising effect on a wide range of pathologies is striking, and which affords a novel alternative to conventional pharmacological interventions.

Hyland, M. E. (2003). "Extended Network Generalized Entanglement Theory: therapeutic mechanisms, empirical predictions, and investigations." J Altern Complement Med **9**(6): 919-936.

Extended Network Generalized Entanglement Theory (Entanglement Theory for short) combines two earlier theories based on complexity theory and quantum mechanics. The theory's assumptions are: the body is a complex, self-organizing system (the extended network) that self-organizes so as to achieve genetically defined patterns (where patterns include morphologic as well as lifestyle patterns). These pattern-specifying genes require feedback that is provided by generalized quantum entanglement. Additionally, generalized entanglement has evolved as a form of communication between people (and animals) and can be used in healing. Entanglement Theory suggests that several processes are involved in complementary and alternative medicine (CAM). Direct subtle therapy creates network change either through lifestyle management, some manual therapies, and psychologically mediated effects of therapy. Indirect subtle therapy is a process of entanglement with other people or physical entities (e.g., remedies, healing sites). Both types of subtle therapy create two kinds of information within the network--either that the network is more disregulated than it is and the network then compensates for this error, or as a guide for network change leading to healing. Most CAM therapies involve a combination of indirect and direct therapies, making empirical evaluation complex. Empirical predictions from this theory are contrasted with those from two other possible mechanisms of healing: (1) psychologic processes and (2) mechanisms involving electromagnetic influence between people (biofield/energy medicine). Topics for empirical study include a hyperfast communication system, the phenomenology of entanglement, predictors of outcome in naturally occurring clinical settings, and the importance of therapist and patient characteristics to outcome.

Hyland, M. E. (2004). "Does a form of 'entanglement' between people explain healing? An examination of hypotheses and methodology." Complement Ther Med **12**(4): 198-208.

Quantum entanglement is a phenomenon in which entangled systems exhibit correlations that cannot be explained by classical physics. It has recently been suggested that a similar process occurs between people and explains anomalous phenomena such as healing. This paper explores the hypothesis that the therapeutic interaction involves some kind of 'entanglement' between people. There are several different versions of the theory that entanglement is possible between people: the versions differ in the way entanglement between people is derived, and the way it has a therapeutic effect. The two main versions are generalised, specific entanglement, and global, emergent entanglement-specific entanglement. Two research ideas are presented for testing the hypothesis of entanglement between people, both of which are based on predicting variation in outcome in naturally occurring contexts (the naturalistic observational study).

Ilan, Y. (2020). "Order Through Disorder: The Characteristic Variability of Systems." Front Cell Dev Biol **8**: 186.

Randomness characterizes many processes in nature, and therefore its importance cannot be overstated. In the present study, we investigate examples of randomness found in various fields, to underlie its fundamental processes. The fields we address include physics, chemistry, biology (biological systems from genes to whole organs), medicine, and environmental science. Through the chosen examples, we explore the seemingly paradoxical nature of life and demonstrate that randomness is preferred under specific conditions. Furthermore, under certain conditions, promoting or making use of variability-

associated parameters may be necessary for improving the function of processes and systems.

Inoue, T., et al. (2014). "Realization of dynamic thermal emission control." Nat Mater **13**(10): 928-931.

Thermal emission in the infrared range is important in various fields of research, including chemistry, medicine and atmospheric science. Recently, the possibility of controlling thermal emission based on wavelength-scale optical structures has been intensively investigated with a view towards a new generation of thermal emission devices. However, all demonstrations so far have involved the 'static' control of thermal emission; high-speed modulation of thermal emission has proved difficult to achieve because the intensity of thermal emission from an object is usually determined by its temperature, and the frequency of temperature modulation is limited to 10-100 Hz even when the thermal mass of the object is small. Here, we experimentally demonstrate the dynamic control of thermal emission via the control of emissivity (absorptivity), at a speed four orders of magnitude faster than is possible using the conventional temperature-modulation method. Our approach is based on the dynamic control of intersubband absorption in n-type quantum wells, which is enhanced by an optical resonant mode in a photonic crystal slab. The extraction of electrical carriers from the quantum wells leads to an immediate change in emissivity from 0.74 to 0.24 at the resonant wavelength while maintaining much lower emissivity at all other wavelengths.

Irmis, F. (2015). "[Spirituality and ethics in psychosomatic medicine]." Cas Lek Cesk **154**(3): 115-121.

A patient has to cope with an illness on a physical, mental and spiritual level. There exists a difference between religiousness and spirituality even though the approach has a common foundation. Nonreligious spirituality relates to an inner experience, transcendent states of consciousness, meaningfulness, responsibility, sympathy, ethics, humanisation, faith. We encounter the spiritual point of view in humanistic psychotherapy, pastoral medicine, work of hospital chaplains, New Age, psychotherapies with religious and alternative aspects, transpersonal psychotherapy, psycho-spiritual crises, unusual states of consciousness, in meditation, Yoga, relaxation, kinesiology, ethicotherapy, reincarnation therapy, positive motivation, holotropic breathing, etc. There is description of different degrees of spiritual development, rational and irrational feeling of spirituality, Quantum Physics, spiritual intelligence, neuro-theology, physiological change, effects on improving adaptation during stress, drugs addiction, etc. Spirituality in relation with ethics is discussed in terms of socio-biology, evolution, emotions, aggressivity, genetics and social influence. The work analyses the effect of stressful situations on the deterioration of moral attitudes: during lack of time, obedience to authority and order. It is described how temperament and personality disorders can affect perception of spirituality, guilt feeling and conscience. Stressful situations, lack of time, relying only on the auxiliary objective methods leads to alienation of physician with a patient. Spirituality can partially improve the doctor-patient relationship, communication and sense of responsibility.

Isensee, K., et al. (2018). "Biomedical applications of mid-infrared quantum cascade lasers - a review." Analyst **143**(24): 5888-5911.

Mid-infrared spectroscopy has been applied to research in biology and medicine for more than 20 years and conceivable applications have been identified. More recently, these applications have been shown to benefit from the use of quantum cascade lasers due to their specific properties, namely high spectral power density, small beam parameter product, narrow emission spectrum and, if needed, tuning capabilities. This review provides an overview of the achievements and illustrates some applications which benefit from the key characteristics of quantum cascade laser-based mid-infrared spectroscopy using examples such as breath analysis, the investigation of serum, non-invasive glucose monitoring in bulk tissue and the combination of spectroscopy and microscopy of tissue thin sections for rapid histopathology.

Ivanova, B. and M. Spiteller (2014). "Solid-state UV-MALDI-MS assay of transition metal dithiocarbamate fungicides." Environ Sci Pollut Res Int **21**(2): 1163-1177.

The determination of transition metal containing dithiocarbamate fungicides represents a challenging aspect of analytical object. They have a low stability, low solubility and stabilize versatile coordination monomers, dimers, disulfides and/or S-oxidized derivatives. Their diverse biological activities and agricultural implementation encompass plant prevention and crop protection against a variety of plants containing fungi and diseases of 400 pathogens and 70 cultures. Nonetheless, those dithiocarbamates (DTCs) are banned for agricultural use in Europe or have expiration at years 2016-2017 because of their highly toxic degradation products and/or metabolites, in particular ethylene thiourea; they found large-scale implementations in materials research and medicine. Despite the broad interdisciplinary of DTC application, due to the above reasons, they have received little attention in the rapidly growing field of analytical chemistry, and in particular, the analytical mass spectrometry. Therefore, the study reported on qualitative, quantitative and structural analysis of ten DTCs (1-10), using the matrix assisted laser

desorption/ionization (UV-MALDI)-Orbitrap-mass spectrometry (MS) contributed considerably to the implementation of the method for environmental and foodstuffs monitoring. Its ultrahigh resolving power and capacity for direct solid-state analysis, at limited number of sample pretreatment steps, at concentration levels of analytes of up to femtogram per gram resulted to achievement of a highly precise analytical information for these non-trivial objects. The presented fully validated method and technique is based on the successful ionization of DTCs embedded in three novel organic salts (M1-M3). In this regard, the reported MS and the single-crystal X-ray diffraction data as well as the quantum chemical one are able to correlate the molecular structures in condense and in the gas phase. Despite the novelty of the fundamental methodological character of the research reported, the promising metrology contributed to the applied aspect of the UV-MALDI-MS as a robust analytical method for environmental and foodstuffs monitoring, which is tested on two commercially available crop protecting products such as Mancozeb(R) and Antracol(R), respectively.

Jain, K. K. (2010). "Advances in the field of nanooncology." BMC Med **8**: 83.

Nanooncology, the application of nanobiotechnology to the management of cancer, is currently the most important chapter of nanomedicine. Nanobiotechnology has refined and extended the limits of molecular diagnosis of cancer, for example, through the use of gold nanoparticles and quantum dots. Nanobiotechnology has also improved the discovery of cancer biomarkers, one such example being the sensitive detection of multiple protein biomarkers by nanobiosensors. Magnetic nanoparticles can capture circulating tumor cells in the bloodstream followed by rapid photoacoustic detection. Nanoparticles enable targeted drug delivery in cancer that increases efficacy and decreases adverse effects through reducing the dosage of anticancer drugs administered. Nanoparticulate anticancer drugs can cross some of the biological barriers and achieve therapeutic concentrations in tumor and spare the surrounding normal tissues from toxic effects. Nanoparticle constructs facilitate the delivery of various forms of energy for noninvasive thermal destruction of surgically inaccessible malignant tumors. Nanoparticle-based optical imaging of tumors as well as contrast agents to enhance detection of tumors by magnetic resonance imaging can be combined with delivery of therapeutic agents for cancer. Monoclonal antibody nanoparticle complexes are under investigation for diagnosis as well as targeted delivery of cancer therapy. Nanoparticle-based chemotherapeutic agents are already on the market, and several are in clinical trials. Personalization of cancer therapies is based on a better understanding of the disease at the molecular level, which is facilitated by nanobiotechnology. Nanobiotechnology will facilitate the combination of diagnostics with therapeutics, which is an important feature of a personalized medicine approach to cancer.

Jebali, A., et al. (2017). "Nano-carbohydrates: Synthesis and application in genetics, biotechnology, and medicine." Adv Colloid Interface Sci **240**: 1-14.

Combining nanoparticles with carbohydrate has triggered an exponential growth of research activities for the design of novel functional bionanomaterials, nano-carbohydrates. Recent advances in versatile synthesis of glycosylated nanoparticles have paved the way towards diverse biomedical applications. The accessibility of a wide variety of these structured nanosystems, in terms of shape, size, and organization around stable nanoparticles, has readily contributed to their development and application in nanomedicine. Glycosylated gold nanoparticles, glycosylated quantum dots, fullerenes, single-wall nanotubes, and self-assembled glyconanoparticles using amphiphilic glycopolymers or glycodendrimers have received considerable attention for their application in powerful imaging, therapeutic, and biodiagnostic devices. Recently, nano-carbohydrates were used for different types of microarrays to detect proteins and nucleic acids.

Jeelani, S., et al. (2014). "Theranostics: A treasured tailor for tomorrow." J Pharm Bioallied Sci **6**(Suppl 1): S6-8.

Emerging as a targeted, safe, and efficient pharmacotherapy is the approach of theranostics, which focuses on patient-centered care. It is a combination of diagnosis and therapeutics. It provides a transition from conventional medicine to personalized medicine. It deals with the custom made treatment plan based on uniqueness of every individual thus resulting in right drug for the right patient at the right time. Genetics plays a significant role in theranostics. Theranostics provides a cost-effective specific successful treatment protocol. Pharmacogenetics, proteomics and biomarker profiling forms the backbone of theranostics. The role of theranostics is interestingly appreciated at multi levels with special consideration in oncology wherein nano formulations in the form of liposomes, dendrimers, polymeric nanoparticles, metallic nanoparticles, quantum dots and carbon nanotubes play a very important role. Thus, theranostics is a holistic transition from trial and error medicine to predictive, preventive and personalized medicine leading to improved quality care of pharmacotherapy.

Jenista, E. R., et al. (2010). "Application of mixed spin iMQCs for temperature and chemical-selective imaging." J Magn Reson **204**(2): 208-218.

The development of accurate and non-invasive temperature imaging techniques has a wide variety of applications in fields such as medicine, chemistry and materials science. Accurate detection of temperature both in phantoms and in vivo can be obtained using iMQCs (intermolecular multiple quantum coherences), as demonstrated in a recent paper. This paper describes the underlying theory of iMQC temperature detection, as well as extensions of that work allowing not only for imaging of absolute temperature but also for imaging of analyte concentrations through chemically-selective spin density imaging.

Jennings, L. E. and N. J. Long (2009). "'Two is better than one'--probes for dual-modality molecular imaging." Chem Commun (Camb)(24): 3511-3524.

Molecular or personalised medicine is the future of patient management and healthcare, and molecular imaging plays a key role towards this goal. However, amongst molecular imaging techniques, no single modality is perfect and sufficient to gain all the necessary information. For instance, optical fluorescence imaging is difficult to quantify--especially in tissue more than a few millimetres in depth within a subject; magnetic resonance imaging (MRI) has superb resolution but low sensitivity and positron emission tomography (PET) has very high sensitivity but poor resolution. The combination of multiple molecular imaging techniques can therefore offer synergistic advantages over any modality alone. However, the problem cannot be solved by simply adding two different classes of imaging probes together, unless they happen to have identical pharmacodynamic properties. Therefore, multi-modal contrast agents or imaging probes have been developed to solve this problem. Despite the great wealth of information that such probes can provide, their development is far from trivial and represents an important challenge to synthetic chemists. In this feature article, we provide an overview of recent findings in the synthesis, evaluation and application of dual-modality molecular imaging probes.

Jeong, S. H., et al. (2010). "Assessment of penetration of quantum dots through in vitro and in vivo human skin using the human skin equivalent model and the tape stripping method." Biochem Biophys Res Commun **394**(3): 612-615.

Quantum dots (QDs) are rapidly emerging as an important class of nanoparticles (NPs) with potential applications in medicine. However, little is known about penetration of QDs through human skin. This study investigated skin penetration of QDs in both in vivo and in vitro human skin. Using the tape stripping method, this study demonstrates for the first time that QDs can actually penetrate through the stratum corneum (SC) of human skin. Transmission electron microscope (TEM) and energy diverse X-ray (EDX) analysis showed accumulation of QDs in the SC of a human skin equivalent model (HSEM) after dermal exposure to QDs. These findings suggest possible transdermal absorption of QDs after dermal exposure over a relatively long period of time.

Jeyamogan, S., et al. (2021). "Application and Importance of Theranostics in the Diagnosis and Treatment of Cancer." Arch Med Res **52**(2): 131-142.

The number of cancer cases worldwide in terms of morbidity and mortality is a serious concern, despite the presence of therapeutic interventions and supportive care. Limitations in the current available diagnosis methods and treatments methods may contribute to the increase in cancer mortality. Theranostics, is a novel approach that has opened avenues for the simultaneous precise diagnosis and treatment for cancer patients. Although still in the early development stage, theranostic agents such as quantum dots, radioisotopes, liposomes and plasmonic nanobubbles can be bound to anticancer drugs, cancer cell markers and imaging agents, with the support of available imaging techniques, provide the potential to facilitate diagnosis, treatment and management of cancer patients. Herein, we discuss the potential benefits of several theranostic tools for the management of cancer. Specifically, quantum dots, radio-labelled isotopes, liposomes and plasmonic nanobubbles coupled with targeting agents and/or anticancer molecules and imaging agents as theranostic agents are deliberated upon in this review. Overall, the use of theranostic agents shows promise in cancer management. Nevertheless, intensive research is required to realize these expectations.

Jia, C., et al. (2009). "Metabolism of echinacoside, a good antioxidant, in rats: isolation and identification of its biliary metabolites." Drug Metab Dispos **37**(2): 431-438.

Echinacoside (ECH) is one of the major active phenylethanoid glycosides (PEGs) in famous traditional Chinese medicine, Herba Cistanches. Although it has various bioactivities, such as antioxidation, neuroprotection, and hepatoprotection, knowledge about its metabolic fate is scant. In the present study, eight phase II metabolites, 3,4 -O-dimethyl-ECH-3 -O-beta-d-glucuronide (M1); 4,4 -O-dimethyl-ECH-3 -O-beta-d-glucuronide (M2); 3,4 -O-dimethyl-ECH-4-O-sulfate ester (M3); 4,4 -O-dimethyl-ECH-3-O-sulfate ester (M4); 3,3 -O-dimethyl-ECH (M5); 3,4 -O-dimethyl-ECH (M6); 4,3 -O-dimethyl-ECH (M7); and 4,4 -O-dimethyl-ECH (M8), were isolated from rat bile sample after intravenous administration of ECH and identified by mass spectra and NMR spectroscopy, including (1)H NMR, (13)C NMR, nuclear Overhauser effect difference spectroscopy, and two-dimensional NMR

(heteronuclear single quantum correlation, heteronuclear multiple-bond correlation spectroscopy, gradient-selected correlation spectroscopy, and nuclear Overhauser effect spectroscopy). Among them, M5 to M8 were O-di-methylated conjugates; M1 and M2 and M3 and M4 were O-dimethyl glucuronides and O-dimethyl sulfates, respectively. In the three types of metabolites of rat, the major metabolites were the methyl ethers and the glucuronides, whereas the sulfates were minor. The regioselectivity of conjugation for ECH and metabolic pathway of ECH were proposed, which gave insight into the mechanism of ECH for its bioactivities in vivo.

Kapusta, J., et al. (2017). "[Evaluation of selected vascular active factors in patients after myocardial infarction subjected to cardiac rehabilitation]." Pol Merkur Lekarski **43**(254): 56-60.

Atherosclerosis is an inflammatory process that develops in the coronary arteries. Clinically active agents such as proinflammatory interleukins, TNF-alpha, tissue inhibitors of metalloproteinases (including TIMP-1), and vascular endothelial growth factor (VEGF), are important factors in the development of acute coronary syndromes. AIM: The aim of the study was to evaluate the effect of cardiac rehabilitation (stage II) on the concentration of selected vascular active factors (IL- 1, IL-6, TIMP-1, VEGF). MATERIALS AND METHODS: The study involved 24 patients after ACS who underwent complex cardiac rehabilitation (stage II) in the Department of Internal Medicine and Cardiac Rehabilitation at the Medical University of Lodz. The study involved 20 men and 4 women aged 42-78 years (average age 58.75 +/- 8.45 years). The ELISA method was used in the vascular endothelial cell assay using readymade sets for determining individual molecules: Human Quantum ELISA Kit (DTM100; R & D Systems, BIOKOM, Poland), Human VEGF Quantikine ELISA Kit (DVE00; R & D Systems, BIOKOM, Poland) Human IL-1 beta / IL-1F2 Quantikine ELISA Kit (DLB50; R & D Systems, BIOKOM, Poland), Human IL-6 Quantikine ELISA Kit (D6050, R & D Systems, BIOKOM, Poland). TIMP-1 concentration is expressed in ng / ml, VEGF in pg / ml, IL-1 in pg / ml, IL-6 pg / ml. The results of the study were analyzed statistically at significance level p <0,05. RESULTS: There was no significant effect of cardiac rehabilitation on vascular endothelial factors: TIMP-1, VEGF, IL-6. Significant effect of cardiac rehabilitation was observed on the increase of IL-1 concentration (p=0.016). CONCLUSIONS: The absence of post-cardiac rehabilitation in patients after ACS, significant changes in vascular endothelial activity, confirm the hypothesis that adequate physical effort does not involve changes in blood concentrations and justifies perception of rehabilitation as a safe and risk-free intervention.

Karabanov, A., et al. (2015). "Dynamic Nuclear Polarization as Kinetically Constrained Diffusion." Phys Rev Lett **115**(2): 020404.

Dynamic nuclear polarization (DNP) is a promising strategy for generating a significantly increased nonthermal spin polarization in nuclear magnetic resonance (NMR) and its applications that range from medicine diagnostics to material science. Being a genuine nonequilibrium effect, DNP circumvents the need for strong magnetic fields. However, despite intense research, a detailed theoretical understanding of the precise mechanism behind DNP is currently lacking. We address this issue by focusing on a simple instance of DNP-so-called solid effect DNP-which is formulated in terms of a quantum central spin model where a single electron is coupled to an ensemble of interacting nuclei. We show analytically that the nonequilibrium buildup of polarization heavily relies on a mechanism which can be interpreted as kinetically constrained diffusion. Beyond revealing this insight, our approach furthermore permits numerical studies of ensembles containing thousands of spins that are typically intractable when formulated in terms of a quantum master equation. We believe that this represents an important step forward in the quest of harnessing nonequilibrium many-body quantum physics for technological applications.

Karakaslar, E. O., et al. (2020). "Predicting Carbon Spectrum in Heteronuclear Single Quantum Coherence Spectroscopy for Online Feedback During Surgery." IEEE/ACM Trans Comput Biol Bioinform **17**(2): 719-725.

(1)H High-Resolution Magic Angle Spinning (HRMAS) Nuclear Magnetic Resonance (NMR) is a reliable technology used for detecting metabolites in solid tissues. Fast response time enables guiding surgeons in real time, for detecting tumor cells that are left over in the excision cavity. However, severe overlap of spectral resonances in 1D signal often render distinguishing metabolites impossible. In that case, Heteronuclear Single Quantum Coherence Spectroscopy (HSQC) NMR is applied which can distinguish metabolites by generating 2D spectra ((1)H- (13)C). Unfortunately, this analysis requires much longer time and prohibits real time analysis. Thus, obtaining 2D spectrum fast has major implications in medicine. In this study, we show that using multiple multivariate regression and statistical total correlation spectroscopy, we can learn the relation between the (1)H and (13)C dimensions. Learning is possible with small sample sizes and without the need for performing the HSQC analysis, we can predict the (13)C dimension by just performing (1)H HRMAS NMR experiment. We show on a rat model of central nervous system tissues (80 samples, 5 tissues) that our

methods achieve 0.971 and 0.957 mean R(2) values, respectively. Our tests on 15 human brain tumor samples show that we can predict 104 groups of 39 metabolites with 97 percent accuracy. Finally, we show that we can predict the presence of a drug resistant tumor biomarker (creatine) despite obstructed signal in (1)H dimension. In practice, this information can provide valuable feedback to the surgeon to further resect the cavity to avoid potential recurrence.

Kassis, A. I., et al. (1983). "Thallium-201: an experimental and a theoretical radiobiological approach to dosimetry." J Nucl Med **24**(12): 1164-1175.

The kinetics of uptake and retention of Tl-201, Rb-86, and K-42 and -43 have been studied in cultured mammalian cells and related to their radiotoxicities. Among the four radionuclides, the intracellular localization of Tl-201, the only emitter of Auger electrons, was important for the manifestation of its cytocidal effects. The results have been found consistent with the short-range nature of Auger electrons and are substantiated by our theoretical dosimetric calculations. The possible implications of this in vitro system for applications of Tl-201 in nuclear medicine are indicated.

Kato, K., et al. (2020). "Intermolecular interaction among Remdesivir, RNA and RNA-dependent RNA polymerase of SARS-CoV-2 analyzed by fragment molecular orbital calculation." J Mol Graph Model **100**: 107695.

COVID-19, a disease caused by a new strain of coronavirus (SARS-CoV-2) originating from Wuhan, China, has now spread around the world, triggering a global pandemic, leaving the public eagerly awaiting the development of a specific medicine and vaccine. In response, aggressive efforts are underway around the world to overcome COVID-19. In this study, referencing the data published on the Protein Data Bank (PDB ID: 7BV2) on April 22, we conducted a detailed analysis of the interaction between the complex structures of the RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2 and Remdesivir, an antiviral drug, from the quantum chemical perspective based on the fragment molecular orbital (FMO) method. In addition to the hydrogen bonding and intra-strand stacking between complementary strands as seen in normal base pairs, Remdesivir bound to the terminus of an primer-RNA strand was further stabilized by diagonal pi-pi stacking with the -1A' base of the complementary strand and an additional hydrogen bond with an intra-strand base, due to the effect of chemically modified functional group. Moreover, stable OH/pi interaction is also formed with Thr687 of the RdRp. We quantitatively revealed the exhaustive interaction within the complex among Remdesivir, template-primer-RNA, RdRp and co-factors, and published the results in the FMODB database.

Kim, K. H., et al. (2014). "4-Methylthio-butanyl derivatives from the seeds of Raphanus sativus and their biological evaluation on anti-inflammatory and antitumor activities." J Ethnopharmacol **151**(1): 503-508.

ETHNOPHARMACOLOGICAL RELEVANCE: Raphanus sativus seeds (Brassicaceae) known as Raphani Semen have long been used as anti-cancer and/or anti-inflammatory agents in Korean traditional medicine. This study was designed to isolate the bioactive constituents from the seed extracts of Raphanus sativus and evaluate their anti-inflammatory and antitumor activities. MATERIAL AND METHODS: Bioassay-guided fractionation and chemical investigation of a methanolic extract of the seeds of Raphanus sativus led to the isolation and identification of seven 4-methylthio-butanyl derivatives. Structural elucidation of the isolated compounds was carried out using 1D and 2D nuclear magnetic resonance (NMR) spectroscopy techniques ((1)H, (13)C, COSY, HMQC and HMBC experiments) and mass spectrometry. RESULTS: The isolated compounds were characterized as in the following: three new 4-methylthio-butanyl derivatives, sinapoyl desulfoglucoraphenin (1), (E)-5-(methylsulfinyl)pent-4-enoxylimidic acid methyl ester (2), and (S)-5-((methylsulfinyl)methyl)pyrrolidine-2-thione (3), together with four known compounds, 5-(methylsulfinyl)-4-pentenenitrile (4), 5-(methylsulfinyl)-pentanenitrile (5), sulforaphene (6), and sulforaphane (7). Full NMR data assignments of the three known compounds 4-6 were also reported for the first time. We evaluated the anti-neuroinflammatory effect of 1-7 in lipopolysaccharide-stimulated murine microglia BV2 cells. Compound 1 significantly inhibited nitrite oxide production with IC50 values of 45.36 muM. Moreover, it also reduced the protein expression of inducible nitric oxide synthase. All isolates were also evaluated for their antiproliferative activities against four human tumor cell lines (A549, SK-OV-3, SK-MEL-2, and HCT-15), and all of them showed antiproliferative activity against the HCT-15 cell, with IC50 values of 8.49-23.97 muM. CONCLUSIONS: 4-Methylthio-butanyl derivatives were one of the main compositions of Raphanus sativus seeds, and activities demonstrated by the isolated compounds support the ethnopharmacological use of Raphanus sativus seeds (Brassicaceae) as anti-cancer and/or anti-inflammatory agents.

Kim, M. J., et al. (2013). "Visible-to-near IR quantum dot-based hypermulticolor high-content screening of herbal medicines for the efficacy monitoring of hair

growth promotion and hair loss inhibition." J Biomol Screen **18**(4): 462-473.

There is a growing interest in alopecia prevention strategies, as the number of alopecia patients is increasing. We examine the efficacy of herbal medicine for hair growth promotion/hair loss inhibition in two cell lines via Western blot and high-content screening (HCS). Nine herbal extracts were obtained from three different herbal medicine mixtures using 3 different extraction methods. Five target proteins-IGF-1 (insulin-like growth factor-1), TGF-beta2 (transforming growth factor-beta2), VEGF (vascular endothelial growth factor), DKK-1 (Dickkopf-1), and Wnt5alpha-were observed for the assessment of hair growth promotion/hair loss inhibition efficacy. The efficacies of nine extracts were compared with minoxidil as control. Efficacy was defined as a rise in the expression levels of IGF-1, VEGF, and Wnt5alpha but a decrease in DKK-1 and TGF-beta2. Intracellular concurrent imaging of these proteins was successfully achieved using HCS, employing visible-to-near infrared probing based on quantum-antibody conjugates and hypermulticolor imaging.

Klimek, R. (2003). "[Neoplasms and medical thermodynamics]." Ginekol Pol **74**(9): 746-753.

Oncology--just as every field of medicine that deals with etiology, diagnostics, pathomechanism and treatment of diseases--is only a part of the general human knowledge, whose all significant achievements must be used to protect human health. This pursuit has as its object not only the benefits form practical discoveries (L. Pasteur, W.C. Roentgen, P. Curie and M. Sklodowska-Curie, V. Schally etc.), but also theoretical generalizations (A. Einstein, W.K. Heisenberg and I. Prigogine). Unfortunately it is the lack and/or slow adaptation of that information, that is responsible for the still unsatisfactory progress in clinical oncology. Responsibility rests not only with oncologists, but primarily with editors of medical journals and textbooks, who have a moral duty to follow the entire general knowledge, especially in the field of the basic research. On the basis of an analysis of the contents of the Polish oncology textbooks and materials from the specialist conferences in gynaecologic oncology, they were found to: 1. Omit the current, particularly domestic literature, 2. Contain mostly works, whose conclusions are textbook information, 3. Rarely include studies in the area of medical thermodynamics, 4. Attempt to explain the effects of the modern technologies, e.g. fotodynamics or nanotechnology using theoretical generalizations which are inadequate for them, and 5. Disregard the rule primum non nocere not only in prevention but even in the treatment of neoplasms. Neoplastic disease has many conditionings and types because of the unique identity of the neoplasms which cause it and which are caused by universal and natural phenomena of the self-organizing dissipative structures. It requires not only early diagnosing but also causative treatment already in the precancerous states, which are better detected by modern methods based on the quantum thermodynamics (lasers, fotodynamics, nuclear magnetic resonance, genetic nanotechnology etc.).

Knoll, J. H. (2007). "Human metaphase chromosome FISH using quantum dot conjugates." Methods Mol Biol **374**: 55-66.

Fluorescence in situ hybridization (FISH) is a powerful, molecular technique with a wide range of applications in medicine and biology. In medicine, FISH uses genomic and cDNA probes to determine the chromosomal position of genes and DNA sequences, which enables detection of ploidy levels and identification of subtle chromosomal rearrangements. Because of its exquisite sensitivity, FISH often enhances conventional cytogenetic analysis and it can provide either diagnostic or prognostic results for particular chromosomal disorders. To achieve the robust probe signals needed for routine clinical application, typical FISH probes consist of recombinant genomic DNA clones often covering multiple genes. These probes can be readily visualized on metaphase chromosomes as they span tens to hundreds of thousands of nucleotides. Visualization of shorter targets has been performed in many research laboratories, and will have significant advantages once they are available clinically. Toward that end, our goal is to make the signals from these shorter probes more intense. We are utilizing quantum dot conjugates to visualize single copy sequence DNA probes as short as 1500 nucleotides in length.

Knopp, D., et al. (2009). "Review: bioanalytical applications of biomolecule-functionalized nanometer-sized doped silica particles." Anal Chim Acta **647**(1): 14-30.

Recent research has looked to develop innovative and powerful novel biofunctionalized nanometer-sized silica particles, controlling and tailoring their properties in a very predictable manner to meet the needs of specific applications. The silica shells of these particles facilitate a wide variety of surface reactions and allow conjugation with biomolecules like proteins and DNA. There exist a multitude of possible applications of fabricated nanoparticles in biotechnology and medicine. In particular, they have proved to be highly useful for biosensing, assay labelling, bioimaging, and in research on a variety of molecular tags in cellular and molecular biology. Techniques commonly rely on the use of silica-coated semiconductor quantum dots, organic dyes, magnetic particles, and Raman active particles. Inorganic-biological hybrid particles combine the

properties of both materials, i.e., the spectroscopic characteristics of the entrapped nanocrystal, and the biomolecular function of the conjugated entity. Rather than being exhaustive, this review focuses on selected examples to illustrate novel concepts and promising applications. Approaches described include the encoding of silica nanoparticles with different groups, and conjugation with various biological entities. Further, promising applications in bioanalysis are considered and discussed.

Kobayashi, T., et al. (2010). "Triplet formation of 6-azauridine and singlet oxygen sensitization with UV light irradiation." Phys Chem Chem Phys **12**(19): 5140-5148.

Excited state characteristics of 6-azauridine (6AUd), which is known as a medicine against psoriasis and neoplastic, were investigated with laser plash photolysis, time-resolved thermal lensing, and near IR single photon counting method. The triplet-triplet absorption spectrum of 6AUd was observed for the first time. The formation quantum yield of excited triplet 6AUd (Phi(ISC)) was estimated by acetone triplet sensitization and actinometry with benzophenone to be 1.00 +/- 0.07 (248 nm excitation) and 0.78 +/- 0.05 (308 nm excitation). This excitation wavelength effect could be explained by intersystem crossing (ISC) to the excited triplet manifolds occurring during the relaxation on the potential energy surface (PES) of the S(1)(npi*) state and be in competition with internal conversion to the S(0) state after the relaxation to the minimum of the S(1)(npi*) state. 6AUd had a lower Phi(ISC) value than 6-azauracil (6AU) with the 308 nm excitation (Phi(ISC) = 0.93 +/- 0.04 for 6AU). The nucleoside has more vibrational modes than 6AU, and therefore the ribose would accelerate intramolecular vibrational energy redistribution and the relaxation to the minimum of the PES of the S(1)(npi*) state. Sensitized singlet oxygen formation of 6AUd was also detected in the O(2)-saturated condition with quantum yields of 0.49 +/- 0.01 with the 248 nm excitation, indicating the high phototoxicity of 6AUd.

Kobeissy, F. H., et al. (2014). "Post-genomics nanotechnology is gaining momentum: nanoproteomics and applications in life sciences." OMICS **18**(2): 111-131.

The post-genomics era has brought about new Omics biotechnologies, such as proteomics and metabolomics, as well as their novel applications to personal genomics and the quantified self. These advances are now also catalyzing other and newer post-genomics innovations, leading to convergences between Omics and nanotechnology. In this work, we systematically contextualize and exemplify an emerging strand of post-genomics life sciences, namely, nanoproteomics and its applications in health and integrative biological systems. Nanotechnology has been utilized as a complementary component to revolutionize proteomics through different kinds of nanotechnology applications, including nanoporous structures, functionalized nanoparticles, quantum dots, and polymeric nanostructures. Those applications, though still in their infancy, have led to several highly sensitive diagnostics and new methods of drug delivery and targeted therapy for clinical use. The present article differs from previous analyses of nanoproteomics in that it offers an in-depth and comparative evaluation of the attendant biotechnology portfolio and their applications as seen through the lens of post-genomics life sciences and biomedicine. These include: (1) immunosensors for inflammatory, pathogenic, and autoimmune markers for infectious and autoimmune diseases, (2) amplified immunoassays for detection of cancer biomarkers, and (3) methods for targeted therapy and automatically adjusted drug delivery such as in experimental stroke and brain injury studies. As nanoproteomics becomes available both to the clinician at the bedside and the citizens who are increasingly interested in access to novel post-genomics diagnostics through initiatives such as the quantified self, we anticipate further breakthroughs in personalized and targeted medicine.

Kodadek, T. (2014). "Chemical tools to monitor and manipulate the adaptive immune system." Chem Biol **21**(9): 1066-1074.

The ability to monitor and manipulate antigen-specific immune responses would have a major impact on several areas of biology and medicine. In this perspective, I consider pharmacological methods to do this, with a focus on the development of abiological "antigen surrogates" capable of binding to the antigen-binding sites of antibodies and B cell receptors with high affinity and selectivity. I describe the application of combinatorial library screening to identify antigen surrogates for monoclonal antibodies of therapeutic interest using chronic lymphocytic leukemia as an example. Furthermore, I discuss the use of multiplexed assays for the quantification of antigen surrogate-antibody complexes as diagnostic tools and antigen surrogate discovery via serum screening. Although antigen surrogates are a fairly new concept, I argue that they will open new avenues for both basic and clinical research and that major advances can be expected over the next few years.

Koning, A. J. and M. C. Duijvestijn (2007). "Nuclear theory for high-energy nuclear reactions of biomedical relevance." Radiat Prot Dosimetry **126**(1-4): 28-34.

A full description of all possible nuclear reactions that take place in a macroscopic device can only be accomplished with a nuclear model code in combination with key experimental data. To address

this issue, the authors demonstrate some of the capabilities of TALYS, a nuclear reaction program which simulates nuclear reactions that involve neutrons, gamma rays, protons, deuterons, tritons, helions and alpha particles, in the 1 keV to 200 MeV energy range. A suite of nuclear reaction models has been implemented into a single code system, enabling to evaluate basically all nuclear reactions beyond the resonance range. The main nuclear models used, such as newly developed optical models, various compound nucleus, fission, gamma-ray strength, level density and pre-equilibrium models, all driven by a comprehensive database of nuclear structure parameters have been briefly mentioned. The predictive power of the code is demonstrated by comparing calculated results with a diverse set of experimental observables. The aim is to show that TALYS represents a robust computational approach that covers the whole path from fundamental nuclear reaction models to the creation of complete data libraries for nuclear applications.

Korpijarvi, V. M., et al. (2016). "High-power temperature-stable GaInNAs distributed Bragg reflector laser emitting at 1180 nm." Opt Lett **41**(4): 657-660.

We report a single-mode 1180 nm distributed Bragg reflector (DBR) laser diode with a high output power of 340 mW. For the fabrication, we employed novel nanoimprint lithography that ensures cost-effective, large-area, conformal patterning and does not require regrowth. The output characteristics exhibited outstanding temperature insensitivity with a power drop of only 30% for an increase of the mount temperature from 20 degrees C to 80 degrees C. The high temperature stability was achieved by using GaInNAs/GaAs quantum wells (QWs), which exhibit improved carrier confinement compared to standard InGaAs/GaAs QWs. The corresponding characteristic temperatures were T₀=110 K and T₁=160 K. Moreover, we used a large detuning between the peak wavelength of the material gain at room temperature and the lasing wavelength determined by the DBR. In addition to good temperature characteristics, GaInNAs/GaAs QWs exhibit relatively low lattice strain with direct impact on improving the lifetime of laser diodes at this challenging wavelength range. The single-mode laser emission could be tuned by changing the mount temperature (0.1 nm/ degrees C) or the drive current (0.5 pm/mA). The laser showed no degradation in a room-temperature lifetime test at 900 mA drive current. These compact and efficient 1180 nm laser diodes are instrumental for the development of compact frequency-doubled yellow-orange lasers, which have important applications in medicine and spectroscopy.

Krishnakumar, V., et al. (2014). "Spectroscopic properties, NLO, HOMO-LUMO and NBO of maltol." Spectrochim Acta A Mol Biomol Spectrosc **121**: 245-253.

Maltol (3-hydroxy-2-methyl-4pyrone) is widely known as metal ions chelator with many practical applications in catalysis, medicine and food chemistry. The FTIR and FT-Raman spectra of maltol have been recorded in the region 4000-400 and 4000-50 cm(-1), respectively. The conformational analysis, optimized geometry, frequency and intensity of the vibrational bands of maltol were obtained by the density functional theory (DFT) with complete relaxation in the potential energy surface using 6-31G* basis set. The observed and the calculated frequencies are found to be in good agreement. The (1)H and (13)C NMR spectra have been recorded and (1)H and (13)C nuclear magnetic resonance chemical shifts of the molecule were also calculated using the gauge independent atomic orbital (GIAO) method and their respective linear correlations were obtained. The electronic properties HOMO and LUMO energies were measured. Thermodynamic properties (heat capacity, entropy and enthalpy) of the title compound were calculated. The Mulliken charges, the values of electric dipole moment (mu) of the molecule were computed using DFT calculations. The first order hyperpolarizability (betao) and related properties (beta, alphao and Deltaalpha) of both are calculated using B3LYP/6-31G* method on the finite-field approach. The calculated first hyperpolarizability shows that the molecules are an attractive molecule for future applications in non-linear optics. The intramolecular contacts have been interpreted using Natural Bond Orbital (NBO).

Krishnan, M., et al. (2010). "Geometry-induced electrostatic trapping of nanometric objects in a fluid." Nature **467**(7316): 692-695.

The ability to trap an object-whether a single atom or a macroscopic entity-affects fields as diverse as quantum optics, soft condensed-matter physics, biophysics and clinical medicine. Many sophisticated methodologies have been developed to counter the randomizing effect of Brownian motion in solution, but stable trapping of nanometre-sized objects remains challenging. Optical tweezers are widely used traps, but require sufficiently polarizable objects and thus are unable to manipulate small macromolecules. Confinement of single molecules has been achieved using electrokinetic feedback guided by tracking of a fluorescent label, but photophysical constraints limit the trap stiffness and lifetime. Here we show that a fluidic slit with appropriately tailored topography has a spatially modulated electrostatic potential that can trap and levitate charged objects in solution for up to

several hours. We illustrate this principle with gold particles, polymer beads and lipid vesicles with diameters of tens of nanometres, which are all trapped without external intervention and independently of their mass and dielectric function. The stiffness and stability of our electrostatic trap is easily tuned by adjusting the system geometry and the ionic strength of the solution, and it lends itself to integration with other manipulation mechanisms. We anticipate that these features will allow its use for contact-free confinement of single proteins and macromolecules, and the sorting and fractionation of nanometre-sized objects or their assembly into high-density arrays.

Kucera, O., et al. (2015). "Spectral perspective on the electromagnetic activity of cells." Curr Top Med Chem **15**(6): 513-522.

In this mini-review, we summarize the current hypotheses, theories and experimental evidence concerning the electromagnetic activity of living cells. We systematically classify the bio-electromagnetic phenomena in terms of frequency and we assess their general acceptance in scientific community. We show that the electromagnetic activity of cells is well established in the low frequency range below 1 kHz and on optical wavelengths, while there is only limited evidence for bio-electromagnetic processes in radio-frequency and millimeter-wave ranges. This lack of generally accepted theory or trustful experimental results is the cause for controversy which accompanies this topic. We conclude our review with the discussion of the relevance of the electromagnetic activity of cells to human medicine.

Kulik, T. V., et al. (2016). "Thermal transformation of bioactive caffeic acid on fumed silica seen by UV-Vis spectroscopy, thermogravimetric analysis, temperature programmed desorption mass spectrometry and quantum chemical methods." J Colloid Interface Sci **470**: 132-141.

Thermochemical studies of hydroxycinnamic acid derivatives and their surface complexes are important for the pharmaceutical industry, medicine and for the development of technologies of heterogeneous biomass pyrolysis. In this study, structural and thermal transformations of caffeic acid complexes on silica surfaces were studied by UV-Vis spectroscopy, thermogravimetric analysis, temperature programmed desorption mass spectrometry (TPD MS) and quantum chemical methods. Two types of caffeic acid surface complexes are found to form through phenolic or carboxyl groups. The kinetic parameters of the chemical reactions of caffeic acid on silica surface are calculated. The mechanisms of thermal transformations of the caffeic chemisorbed surface complexes are proposed. Thermal decomposition of caffeic acid complex chemisorbed through grafted ester group proceeds via three parallel reactions, producing ketene, vinyl and acetylene derivatives of 1,2-dihydroxybenzene. Immobilization of phenolic acids on the silica surface improves greatly their thermal stability.

Kumar, G., et al. (1999). "The Internal Medicine Center--an integrated solution for information on internal medicine on the World Wide Web." Int J Med Inform **55**(1): 77-81.

The World Wide Web (WWW) has grown from being a resource center for a select group of scientists to a large database of information that is available to both professionals and public. The amount of medical information on the Web has been increasing exponentially and thus, it has become increasingly difficult for anyone to be able to search for a specific quantum of information among this mass. Even in mid 1996, it was noted that the amount of information on internal medicine was growing rapidly. Hence, on 21 March 1997, the Internal Medicine Center (IMC) was created and launched. The IMC is an unique concept and it represents the first time that medical data on the web has been organized into a form that intimately parallels clinical medicine. The rationale behind the creation of the IMC can be summarized in three words: information, speed and convenience. The interface used by this center reflects these goals because overuse of large image files are avoided, hence decreasing the access time and yet keeping the information in an easily comprehensible manner. In conclusion, the IMC serves as a useful tool for the layman as well as the expert because the comprehensive information that it offers can be accessed rapidly and conveniently.

Kumar, R. (2017). "Clinical Practice in Community Medicine: Challenges and Opportunities." Indian J Community Med **42**(3): 131-133.

Clinical practice with community health perspective makes community medicine a unique specialty. In their health centers, community physicians not only implement disease prevention programs, assess community health needs, manage healthcare teams and advocate for health promoting policies but also diagnose and treat diseases. However, participation of community medicine faculty in the delivery of clinical care varies from place to place due to administrative constraints. Health centers attached with medical college are not dependent on community medicine faculty for clinical service as these centers have their own medical and paramedical staff; whereas, other clinical departments in medical colleges depend on their faculty for delivery of clinical care in the hospital. Consequently, a perception is gaining ground that community medicine is a para-clinical specialty.

Strategies for a fixed tenured rotation of faculty in the health centers should be evolved. All faculty members of community medicine must also provide clinical care in the health centers and the quantum of clinical services provided by each one of them should be reported widely to all stakeholders. Community medicine residency programs must ensure that trainee community physicians acquire competency to deliver comprehensive primary health care (promotive, preventive, curative, and rehabilitative) in a health center.

Kumar, S., et al. (2018). "Induced Pluripotent Stem Cells in Disease Modeling and Gene Identification." Methods Mol Biol **1706**: 17-38.

Experimental modeling of human inherited disorders provides insight into the cellular and molecular mechanisms involved, and the underlying genetic component influencing, the disease phenotype. The breakthrough development of induced pluripotent stem cell (iPSC) technology represents a quantum leap in experimental modeling of human diseases, providing investigators with a self-renewing and, thus, unlimited source of pluripotent cells for targeted differentiation. In principle, the entire range of cell types found in the human body can be interrogated using an iPSC approach. Therefore, iPSC technology, and the increasingly refined abilities to differentiate iPSCs into disease-relevant target cells, has far-reaching implications for understanding disease pathophysiology, identifying disease-causing genes, and developing more precise therapeutics, including advances in regenerative medicine. In this chapter, we discuss the technological perspectives and recent developments in the application of patient-derived iPSC lines for human disease modeling and disease gene identification.

Kumart, S. A. and M. I. Khan (2010). "Heterofunctional nanomaterials: fabrication, properties and applications in nanobiotechnology." J Nanosci Nanotechnol **10**(7): 4124-4134.

Nanotechnology and nanoengineering includes a novel class of materials that are gaining significant recognition to pursuit technological/biological advances in diverse fields including, biology, medicine, electronics, engineering etc. due to their unique size- and shape-dependent intrinsic physicochemical, optoelectronic and biological properties. Characteristics such as high surface to volume ratios and quantum confinement results in materials that are qualitatively different from their bulk counterparts. These properties not only make them suitable for numerous applications in existing and emerging technologies, but also have outstanding role in many fields that provide inspiration for their fabrication. In Today's trend nanotechnology is spreading vigorously where researchers all over the world are focusing towards their synthesis and applications. Therefore, this review is helpful for the researchers in the field of nanobiotechnology/nanomedicine, providing a brief overview of nanotechnology, covering nanomaterial synthesis methods (with emphasis on environmentally benign greener approaches), their properties, and applications; such as drug delivery, bio-labeling, nanotoxicity etc. The influence of synthesis methods and surface coatings/stabilizing agents and their subsequent applications is discussed, and a broad outline on the biomedical applications into which they have been implemented is also presented.

Kundrotas, G., et al. (2019). "Uptake and distribution of carboxylated quantum dots in human mesenchymal stem cells: cell growing density matters." J Nanobiotechnology **17**(1): 39.

BACKGROUND: Human mesenchymal stem cells (MSCs) have drawn much attention in the field of regenerative medicine for their immunomodulatory and anti-inflammatory effects. MSCs possess specific tumor-oriented migration and incorporation highlighting the potential for MSCs to be used as an ideal carrier for anticancer agents. Bone marrow is the main source of MSCs for clinical applications. MSCs tracking in vivo is a critical component of the safety and efficacy evaluation of therapeutic cell products; therefore, cells must be labeled with contrast agents to enable visualization of the MSCs migration in vivo. Due to their unique properties, quantum dots (QDs) are emerging as optimal tools in long-term MSC optical imaging applications. The aim of this study was to investigate the uptake dynamics, cytotoxity, subcellular and extracellular distribution of non-targeted carboxylated quantum dots in human bone marrow MSCs at different cell growing densities. RESULTS: QDs had no negative impact on MSC viability throughout the experiment and accumulated in all observed cells efficiently; however, in some MSCs QDs induced formation of lipid droplets. At low cell growing densities QDs distribute within MSCs cytoplasm already after 1 h of incubation reaching saturation after 6 h. After 24 h QDs localize mainly in the perinuclear region of the cells in endosomes. Interestingly, in more confluent culture QDs localize mostly outside MSCs. QDs abundantly mark MSC long filopodia-like structures attaching neighboring cells. At high cell density cultivation, we for the first time demonstrated that carboxylated QDs localize in human bone marrow MSC extracellular matrix. Moreover, we observed that average photoluminescence lifetime of QDs distributed in extracellular matrix are longer than lifetimes of QDs entrapped in endocytic vesicles; thus,

for the first time showing the possibility to identify and distinguish localization of QDs in various extracellular and intracellular structures using fluorescence-lifetime imaging microscopy without additional staining assays. CONCLUSION: Carboxylated QDs can be used as nonspecific and effective dye for staining of human bone marrow MSCs and their specific extracellular structures. These results are promising in fundamental stem cell biology as well as in cellular therapy, anticancer drug delivery and tissue engineering.

Kundu, A., et al. (2018). "Facile approach to synthesize highly fluorescent multicolor emissive carbon dots via surface functionalization for cellular imaging." J Colloid Interface Sci **513**: 505-514.

Luminescent nanomaterials are encouraging scaffolds for diverse applications such as chemical sensors and biosensors, imaging, drug delivery, diagnostics, catalysis, energy, photonics, medicine, and so on. Carbon dots (CDs) are a new class of luminescent carbonaceous nanomaterial that have appeared recently and reaped tremendous scientific interest. Herein, we have exploited a simple approach to prepare tuneable and highly fluorescent CDs via surface functionalization. The successful synthesis of CDs is manifested from several investigations like high-resolution transmission electron microscopy (HRTEM), X-ray diffraction (XRD), Fourier transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS). The CDs exhibit excellent water solubility and with increasing nitrogen content fluorescence quantum yield increases whereas cell toxicity decreases. The CD synthesized at high temperature (180 degrees C) shows very high quantum yield (more than 56%). The tuneable optical properties of CDs are systematically studied using UV-vis and fluorescence spectroscopy. The cell viability evaluation and in vitro imaging study reveals that the synthesized CDs can be employed as a potential fluorescent probe for bio-imaging without further modification.

Kundu, S., et al. (2017). "Exploiting the biomimetic and luminescence properties of multivalent dendrimer-semiconductor nanohybrid materials in the ultra-low level determination of folic acid." Analyst **142**(13): 2491-2499.

In view of the enhanced generation of folate receptors in cancerous cells and diseases linked to the deficiency of folic acid, such as anemia, mental devolution, congenital malformation, etc., the development of a simple method for the ultra-sensitive determination of folic acid remains a long-standing issue for practical applications in medicine and biotechnology. Thus, the proposed luminescence based strategy involving multifunctional poly(amidoamine) (PAMAM) dendrimer encapsulated quantum dots (QDs) as a probe provides a simple, fast and efficient method for the selective determination of folic acid at the nano-molar level. Absorption and Fourier transform infra-red (FTIR) spectroscopy provide evidence of the binding of folic acid with dendrimer amine groups. The emission quenching of dendrimer encapsulated CdS QDs follows a linear Stern-Volmer plot with an exceedingly high value of the Stern-Volmer constant (KSV = 8.4 x 10(6) M(-1)) facilitating a higher detection efficiency. Similar quenching analysis with dendrimer-ZnS QDs showed a slightly lower Stern-Volmer constant (KSV = 2.29 x 10(6) M(-1)). The lower probing efficiency of the protein or amino acid capping of QDs has been explained through zeta potential measurements. The solvent polarity dependence suggests a charge transfer process responsible for the emission quenching of CdS QDs, which is static in nature as revealed by lifetime measurements. The determination of folic acid at this low level is not affected by possible interfering molecules, such as vitamin C, vitamin B12 and uric acid. Calorimetric measurements showed that the exothermic binding of folic acid with a dendrimer follows enthalpy-entropy compensation. The detailed mechanistic aspect of interactions of folic acid with the QD probe helps in a better understanding of the detection process, which in turn can assist in developing a dendrimer based material for image analysis and drug delivery in folate receptor rich cells.

Kuppers, B. (1992). "[Complementarity and Gestalt circle--Viktor von Weizsacker and the importance of a general theory of illness]." Psychother Psychosom Med Psychol **42**(5): 167-174.

Two developments have led to the elaboration of a complementarity theory in modern natural science--the Copenhagen interpretation of quantum mechanics and Viktor von Weizsackers introduction of the subject into biology. The revolutionary implications of these developments are discernible in modern literature. The author seeks to show that a paradigm shift in positivistic clinical medicine is necessitated by the history and theory of science.

Kuznetsova, I. M., et al. (2012). "Reevaluation of ANS binding to human and bovine serum albumins: key role of equilibrium microdialysis in ligand - receptor binding characterization." PLoS One **7**(7): e40845.

In this work we return to the problem of the determination of ligand-receptor binding stoichiometry and binding constants. In many cases the ligand is a fluorescent dye which has low fluorescence quantum yield in free state but forms highly fluorescent complex with target receptor. That is why many researchers use dye fluorescence for determination of its binding parameters with receptor, but they leave out of account

that fluorescence intensity is proportional to the part of the light absorbed by the solution rather than to the concentration of bound dye. We showed how ligand-receptor binding parameters can be determined by spectrophotometry of the solutions prepared by equilibrium microdialysis. We determined the binding parameters of ANS - human serum albumin (HSA) and ANS - bovine serum albumin (BSA) interaction, absorption spectra, concentration and molar extinction coefficient, as well as fluorescence quantum yield of the bound dye. It was found that HSA and BSA have two binding modes with significantly different affinity to ANS. Correct determination of the binding parameters of ligand-receptor interaction is important for fundamental investigations and practical aspects of molecule medicine and pharmaceutics. The data obtained for albumins are important in connection with their role as drugs transporters.

Kuznetsova, V., et al. (2020). "Spectral-Time Multiplexing in FRET Complexes of AgInS2/ZnS Quantum Dot and Organic Dyes." Nanomaterials (Basel) **10**(8).

Nowadays, multiplex analysis is very popular, since it allows to detect a large number of biomarkers simultaneously. Traditional multiplex analysis is usually based on changes of photoluminescence (PL) intensity and/or PL band spectral positions in the presence of analytes. Using PL lifetime as an additional parameter might increase the efficiency of multiplex methods. Quantum dots (QDs) can be used as luminescent markers for multiplex analysis. Ternary in-based QDs are a great alternative to the traditional Cd-based one. Ternary QDs possess all advantages of traditional QDs, including tunable photoluminescence in visible range. At the same time ternary QDs do not have Cd-toxicity, and moreover they possess long spectral dependent lifetimes. This allows the use of ternary QDs as a donor for time-resolved multiplex sensing based on Forster resonance energy transfer (FRET). In the present work, we implemented FRET from AgInS2/ZnS ternary QDs to cyanine dyes absorbing in different spectral regions of QD luminescence with different lifetimes. As the result, FRET-induced luminescence of dyes differed not only in wavelengths but also in lifetimes of luminescence, which can be used for time-resolved multiplex analysis in biology and medicine.

Leung, K. (2004). VivoTag-S 680-anti-human mammaglobin-A monoclonal antibody. Molecular Imaging and Contrast Agent Database (MICAD). Bethesda (MD).

Optical fluorescence imaging is increasingly used to monitor biological functions of specific targets (1-3). However, the intrinsic fluorescence of biomolecules poses a problem when fluorophores that absorb visible light (350-700 nm) are used. Near-infrared (NIR) fluorescence (700-1,000 nm) detection avoids the background fluorescence interference of natural biomolecules, providing a high contrast between target and background tissues. NIR fluorophores have a wider dynamic range and minimal background as a result of reduced scattering compared with visible fluorescence detection. They also have high sensitivity, resulting from low infrared background, and high extinction coefficients, which provide high quantum yields. The NIR region is also compatible with solid-state optical components, such as diode lasers and silicon detectors. NIR fluorescence imaging is becoming a noninvasive compliment to radionuclide imaging in small animals. The primary function of the lymphatic system is to drain ~10% of the interstitial fluid from small capillaries to lymphatic vessels through lymph nodes (LNs) and finally to the venous system (4-8). LNs form a natural filter for the lymphatic drainage and prevent the possible migration of cancer cells from the lymphatic system into the rest of the body or into the venous system. As the first LN that receives lymph drainage from a tumor bed, the sentinel LN is very likely to contain cancer cells if the primary tumor has spread via the lymphatic system. However, with advances of new imaging agents and techniques, imaging and mapping of both the lymphatic vessels and the LNs are now possible with x-ray-computed tomography, ultrasound, nuclear medicine, and magnetic resonance imaging (9-11). If the sentinel LN contains tumor cells, then the axillary LNs (ALNs) will be evaluated further for the presence of tumor cells. Therefore, there is a need for a specific biomarker for identification of ALNs containing tumor cells. Mammaglobin-A belongs to a family of epithelial secretory proteins (secretoglobins). Mammaglobin-A gene (SCGB2A2) encodes a 10.5-kDa glycoprotein that is exclusively expressed in normal breast tissue. In an analysis of 35 breast tumor biopsies, mammaglobin-A mRNA levels increased at least ten-fold relative to normal breast tissue in 23% of cases (12). In another study, mammaglobin-A protein levels increased drastically in 81 of 100 breast tumors (13). Mammaglobin-A can be used as a biomarker for the detection of breast tumor micrometastasis in sentinel LNs (14). Tafreshi et al. (15) performed mammaglobin-A protein expression studies in 250 breast cancer samples showing positive staining in ~90% of invasive ductal carcinoma, 80% of intraductal carcinoma, and 45% of LN with macrometastasis. Tafreshi et al. (15) conjugated the NIR fluoresecent dye VivoTag-S 680 to a murine monoclonal antibody against human mammaglobin-A (MamAb) as an imaging probe (MamAb-680) for the noninvasive detection of breast tumor metastasis in LNs in mice.

Levy, M., et al. (2019). "Quantum dot therapeutics: a new class of radical therapies." J Biol Eng **13**: 48.

Traditional therapeutics and vaccines represent the bedrock of modern medicine, where isolated biochemical molecules or designed proteins have led to success in treating and preventing diseases. However, several adaptive pathogens, such as multidrug-resistant (MDR) superbugs, and rapidly evolving diseases, such as cancer, can evade such molecules very effectively. This poses an important problem since the rapid emergence of multidrug-resistance among microbes is one of the most pressing public health crises of our time-one that could claim more than 10 million lives and 100 trillion dollars annually by 2050. Several non-traditional antibiotics are now being developed that can survive in the face of adaptive drug resistance. One such versatile strategy is redox perturbation using quantum dot (QD) therapeutics. While redox molecules are nominally used by cells for intracellular signaling and other functions, specific generation of such species exogenously, using an electromagnetic stimulus (light, sound, magnetic field), can specifically kill the cells most vulnerable to such species. For example, recently QD therapeutics have shown tremendous promise by specifically generating superoxide intracellularly (using light as a trigger) to selectively eliminate a wide range of MDR pathogens. While the efficacy of such QD therapeutics was shown using in vitro studies, several apparent contradictions exist regarding QD safety and potential for clinical applications. In this review, we outline the design rules for creating specific QD therapies for redox perturbation; summarize the parameters for choosing appropriate materials, size, and capping ligands to ensure their facile clearance; and highlight a potential path forward towards developing this new class of radical QD therapeutics.

Lewis, M. J. (2003). "Biomagnetism: a new tool in sport and exercise science." J Sports Sci **21**(10): 793-802.

Biomagnetometry is a non-invasive technique for detecting magnetic fields associated with the electrophysiology and magnetic susceptibility of body tissues. The aims of this paper are to provide a review of the discipline of biomagnetism and its measurement using a superconducting quantum interference device (SQUID), and to discuss the potential utility of this technique in sport and exercise science. A tutorial section is presented to provide an introduction to the theory and practical application of SQUID biomagnetometry. A review of the biomagnetism literature demonstrates the variety of previous biomagnetic investigations and suggests several potential applications of biomagnetometry in sport and exercise science. A discussion of these includes an assessment of the advantages of measuring biomagnetic fields as opposed to electrical potentials, with particular reference to the improved precision and accuracy of physiological source modelling using biomagnetic data. There is evidence to suggest that SQUID biomagnetometry would provide useful (and perhaps unique) information on functional, anatomical and physiological assessments in sport and exercise science. Further investigations of biomagnetometry in this discipline should focus on three main areas: cardiology, encephalography and neurology, and body composition assessment.

Lyu, Y., et al. (2016). "Intraparticle Molecular Orbital Engineering of Semiconducting Polymer Nanoparticles as Amplified Theranostics for in Vivo Photoacoustic Imaging and Photothermal Therapy." ACS Nano **10**(4): 4472-4481.

Optical theranostic nanoagents that seamlessly and synergistically integrate light-generated signals with photothermal or photodynamic therapy can provide opportunities for cost-effective precision medicine, while the potential for clinical translation requires them to have good biocompatibility and high imaging/therapy performance. We herein report an intraparticle molecular orbital engineering approach to simultaneously enhance photoacoustic brightness and photothermal therapy efficacy of semiconducting polymer nanoparticles (SPNs) for in vivo imaging and treatment of cancer. The theranostic SPNs have a binary optical component nanostructure, wherein a near-infrared absorbing semiconducting polymer and an ultrasmall carbon dot (fullerene) interact with each other to induce photoinduced electron transfer upon light irradiation. Such an intraparticle optoelectronic interaction augments heat generation and consequently enhances the photoacoustic signal and maximum photothermal temperature of SPNs by 2.6- and 1.3-fold, respectively. With the use of the amplified SPN as the theranostic nanoagent, it permits enhanced photoacoustic imaging and photothermal ablation of tumor in living mice. Our study thus not only introduces a category of purely organic optical theranostics but also highlights a molecular guideline to amplify the effectiveness of light-intensive imaging and therapeutic nanosystems.

Ma, B., et al. (2016). "Logical design of anti-prion agents using NAGARA." Biochem Biophys Res Commun **469**(4): 930-935.

To accelerate the logical drug design procedure, we created the program "NAGARA," a plugin for PyMOL, and applied it to the discovery of small compounds called medical chaperones (MCs) that stabilize the cellular form of a prion protein

(PrP(C)). In NAGARA, we constructed a single platform to unify the docking simulation (DS), free energy calculation by molecular dynamics (MD) simulation, and interfragment interaction energy (IFIE) calculation by quantum chemistry (QC) calculation. NAGARA also enables large-scale parallel computing via a convenient graphical user interface. Here, we demonstrated its performance and its broad applicability from drug discovery to lead optimization with full compatibility with various experimental methods including Western blotting (WB) analysis, surface plasmon resonance (SPR), and nuclear magnetic resonance (NMR) measurements. Combining DS and WB, we discovered anti-prion activities for two compounds and tegobuvir (TGV), a non-nucleoside non-structural protein NS5B polymerase inhibitor showing activity against hepatitis C virus genotype 1. Binding profiles predicted by MD and QC are consistent with those obtained by SPR and NMR. Free energy analyses showed that these compounds stabilize the PrP(C) conformation by decreasing the conformational fluctuation of the PrP(C). Because TGV has been already approved as a medicine, its extension to prion diseases is straightforward. Finally, we evaluated the affinities of the fragmented regions of TGV using QC and found a clue for its further optimization. By repeating WB, MD, and QC recursively, we were able to obtain the optimum lead structure.

Ma, X. L., et al. (2014). "[Optimization of experimental parameters for quantitative NMR (qNMR) and its application in quantitative analysis of traditional Chinese medicines]." Yao Xue Xue Bao **49**(9): 1248-1257.

Quantitative NMR (qNMR) is a technology based on the principle of NMR. This technology does not need the references of the determined components, which supplies a solution for the problem of reference scarcity in the quantitative analysis of traditional Chinese medicines. Moreover, this technology has the advantages of easy operation, non-destructiveness for the determined sample, high accuracy and repeatability, in comparison with HPLC, LC-MS and GC-MS. NMR technology has achieved quantum leap in sensitivity and accuracy with the development of NMR hardware. In addition, the choice of appropriate experimental parameters of the pre-treatment and measurement procedure as well as the post-acquisition processing is also important for obtaining high-quality and reproducible NMR spectra. This review summarizes the principle of qHNMR, the various experimental parameters affecting the accuracy and the precision of qHNMR, such as signal to noise ratio, relaxation delay, pulse width, acquisition time, window function, phase correction and baseline correction, and their corresponding optimized methods. Moreover, the application of qHNMR in the fields of quantitation of single or multi-components of traditional Chinese medicines, the purity detection of references, and the quality analysis of foods has been discussed. In addition, the existing questions and the future application prospects of qNMR in natural product areas are also presented.

Ma, Z., et al. (2020). "Cross-Link-Functionalized Nanoparticles for Rapid Excretion in Nanotheranostic Applications." Angew Chem Int Ed Engl **59**(46): 20552-20560.

Most NIR-IIb fluorophores are nanoparticle-based probes with long retention (approximately 1 month or longer) in the body. Here, we applied a novel cross-linked coating to functionalize core/shell lead sulfide/cadmium sulfide quantum dots (PbS/CdS QDs) emitting at approximately 1600 nm. The coating was comprised of an amphiphilic polymer followed by three crosslinked amphiphilic polymeric layers (P(3) coating), imparting high biocompatibility and >90 % excretion of QDs within 2 weeks of intravenous administration. The P(3) -QDs were conjugated to an engineered anti-CD8 diabody (Cys-diabody) for in vivo molecular imaging of CD8+ cytotoxic T lymphocytes (CTLs) in response to anti-PD-L1 therapy. Two-plex molecular imaging in combination with down-conversion Er nanoparticles (ErNPs) was performed for real-time in vivo monitoring of PD-L1 positive tumor cells and CTLs with cellular resolution by non-invasive NIR-IIb light sheet microscopy. Imaging of angiogenesis in the tumor microenvironment and of lymph nodes deep in the body with a signal-to-background ratio of up to approximately 170 was also achieved using P(3) -QDs.

Mahapatra, A. K., et al. (2014). "Tiny technology proves big: a challenge at engineering, medicine and pharmaceutical sciences interface." Crit Rev Ther Drug Carrier Syst **31**(1): 1-47.

Nanoscale materials with a broad spectrum of applications are providing a new foundation for technological integration and innovation. In this article, we review various polymers being used, their polymeric properties, nanoparticle (NP) fabrication, and mechanisms and kinetics of drug release. Specific information is given on each polymer regarding transportation, fate, and delivery issues. Nanoparticles have been developed to deliver conventional drug molecules, peptides and proteins, vaccines, and genes or nucleotides. Nanoparticles have wide application in fields such as cancer therapeutics and targeted drug delivery, including transbarrier brain delivery, dermal and transdermal delivery, intraocular delivery, parenteral delivery, and imaging and diagnostics. In

this review, we focus on the potentials of nanotechnology in medicine, and we discuss different nanoparticulate drug delivery systems, including polymeric NPs, metal and metal oxide NPs, ceramics, quantum dots, carbon nanotubes, polymeric micelles, and dendrimers along with their applications in therapeutics, imaging, and diagnostics. In addition, we identify several interesting developments that will affect the future of nanotechnology and nanomedicine.

Mai, S. and L. Gonzalez (2020). "Molecular Photochemistry: Recent Developments in Theory." Angew Chem Int Ed Engl **59**(39): 16832-16846.

Photochemistry is a fascinating branch of chemistry that is concerned with molecules and light. However, the importance of simulating light-induced processes is reflected also in fields as diverse as biology, material science, and medicine. This Minireview highlights recent progress achieved in theoretical chemistry to calculate electronically excited states of molecules and simulate their photoinduced dynamics, with the aim of reaching experimental accuracy. We focus on emergent methods and give selected examples that illustrate the progress in recent years towards predicting complex electronic structures with strong correlation, calculations on large molecules, describing multichromophoric systems, and simulating non-adiabatic molecular dynamics over long time scales, for molecules in the gas phase or in complex biological environments.

Maida, V. and P. M. Cheon (2014). "Prognosis: the "missing link" within the CanMEDS competency framework." BMC Med Educ **14**: 93.

BACKGROUND: The concept of prognosis dates back to antiquity. Quantum advances in diagnostics and therapeutics have relegated this once highly valued core competency to an almost negligible role in modern medical practice. Medical curricula are devoid of teaching opportunities focused on prognosis. This void is driven by a corresponding relative dearth within physician competency frameworks. This study aims to assess the level of content related to prognosis within CanMEDS (Canadian Medical Education Directives for Specialists), a leading and prototypical physician competency framework. METHODS: A quantitative content analysis of CanMEDS competency framework was carried out to measure the extent of this deficiency. Foxit Reader 5.1 (Foxit Corporation), a keyword scanning software, was used to assess the CanMEDS 2005 framework documents of 29 physician specialties and 37 subspecialties across the seven physician roles (medical expert, communicator, collaborator, manager, health advocate, scholar, and professional). The keywords used in the search included prognosis, prognostic, prognosticate, and prognostication. RESULTS: Of the 29 specialties six (20.7%) contained at least one citation of the keyword "prognosis", and one (3.4%) contained one citation of the keyword "prognostic". Of the 37 subspecialties, sixteen (43.2%) contained at least one citation of the keyword "prognosis", and three (8.1%) contained at least one citation of the keyword "prognostic". The terms "prognosticate" and "prognostication" were completely absent from all CanMEDS 2005 documents. Overall, the combined citations for "prognosis" and "prognostic" were linked with the following competency roles: Medical Expert (80.3%), Scholar (11.5%), and Communicator (8.2%). CONCLUSIONS: Given the fundamental and foundational importance of prognosis within medical practice, it is recommended that physicians develop appropriate attitudes, skills and knowledge related to the formulation and communication of prognosis. The deficiencies within CanMEDS, demonstrated by this study, should be addressed in advance of the launch of its updated version in 2015.

Maisch, T., et al. (2014). "Fast and effective photodynamic inactivation of multiresistant bacteria by cationic riboflavin derivatives." PLoS One **9**(12): e111792.

Photodynamic inactivation of bacteria (PIB) proves to be an additional method to kill pathogenic bacteria. PIB requires photosensitizer molecules that effectively generate reactive oxygen species like singlet oxygen when exposed to visible light. To allow a broad application in medicine, photosensitizers should be safe when applied in humans. Substances like vitamin B2, which are most likely safe, are known to produce singlet oxygen upon irradiation. In the present study, we added positive charges to flavin derivatives to enable attachment of these molecules to the negatively charged surface of bacteria. Two of the synthesized flavin derivatives showed a high quantum yield of singlet oxygen of approximately 75%. Multidrug resistant bacteria like MRSA (Methicillin resistant Staphylococcus aureus), EHEC (enterohemorrhagic Escherichia coli), Pseudomonas aeruginosa, and Acinetobacter baumannii were incubated with these flavin derivatives in vitro and were subsequently irradiated with visible light for seconds only. Singlet oxygen production in bacteria was proved by detecting its luminescence at 1270 nm. After irradiation, the number of viable bacteria decreased up to 6 log10 steps depending on the concentration of the flavin derivatives and the light dosimetry. The bactericidal effect of PIB was independent of the bacterial type and the corresponding antibiotic resistance pattern. In contrast, the photosensitizer concentration and light parameters used for bacteria killing did not affect cell viability of human keratinocytes (therapeutic window).

Multiresistant bacteria can be safely and effectively killed by a combination of modified vitamin B2 molecules, oxygen and visible light, whereas normal skin cells survive. Further work will include these new photosensitizers for topical application to decolonize bacteria from skin and mucosa.

Makhouri, F. R. and J. B. Ghasemi (2018). "In Silico Studies in Drug Research Against Neurodegenerative Diseases." Curr Neuropharmacol **16**(6): 664-725.

BACKGROUND: Neurodegenerative diseases such as Alzheimer's disease (AD), amyotrophic lateral sclerosis, Parkinson's disease (PD), spinal cerebellar ataxias, and spinal and bulbar muscular atrophy are described by slow and selective degeneration of neurons and axons in the central nervous system (CNS) and constitute one of the major challenges of modern medicine. Computeraided or in silico drug design methods have matured into powerful tools for reducing the number of ligands that should be screened in experimental assays. METHODS: In the present review, the authors provide a basic background about neurodegenerative diseases and in silico techniques in the drug research. Furthermore, they review the various in silico studies reported against various targets in neurodegenerative diseases, including homology modeling, molecular docking, virtual high-throughput screening, quantitative structure activity relationship (QSAR), hologram quantitative structure activity relationship (HQSAR), 3D pharmacophore mapping, proteochemometrics modeling (PCM), fingerprints, fragment-based drug discovery, Monte Carlo simulation, molecular dynamic (MD) simulation, quantum-mechanical methods for drug design, support vector machines, and machine learning approaches. RESULTS: Detailed analysis of the recently reported case studies revealed that the majority of them use a sequential combination of ligand and structure-based virtual screening techniques, with particular focus on pharmacophore models and the docking approach. CONCLUSION: Neurodegenerative diseases have a multifactorial pathoetiological origin, so scientists have become persuaded that a multi-target therapeutic strategy aimed at the simultaneous targeting of multiple proteins (and therefore etiologies) involved in the development of a disease is recommended in future.

Malish, R. G., et al. (2020). "Finding Opportunities for Health-Care System Advancement in the COVID-19 Crisis." Disaster Med Public Health Prep: 1-6.

The coronavirus disease 2019 (COVID-19) pandemic forced American medical systems to adapt to high patient loads of respiratory disease. Its disruption of normal routines also brought opportunities for broader reform. The purpose of this article is to describe how the Carl R. Darnall Army Medical Center (CRDAMC), a medium-sized Army hospital, capitalized on opportunities to advance its strategic aims during the pandemic. Specifically, the hospital sequentially adopted virtual video visits, surged on preventative screenings, and made-over its image to appeal to patients seeking urgent care. These campaigns supported COVID-19 efforts and larger strategic goals simultaneously, and they will endure for years to come. Predictably, CRDAMC encountered obstacles in the course of its transformation. These obstacles and their follow-on lessons are provided to assist future medical leaders seeking quantum change in the opportunities made available by health crises.

Malmir, S., et al. (2020). "Antibacterial properties of a bacterial cellulose CQD-TiO2 nanocomposite." Carbohydr Polym **234**: 115835.

Antibacterial dressing can prevent the occurrence of many infections of wounds. Bacterial cellulose (BC) has the ability to carry and transfer the medicine to achieve a wound healing bandage. In this study, Carbon Quantum Dots-Titanium dioxide (CQD-TiO2) nanoparticles (NP) were added to BC as antibacterial agents. FTIR Spectroscopy illuminated that NPs were well-bonded to BC. Interestingly, MIC test proved that BC/CQD-TiO2 nanostructure (NS) has anti-bacterial properties against Staphylococcus aureus. The findings indicated that, CQD-TiO2 NPs have stronger antibacterial properties with better tensile strength compared to CQD NPs, in a concentration-dependent manner. Toxicity of CQD-TiO2 NPs on human L929 fibroblast cells was also evaluated. Most importantly, the results of the scratch test indicated that the NS was effective in wound healing in L929 cells. The approach in this study may provide an alternative to make an antibacterial wound dressing to achieve an effective drug-based bandage.

Manabe, N., et al. (2006). "Quantum dot as a drug tracer in vivo." IEEE Trans Nanobioscience **5**(4): 263-267.

Quantum dots (QDs) have been applied to a wide range of biological studies by taking advantage of their fluorescence properties. There is almost no method to trace small molecules including medicine. Here, we used QDs for fluorescent tracers for medicine and analyzed their kinetics and dynamics. We conjugated QDs with captopril, anti-hypertensive medicine, by an exchange reaction while retaining the medicinal properties. We investigated the medicinal effect of QD-conjugated captopril (QD-cap) in vitro and in vivo. We also evaluated the concentration and the distribution of the QD-cap in the blood and the organs with their fluorescence. We demonstrate that the QD-cap inhibits the activity of ACE in vitro. The QD-cap reduced the blood pressure of hypertensive model

rats. The concentration of the QD-cap in the blood was measured by using the standard curve of the fluorescence intensity. The blood concentration of the QD-cap decrease exponentially and QD-cap has approximately the same half-life as that of captopril. In addition, the fluorescence of the QDs revealed that QD-cap accumulates in the liver, lungs, and spleen. We succeeded in analyzing the dynamics and kinetics of small molecules using fluorescence of QDs.

Mangoni, M., et al. (2012). "Stem cell tracking: toward clinical application in oncology?" Tumori **98**(5): 535-542.

Noninvasive cellular imaging allows the tracking of grafted cells as well as the monitoring of their migration, suggesting potential applications to track both cancer and therapeutic stem cells. Cell tracking can be performed by two approaches: direct labeling (cells are labeled with tags) and indirect labeling (cells are transfected with a reporter gene and visualized after administration of a reporter probe). Techniques for in vivo detection of grafted cells include optic imaging, nuclear medicine imaging, magnetic resonance imaging, microCT imaging and ultrasound imaging. The ideal imaging modality would bring together high sensitivity, high resolution and low toxicity. All of the available imaging methods are based on different principles, have different properties and different limitations, so several of them can be considered complementary. Transfer of these preclinical cellular imaging modalities to stem cells has already been reported, and transfer to clinical practice within the next years can be reasonably considered.

Maniam, S., et al. (2019). "Harnessing Brightness in Naphthalene Diimides." Chemistry **25**(29): 7044-7057.

The development of brightly emissive compounds is of great research and commercial interest, with established and emerging applications across chemistry, biology, physics, medicine and engineering. Among the many types of molecules available, naphthalene diimides have been widely used for both fundamental photophysical studies and in practical applications that utilise fluorescence as an information readout. The monomeric naphthalene diimide is weakly fluorescent, however through various methods of core-derivatisation, it can be developed to be highly fluorescent and further functionalised to add utility. In this review, we highlight recent advances made in naphthalene diimide chemistry that have led to development of molecules with improved optical properties, and the design strategies utilised to produce bright fluorescence emission as small molecules or in supramolecular architectures.

Manoukian, O. S., et al. (2017). "Electrospun Nanofiber Scaffolds and Their Hydrogel Composites for the Engineering and Regeneration of Soft Tissues." Methods Mol Biol **1570**: 261-278.

Electrospinning has emerged as a simple, elegant, and scalable technique that can be used to fabricate polymeric nanofibers. Pure polymers as well as blends and composites of both natural and synthetic ones have been successfully electrospun into nanofiber matrices for many biomedical applications. Tissue-engineered medical implants, such as polymeric nanofiber scaffolds, are potential alternatives to autografts and allografts, which are short in supply and carry risks of disease transmission. These scaffolds have been used to engineer various soft tissues, including connective tissues, such as skin, ligament, and tendon, as well as nonconnective ones, such as vascular, muscle, and neural tissue. Electrospun nanofiber matrices show morphological similarities to the natural extracellular matrix (ECM), characterized by ultrafine continuous fibers, high surface-to-volume ratios, high porosities, and variable pore-size distributions. The physiochemical properties of nanofiber matrices can be controlled by manipulating electrospinning parameters so that they meet the requirements of a specific application.Nanostructured implants show improved biological performance over bulk materials in aspects of cellular infiltration and in vivo integration, taking advantage of unique quantum, physical, and atomic properties. Furthermore, the topographies of such scaffolds has been shown to dictate cellular attachment, migration, proliferation, and differentiation, which are critical in engineering complex functional tissues with improved biocompatibility and functional performance. This chapter discusses the use of the electrospinning technique in the fabrication of polymer nanofiber scaffolds utilized for the regeneration of soft tissues. Selected scaffolds will be seeded with human mesenchymal stem cells (hMSCs), imaged using scanning electron and confocal microscopy, and then evaluated for their mechanical properties as well as their abilities to promote cell adhesion, proliferation , migration, and differentiation.

Mansur, A. A., et al. (2014). "Fluorescent nanohybrids based on quantum dot-chitosan-antibody as potential cancer biomarkers." ACS Appl Mater Interfaces **6**(14): 11403-11412.

Despite undeniable advances in medicine in recent decades, cancer is still one of the main challenges faced by scientists and professionals in the health sciences as it remains one of the world's most devastating diseases with millions of fatalities and new cases every year. Thus, in this work, we endeavored to synthesize and characterize novel multifunctional

immunoconjugates composed of quantum dots (QDs) as the fluorescent inorganic core and antibody-modified polysaccharide as the organic shell, focusing on their potential applications for in vitro diagnosis of non-Hodgkin lymphoma (NHL) cancer tumors. Chitosan was covalently conjugated with anti-CD20 polyclonal antibody (pAbCD20) via formation of amide bonds between amines and carboxyl groups. In the sequence, these biopolymer-antibody immunoconjugates were utilized as direct capping ligands for biofunctionalization of CdS QDs (CdS/chitosan-pAbCD20) using a single-step process in aqueous medium at room temperature. The nanostructures were characterized by UV-vis spectroscopy, photoluminescence spectroscopy (PL), FTIR, and transmission electron microscopy (TEM) with selected area electron diffraction. The TEM images associated with the UV-vis optical absorption results indicated formation of ultrasmall nanocrystals with average diameters in the range of 2.5-3.0 nm. Also, the PL results demonstrated that the immunoconjugates exhibited "green" fluorescent activity under ultraviolet excitation. Moreover, using in vitro laser light scattering immunoassay (LIA), the QDs/immunoconjugates have shown binding affinity against antigen CD20 (aCD20) expressed by lymphocyte-B cancer cells. In summary, innovative fluorescent nanoimmunoconjugate templates were developed with promising perspectives to be used in the future for detection and imaging of cancer tumors.

Mansur, H. S. (2010). "Quantum dots and nanocomposites." Wiley Interdiscip Rev Nanomed Nanobiotechnol **2**(2): 113-129.

Quantum dots (QDs), also known as semiconducting nanoparticles, are promising zero-dimensional advanced materials because of their nanoscale size and because they can be engineered to suit particular applications such as nonlinear optical devices (NLO), electro-optical devices, and computing applications. QDs can be joined to polymers in order to produce nanocomposites which can be considered a scientific revolution of the 21st century. One of the fastest moving and most exciting interfaces of nanotechnology is the use of QDs in medicine, cell and molecular biology. Recent advances in nanomaterials have produced a new class of markers and probes by conjugating semiconductor QDs with biomolecules that have affinities for binding with selected biological structures. The nanoscale of QDs ensures that they do not scatter light at visible or longer wavelengths, which is important in order to minimize optical losses in practical applications. Moreover, at this scale, quantum confinement and surface effects become very important and therefore manipulation of the dot diameter or modification of its surface allows the properties of the dot to be controlled. Quantum confinement affects the absorption and emission of photons from the dot. Thus, the absorption edge of a material can be tuned by control of the particle size. This paper reviews developments in the myriad of possibilities for the use of semiconductor QDs associated with molecules producing novel hybrid nanocomposite systems for nanomedicine and bioengineering applications.

Manzalini, A. and B. Galeazzi (2019). "Explaining Homeopathy with Quantum Electrodynamics." Homeopathy **108**(3): 169-176.

BACKGROUND: Every living organism is an open system operating far from thermodynamic equilibrium and exchanging energy, matter and information with an external environment. These exchanges are performed through non-linear interactions of billions of different biological components, at different levels, from the quantum to the macro-dimensional. The concept of quantum coherence is an inherent property of living cells, used for long-range interactions such as synchronization of cell division processes. There is support from recent advances in quantum biology, which demonstrate that coherence, as a state of order of matter coupled with electromagnetic (EM) fields, is one of the key quantum phenomena supporting life dynamics. Coherent phenomena are well explained by quantum field theory (QFT), a well-established theoretical framework in quantum physics. Water is essential for life, being the medium used by living organisms to carry out various biochemical reactions and playing a fundamental role in coherent phenomena. METHODS: Quantum electrodynamics (QED), which is the relativistic QFT of electrodynamics, deals with the interactions between EM fields and matter. QED provides theoretical models and experimental frameworks for the emergence and dynamics of coherent structures, even in living organisms. This article provides a model of multi-level coherence for living organisms in which fractal phase oscillations of water are able to link and regulate a biochemical reaction. A mathematical approach, based on the eigenfunctions of Laplace operator in hyper-structures, is explored as a valuable framework to simulate and explain the oneness dynamics of multi-level coherence in life. The preparation process of a homeopathic medicine is analyzed according to QED principles, thus providing a scientific explanation for the theoretical model of "information transfer" from the substance to the water solution. A subsequent step explores the action of a homeopathic medicine in a living organism according to QED principles and the phase-space attractor's dynamics. RESULTS: According to the developed model, all levels of a living organism-organelles, cells, tissues, organs, organ systems, whole organism-are characterized by their

own specific wave functions, whose phases are perfectly orchestrated in a multi-level coherence oneness. When this multi-level coherence is broken, a disease emerges. An example shows how a homeopathic medicine can bring back a patient from a disease state to a healthy one. In particular, by adopting QED, it is argued that in the preparation of homeopathic medicines, the progressive dilution/succussion processes create the conditions for the emergence of coherence domains (CDs) in the aqueous solution. Those domains code the original substance information (in terms of phase oscillations) and therefore they can transfer said information (by phase resonance) to the multi-level coherent structures of the living organism. CONCLUSIONS: We encourage that QED principles and explanations become embodied in the fundamental teachings of the homeopathic method, thus providing the homeopath with a firm grounding in the practice of rational medicine. Systematic efforts in this direction should include multiple disciplines, such as quantum physics, quantum biology, conventional and homeopathic medicine and psychology.

Marabello, D., et al. (2019). "Developing new SrI2 and beta-D-fructopyranose-based metal-organic frameworks with nonlinear optical properties." Acta Crystallogr B Struct Sci Cryst Eng Mater **75**(Pt 2): 210-218.

In the context of personalized medicine, there is a growing interest in materials bearing at the same time diagnostic and therapy functions. This article reports a cheap and easily reproducible procedure to obtain materials with a high potential for these applications. Three new strontium iodide-fructose-based metal-organic frameworks with formulae [Sr(C6H12O6)2]I2, [Sr2(C6H12O6)3(H2O)3]I4.0.5H2O and [Sr(C6H12O6)(H2O)3I]I differing in stoichiometry, symmetry and crystal packing, were obtained and characterized by X-ray diffraction. Bulk quantum simulations show that both the ions and the sugar are crucial in determining the predicted nonlinear response; also, the relative arrangement of various functional groups in the unit cell plays a role in the computed optical properties. Small fragments of the three compounds were selected for in vacuo calculations, proving that the reduced dimensions of the particles have a great influence on the nonlinear optical response. Despite the similar chemical composition of the three compounds, second harmonic generation measurements and in crystal and in vacuo theoretical calculations agree that one of the compounds is a much more efficient second harmonic emitter than the other two, and is thus a suitable candidate for bio-sensor applications.

Marchetti, A., et al. (2017). "Understanding Surface and Interfacial Chemistry in Functional Nanomaterials via Solid-State NMR." Adv Mater **29**(14).

Surface and interfacial chemistry is of fundamental importance in functional nanomaterials applied in catalysis, energy storage and conversion, medicine, and other nanotechnologies. It has been a perpetual challenge for the scientific community to get an accurate and comprehensive picture of the structures, dynamics, and interactions at interfaces. Here, some recent examples in the major disciplines of nanomaterials are selected (e.g., nanoporous materials, battery materials, nanocrystals and quantum dots, supramolecular assemblies, drug-delivery systems, ionomers, and graphite oxides) and it is shown how interfacial chemistry can be addressed through the perspective of solid-state NMR characterization techniques.

Maria-Hormigos, R., et al. (2016). "Labs-on-a-chip meet self-propelled micromotors." Lab Chip **16**(13): 2397-2407.

This frontier review covers recent advances in the field of nanomaterial-based micromotors for the development of novel labs-on-a-chip (LOCs). In this review, we will discuss how carbon nanomaterials "on-board" of micromotors offer particular promise for diverse LOC applications. New trends in the field, directed towards the use of quantum dots and nanoparticles as functional materials for sophisticated micromotors, will be reviewed. Micromotor strategies using functionalized catalytic microengines to capture and transport (bio)molecules between the different reservoirs of LOC devices will also be covered. These recent advances are bringing closer our hopes for personalized medicine and food safety assurance, among others.

Marshall, N. W., et al. (2011). "Quality control measurements for digital x-ray detectors." Phys Med Biol **56**(4): 979-999.

This paper describes a digital radiography (DR) quality control protocol for DR detectors from the forthcoming report from the Institute of Physics and Engineering in Medicine (IPEM). The protocol was applied to a group of six identical caesium iodide (CsI) digital x-ray detectors to assess reproducibility of methods, while four further detectors were assessed to examine the wider applicability. Twelve images with minimal spatial frequency processing are required, from which the detector response, lag, modulation transfer function (MTF), normalized noise power spectrum (NNPS) and threshold contrast-detail (c-d) detectability are calculated. The x-ray spectrum used was 70 kV and 1 mm added copper filtration, with a

target detector air kerma of 2.5 microGy for the NNPS and c-d results. In order to compare detector performance with previous imaging technology, c-d data from four screen/film systems were also acquired, at a target optical density of 1.5 and an average detector air kerma of 2.56 microGy. The DR detector images were typically acquired in 20 min, with a further 45 min required for image transfer and analysis. The average spatial frequency for the 50% point of the MTF for six identical detectors was 1.29 mm(-1) +/- 0.05 (3.9% coefficient of variation (cov)). The air kerma set for the six systems was 2.57 microGy +/- 0.13 (5.0% cov) and the NNPS at this air kerma was 1.42 x 10(-5) mm(2) (6.5% cov). The detective quantum efficiency (DQE) measured for the six identical detectors was 0.60 at 0.5 mm(-1), with a maximum cov of 10% at 2.9 mm(-1), while the average DQE was 0.56 at 0.5 mm(-1) for three CsI detectors from three different manufacturers. Comparable c-d performance was found for these detectors (5.9% cov) with an average threshold contrast of 0.46% for 11 mm circular discs. The average threshold contrast for the S/F systems was 0.70% at 11 mm, indicating superior imaging performance for the digital systems. The protocol was found to be quick, reproducible and gave an in-depth assessment of performance for a range of digital x-ray detectors.

Mason, R. P. (2016). "Imaging free radicals in organelles, cells, tissue, and in vivo with immuno-spin trapping." Redox Biol **8**: 422-429.

The accurate and sensitive detection of biological free radicals in a reliable manner is required to define the mechanistic roles of such species in biochemistry, medicine and toxicology. Most of the techniques currently available are either not appropriate to detect free radicals in cells and tissues due to sensitivity limitations (electron spin resonance, ESR) or subject to artifacts that make the validity of the results questionable (fluorescent probe-based analysis). The development of the immuno-spin trapping technique overcomes all these difficulties. This technique is based on the reaction of amino acid- and DNA base-derived radicals with the spin trap 5, 5-dimethyl-1-pyrroline N-oxide (DMPO) to form protein- and DNA-DMPO nitroxide radical adducts, respectively. These adducts have limited stability and decay to produce the very stable macromolecule-DMPO-nitrone product. This stable product can be detected by mass spectrometry, NMR or immunochemistry by the use of anti-DMPO nitrone antibodies. The formation of macromolecule-DMPO-nitrone adducts is based on the selective reaction of free radical addition to the spin trap and is thus not subject to artifacts frequently encountered with other methods for free radical detection. The selectivity of spin trapping for free radicals in biological systems has been proven by ESR. Immuno-spin trapping is proving to be a potent, sensitive (a million times higher sensitivity than ESR), and easy (not quantum mechanical) method to detect low levels of macromolecule-derived radicals produced in vitro and in vivo. Anti-DMPO antibodies have been used to determine the distribution of free radicals in cells and tissues and even in living animals. In summary, the invention of the immuno-spin trapping technique has had a major impact on the ability to accurately and sensitively detect biological free radicals and, subsequently, on our understanding of the role of free radicals in biochemistry, medicine and toxicology.

Matlashov, A. N., et al. (2011). "SQUIDs vs. Induction Coils for Ultra-Low Field Nuclear Magnetic Resonance: Experimental and Simulation Comparison." IEEE Trans Appl Supercond **21**(3): 465-468.

Nuclear magnetic resonance (NMR) is widely used in medicine, chemistry and industry. One application area is magnetic resonance imaging (MRI). Recently it has become possible to perform NMR and MRI in the ultra-low field (ULF) regime requiring measurement field strengths of the order of only 1 Gauss. This technique exploits the advantages offered by superconducting quantum interference devices or SQUIDs. Our group has built SQUID based MRI systems for brain imaging and for liquid explosives detection at airport security checkpoints. The requirement for liquid helium cooling limits potential applications of ULF MRI for liquid identification and security purposes. Our experimental comparative investigation shows that room temperature inductive magnetometers may provide enough sensitivity in the 3-10 kHz range and can be used for fast liquid explosives detection based on ULF NMR technique. We describe experimental and computer-simulation results comparing multichannel SQUID based and induction coils based instruments that are capable of performing ULF MRI for liquid identification.

Matousovic, K. and L. Podracka (2012). "[To salt or not to salt in kidney diseases? Not more than quantum satis!]." Vnitr Lek **58**(7-8): 531-535.

The salt intake in former Czechoslovakia is twice as high as recommended 5 g/24 hours, which corresponds to 85 mmol//24 hours of sodium in the urine. In the population, the systemic blood pressure level correlates with a urinary excretion of sodium/24 hours. On the other hand, limited salt intake decreases blood pressure in salt-sensitive hypertensive patients. Albuminuria also positively correlates with a salt intake in the population. In patients with renal disease, a diet with low salt content suppresses proteinuria, and,

in contrast, proteinuria is elevated with increased salt intake. The positive influence of the decreased salt intake on the progression of renal insufficiency was confirmed in many experimental studies. However, in humans, this finding was not unequivocally established in control randomized studies. The high salt intake worsens metabolic acidosis in patients with renal insufficiency. Salt is detrimental to the kidneys either by increased systemic and intraglomerular blood pressures or by pressure independent mechanisms of the tissue injury, which are mediated by a higher sodium concentration. The present knowledge concerning the relationship between sodium intake and extracellular fluid volume probably will be modified in light of new discoveries about the osmotically inactive sodium. The public enlightenment and medical application of these new findings related to harmful effects on an inappropriate salt intake in treatment of the kidney disease and in other fields of medicine is strongly desirable.

Matricardi, P. M., et al. (2016). "EAACI Molecular Allergology User's Guide." Pediatr Allergy Immunol **27 Suppl 23**: 1-250.

The availability of allergen molecules ('components') from several protein families has advanced our understanding of immunoglobulin E (IgE)-mediated responses and enabled 'component-resolved diagnosis' (CRD). The European Academy of Allergy and Clinical Immunology (EAACI) Molecular Allergology User's Guide (MAUG) provides comprehensive information on important allergens and describes the diagnostic options using CRD. Part A of the EAACI MAUG introduces allergen molecules, families, composition of extracts, databases, and diagnostic IgE, skin, and basophil tests. Singleplex and multiplex IgE assays with components improve both sensitivity for low-abundance allergens and analytical specificity; IgE to individual allergens can yield information on clinical risks and distinguish cross-reactivity from true primary sensitization. Part B discusses the clinical and molecular aspects of IgE-mediated allergies to foods (including nuts, seeds, legumes, fruits, vegetables, cereal grains, milk, egg, meat, fish, and shellfish), inhalants (pollen, mold spores, mites, and animal dander), and Hymenoptera venom. Diagnostic algorithms and short case histories provide useful information for the clinical workup of allergic individuals targeted for CRD. Part C covers protein families containing ubiquitous, highly cross-reactive panallergens from plant (lipid transfer proteins, polcalcins, PR-10, profilins) and animal sources (lipocalins, parvalbumins, serum albumins, tropomyosins) and explains their diagnostic and clinical utility. Part D lists 100 important allergen molecules. In conclusion, IgE-mediated reactions and allergic diseases, including allergic rhinoconjunctivitis, asthma, food reactions, and insect sting reactions, are discussed from a novel molecular perspective. The EAACI MAUG documents the rapid progression of molecular allergology from basic research to its integration into clinical practice, a quantum leap in the management of allergic patients.

Mattox, T. M., et al. (2015). "Chemical Control of Plasmons in Metal Chalcogenide and Metal Oxide Nanostructures." Adv Mater **27**(38): 5830-5837.

The field of plasmonics has grown to impact a diverse set of scientific disciplines ranging from quantum optics and photovoltaics to metamaterials and medicine. Plasmonics research has traditionally focused on noble metals; however, any material with a sufficiently high carrier density can support surface plasmon modes. Recently, researchers have made great gains in the synthetic (both intrinsic and extrinsic) control over the morphology and doping of nanoscale oxides, pnictides, sulfides, and selenides. These synthetic advances have, collectively, blossomed into a new, emerging class of plasmonic metal chalcogenides that complement traditional metallic materials. Chalcogenide and oxide nanostructures expand plasmonic properties into new spectral domains and also provide a rich suite of chemical controls available to manipulate plasmons, such as particle doping, shape, and composition. New opportunities in plasmonic chalcogenide nanomaterials are highlighted in this article, showing how they may be used to fundamentally tune the interaction and localization of electromagnetic fields on semiconductor surfaces in a way that enables new horizons in basic research and energy-relevant applications.

Mayer, T. A. (1992). "Industrial models of continuous quality improvement. Implications for emergency medicine." Emerg Med Clin North Am **10**(3): 523-547.

CQI or TQM programs were developed from industrial models dating back to the 1930s. The original philosophic underpinnings guiding CQI included SPC, in which rigorous statistical methods were used to study industrial flow processes. As originally adopted by the Japanese, CQI is credited, to a significant degree, with the emergence of the Japanese economy as a major world leader. Nonetheless, the original CQI concepts were developed and implemented by American researchers, including Deming and Juran. The application of industrial models of quality improvement to service businesses in general and the health care industry in particular have met with substantial success in a number of different settings. Far from representing a management fad, CQI represents a solid management philosophy with a strong statistical background that stands in sharp

contrast to traditional management in this country. CQI recognizes that the majority of defects result from a failure of the processes through which the product or service is generated, as opposed to the workers themselves. To a significant degree, CQI empowers service providers (through the strong commitment of top management) to participate in improving the processes through which products and services are delivered. As efforts unfold to contain health care costs and maintain quality in the face of declining resources, CQI programs are likely to be essential to success. Nonetheless, adopting CQI requires a significant commitment on the part of top management to the training and retraining of health care providers and the recognition that traditional management philosophies and techniques have largely failed to produce the quantum leaps in quality that will be required in the coming years.

Maysinger, D. and J. Lovric (2007). "Quantum dots and other fluorescent nanoparticles: quo vadis in the cell?" Adv Exp Med Biol **620**: 156-167.

An exponentially growing number of nanotechnology-based products are providing new platforms for research in different scientific disciplines (e.g., life sciences and medicine). Biocompatible nanoparticles are expected to significantly impact the development of new approaches in medical diagnoses and drug delivery; however, very little is known about the effects of long-term exposure of different nanoparticles in different cell types and tissues. The first objective of this chapter is to provide a brief account of the current status of fluorescent nanoparticles (i.e., quantum dots, fluorescently-labeled micelles, and FloDots) that serve as tools for bioimaging and therapeutics. The second objective of this chapter is to describe the modes and mechanisms of nanoparticle-cell interactions and the "potential" toxic consequences thereof.

Meads, S. (1994). "Contracting out in NZ: evolutionary or revolutionary? Lessons from the UK experience." N Z Health Hospital **46**(1): 13-15.

Despite the worldwide trend to Facilities Management Contracting and the documented improvements in organisational efficiency, the NZ health sector has yet to grasp the benefits of awarding a single contract to manage a comprehensive range of services. This appears contradictory for an industry which has considerable assets tied up in supporting its core business and is under huge pressure to reduce costs and improve service. NZ is therefore faced with two options: an "evolutionary" route which could take us over a decade to achieve the same benefits as they are currently enjoying in the UK NHS, or "revolutionary" route, taking a quantum leap forward, both in the way contracts are specified and the way services are structured and managed. In this article Sarah Meads, General Manager of Serco Health Services, takes a look at how New Zealand health providers could learn from the NHS experience of contracting out since the introduction of Compulsory Competitive Tendering in 1983. Serco Health Services is the division of Serco Group NZ Limited responsible for assisting healthcare providers to review and manage a wide range of non-core support services. It shares resource and expertise with similar divisions working with the NHS and health-care organisations in Hong Kong.

Medical Advisory, S. (2006). "Nanotechnology: an evidence-based analysis." Ont Health Technol Assess Ser **6**(19): 1-43.

OBJECTIVE: Due to continuing advances in the development of structures, devices, and systems with a length of about 1 to 100 nanometres (nm) (1 nm is one billionth of a metre), the Medical Advisory Secretariat conducted a horizon scanning appraisal of nanotechnologies as new and emerging technologies, including an assessment of the possibly disruptive impact of future nanotechnologies. The National Cancer Institute (NCI) in the United States proclaimed a 2015 challenge goal of eliminating suffering and death from cancer. To help meet this goal, the NCI is engaged in a concerted effort to introduce nanotechnology "to radically change the way we diagnose, treat and prevent cancer." It is the NCI's position that "melding nanotechnology and cancer research and development efforts will have a profound, disruptive effect on how we diagnose, treat, and prevent cancer." Thus, this appraisal sought to determine the systemic effects of nanotechnologies that target, image and deliver drugs, for example, with respect to health human resources, training, and new specialties; and to assess the current status of these nanotechnologies and their projected timeline to clinical utilization. CLINICAL NEED: TARGET POPULATION AND CONDITION Cancer is a heterogeneous set of many malignant diseases. In each sex, 3 sites account for over one-half of all cancers. In women, these are the breast (28%), colorectum (13%) and lungs (12%). In men, these are the prostate (28%), lungs (15%), and the colorectum (13%). It is estimated that 246,000 people in Ontario (2% of the population) have been diagnosed with cancer within the past 10 years and are still alive. Most were diagnosed with cancer of the breast (21%), prostate (20%), or colon or rectum (13%). The number of new cancer cases diagnosed each year in Ontario is expected to increase from about 53,000 in 2001 to 80,000 in 2015. This represents more than a 50% increase in new cases over this period. An aging population, population growth,

and rising cancer risk are thought to be the main factors that will contribute to the projected increase in the number of new cases. THE TECHNOLOGY BEING REVIEWED - MEDICAL ADVISORY SECRETARIAT DEFINITION OF NANOTECHNOLOGY: FIRST-GENERATION NANOTECHNOLOGIES: Early application of nanotechnology-enabled products involved drug reformulation to deliver some otherwise toxic drugs (e.g., antifungal and anticancer agents) in a safer and more effective manner. Examples of first-generation nanodevices include the following: liposomes;albumin bound nanoparticles;gadolinium chelate for magnetic resonance imaging (MRI);iron oxide particles for MRI;silver nanoparticles (antibacterial wound dressing); andnanoparticulate dental restoratives.First-generation nanodevices have been in use for several years; therefore, they are not the focus of this report. SECOND-GENERATION NANOTECHNOLOGIES: Second-generation nanotechnologies are more sophisticated than first- generation nanotechnologies, due to novel molecular engineering that enables the devices to target, image, deliver a therapeutic agent, and monitor therapeutic efficacy in real time. Details and examples of second-generation nanodevices are discussed in the following sections of this report. REVIEW STRATEGY: The questions asked were as follows: What is the status of these multifunctional nanotechnologies? That is, what is the projected timeline to clinical utilization?What are the systemic effects of multifunctional nanodevices with integrated applications that target, image, and deliver drugs? That is, what are the implications of the emergence of nanotechnology on health human resources training, new specialties, etc.?The Medical Advisory Secretariat used its usual search techniques to conduct the literature review by searching relevant databases. Outcomes of interest were improved imaging, improved sensitivity or specificity, improved response rates to therapeutic agents, and decreased toxicity. RESULTS: The search yielded 1 health technology assessment on nanotechnology by The Centre for Technology Assessment TA-Swiss and, in the grey literature, a technology review by RAND. These, in addition to data from the National Cancer Institute (United States) formed the basis for the conclusions of the review. With respect to the question as to how soon until nanotechnology is used in patient care, overall, the use of second-generation nanodevices, (e.g., quantum dots [QDs]), nanoshells, dendrimers) that can potentially target, image, and deliver drugs; and image cell response to therapy in real time are still in the preclinical benchwork stage. Table 1 summarizes the projected timelines to clinical utilization. Table 1:Summary of Timelines to Clinical Use*Organization/YearSecond-Generation NanodeviceEstimate of When Nanodevice Will be in Clinical UseNCI 2001Imaging/detection (e.g., QDs)Therapeutic (e.g., nanoshell)Combined (e.g., dendrimer)~2006-2016~2006-2016~2016-2020NCI 2004Imaging/detectionTherapeuticCombined~2009-2019~2009-2019~2019-2024RAND 2006Combinedunlikely before 2021Swiss 2003ImagingTherapeuticCombined~2005-2010~2008-2013~ 2010-2013*NCI refers to National Cancer Institute; QD, quantum dot.Medical Advisory Secretariat Estimated Timeline for Ontario Upon synthesizing the estimated timelines from the NCI, the Swiss technology assessment and the RAND reports (Figure 1), it appears that: the clinical use of separate imaging and therapeutic nanodevices is estimated to start occurring around 2010;the clinical use of combined imaging and therapeutic nanodevices is estimated to start occurring around 2020;changes in the way disease is diagnosed, treated and monitored are anticipated; andthe full (and realistic) extent of these changes within the next 10 to 20 years is uncertain.Figure 1:Medical Advisory Secretariat Estimated Timeline for the Clinical Use of Second-Generation Nanodevices in OntarioWith respect to the question on potential systemic effects of second-generation nanodevices (i.e., the implications of the emergence of these nanodevices on health human resources training, new specialties etc.), Table 2 summarizes the findings from the review. Table 2:Potential Systemic Effects Caused by Second Generation Nanodevices*ImagingTherapeuticCombined (Detect, Image, Treat, Monitor)Increased sensitivity and specificity of QDs or other nanodevices could lead to the replacement of existing technologies (e.g., PSA testing, mammogram).Sudden demand in use of MRI due to use of nanodevices that are activated in the presence of a magnetic field.Universal demand to detect cancer- how will patients be prioritized for this?Sudden demand in use of MRI due to use of nanodevices that are activated in the presence of a magnetic field.Cost: possibly more expensive than current screening modalities.Possibly more expensive than existing therapies (gold nanoshells)Many functions can be performed on one device --> possibly faster, more cost-effective than individual devices.Report of results: possibly faster than existing technologies.Possibly faster determination of therapeutic efficacy (vs. existing technologies)Increase in life expectancy of population? Free-up beds in hospitals?Nanodevices may be able to pinpoint with more accuracy when cancer starts.Ethical question: when does disease start?Increased demand for imaging by people who are asymptomatic and concerned they may get cancer.Nano-radiologist or medical nano-oncologist provides treatment rather than conventional

radiologists or medical oncologists.Creation of nano-nursing compared to conventional nursing.Nano-radiologist or medical nano-oncologist provides treatment, rather than conventional radiologists or medical oncologists.Creation of nano-nursing compared to conventional nursing.Uncertainty regarding how many "traditional" cancer radiologists/oncologists should be retained and trained.

Mehl-Madrona, L. (2008). "Narratives of exceptional survivors who work with aboriginal healers." J Altern Complement Med **14**(5): 497-504.

BACKGROUND: The commonalities are described of 47 people who sought traditional aboriginal healers for help with their cancer. All had 10% or less chance of survival at 5 years given the site and stage of their cancer from actuarial table calculations. SUBJECTS AND DESIGN: The subjects were compared to a similar group of people who were also working with aboriginal healers and who did not survive past 5 years. Narratives were obtained from the people before and after their work with the healer. These stories were enriched through interviews with family members, friends, health care providers, and the healers themselves, whenever possible. Panels of naive medical students, graduate students, patients, and health care providers were used to evaluate the stories and to pick themes that consistently emerged (dimension analysis). Once stable dimensions emerged, scenarios were developed to rate patients along these dimensions from "1" to "5." New panels did the ratings, with at least 3 panels of 3 people per narrative. Comparisons were made between these 2 groups of people, and differences emerged on the dimensions of Present-centeredness; Forgiveness of others; Release of blame, bitterness, and chronic anger; Orientation to process versus outcome; Sense of Humor; Refusal to accept death as immediate prognosis; Plausible (to the patient, his or her family, and the healers) explanation for why he or she got well, including a story reflecting a belief about how he or she can stay well; Supportive community who believes in the person's cure and protects the person from outsiders who think the person will die; People experience a quantum change, in which major improvements in self-esteem and quality of relationships occurs; and Spiritual transformation. CONCLUSIONS: The 2 groups of people reported equal increases on the dimensions of Sense of Meaning and Purpose and Faith and Hope, which may be intrinsic to the style of healing of aboriginal elders.

Meinlschmidt, G. and M. Tegethoff (2017). "[Psychotherapy: Quo vadis?]." Fortschr Neurol Psychiatr **85**(8): 479-494.

Background: The science and practice of psychotherapy is continuously developing. The goal of this article is to describe new impulses, guiding current advancements in the field. Methods: This paper provides a selective narrative review, synthesizing and condensing relevant literature identified through various sources, including MEDLINE, EMBASE, PsycINFO, and "Web of Science", as well as citation tracking, to elaborate key developments in the field of psychotherapy Results: We describe several dynamics: 1) Following up the so-called "third wave of cognitive behavioral therapy", new interventions arise that have at their core fostering interpersonal virtues, such as compassion, forgiveness, and gratitude; 2) Based on technological quantum leaps, new interventions arise that exploit current developments in the field of new media, information, and communication technologies, as well as brain imaging, such as digital interventions for mental disorders and new forms of neurofeedback; 3) Inspired by the field of positive psychology, there is a revival of the promotion of strength and resilience in therapeutic contexts; 4) In light of the new paradigm "precision medicine", the issue of differential and adaptive indication of psychotherapy, addressed with new methods, regains relevance and drives a new field of "precision psychotherapy". 5) Last but not least, the "embodied turn" opens the door for body psychotherapy to gain relevance in academic psychotherapy. Conclusion: These and further developments, such as the use of systemic and network approaches as well as machine learning techniques, outline the vivid activities in the field of psychotherapy.

Meng, Z., et al. (2017). "Peptide-Coated Semiconductor Polymer Dots for Stem Cells Labeling and Tracking." Chemistry **23**(28): 6836-6844.

Stem cell therapy is rapidly moving toward translation to clinical application. To elucidate the therapeutic effect, a robust method that allows tracking of the stem cells over an extended period of time is required. Herein, semiconducting polymer dots (Pdots) are demonstrated for their use in bright labeling and tracking of human mesenchymal stem cells (MSCs) in vitro and in vivo. The Pdots coated with a cell-penetrating peptide (R8) showed remarkable endocytic uptake efficiency that was 15 times higher than that of carboxyl Pdots and more than 200 times than that of bare Pdots. The Pdot-labeled MSCs can be traced for 15 generations in vitro and tracked over 2 weeks in vivo after subcutaneous transplantation. The labeled MSCs administered through the tail vein were preferentially accumulated in the lung; this was distinctive from the distribution of free Pdots, which were primarily distributed in the liver. Based on the properties of bright labeling, excellent tracking capability, and great biocompatibility, the Pdots will be

valuable in the applications of stem cell biology and regenerative medicine.

Mescher, H., et al. (2020). "Flexible Inkjet-Printed Triple Cation Perovskite X-ray Detectors." ACS Appl Mater Interfaces **12**(13): 15774-15784.

Flexible direct conversion X-ray detectors enable a variety of novel applications in medicine, industry, and science. Hybrid organic-inorganic perovskite semiconductors containing elements of high atomic number combine an efficient X-ray absorption with excellent charge transport properties. Due to their additional cost-effective and low-temperature processability, perovskite semiconductors represent promising candidates to be used as active materials in flexible X-ray detectors. Inspired by the promising results recently reported on X-ray detectors that are based on either triple cation perovskites or inkjet-printed perovskite quantum dots, we here investigate flexible inkjet-printed triple cation perovskite X-ray detectors. The performance of the detectors is evaluated by the X-ray sensitivity, the dark current, and the X-ray stability. Exposed to 70 kVp X-ray radiation, reproducible and highly competitive X-ray sensitivities of up to 59.9 muC/(Gyaircm(2)) at low operating voltages of 0.1 V are achieved. Furthermore, a significant dark current reduction is demonstrated in our detectors by replacing spin-coated poly(3,4-ethylenedioxythiophene)/poly(styrenesulfonate) (PEDOT:PSS) with sputtered NiOx hole transport layers. Finally, stable operation of a flexible X-ray detector for a cumulative X-ray exposure of 4 Gyair is presented, and the applicability of our devices as X-ray imaging detectors is shown. The results of this study represent a proof of concept toward flexible direct conversion X-ray detectors realized by cost-effective and high-throughput digital inkjet printing.

Mi, H. W., et al. (2011). "Single-molecule imaging of BMP4 dimerization on human periodontal ligament cells." J Dent Res **90**(11): 1318-1324.

We expressed bone morphogenetic protein 4 (BMP4) fused with enhanced green fluorescent protein (BMP4-EGFP) in the secretory pathways of producer cells. Fluorescent EGFP was acquired only after we interrupted the transport of BMP4-EGFP by culturing cells at a lower temperature (20 degrees C), and the dynamics of BMP4-EGFP could be monitored by single-molecule microscopy. Western blotting analysis confirmed that exposure to low temperature helped the integrated formation of BMP4-EGFP fusion proteins. In this study, for the first time, we could image the fluorescently labeled BMP4 molecules localized on the plasma membrane of living hPDL cells. The one-step photobleaching with EGFP and the "blinking" behavior of quantum dots suggest that the fluorescent spots represent the events of single BMP4 molecules. Single-molecule tracking showed that the BMP receptors (BMPR) dimerize after BMP4 stimulation, or that a complex of one BMP4 molecule and a pre-formed BMPR dimer develops first, followed by the binding of the second BMP4 molecule. Furthermore, BMP4-EGFP enhanced the osteogenic differentiation of hPDL cells via signal transduction involving BMP receptors. This single-molecule imaging technique might be a valuable tool for the future development of BMP4 gene therapy and regenerative medicine mediated by hPDLs.

Milgrom, L. R. (2002). "Patient-practitioner-remedy (PPR) entanglement. Part 1: a qualitative, non-local metaphor for homeopathy based on quantum theory." Homeopathy **91**(4): 239-248.

A metaphor for homeopathy is developed in which the potentised medicine, the patient, and the practitioner are seen as forming a non-local therapeutically 'entangled' triad, qualitatively described in terms of the transactional interpretation of quantum mechanics.

Milgrom, L. R. (2003). "Patient-practitioner-remedy (PPR) entanglement. Part 2: Extending the metaphor for homeopathy using molecular quantum theory." Homeopathy **92**(1): 35-43.

A quantum metaphor developed previously for homeopathy, involving triadic patient-practitioner-remedy (PPR) entanglement, is extended by importing concepts used in chemistry to describe the electronic structures of molecules. In particular, the electronic energy states of triangular tri-atomic molecules are used metaphorically to predict that (a) the more a homeopathic medicine is potentised, the deeper the level of cure is likely to be, and (b) the practitioner can be included as a beneficiary of the therapeutic process. The model also predicts that remedy attenuation and degree of PRR interaction could (in the quantum theoretical sense) represent a pair of complementary conjugate variables.

Milgrom, L. R. (2004). "Patient-Practitioner-Remedy (PPR) Entanglement, Part 7: a gyroscopic metaphor for the vital force and its use to illustrate some of the empirical laws of homeopathy." Forsch Komplementarmed Klass Naturheilkd **11**(4): 212-223.

BACKGROUND: One of the principle obstacles to homeopathy's general acceptance has been its perceived lack of sound theoretical basis within accepted deterministic bio-medical thought. This impasse might be circumvented if instead, appeal was made to the nondeterministic concepts of the physical sciences, e.g., quantum theory and its notions of entanglement, nonlocality, and uncertainty; Weak Quantum Theory (WQT) and Patient-Practitioner-

Remedy (PPR) Entanglement representing two new complementary strands of thought with the potential to create a new theoretical basis for homeopathy. OBJECTIVE: The goal of this present study was to generate a preliminary mathematical model of the action and reaction of the Vital Force to diseases and remedies within the developing contexts of WQT and PPR Entanglement, based on the metaphor of a hypothetical 'quantized' gyroscope as its physical representation. METHODS: The physics of gyroscopic motion was combined with the quantum theory describing rotating objects (without some of its imposed limitations, e.g., Planck's constant, in line with the relaxation of some of orthodox quantum theory's axioms as proposed by WQT). Thus, increase or decrease in the rate of spin of the Vital Force's hypothetical gyroscope was described in terms of quantized 'shift operators' constructed mathematically from the known 'complementarity' of a remedy's primary and secondary symptoms, expressed in the notation of complex numbers. Ultimately, this generates a hypothetical 'wave function' for the Vital Force. RESULTS: This hypothetical 'wave function' has been used to illustrate certain empirical observations of homeopathy and conventional medicine, e.g., the biphasal action of remedies encapsulated in the Arndt-Schulz Law, Wilder's Law of Initial Value, and some of the results of homeopathic provings. CONCLUSION: This preliminary theoretical analysis suggests that perhaps these less well-known empirical observations should be reinvestigated and, if confirmed, could begin ultimately to provide a much-needed alternative to the doubleblind placebo-controlled trial as a means of investigating and testing the efficacy of homeopathy.

Mohid, S. A. and A. Bhunia (2020). "Combining Antimicrobial Peptides with Nanotechnology: An Emerging Field in Theranostics." Curr Protein Pept Sci **21**(4): 413-428.

The emergence of multidrug-resistant pathogens and their rapid adaptation against new antibiotics is a major challenge for scientists and medical professionals. Different approaches have been taken to combat this problem, which includes rationally designed potent antimicrobial peptides (AMPs) and several nanoparticles and quantum dots. AMPs are considered as a new generation of super antibiotics that hold enormous potential to fight against bacterial resistance by the rapidly killing planktonic as well as their biofilm form while keeping low toxicity profile against eukaryotic cells. Various nanoparticles and quantum dots have proved their effectiveness against a vast array of infections and diseases. Conjugation and functionalization of nanoparticles with potentially active antimicrobial peptides have added advantages that widen their applications in the field of drug discovery as well as delivery system including imaging and diagnostics. This article reviews the current progress and implementation of different nanoparticles and quantum dots conjugated antimicrobial peptides in terms of bio-stability, drug delivery, and therapeutic applications.

Molski, M. (2010). "Biosupersymmetry." Biosystems **100**(1): 47-54.

The growth of biological systems described by the Gompertz and West-Brown-Enquist functions is considered in the framework of the space-like supersymmetric quantum mechanics. It has been shown that the supersymmetric effect of a fermion-boson conversion has a biological analogue in the phenomenon of a growth-regression transformation under the influence of a cycle-non-specific drug of a constant concentration. The results obtained reveal that the biological growth can be viewed as the macroscopic quantum phenomenon endowed with the space-like supersymmetric properties not established so far in the domain of biology and medicine.

Molski, M. (2011). "Quasi-quantum model of potentization." Homeopathy **100**(4): 259-263.

Analytical time-dependent functions describing the change of the concentration of the solvent S(t) and the homeopathic active substance A(t) during decimal and centesimal dilution are derived. The function S(t) is a special case of the West-Brown-Enquist curve describing ontogenic growth, the increase in concentration of the solvent during potentization resembles the growth of biological systems. It is demonstrated that the macroscopic S(t) function is the ground state solution of the microscopic non-local Horodecki-Feinberg equation for the time-dependent Hulthen potential at the critical screening. In consequence potentization belongs to the class of quasi-quantum phenomena playing an important role both in biological systems and homeopathy. A comparison of the results predicted by the model proposed with the results of experiments on delayed luminescence of a homeopathic medicine is made.

Mooney, H. (2008). "Franchise. Quantum leap." Health Serv J: 24-26.

The Royal Marsden's chemotherapy unit in Kingston will not only treat its own patients who live locally, but also accept referrals from local GPs. The move is part of a trend by well-known hospitals to open franchises, led by the Moorfields Eye Hospital which has 11 satellite units, including one in Dubai. Franchising by specialist hospitals can increase services, raise income and expand their brand. It also allows specialist staff to work in a range of settings.

Morrison, R., et al. (1994). "Three-dimensional computerized tomography: a quantum leap in diagnostic imaging?" J Foot Ankle Surg **33**(1): 72-76.

Ever since the discovery of radium by Madame Curie, men and women of vision and science have labored to improve radiation technology. Over a period of approximately 85 years, we have gone from this initial discovery to three-dimensional computerized transmission tomography; one of the latest techniques in modern day x-ray imaging. Its uses are vast and unparalleled in many facets of medicine and surgery, outlining pathology as never before seen, and possibly, never before completely understood. Three-dimensional computerized tomography is rapidly gaining popularity in cross-sectional imaging of the foot and ankle. It has proven invaluable in elucidating osseous and soft tissue pathology. Abnormalities of the musculoskeletal system that exhibit complex anatomy are often difficult to interpret using standard radiographic techniques. Overall, three-dimensional computerized tomography has established itself as a means by which clinicians may appreciate the three-dimensional disposition of anatomy and disease.

Moses, W. W. (2009). "Photodetectors for Nuclear Medical Imaging." Nucl Instrum Methods Phys Res A **610**(1): 11-15.

There have been a number of recent advances in photodetector technology, notably in photomultiplier tubes with high quantum efficiency (up to ~50%), hybrid photodetectors, and silicon-based Geiger-mode photodetectors. This paper looks at the potential benefits that these technologies can bring to nuclear medicine, notably SPECT and PET. We find that while the potential benefits to SPECT are relatively small, they can bring performance improvements in many areas for PET.

Motlagh, N. S., et al. (2016). "Fluorescence properties of several chemotherapy drugs: doxorubicin, paclitaxel and bleomycin." Biomed Opt Express **7**(6): 2400-2406.

Several chemo-drugs act as the biocompatible fluorophores. Here, the laser induced fluorescence (LIF) properties of doxorubicin, paclitaxel and bleomycin are investigated. The absorption lines mostly lie over UV range according to the UV-VIS spectra. Therefore, a single XeCl laser provokes the desired transitions of the chemo-drugs of interest at 308 nm. It is shown that LIF spectra are strongly dependent on the fluorophore concentration giving rise to the sensible red shift. This happens when large overlapping area appears between absorption and emission spectra accordingly. The red shift is taken into account as a characteristic parameter of a certain chemo-drug. The fluorescence extinction (alpha) and self-quenching (k) coefficients are determined based on the best fitting of the adopted Lambert-Beer equation over experimental data. The quantum yield of each chemo-drug is also measured using the linearity of the absorption and emission rates.

Muehsam, D., et al. (2015). "An Overview of Biofield Devices." Glob Adv Health Med **4**(Suppl): 42-51.

Advances in biophysics, biology, functional genomics, neuroscience, psychology, psychoneuroimmunology, and other fields suggest the existence of a subtle system of "biofield" interactions that organize biological processes from the subatomic, atomic, molecular, cellular, and organismic to the interpersonal and cosmic levels. Biofield interactions may bring about regulation of biochemical, cellular, and neurological processes through means related to electromagnetism, quantum fields, and perhaps other means of modulating biological activity and information flow. The biofield paradigm, in contrast to a reductionist, chemistry-centered viewpoint, emphasizes the informational content of biological processes; biofield interactions are thought to operate in part via low-energy or "subtle" processes such as weak, nonthermal electromagnetic fields (EMFs) or processes potentially related to consciousness and nonlocality. Biofield interactions may also operate through or be reflected in more well-understood informational processes found in electroencephalographic (EEG) and electrocardiographic (ECG) data. Recent advances have led to the development of a wide variety of therapeutic and diagnostic biofield devices, defined as physical instruments best understood from the viewpoint of a biofield paradigm. Here, we provide a broad overview of biofield devices, with emphasis on those devices for which solid, peer-reviewed evidence exists. A subset of these devices, such as those based upon EEG- and ECG-based heart rate variability, function via mechanisms that are well understood and are widely employed in clinical settings. Other device modalities, such a gas discharge visualization and biophoton emission, appear to operate through incompletely understood mechanisms and have unclear clinical significance. Device modes of operation include EMF-light, EMF-heat, EMF-nonthermal, electrical current, vibration and sound, physical and mechanical, intentionality and nonlocality, gas and plasma, and other (mode of operation not well-understood). Methodological issues in device development and interfaces for future interdisciplinary research are discussed. Devices play prominent cultural and scientific roles in our society, and it is likely that device technologies will be one of the most influential access points for the furthering of biofield research and the dissemination of biofield concepts. This developing

field of study presents new areas of research that have many important implications for both basic science and clinical medicine.

Mujika, J. I. and X. Lopez (2017). "Unveiling the Catalytic Role of B-Block Histidine in the N-S Acyl Shift Step of Protein Splicing." J Phys Chem B **121**(33): 7786-7796.

Protein splicing is a post-translational modification that involves the excision of a segment denoted as "intein" and the joining of its two flanking segments. The process is autocatalytic, making inteins appealing for many applications in biotechnology, bioengineering, or medicine. The canonical mechanism of protein splicing is composed of four sequential steps, and is initialized by an N-S or N-O acyl shift to form a linear ester. It is well-established that a histidine, the most conserved amino acid in all inteins, catalyzes this initial step, even though its role remains to be understood. In this study, we combine molecular dynamics simulations and quantum mechanics/molecular mechanics (QM/MM) hybrid calculations to investigate the alternative reaction pathways proposed for the N-S acyl shift in Mycobacterium tuberculosis RecA intein. The results rule out the histidine acting as a base and activating the side chain of Cys1; instead, an aspartate performs this action. In the reaction mechanism proposed herein, denoted as the "Asp422 activated" mechanism, two sequential roles are attributed to the histidine: (i) ground-state destabilization by straining the scissile peptide bond and (ii) protonation of the leaving amide group. In summary, the study provides relevant data to understand the catalytic role of this histidine, and proposes a reaction pathway for the N-S acyl shift reaction in protein splicing that fits with the available experimental data.

Mulder, W. J., et al. (2009). "Nanoparticulate assemblies of amphiphiles and diagnostically active materials for multimodality imaging." Acc Chem Res **42**(7): 904-914.

Modern medicine has greatly benefited from recent dramatic improvements in imaging techniques. The observation of physiological events through interactions manipulated at the molecular level offers unique insight into the function (and dysfunction) of the living organism. The tremendous advances in the development of nanoparticulate molecular imaging agents over the past decade have made it possible to noninvasively image the specificity, pharmacokinetic profiles, biodistribution, and therapeutic efficacy of many novel compounds. Several types of nanoparticles have demonstrated utility for biomedical purposes, including inorganic nanocrystals, such as iron oxide, gold, and quantum dots. Moreover, natural nanoparticles, such as viruses, lipoproteins, or apoferritin, as well as hybrid nanostructures composed of inorganic and natural nanoparticles, have been applied broadly. However, among the most investigated nanoparticle platforms for biomedical purposes are lipidic aggregates, such as liposomal nanoparticles, micelles, and microemulsions. Their relative ease of preparation and functionalization, as well as the ready synthetic ability to combine multiple amphiphilic moieties, are the most important reasons for their popularity. Lipid-based nanoparticle platforms allow the inclusion of a variety of imaging agents, ranging from fluorescent molecules to chelated metals and nanocrystals. In recent years, we have created a variety of multifunctional lipid-based nanoparticles for molecular imaging; many are capable of being used with more than one imaging technique (that is, with multimodal imaging ability). These nanoparticles differ in size, morphology, and specificity for biological markers. In this Account, we discuss the development and characterization of five different particles: liposomes, micelles, nanocrystal micelles, lipid-coated silica, and nanocrystal high-density lipoprotein (HDL). We also demonstrate their application for multimodal molecular imaging, with the main focus on magnetic resonance imaging (MRI), optical techniques, and transmission electron microscopy (TEM). The functionalization of the nanoparticles and the modulation of their pharmacokinetics are discussed. Their application for molecular imaging of key processes in cancer and cardiovascular disease are shown. Finally, we discuss a recent development in which the endogenous nanoparticle HDL was modified to carry different diagnostically active nanocrystal cores to enable multimodal imaging of macrophages in experimental atherosclerosis. The multimodal characteristics of the different contrast agent platforms have proven to be extremely valuable for validation purposes and for understanding mechanisms of particle-target interaction at different levels, ranging from the entire organism down to cellular organelles.

Mulliken, R. S. (1967). "Spectroscopy, molecular orbitals, and chemical bonding." Science **157**(3784): 13-24.

Murugavel, S., et al. (2019). "Synthesis, computational quantum chemical study, in silico ADMET and molecular docking analysis, in vitro biological evaluation of a novel sulfur heterocyclic thiophene derivative containing 1,2,3-triazole and pyridine moieties as a potential human topoisomerase IIalpha inhibiting anticancer agent." Comput Biol Chem **79**: 73-82.

Computational quantum chemical study and biological evaluation of a synthesized novel sulfur

heterocyclic thiophene derivative containing 1,2,3-triazole and pyridine moieties namely BTPT [2-(1-benzyl-5-methyl-1H-1,2,3-triazol-4-yl)-6-methoxy-4-(thiophen-2-yl) pyridine] was presented in this study. The crystal structure was determined by SCXRD method. For the title compound BTPT, spectroscopic characterization like (1)H NMR, (13)C NMR, FTIR, UV-vis were carried out theoretically by computational DFT method and compared with experimental data. Druglikeness parameters of BTPT were found through in silico pharmacological ADMET properties estimation. The molecular docking investigation was performed with human topoisomerase IIalpha (PDB ID:1ZXM) targeting ATP binding site. In vitro cytotoxicity activity of BTPT/doxorubicin were examined by MTT assay procedure against three human cancer cell lines A549, PC-3, MDAMB-231 with IC50 values of 0.68/0.70, 1.03/0.77 and 0.88/0.98 muM, respectively. Our title compound BTPT reveals notable cytotoxicity against breast cancer cell (MDAMB-231), moderate activity with human lung cancer cell (A-549) and less inhibition with human prostate cancer cell (PC-3) compared to familiar cancer medicine doxorubicin. From the results, BTPT could be observed as a potential candidate for novel anticancer drug development process.

Naik, G. G., et al. (2020). "Multi-Functional Carbon Dots from an Ayurvedic Medicinal Plant for Cancer Cell Bioimaging Applications." J Fluoresc **30**(2): 407-418.

The combination of an Ayurvedic wisdom and nanotechnology may help us to resolve the complex healthcare challenges. A facile and economical one-pot hydrothermal synthesis method has been adopted for preparing a blue fluorescent carbon dots (CDs) with a quantum yield of 15.10% from an Ayurvedic medicinal plant Andrographis paniculata (AP). The Andrographis paniculata derived CDs (AAPCDs) were then characterized using different techniques. Through High Performance Thin Layer Chromatography (HPTLC) profiling of the AP extract and the CDs, it was found that some of the phytoconstituents are retained as such while others may have been converted into their derivatives during the process of formation of CDs. The CDs are designed to possess cellular imaging of human breast carcinoma cells (MCF-7), apart from free radicals sensing and scavenging capabilities. AAPCDs showed minimal cytotoxicity in Multi Drug Resistant clinically isolated strains of gram positive and gram negative bacteria which may be employed for microbiology oriented experiments. These results suggest potential of multi-functional AAPCDs as nano-probes for various pharmaceutical, biomedical and bioengineering applications.

Nair, R. V., et al. (2020). "A dual signal on-off fluorescent nanosensor for the simultaneous detection of copper and creatinine." Mater Sci Eng C Mater Biol Appl **109**: 110569.

The transition of conventional medicine to personalized medicine has paved the way for sensing new biomolecules. Consequently, this field attracted wide interest due to its capability to provide information on point of care basis. Multi-analyte sensors that emerged recently can perform quick and affordable analysis with minimum quantity of blood samples compared to traditional sensing of individual analytes. The present study focuses on the development of a quantum dot (Qd) based nanosensor for the simultaneous detection of copper and creatinine; two biologically relevant molecules. The sensor was designed by forming a complex of Qd with 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and picric acid through carboxylic bond formation of Qd-EDC with picric acid. The dual independent emissions of the Qd-EDC complex was used for the simultaneous detection of creatinine and copper by a turn on/turn off method and was successfully demonstrated with a sensitivity of nanomolar to millimolar, and micromolar to millimolar range respectively. The multianalyte sensor thus developed has quick response and works well under normal conditions of temperature and pH. It is also shown to work in cellular environment and blood serum. A simple image based detection of creatinine using the sensor strips has also been attempted by means of a mobile camera and validated with human blood samples.

Narayan, S. K. and J. K. Dutta (2005). "Creutzfeldt-Jakob disease." J Assoc Physicians India **53**: 791-795.

Cruetzfeldt-Jakob disease is a prion protein disease causing a transmissible, subacute, fatal neurodegenerative disease characterized by a spongiform encephalopathy. Though rare, ever since Pruisner described the pathogenesis in 1982, this disease kept the clinicians as well as biologists spellbound, because of its distinct clinical picture and the novel mechanism of transmission. There was a further quantum leap in the interest in the disease with the establishment of its new clinical variant, the so called 'mad cow disease' in the late 1990s and had led to more stringent measures to ensure the quality of cattle-feeds and cattle-derived food products. The sporadic genetic variants, the commonest form of the disease, continue to challenge the genetic scientists. Advances in neuroimaging, cerebrospinal fluid marker proteins and genetic linkage studies now offer excellent diagnostic methods, while advances in therapeutic medicine which use products from cadaveric extracts such as growth hormone for treatment of hypopituitarism, dural grafts for neurosurgical

procedures and cornea for transplantation etc. have thrown new challenges in controlling this serious disease.

Nekoueian, K., et al. (2019). "Carbon-based quantum particles: an electroanalytical and biomedical perspective." Chem Soc Rev **48**(15): 4281-4316.

Carbon-based quantum particles, especially spherical carbon quantum dots (CQDs) and nanosheets like graphene quantum dots (GQDs), are an emerging class of quantum dots with unique properties owing to their quantum confinement effect. Many reviews appeared recently in the literature highlighting their optical properties, structures, and applications. These papers cover a broad spectrum of carbon-based nanoparticles, excluding a more detailed discussion about some important aspects related to the definition of carbon-based particles and the correlation of optical and electrochemical aspects in relation to sensing and biomedical applications. A large part of this review is devoted to these aspects. It aims, in particular, to act as a bridge between optical and electrochemical aspects of carbon-based quantum particles, both of which are associated with the electronic nature of carbon-based quantum particles. A special focus will be on their use in electroanalysis, notably their benefits in redox, and in electrochemical analysis with emphasis on their application as sensors. Electroanalysis is an easy and cost-effective means of providing qualitative and quantitative information of a specific analyte in solution in a time scale of some minutes. The integration of carbon-based quantum particles into these detection schemes as well as their incorporation into composite nanomaterials have largely improved detection limits with possibilities for their integration in aspects ranging from point-of-care devices to personalized medicine. This review will focus on some of these aspects while also covering the nanomedical aspects of carbon-based quantum particles, ultimately correlated for such developments.

Nelson, J., et al. (2012). "SU-D-217A-03: Nuclear Medicine Uniformity Assessment Using 2D Noise Power Spectrum." Med Phys **39**(6Part3): 3621.

PURPOSE: Nuclear medicine quality control programs require daily evaluation for the presence of potential non-uniformities by commonly utilizing a traditional pixel value-based assessment (Integral CFOVUniformity). While this method effectively captures regional non- uniformities in the image, it does not adequately reflect subtle periodic structures that are visually apparent and clinically unacceptable, therefore requiring the need for additional visual inspection of the image. The goal of this project was to develop a new uniformity assessment metric by targetingstructural patterns and more closely correlating with visual inspection. METHODS: The new quantitative uniformity assessment metric is based on the 2D Noise Power Spectrum (NPS). A full 2D NPS was performed on each image. The NPS was thresholded to remove quantum noise and further filtered by the visual response function. A score, the Structure Noise Index (SNI), was then applied to each based on the average magnitude of the structured noise in the processed image. To verify the validity of the new metric, 50 daily uniformity images with varying degrees of visual structured and non-structured non-uniformity were scored by 5 expert nuclear medicine physicists. The correlation between the visual score and SNI were assessed. The Integral CFOV was also compared against the visual score. RESULTS: Our new SNI assessment metric compared to the Integral CFOV showed in increase in sensitivity from 67% to 100% in correctly identifying structured non-uniformities. The overall positive predictive value also increased from 55% to 72%. CONCLUSIONS: Our new uniformity metric correlates much more closely with visual assessment of structured non- uniform NM images than the traditional pixel-based method. Using this new metric in conjunction with the traditional pixel value-based assessment will allow a more accurate quantitative assessment of nuclear medicineuniformity.

Nelson, J. S., et al. (2014). "Improved nuclear medicine uniformity assessment with noise texture analysis." J Nucl Med **55**(1): 169-174.

UNLABELLED: Because gamma cameras are generally susceptible to environmental conditions and system vulnerabilities, they require routine evaluation of uniformity performance. The metrics for such evaluations are commonly pixel value-based. Although these metrics are typically successful at identifying regional nonuniformities, they often do not adequately reflect subtle periodic structures; therefore, additional visual inspections are required. The goal of this project was to develop, test, and validate a new uniformity analysis metric capable of accurately identifying structures and patterns present in nuclear medicine flood-field uniformity images. METHODS: A new uniformity assessment metric, termed the structured noise index (SNI), was based on the 2-dimensional noise power spectrum (NPS). The contribution of quantum noise was subtracted from the NPS of a flood-field uniformity image, resulting in an NPS representing image artifacts. A visual response filter function was then applied to both the original NPS and the artifact NPS. A single quantitative score was calculated on the basis of the magnitude of the artifact. To verify the validity of the SNI, an observer study was performed with 5 expert nuclear medicine physicists. The correlation between the SNI and the visual score was assessed with Spearman rank correlation analysis.

The SNI was also compared with pixel value-based assessment metrics modeled on the National Electrical Manufacturers Association standard for integral uniformity in both the useful field of view (UFOV) and the central field of view (CFOV). RESULTS: The SNI outperformed the pixel value-based metrics in terms of its correlation with the visual score (rho values for the SNI, integral UFOV, and integral CFOV were 0.86, 0.59, and 0.58, respectively). The SNI had 100% sensitivity for identifying both structured and nonstructured nonuniformities; for the integral UFOV and CFOV metrics, the sensitivities were only 62% and 54%, respectively. The overall positive predictive value of the SNI was 87%; for the integral UFOV and CFOV metrics, the positive predictive values were only 67% and 50%, respectively. CONCLUSION: The SNI accurately identified both structured and nonstructured flood-field nonuniformities and correlated closely with expert visual assessment. Compared with traditional pixel value-based analysis, the SNI showed superior performance in terms of its correlation with visual perception. The SNI method is effective for detecting and quantifying visually apparent nonuniformities and may reduce the need for more subjective visual analyses.

Ni, X., et al. (2018). "Fluorescent Nanoparticles for Noninvasive Stem Cell Tracking in Regenerative Medicine." J Biomed Nanotechnol **14**(2): 240-256.

Stem cell-based therapies have emerged as promising platforms with the potential to treat serious diseases that are incurable by traditional medical approaches. To optimize the overall outcomes, it is important to understand the fate of transplanted stem cells (e.g., localization, migration, engraftment, survival, proliferation and differentiation). Fluorescent nanoparticles with good photostability and minimal perturbation of cell functions hold great promise for distinguishing transplanted stem cells from host tissues with high resolution, showing advantages over traditional histological methods. This review aims to summarize the recent advances in the use of fluorescent nanoparticles for the direct labelling of stem cells and the applications of such nanoparticles in stem cell tracking. The relevant fluorescent nanoparticles, including quantum dots, organic fluorogen-doped nanoparticles, fluorescent nanodiamonds, and upconversion nanoparticles are discussed. The advantages and limitations of the currently available fluorescent trackers are summarized, and perspectives on new research opportunities are discussed.

Nie, S. (2009). "Biomedical nanotechnology for molecular imaging, diagnostics, and targeted therapy." Annu Int Conf IEEE Eng Med Biol Soc **2009**: 4578-4579.

Biomedical nanotechnology is a cross-disciplinary area of research in science, engineering and medicine with broad applications for molecular imaging, molecular diagnosis, and targeted therapy. The basic rationale is that nanometer-sized particles such as semiconductor quantum dots and iron oxide nanocrystals have optical, magnetic or structural properties that are not available from either molecules or bulk solids. When linked with biotargeting ligands such as monoclonal antibodies, peptides or small molecules, these nanoparticles can be used to target diseased cells and organs (such as malignant tumors and cardiovascular plaques) with high affinity and specificity. In the "mesoscopic" size range of 5-100 nm diameter, nanoparticles also have large surface areas and functional groups for conjugating to multiple diagnostic (e.g., optical, radioisotopic, or magnetic) and therapeutic (e.g., anticancer) agents.

Nie, S., et al. (2007). "Nanotechnology applications in cancer." Annu Rev Biomed Eng **9**: 257-288.

Cancer nanotechnology is an interdisciplinary area of research in science, engineering, and medicine with broad applications for molecular imaging, molecular diagnosis, and targeted therapy. The basic rationale is that nanometer-sized particles, such as semiconductor quantum dots and iron oxide nanocrystals, have optical, magnetic, or structural properties that are not available from molecules or bulk solids. When linked with tumor targeting ligands such as monoclonal antibodies, peptides, or small molecules, these nanoparticles can be used to target tumor antigens (biomarkers) as well as tumor vasculatures with high affinity and specificity. In the mesoscopic size range of 5-100 nm diameter, nanoparticles also have large surface areas and functional groups for conjugating to multiple diagnostic (e.g., optical, radioisotopic, or magnetic) and therapeutic (e.g., anticancer) agents. Recent advances have led to bioaffinity nanoparticle probes for molecular and cellular imaging, targeted nanoparticle drugs for cancer therapy, and integrated nanodevices for early cancer detection and screening. These developments raise exciting opportunities for personalized oncology in which genetic and protein biomarkers are used to diagnose and treat cancer based on the molecular profiles of individual patients.

Nilewski, L., et al. (2019). "Highly Oxidized Graphene Quantum Dots from Coal as Efficient Antioxidants." ACS Appl Mater Interfaces **11**(18): 16815-16821.

Graphene quantum dots (GQDs) have recently been employed in various fields including medicine as antioxidants, primarily because of favorable biocompatibility in comparison to common inorganic quantum dots, although the structural features that lead to the biological activities of GQDs are poorly

understood. Here, we report that coal-derived GQDs and their poly(ethylene glycol)-functionalized derivatives serve as efficient antioxidants, and we evaluate their electrochemical, chemical, and in vitro biological activities.

Ning, Y., et al. (2020). "Split and Use: Structural Isomers for Diagnosis and Therapy." J Am Chem Soc **142**(14): 6761-6768.

Diagnostics and therapeutics are generally separate entities in medicine. Theranostics, agents that provide for both modalities, are being developed. However, they often require complex syntheses so as to incorporate within one molecular structure both diagnostic and therapeutic elements. Moreover, their use is often complicated by the disparate dosage requirements for diagnosis and therapy. Herein, we report that closely related porphyrinoid regioisomers produced from the same 1,3-dipolar cycloaddition reaction give rise to products that as their corresponding ytterbium(III) complexes may be split and used for the separate biological functions that are required for theranostics. Specifically, the cis isomer is luminescent and suitable for NIR imaging, while the trans isomer produces singlet oxygen with a good quantum yield and is thus attractive for use in photodynamic therapy (PDT). Both in vitro and in vivo experiments provide support for the complementary biological functions of the two regioisomers. The present study reveals how ostensibly related regioisomers may be used to switch between diagnosis and therapy. More broadly, it serves to highlight a new approach to creating paired sets of molecules that may be used in combination as effective theranostics.

Nissel, H. (1998). "[Acupuncture: an information therapy?]." Wien Med Wochenschr **148**(19): 439-442.

Even though modern medicine continues to be governed by the morphological point of view, cybernetics and systems theory are beginning to gain in importance. The concept of "Infomedicine" serves as the basis for a discussion of regulation and the information mechanisms necessary for this to occur. Some of the new insights being made in physics, such as the theory of relativity, quantum physics, and chaos theory provide many valuable explanations. Acupuncture represents a regulation and information therapy, and many parallels can be drawn between traditional Chinese medicine and the discoveries being made in today's physics.

Noori Tahneh, A., et al. (2017). "Density functional theory study of structural and electronic properties of trans and cis structures of thiothixene as a nano-drug." J Mol Model **23**(12): 356.

The geometrical structure, electronic and optical properties, electronic absorption spectra, vibrational frequencies, natural charge distribution, MEP analysis and thermodynamic properties of the trans and cis structures of the drug thiothixene were investigated using density functional theory (DFT) and time-dependent DFT (TDDFT) methods with the B3LYP hybrid functional and 6-311 + G(d,p) basis set. The results of the calculations demonstrate that the cis structure of thiothixene has appropriate quantum properties that can act as an active medicine. The relative energies of trans and cis structures of thiothixene shows that the cis structure is more stable than the trans structure, with a small energy difference. TDDFT calculations show that the cis structure of thiothixene has the best absorption properties. The calculated NLO properties show that the NLO properties of the cis structure of thiothixene are higher than the trans structure, and the fact that the chemical hardness of the cis structure is lower than that of the trans structure that indicates that the reactivity and charge transfer of the cis isomer of thiothixene is higher than that of trans thiothixene. The molecular electrostatic potential (MEP) maps of both structures of thiothixene demonstrate that the oxygen atoms of the molecule are appropriate areas for electrophilic reactions. The vibrational frequencies of the two conformations of thiothixene demonstrate that both structures of thiothixene have almost similar modes of vibrations. The calculated thermodynamic parameters show that these quantities increase with enhancing temperature due to the enhancement of molecular vibrational intensities with temperature. Graphical abstract Trans/Cis isomerization of thiothixene drug.

Norbury, J. W., et al. (1986). "Predicting charmonium and bottomonium spectra with a quark harmonic oscillator." Am J Phys **54**(11): 1031-1034.

We present a simple application of the three-dimensional harmonic oscillator which should provide a very nice particle physics example to be presented in introductory undergraduate quantum mechanics course. The idea is to use the nonrelativistic quark model to calculate the spin-averaged mass levels of the charmonium and bottomonium spectra.

Pham, M. and I. McRae (2015). "Who provides GP after-hours care?" Health Policy **119**(4): 447-455.

Understanding the demographic and financial factors likely to influence the supply side of after-hours GP care is crucial in meeting the increasing demand for these services. This study answers two questions: which GPs are more likely to provide after-hours GP care, and of those who do, which are more likely to take a heavier load. Data from the first wave of the Medicine in Australia: Balancing Employment and Life

(MABEL) survey is used, with logistic regression applied to address the decision to undertake after-hours work and linear regression to address the question of the quantum of work. The results show that female, older, and urban GPs are less likely to work outside of normal hours. GPs who are employees are less likely to participate in after-hours work than GPs who are principals or partners of a practice. On the other hand, principals and partners, are likely work more hours in the after-hours period than employee GPs if they do participate in this work. Similarly, those GPs in solo practice who work after-hours also tend to take a heavier after-hours workload than the GPs who are not in solo practice. The role of GP wages and family income does not seem to be compelling. These conclusions are likely to relate to the ways doctors behave independent of the health system.

Pham, S. H., et al. (2020). "Stimuli-Responsive Nanomaterials for Application in Antitumor Therapy and Drug Delivery." Pharmaceutics **12**(7).

The new era of nanotechnology has produced advanced nanomaterials applicable to various fields of medicine, including diagnostic bio-imaging, chemotherapy, targeted drug delivery, and biosensors. Various materials are formed into nanoparticles, such as gold nanomaterials, carbon quantum dots, and liposomes. The nanomaterials have been functionalized and widely used because they are biocompatible and easy to design and prepare. This review mainly focuses on nanomaterials responsive to the external stimuli used in drug-delivery systems. To overcome the drawbacks of conventional therapeutics to a tumor, the dual- and multi-responsive behaviors of nanoparticles have been harnessed to improve efficiency from a drug delivery point of view. Issues and future research related to these nanomaterial-based stimuli sensitivities and the scope of stimuli-responsive systems for nanomedicine applications are discussed.

Pilme, J., et al. (2014). "QTAIM Analysis in the Context of Quasirelativistic Quantum Calculations." J Chem Theory Comput **10**(11): 4830-4841.

Computational chemistry currently lacks ad hoc tools for probing the nature of chemical bonds in heavy and superheavy-atom systems where the consideration of spin-orbit coupling (SOC) effects is mandatory. We report an implementation of the Quantum Theory of Atoms-In-Molecules in the framework of two-component relativistic calculations. Used in conjunction with the topological analysis of the Electron Localization Function, we show for astatine (At) species that SOC significantly lowers At electronegativity and boosts its propensity to make charge-shift bonds. Relativistic spin-dependent effects are furthermore able to change some bonds from mainly covalent to charge-shift type. The implication of the disclosed features regarding the rationalization of the labeling protocols used in nuclear medicine for (211)At radioisotope nicely illustrates the potential of the introduced methodology for investigating the chemistry of (super)heavy elements.

Pincus, D. (2012). "Self-organizing biopsychosocial dynamics and the patient-healer relationship." Forsch Komplementmed **19 Suppl 1**: 22-29.

The patient-healer relationship has an increasing area of interest for complementary and alternative medicine (CAM) researchers. This focus on the interpersonal context of treatment is not surprising as dismantling studies, clinical trials and other linear research designs continually point toward the critical role of context and the broadband biopsychosocial nature of therapeutic responses to CAM. Unfortunately, the same traditional research models and methods that fail to find simple and specific treatment-outcome relations are similarly failing to find simple and specific mechanisms to explain how interpersonal processes influence patient outcomes. This paper presents an overview of some of the key models and methods from nonlinear dynamical systems that are better equipped for empirical testing of CAM outcomes on broadband biopsychosocial processes. Suggestions are made for CAM researchers to assist in modeling the interactions among key process dynamics interacting across biopsychosocial scales: empathy, intra-psychic conflict, physiological arousal, and leukocyte telomerase activity. Finally, some speculations are made regarding the possibility for deeper cross-scale information exchange involving quantum temporal nonlocality.

Pla, J. J., et al. (2013). "High-fidelity readout and control of a nuclear spin qubit in silicon." Nature **496**(7445): 334-338.

Detection of nuclear spin precession is critical for a wide range of scientific techniques that have applications in diverse fields including analytical chemistry, materials science, medicine and biology. Fundamentally, it is possible because of the extreme isolation of nuclear spins from their environment. This isolation also makes single nuclear spins desirable for quantum-information processing, as shown by pioneering studies on nitrogen-vacancy centres in diamond. The nuclear spin of a (31)P donor in silicon is very promising as a quantum bit: bulk measurements indicate that it has excellent coherence times and silicon is the dominant material in the microelectronics industry. Here we demonstrate electrical detection and coherent manipulation of a single (31)P nuclear spin qubit with sufficiently high fidelities for fault-tolerant quantum computing. By integrating single-shot readout

of the electron spin with on-chip electron spin resonance, we demonstrate quantum non-demolition and electrical single-shot readout of the nuclear spin with a readout fidelity higher than 99.8 percent-the highest so far reported for any solid-state qubit. The single nuclear spin is then operated as a qubit by applying coherent radio-frequency pulses. For an ionized (31)P donor, we find a nuclear spin coherence time of 60 milliseconds and a one-qubit gate control fidelity exceeding 98 percent. These results demonstrate that the dominant technology of modern electronics can be adapted to host a complete electrical measurement and control platform for nuclear-spin-based quantum-information processing.

Poccia, N. and A. Bianconi (2011). "The Physics of Life and Quantum Complex Matter: A Case of Cross-Fertilization." Life (Basel) **1**(1): 3-6.

Progress in the science of complexity, from the Big Bang to the coming of humankind, from chemistry and biology to geosciences and medicine, and from materials engineering to energy sciences, is leading to a shift of paradigm in the physical sciences. The focus is on the understanding of the non-equilibrium process in fine tuned systems. Quantum complex materials such as high temperature superconductors and living matter are both non-equilibrium and fine tuned systems. These topics have been subbjects of scientific discussion in the Rome Symposium on the "Quantum Physics of Living Matter".

Popilock, R., et al. (2008). "CT artifact recognition for the nuclear technologist." J Nucl Med Technol **36**(2): 79-81.

The goal of this article is to make the PET/CT and SPECT/CT operator aware of common artifacts found in CT. In diagnostic imaging, the ability to render an accurate diagnosis requires the technologist to take steps to optimize image quality and recognize when image quality has been compromised-that is, when there is an image artifact. One way these artifacts occur is through the inability of the CT linear attenuation image to precisely represent the linear attenuation map of a 2-dimensional section through the body. The reasons for this inability are multifold. First, CT is subject to the laws of x-ray quantum physics resulting in noise in all CT images. Moreover, all current CT x-ray systems generate a spectrum of energies. Also, CT scanners use detectors of finite dimension, as are the x-ray focal spots; reconstruct images from a finite number of samples distributed over a finite number of views; and acquire the data for each reconstruction over a finite period.

Posadzki, P. and N. Glass (2009). "Mind-body medicine: a conceptual (re)synthesis?" Adv Mind Body Med **24**(3): 8-14.

The aim of this paper is to review the literature on mind-body medicine (MBM) in a narrative manner. A coherent construct is explored and developed that includes a conceptual synthesis of existing theories that is grounded in qualitative paradigms. Theoretical reflections on MBM are addressed in order to overview its practical implications. The logic and underlying principles of MBM are highlighted with regard to the benefits that this modality is reputed to produce. Its therapeutic and preventive values, as well as strategies for its development and promotion, are also considered. The paper proposes several recommendations for future healthcare practices. These include the need to build a complex, multidimensional model of MBM and the integral practical implications. The core information regarding the essence of MBM is discussed in relation to the existing literature and, in particular, quantum physics.

Pospelov, A. P., et al. (2020). "Selective detection of complex gas mixtures using point contacts: concept, method and tools." Beilstein J Nanotechnol **11**: 1631-1643.

Of all modern nanosensors using the principle of measuring variations in electric conductance, point-contact sensors stand out in having a number of original sensor properties not manifested by their analogues. The nontrivial nature of point-contact sensors is based on the unique properties of Yanson point contacts used as the sensing elements. The quantum properties of Yanson point contacts enable the solution of some of the problems that could not be solved using conventional sensors measuring conductance. In the present paper, we demonstrate this by showing the potential of quantum point-contact sensors to selectively detect components of a gas mixture in real time. To demonstrate the high efficiency of the proposed approach, we analyze the human breath, which is the most complex of the currently known natural gas mixtures with extremely low concentrations of its components. Point-contact sensors allow us to obtain a spectroscopic profile of the mixture. This profile contains information about the complete set of energy interactions occurring in the point contact/breath system when the breath constituents adsorb to and desorb from the surface of the point-contact conduction channel. With this information we can unambiguously characterize the analyzed system, since knowing the energy parameters is key to successfully identifying and modeling the physicochemical properties of various quantum objects. Using the point-contact spectroscopic profile of a

complex gas mixture it is possible to get a functional dependence of the concentration of particular breath components on the amplitude of the sensor output signal. To demonstrate the feasibility of the proposed approach, we analyze the point-contact profiles from the breath of several patients and compare them with the concentrations of serotonin and cortisol in the body of each patient. The obtained results demonstrate that the proposed methodology allows one to get an effective calibration function for a non-invasive analysis of the level of serotonin and cortisol in the human body using the point-contact breath test. The present study indicates some necessary prerequisites for the design of fast detection methods using differential sensor analysis in real time, which can be implemented in various areas of science and technology, among which medicine is one of the most important.

Potekhin, S. A. and R. S. Khusainova (2005). "Spin-dependent absorption of water molecules." Biophys Chem **118**(2-3): 84-87.

The effects of spin state of water molecules on its absorption on lyophilized DNA, lysozyme and some inorganic sorbents were studied. It was shown that the absorption rates of ortho and para water from vapor differ noticeably. The para isomer binding with preparations is distinctly faster than that of the ortho isomer in all cases. Clear-cut distinction in the sorption kinetics is determined by the difference in quantum statistics for spin isomers, which in its turn can give rise to remarkable differences in physico-chemical properties of ortho and para water. This finding opens a wide field of activity in studying fundamental and applied problems relating to the role of the spin state of water molecules in physics, chemistry, biology and medicine.

Prasanth, D., et al. (2020). "Microgravity Modulates Effects of Chemotherapeutic Drugs on Cancer Cell Migration." Life (Basel) **10**(9).

Microgravity or the condition of apparent weightlessness causes bone, muscular and immune system dysfunctions in astronauts following spaceflights. These organ and system-level dysfunctions correlate with changes induced at the single cell level both by simulated microgravity on earth as well as microgravity conditions in outer space (as in the international space station). Reported changes in single bone cells, muscle cells and white blood cells include structural/morphological abnormalities, changes in gene expression, protein expression, metabolic pathways and signaling pathways, suggesting that cells mount some response or adjustment to microgravity. However, the implications of such adjustments on many cellular functions and responses are not clear largely because the primary mechanism of gravity sensing in animal cells is unknown. Here, we used a rotary cell culture system developed by NASA to subject leukemic and erythroleukemic cancer cells to microgravity for 48 h and then quantified their innate immune response to common anti-cancer drugs using biophysical parameters and our recently developed quantum-dot-based fluorescence spectroscopy. We found that leukemic cancer cells treated with daunorubicin show increased chemotactic migration ($p < 0.01$) following simulated microgravity (microg) compared to normal gravity on earth (1 g). However, cells treated with doxorubicin showed enhanced migration both in 1 g and following microg. Our results show that microgravity modulates cancer cell response to chemotherapy in a drug-dependent manner. These results suggest using simulated microgravity as an immunomodulatory tool for the development of new immunotherapies for both space and terrestrial medicine.

Preston, T. C. and R. Signorell (2012). "From plasmon spectra of metallic to vibron spectra of dielectric nanoparticles." Acc Chem Res **45**(9): 1501-1510.

Light interacts surprisingly differently with small particles than with bulk or gas phase materials. This can cause rare phenomena such as the occurence of a "blue moon". Spectroscopic particle phenomena of similar physical origin have also spawned countless applications ranging from remote sensing to medicine. Despite the broad interest in particle spectra, their interpretation still poses many challenges. In this Account, we discuss the challenges associated with the analysis of infrared, or vibron, extinction spectra of small dielectric particles. The comparison with the more widely studied plasmon spectra of metallic nanoparticles reveals many common features. The shape, size, and architecture of particles influence the band profiles in vibron and plasmon spectra in similar ways. However, the molecular structure of dielectric particles produces infrared spectral features that are more diverse and detailed or even unique to vibron spectra. More complexity means higher information content, but that also makes the spectra more difficult to interpret. Conventional models such as classical electromagnetic theory with a continuum description of the wavelength-dependent optical constants are often no longer applicable to these spectra. In cases where accurate optical constants are not available and for ultrafine particles, where the molecular structure and quantum effects become essential, researchers must resort to molecular models for light-particle interaction that do not require the prior knowledge of optical constants. In this Account, we illustrate how vibrational exciton approaches combined with

molecular dynamics simulations and solid-state density functional calculations provide a viable solution to these challenges. Molecular models reveal two important characteristics of vibron spectra of small molecularly structured particles. The band profiles in vibron spectra are largely determined by transition dipole coupling between the molecules in a particle. Below a specific particle size limit, conventional models fail. Molecular models explain many other phenomena in particle spectra, such as size, shape, and mixing effects, providing the foundation for a better understanding of the interaction of solar radiation with aerosols and clouds and for the design of dielectric nanomaterials.

Prina-Mello, A., et al. (2010). "Comparative flow cytometric analysis of immunofunctionalized nanowire and nanoparticle signatures." Small **6**(2): 247-255.

Flow cytometry is one of the gold-standard techniques used in clinical medicine for quantitative immunoassaying. The continuous development of its probes, commonly fluorescent nanoparticles, is important. Lately, the introduction of quantitative multiplexed immunoassay has challenged the use of nanoparticles as probes. Functionalized fluorescent silica-based magnetic nanowires are investigated under flow cytometry as a novel probe category. The preparation and full characterization of these multimodal nanowires is reported and compared to those of silica-based magnetic nanoparticles by flow cytometry. Full characterization includes transmission electron microscopy and fluorescence microscopy imaging, flow cytometric assaying, superconducting quantum interference device (SQUID) magnetization, and Mossbauer spectroscopy measurements. This work shows that loaded silica nanowires have intrinsic geometrical advantages when compared to similar spherical particles due to their unique "flow cytometry fingerprint" when utilized as magnetic carriers for immunodetection applications. These advantages account for a 17% yield in detecting the functional binding between THP-1 and ICAM-1, by utilizing a much lower concentration than that required for the nanoparticles.

Prince, R. H. and M. Reiss (1990). "Psychiatry and the irrational: does our scientific world view interfere with the adaptation of psychotics?" Psychiatr J Univ Ott **15**(3): 137-143.

Perhaps even more strongly than others in our contemporary Western world, psychiatrists cling to an exceptionally rigid scientific world view. When psychotic patients speak of such matters as their experiences with spirits or of being possessed or of their preoccupations with meaningful coincidences, psychiatrists discount their views as mere psychotic delusions. We suggest that psychiatrists should deal with their patient's attempts at explaining their symptoms by negotiation and compromise, just as any other physician would do when confronted with patient explanations for symptoms which do not coincide with the tenets of scientific medicine. Rather than relegating the psychotic to a meaning-vacuum by dismissing his or her explanations as totally false and non-negotiable, the therapist should help patients find meaning by linking their views and experiences to those of important thinkers within Western cultures. Almost all elements of psychotic thought including beliefs in disembodied spirits, synchronicity (meaningful coincidences), and the possibility of non-material, actions-at-a-distance can be found among respected Western philosophers, psychiatrists, religious leaders and quantum physicists. An example of the world view of a psychotic patient is presented in which a variety of idiosyncratic beliefs are described including convictions of the reality of synchronicity. We demonstrate that highly similar synchronicity beliefs have been entertained by many major Western intellectuals. We contend that on this basis and along with negotiation and compromise, a therapeutic alliance can be established which may provide a measure of symptom relief as well as improvements in rehabilitation potential.

Prudent, M., et al. (2012). "Proteomic analysis of Intercept-treated platelets." J Proteomics **76 Spec No.**: 316-328.

In the past decades, transfusion medicine has been driven by the quest for increased safety against transfusion-transmitted infections, mainly by better donor selection and by the development of improved serological and nucleic-acid-based screening assays. Recently, pathogen reduction technologies became available and started to be implemented in several countries, with the primary goal to fight against bacterial contamination of blood products, a rare but dramatic event against which there was no definitive measure. Though pathogen reduction technologies represent a quantum leap in transfusion safety, the biomedical efficacy of platelet concentrates (PCs) treated with various pathogen reduction techniques has been recently questioned by clinical studies. Here, a gel-based proteomic analysis of PCs (n=5), Intercept-treated or untreated, from pooled buffy-coat (10 donors per PC) at Days 1, 2 and 8, shows that the Intercept process that is the most widespread pathogen reduction technique to date, has relatively low impact on the proteome of treated platelets: the process induces modifications of DJ-1 protein, glutaredoxin 5, and G(i)alpha 2 protein. As for the impact of storage, chloride intracellular channel protein 4 (CLIC4) and actin increased independently of Intercept treatment

during storage. Whereas alteration of the DJ-1 protein and glutaredoxin 5 points out an oxidative stress-associated lesion, modification of G(i)alpha2 directly connects a possible Intercept-associated lesion to haemostatic properties of Intercept-treated platelets. This article is part of a Special Issue entitled: Integrated omics.

Qian, C., et al. (2018). "Facile synthetic Photoluminescent Graphene Quantum dots encapsulated beta-cyclodextrin drug carrier system for the management of macular degeneration: Detailed analytical and biological investigations." J Photochem Photobiol B **189**: 244-249.

Drug administration by effective nano-carriers is an emerging and growing technology in the field of bio-medicine and particularly Age -related macular degeneration (AMD). This developed nanomaterials based methods with drug administration maximizes the biocompatibility and systemically increases drug delivery profile for the drugs. Herein, we described the effective drug molecules delivery profiles by the hydrothermally synthesized graphene quantum dots (GQDs) encapsulated with supramolecular beta-cyclodextrin (beta-CD) as a drug delivery system for AMD. The drug release profiles were analysed and plotted by two different types of drugs ((Bevacizumab (Bev) and Ranibizumab (Ran))) and compounds displayed an initial burst delivery percentage of 55.7+/-1.6% and 52.2+/-2.6, respectively, within 15min. After 1h, 94.2% (Ran) and 93.1% (Bev) of loaded drug molecules were released from the beta-CD encapsulated GQDs in sustained manner. The biocompatibility of the synthesized carriers was investigated quantitatively and qualitatively with the mouse Fibroblast L929 cell line. The biological cell analysis observed by calculated cell count and green fluorescence visualization has been clearly confirmed the samples are non-toxic and highly compatible to the cells with more than 90% cell viability after 5days cell culture. The observed material properties and biological results demonstrated that the suitability of the developed nano-carriers for the drug delivery system in the AMD.

Qin, Y. G. (2007). "[The main mechanism of the reinforcing-reducing method in Huangdi's Internal Classic is to promote qi with thought]." Zhongguo Zhen Jiu **27**(3): 217-221.

Based on Huangdi' s Internal Classic and a great deal of clinical verification, in combination with new discoveries of the nerve, the meridian electromagnetic field and the quantum physics for role of thought outside body, it is proved that the main mechanism of the reinforcing-reducing method in Huangdi's Internal Classic is to promote flow of qi with the doctor's thought, with the needle very few twisted and rotated; discover new mechanisms of the reinforcing-reducing method, newly explain and clinically verify many basic standpoints about the reinforcing-reducing, and name as "acupuncture therapy of promoting qi with thought". The method has a strong reinforcing-reducing function and do not need the needle feeling, and is directly related with doctor's idea. It is emphasized specially that it can be carefully adopted only when full syndrome differentiation is made and strictly obey the contraindications in Huangdi's Internal Classic, otherwise it has very serious danger. This kind of model that doctor's mental effect is translated into the patient's biological effect put forward new problem, new thinking for brain sciences and modern acupuncture studies.

Quach, J. Q., et al. (2011). "Reconfigurable quantum metamaterials." Opt Express **19**(12): 11018-11033.

By coupling controllable quantum systems into larger structures we introduce the concept of a quantum metamaterial. Conventional meta-materials represent one of the most important frontiers in optical design, with applications in diverse fields ranging from medicine to aerospace. Up until now however, metamaterials have themselves been classical structures and interact only with the classical properties of light. Here we describe a class of dynamic metamaterials, based on the quantum properties of coupled atom-cavity arrays, which are intrinsically lossless, reconfigurable, and operate fundamentally at the quantum level. We show how this new class of metamaterial could be used to create a reconfigurable quantum superlens possessing a negative index gradient for single photon imaging. With the inherent features of quantum superposition and entanglement of metamaterial properties, this new class of dynamic quantum metamaterial, opens a new vista for quantum science and technology.

Quarta, A., et al. (2007). "Fluorescent-magnetic hybrid nanostructures: preparation, properties, and applications in biology." IEEE Trans Nanobioscience **6**(4): 298-308.

Research on nanocomposite materials aims at developing nanoscale composites with innovative optical, chemical, and magnetic properties, all combined in one single nanostructure. In this scenario, nanostructures which show simultaneously fluorescent and magnetic features are of particular interest for pharmaceutical and biomedical applications. In this review, we will focus our attention on magnetic-fluorescent nanocomposite based on colloidal iron oxide nanocrystals combined with different classes of fluorophores which can be either organic dyes, such as fluoresceins, cyanines, porphyrins, or colloidal

quantum dots. We will give an overview of the preparation methods of the magnetic-fluorescent nanocomposites that are now available and we will outline the most significant in vitro studies of such nanocomposites on living cells. Some examples of their applications in biology and medicine will also be discussed.

Raffa, V., et al. (2010). "Progress in nanotechnology for healthcare." Minim Invasive Ther Allied Technol **19**(3): 127-135.

This review based on the Wickham lecture given by AC at the 2009 SMIT meeting in Sinaia outlines the progress made in nano-technology for healthcare. It describes in brief the nature of nano-materials and their unique properties which accounts for the significant research both in scientific institutions and industry for translation into new therapies embodied in the emerging field of nano-medicine. It stresses that the potential of nano-medicine to make significant inroads for more effective therapies both for life-threatening and life-disabling disorders will only be achieved by high-quality life science research. The first generation of passive nano-diagnostics based on nanoparticle contrast agents for magnetic resonance imaging is well established in clinical practice and new such contrast agents are undergoing early clinical evaluation. Likewise active (second generation) nano-therapies, exemplified by targeted control drug release systems are undergoing early clinical evaluation. The situation concerning other nano-materials such as carbon nanotubes (CNTs) and boron nitride nanotubes (BNNTs) is less advanced although considerable progress has been made on their coating for aqueous dispersion and functionalisation to enable carriage of drugs, genes and fluorescent markers. The main problem related to the clinical use of these nanotubes is that there is no consent among scientists on the fate of such nano-materials following injection or implantation in humans. Provided carbon nanotubes are manufactured to certain medical criteria (length around 1 mum, purity of 97-99% and low Fe content) they exhibit no cytotoxicity on cell cultures and demonstrate full bio-compatibility on in vivo animal studies. The results of recent experimental studies have demonstrated the potential of technologies based on CNTs for low voltage wireless electro-chemotherapy of tumours and for electro-stimulation therapies for cardiac, neurodegenerative and skeletal and visceral muscle disorders.

Rai, A., et al. (2021). "Recent Advances and Implication of Bioengineered Nanomaterials in Cancer Theranostics." Medicina (Kaunas) **57**(2).

Cancer is one of the most common causes of death and affects millions of lives every year. In addition to non-infectious carcinogens, infectious agents contribute significantly to increased incidence of several cancers. Several therapeutic techniques have been used for the treatment of such cancers. Recently, nanotechnology has emerged to advance the diagnosis, imaging, and therapeutics of various cancer types. Nanomaterials have multiple advantages over other materials due to their small size and high surface area, which allow retention and controlled drug release to improve the anti-cancer property. Most cancer therapies have been known to damage healthy cells due to poor specificity, which can be avoided by using nanosized particles. Nanomaterials can be combined with various types of biomaterials to make it less toxic and improve its biocompatibility. Based on these properties, several nanomaterials have been developed which possess excellent anti-cancer efficacy potential and improved diagnosis. This review presents the latest update on novel nanomaterials used to improve the diagnostic and therapeutic of pathogen-associated and non-pathogenic cancers. We further highlighted mechanistic insights into their mode of action, improved features, and limitations.

Raikwar, S. P., et al. (2018). "Neuro-Immuno-Gene- and Genome-Editing-Therapy for Alzheimer's Disease: Are We There Yet?" J Alzheimers Dis **65**(2): 321-344.

Alzheimer's disease (AD) is a highly complex neurodegenerative disorder and the current treatment strategies are largely ineffective thereby leading to irreversible and progressive cognitive decline in AD patients. AD continues to defy successful treatment despite significant advancements in the field of molecular medicine. Repeatedly, early promising preclinical and clinical results have catapulted into devastating setbacks leading to multi-billion dollar losses not only to the top pharmaceutical companies but also to the AD patients and their families. Thus, it is very timely to review the progress in the emerging fields of gene therapy and stem cell-based precision medicine. Here, we have made sincere efforts to feature the ongoing progress especially in the field of AD gene therapy and stem cell-based regenerative medicine. Further, we also provide highlights in elucidating the molecular mechanisms underlying AD pathogenesis and describe novel AD therapeutic targets and strategies for the new drug discovery. We hope that the quantum leap in the scientific advancements and improved funding will bolster novel concepts that will propel the momentum toward a trajectory leading to a robust AD patient-specific next generation precision medicine with improved cognitive function and excellent life quality.

Ramanery, F. P., et al. (2013). "One-step colloidal synthesis of biocompatible water-soluble ZnS quantum

dot/chitosan nanoconjugates." Nanoscale Res Lett **8**(1): 512.

Quantum dots (QDs) are luminescent semiconductor nanocrystals with great prospective for use in biomedical and environmental applications. Nonetheless, eliminating the potential cytotoxicity of the QDs made with heavy metals is still a challenge facing the research community. Thus, the aim of this work was to develop a novel facile route for synthesising biocompatible QDs employing carbohydrate ligands in aqueous colloidal chemistry with optical properties tuned by pH. The synthesis of ZnS QDs capped by chitosan was performed using a single-step aqueous colloidal process at room temperature. The nanobioconjugates were extensively characterised by several techniques, and the results demonstrated that the average size of ZnS nanocrystals and their fluorescent properties were influenced by the pH during the synthesis. Hence, novel 'cadmium-free' biofunctionalised systems based on ZnS QDs capped by chitosan were successfully developed exhibiting luminescent activity that may be used in a large number of possible applications, such as probes in biology, medicine and pharmacy.

Rao, P. V. and S. H. Gan (2015). "Recent Advances in Nanotechnology-Based Diagnosis and Treatments of Diabetes." Curr Drug Metab **16**(5): 371-375.

Nanotechnology is a field encompassing nanostructures, nanomaterials and nanoparticles, which are of increasing importance to researchers and industrial players alike. Nanotechnology addresses the construction and consumption of substances and devices on the nanometer scale. Nanomedicine is a new field that combines nanotechnology with medicine to boost human health care. Nanomedicine is an interdisciplinary field that includes various areas of biology, chemistry, physics and engineering. The most important problems related to diabetes management, such as self-monitoring of blood glucose levels and insulin injections, can now be conquered due to progress in nanomedicine, which offers glucose nanosensors, the layer-by-layer technique, carbon nanotubes, quantum dots, oral insulins, microspheres, artificial pancreases and nanopumps. In this review, the key methodological and scientific characteristics of nanomedicine related to diabetes treatment, glucose monitoring and insulin administration are discussed.

Rasool, M., et al. (2015). "Recent Developments in Nanomedicines for Management of Various Health Issues Via Metabolism and Physico-Chemical Properties." Curr Drug Metab **16**(5): 389-396.

During the last decade the nanotechnologists began research on applications of nanomaterials for medicine and therapeutics. Various nanoparticles (nanomedicines) are being used worldwide for the diagnosis and management in a number of disorders including cancer and neurodegenerative disorders. The successful non-viral gene therapy is now possible with the advancements in nanotechnology. Mostly nanoparticles are divided into two main classes: organic and inorganic nanoparticles. Diverse features of nanomedicines with surface modification help to make them biocompatible with addition of varying polymer that facilitates targeted delivery of drug and its controlled release into the cells, tissues and organs. Liposomes, quantum dots, silver and gold nanoparticles are the most common examples of nanomedicines.

Rassel, S., et al. (2020). "Noninvasive blood glucose detection using a quantum cascade laser." Analyst **145**(7): 2441-2456.

A Quantum Cascade Laser (QCL) was invented in the late 90s as a promising mid-infrared light source and it has contributed to the fields of industry, military, medicine, and biology. The room temperature operation, watt-level output power, compact size, and wide tuning capability of this laser advanced the field of noninvasive blood glucose detection with the use of transmission, absorption, and photoacoustic spectroscopy. This review provides a complete overview of the recent progress and technical details of these spectroscopy techniques, using QCL as an infrared light source for detecting blood glucose concentrations in diabetic patients.

Ratnikova, T. A., et al. (2012). "Biophysical methods for assessing plant responses to nanoparticle exposure." Methods Mol Biol **926**: 383-398.

As nanotechnology rapidly emerges into a new industry-driven by its enormous potential to revolutionize electronics, materials, and medicine-exposure of living species to discharged nanoparticles has become inevitable. Despite the increased effort on elucidating the environmental impact of nanotechnology, literature on higher plants exposure to nanoparticles remains scarce and often contradictory. Here we present our biophysical methodologies for the study of carbon nanoparticle uptake by Allium cepa cells and rice plants. We address the three essential aspects for such studies: identification of carbon nanoparticles in the plant species, quantification of nanotransport and aggregation in the plant compartments, and evaluation of plant responses to nanoparticle exposure on the cellular and organism level. Considering the close connection between plant and mammalian species in ecological systems especially in the food chain, we draw a direct comparison on the uptake of carbon nanoparticles in plant and mammalian cells. In addition to the above

studies, we present methods for assessing the effects of quantum dot adsorption on algal photosynthesis.

Reen, F. J., et al. (2015). "The Sound of Silence: Activating Silent Biosynthetic Gene Clusters in Marine Microorganisms." Mar Drugs **13**(8): 4754-4783.

Unlocking the rich harvest of marine microbial ecosystems has the potential to both safeguard the existence of our species for the future, while also presenting significant lifestyle benefits for commercial gain. However, while significant advances have been made in the field of marine biodiscovery, leading to the introduction of new classes of therapeutics for clinical medicine, cosmetics and industrial products, much of what this natural ecosystem has to offer is locked in, and essentially hidden from our screening methods. Releasing this silent potential represents a significant technological challenge, the key to which is a comprehensive understanding of what controls these systems. Heterologous expression systems have been successful in awakening a number of these cryptic marine biosynthetic gene clusters (BGCs). However, this approach is limited by the typically large size of the encoding sequences. More recently, focus has shifted to the regulatory proteins associated with each BGC, many of which are signal responsive raising the possibility of exogenous activation. Abundant among these are the LysR-type family of transcriptional regulators, which are known to control production of microbial aromatic systems. Although the environmental signals that activate these regulatory systems remain unknown, it offers the exciting possibility of evoking mimic molecules and synthetic expression systems to drive production of potentially novel natural products in microorganisms. Success in this field has the potential to provide a quantum leap forward in medical and industrial bio-product development. To achieve these new endpoints, it is clear that the integrated efforts of bioinformaticians and natural product chemists will be required as we strive to uncover new and potentially unique structures from silent or cryptic marine gene clusters.

Reimers, J. R., et al. (2009). "Weak, strong, and coherent regimes of Frohlich condensation and their applications to terahertz medicine and quantum consciousness." Proc Natl Acad Sci U S A **106**(11): 4219-4224.

In 1968, Frohlich showed that a driven set of oscillators can condense with nearly all of the supplied energy activating the vibrational mode of lowest frequency. This is a remarkable property usually compared with Bose-Einstein condensation, superconductivity, lasing, and other unique phenomena involving macroscopic quantum coherence. However, despite intense research, no unambiguous example has been documented. We determine the most likely experimental signatures of Frohlich condensation and show that they are significant features remote from the extraordinary properties normally envisaged. Frohlich condensates are classified into 3 types: weak condensates in which profound effects on chemical kinetics are possible, strong condensates in which an extremely large amount of energy is channeled into 1 vibrational mode, and coherent condensates in which this energy is placed in a single quantum state. Coherent condensates are shown to involve extremely large energies, to not be produced by the Wu-Austin dynamical Hamiltonian that provides the simplest depiction of Frohlich condensates formed using mechanically supplied energy, and to be extremely fragile. They are inaccessible in a biological environment. Hence the Penrose-Hameroff orchestrated objective-reduction model and related theories for cognitive function that embody coherent Frohlich condensation as an essential element are untenable. Weak condensates, however, may have profound effects on chemical and enzyme kinetics, and may be produced from biochemical energy or from radio frequency, microwave, or terahertz radiation. Pokorny's observed 8.085-MHz microtubulin resonance is identified as a possible candidate, with microwave reactors (green chemistry) and terahertz medicine appearing as other feasible sources.

Rein, G. (2004). "Bioinformation within the biofield: beyond bioelectromagnetics." J Altern Complement Med **10**(1): 59-68.

This review article extends previous scientific definitions of the biofield (endogenous energy fields of the body) to include nonclassical and quantum energy fields. The biofield is defined further in terms of its functional property to act as a resonance target for external forms of energy used as treatment modalities in energy medicine. The functional role of the biofield in the body's innate self-healing mechanisms is hypothesized, based on the concept of bioinformation which, mediated by consciousness, functions globally at the quantum level to supply coherence, phase, spin, and pattern information to regulate and heal all physiologic processes. This model is used to explain a wide variety of anomalies reported in the scientific literature, which can not be explained by traditional biophysics and bioelectromagnetics.

Reis, H., et al. (2015). "Reliable but Timesaving: In Search of an Efficient Quantum-chemical Method for the Description of Functional Fullerenes." Curr Top Med Chem **15**(18): 1845-1858.

Fullerene and its derivatives are currently one of the most intensively investigated species in the area of nanomedicine and nanochemistry. Various unique properties of fullerenes are responsible for their wide

range applications in industry, biology and medicine. A large pool of functionalized C60 and C70 fullerenes is investigated theoretically at different levels of quantum-mechanical theory. The semiempirial PM6 method, density functional theory with the B3LYP functional, and correlated ab initio MP2 method are employed to compute the optimized structures, and an array of properties for the considered species. In addition to the calculations for isolated molecules, the results of solution calculations are also reported at the DFT level, using the polarizable continuum model (PCM). Ionization potentials (IPs) and electron affinities (EAs) are computed by means of Koopmans' theorem as well as with the more accurate but computationally expensive DeltaSCF method. Both procedures yield comparable values, while comparison of IPs and EAs computed with different quantum-mechanical methods shows surprisingly large differences. Harmonic vibrational frequencies are computed at the PM6 and B3LYP levels of theory and compared with each other. A possible application of the frequencies as 3D descriptors in the EVA (EigenVAlues) method is shown. All the computed data are made available, and may be used to replace experimental data in routine applications where large amounts of data are required, e.g. in structure-activity relationship studies of the toxicity of fullerene derivatives.

Richards, K. (2013). "Wellpower: the foundation of innovation." Nurs Econ **31**(2): 94-98.

The financial and human costs of compassion fatigue and burnout can be devastating. In the haste to "get more done," are we hardwiring our caregivers for disaster? The lifestyle choices we make and the degree of self-care we practice are paramount to not only our individual quality and quantity of life and our immediate circle of influence but holds the profound potential to create quantum change within our health care system. For nurses, who are the most influential force for health care reform in America, the time to emulate wellness has never been more critical. By creating healthy habits for ourselves, we flourish as ambassadors of self-care for our patients, families, colleagues, and communities. As we move forward with health care reform, the most powerful influence that we, as nurse leaders can wield is to practice regular self-care, healthy lifestyles, and preventative medicine.

Richter, S. (1976). "[Wolfgang Pauli and the origin of the spin-concept]." Gesnerus **33**(3-4): 253-270.

Rieth, M. and W. Schommers (2002). "Computational engineering of metallic nanostructures and nanomachines." J Nanosci Nanotechnol **2**(6): 679-685.

Small structures with dimensions in the nanometer regime play an important role within a lot of modern technological branches like, for example, genetics, chip fabrication, material science, medicine, or chemistry. While highly sophisticated characterization methods would be necessary to study such nanostructures, computational methods and models have made their entrance into the field of nanotechnology. The present work gives an overview of the problems connected with quantum mechanics, many-particle systems, and nanophysical models. Further, the application of molecular dynamics (MD)--a typical computational method suitable for modelling at the nanolevel--is introduced and outlined. The setup and use of specific MD models, advanced computation techniques, and efficient algorithms are discussed, while the focus is laid on the subjects nanodesign and nanoengineering which are demonstrated for the example of metallic nanostructures. Finally, the introduced techniques and methods are applied to stability studies of theoretical nanomachines.

Robidillo, C. J. T. and J. G. C. Veinot (2020). "Functional Bio-inorganic Hybrids from Silicon Quantum Dots and Biological Molecules." ACS Appl Mater Interfaces **12**(47): 52251-52270.

Quantum dots (QDs) are semiconductor nanoparticles that exhibit photoluminescent properties useful for applications in the field of diagnostics and medicine. Successful implementation of these QDs for bio-imaging and bio/chemical sensing typically involves conjugation to biologically active molecules for recognition and signal generation. Unfortunately, traditional and widely studied QDs are based upon heavy metals and other toxic elements (e.g., Cd- and Pb-based QDs), which precludes their safe use in actual biological systems. Silicon quantum dots (SiQDs) offer the same advantages as these heavy-metal-based QDs with the added benefits of nontoxicity and abundance. The preparation of functional bio-inorganic hybrids from SiQDs and biomolecules has lagged significantly compared to their traditional toxic counterparts because of the challenges associated with the synthesis of water-soluble SiQDs and their relative instability in aqueous environments. Advances in SiQD synthesis and surface functionalization, however, have made possible the preparation of functional bio-inorganic hybrids from SiQDs and biological molecules through different bioconjugation reactions. In this contribution, we review the various bioconjugate reactions by which SiQDs have been linked to biomolecules and implemented as platforms for bio-imaging and bio/chemical sensing. We also highlight the challenges that need to be addressed and overcome for these materials to reach their full potential. Lastly, we give prospective applications where this unique class of nontoxic and biocompatible materials can be of great utility in the future.

Robson, B. (2005). "Clinical and pharmacogenomic data mining: 3. Zeta theory as a general tactic for clinical bioinformatics." J Proteome Res **4**(2): 445-455.

A new approach, a Zeta Theory of observations, data, and data mining, is being forged from a theory of expected information into an even more cohesive and comprehensive form by the challenge of general genomic, pharmacogenomic, and proteomic data. In this paper, the focus is not on studies using the specific tool FANO (CliniMiner) but on extensions to a new broader theoretical approach, aspects of which can easily be implemented into, or otherwise support, excellent existing methods, such as forms of multivariate analysis and IBM's product Intelligent Miner. The theory should perhaps be distinguished from an existing purely number-theoretic area sometimes also known as Zeta Theory, which focuses on the Riemann Zeta Function and the ways in which it governs the distribution of prime numbers. However, Zeta Theory as used here overlaps heavily with it and actually makes use of these same matters. The distinction is that it enters from a Bayesian information theory and data representation perspective. It could thus be considered an application of the 'mathematician's version'. The application is by no means confined to areas of modern biomedicine, and indeed its generality, even merging into quantum mechanics, is a key feature. Other areas with some similar challenges as modern biology, and which have inspired data mining methods such as IBM's Intelligent Miner, include commerce. But for several reasons discussed, modern molecular biology and medicine seem particularly challenging, and this relates to the often irreducible high dimensionality of the data. This thus remains our main target.

Robson, B. (2007). "The new physician as unwitting quantum mechanic: is adapting Dirac's inference system best practice for personalized medicine, genomics, and proteomics?" J Proteome Res **6**(8): 3114-3126.

What is the Best Practice for automated inference in Medical Decision Support for personalized medicine? A known system already exists as Dirac's inference system from quantum mechanics (QM) using bra-kets <A | B> and bras <A| and kets |B> where A and B are states, events, or measurements representing, say, clinical and biomedical rules. Dirac's system should theoretically be the universal best practice for all inference, though QM is notorious as sometimes leading to bizarre conclusions that appear not to be applicable to the macroscopic world of everyday world human experience and medical practice. It is here argued that this apparent difficulty vanishes if QM is assigned one new multiplication function @, which conserves conditionality appropriately, making QM applicable to classical inference including a quantitative form of the predicate calculus. An alternative interpretation with the same consequences is if every i = radical-1 in Dirac's QM is replaced by h, an entity distinct from 1 and i and arguably a hidden root of 1 such that h2 = 1. With that exception, this paper is thus primarily a review of the application of Dirac's system, by application of linear algebra in the complex domain to help manipulate information about associations and ontology in complicated data. Any combined bra-ket <A | B> can be shown to be composed only of the sum of QM-like bra and ket weights c(<A|) and c(|B>), times an exponential function of Fano's mutual information measure I(A; B) about the association between A and B, that is, an association rule from data mining. With the weights and Fano measure re-expressed as expectations on finite data using Riemann's Incomplete (i.e., Generalized) Zeta Functions, actual counts of observations for real world sparse data can be readily utilized. Finally, the paper compares identical character, distinguishability of states events or measurements, correlation, mutual information, and orthogonal character, important issues in data mining and biomedical analytics, as in QM.

Robson, B. (2014). "Hyperbolic Dirac Nets for medical decision support. Theory, methods, and comparison with Bayes Nets." Comput Biol Med **51**: 183-197.

We recently introduced the concept of a Hyperbolic Dirac Net (HDN) for medical inference on the grounds that, while the traditional Bayes Net (BN) is popular in medicine, it is not suited to that domain: there are many interdependencies such that any "node" can be ultimately conditional upon itself. A traditional BN is a directed acyclic graph by definition, while the HDN is a bidirectional general graph closer to a diffuse "field" of influence. Cycles require bidirectionality; the HDN uses a particular type of imaginary number from Diracs quantum mechanics to encode it. Comparison with the BN is made alongside a set of recipes for converting a given BN to an HDN, also adding cycles that do not usually require reiterative methods. This conversion is called the P-method. Conversion to cycles can sometimes be difficult, but more troubling was that the original BN had probabilities needing adjustment to satisfy realism alongside the important property called "coherence". The more general and simpler K-method, not dependent on the BN, is usually (but not necessarily) derived by data mining, and is therefore also introduced. As discussed, BN developments may converge to an HDN-like concept, so it is reasonable to consider the HDN as a BN extension.

Robson, B. and S. Boray (2016). "Data-mining to build a knowledge representation store for clinical decision support. Studies on curation and validation based on

machine performance in multiple choice medical licensing examinations." Comput Biol Med **73**: 71-93.

Extracting medical knowledge by structured data mining of many medical records and from unstructured data mining of natural language source text on the Internet will become increasingly important for clinical decision support. Output from these sources can be transformed into large numbers of elements of knowledge in a Knowledge Representation Store (KRS), here using the notation and to some extent the algebraic principles of the Q-UEL Web-based universal exchange and inference language described previously, rooted in Dirac notation from quantum mechanics and linguistic theory. In a KRS, semantic structures or statements about the world of interest to medicine are analogous to natural language sentences seen as formed from noun phrases separated by verbs, prepositions and other descriptions of relationships. A convenient method of testing and better curating these elements of knowledge is by having the computer use them to take the test of a multiple choice medical licensing examination. It is a venture which perhaps tells us almost as much about the reasoning of students and examiners as it does about the requirements for Artificial Intelligence as employed in clinical decision making. It emphasizes the role of context and of contextual probabilities as opposed to the more familiar intrinsic probabilities, and of a preliminary form of logic that we call presyllogistic reasoning.

Robson, B. and S. Boray (2016). "Studies of the role of a smart web for precision medicine supported by biobanking." Per Med **13**(4): 361-380.

Both the extraction of medical knowledge from data mining many patient records and from authoritative natural language text on the Internet are important for clinical decision support and biomedical research. The samples in biobanks represent a further kind of information repository of recognized increasing importance, so mechanisms being developed for a smart web for medicine should take them into account. While this paper is primarily a review of Quantum Universal Exchange Language as an XML extension to enable a future smart web for healthcare and biomedicine, it is the first time that we have discussed the connection with biobanks and the design of Quantum Universal Exchange Language's XML-like tags to support their use.

Robson, B., et al. (2013). "Suggestions for a Web based universal exchange and inference language for medicine." Comput Biol Med **43**(12): 2297-2310.

Mining biomedical and pharmaceutical data generates huge numbers of interacting probabilistic statements for inference, which can be supported by mining Web text sources. This latter can also be probabilistic, in a sense described in this report. However, the diversity of tools for probabilistic inference is troublesome, suggesting a need for a unifying best practice. Physicists often claim that quantum mechanics is the universal best practice for probabilistic reasoning. We discuss how the Dirac notation and algebra suggest the form and algebraic and semantic meaning of XML-like Web tags for a clinical and biomedical universal exchange language formulated to make sense directly to the eye of the physician and biomedical researcher.

Rode, A., et al. (2018). "Carbon Nanotubes: Classification, Method of Preparation and Pharmaceutical Application." Curr Drug Deliv **15**(5): 620-629.

Nanoscience and nanotechnology are emerging areas in the pharmaceutical sciences and the need of modernizing world. Nanoscience is the world of atoms, macromolecular assemblies, macromolecules, quantum dots, and molecules. Nanoscience is the study, and understanding control of phenomena and manipulation of material at the nanoscale. Carbon nanotubes are a tube like material mainly made up of carbon. Only carbon nanotubes are the macromolecules of graphite consisting of sheets of carbon, which is weaved into the cylinder. Graphite sheets look like a hexagonal in shape Nano carbon tubes are about 2 millimetres long and these are one hundred times as stiff as steel. The arrangement of atom in a carbon nanotube is in a form of hexagonal as like as graphite. Carrying capacity of carbon nanotube is 1000 times higher than that of copper thermal stability of it is 4000k, it can be semiconducting or metallic, depending on their diameter and chirality of the atom. These carbon nanotubes having various classifications like single walled CNT's, Multiwalled CNT's, Nano horns, Nano buds, polymerized single walled nanotubes. The review is more focused towards the methods of preparation of nanotubes and their general various applications in pharmacy and medicine along with toxicity. These carbon Nano tubes can be prepared by using various methods with successful ease or application in pharmaceuticals, i.e. gas storage, adsorption, catalyst supported, delivery of drug through targeted system, electrochemistry, bio sensing, fuel cell, photodynamic cells, etc. CNT's are advanced technology in the era of nanotechnology in pharmaceutical sciences which are more emphasizing on patient's compliance and safety. Possessing a broad area of application along with targeted drug delivery. The Scientists are still exploring the various applications of it.

Rode, J. E., et al. (2011). "Phenylisoserine in the gas-phase and water: Ab initio studies on neutral and zwitterion conformers." J Mol Model **17**(5): 961-970.

The conformational landscape of phenylisoserine (PhIS) was studied. Trial structures were generated by allowing for all combinations of

single-bond rotamers. Based on the B3LYP/aug-cc-pVDZ calculations 54 conformers were found to be stable in the gas phase. The six most stable conformers were further optimized at the B3LYP/aug-cc-pVTZ and MP2/aug-cc-pVDZ levels for which characteristic intramolecular hydrogen bond types were classified. To estimate the influence of water on PhIS conformation, the IEF-PCM/B3LYP/aug-cc-pVDZ calculations were carried out and showed 51 neutral and six zwitterionic conformers to be stable in water solution. According to DFT calculations, the conformer equilibrium in the gas phase is dominated by one conformer, whereas the MP2 calculations suggest three PhIS structures to be significantly populated. Comparison of DFT and MP2 energies of all 57 structures stable in water indicates that, in practice, one zwitterionic and one neutral conformer determine the equilibrium in water. Based on the AIM calculations, we found that for the neutral conformers in vacuum and in water, d(H...B) is linearly correlated with Laplacian at the H-bond critical point. Figure Phenylisoserine (PhIS) is an active side chain of cytotoxic Paclitaxel medicine. The conformational landscape of phenylisoserine was studied. One zwitterionic and one neutralconformer determine the equilibrium in water whereas in the gas phase the MP2 calculations suggest three PhIS structures to be significantly populated.

Rogers, D. W. and A. A. Zavitsas (2017). "Long Chain Saturated and Unsaturated Carboxylic Acids: Filling a Large Gap of Knowledge in Their Enthalpies of Formation." J Org Chem **82**(1): 673-679.

Despite their abundance in nature and their importance in biology, medicine, nutrition, and in industry, gas phase enthalpies of formation of many long chain saturated and unsaturated fatty acids and of dicarboxylic acids are either unavailable or have been estimated with large uncertainties. Available experimental values for stearic acid show a spread of 68 kJ mol(-1). This work fills the knowledge gap by obtaining reliable values by quantum theoretical calculations using G4 model chemistry. Compounds with up to 20 carbon atoms are treated. The theoretical results are in excellent agreement with well established experimental values when such values exist, and they provide a large number of previously unavailable values.

Rohrich, R. J. (2008). "What if the world had 100 people? Counting our blessings in a quantum world." Plast Reconstr Surg **122**(2): 659-661.

Rojas-Chapana, J. A. and M. Giersig (2006). "Multi-walled carbon nanotubes and metallic nanoparticles and their application in biomedicine." J Nanosci Nanotechnol **6**(2): 316-321.

Interdisciplinary research has become a matter of paramount importance for novel applications of nanomaterials in biology and medicine. As such, many disciplines-physics, chemistry, microbiology, cell biology, and material science-all contribute to the design, synthesis and fabrication of functional and biocompatible devices at the nanometer scale. Since the most areas of cell biology and biomedicine deal with functional entities such as DNA and proteins, mimicry of these structures and function in the nanosize range offers exciting opportunities for the development of biosensors, biochips, and bioplatforms. In this report we highlight the potential benefits and challenges that arise in the manufacture of biocompatible nanoparticles and nano-networks that can be coupled with biological objects. Among the challenges facing us are those concerned with making the necessary advances in enabling affordability, innovation, and quality of manufactured nanodevices for rapid progress in the emerging field of bio-nanotechnology. The convergence of nanotechnology and biomedicine makes nanoscale research highly promising for new discoveries that can cost-effectively accelerate progress in moving from basic research to practical prototypes and products.

Romero-Morelos, P., et al. (2011). "[The nanotechnology as a support for diagnosis and prognosis in cancer research]." Rev Med Inst Mex Seguro Soc **49**(6): 621-630.

Recently, technological advances have greatly increased, generating the development of nanotechnology, which is responsible for the design of structures and materials in the nanometer scale. This creates one of the most important cutting-edge sciences, integrating physics, chemistry, engineering and biology sciences. Specifically the integration with biology results in a new science called nanobiotechnology, specifically nanomedicine, which has the goal of mainly looking for more precise molecular diagnostic and prognostic processes, as well as the new design of drugs in the personalized medicine field. On the other hand, at molecular level in medical research, the nanoparticles are most commonly used as tools. Molecular diagnostics uses gold nanoparticles, paramagnetic nanoparticles and quantum dots, which can be used for the diagnosis and treatment of several diseases, including cancer. Quantum dots are the most promising tools for diagnosis and therapy in cancer research.

Ronconi, L. and P. J. Sadler (2008). "Applications of heteronuclear NMR spectroscopy in biological and medicinal inorganic chemistry." Coord Chem Rev **252**(21): 2239-2277.

There is a wide range of potential applications of inorganic compounds, and metal coordination complexes in particular, in medicine but progress is hampered by a lack of methods to study their speciation. The biological activity of metal complexes

is determined by the metal itself, its oxidation state, the types and number of coordinated ligands and their strength of binding, the geometry of the complex, redox potential and ligand exchange rates. For organic drugs a variety of readily observed spin I = 1/2 nuclei can be used ((1)H, (13)C, (15)N, (19)F, (31)P), but only a few metals fall into this category. Most are quadrupolar nuclei giving rise to broad lines with low detection sensitivity (for biological systems). However we show that, in some cases, heteronuclear NMR studies can provide new insights into the biological and medicinal chemistry of a range of elements and these data will stimulate further advances in this area.

Ronkainen, N. J. and S. L. Okon (2014). "Nanomaterial-Based Electrochemical Immunosensors for Clinically Significant Biomarkers." Materials (Basel) **7**(6): 4669-4709.

Nanotechnology has played a crucial role in the development of biosensors over the past decade. The development, testing, optimization, and validation of new biosensors has become a highly interdisciplinary effort involving experts in chemistry, biology, physics, engineering, and medicine. The sensitivity, the specificity and the reproducibility of biosensors have improved tremendously as a result of incorporating nanomaterials in their design. In general, nanomaterials-based electrochemical immunosensors amplify the sensitivity by facilitating greater loading of the larger sensing surface with biorecognition molecules as well as improving the electrochemical properties of the transducer. The most common types of nanomaterials and their properties will be described. In addition, the utilization of nanomaterials in immunosensors for biomarker detection will be discussed since these biosensors have enormous potential for a myriad of clinical uses. Electrochemical immunosensors provide a specific and simple analytical alternative as evidenced by their brief analysis times, inexpensive instrumentation, lower assay cost as well as good portability and amenability to miniaturization. The role nanomaterials play in biosensors, their ability to improve detection capabilities in low concentration analytes yielding clinically useful data and their impact on other biosensor performance properties will be discussed. Finally, the most common types of electroanalytical detection methods will be briefly touched upon.

Rosch, P. J. and H. M. Kearney (1985). "Holistic medicine and technology: a modern dialectic." Soc Sci Med **21**(12): 1405-1409.

This is an attempt to present a comprehensive overview of two major trends in American medicine which suggests significant evolutionary biopsychosocial developments in the remaining decades of the 20th century. Comments have been confined to the U.S. because it is the geographical country of residence and practice of the authors, and because the U.S. appears to be the locus of two contemporaneous and seemingly antithetical popular movements: quantum leaps in the development and use of medical technology and a groundswell of interest and enthusiasm for health enhancement or wellness which advocates a natural approach to health and emphasizes the central role of the individual in the preservation of health and the prevention of illness. The dynamics of this modern dialectic in American medicine have generated important qualitative consequences in the nature of the doctor-patient relationship and the delivery of health care. They have also, it is submitted, generated the search for a new paradigm which will permit a workable equilibrium between the disparate imperatives of both movements. The delicate process of developing that equilibrium is made more difficult by the co-existence of a host of complex factors, many of which are inextricably interwoven with one or the other of these two major trends.(ABSTRACT TRUNCATED AT 250 WORDS)

Rosen, P. (1987). "The future of emergency medicine." Emerg Med Clin North Am **5**(1): 133-147.

I have made some predictions about what I feel will be the future of our specialty. I have carefully avoided entering into details of our practice because these will evolve gradually rather than in predictable quantum jumps. Although I fear and believe that the economic future of medicine lies with the corporate entity, and that more and more physicians will become employees of such corporations, I don't believe that this alters the professional responsibilities, nor do I think it will interfere with professional satisfactions. I believe that so long as the field continues to believe its primary mission is that of the life or limb threat, that there will continue to be a need for the specialty of Emergency Medicine. Finally I believe that given that mission, there is now and will continue to be in the future, no more fulfilling career.

Rosenow, U. F. (1995). "Notes on the legacy of the Rontgen rays." Med Phys **22**(11 Pt 2): 1855-1867.

The discovery of the Rontgen rays and the events connected to it are extraordinary in many respects. Rontgen never disclosed the full details of the experiment which led to the discovery on November 8, 1895. He observed the x-rays by chance. Neither he nor any other scientist had an idea that such radiation might exist. However, it needed a Rontgen to make the discovery, an experimenter of his superior capabilities. His achievement was the culmination point of the development of physics as an experimental science in the 19th Century. This development of physics is described in this report in some detail, together with the institutional structure of university physics in Germany and the status of technical achievements at the time of

Rontgen. Rontgen was suspicious, if not disdainful, of theoretical physics which slowly had gained in importance and in institutional representation. Thus, Rontgen's famous discovery, possible only to a mind not prejudiced by theoretical considerations or expectations, happened at a point in the history of physics when predominantly theoretical concepts introduced the paradigm change from "classical" to "modern" physics: Maxwell's electromagnetic theory, Planck's quantum hypothesis, and Einstein's relativity principle and explanation of the photo-electric effect. The tremendous speed by which the news of the "new kind of rays" spread around the world and the sensation this news caused launched an intensity of research on x-rays unprecedented in other areas of research and is reflected in a description of the publication history. The traditional working style of the Institute Director Rontgen, the structure of his Institute, his lack of interest in theory, the burden of his sudden fame and other factors made it practically impossible for him to compete with the rapid development and to contribute substantially to the research on x-rays. Even the award of the first Nobel Prize in physics in 1901 did not stimulate him to undertake new research activities. He even succeeded in avoiding presentation of his Nobel Lecture. He took the role of the interested observer, sometimes diverted by priority disputes, mainly with Lenard, or by sensational press reports, and retreated increasingly into final solitude, possibly his answer also to the abundance of honors heaped upon him. The impact of his discovery was, however, enormous. In physics it gave impulses to the discovery of radioactivity, of the identification of the electron, and the development of the model of the atom; and in medicine in its immediate applications in diagnosis and therapy.

Rossi, D., et al. (2017). "(R)-(-)-Aloesaponol III 8-Methyl Ether from Eremurus persicus: A Novel Compound against Leishmaniosis." Molecules **22**(4).

Leishmaniosis is a neglected tropical disease which affects several millions of people worldwide. The current drug therapies are expensive and often lack efficacy, mainly due to the development of parasite resistance. Hence, there is an urgent need for new drugs effective against Leishmania infections. As a part of our ongoing study on the phytochemical characterization and biological investigation of plants used in the traditional medicine of western and central Asia, in the present study, we focused on Eremurus persicus root extract in order to evaluate its potential in the treatment of leishmaniosis. As a result of our study, aloesaponol III 8-methyl ether (ASME) was isolated for the first time from Eremurus persicus root extract, its chemical structure elucidated by means of IR and NMR experiments and the (R) configuration assigned by optical activity measurements: chiroptical aspects were investigated with vibrational circular dichroism (VCD) and electronic circular dichroism (ECD) spectroscopies and DFT (density functional theory) quantum mechanical calculations. Concerning biological investigations, our results clearly proved that (R)-ASME inhibits Leishmania infantum promastigotes viability (IC50 73 microg/mL), inducing morphological alterations and mitochondrial potential deregulation. Moreover, it is not toxic on macrophages at the concentration tested, thus representing a promising molecule against Leishmania infections.

Ruan, S., et al. (2015). "Noninvasive In Vivo Diagnosis of Brain Glioma Using RGD-Decorated Fluorescent Carbonaceous Nanospheres." J Biomed Nanotechnol **11**(12): 2148-2157.

Fluorescent carbonaceous nanospheres (CDs) have gained significant attention because of their promising applications, especially in biology and medicine, due to their unique properties. However, the application of CDs in the noninvasive imaging of diseased tissues has been restricted by the poor targeting efficiency of CDs. In this study, CDs were prepared from sucrose and glutamic acid with a particle size of 122.5 nm. Due to quantum confinement in the nanoparticles, CDs exhibited emission from 450 to 600 nm upon excitation at approximately 400 nm. This feature made it possible to use the CDs for low-background bioimaging of deep diseased tissues. RGD, a ligand that can target alpha(v)beta3, which is highly expressed on most tumor and neovascular cells, was decorated onto the CDs after PEGylation. The product, RGD-PEG-CDs, possessed low cytotoxicity, as determined by MTT assay. In vitro, RGD-PEG-CDs targeted U87 (a human brain glioma cell line) cells with a higher cellular uptake intensity than CDs and PEGylated CDs (PEG-CDs), and endosomes were involved in the uptake procedure. The internalization of RGD-PEG-CDs, PEG-CDs and CDs all were primarily mediated by macropinocytosis and a clathrin-mediated pathway, which were energy-dependent. Additionally, the uptake of RGD-PEG-CDs could be significantly inhibited by free RGD, indicating that the uptake was mediated by the receptor of RGD. In vivo, RGD-PEG-CDs accumulated in U87 glioma at high intensity, at values that were 1.67- and 1.64-fold higher than those of PEG-CDs and CDs. Furthermore, RGD-PEG-CDs exhibited good colocalization with neovasculature. In conclusion, RGD-PEG-CDs could be successfully used for noninvasive U87 glioma imaging.

Rusakova, I. L. and Y. Y. Rusakov (2021). "Quantum chemical calculations of (77) Se and (125) Te nuclear magnetic resonance spectral parameters and their structural applications." Magn Reson Chem **59**(4): 359-407.

An accurate quantum chemical (QC) modeling of (77) Se and (125) Te nuclear magnetic

resonance (NMR) spectra is deeply involved in the NMR structural assignment for selenium and tellurium compounds that are of utmost importance both in organic and inorganic chemistry nowadays due to their huge application potential in many fields, like biology, medicine, and metallurgy. The main interest of this review is focused on the progress in QC computations of (77) Se and (125) Te NMR chemical shifts and indirect spin-spin coupling constants involving these nuclei. Different computational methodologies that have been used to simulate the NMR spectra of selenium and tellurium compounds since the middle of the 1990s are discussed with a strong emphasis on their accuracy. A special accent is placed on the calculations resorting to the relativistic methodologies, because taking into account the relativistic effects appreciably influences the precision of NMR calculations of selenium and, especially, tellurium compounds. Stereochemical applications of quantum chemical calculations of (77) Se and (125) Te NMR parameters are discussed so as to exemplify the importance of integrated approach of experimental and computational NMR techniques.

Russell, A. L., et al. (2018). "Characterization and cost-benefit analysis of automated bioreactor-expanded mesenchymal stem cells for clinical applications." Transfusion **58**(10): 2374-2382.

BACKGROUND: Expanding quantities of mesenchymal stem cells (MSCs) sufficient to treat large numbers of patients in cellular therapy and regenerative medicine clinical trials is an ongoing challenge for cell manufacturing facilities. STUDY DESIGN AND METHODS: We evaluated options for scaling up large quantities of bone marrow-derived MSCs (BM-MSCs) using methods that can be performed in compliance with Good Manufacturing Practices (GMP). We expanded BM-MSCs from fresh marrow aspirate in alphaMEM supplemented with 5% human platelet lysate using both an automated cell expansion system (Quantum, Terumo BCT) and a manual flask-based method using multilayer flasks. We compared MSCs expanded using both methods and assessed their differentiation to adipogenic and osteogenic tissue, capacity to suppress T-cell proliferation, cytokines, and growth factor secretion profile and cost-effectiveness of manufacturing enough BM-MSCs to administer a single dose of 100 x 10(6) cells per subject in a clinical trial of 100 subjects. RESULTS: We have established that large quantities of clinical-grade BM-MSCs manufactured with an automated hollow-fiber bioreactor were phenotypically (CD73, CD90, CD105) and functionally (adipogenic and osteogenic differentiation and cytokine and growth factor secretion) similar to manually expanded BM-MSCs. In addition, MSC manufacturing costs significantly less and required less time and effort when using the Quantum automated cell expansion system over the manual multilayer flasks method. CONCLUSION: MSCs manufactured by an automated bioreactor are physically and functionally equivalent to the MSCs manufactured by the manual flask method and have met the standards required for clinical application.

Sabapathy, V. and S. Kumar (2016). "hiPSC-derived iMSCs: NextGen MSCs as an advanced therapeutically active cell resource for regenerative medicine." J Cell Mol Med **20**(8): 1571-1588.

Mesenchymal stem cells (MSCs) are being assessed for ameliorating the severity of graft-versus-host disease, autoimmune conditions, musculoskeletal injuries and cardiovascular diseases. While most of these clinical therapeutic applications require substantial cell quantities, the number of MSCs that can be obtained initially from a single donor remains limited. The utility of MSCs derived from human-induced pluripotent stem cells (hiPSCs) has been shown in recent pre-clinical studies. Since adult MSCs have limited capability regarding proliferation, the quantum of bioactive factor secretion and immunomodulation ability may be constrained. Hence, the alternate source of MSCs is being considered to replace the commonly used adult tissue-derived MSCs. The MSCs have been obtained from various adult and foetal tissues. The hiPSC-derived MSCs (iMSCs) are transpiring as an attractive source of MSCs because during reprogramming process, cells undergo rejuvination, exhibiting better cellular vitality such as survival, proliferation and differentiations potentials. The autologous iMSCs could be considered as an inexhaustible source of MSCs that could be used to meet the unmet clinical needs. Human-induced PSC-derived MSCs are reported to be superior when compared to the adult MSCs regarding cell proliferation, immunomodulation, cytokines profiles, microenvironment modulating exosomes and bioactive paracrine factors secretion. Strategies such as derivation and propagation of iMSCs in chemically defined culture conditions and use of footprint-free safer reprogramming strategies have contributed towards the development of clinically relevant cell types. In this review, the role of iPSC-derived mesenchymal stromal cells (iMSCs) as an alternate source of therapeutically active MSCs has been described. Additionally, we also describe the role of iMSCs in regenerative medical applications, the necessary strategies, and the regulatory policies that have to be enforced to render iMSC's effectiveness in translational medicine.

Sadeghi, S., et al. (2021). "Cation exchange mediated synthesis of bright Au@ZnTe core-shell nanocrystals." Nanotechnology **32**(2): 025603.

The synthesis of heterostructured core-shell nanocrystals has attracted significant attention due to their wide range of applications in energy, medicine and environment. To further extend the possible nanostructures, non-epitaxial growth is introduced to form heterostructures with large lattice mismatches, which cannot be achieved by classical epitaxial growth techniques. Here, we report the synthetic procedure of Au@ZnTe core-shell nanostructures by cation exchange reaction for the first time. For that, bimetallic Au@Ag heterostructures were synthesized by using PDDA as stabilizer and shape-controller. Then, by addition of Te and Zn precursors in a step-wise reaction, the zinc and silver cation exchange was performed and Au@ZnTe nanocrystals were obtained. Structural and optical characterization confirmed the formation of the Au@ZnTe nanocrystals. The optimization of the synthesis led to the bright nanocrystals with a photoluminescence quantum yield up to 27%. The non-toxic, versatile synthetic route, and bright emission of the synthesized Au@ZnTe nanocrystals offer significant potential for future bio-imaging and optoelectronic applications.

Sadeghpour, S. D., et al. (2020). "Predictive and fluorescent nanosensing experimental methods for evaluating anthrax protective antigen and lethal factor interactions for therapeutic applications." Int J Biol Macromol **160**: 1158-1167.

Recently, specific interaction of anthrax protective antigen domain 4 (PAD4) and lethal factor domain 1 (LFD1) have been considered for the design of novel diagnostic and therapeutic systems in medicine. In this study, theoretical and experimental approaches were used to monitor the interactions of PAD4 and LFD1. CLusPro server and Dimplot software were used to predict the interaction of these domains. Results, revealed interactive sites between PAD4 and LFD1 on loop regions of both C and N terminal of PAD4. In experimental methods, PAD4 and LFD1 were expressed in Escherichia coli and purified for usage in Magnetic Bead (MB) and Multi-Walled Carbon Nanotubes (MWCNTs) based bio-sensing platforms. In the magnetic-based system, the magnetic sedimentation of QD-PAD4 by MBs-LFD1 and the observation of the fluorescence spectrum related to QD-PAD4 in the precipitated materials confirmed the interaction of PAD4 with LFD1 protein. In the MWCNTs-based method, the QD-PAD4 fluorescence was quenched by absorption on MWCNTs. Upon the addition of LFD1, fluorescence emission was recovered, indicating interaction of LFD1 with QD-PAD4, which results the separation of QD-PAD4 from MWCNTs surfaces and fluorescence restoration. Finally, new approaches showed the interaction of PAD4 and LFD1, which can be used as an attractive model in medicine.

Saeed, H. K., et al. (2020). "Making the Right Link to Theranostics: The Photophysical and Biological Properties of Dinuclear Ru(II)-Re(I) dppz Complexes Depend on Their Tether." J Am Chem Soc **142**(2): 1101-1111.

The synthesis of new dinuclear complexes containing linked Ru(II)(dppz) and Re(I)(dppz) moieties is reported. The photophysical and biological properties of the new complex, which incorporates a N,N'-bis(4-pyridylmethyl)-1,6-hexanediamine tether ligand, are compared to a previously reported Ru(II)/Re(I) complex linked by a simple dipyridyl alkane ligand. Although both complexes bind to DNA with similar affinities, steady-state and time-resolved photophysical studies reveal that the nature of the linker affects the excited state dynamics of the complexes and their DNA photocleavage properties. Quantum-based DFT calculations on these systems offer insights into these effects. While both complexes are live cells permeant, their intracellular localizations are significantly affected by the nature of the linker. Notably, one of the complexes displayed concentration-dependent localization and possesses photophysical properties that are compatible with SIM and STED nanoscopy. This allowed the dynamics of its intracellular localization to be tracked at super resolutions.

Sajjadi, M., et al. (2021). "Carbon-based nanomaterials for targeted cancer nanotherapy: recent trends and future prospects." J Drug Target: 1-26.

Carbon-based nanomaterials are becoming attractive materials due to their unique structural dimensions and promising mechanical, electrical, thermal, optical and chemical characteristics. Carbon nanotubes, graphene, graphene oxide, carbon and graphene quantum dots have numerous applications in diverse areas, including biosensing, drug/gene delivery, tissue engineering, imaging, regenerative medicine, diagnosis, and cancer therapy. Cancer remains one of the major health problems all over the world, and several therapeutic approaches are focussed on designing targeted anticancer drug delivery nanosystems by applying benign and less hazardous resources with high biocompatibility, ease of functionalization, remarkable targeted therapy issues, and low adverse effects. This review highlights the recent development on these carbon based-nanomaterials in the field of targeted cancer therapy and discusses their possible and promising diagnostic and therapeutic applications for the treatment of cancers.

Sanchez, D. N. R., et al. (2017). "Effects of Canine and Murine Mesenchymal Stromal Cell Transplantation on Peripheral Nerve Regeneration." Int J Stem Cells **10**(1): 83-92.

Background and Objectives: Maintaining a permissive microenvironment is essential for adequate nerve regeneration. Cell-based therapy has the potential based cell replacement and promotion of axonal growth. The adipose tissue derived mesenchymal stromal cells (Ad-MSC) attract interest because neuroregenerative and anti-inflammatory properties. The aim of this study was to evaluate the effects of canine and murine Ad-MSC transplantation on the sciatic nerve regeneration. Methods: Forty Wistar rats were divided randomly into: control group - CG (n=8); denervated group - DG (n=8); decellularized vein group - VG (n=8); decellularized veincanine MSC-cMSC (n=8); descellularized veinmurine MSC-mMSC (n=8). After 10-mm nerve gap, the tubulation technique was performed with decellularized vein filled with 10(6) MSC labeled with quantum dots (Qtracker 665((R))). The sciatic nerve functional index (SFI) and electroneuromyography (ENMG) measurements were carried and morphometric and immunohistochemistry analysis of the tissue. Results: The SFI values were higher in the cMSC and mMSC groups at day 27 ($p<0.020$) and day 35 ($p<0.011$). The ENMG analysis also revealed better results in the mMSC group. Density, number, and total area of the fibers were increased in the mMSC and cMSC groups. Brain-derived neurotrophic factor BDNF and S-100 protein positive immunoreactivity showed a higher expression for both in the nerve of the mMSC and cMSC groups. The MSC labeled with quantum dots were detected at day 35, indicating neuronal survival long after the nerve damage. Conclusions: Murine and canine Ad-MSC associated with decellularized vein scaffold had positive effects on sciatic nerve regeneration in rats.

Santos, J. C., et al. (2013). "One-step biofunctionalization of quantum dots with chitosan and N-palmitoyl chitosan for potential biomedical applications." Molecules **18**(6): 6550-6572.

Carbohydrates and derivatives (such as glycolipids, glycoproteins) are of critical importance for cell structure, metabolism and functions. The effects of carbohydrate and lipid metabolic imbalances most often cause health disorders and diseases. In this study, new carbohydrate-based nanobioconjugates were designed and synthesized at room temperature using a single-step aqueous route combining chitosan and acyl-modified chitosan with fluorescent inorganic nanoparticles. N-palmitoyl chitosan (C-Pal) was prepared aiming at altering the lipophilic behavior of chitosan (CHI), but also retaining its reasonable water solubility for potential biomedical applications. CHI and C-Pal were used for producing biofunctionalized CdS quantum dots (QDs) as colloidal water dispersions. Fourier transform infrared spectroscopy (FTIR), thermal analysis (TG/DSC), surface contact angle (SCA), and degree of swelling (DS) in phosphate buffer were used to characterize the carbohydrates. Additionally, UV-Visible spectroscopy (UV-Vis), photoluminescence spectroscopy (PL), dynamic light scattering (DLS), scanning and transmission electron microscopy (SEM/TEM) were used to evaluate the precursors and nanobioconjugates produced. The FTIR spectra associated with the thermal analysis results have undoubtedly indicated the presence of N-palmitoyl groups "grafted" to the chitosan chain (C-Pal) which significantly altered its behavior towards water swelling and surface contact angle as compared to the unmodified chitosan. Furthermore, the results have evidenced that both CHI and C-Pal performed as capping ligands on nucleating and stabilizing colloidal CdS QDs with estimated average size below 3.5 nm and fluorescent activity in the visible range of the spectra. Therefore, an innovative "one-step" process was developed via room temperature aqueous colloidal chemistry for producing biofunctionalized quantum dots using water soluble carbohydrates tailored with amphiphilic behavior offering potential applications as fluorescent biomarkers in the investigation of glycoconjugates for the nutrition, biology, pharmaceutical, and medicine fields.

Santoshi, S., et al. (2011). "Rational design of novel anti-microtubule agent (9-azido-noscapine) from quantitative structure activity relationship (QSAR) evaluation of noscapinoids." J Biomol Screen **16**(9): 1047-1058.

An anticough medicine, noscapine [(S)-3-((R)4-methoxy-6-methyl-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinolin-5 -yl)-6,7-dimethoxyiso-benzofuran-1(3H)-one], was discovered in the authors' laboratory as a novel type of tubulin-binding agent that mitigates polymerization dynamics of microtubule polymers without changing overall subunit-polymer equilibrium. To obtain systematic insight into the relationship between the structural framework of noscapine scaffold and its antitumor activity, the authors synthesized strategic derivatives (including two new ones in this article). The IC(50) values of these analogs vary from 1.2 to 56.0 microM in human acute lymphoblastic leukemia cells (CEM). Geometrical optimization was performed using semiempirical quantum chemical calculations at the 3-21G* level. Structures were in agreement with nuclear magnetic resonance analysis of molecular flexibility in solution and crystal structures. A genetic function approximation algorithm of variable selection was used to generate the quantitative structure activity relationship (QSAR) model. The robustness of the QSAR model (R(2) = 0.942) was analyzed by values of the internal cross-validated regression coefficient (R(2) (LOO) = 0.815) for the training set and determination coefficient (R(2) (test) = 0.817) for the test set.

Validation was achieved by rational design of further novel and potent antitumor noscapinoid, 9-azido-noscapine, and reduced 9-azido-noscapine. The experimentally determined value of pIC(50) for both the compounds (5.585 M) turned out to be very close to predicted pIC(50) (5.731 and 5.710 M).

Santra, S., et al. (2004). "Luminescent nanoparticle probes for bioimaging." J Nanosci Nanotechnol **4**(6): 590-599.

Bioimaging with luminescent nanoparticle probes have recently attracted widespread interest in biology and medicine. In comparison with commonly used organic dyes, luminescent nanoparticles are better in terms of photostability and sensitivity. These optical features of nanoparticle probes are critical for real time tracking and monitoring of biological events in the cellular level, which may not be accomplished using regular fluorescent dyes. Nanoparticle probes are also shown highly suitable for immunoassay and other diagnostic and therapeutic applications. In this article, we describe a variety of optical nanoparticle probes such as quantum dots, metal nanoparticles, dye-doped nanoparticles etc. for bioimaging applications.

Saraceno, R., et al. (2013). "Emerging applications of nanomedicine in dermatology." Skin Res Technol **19**(1): e13-19.

BACKGROUND: Nanotechnology is a new branch of engineering consisting of the usage of nanoscale particles (100 nm and smaller). Nanomedicine is the application of nanoscale technologies for diagnostic and therapeutic purposes in medicine. Nanodermatology, nanotechnology applied to dermatology, represents one of the most advanced field for which an increasing interest, both economic and scientific, is rising. The skin is the first point of contact for a whole host of nanomaterials, ranging from topical preparations, articles of clothing and household products, to sporting goods and industrial manufactured goods. Applications of nanomedicine in dermatology include new direction in medical diagnosis, monitoring and treatment. Gold nanoparticle, quantum dots and magnetic nanoparticles are used in non-invasive nanoimaging of high-resolution dermoscopy, microscopy, nanopunch, and spectroscopy, offering advanced diagnostic and therapeutic modalities. Nanotherapeutics has been considered in immunotherapy, genetherapy, and drug therapy. In drug therapy, because of size reduction or encapsulation of drug particles, the therapeutic potential of water insoluble and unstable drugs improve, and also facilitate the delivery of small molecules across blood, skin, nails, and pilosebaceous unit. AIMS: To review therapeutic applications and benefits of nanomedicine in esthetic dermatology, treatment of malignancies, and inflammatory skin diseases.

Sasinowski, F. J. and A. J. Varond (2016). "FDA's Flexibility in Subpart H Approvals: Assessing Quantum of Effectiveness Evidence." Food Drug Law J **71**(1): 135-157.

This article examines the strength of scientific and clinical evidence for FDA's nineteen non-AIDS, non-cancer Subpart H approval determinations over the Accelerated Approval program's twenty-four year existence. The authors researched the bases for FDA's determinations when an unvalidated surrogate or intermediate clinical endpoint is "reasonably likely to predict clinical benefit." The four key factors set forth in FDA's "Guidance for Industry, Expedited Programs for Serious Conditions - Drugs and Biologics" were applied to past Subpart H approvals. For the nineteen precedents, the authors found wide variances between the quantum and quality of evidence on each of the four factors, indicating that a lack of evidence on any single factor was not disqualifying in and of itself. The results of this study, therefore, show that FDA exercises extraordinarily more regulatory flexibility than either FDA's foundational statutes or even FDA' s most recent 2014 Expedited Programs Guidance explicitly express. Given recent legislative exhortations and the increasing promise of personalized medicine and translational sciences, the authors conclude that Subpart H should be further explored and utilized. The authors provide a detailed analysis of the orecedents established in the nineteen approvals.

Satti, J. A. (2012). "Practical implications of nanodosimetry in medicine." Dose Response **10**(3): 355-363.

The grandiose promises made decades ago of cost reduction, miracle cures for cancers and universal availability of nanomedicine are still a far cry. Even we do not have any viable model to exploit nanotechnology in medicine. The most important arena of the nanotechnology is the development of nanoscale drugs for routine clinical practice. The current chemo protocols are based on maximum tolerable dose philosophy. Such a dose, when translated into active nanoscale clusters, quantitatively outnumbers the cells in an average human body. These nanoscale drug issues are discussed in this paper. A theoretical framework for commonly used drug aspirin has been considered as an example. The possible quantum physical effects have also been theoretically evaluated. Further, the amount of drug molecules in a standardized aspirin dose of 100 milligram has been computed into nanoclusters. The calculations show that the processing of nanoscale drug is a monumental task which requires new types of manufacturing facilities.

Also there is a need to develop new protocols which will help realize the practical implementation of nanodosimetry in day to day drug administrations. These protocols will need to examine the implications of dose-responses such as necrosis, apoptosis and hormesis in medicine for routine clinical practice.

Savelli, S., et al. (2018). "Pooled human serum: A new culture supplement for bioreactor-based cell therapies. Preliminary results." Cytotherapy **20**(4): 556-563.

BACKGROUND: Bone Marrow MSCs are an appealing source for several cell-based therapies. Many bioreactors, as the Quantum Cell Expansion System, have been developed to generate a large number of MSCs under Good Manufacturing Practice conditions by using Human Platelet Lysate (HPL). Previously we isolated in the human bone marrow a novel cell population, named Mesodermal Progenitor Cells (MPCs), which we identified as precursors of MSCs. MPCs could represent an important cell source for regenerative medicine applications. As HPL gives rise to a homogeneus MSC population, limiting the harvesting of other cell types, in this study we investigated the efficacy of pooled human AB serum (ABS) to provide clinically relevant numbers of both MSCs and MPCs for regenerative medicine applications by using the Quantum System. METHODS: Bone marrow aspirates were obtained from healthy adult individuals undergoing routine total hip replacement surgery and used to generate primary cultures in the bioreactor. HPL and ABS were tested as supplements to culture medium. Morphological observations, cytofluorimetric analysis, lactate and glucose level assessment were performed. RESULTS: ABS gave rise to both heterogeneous MSC and MPC population. About 95% of cells cultured in HPL showed a fibroblast-like morphology and typical mesenchymal surface markers, but MPCs were scarcely represented. DISCUSSION: The use of ABS appeared to sustain a large scale MSC production, as well as the recovery of a subset of MPCs, and resulted a suitable alternative to HPL in the cell generation based on the Quantum System.

Saxena, V. and G. Portale (2020). "Contribution of Ex-Situ and In-Situ X-ray Grazing Incidence Scattering Techniques to the Understanding of Quantum Dot Self-Assembly: A Review." Nanomaterials (Basel) **10**(11).

Quantum dots are under intense research, given their amazing properties which favor their use in electronics, optoelectronics, energy, medicine and other important applications. For many of these technological applications, quantum dots are used in their ordered self-assembled form, called superlattice. Understanding the mechanism of formation of the superlattices is crucial to designing quantum dots devices with desired properties. Here we review some of the most important findings about the formation of such superlattices that have been derived using grazing incidence scattering techniques (grazing incidence small and wide angle X-ray scattering (GISAXS/GIWAXS)). Acquisition of these structural information is essential to developing some of the most important underlying theories in the field.

Schatti, J., et al. (2017). "Tailoring the volatility and stability of oligopeptides." J Mass Spectrom **52**(8): 550-556.

Amino acids are essential building blocks of life, and fluorinated derivatives have gained interest in chemistry and medicine. Modern mass spectrometry has enabled the study of oligo- and polypeptides as isolated entities in the gas phase, but predominantly as singly or even multiply charged species. While laser desorption of neutral peptides into adiabatically expanding supersonic noble gas jets is possible, UV-VIS spectroscopy, electric or magnetic deflectometry as well as quantum interferometry would profit from the possibility to prepare thermally slow molecular beams. This has typically been precluded by the fragility of the peptide bond and the fact that a peptide would rather 'fry', i.e. denature and fragment than 'fly'. Here, we explore how tailored perfluoroalkyl functionalization can reduce the intermolecular binding and thus increase the volatility of peptides and compare it to previously explored methylation, acylation and amidation of peptides. We show that this strategy is essential and enables the formation of thermal beams of intact neutral tripeptides, whereas only fragments were observed for an extensively fluoroalkyl-decorated nonapeptide. (c) 2017 The Authors. Journal of Mass Spectrometry Published by John Wiley & Sons Ltd.

Schlaudraff, U. (2004). "[Established certainty: experiences with clinical chaplaincy between doubt, evidence and revelation]." Z Arztl Fortbild Qualitatssich **98**(5): 413-421.

Medicine must not be understood just as applied science. Modern physics, namely Quantum Theory, the theory of complementarity, and the "End of Certainty" (Ilya Prigogine) have proved the cogency of the perception of medicine as a mixture of the art of uncertainty and the science of probability. Research into chaos and order has revealed the dynamic structure of complex systems that no longer allow for undoubted prognosis. The only thing a physician can definitely promise is his readiness never to abandon a patient and to keep up personal integrity. Thus it is not only knowledge and skill that matter. It is background and authenticity that counts, which will make the doctor a guarantee of a covenant relationship that the patient may rely on. The importance of standing surety for

someone in a therapeutic setting is demonstrated by giving examples from literature and personal experience in clinical chaplaincy.

Schmahl, F. W. (1998). "Some theoretical remarks regarding the integration of somatic and psychosocial risk factors of coronary artery disease in preventive programmes in occupational medicine." Int J Occup Med Environ Health **11**(4): 285-289.

In occupational medicine, as well as in many other medical areas, we still find too frequently a disturbing polarization of 'natural science oriented' versus 'psychosocial oriented' medicine. This has its roots in Descartes' traditional division of res cogitans (thinking substance) and res extensa (extended or corporeal substance). It would be important for medicine to integrate modern physics, where quantum theory plays an essential role, into its natural science base. In modern physics, the Cartesian division can no longer be consistently maintained as it has been in classical physics and related natural sciences. Taking the recent developments and new aspects of modern natural science into consideration for application in medical thinking would facilitate greatly the desirable unified, holistic approach, necessary to overcome the problems of the Cartesian division still present, and to better integrate somatic and psychosocial aspects of medicine. This is important for the general planning of programmes of preventive medicine in occupational health as well as in other medical fields. It is also essential specifically in treating individual patients and their medical problems. This is demonstrated here using the example of coronary artery disease (CAD). Treatment and prevention of CAD, a main cause of morbidity and mortality in industrialized countries, is a major challenge for all of medicine, including occupational medicine.

Schmid, G. B. (2005). "Much ado about entanglement: a novel approach to test nonlocal communication via violation of 'local realism'." Forsch Komplementarmed Klass Naturheilkd **12**(4): 214-222.

BACKGROUND: The term 'entanglement' is often used in recent literature to help explain an apparent nonlocal communication within a psychophysical context, and is here strictly taken as equivalent to a violation of what physicists call 'local realism'. METHODS: Conceptual basics of nonlocal communication in psychophysical experiments are introduced in analogy to their usage in quantum physics to investigate local realism. Violations of local realism are tested using an algorithm adopted from the Information Theoretic Bell Inequality (ITBI) known to quantum theory. The algorithm involves a generic distant mentation experiment. RESULTS: An experimental design and an analytical method to test psychophysical entanglement presumed to be involved in a medical or psychological context are introduced. The mathematical foundations are presented in a didactically simple-to-follow approach. CONCLUSIONS: The ITBI can be extended into the fields of medicine and psychological science, thereby providing a guideline for researchers to follow in order to estimate whether or not some kind of 'action at a distance' may be real in the phenomenon under investigation.

Schmidt, J. M. (2014). "New approaches within the history and theory of medicine and their relevance for homeopathy." Homeopathy **103**(2): 153-159.

Conventional sciences have brought forth a wealth of knowledge and benefits, but they have not always been clear and precise about their legitimate scope and methodological limitations. In contrast, new and critical approaches in modern sciences question and reflect their own presuppositions, dependencies, and constraints. Examples are quantum physics, theory and history of science, as well as theory and history of medicine, sociology, and economics. In this way, deprecative dogmatism and animosity amongst sciences ought to be lessened, while the field opens up for each science to redefine its appropriate place in society. This would appear to be a chance for homeopathy, as new approaches, especially within the social and economic sciences, suggest that being a follower of Samuel Hahnemann (1755-1843) may have advantages and privileges that conventional medicine seems to be lacking and whose relevance was overlooked during the rise of economic thinking in the last two centuries.

Schottelius, M., et al. (2009). "Ligands for mapping alphavbeta3-integrin expression in vivo." Acc Chem Res **42**(7): 969-980.

The alpha(v)beta(3)- and alpha(5)beta(1)-integrins play a key role in angiogenesis, the formation of new vessels in tissues that lack them. By serving as receptors for a variety of extracellular matrix proteins containing an arginine-glycine-aspartic acid (RGD) sequence, these integrins mediate migration of endothelial cells into the basement membrane and regulate their growth, survival, and differentiation. Besides being involved in angiogenesis, the alpha(v)beta(3)-integrin is also presented on tumor cells of various origin, where it is involved in the processes that govern metastasis. Because the alpha(v)beta(3)-integrin is an attractive target for cancer treatment, high-affinity ligands containing the RGD sequence, for example, cyclic pentapeptides, have been developed. They inhibit angiogenesis, induce endothelial apoptosis, decrease tumor growth, and reduce invasiveness and spread of metastasis. This

development finally resulted in cyclo(RGDf(NMe)V) (cilengitide), which is a drug for the treatment of glioblastoma (currently in phase III clinical trials). With the growing focus on individualized medicine, clinicians would like to be able to assess the severity of the disease and monitor therapy for each patient. Such measurements would be based on a noninvasive visualization and quantification the alpha(v)beta(3)-integrin expression levels before, during, and after antiangiogenic therapy. A wide spectrum of in vivo imaging probes for the nuclear imaging modalities positron emission tomography (PET) and single-photon emission computed tomography (SPECT), for optical imaging, and for magnetic resonance imaging (MRI) have been developed with these goals in mind. In this Account, we describe the synthesis and preclinical and clinical assessments of dedicated targeting probes. These molecules ideally accumulate selectively and in high concentrations in alpha(v)beta(3)-integrin-expressing tissues, have low uptake and retention in nontarget tissues, and are highly stable against in vivo degradation. [(123)I]cyclo(RGDyV) was the first radiolabeled "imaging analogue" of cilengitide that we evaluated preclinically in detail. Subsequent studies focused on cyclo(RGDfK) and cyclo(RGDyK), which allowed conjugation with various signaling moieties, such as prosthetic groups, bifunctional chelators (DTPA, DOTA, NOTA, TETA, and TE2A for labeling with (111)In or (177)Lu for SPECT and (86)Y, (68)Ga, or (64)Cu for PET), or fluorescent dyes (Cy5.5, cypate). Furthermore, pharmacokinetic modifiers such as carbohydrates, charged amino acids, or PEG analogues were coupled to the peptide core without significantly affecting the binding affinity. Finally, dimers, tetramers, octamers, and polymers and decorated quantum dots with several dozens of peptide units were constructed and investigated. Some of these multimers demonstrated significantly improved affinity (avidity) and targeting efficiency in vivo. Besides peptidic alpha(v)beta(3)-integrin ligands, researchers have investigated radiolabeled antibodies such as Abegrin and used molecular modeling to design small peptidomimetics with improved activity, in vivo stability, and subtype selectivity (e.g., (111)In-TA138). Furthermore, there is an increasing interest in nanoparticles such as nanotubes, quantum dots, or paramagnetic particles coated with cyclic RGD analogues as targeting agents. [(18)F]Galacto-RGD, a glycosylated cyclo(RGDfK) analogue, was the first such substance applied in patients and has been successfully assessed in more than 100 patients so far. Because of modification with carbohydrates, rapid renal excretion, and inherently low background activity in most regions of the body, imaging of alpha(v)beta(3) expression with high tumor/background ratios and high specificity is possible. Other (18)F-labeled RGD analogues recently developed by Siemens and GE Healthcare have entered clinical trials.

Schwartz, G. E. and L. G. Russek (1997). "Dynamical energy systems and modern physics: fostering the science and spirit of complementary and alternative medicine." Altern Ther Health Med **3**(3): 46-56.

When systems theory is carefully applied to the concept of energy, some novel and far-reaching implications for modern physics and complementary medicine emerge. The heart of systems theory is dynamic interactions: systems do not simply act on systems, they interact with them in complex ways. By definition, systems at any level (e.g., physical, biological, social, ecological) are open to information, energy, and matter to varying degrees, and therefore interact with other systems to varying degrees. We first show how resonance between two tuning forks, a classic demonstration in physics, can be seen to reflect synchronized dynamic interactions over time. We then derive how the dynamic interaction of systems in mutual recurrent feedback relationships naturally create dynamic "memories" for their interactions over time. The mystery of how a photon (or electron) "knows" ahead of time whether to function as a particle or wave in the single slit/double slit quantum physics paradigm is potentially solved when energetic interactions inherent in the experimental system are recognized. The observation that energy decreases with the square of distance is shown not to be immutable when viewed from a dynamical energy systems perspective. Implications for controversial claims in complementary and alternative medicine, such as memory for molecules retained in water (homeopathy), remote diagnosis, and prayer and healing, are considered. A dynamical energy systems framework can facilitate the development of what might be termed "relationship consciousness," which has the potential to nurture both the science and spirit of complementary medicine and might help to create integrated medicine.

Schwartz, G. E. and E. P. Schloss (2006). "World hypotheses and the evolution of integrative medicine: combining categorical diagnoses and cause-effect interventions with whole systems research and nonvisualizable (seemingly "impossible") healing." Explore (NY) **2**(6): 509-514.

It has been proposed that to understand (1) the evolution of science and medicine, and (2) the integration of conventional, complementary and alternative medicine, it is essential to consider at least eight universal implicit meta-cognitive hypotheses. It has been suggested that these implicit "world" hypotheses can be applied in every discipline of science. The present paper reviews the eight world hypotheses and proposes an additional hypothesis,

termed the nonvisualizable or "Nth" world hypothesis (adopting the mathematical concept of "N"; eg, as in N dimensional space). Drawing on contemporary mathematics and quantum physics, we propose that certain theories and data-by their inherent nature-can not be visualized, and therefore may seem "unimaginable" and "impossible" (if not "unbelievable"), even though they are real. Certain seemingly anomalous observations in mind-body and energy medicine, including areas historically labeled as parapsychology or spiritual energy healing, often elicit strongly skeptical and dismissive reactions. We propose that these skeptical and dismissive reactions to purportedly impossible (yet logical) theories and seemingly unbelievable (yet replicable) data can be tempered when the Nth world hypothesis is understood and incorporated. Integrity in evidence-based science and medicine may require that scientists and nonscientists alike develop comfort and humility in accepting the human mind's restricted ability to envision and imagine certain nonvisualizable-yet fundamental and real-concepts and effects, as illustrated in contemporary physics and complementary and alternative medicine.

Schwartz, S. A. (2010). "Nonlocality and exceptional experiences: a study of genius, religious epiphany, and the psychic." Explore (NY) **6**(4): 227-236.

Two hundred years of reductive materialism has failed to explain the extraordinary experiences we know as moments of genius, religious epiphany, and psychic insight. This paper proposes that these three experiences are in essence the same experience, differentiated only by intention and context. It reaches this conclusion based on well-conducted experimental research across the continuum of science--work that proposes a new interdependent model of consciousness that takes into consideration a nonlocal linkage or entanglement, as an aspect of consciousness not limited by space and time. The paper surveys some of the most important relevant research from quantum biology, physics, psychology, medicine, anthropology, and parapsychology. It proposes that more attention should be paid to the autobiographies, correspondence, and journals of men and women to whom history unequivocally accords the designation of genius, saint, or psychic, offering examples from these sources. And it presents comparisons between ethnohistorical material and spiritual traditions, suggesting they arrive at a similar worldview. Finally, it proposes that meditation research, some examples of which are cited, be seen in the context of psychophysical self-regulation, and that it offers one powerful avenue for producing these exceptional experiences.

Scott, I. (2014). "Ten clinician-driven strategies for maximising value of Australian health care." Aust Health Rev **38**(2): 125-133.

OBJECTIVE: To articulate the concept of high-value care (i.e. clinically relevant, patient-important benefit at lowest possible cost) and suggest strategies by which clinicians can promote such care in rendering the Australian healthcare system more affordable and sustainable. METHODS: Strategies were developed by the author based on personal experience in clinical practice, evidence-based medicine and quality improvement. Relevant literature was reviewed in retrieving studies supporting each strategy. RESULTS: Ten strategies were developed: (1) minimise errors in diagnosis; (2) discontinue low- or no-value practices that provide little benefit or cause harm; (3) defer the use of unproven interventions; (4) select care options according to comparative cost-effectiveness; (5) target clinical interventions to those who derive greatest benefit; (6) adopt a more conservative approach nearing the end of life; (7) actively involve patients in shared decision making and self-management; (8) minimise day-to-day operational waste; (9) convert healthcare institutions into rapidly learning organisations; and (10) advocate for integrated patient care across all clinical settings. CONCLUSIONS: Clinicians and their professional organisations, in partnership with managers, can implement strategies capable of maximising value and sustainability of health care in Australia. What is known about this topic? Value-based care has emerged as a unitary concept that integrates quality and cost, and is being increasingly used to inform healthcare policy making and reform. What does this paper add? There is scant literature that translates the concept of high value care into actionable enhancement strategies for clinicians in everyday practice settings. This article provides 10 strategies with supporting studies in an attempt to fill this gap. What are the implications for practitioners? If all practitioners, in partnership with healthcare managers, attempted to enact all 10 strategies in their workplaces, a significant quantum of healthcare resources could be redirected from low- to high-value care, culminating in much greater health benefit from the healthcare dollars currently being spent. However, such reforms will require a shift in clinician thinking and practice away from volume-based care to value-based care.

Sen, A. and H. C. Gifford (2016). "Accounting for anatomical noise in search-capable model observers for planar nuclear imaging." J Med Imaging (Bellingham) **3**(1): 015502.

Model observers intended to predict the diagnostic performance of human observers should account for the effects of both quantum and anatomical

noise. We compared the abilities of several visual-search (VS) and scanning Hotelling-type models to account for anatomical noise in a localization receiver operating characteristic (LROC) study involving simulated nuclear medicine images. Our VS observer invoked a two-stage process of search and analysis. The images featured lesions in the prostate and pelvic lymph nodes. Lesion contrast and the geometric resolution and sensitivity of the imaging collimator were the study variables. A set of anthropomorphic mathematical phantoms was imaged with an analytic projector based on eight parallel-hole collimators with different sensitivity and resolution properties. The LROC study was conducted with human observers and the channelized nonprewhitening, channelized Hotelling (CH) and VS model observers. The CH observer was applied in a "background-known-statistically" protocol while the VS observer performed a quasi-background-known-exactly task. Both of these models were applied with and without internal noise in the decision variables. A perceptual search threshold was also tested with the VS observer. The model observers without inefficiencies failed to mimic the average performance trend for the humans. The CH and VS observers with internal noise matched the humans primarily at low collimator sensitivities. With both internal noise and the search threshold, the VS observer attained quantitative agreement with the human observers. Computational efficiency is an important advantage of the VS observer.

Sentis, G., et al. (2016). "Quantum Change Point." Phys Rev Lett **117**(15): 150502.

Sudden changes are ubiquitous in nature. Identifying them is crucial for a number of applications in biology, medicine, and social sciences. Here we take the problem of detecting sudden changes to the quantum domain. We consider a source that emits quantum particles in a default state, until a point where a mutation occurs that causes the source to switch to another state. The problem is then to find out where the change occurred. We determine the maximum probability of correctly identifying the change point, allowing for collective measurements on the whole sequence of particles emitted by the source. Then, we devise online strategies where the particles are measured individually and an answer is provided as soon as a new particle is received. We show that these online strategies substantially underperform the optimal quantum measurement, indicating that quantum sudden changes, although happening locally, are better detected globally.

Sethiya, N. K., et al. (2009). "An update on Shankhpushpi, a cognition-boosting Ayurvedic medicine." Zhong Xi Yi Jie He Xue Bao **7**(11): 1001-1022.

Shankhpushpi is an Ayurvedic drug used for its action on the central nervous system, especially for boosting memory and improving intellect. Quantum of information gained from Ayurvedic and other Sanskrit literature revealed the existence of four different plant species under the name of Shankhpushpi, which is used in various Ayurvedic prescriptions described in ancient texts, singly or in combination with other herbs. The sources comprise of entire herbs with following botanicals viz., Convulvulus pluricaulis Choisy. (Convulvulaceae), Evolvulus alsinoides Linn. (Convulvulaceae), Clitoria ternatea Linn. (Papilionaceae) and Canscora decussata Schult. (Gentianaceae). A review on the available scientific information in terms of pharmacognostical characteristics, chemical constituents, pharmacological activities, preclinical and clinical applications of controversial sources of Shankhpushpi is prepared with a view to review scientific work undertaken on Shankhpushpi. It may provide parameters of differentiation and permit appreciation of variability of drug action by use of different botanical sources.

Shah, N., et al. (2017). "Role of Ultrasound-Based Prenatal Prediction of Pulmonary Function in Congenital Diaphragmatic Hernia: Does It Have Prognostic Significance Postnatally?" J Obstet Gynaecol India **67**(1): 33-36.

BACKGROUND AND OBJECTIVES: The incidence of congenital diaphragmatic hernia (CDH) in India is 1 in 1000. About 60 % of these are isolated, and the survival prognosis in them depends upon the quantum of contralateral functional lung. Out of the various pulmonary and extrapulmonary sonological predictors, observed to expected lung-head ratio (O/E LHR) is an efficient gestation-independent predictor of pulmonary function. This study was carried out to see the correlation of this prenatal predictor with the postnatal outcome depending on the pulmonary function. METHODOLOGY: This study was carried out at Apollo Center of Fetal Medicine, New Delhi, from January 2009 to December 2015. A total of 14 fetuses with isolated left-sided CDH were included. The contralateral lung area was measured in 2D transverse view of the thorax at the level of four-chamber view of the heart by tracing method. The obtained value (square mm) was then divided by the expected mean lung area at that gestation and multiplied with 100 to express O/E LHR as percentage. These were then classified as severe (O/E LHR <25 %), moderate (25-45 %) or mild (>45 %) varieties of CDH. The parents to be were counselled for termination or continuation of pregnancy based on severity of CDH and total lung area. The patients were

followed up for obstetrical and neonatal outcome till the time of first postoperative visit (diaphragmatic repair). RESULTS: The survival correlation in mild cases was 100 % (n = 5 out of 5) and 50 % in moderate cases (n = 2 out of 4), and both severe cases were terminated. There was a significant difference ($p < 0.01$) in the survival rate in the mild versus severe cases. CONCLUSIONS: The prenatal predictor for postnatal pulmonary function correlates well with the neonatal outcome and hence is an important tool in prenatal counseling and triaging those who require termination of pregnancy versus expectant management. An obstetrician who is a first point of contact to the pregnant women can understand this and use it for counseling and differentiating the patients who need termination with regard to CDH.

Shahdost-Fard, F. and M. Roushani (2016). "Conformation switching of an aptamer based on cocaine enhancement on a surface of modified GCE." Talanta **154**: 7-14.

An ultrasensitive aptasensor was fabricated as an electrochemical nanotool based on the conformation switching of an aptamer (Apt). The Apt which was covalently attached on the surface of a glassy carbon electrode (GCE) covered with cadmium telluride (CdTe) quantum dots (QDs) works as a unique modifier for assaying cocaine. The Apt was combined with cocaine to form a three-way junction complex; this complex increased the steric hindrance of the modified GCE surface and resulted in a variation of the corresponding current of a redox probe. In the present study, DPV technique for cocaine detection was applied and resulted in an unprecedented detection limit (LOD) of 5.0+/-0.1pmolL(-1), which is more sensitive than previously reported methods. One of the greatest advantages of this aptasensor is the elimination of enzymes or antibodies. It is also relatively a highly sensitive, simple, reproducible, and controllable nanotool. Likewise, it can be easily miniaturized, which is a necessary condition for the high-throughput system and on-site applications. The offered nanotool has a great promise for the routine analysis of the ultra-trace amounts of cocaine, which is important for law enforcement and clinical medicine. It is notable to say that further attempts are under way in our laboratory for the construction of other aptasensors with higher performance for specific targets such as the detection of methadone (MTD) and ibuprofen (IBP).

Sharifi, M., et al. (2020). "Development of point-of-care nanobiosensors for breast cancers diagnosis." Talanta **217**: 121091.

Nanobiosensors have played a key role as portable devices in the rapid breast cancer diagnosis and in clinical medicine like point-of-care devices. However, understanding biomarkers and nanomaterials is crucial for improving the performance of nanobiosensors for all stages of different diseases or treatment. Therefore, this study not only investigates the effect of biomarkers and nanomaterials such as metallic, carbon structures and quantum dot on the accuracy of nanobiosensors for early detection of breast cancer, but also exhibits how they are used in vivo and in vitro and their application in point-of-care devices for personalized cancer diagnosis. Afterwards, application of fluidics and microchips as point-of-care nanobiosensors in the early detection of biomarkers associated with breast cancer diagnosis was discussed. Furthermore, the integration of nanobiosensors in nanomotors platforms for the treatment of breast cancer was overviewed. Finally, the ongoing challenges and future trends on the detection limit of nanobiosensors, their application in point-of-care clinical diagnostics and the approaches implemented for their improvements by highlighting the successful reports on the revolution of personalized diagnostics were surveyed.

Sharma, S., et al. (2019). "Bioresponse Inspired Nanomaterials for Targeted Drug and Gene Delivery." Pharm Nanotechnol **7**(3): 220-233.

The traditional drug delivery techniques are unresponsive to the altering metabolic states of the body and fail to achieve target specific drug delivery, which results in toxic plasma concentrations. In order to harmonize the drug release profiles, diverse biological and pathological pathways and factors involved have been studied and consequently, nanomaterials and nanostructures are engineered in a manner so that they respond and interact with the target cells and tissues in a controlled manner to induce promising pharmacological responses with least undesirable effects. The bioinspired nanoparticles such as carbon nanotubes, metallic nanoparticles, and quantum dots sense the localized host environment for diagnosis and treatment of pathological states. These biocompatible polymeric- based nanostructures bind drugs to the specific receptors, which renders them as ideal vehicles for the delivery of drugs and gene. The ultimate goal of bioinspired nanocomposites is to achieve personalized diagnostic and therapeutic outcomes. This review briefly discussed current trends; role, recent advancements as well as different approaches, which are being used for designing and fabrication of some bioinspired nanocarriers.

Sharma, S. D., et al. (2017). "MRI-based quantitative susceptibility mapping (QSM) and R2* mapping of liver iron overload: Comparison with SQUID-based biomagnetic liver susceptometry." Magn Reson Med **78**(1): 264-270.

PURPOSE: We aimed to determine the agreement between quantitative susceptibility mapping (QSM)-based biomagnetic liver susceptometry (BLS) and confounder-corrected R2* mapping with superconducting quantum interference device (SQUID)-based biomagnetic liver susceptometry in patients with liver iron overload. METHODS: Data were acquired from two healthy controls and 22 patients undergoing MRI and SQUID-BLS as part of routine monitoring for iron overload. Magnetic resonance imaging was performed on a 3T system using a three-dimensional multi-echo gradient-echo acquisition. Both magnetic susceptibility and R2* of the liver were estimated from this acquisition. Linear regression was used to compare estimates of QSM-BLS and R2* to SQUID-BLS. RESULTS: Both QSM-BLS and confounder-corrected R2* were sensitive to the presence of iron in the liver. Linear regression between QSM-BLS and SQUID-BLS demonstrated the following relationship: QSM-BLS = (-0.22 +/- 0.11) + (0.49 +/- 0.05) . SQUID-BLS with r(2) = 0.88. The coefficient of determination between liver R2* and SQUID-BLS was also r(2) = 0.88. CONCLUSION: We determined a strong correlation between both QSM-BLS and confounder-corrected R2* to SQUID-BLS. This study demonstrates the feasibility of QSM-BLS and confounder-corrected R2* for assessing liver iron overload, particularly when SQUID systems are not accessible. Magn Reson Med 78:264-270, 2017. (c) 2016 International Society for Magnetic Resonance in Medicine.

Shcharbin, D., et al. (2015). "Phosphorus-containing nanoparticles: biomedical patents review." Expert Opin Ther Pat **25**(5): 539-548.

INTRODUCTION: The beginning of the nano-era started with the appearance of artificial nanosized supramolecular systems called nanomaterials and nanoparticles (NPs). AREAS COVERED: In the present review, we have analyzed the patents on phosphorus-based nanomaterials (fullerenes, quantum dots [QDs], graphene, liposomes, dendrimers, gold and silver NPs) in biology and medicine. Their impact in treatment of cancer, viral infections and cardiovascular diseases is discussed. EXPERT OPINION: Liposomes and dendrimers had the highest number of biomedical patents. The third candidates were QDs and the fourth and fifth were gold and silver NPs. Fullerenes and carbon nanotubes have the fewest applications in biology and medicine. Thus, our first conclusion was about the 'unifying nanotoxicology paradigm', that 'soft' NPs are significantly more biocompatible than 'hard' NPs. There has been a trend of these nanomaterials being applied in medicine drug and gene delivery, visualization of cells and pathologic processes, using them as antivirals and antimicrobials, contrast agents, antioxidants and photosensitizers. It was unexpected that no patents were found in which phosphorus NPs were used in 3D printing of bones and other biological tissues. The conclusion reached is that nanomaterials are promising tools in future medical applications.

Smith, A. M., et al. (2008). "Bioconjugated quantum dots for in vivo molecular and cellular imaging." Adv Drug Deliv Rev **60**(11): 1226-1240.

Semiconductor quantum dots (QDs) are tiny light-emitting particles on the nanometer scale, and are emerging as a new class of fluorescent labels for biology and medicine. In comparison with organic dyes and fluorescent proteins, they have unique optical and electronic properties, with size-tunable light emission, superior signal brightness, resistance to photobleaching, and broad absorption spectra for simultaneous excitation of multiple fluorescence colors. QDs also provide a versatile nanoscale scaffold for designing multifunctional nanoparticles with both imaging and therapeutic functions. When linked with targeting ligands such as antibodies, peptides or small molecules, QDs can be used to target tumor biomarkers as well as tumor vasculatures with high affinity and specificity. Here we discuss the synthesis and development of state-of-the-art QD probes and their use for molecular and cellular imaging. We also examine key issues for in vivo imaging and therapy, such as nanoparticle biodistribution, pharmacokinetics, and toxicology.

Smith, A. M., et al. (2010). "Imaging dynamic cellular events with quantum dots The bright future." Biochem (Lond) **32**(3): 12.

Semiconductor quantum dots (QDs) are tiny light-emitting particles that have emerged as a new class of fluorescent labels for biology and medicine. Compared with traditional fluorescent probes, QDs have unique optical and electronic properties such as size-tuneable light emission, narrow and symmetric emission spectra, and broad absorption spectra that enable the simultaneous excitation of multiple fluorescence colours.

Smith, C. U. (2001). "Renatus renatus: the Cartesian tradition in British neuroscience and the neurophilosophy of John Carew Eccles." Brain Cogn **46**(3): 364-372.

J. C. Eccles (1903-1997) had a highly distinguished career in neurophysiology, being awarded the Nobel Prize for Medicine or Physiology in 1963. This paper sets him within the Cartesian tradition of British neurophysiology initiated by Thomas Henry Huxley in the mid-19th century. It shows how the mind-brain problematique of the Cartesian tradition troubled him throughout his career, leading him finally

to a solution in terms of quantum microphysics and microphysiology. This position, which has subsequently become fashionable, is discussed and shown (at least in the form Eccles espoused) to provide no solution to the problem posed by Descartes in the early 17th century.

Smith, C. W. (2004). "Quanta and coherence effects in water and living systems." J Altern Complement Med **10**(1): 69-78.

OBJECTIVE: To review the progress the author has made over the past 5 years in understanding coherence effects in water and living systems using quantum mechanical models. BACKGROUND: The implications of existing theoretical work on water are discussed. METHODS: Available techniques for the measurement of frequencies imprinted in water are described or referenced. RESULTS: The importance of frequency is shown in respect of the understanding of the mechanisms of homeopathy, acupuncture and how bio-information may be stored in water and also in respect of chemical and electrical sensitivities or hypersensitivities; hypersensitivity being that degree of sensitivity that seriously interferes with normal functioning. CONCLUSION: Water and living systems have macroscopic quantum properties that can give rise to a memory for frequencies, long-range effects, and entanglement between separated systems.

Smith, M. Q., et al. (2009). "Multiplexed fluorescence imaging of tumor biomarkers in gene expression and protein levels for personalized and predictive medicine." Curr Mol Med **9**(8): 1017-1023.

Combining groundbreaking research and developments in cancer biomarkers, nanotechnology and molecular targeted medicine, a new realm of therapy is possible: personalized and predictive medicine. Developing a method to detect the overexpression of several tumor marker genes simultaneously, knowing that a single cell generally expresses more than one altered gene, should have a high predictive value for identifying cancer cells amidst the normal cellular background. Theoretically, a cancer's unique molecular profile can be used to predict its invasive and metastatic potential, its ability to evade immune surveillance, and its potential response to treatment. Fluorescent probes have been developed to detect the levels of expression of various biomarkers in tumor cells and tissues. Expression of biomarker messenger RNAs (mRNAs) or the presence of a specific mutation in an oncogene in cancer cells can be detected using molecular beacons (MBs) that only emit fluorescent signals after binding to its specific target mRNAs. Antibodies or ligands labeled with fluorophores or fluorescent quantum dots (QDs) have been successfully used to identify specific proteins expressed in cells. Furthermore, multiplex imaging using both MBs and antibodies labeled with a fluorescent probe on the same sample may provide important information correlating the level of mRNA expression and the subsequent level of protein production for a given biomarker. This technology will be useful in research investigating cancer biology, molecular imaging and molecular profiling. With the identification of biomarkers that are related to aggressive tumor types, we may be able to predict within certain patient populations who will develop invasive cancers, and what their prognosis will be given different treatment modalities, ultimately delivering medical care and treatment strategies that are specifically tailored to each individual patient, making personalized and predictive medicine a reality.

Smith, R. C., et al. (2013). "An evidence-based patient-centered method makes the biopsychosocial model scientific." Patient Educ Couns **91**(3): 265-270.

OBJECTIVE: To review the scientific status of the biopsychosocial (BPS) model and to propose a way to improve it. DISCUSSION: Engel's BPS model added patients' psychological and social health concerns to the highly successful biomedical model. He proposed that the BPS model could make medicine more scientific, but its use in education, clinical care, and, especially, research remains minimal. Many aver correctly that the present model cannot be defined in a consistent way for the individual patient, making it untestable and non-scientific. This stems from not obtaining relevant BPS data systematically, where one interviewer obtains the same information another would. Recent research by two of the authors has produced similar patient-centered interviewing methods that are repeatable and elicit just the relevant patient information needed to define the model at each visit. We propose that the field adopt these evidence-based methods as the standard for identifying the BPS model. CONCLUSION: Identifying a scientific BPS model in each patient with an agreed-upon, evidence-based patient-centered interviewing method can produce a quantum leap ahead in both research and teaching. PRACTICE IMPLICATIONS: A scientific BPS model can give us more confidence in being humanistic. In research, we can conduct more rigorous studies to inform better practices.

Smith, R. C., et al. (2014). "Addressing mental health issues in primary care: an initial curriculum for medical residents." Patient Educ Couns **94**(1): 33-42.

OBJECTIVE: Many express concern that modern medicine fails to provide adequate psychosocial and mental health care. Our educational system has not trained the primary care providers who care for most of these patients. Our objective here is to

propose a quantum change: prepare residents and students during all years of training so that they are as effective in treating psychosocial and mental health issues as they are medical problems. METHOD: We operationalize this objective, following Kern, by developing an intensive 3-year curriculum in psychosocial and mental health care for medical residents based on models with a strong evidence-base. RESULTS: We report an intensive curriculum that can guide others with similar training interests and also initiate the conversation about how best to prepare residency graduates to provide effective mental health and psychosocial care. CONCLUSION: Identifying specific curricula informs education policy-makers of the specific requirements they will need to meet if psychosocial and mental health training are to improve. PRACTICE IMPLICATIONS: Training residents in mental health will lead to improved care for this very prevalent primary care population.

Sobhani, H. and E. Dadar (2019). "Terahertz vortex generation methods in rippled and vortex plasmas." J Opt Soc Am A Opt Image Sci Vis **36**(7): 1187-1196.

Terahertz vortices have strong potential for many applications such as imaging and sensing in medicine, biomedical engineering, rotations of molecules, quantum condensation, optical tweezers, manipulation of electron beams, and communications. However, owing to recent developments, there has been less research about vortex generation in the terahertz domain. Due to the damaging limit and low conversion efficiency, a few schemes to generate terahertz vortices based on plasma have recently been reported. Generally, to excite the helicity of the terahertz vortices, two scenarios have been reported: one is transferring the orbital angular momentum from the plasma vortex to the emitted terahertz radiation, and the other is exciting the helicity of the terahertz vortices using twisted input lasers. This paper is a review of recent studies on terahertz vortex generation based on the rippled and vortex plasma substrata.

Solanki, A., et al. (2008). "Nanotechnology for regenerative medicine: nanomaterials for stem cell imaging." Nanomedicine (Lond) **3**(4): 567-578.

Although stem cells hold great potential for the treatment of many injuries and degenerative diseases, several obstacles must be overcome before their therapeutic application can be realized. These include the development of advanced techniques to understand and control functions of microenvironmental signals and novel methods to track and guide transplanted stem cells. The application of nanotechnology to stem cell biology would be able to address those challenges. This review details the current challenges in regenerative medicine, the current applications of nanoparticles in stem cell biology and further potential of nanotechnology approaches towards regenerative medicine, focusing mainly on magnetic nanoparticle- and quantum dot-based applications in stem cell research.

Sommer, K. J., et al. (2014). "[Process design in high-reliability organizations]." Urologe A **53**(5): 645-649.

Modern medicine is a highly complex service industry in which individual care providers are linked in a complicated network. The complexity and interlinkedness is associated with risks concerning patient safety. Other highly complex industries like commercial aviation have succeeded in maintaining or even increasing its safety levels despite rapidly increasing passenger figures. Standard operating procedures (SOPs), crew resource management (CRM), as well as operational risk evaluation (ORE) are historically developed and trusted parts of a comprehensive and systemic safety program. If medicine wants to follow this quantum leap towards increased patient safety, it must intensively evaluate the results of other high-reliability industries and seek step-by-step implementation after a critical assessment.

Somogyi, B. and A. Gali (2014). "Computational design of in vivo biomarkers." J Phys Condens Matter **26**(14): 143202.

Fluorescent semiconductor nanocrystals (or quantum dots) are very promising agents for bioimaging applications because their optical properties are superior compared to those of conventional organic dyes. However, not all the properties of these quantum dots suit the stringent criteria of in vivo applications, i.e. their employment in living organisms that might be of importance in therapy and medicine. In our review, we first summarize the properties of an 'ideal' biomarker needed for in vivo applications. Despite recent efforts, no such hand-made fluorescent quantum dot exists that may be considered as 'ideal' in this respect. We propose that ab initio atomistic simulations with predictive power can be used to design 'ideal' in vivo fluorescent semiconductor nanoparticles. We briefly review such ab initio methods that can be applied to calculate the electronic and optical properties of very small nanocrystals, with extra emphasis on density functional theory (DFT) and time-dependent DFT which are the most suitable approaches for the description of these systems. Finally, we present our recent results on this topic where we investigated the applicability of nanodiamonds and silicon carbide nanocrystals for in vivo bioimaging.

Song, F. and W. C. Chan (2011). "Principles of conjugating quantum dots to proteins via carbodiimide chemistry." Nanotechnology **22**(49): 494006.

The covalent coupling of nanomaterials to bio-recognition molecules is a critical intermediate step in using nanomaterials for biology and medicine. Here we investigate the carbodiimide-mediated conjugation of fluorescent quantum dots to different proteins (e.g., immunoglobulin G, bovine serum albumin, and horseradish peroxidase). To enable these studies, we developed a simple method to isolate quantum dot bioconjugates from unconjugated quantum dots. The results show that the reactant concentrations and protein type will impact the overall number of proteins conjugated onto the surfaces of the quantum dots, homogeneity of the protein-quantum dot conjugate population, quantum efficiency, binding avidity, and enzymatic kinetics. We propose general principles that should be followed for the successful coupling of proteins to quantum dots.

Sonmez, M., et al. (2015). "SYNTHESIS AND APPLICATIONS OF Fe3O4/SiO2 CORE-SHELL MATERIALS." Curr Pharm Des **21**(37): 5324-5335.

Multifunctional nanoparticles based on magnetite/silica core-shell, consisting of iron oxides coated with silica matrix doped with fluorescent components such as organic dyes (fluorescein isothiocyanate - FITC, Rhodamine 6G) or quantum dots, have drawn remarkable attention in the last years. Due to the bi-functionality of these types of nanoparticles (simultaneously having magnetic and fluorescent properties), they are successfully used in highly efficient human stem cell labeling, magnetic carrier for photodynamic therapy, drug delivery, hyperthermia and other biomedical applications. Another application of core-shell-based nanoparticles, in which the silica is functionalized with aminosilanes, is for immobilization and separation of various biological entities such as proteins, antibodies, enzymes etc. as well as in environmental applications, as adsorbents for heavy metal ions. In vitro tests on human cancerous cells, such as A549 (human lung carcinoma), breast, human cervical cancer, THP-1 (human acute monocytic leukaemia) etc. , were conducted to assess the potential cytotoxic effects that may occur upon contact of nanoparticles with cancerous tissue. Results show that core-shell nanoparticles doped with cytostatics (cisplatin, doxorubicin, etc.), are easily adsorbed by affected tissue and in some cases lead to an inhibition of cell proliferation and induce cell death by apoptosis. The goal of this review is to summarize the advances in the field of core-shell materials, particularly those based on magnetite/silica with applicability in medicine and environmental protection. This paper briefly describes synthesis methods of silica-coated magnetite nanoparticles (Stober method and microemulsion), the method of encapsulating functional groups based on aminosilanes in silica shell, as well as applications in medicine of these types of simple or modified nanoparticles for cancer therapy, MRI, biomarker immobilization, drug delivery, biocatalysis etc., and in environmental applications (removal of heavy metal ions and catalysis).

Sonvico, F., et al. (2005). "Metallic colloid nanotechnology, applications in diagnosis and therapeutics." Curr Pharm Des **11**(16): 2095-2105.

In recent years the fields of medicine and biology assist to an ever-growing innovation related to the development of nanotechnologies. In the pharmaceutical domain, for example, liposomes, polymer based micro and nanoparticles have been subjects of intense research and development during the last three decades. In this scenario metallic particles, which use was already suggested in the first half of the '80, are now experiencing a real renaissance. In the field of diagnosis, magnetic resonance imaging is one of the first and up to now the most developed application of metallic particles. But beside this application, a very new generation of biosensors based on the optical properties of colloidal gold and fluorescent nanocrystals, called quantum dots seems to be ready to be implemented in diagnosis and medical imaging. Concerning therapeutic applications, the potentialities of metal nanoparticles to help fulfilling the need of time and space controlled release of drugs has been intuited for a long time. Nowadays, magnetically guided carriers or thermal responsive matrices, in which drug release is triggered by the heating of metal nanoparticles, are effective examples of their application in drug delivery, while more recently efforts to develop metallic nanoobjects to be used as vectors of nucleic acids for vaccination and transfection have been multiplied. In the future, one of the most interesting challenges is certainly the use of metallic nanoparticles for an innovating, effective and selective physical treatment of solid tumors via targeted intracellular hyperthermia.

Srivastava, A., et al. (2017). "Spectroscopic (far or terahertz, mid-infrared and Raman) investigation, thermal analysis and biological activity of piplartine." Spectrochim Acta A Mol Biomol Spectrosc **184**: 368-381.

Research in the field of medicinal plants including Piper species like long pepper (Piper longum L.- Piperaceae) is increasing all over the world due to its use in traditional and Ayurvedic medicine. Piplartine (piperlongumine, 5,6-dihydro-1-[(2E)-1-oxo-3-(3,4,5-trimethoxyphenyl)-2-propenyl]-2(1H)-

pyridinone), a biologically active alkaloid/amide was isolated from the phytochemical investigations of Piper species, as long pepper. This alkaloid has cytotoxic, anti-fungal, anti-diabetic, anti-platelet aggregation, anti-tumoral, anxiolytic, anti-depressant, anti-leishmanial, and genotoxic activities, but, its anticancer property is the most promising and has been widely explored. The main purpose of the work is to present a solid state characterization of PPTN using thermal analysis and vibrational spectroscopy. Quantum mechanical calculations based on the density functional theory was also applied to investigate the molecular conformation and vibrational spectrum, which was compared with experimental results obtained by Raman scattering, far (terahertz) and mid-infrared adsorption spectroscopy. NBO analysis has been performed which predict that most intensive interactions in PPTN are the hyperconjugative interactions between n(1) N6 and pi*(O1C7) having delocalization energy of 50.53kcal/mol, Topological parameters have been analyzed using 'AIM' analysis which governs the three bond critical points (BCPs), one di-hydrogen, and four ring critical points (RCPs). MEP surface has been plotted which forecast that the most negative region is associated with the electronegative oxygen atoms (sites for nucleophilic activity). Theoretically, to confirm that the title compound has anti-cancer, anti-diabetic and anti-platelet aggregation activities, it was analyzed by molecular docking interactions with the corresponding target receptors. The obtained values of H-bonding parameters and binding affinity prove that its anti-cancer activity is the more prominent than the other properties.

Stagi, L., et al. (2019). "From 2-D to 0-D Boron Nitride Materials, The Next Challenge." Materials (Basel) **12**(23).

The discovery of graphene has paved the way for intense research into 2D materials which is expected to have a tremendous impact on our knowledge of material properties in small dimensions. Among other materials, boron nitride (BN) nanomaterials have shown remarkable features with the possibility of being used in a large variety of devices. Photonics, aerospace, and medicine are just some of the possible fields where BN has been successfully employed. Poor scalability represents, however, a primary limit of boron nitride. Techniques to limit the number of defects, obtaining large area sheets and the production of significant amounts of homogenous 2D materials are still at an early stage. In most cases, the synthesis process governs defect formation. It is of utmost importance, therefore, to achieve a deep understanding of the mechanism behind the creation of these defects. We reviewed some of the most recent studies on 2D and 0D boron nitride materials. Starting with the theoretical works which describe the correlations between structure and defects, we critically described the main BN synthesis routes and the properties of the final materials. The main results are summarized to present a general outlook on the current state of the art in this field.

Starck, S. A., et al. (2005). "The use of detective quantum efficiency (DQE) in evaluating the performance of gamma camera systems." Phys Med Biol **50**(7): 1601-1609.

The imaging properties of an imaging system can be described by its detective quantum efficiency (DQE). Using the modulation transfer function calculated from measured line spread functions and the normalized noise power spectrum calculated from uniformity images, DQE was calculated with the number of photons emitted from a plane source as a measure for the incoming SNR2. Measurements were made with 99mTc, using three different pulse height windows at 2 cm and 12 cm depths in water with high resolution and all purpose collimators and with two different crystal thicknesses. The results indicated that at greater depths a 15% window is the best choice. The choice of collimator depends on the details in the organ being investigated. There is a break point at 0.5 cycles cm-1 and 1.2 cycles cm-1 at 12 cm and 2 cm depths, respectively. A difference was found in DQE between the two crystal thicknesses, with a slightly better result for the thick crystal for measurements at 12 cm depth. At 2 cm depth, the thinner crystal was slightly better for frequencies over 0.5 cm-1. The determination of DQE could be a method to optimize the parameters for different nuclear medicine investigations. The DQE could also be used in comparing different gamma camera systems with different collimators to obtain a figure of merit.

Stasheuski, A. S., et al. (2014). "Photophysical properties and singlet oxygen generation efficiencies of water-soluble fullerene nanoparticles." Photochem Photobiol **90**(5): 997-1003.

As various fullerene derivatives have been developed, it is necessary to explore their photophysical properties for potential use in photoelectronics and medicine. Here, we address the photophysical properties of newly synthesized water-soluble fullerene-based nanoparticles and polyhydroxylated fullerene as a representative water-soluble fullerene derivative. They show broad emission band arising from a wide-range of excitation energies. It is attributed to the optical transitions from disorder-induced states, which decay in the nanosecond time range. We determine the kinetic properties of the singlet oxygen ((1)O2) luminescence generated by the fullerene nanoparticles and polyhydroxylated fullerene

to consider the potential as photodynamic agents. Triplet state decay of the nanoparticles was longer than (1)O2 lifetime in water. Singlet oxygen quantum yield of a series of the fullerene nanoparticles is comparably higher ranging from 0.15 to 0.2 than that of polyhydroxylated fullerene, which is about 0.06.

Stenta, M. and M. Dal Peraro (2011). "An introduction to quantum chemical methods applied to drug design." Front Biosci (Elite Ed) **3**: 1061-1078.

The advent of molecular medicine allowed identifying the malfunctioning of subcellular processes as the source of many diseases. Since then, drugs are not only discovered, but actually designed to fulfill a precise task. Modern computational techniques, based on molecular modeling, play a relevant role both in target identification and drug lead development. By flanking and integrating standard experimental techniques, modeling has proven itself as a powerful tool across the drug design process. The success of computational methods depends on a balance between cost (computation time) and accuracy. Thus, the integration of innovative theories and more powerful hardware architectures allows molecular modeling to be used as a reliable tool for rationalizing the results of experiments and accelerating the development of new drug design strategies. We present an overview of the most common quantum chemistry computational approaches, providing for each one a general theoretical introduction to highlight limitations and strong points. We then discuss recent developments in software and hardware resources, which have allowed state-of-the-art of computational quantum chemistry to be applied to drug development.

Stewart, F., et al. (2021). "Ultrasound mediated delivery of quantum dots from a proof of concept capsule endoscope to the gastrointestinal wall." Sci Rep **11**(1): 2584.

Biologic drugs, defined as therapeutic agents produced from or containing components of a living organism, are of growing importance to the pharmaceutical industry. Though oral delivery of medicine is convenient, biologics require invasive injections because of their poor bioavailability via oral routes. Delivery of biologics to the small intestine using electronic delivery with devices that are similar to capsule endoscopes is a promising means of overcoming this limitation and does not require reformulation of the therapeutic agent. The efficacy of such capsule devices for drug delivery could be further improved by increasing the permeability of the intestinal tract lining with an integrated ultrasound transducer to increase uptake. This paper describes a novel proof of concept capsule device capable of electronic application of focused ultrasound and delivery of therapeutic agents. Fluorescent markers, which were chosen as a model drug, were used to demonstrate in vivo delivery in the porcine small intestine with this capsule. We show that the fluorescent markers can penetrate the mucus layer of the small intestine at low acoustic powers when combining microbubbles with focused ultrasound during in vivo experiments using porcine models. This study illustrates how such a device could be potentially used for gastrointestinal drug delivery and the challenges to be overcome before focused ultrasound and microbubbles could be used with this device for the oral delivery of biologic therapeutics.

Steyer, G. J., et al. (2009). "Cryo-Imaging of Fluorescently-Labeled Single Cells in a Mouse." Proc SPIE Int Soc Opt Eng **7262**: 72620W-72620W72628.

We developed a cryo-imaging system to provide single-cell detection of fluorescently labeled cells in mouse, with particular applicability to stem cells and metastatic cancer. The Case cryo-imaging system consists of a fluorescence microscope, robotic imaging positioner, customized cryostat, PC-based control system, and visualization/analysis software. The system alternates between sectioning (10-40 mum) and imaging, collecting color brightfield and fluorescent block-face image volumes >60GB. In mouse experiments, we imaged quantum-dot labeled stem cells, GFP-labeled cancer and stem cells, and cell-size fluorescent microspheres. To remove subsurface fluorescence, we used a simplified model of light-tissue interaction whereby the next image was scaled, blurred, and subtracted from the current image. We estimated scaling and blurring parameters by minimizing entropy of subtracted images. Tissue specific attenuation parameters were found [u(T) : heart (267 +/- 47.6 mum), liver (218 +/- 27.1 mum), brain (161 +/- 27.4 mum)] to be within the range of estimates in the literature. "Next image" processing removed subsurface fluorescence equally well across multiple tissues (brain, kidney, liver, adipose tissue, etc.), and analysis of 200 microsphere images in the brain gave 97+/-2% reduction of subsurface fluorescence. Fluorescent signals were determined to arise from single cells based upon geometric and integrated intensity measurements. Next image processing greatly improved axial resolution, enabled high quality 3D volume renderings, and improved enumeration of single cells with connected component analysis by up to 24%. Analysis of image volumes identified metastatic cancer sites, found homing of stem cells to injury sites, and showed microsphere distribution correlated with blood flow patterns.We developed and evaluated cryo-imaging to provide single-cell detection of fluorescently labeled cells in mouse. Our cryo-imaging system provides extreme (>60GB), micron-

scale, fluorescence, and bright field image data. Here we describe our image pre-processing, analysis, and visualization techniques. Processing improves axial resolution, reduces subsurface fluorescence by 97%, and enables single cell detection and counting. High quality 3D volume renderings enable us to evaluate cell distribution patterns. Applications include the myriad of biomedical experiments using fluorescent reporter gene and exogenous fluorophore labeling of cells in applications such as stem cell regenerative medicine, cancer, tissue engineering, etc.

Stuppner, S., et al. (2020). "Near-Infrared Spectroscopy as a Rapid Screening Method for the Determination of Total Anthocyanin Content in Sambucus Fructus." Sensors (Basel) **20**(17).

Elderberry (Sambucus nigra L., fructus) is a very potent herbal drug, deriving from traditional European medicine (TEM). Ripe elderberries are rich in anthocyanins, flavonols, flavonol esters, flavonol glycosides, lectins, essential oils, unsaturated fatty acids and vitamins. Nevertheless, unripe elderflower fruits contain a certain amount of sambunigrin, a toxic cyanogenic glycoside, whose concentration decreases in the ripening process. Therefore, quality assurance must be carried out. The standard method described in literature is the photometric determination (pH-differential method) of the total anthocyanin content (TAC) that is the highest when the berries are ripe. The drawback of the pH-differential method is the extensive sample preparation and the low accuracy of the method. Therefore, the goal of this publication was to develop a fast non invasive near-infrared (NIR) method for the determination of TAC in whole berries. TAC of elderberries was measured using pH-differentiation method where TAC values of 632.87 mg/kg to 4342.01 mg/kg were measured. Additionally, cyanidin-3-O-glucoside, cyanidin-3-O-sambubioside and cyanidin-3-O-sambubioside-5-O-glucoside which represent more than 98% of TAC in elderberry were quantified using ultra high performance liquid chromatography-multiple wavelength detection-ultra high resolution-quadrupole-time of flight-mass spectrometry (UHPLC-MWD-UHR-Q-TOF-MS) and their sum parameter was determined, ranging between 499.43 mg/kg and 8199.07 mg/kg. Using those two methods as reference, whole elderberries were investigated by NIR spectroscopy with the Buchi NIRFlex N-500 benchtop spectrometer. According to the constructed partial least squares regression (PLSR) models the performance was as follows: a relative standard deviation (RSDPLSR) of 13.5% and root mean square error of calibration (RMSECV/RMSEC) of 1.31 for pH-differentiation reference and a RSDPLSR of 12.9% and RMSECV/RMSEC of 1.28 for the HPLC reference method. In this study, we confirm that it is possible to perform a NIR screening for TAC in whole elderberries. Using quantum chemical calculations, we obtained detailed NIR band assignments of the analyzed compounds and interpreted the wavenumber regions established in PLSR models as meaningful for anthocyanin content. The NIR measurement turned out to be a fast and cost-efficient alternative for the determination of TAC compared to pH-differential method and UHPLC-MWD-UHR-Q-TOF-MS. Due to the benefit of no sample preparation and extraction the technology can be considered as sustainable green technology. With the above mentioned inversely proportional ratio of TAC to total amount of toxic cyanogenic glycosides, NIR proves to be a reliable screening method for the ideal harvest time with maximal content of TAC and lowest content of cyanogenic glycosides in elderberry.

Sugden, J. K. (2004). "Photochemistry of dyes and fluorochromes used in biology and medicine: some physicochemical background and current applications." Biotech Histochem **79**(2): 71-90.

An overview of the basic principles of photochemistry is presented to facilitate discussion of fluorescence, quenching and quantum yields. These topics in turn provide the foundation for an account of fluorescence spectroscopy and its application to microscopy. A brief overview of light microscopy and the application of fluorescence microscopy is given. The influences of molecular features, such as aromatic character and substitution patterns, on color and fluorescence are described. The concept of color fading is considered with particular reference to its effect on microscopic preparations. A survey of representative fluorescent probes is provided, and their sensitivity, application, and limitations are described. The phototoxicity of fluorescent molecules is discussed using biomembranes and DNA as examples of targets of toxicity. Photodynamic therapy, a relatively new clinical application of phototoxicity, is described. Both anticancer and antimicrobial applications are noted, and an assessment is given of the current ideas on the ideal physicochemical properties of the sensitizing agents for such applications.

Sukhorukov, G. B., et al. (2007). "Multifunctionalized polymer microcapsules: novel tools for biological and pharmacological applications." Small **3**(6): 944-955.

We describe recent developments with multifunctional nanoengineered polymer capsules. In addition to their obvious use as a delivery system, multifunctional nanocontainers find wide application in enzymatic catalysis, controlled release, and directed drug delivery in medicine. The multifunctionality is provided by the following components: 1) Luminescent semiconductor nanocrystals (quantum dots) that

facilitate imaging and identification of different capsules, 2) superparamagnetic nanoparticles that allow manipulation of the capsules in a magnetic field, 3) surface coatings, which target the capsules to desired cells, 4) metallic nanoparticles in the capsule wall that act as an absorbing antenna for electromagnetic fields and provide heat for controlled release, and 5) enzymes and pharmaceutical agents that allow specific reactions. The unique advantage of multifunctional microcapsules in comparison to other systems is that they can be simultaneously loaded/functionalized with the above components, allowing for the combination of their properties in a single object.

Sukhorukov, G. B., et al. (2005). "Nanoengineered polymer capsules: tools for detection, controlled delivery, and site-specific manipulation." Small **1**(2): 194-200.

We present the concept of multifunctional nanoengineered polymer capsules and outline their applications as new drug delivery systems or supramolecular toolboxes containing, for example, enzymes capable of converting nontoxic prodrugs into toxic drugs at a designated location. Such functionalized nanocontainers offer a wide range of applications including enzymatic catalysis, controlled release, and directed drug delivery in medicine due to their multifunctionality. The unique advantage of capsules in comparison to other systems is that they can be functionalized or loaded simultaneously with the above-mentioned components, thus permitting multifunctional processes in single cells.

Sulimov, V. B., et al. (2019). "Advances in Docking." Curr Med Chem **26**(42): 7555-7580.

BACKGROUND: Design of small molecules which are able to bind to the protein responsible for a disease is the key step of the entire process of the new medicine discovery. Atomistic computer modeling can significantly improve effectiveness of such design. The accurate calculation of the free energy of binding a small molecule (a ligand) to the target protein is the most important problem of such modeling. Docking is one of the most popular molecular modeling methods for finding ligand binding poses in the target protein and calculating the protein-ligand binding energy. This energy is used for finding the most active compounds for the given target protein. This short review aims to give a concise description of distinctive features of docking programs focusing on computation methods and approximations influencing their accuracy. METHODS: This review is based on the peer-reviewed research literature including author's own publications. The main features of several representative docking programs are briefly described focusing on their characteristics influencing docking accuracy: force fields, energy calculations, solvent models, algorithms of the best ligand pose search, global and local optimizations, ligand and target protein flexibility, and the simplifications made for the docking accelerating. Apart from other recent reviews focused mainly on the performance of different docking programs, in this work, an attempt is made to extract the most important functional characteristics defining the docking accuracy. Also a roadmap for increasing the docking accuracy is proposed. This is based on the new generation of docking programs which have been realized recently. These programs and respective new global optimization algorithms are described shortly. RESULTS: Several popular conventional docking programs are considered. Their search of the best ligand pose is based explicitly or implicitly on the global optimization problem. Several algorithms are used to solve this problem, and among them, the heuristic genetic algorithm is distinguished by its popularity and an elaborate design. All conventional docking programs for their acceleration use the preliminary calculated grids of protein-ligand interaction potentials or preferable points of protein and ligand conjugation. These approaches and commonly used fitting parameters restrict strongly the docking accuracy. Solvent is considered in exceedingly simplified approaches in the course of the global optimization and the search for the best ligand poses. More accurate approaches on the base of implicit solvent models are used frequently for more careful binding energy calculations after docking. The new generation of docking programs are developed recently. They find the spectrum of low energy minima of a protein-ligand complex including the global minimum. These programs should be more accurate because they do not use a preliminary calculated grid of protein-ligand interaction potentials and other simplifications, the energy of any conformation of the molecular system is calculated in the frame of a given force field and there are no fitting parameters. A new docking algorithm is developed and fulfilled specially for the new docking programs. This algorithm allows docking a flexible ligand into a flexible protein with several dozen mobile atoms on the base of the global energy minimum search. Such docking results in improving the accuracy of ligand positioning in the docking process. The adequate choice of the method of molecular energy calculations also results in the better docking positioning accuracy. An advancement in the application of quantum chemistry methods to docking and scoring is revealed. CONCLUSION: The findings of this review confirm the great demand in docking programs for discovery of new medicine substances with the help of molecular modeling. New trends in docking programs design are revealed. These trends are focused on the increase of the docking accuracy at the

expense of more accurate molecular energy calculations without any fitting parameters, including quantum-chemical methods and implicit solvent models, and by using new global optimization algorithms which make it possible to treat flexibility of ligands and mobility of protein atoms simultaneously. Finally, it is shown that all the necessary prerequisites for increasing the docking accuracy can be accomplished in practice.

Sullivan, K. M. (1994). "Forensic applications of DNA fingerprinting." Mol Biotechnol **1**(1): 13-27.

In many ways, DNA profiling technology is very similar to the conventional techniques used for forensic identification. As with, for example, blood grouping techniques, the molecular characteristics of the scene of crime sample may be determined and compared with those of the scene of reference samples from suspects and victim. If the molecular characteristics of the crime sample and the suspect are different, then they cannot be from the same person, whereas if they match, then the possibility remains that they may be from a single source. Similar material, such as blood or semen stains, may be used for both biochemical and genetic tests, and the main applications of identification and relationship testing are shared by both techniques. At this point, the similarity ends; DNA profiling has the following characteristics: 1. It is more sensitive, being able to generate sound data from only a tiny amount of even partially degraded biological material. 2. It is capable of resolving mixtures of semen or tissue from up to several individuals. 3. It has a far greater power of discrimination between individuals--sometimes up to 1 millionfold higher than conventional techniques. 4. It provides considerably more information on the nature of relationships, particularly in cases of incest. As such, the technique represents a quantum leap in forensic identification and relationship testing.

Sun, C., et al. (2020). "Development of a ZnCdS@ZnS quantum dots-based label-free electrochemiluminescence immunosensor for sensitive determination of aflatoxin B1 in lotus seed." Mikrochim Acta **187**(4): 236.

In this study, we designed a ZnCdS@ZnS quantum dots (QDs)-based label-free electrochemiluminescence (ECL) immunosensor for sensitive determination of aflatoxin B1 (AFB1). A Nafion solution assembled abundant QDs on the surface of a Au electrode as ECL signal probes, with specially coupled anti-AFB1 antibodies as the capturing element. As the reduction reaction between S2O8(2-) in the electrolyte and QDs on the electrode led to ECL emission, the decreased ECL signals resulting from target AFB1 in the samples were recorded for quantification. We evaluated electrochemical impedance spectroscopy and ECL measurements along each step in the construction of the proposed immunosensor. After systematic optimization of crucial parameters, the ECL immunosensor exhibited a good sensitivity, with a low detection limit of 0.01 ng/mL for AFB1 in a wide concentration range of 0.05-100 ng/mL. Testing with lotus seed samples confirmed the satisfactory selectivity, stability, and reproducibility of the developed ECL immunosensor for rapid, efficient, and sensitive detection of AFB1 at trace levels in complex matrices. This study provides a powerful and universal analytical platform for a variety of analytes that can be used in broad applications for real-time analysis, such as food and traditional Chinese medicine safety testing, environmental pollution monitoring, and disease diagnostics. Graphical abstract Development of a ZnCdS@ZnS quantum dots based label-free electrochemiluminescence immunosensor for sensitive detection of aflatoxin B1 in lotus seed.

Sun, Y. N., et al. (2017). "Chemical Components from Aloe and their Inhibition of Indoleamine 2, 3-dioxygenase." Pharmacogn Mag **13**(49): 58-63.

BACKGROUND: In Korea, Aloe is routinely ingested as a traditional medicine or as a component of health beverages. OBJECTIVE: To research the inhibition of indoleamine 2, 3-dioxygenase (IDO) activities of components from Aloe. MATERIALS AND METHODS: the compounds were isolated by a combination of silica gel and YMC Rp-18 column chromatography, and their structures were identified by analysis of spectroscopic data (1D, 2D-NMR, and MS). All of the isolated compounds were examined for their ability to inhibit IDO, which actively suppresses immune functions by catalyzing the rate limiting reaction in the conversion of tryptophan to kynurenine. RESULTS: In this phytochemical study, 18 known compounds were isolated from aqueous dissolved Aloe exudates. All of the isolated compounds were examined for their ability to inhibit IDO activities for a series of anthraquinone derivatives (1-7) isolated from the Aloe extract; the IC50 values of these compounds ranged from 39.41 to 53.93 microM. Enzyme kinetic studies of their modes of inhibition indicated that all of the compounds were uncompetitive inhibitors. CONCLUSION: The aqueous dissolved Aloe exudate can be used as a source of novel natural IDO inhibitors and merit testing as therapeutic agents in the treatments of cancer and immunopathologic diseases, such as autoimmune, inflammatory, and allergic disorders. SUMMARY: In this study, 18 known compounds were isolated from aqueous dissolved Aloe exudates. All of the isolated compounds were examined for their ability to inhibit indoleamine 2, 3-dioxygenase (IDO)

activities for a series of anthraquinone derivatives (1-7) isolated from the Aloe extract. Abbreviation used: IDO: inhibit indoleamine 2, 3-dioxygenase, TMS: tetramethylsilane, HMQC: heteronuclear multiple quantum correlation, HMBC: heteronuclear multiple bond correlation, COSY: 1H-1H correlation spectroscopy, ESI-MS: Electrospray ionization mass spectrometry, DMSO: dimethyl sulfoxide.

Sun, Z., et al. (2018). "Haemostatic bioactivity of novel Schizonepetae Spica Carbonisata-derived carbon dots via platelet counts elevation." Artif Cells Nanomed Biotechnol **46**(sup3): S308-S317.

Schizonepetae Spica Carbonisata (SSC) has pronounced haemostatic effects for hundreds of years and has been acknowledged in the 2015 Pharmacopoeia of the People's Republic of China (PPRC) as a haemostatic charcoal drug. However, after years of efforts, the underlying mechanism and the material basis is still less defined. In this research, we developed a novel CDs derived from SSC (SSC-CDs) with an average diameter of 1.29-6.87 nm and a quantum yield of 6.31%. SSC was prepared using a modified pyrolysis method and no further modification and external surface passivation agent is required. With abundant surface groups, SSC-CDs showed distinct solubility and bioactivity. In this study, we innovatively used the Deinagkistrodon acutus (D. acutus) venom model as well as the classical haemorrhagic animal model to evaluate the haemostatic bioactivity of SSC-CDs. The results indicated that SSC-CDs had outstanding haemostatic bioactivity and might inhibit the haemorrhagic activity via PLT elevation. According to the results of this study and our previous work, we discovered that CDs derived from different kinds of charcoal drugs presented similarities and differences in the structural feature, physicochemical property and bioactivity. In order to further explore the self-bioactivities, we first named this kind of CDs as "Chinese Medicine charcoal drug nanoparticles" (CMNP). These results may not only provide evidence for further researches of self-bioactivities of CDs but give new insights into potential biomedical and healthcare applications of CDs, therefore, make contributions to future drug discovery.

Sung, G. T. and I. S. Gill (2003). "Robotic renal and adrenal surgery." Surg Clin North Am **83**(6): 1469-1482.

Technology today is evolving at a dramatic rate. Quantum development has occurred in the area of robotic enhancement technology (RET) in the last decade. Incorporation of RET with advanced telecommunication technologies is a recent integration in medicine, with growth potential and application in the delivery of modern health care. There remain, however, many areas which need to be further improved and evaluated before clinical applications of the robot become accepted in adrenal and renal minimally invasive surgery.

Sung, S. Y., et al. (2019). "Graphene Quantum Dots-Mediated Theranostic Penetrative Delivery of Drug and Photolytics in Deep Tumors by Targeted Biomimetic Nanosponges." Nano Lett **19**(1): 69-81.

Dual-targeted delivery of drugs and energy by nanohybrids can potentially alleviate side effects and improve the unique features required for precision medicine. To realize this aim, however, the hybrids which are often rapidly removed from circulation and the piled up tumors periphery near the blood vessels must address the difficulties in low blood half-lives and tumor penetration. In this study, a sponge-inspired carbon composites-supported red blood cell (RBC) membrane that doubles as a stealth agent and photolytic carrier that transports tumor-penetrative agents (graphene quantum dots and docetaxel (GQD-D)) and heat with irradiation was developed. The RBC-membrane enveloped nanosponge (RBC@NS) integrated to a targeted protein that accumulates in tumor spheroids via high lateral bilayer fluidity exhibits an 8-fold increase in accumulation compared to the NS. Penetrative delivery of GQDs to tumor sites is actuated by near-infrared irradiation through a one-atom-thick structure, facilitating penetration and drug delivery deep into the tumor tissue. The synergy of chemotherapy and photolytic effects was delivered by the theranostic GQDs deep into tumors, which effectively damaged and inhibited the tumor in 21 days when treated with a single irradiation. This targeted RBC@GQD-D/NS with the capabilities of enhanced tumor targeting, NIR-induced drug penetration into tumors, and thermal ablation for photolytic therapy promotes tumor suppression and exhibits potential for other biomedical applications.

Surendiran, A., et al. (2009). "Novel applications of nanotechnology in medicine." Indian J Med Res **130**(6): 689-701.

Current modalities of diagnosis and treatment of various diseases, especially cancer have major limitations such as poor sensitivity or specificity and drug toxicities respectively. Newer and improved methods of cancer detection based on nanoparticles are being developed. They are used as contrast agents, fluorescent materials, molecular research tools and drugs with targeting antibodies. Paramagnetic nanoparticles, quantum dots, nanoshells and nanosomes are few of the nanoparticles used for diagnostic purposes. Drugs with high toxic potential like cancer chemotherapeutic drugs can be given with a better safety profile with the utility of nanotechnology.

These can be made to act specifically at the target tissue by active as well as passive means. Other modalities of therapy such as heat induced ablation of cancer cells by nanoshells and gene therapy are also being developed. This review discusses the various platforms of nanotechnology being used in different aspects of medicine like diagnostics and therapeutics. The potential toxicities of the nanoparticles are also described in addition to hypothetical designs such as respirocytes and microbivores. The safety of nanomedicine is not yet fully defined. However, it is possible that nanomedicine in future would play a crucial role in the treatment of human diseases and also in enhancement of normal human physiology.

Sweeney, B. P. (2004). "Watson and Crick 50 years on. From double helix to pharmacogenomics." Anaesthesia **59**(2): 150-165.

The second half of the 20th century has seen quantum leaps in our understanding of molecular biology. The technological advances, which facilitated the recent successful completion of the Human Genome Project, have provided the tools for deciphering the complexity of the human condition. At present, the function of only 50% of genes is known. However, as understanding of the human genome improves, a plethora of gene targets for treating disease will be uncovered - leading to therapies which will be considered revolutionary. Genome related science has begun to impact almost every facet of medicine including anaesthesia and intensive care. Better understanding of interindividual differences will enable better prediction of illness susceptibility as well as response to treatment. These insights will permit therapies to be tailored to individuals or racial groups. At present, there is only rudimentary knowledge of factors controlling gene regulation, but in the future, better understanding of gene-environment interactions and gene expression will enable pharmaceutical companies to develop new therapies and permit clinicians to optimise their effects, without recourse to current laborious testing regimens. As genomic science progresses, new ethical, legal, social and philosophical dilemmas will also continue to emerge.

Szefler, B. (2018). "Nanotechnology, from quantum mechanical calculations up to drug delivery." Int J Nanomedicine **13**: 6143-6176.

There are several reasons why nanotechnology is currently considered as the leader among the most intensively developing research trends. Nanomatter often exhibits new properties, other than those of the morphology of a continuous solid. Also, new phenomena appear at the nanoscale, which are unknown in the case of microcrystalline objects. For this reason, nanomaterials have already found numerous applications that are described in this review. However, among intensively developed various branches of nanotechnology, nanomedicine and pharmacology stand out particularly, which opens new possibilities for the development of these disciplines, gives great hope for the creation of new drugs in which toxicological properties are reduced to a minimum, reduces the doses of medicines, offers targeted treatment and increases diagnostic possibilities. Nanotechnology is the source of a great revolution in medicine. It gives great hope for better and faster treatment of many diseases and gives hope for a better tomorrow. However, the creation of new "nanodrugs" requires a special understanding of the properties of nanoparticles. This article is a review work which determines and describes the way of creating new nanodrugs from ab initio calculations by docking and molecular dynamic applications up to a new medicinal product, as a proposal for the personalized medicine, in the early future.

Taghva, A., et al. (2010). "From atom to brain: applications of molecular imaging to neurosurgery." World Neurosurg **73**(5): 477-485.

Molecular imaging is a field born out of the happy marriage of molecular biology and radiology. The first installment of this two-part series on molecular imaging demonstrated basic principles for practitioners in the field of the neurosciences. This installment seeks to provide some illustrative examples, insights, and specific applications to the neurosciences. The fields of functional neurosurgery including the treatment of neuropsychiatric disorders, novel treatments and imaging of tumors, neuroregenerative medicine, and nanotechnology in vascular disorders are covered. Finally, we give some parting thoughts on the future of molecular imaging, including advances in the imaging of neurodegenerative disorders.

Tak, Y. K., et al. (2012). "Highly sensitive polymerase chain reaction-free quantum dot-based quantification of forensic genomic DNA." Anal Chim Acta **721**: 85-91.

Forensic DNA samples can degrade easily due to exposure to light and moisture at the crime scene. In addition, the amount of DNA acquired at a criminal site is inherently limited. This limited amount of human DNA has to be quantified accurately after the process of DNA extraction. The accurately quantified extracted genomic DNA is then used as a DNA template in polymerase chain reaction (PCR) amplification for short tandem repeat (STR) human identification. Accordingly, highly sensitive and human-specific quantification of forensic DNA samples is an essential issue in forensic study. In this work, a quantum dot (Qdot)-labeled Alu sequence was developed as a probe

to simultaneously satisfy both the high sensitivity and human genome selectivity for quantification of forensic DNA samples. This probe provided PCR-free determination of human genomic DNA and had a 2.5-femtogram detection limit due to the strong emission and photostability of the Qdot. The Qdot-labeled Alu sequence has been used successfully to assess 18 different forensic DNA samples for STR human identification.

Takeda, M., et al. (2008). "In vivo single molecular imaging and sentinel node navigation by nanotechnology for molecular targeting drug-delivery systems and tailor-made medicine." Breast Cancer **15**(2): 145-152.

The recent advances in nanotechnology have a great potential to improve the prevention, diagnosis, and treatment of human diseases. Nanomaterials for medical applications are expected to grasp pharmacokinetics and the toxicity for application to medical treatment on the aspect of safety of the nanomaterials and nanodevices. We describe a generation of CdSe nanoparticles [quantum dots (QDs)] conjugated with monoclonal anti-HER2 antibody (Trastuzumab), for single molecular in vivo imaging of breast cancer cells. We established a high-resolution in vivo 3D microscopic system for a novel imaging method at the molecular level. The cancer cells expressing HER2 protein were visualized by the nanoparticles in vivo at subcellular resolution, suggesting future utilization of the system in medical applications to improve drug-delivery systems to target the primary and metastatic tumors for made-to-order treatment. We also describe sentinel node navigation using fluorescent nanoparticles for breast cancer surgery in experimental model, which have shown the potential to be an alternative to existing tracers in the detection of the sentinel node if we select the appropriate particle size and wavelength. Future innovation in cancer imaging by nanotechnology and novel measurement technology will provide great improvement, not only in the clinical field but also in basic medical science for the development of medicine.

Tan, A., et al. (2011). "Quantum dots and carbon nanotubes in oncology: a review on emerging theranostic applications in nanomedicine." Nanomedicine (Lond) **6**(6): 1101-1114.

Cancer is one of the main causes of death in the world, and according to the WHO it is projected to continue rising. Current diagnostic modalities for the detection of cancer include the use of x-rays, magnetic resonance imaging and positron emission tomography, among others. The treatment of cancer often involves the use (or combination) of chemotherapeutic drugs, radiotherapy and interventional surgery (for solid and operable tumors). The application of nanotechnology in biology and medicine is advancing rapidly. Recent evidence suggests that quantum dots (QDs) can be used to image cancer cells as they display superior fluorescent properties compared with conventional chromophores and contrast agents. In addition, carbon nanotubes (CNTs) have emerged as viable candidates for novel chemotherapeutic drug delivery-platforms. The unique photothermal properties of CNTs also allow them to be used in conjunction with near infrared radiation and lasers to thermally ablate cancer cells. Furthermore, mounting evidence indicates that it is possible to conjugate QDs to CNTs, making it possible to exploit their novel attributes in the realm of cancer theranostics (diagnostics and therapy). Here we review the current literature pertaining to the applications of QDs and CNTs in oncology, and also discuss the relevance and implications of nanomedicine in a clinical setting.

Tan, L. L. and L. Shang (2019). "Smart Delivery Systems Based on Poly(glycidyl methacrylate)s-Coated Organic/Inorganic Core-Shell Nanohybrids." Macromol Rapid Commun **40**(17): e1800879.

Smart delivery systems have gained momentum over the last few decades due to their potential to realize enhanced therapeutic efficacy. Poly(glycidyl methacrylate)s (PGMAs), which spring up like mushrooms, have drawn great attention in the theranostics field, especially in multifunctional theranostic systems. The marriage of PGMAs with functional inorganic cores is expected to integrate diagnosis (e.g., fluorescence, X-ray computed tomography, magnetic resonance, photoacoustic and upconversion luminescence imaging), treatment, or multimodal synergistic therapies (e.g., chemotherapy, gene therapy, photothermal therapy) in one pot for personalized medicine. In this review, recent progress in various PGMA-coated nanohybrids based on the type of integrated inorganic nanoparticle, including silica nanoparticles, magnetic nanoparticles, quantum dots, gold nanoparticles, gold nanorods, metal-organic frameworks, cellulose nanocrystals, and their core-shell nanostructures is systematically reviewed. Future work in this field is anticipated to be devoted to developing efficient real-time-imaging-guided multimodal synergistic therapies.

Tan, M. A. and H. Takayama (2019). "Recent Progress in the Chemistry of Pandanus Alkaloids." Alkaloids Chem Biol **82**: 1-28.

The genus Pandanus (Pandanaceae) is widely distributed in the tropical and subtropical regions. With about 700 species worldwide, three Pandanus species (P. amaryllifolius, P. utilis, and P. dubius) have been investigated and found to contain new alkaloids

possessing a pyrrolidinyl-alpha,beta-unsaturated gamma-lactone, a gamma-butylidene-alpha-methyl-alpha,beta-unsaturated gamma-lactam, and/or indolizidine residues. Several total syntheses of Pandanus alkaloids have been accomplished. Several pharmacological studies on Pandanus species, including scientific validations of their antibacterial, antiinflammatory, antidiarrheal, and cytotoxic activities, have been conducted in relation to their traditional folk medicine uses.

Tan, S. K. (2003). "From genesis to genes." Ann Acad Med Singap **32**(5): 710-714.

Since the beginning of time, our ancestors have been plagued by illnesses and injuries that are not too different from today's diseases. Evidence from prehistoric times and ancient civilisations have shown man's attempts at trying to understand the nature and treatment of these conditions. It was not till the early 19th century that the scientific basis of modern medicine was firmly established when microorganisms were discovered and found to be the cause of many of these illnesses. The 20th century saw quantum leaps made in the understanding of the function of the human body and the therapeutic measures aimed at restoration of any such malfunction. The end of the last millennium was marked by historic achievements made in the Life Sciences, in particular the completion of the sequencing of the Human Genome--the code of life. The beginning of the 21st century has already seen many breakthroughs in medical sciences, especially in the fields of stem cell technology and gene therapy. The number of known illnesses directly related to genetic defects or abnormalities have increased exponentially. Many of today's scourges can be prevented or more effectively treated. Our ability to utilise this new knowledge to combat the ravages of the ageing process and its associated illnesses--degenerative diseases and cancers offer much hope for the future.

Taneja, P., et al. (2021). "Advancement of nanoscience in development of conjugated drugs for enhanced disease prevention." Life Sci **268**: 118859.

Nanoscience and nanotechnology is a recently emerging and rapid developing field of science and has also been explored in the fields of Biotechnology and Medicine. Nanoparticles are being used as tools for diagnostic purposes and as a medium for the delivery of therapeutic agents to the specific targeted sites under controlled conditions. The physicochemical properties of these nanoparticles give them the ability to treat various chronic human diseases by site specific drug delivery and to use in diagnosis, biosensing and bioimaging devices, and implants. According to the type of materials used nanoparticles can be classified as organic (micelles, liposomes, nanogels and dendrimers) and inorganic (including gold nanoparticles (GNPs), super-paramagnetic iron oxide nanomaterials (SPIONs), quantum dots (QDs), and paramagnetic lanthanide ions). Different types of nanoparticle are being used in conjugation with various types of biomoities (such as peptide, lipids, antibodies, nucleotides, plasmids, ligands and polysaccharides) to form nanoparticle-drug conjugates which has enhanced capacity of drug delivery at targeted sites and hence improved disease treatment and diagnosis. In this study, the summary of various types of nanoparticle-drug conjugates that are being used along with their mechanism and applications are included. In addition, the various nanoparticle-drug conjugates which are being used and which are under clinical studies along with their future opportunities and challenges are also discussed in this review.

Tang, D., et al. (2017). "Evaluation of TSPO PET Ligands [(18)F]VUIIS1009A and [(18)F]VUIIS1009B: Tracers for Cancer Imaging." Mol Imaging Biol **19**(4): 578-588.

PURPOSE: Positron emission tomography (PET) ligands targeting translocator protein (TSPO) are potential imaging diagnostics of cancer. In this study, we report two novel, high-affinity TSPO PET ligands that are 5,7 regioisomers, [(18)F]VUIIS1009A ([(18)F]3A) and [(18)F]VUIIS1009B ([(18)F]3B), and their initial in vitro and in vivo evaluation in healthy mice and glioma-bearing rats. PROCEDURES: VUIIS1009A/B was synthesized and confirmed by X-ray crystallography. Interactions between TSPO binding pocket and novel ligands were evaluated and compared with contemporary TSPO ligands using 2D (1)H-(15)N heteronuclear single quantum coherence (HSQC) spectroscopy. In vivo biodistribution of [(18)F]VUIIS1009A and [(18)F]VUIIS1009B was carried out in healthy mice with and without radioligand displacement. Dynamic PET imaging data were acquired simultaneously with [(18)F]VUIIS1009A/B injections in glioma-bearing rats, with binding reversibility and specificity evaluated by radioligand displacement. In vivo radiometabolite analysis was performed using radio-TLC, and quantitative analysis of PET data was performed using metabolite-corrected arterial input functions. Imaging was validated with histology and immunohistochemistry. RESULTS: Both VUIIS1009A (3A) and VUIIS1009B (3B) were found to exhibit exceptional binding affinity to TSPO, with observed IC50 values against PK11195 approximately 500-fold lower than DPA-714. However, HSQC NMR suggested that VUIIS1009A and VUIIS1009B share a common binding pocket within mammalian TSPO (mTSPO) as DPA-714 and to a lesser extent, PK11195.

[(18)F]VUIIS1009A ([(18)F]3A) and [(18)F]VUIIS1009B ([(18)F]3B) exhibited similar biodistribution in healthy mice. In rats bearing C6 gliomas, both [(18)F]VUIIS1009A and [(18)F]VUIIS1009B exhibited greater binding potential (k 3/k 4)in tumor tissue compared to [(18)F]DPA-714. Interestingly, [(18)F]VUIIS1009B exhibited significantly greater tumor uptake (V T) than [(18)F]VUIIS1009A, which was attributed primarily to greater plasma-to-tumor extraction efficiency. CONCLUSIONS: The novel PET ligand [(18)F]VUIIS1009B exhibits promising characteristics for imaging glioma; its superiority over [(18)F]VUIIS1009A, a regioisomer, appears to be primarily due to improved plasma extraction efficiency. Continued evaluation of [(18)F]VUIIS1009B as a high-affinity TSPO PET ligand for precision medicine appears warranted.

Tang, M., et al. (2009). "The effect of quantum dots on synaptic transmission and plasticity in the hippocampal dentate gyrus area of anesthetized rats." Biomaterials **30**(28): 4948-4955.

Recently, quantum dots (QDs) have attracted widespread interest in biology and medicine. They are rapidly being used as new tools for both diagnostic and therapeutic purposes. Critical issues for further applications of QDs include the assessment of biocompatibility and biosafety of QDs. Most of previous researches concerning QD cytotoxicity focused on in vitro studies. In the present study, the impairments of acute exposure to well-modified and unmodified QDs (streptavidin-CdSe/ZnS and CdSe QDs, respectively) on synaptic transmission and plasticity were examined in adult rat hippocampal dentate gyrus (DG) area in vivo. The input/output (I/O) functions, paired-pulse ratio (PPR), field excitatory postsynaptic potential (fEPSP) and population spike (PS) amplitude were measured. The results showed that PPR and long-term potentiation (LTP) were all significantly decreased in these two types of QD-exposed rats compared to those in control rats. While the I/O functions and the amplitudes of fEPSP slope and PS amplitude of the baseline were significantly increased under QD exposure. These findings suggest that exposure to QDs, no matter whether they are well modified or not, could impair synaptic transmission and plasticity in the rat DG area in vivo and reveal the potential risks of QD applications in biology and medicine, especially in the toxin-susceptible central nervous system (CNS).

Tang, M., et al. (2008). "Mechanisms of unmodified CdSe quantum dot-induced elevation of cytoplasmic calcium levels in primary cultures of rat hippocampal neurons." Biomaterials **29**(33): 4383-4391.

Quantum dots (QDs) have shown great promise for applications in biology and medicine, which is being challenged by their potential nanotoxicity. Reactive oxygen species (ROS) produced by QDs are believed to be partially responsible for QD cytotoxicity. Cytoplasmic Ca(2+) plays an important role in the development of ROS injury. Here we found unmodified cadmium selenium (CdSe) QDs could elevate cytoplasmic calcium levels ([Ca(2+)](i)) in primary cultures of hippocampal neurons, involved both extracellular Ca(2+) influx and internal Ca(2+) release. More specifically, verapamil and mibefradil (L-type and T-type calcium channels antagonists, respectively) failed to prevent extracellular Ca(2+) influx under QD insult, while omega-conotoxin (N-type antagonist) could partially block this Ca(2+) influx. Surprisingly, this Ca(2+) influx could be well blocked by voltage-gated sodium channels (VGSCs) antagonist, tetrodotoxin (TTX). QD-induced internal Ca(2+) release could be avoided by clonazepam, a specific inhibitor of mitochondrial sodium-calcium exchangers (MNCX), and also by TTX. Furthermore, dantrolene, an antagonist of ryanodine (Ry) receptors in endoplasmic reticulum (ER), almost abolished internal Ca(2+) release, while 2-APB [inositol triphosphate (IP(3)) receptors antagonist] failed to block this Ca(2+) release, indicating that released Ca(2+) from mitochondria, which was induced by extracellular Na(+) influx, further triggered much more Ca(2+) release from ER. Our results imply that more research on the biocompatibility and biosafety of QD is both warranted and necessary.

Tang, M., et al. (2008). "Unmodified CdSe quantum dots induce elevation of cytoplasmic calcium levels and impairment of functional properties of sodium channels in rat primary cultured hippocampal neurons." Environ Health Perspect **116**(7): 915-922.

BACKGROUND: The growing applications of nanotechnologic products, such as quantum dots (QDs), increase the likelihood of exposure. Furthermore, their accumulation in the bioenvironment and retention in cells and tissues are arousing increasing worries about the potentially harmful side effects of these nanotechnologic products. Previous studies concerning QD cytotoxicity focused on the reactive oxygen species produced by QDs. Cellular calcium homeostasis dysregulation caused by QDs may be also responsible for QD cytotoxicity. Meanwhile the interference of QDs with voltage-gated sodium channel (VGSC) current (I(Na)) may lead to changes in electrical activity and worsen neurotoxicologic damage. OBJECTIVE: We aimed to investigate the potential for neurotoxicity of cadmium selenium QDs in a hippocampal neuronal culture model, focusing on cytoplasmic calcium levels and VGSCs function.

METHODS: We used confocal laser scanning and standard whole-cell patch clamp techniques. RESULTS: We found that a) QDs induced neuron death dose dependently; b) cytoplasmic calcium levels were elevated for an extended period by QD treatment, which was due to both extracellular calcium influx and internal calcium release from endoplasmic reticulum; and c) QD treatment enhanced activation and inactivation of I(Na), prolonged the time course of activation, slowed I(Na) recovery, and reduced the fraction of available VGSCs. CONCLUSION: Results in this study provide new insights into QD toxicology and reveal potential risks of their future applications in biology and medicine.

Tang, W., et al. (2015). "A single quantum dot-based biosensor for DNA point mutation assay." Analyst **140**(17): 5936-5943.

Sensitive and selective detection of point mutation is essential to molecular biology research and early clinical diagnosis. Here, we demonstrate a single quantum dot (QD)-based biosensor for DNA point mutation assay. In this assay, a mutant target (G/C) remains unchanged after the endonuclease treatment, and the polymerase chain reaction (PCR) may be initiated with the assistance of primers and polymerase, generating a large number of mutant targets. The amplified mutant targets can be captured by biotinylated probes during the process of denaturation and annealing, and Cy5-dGTP may be assembled into the biotinylated probe with the catalysis of polymerase, leading to the formation of Cy5-labeled biotinylated probes. The Cy5-labeled biotinylated probes can be further assembled onto the QD surface to obtain a Cy5-DNA-QD complex, resulting in the generation of fluorescence resonance energy transfer (FRET) between the QD donor and the Cy5 receptor. The mutant targets can be quantitatively evaluated by the measurement of Cy5 counts by total internal reflection fluorescence (TIRF) microscopy. While in the presence of wild-type targets (T/A), no Cy5-dGTP can be assembled into the biotinylated probe due to the presence of a mismatch and consequently no FRET is observed. This single QD-based biosensor exhibits high sensitivity with a detection limit of 5.3 aM (or 32 copies) and can even discriminate as low as 0.01% variant frequency from the mixture of mutant targets and wild-type ones. Importantly, this biosensor can be used for genomic analysis in human lung cancer cells, and may be further applied for an early clinical diagnosis and personalized medicine.

Tarassoli, S. P. (2019). "Artificial intelligence, regenerative surgery, robotics? What is realistic for the future of surgery?" Ann Med Surg (Lond) **41**: 53-55.

The potential of surgery lies in the technological advances that would complement it. The landscape of the field will differ depending on the time period being looked at and would no doubt include conjecture. Initial breakthroughs will need to pave the way for future medical technology and apply to the surgical sciences. Within the next 10 years we would expect to see the emergence of big data analysis, cuttingedge image processing techniques for surgical planning and better implementation of virtual and augmented reality in operating theatres for both patient care and teaching purposes. Over the next 50 to 100 years, the use of quantum computing should lead to increased automation in our healthcare systems. The inception of novel biomaterial invention and advanced genetic engineering will usher in the new age of regenerative medicine in the clinical setting. The future of surgery includes many predictions and promises, but it is apparent that the development will lead to bettering outcome and focus on patient care.

Tariq, A., et al. (2017). "Phosphorous Application Improves Drought Tolerance of Phoebe zhennan." Front Plant Sci **8**: 1561.

Phoebe zhennan (Gold Phoebe) is a threatened tree species in China and a valuable and important source of wood and bioactive compounds used in medicine. Apart from anthropogenic disturbances, several biotic constraints currently restrict its growth and development. However, little attention has been given to building adaptive strategies for its conservation by examining its morphological and physio-biochemical responses to drought stress, and the role of fertilizers on these responses. A randomized experimental design was used to investigate the effects of two levels of irrigation (well-watered and drought-stressed) and phosphorous (P) fertilization treatment (with and without P) to assess the morphological and physio-biochemical responses of P. zhennan seedlings to drought stress. In addition, we evaluated whether P application could mitigate the negative impacts of drought on plant growth and metabolism. Drought stress had a significant negative effect on the growth and metabolic processes of P. zhennan. Despite this, reduced leaf area, limited stomatal conductance, reduced transpiration rate, increased water use efficiency, enhanced antioxidant enzymes activities, and osmolytes accumulation suggested that the species has good adaptive strategies for tolerating drought stress. Application of P had a significant positive effect on root biomass, signifying its improved water extracting capacity from the soil. Moreover, P fertilization significantly increased leaf relative water content, net photosynthetic rate, and maximal quantum efficiency of PSII under drought stress conditions. This may be attributable to several factors, such as enhanced

root biomass, decreased malondialdehyde content, and the up-regulation of chloroplast pigments, osmolytes, and nitrogenous compounds. However, P application had only a slight or negligible effect on the growth and metabolism of well-watered plants. In conclusion, P. zhennan has a strong capability for drought resistance, while P application facilitates and improves drought tolerance mostly through physio-biochemical adjustments, regardless of water availability. It is imperative to explore the underlying metabolic mechanisms and effects of different levels of P fertilization on P. zhennan under drought conditions in order to design appropriate conservation and management strategies for this species, which is at risk of extinction.

Tayo, L. L. (2017). "Stimuli-responsive nanocarriers for intracellular delivery." Biophys Rev **9**(6): 931-940.

The emergence of different nanoparticles (NPs) has made a significant revolution in the field of medicine. Different NPs in the form of metallic NPs, dendrimers, polymeric NPs, carbon quantum dots and liposomes have been functionalized and used as platforms for intracellular delivery of biomolecules, drugs, imaging agents and nucleic acids. These NPs are designed to improve the pharmacokinetic properties of the drug, improve their bioavailability and successfully surpass physiological or pathological obstacles in the biological system so that therapeutic efficacy is achieved. In this review I present some of the current approaches used in intracellular delivery systems, with a focus on various stimuli-responsive nanocarriers, including cell-penetrating peptides, to highlight their various biomedical applications.

Tchapet Njafa, J. P. and S. G. Nana Engo (2018). "Quantum associative memory with linear and non-linear algorithms for the diagnosis of some tropical diseases." Neural Netw **97**: 1-10.

This paper presents the QAMDiagnos, a model of Quantum Associative Memory (QAM) that can be a helpful tool for medical staff without experience or laboratory facilities, for the diagnosis of four tropical diseases (malaria, typhoid fever, yellow fever and dengue) which have several similar signs and symptoms. The memory can distinguish a single infection from a polyinfection. Our model is a combination of the improved versions of the original linear quantum retrieving algorithm proposed by Ventura and the non-linear quantum search algorithm of Abrams and Lloyd. From the given simulation results, it appears that the efficiency of recognition is good when particular signs and symptoms of a disease are inserted given that the linear algorithm is the main algorithm. The non-linear algorithm helps confirm or correct the diagnosis or give some advice to the medical staff for the treatment. So, our QAMDiagnos that has a friendly graphical user interface for desktop and smart-phone is a sensitive and a low-cost diagnostic tool that enables rapid and accurate diagnosis of four tropical diseases.

Teleanu, D. M., et al. (2019). "Neurotoxicity of Nanomaterials: An Up-to-Date Overview." Nanomaterials (Basel) **9**(1).

The field of nanotechnology, through which nanomaterials are designed, characterized, produced, and applied, is rapidly emerging in various fields, including energy, electronics, food and agriculture, environmental science, cosmetics, and medicine. The most common biomedical applications of nanomaterials involve drug delivery, bioimaging, and gene and cancer therapy. Since they possess unique properties which are different than bulk materials, toxic effects and long-term impacts on organisms are not completely known. Therefore, the purpose of this review is to emphasize the main neurotoxic effects induced by nanoparticles, liposomes, dendrimers, carbon nanotubes, and quantum dots, as well as the key neurotoxicology assays to evaluate them.

Teles Fujishima, M. A., et al. (2018). "An Antioxidant Potential, Quantum-Chemical and Molecular Docking Study of the Major Chemical Constituents Present in the Leaves of Curatella americana Linn." Pharmaceuticals (Basel) **11**(3).

Reactive oxygen species (ROS) are continuously generated in the normal biological systems, primarily by enzymes as xanthine oxidase (XO). The inappropriate scavenging or inhibition of ROS has been considered to be linked with aging, inflammatory disorders, and chronic diseases. Therefore, many plants and their products have been investigated as natural antioxidants for their potential use in preventive medicine. The leaves and bark extracts of Curatella americana Linn. were described in scientific research as anti-inflammatory, vasodilator, anti-ulcerogenic, and hypolipidemic effects. So, the aim of this study was to evaluate the antioxidant potentials of leaf hydroalcoholic extract from C. americana (HECA) through the scavenging DPPH assay and their main chemical constituents, evaluated by the following quantum chemical approaches (DFT B3LYP/6-31G**): Maps of Molecular Electrostatic Potential (MEP), Frontier Orbital's (HOMO and LUMO) followed by multivariate analysis and molecular docking simulations with the xanthine oxidase enzyme. The hydroalcoholic extract showed significant antioxidant activity by free radical scavenging probably due to the great presence of flavonoids, which were grouped in the PCA and HCA analysis with the standard gallic acid. In the molecular

docking study, the compounds studied presented the binding free energy (DeltaG) values close each other, due to the similar interactions with amino acids residues at the activity site. The descriptors Gap and softness were important to characterize the molecules with antioxidant potential by capturing oxygen radicals.

Teoh, G. Z., et al. (2015). "Role of nanotechnology in development of artificial organs." Minerva Med **106**(1): 17-33.

Improvements in our understanding of the interactions between implants and cells have directed attention towards nanoscale technologies. To date, nanotechnology has played a helping hand in the development of synthetic artificial organs and regenerative medicine. This includes the production of smart nanocomposite materials; fluorescent nanoparticles like Quantum Dots (QD) and magnetic nano particles (MNP) for stem cell tracking; and carbon nanotubes (CNT) and graphene for enhancement of material properties. The scope of this paper includes the role of nanoparticles in the development of nanomaterials; the chemical surface modifications possible to improve implant function and an overview of the performance of nano-engineered organs thus far. This includes implants developed for aesthetic purposes like nasal and auricular scaffolds, plastic and reconstructive surgical constructs (i.e. dermal grafts), hollow organs for cardiothoracic applications; and last but not least, orthopedic implants. The five-year outlook for nano-enhanced artificial organs is also discussed, highlighting the key research and development areas, available funds and the hurdles we face in accomplishing progression from prototypes on the laboratory bench to off-the-shelf products for the consumer market. Ultimately, this review aims to delineate the advantages of incorporating nanotechnology, as an individual entity or as a part of a construct for the development of tissue engineering scaffolds and/or artificial organs, and unravel the mechanisms of tissue cell-biomaterial interactions at the nanoscale, allowing for better progress in the development and optimization of unique nanoscale surface features for a wide range of applications.

Teradal, N. L. and R. Jelinek (2017). "Carbon Nanomaterials in Biological Studies and Biomedicine." Adv Healthc Mater **6**(17).

The "carbon nano-world" has made over the past few decades huge contributions in diverse scientific disciplines and technological advances. While dramatic advances have been widely publicized in using carbon nanomaterials such as fullerenes, carbon nanotubes, and graphene in materials sciences, nano-electronics, and photonics, their contributions to biology and biomedicine have been noteworthy as well. This Review focuses on the use of carbon nanotubes (CNTs), graphene, and carbon quantum dots [encompassing graphene quantum dots (GQDs) and carbon dots (C-dots)] in biologically oriented materials and applications. Examples of these remarkable nanomaterials in bio-sensing, cell- and tissue-imaging, regenerative medicine, and other applications are presented and discussed, emphasizing the significance of their unique properties and their future potential.

Terrett, N. (2010). "Molecular Medicine - CHI's 17th International Tri-Conference: Mastering Medicinal Chemistry - CHI's Seventh Annual Conference." IDrugs **13**(4): 209-213.

CHI's 17th International Tri-Conference on Molecular Medicine, held in San Francisco, included topics covering new developments in the field of medicinal chemistry. This conference report highlights selected presentations on fragment-based drug discovery, quantum mechanical energy decomposition for the analysis of SARs, medicinal chemistry strategies and the role of imaging in drug discovery. Investigational drugs discussed include MLN-4924 (Millennium Pharmaceuticals Inc), GDC-0449 (Chugai Pharmaceutical Co Ltd/Curis Inc/F Hoffmann-La Roche Ltd/Genentech Inc/NCI), RDEA-119 (Ardea Biosciences Inc/Bayer HealthCare AG) and tafamidis (Fx-1006A; FoldRx Pharmaceuticals Inc).

Terrovitis, J. V., et al. (2010). "Assessment and optimization of cell engraftment after transplantation into the heart." Circ Res **106**(3): 479-494.

Myocardial regeneration using stem and progenitor cell transplantation in the injured heart has recently become a major goal in the treatment of cardiac disease. Experimental studies and clinical applications have generally been encouraging, although the functional benefits that have been attained clinically are modest and inconsistent. Low cell retention and engraftment after myocardial delivery is a key factor limiting the successful application of cell therapy, irrespective of the type of cell or the delivery method. To improve engraftment, accurate methods for tracking cell fate and quantifying cell survival need to be applied. Several laboratory techniques (histological methods, real-time quantitative polymerase chain reaction, radiolabeling) have provided invaluable information about cell engraftment. In vivo imaging (nuclear medicine modalities, bioluminescence, and MRI) has the potential to provide quantitative information noninvasively, enabling longitudinal assessment of cell fate. In the present review, we present several available methods for assessing cell engraftment, and we critically discuss their strengths and limitations. In addition to providing insights about

the mechanisms mediating cell loss after transplantation, these methods can evaluate techniques for augmenting engraftment, such as tissue engineering approaches, preconditioning, and genetic modification, allowing optimization of cell therapies.

Thakkar, U. G., et al. (2016). "Infusion of autologous adipose tissue derived neuronal differentiated mesenchymal stem cells and hematopoietic stem cells in post-traumatic paraplegia offers a viable therapeutic approach." Adv Biomed Res **5**: 51.

BACKGROUND: Spinal cord injury (SCI) is not likely to recover by current therapeutic modalities. Stem cell (SC) therapy (SCT) has promising results in regenerative medicine. We present our experience of co-infusion of autologous adipose tissue derived mesenchymal SC differentiated neuronal cells (N-Ad-MSC) and hematopoietic SCs (HSCs) in a set of patients with posttraumatic paraplegia. MATERIALS AND METHODS: Ten patients with posttraumatic paraplegia of mean age 3.42 years were volunteered for SCT. Their mean age was 28 years, and they had variable associated complications. They were subjected to adipose tissue resection for in vitro generation of N-Ad-MSC and bone marrow aspiration for generation of HSC. Generated SCs were infused into the cerebrospinal fluid (CSF) below injury site in all patients. RESULTS: Total mean quantum of SC infused was 4.04 ml with a mean nucleated cell count of 4.5 x 10(4)/muL and mean CD34+ of 0.35%, CD45-/90+ and CD45-/73+ of 41.4%, and 10.04%, respectively. All of them expressed transcription factors beta-3 tubulin and glial fibrillary acid protein. No untoward effect of SCT was noted. Variable and sustained improvement in Hauser's index and American Spinal Injury Association score was noted in all patients over a mean follow-up of 2.95 years. Mean injury duration was 3.42 years against the period of approximately 1-year required for natural recovery, suggesting a positive role of SCs. CONCLUSION: Co-infusion of N-Ad-MSC and HSC in CSF is safe and viable therapeutic approach for SCIs.

Thetakala, R. K., et al. (2017). "The relationship of forensic odontology with various dental specialties in the articles published in a National and an International Forensic Odontology Journal: A 5-year content analysis." J Forensic Dent Sci **9**(2): 65-72.

Aims: The aim of this study is to assess the quantum of articles published by various dental specialties in a National and an International Forensic Odontology Journal from January 1, 2010, to December 31, 2014. Settings and Design: The present study is a 5-year retrospective content analysis study. Subjects and Methods: Data were collected from two forensic odontology journals (Journal of Forensic Odonto Stomatology [JOFS] and Journal of Forensic Dental Sciences [JFDS]) which are subscribed by institutional library. The article contents were scrutinized by one investigator and categorized into nine individual dental specialties based on the new working classification proposed for forensic odontology. Statistical Analysis Used: The quantum of articles published by various dental specialties and the various focus areas in each specialty were assessed using Chi-square test. Results: Among all the published articles, a maximum number of articles were related to the Department of Oral Medicine and Radiology (32.6%) in JFDS with Cheiloscopy (46.7%) being more focused area and to the Department of Prosthodontics (25.7%) in JFOS with Bite mark analysis (66.7%) being more focused area. Conclusions: There was a scarcity of information about the relationship of forensic odontology with various dental specialties in the articles published in JFDS and JFOS. The editorial board of journals should expand and elaborate their scope of journals to various focus areas of forensic odontology. This will encourage the researchers to explore in the different focus areas which are most neglected as of now.

Thomas, A., et al. (2016). "Options for the Development of Noninvasive Glucose Monitoring: Is Nanotechnology an Option to Break the Boundaries?" J Diabetes Sci Technol **10**(3): 782-789.

Nowadays nanotechnology has many applications in products used in various areas of daily life; however, this technology has also an option in modern medicine and pharmacy. Therefore, this technology is also an attractive option for the field of diagnosis and treatment of diabetes. Many people with diabetes measure their blood glucose levels regularly to determine the insulin dose. Ideally glucose values would be measured noninvasively (NI). However, none of all the NI approaches studied in the past decades enabled reliable NI measurements under all daily life conditions. Particularly an unfavorable signal-to-noise ratio turned out to be problematic. Based on the known physical possibilities for NI glucose monitoring the focus of this review is on nanotechnology approaches. Functional prototypes exist for some of these that showed promising results under defined laboratory conditions, indicating a good sensitivity and selectivity for glucose. On the second hand is to optimize the technological process of manufacturing. In view of the rapid progress in micro- and nanoelectronics hopefully NI glucose monitoring systems can be developed in the near future.

Thomford, N. E., et al. (2018). "Natural Products for Drug Discovery in the 21st Century: Innovations for Novel Drug Discovery." Int J Mol Sci **19**(6).

The therapeutic properties of plants have been recognised since time immemorial. Many pathological conditions have been treated using plant-derived medicines. These medicines are used as concoctions or concentrated plant extracts without isolation of active compounds. Modern medicine however, requires the isolation and purification of one or two active compounds. There are however a lot of global health challenges with diseases such as cancer, degenerative diseases, HIV/AIDS and diabetes, of which modern medicine is struggling to provide cures. Many times the isolation of "active compound" has made the compound ineffective. Drug discovery is a multidimensional problem requiring several parameters of both natural and synthetic compounds such as safety, pharmacokinetics and efficacy to be evaluated during drug candidate selection. The advent of latest technologies that enhance drug design hypotheses such as Artificial Intelligence, the use of 'organ-on chip' and microfluidics technologies, means that automation has become part of drug discovery. This has resulted in increased speed in drug discovery and evaluation of the safety, pharmacokinetics and efficacy of candidate compounds whilst allowing novel ways of drug design and synthesis based on natural compounds. Recent advances in analytical and computational techniques have opened new avenues to process complex natural products and to use their structures to derive new and innovative drugs. Indeed, we are in the era of computational molecular design, as applied to natural products. Predictive computational softwares have contributed to the discovery of molecular targets of natural products and their derivatives. In future the use of quantum computing, computational softwares and databases in modelling molecular interactions and predicting features and parameters needed for drug development, such as pharmacokinetic and pharmacodynamics, will result in few false positive leads in drug development. This review discusses plant-based natural product drug discovery and how innovative technologies play a role in next-generation drug discovery.

Tian, J. X., et al. (2014). "Characterisation and identification of dihydroindole-type alkaloids from processed semen strychni by high-performance liquid chromatography coupled with electrospray ionisation ion trap time-of-flight mass spectrometry." Phytochem Anal **25**(1): 36-44.

INTRODUCTION: For centuries, Semen Strychni (the ripened seeds of Strychnos nux-vomica) has been used extensively as a herbal medicine in Asian countries. However, the chemical composition of the dihydroindole-type alkaloids contained in processed Semen Strychni is not fully understood. OBJECTIVE: To develop an improved strategy using mass defect filtering (MDF) in combination with MS(n) analysis and theoretical calculations for identification and structural characterisation of dihydroindole-type alkaloids in processed Semen Strychni extracts. METHODS: The experimental work was conducted using a high-performance liquid chromatography coupled with electrospray ionisation ion trap time-of-flight mass spectrometry (HPLC-ESI/IT-TOF/MS) system. Upon acquisition of full-scan MS data, the potential dihydroindole-type alkaloids were screened using a well-defined mass defect range of 50 mDa. With the assistance of MS(n) analysis, the diagnostic fragment ions (DFIs) were used as primary screening references for targeting the characteristic analogues. For better discrimination of the isomers, quantum chemical calculations were utilised to provide additional structural information. RESULTS: Twenty-four dihydroindole-type alkaloids, including four that were previously not described, were tentatively identified. CONCLUSION: A new, rapid and sensitive method was developed for the discovery and characterisation of dihydroindole-type alkaloids in extracts of processed Semen Strychni. The successful application of this method indicates a potential for adaptation to other classes of natural product from other sources.

Tian, Y., et al. (2018). "Affinity Binding-Induced Hg(2+) Release and Quantum Dot Doping for General, Label-Free, and Homogenous Fluorescence Protein Assay." ACS Sens **3**(7): 1401-1408.

Herein, a general protein conversion and analysis strategy was developed for homogeneous, label-free, and sensitive protein detection, on the basis of the affinity binding-induced Hg(2+) release for protein conversion, and the succeeding Hg(2+) doping-induced ZnSe quantum dot (QD) photoluminescence for signal readout. Two DNA motifs were designed, each of which was conjugated with a protein-specific recognition ligand. The mercury ions were initially introduced into one DNA motif by T-Hg(2+)-T interaction. The Hg(2+) releasing was then accomplished after protein recognition-initiated strand exchange reaction between two DNA motifs. Then, the simultaneous incorporation of the released Hg(2+) into ZnSe QD resulted in a doping-dependent fluorescence emission at 560 nm correlated with protein analysis. The protein assay is outperformed only by a simple one-step mixing operation but no separation or washing steps. Also, the use of doped QD as a fluorogenic reporter can avoid the fluorophore and/or quencher labeling, and eliminate complex DNA manipulation procedures for signal readout or amplification involved in most existing nucleic acid-based protein conversion and analysis methods. The versatile and sensitive detection toward multivalent proteins was verified with

the detection limits achieved at 0.034 nM for anti-Dig antibody, 0.012 nM for streptavidin, and 0.025 nM for thrombin. Thus, it shows great promise for protein analysis to accommodate the applications in disease diagnosis, biomarker screening, and clinical medicine.

Tiller, W. A. (2004). "A personal perspective on energies in future energy medicine." J Altern Complement Med **10**(5): 867-877.

This paper deals with the evolution of medicine from chemical medicine to energy medicine to information medicine as, first, standard electric, magnetic, and electromagnetic fields are applied to a patient and, second, as subtle energy fields are applied to the patient. Next, a brief reporting is given on our specific intention imprinting of a simple electrical device, which, when turned on in a given space, lifts the inner symmetry state of that space and tunes that space so that the specific intention, acting on the materials in that space, causes well-designed target experiments running in that space to yield results in full accord with the specific intention. A new theoretical model of nature is provided to explain these seemingly anomalous phenomena. A new perspective on what constitutes the whole person is also provided and one finds that human consciousness will become an important experimental variable in future medicine.

Toda, M., et al. (2019). "In Vivo Fluorescence Visualization of Anterior Chamber Injected Human Corneal Endothelial Cells Labeled With Quantum Dots." Invest Ophthalmol Vis Sci **60**(12): 4008-4020.

Purpose: The injection of cultured human corneal endothelial cells (cHCECs) into the anterior chamber (AC) is a newly developed modality for the successful treatment of corneal endothelium dysfunction. Here, we investigated whether or not cHCECs could be labeled using quantum dots (QDs) composed of semiconductor nanoparticle octa-arginine (R8) to trace injected cHCECs and examined the utility of in vivo fluorescence imaging to analyze the dynamics and accumulation of QD-labeled injected cHCECs in a corneal endothelial dysfunction mouse model. Methods: The cHCECs, either of high quality or with cell-state transition, were labeled by adding a mixture of QDs655 and R8. The labeling efficiency and the unchanging of the cell phenotypes by the labeling was confirmed by flow cytometry. The labeled cHCECs were injected into the AC of either healthy mice or mice with corneal endothelium damaged by cryogenic treatment. The kinetics of the injected cHCECs was traced quantitatively via multiphoton confocal laser microscopy. Results: QD labeling induced no morphologic change in the cHCECs or in the expression of the functional markers of cHCECs (i.e., Na+/K+-ATPase and zonula occludens-1). The injected cHCECs-QDs were quantitatively detected, and the retention of cHCECs-QDs was evident, from 3 to 48 hours post cell injection on the posterior surface in the cryogenically injured corneal endothelium mouse model eyes, yet not in the noninjured healthy control eyes. Conclusions: The findings of this study show that in the field of regenerative medicine, QD labeling of cells presents a convenient and sensitive method of finely monitoring the fate of injected cells in vivo.

Tomczak, N., et al. (2012). "Enabling biomedical research with designer quantum dots." Methods Mol Biol **811**: 245-265.

Quantum Dots (QDs) are a new class of semiconductor nanoparticulate luminophores, which are actively researched for novel applications in biology and nanomedicine. In this review, the recent progress in the design and applications of QD labels for in vitro and in vivo imaging of cells is presented. Surface chemical engineering of hydrophobic QDs is required to render them water soluble and biocompatible. Further surface modification and attachment of bioactive molecules to the surface of QDs, such as peptides, aptamers, or antibodies are intensively explored for targeted imaging of living cells, and disease states in animals. Specially designed surface coatings can drastically decrease nonspecific interactions between QDs and cells, minimize degradation of QDs under in vivo physiological conditions, reduce the cytotoxicity of QDs, and prolong circulation lifetimes in animals. New generations of QD probes are also promising for imaging cellular processes at the single-molecule level. Ultimately, QDs as components of complex therapeutic nanosystems are poised to contribute significantly to the field of personalized medicine.

Tong, H., et al. (2013). "Polyethylenimine600-beta-cyclodextrin: a promising nanopolymer for nonviral gene delivery of primary mesenchymal stem cells." Int J Nanomedicine **8**: 1935-1946.

Genetically modified mesenchymal stem cells (MSCs) have great potential in the application of regenerative medicine and molecular therapy. In the present manuscript, we introduce a nanopolymer, polyethylenimine600-beta-cyclodextrin (PEI600-beta-CyD), as an efficient polyplex-forming plasmid delivery agent with low toxicity and ideal transfection efficiency on primary MSCs. PEI600-beta-CyD causes significantly less cytotoxicity and apoptosis on MSCs than 25 kDa high-molecular-weight PEI (PEI25kDa). PEI600-beta-CyD also exhibits similar transfection efficiency as PEI25kDa on MSCs, which is higher than that of PEI600Da. Quantum dot-labeled plasmids show that PEI600-beta-CyD or PEI25kDa delivers the plasmids in a more scattered manner than PEI600Da

does. Further study shows that PEI600-beta-CyD and PEI25kDa are more capable of delivering plasmids into the cell lysosome and nucleus than PEI600Da, which correlates well with the results of their transfection-efficiency assay. Moreover, among the three vectors, PEI600-beta-CyD has the most capacity of enhancing the alkaline phosphatase activity of MSCs by transfecting bone morphogenetic protein 2, 7, or special AT-rich sequence-binding protein 2. These results clearly indicate that PEI600-beta-CyD is a safe and effective candidate for the nonviral gene delivery of MSCs because of its ideal inclusion ability and proton sponge effect, and the application of this nanopolymer warrants further investigation.

Tong, S., et al. (2012). "Engineering imaging probes and molecular machines for nanomedicine." Sci China Life Sci **55**(10): 843-861.

Nanomedicine is an emerging field that integrates nanotechnology, biomolecular engineering, life sciences and medicine; it is expected to produce major breakthroughs in medical diagnostics and therapeutics. Due to the size-compatibility of nano-scale structures and devices with proteins and nucleic acids, the design, synthesis and application of nanoprobes, nanocarriers and nanomachines provide unprecedented opportunities for achieving a better control of biological processes, and drastic improvements in disease detection, therapy, and prevention. Recent advances in nanomedicine include the development of functional nanoparticle based molecular imaging probes, nano-structured materials as drug/gene carriers for in vivo delivery, and engineered molecular machines for treating single-gene disorders. This review focuses on the development of molecular imaging probes and engineered nucleases for nanomedicine, including quantum dot bioconjugates, quantum dot-fluorescent protein FRET probes, molecular beacons, magnetic and gold nanoparticle based imaging contrast agents, and the design and validation of zinc finger nucleases (ZFNs) and TAL effector nucleases (TALENs) for gene targeting. The challenges in translating nanomedicine approaches to clinical applications are discussed.

Tong, W. F., et al. (2002). "Somatic cell nuclear transfer (cloning): implications for the medical practitioner." Singapore Med J **43**(7): 369-376.

The current century will bring tremendous changes to the science and the practice of medicine. This century will be acknowledged as the century of Biology as the fusion of molecular genetics and experimental embryology pushes the barriers of science beyond perimeters that we have thought existed, as much as the past century was the century of Physics, with all the exact scientific calculations and predictions, resulting in electricity, nuclear power and quantum physics. The first major breakthrough has been the pioneering work of Wilmut and Campbell, first with the birth of Megan and Moran in 1995 (1), followed by the birth of Dolly the sheep, the first reported mammalian clone from a fully differentiated adult cell, reported in July 1996 (2). However, current cloning techniques are an extension of over 40 years of research using nuclei derived from non-human embryonic and fetal cells. However, following the birth of Dolly, the prospects of cloning technology have extended to ethically hazier areas of human cloning and embryonic stem cell research. This review hopes to bring the reader closer to the science and the ethics of this new technology, and what the implications are for the medical practitioner.

Townsend, L. W., et al. (1986). "Comparison of abrasion model differences in heavy ion fragmentation: optical versus geometric models." Phys Rev C Nucl Phys **34**(4): 1491-1494.

Using an abrasion-ablation collision model, which includes contributions from frictional-spectator interactions and electromagnetic dissociation, analyses of the sensitivities of predicted fragmentation cross sections to the choice of a particular abrasion formalism are made using both geometric and optical potential abrasion models. Most cross section differences obtained using the two abrasion models are less than the present experimental uncertainties, suggesting that either abrasion model is suitable for estimating isotopic and elemental fragment distributions.

Tozzini, V. (2010). "Multiscale modeling of proteins." Acc Chem Res **43**(2): 220-230.

The activity within a living cell is based on a complex network of interactions among biomolecules, exchanging information and energy through biochemical processes. These events occur on different scales, from the nano- to the macroscale, spanning about 10 orders of magnitude in the space domain and 15 orders of magnitude in the time domain. Consequently, many different modeling techniques, each proper for a particular time or space scale, are commonly used. In addition, a single process often spans more than a single time or space scale. Thus, the necessity arises for combining the modeling techniques in multiscale approaches. In this Account, I first review the different modeling methods for bio-systems, from quantum mechanics to the coarse-grained and continuum-like descriptions, passing through the atomistic force field simulations. Special attention is devoted to their combination in different possible multiscale approaches and to the questions and problems related to their coherent matching in the

space and time domains. These aspects are often considered secondary, but in fact, they have primary relevance when the aim is the coherent and complete description of bioprocesses. Subsequently, applications are illustrated by means of two paradigmatic examples: (i) the green fluorescent protein (GFP) family and (ii) the proteins involved in the human immunodeficiency virus (HIV) replication cycle. The GFPs are currently one of the most frequently used markers for monitoring protein trafficking within living cells; nanobiotechnology and cell biology strongly rely on their use in fluorescence microscopy techniques. A detailed knowledge of the actions of the virus-specific enzymes of HIV (specifically HIV protease and integrase) is necessary to study novel therapeutic strategies against this disease. Thus, the insight accumulated over years of intense study is an excellent framework for this Account. The foremost relevance of these two biomolecular systems was recently confirmed by the assignment of two of the Nobel prizes in 2008: in chemistry for the discovery of GFP and in medicine for the discovery of HIV. Accordingly, these proteins were studied with essentially all of the available modeling techniques, making them ideal examples for studying the details of multiscale approaches in protein modeling.

Tripathi, S. K., et al. (2015). "Quantum Dots and their Potential Role in Cancer Theranostics." Crit Rev Ther Drug Carrier Syst **32**(6): 461-502.

The emergence of cancer nanomedicine is the result of fruitful advances in the fields of nanotechnology, bioimaging, formulation development, and molecular biology. Quantum dots (QDs) are the luminescent nanocrystals (NCs) that provide a multifunctional platform for imaging the biosystems following controlled delivery of therapeutic drugs, proteins, peptides, oligonucleotides, and genes. These engineered fluorescent probes with integrated imaging and carrier functionalities have become excellent tools for molecular diagnostics and delivery of therapeutics molecules. Flexible surface chemistry, unique optical properties, high sensitivity, and multiplexing capabilities of QDs certainly make them a most promising tool for personalized medicine. This review focuses on state-of-art advances in synthesizing QDs and highlights the approaches used for functionalization of QDs with desired ligands for targeted carriage to specific sites. Discussed is the role of QDs in antitumor therapy through drug delivery and gene delivery and the recently emerged photodynamic therapy (PDT). We also endeavor to critically address the major impediments in the clinical development of these multifunctional nanoplatforms, with a special focus on plausible advancements for the near future.

Tsentalovich, Y. P., et al. (2011). "Deactivation of excited states of kynurenine covalently linked to nitroxides." Photochem Photobiol **87**(1): 22-31.

Due to ability of stable nitroxides to interact with free radicals, they are used as antioxidants for therapeutic and research goals in biology and medicine. A modern trend in medical chemistry is the design of multifunctional molecules such as UV absorbers covalently bound to nitroxides, which provides both UV protection and antioxidant properties combined in the same molecule. In the present work, we report the synthesis of conjugates of a natural UV filter kynurenine (KN) with nitroxides (KN-RNO(*) conjugates) and the study of their photochemical properties in aqueous and methanol solutions. Due to the spin-exchange interaction between KN and nitroxide moieties, the triplet lifetimes in conjugates are much shorter than in KN molecule, but the triplet quantum yields are significantly higher. The reaction of intramolecular electron transfer between photoexcited KN and nitroxide moieties is the main factor determining the quantum yield of KN-RNO(*) conjugates photodecomposition. Consequently, KN-RNO(*) conjugates in aqueous solution are photochemically less stable than the parent KN molecule. Nevertheless, the photostability of KN-RNO(*) conjugates is much higher than that of cinnamates which are widely used as UV absorbers in modern sunscreen formulations. Thus, the combination of the endogenous chromophore KN with nitroxides is very promising for medical applications.

Tsiafoulis, C. G., et al. (2011). "A new method for the determination of free L-carnitine in serum samples based on high field single quantum coherence filtering 1H-NMR spectroscopy." Anal Bioanal Chem **399**(6): 2285-2294.

The rapid and accurate determination of specific metabolites present in biofluids is a very demanding task which is essential in both medicine and chemistry. L-carnitine (3-hydroxy-4-N-trimethylammonium butyrate) is an important metabolite which participates in a series of biological paths and therefore its determination is of diagnostic importance. A single quantum coherence filtering (1)H NMR methodology was used for the accurate and rapid determination of L-carnitine in human serum samples. The methodology is based on spectral simplification, and specifically on the distinction of the N-methyl proton signal of L-carnitine that is greatly overlapped in the (1)H-NMR spectrum of serum. The quantitative results provided by the proposed method are in excellent agreement with those obtained by the enzymatic method, which is widely used. The proposed method is rapid (~20 min of experimental time), selective, sensitive, and has good analytical

characteristics (accuracy, reproducibility). Selected protein precipitation methods were also investigated and sample pretreatment with EtOH is suggested.

Turner, R. J., et al. (2012). "Microbial processing of tellurium as a tool in biotechnology." Biotechnol Adv **30**(5): 954-963.

Here, we overview the most recent advances in understanding the bacterial mechanisms that stay behind the reduction of tellurium oxyanions in both planktonic cells and biofilms. This is a topic of interest for basic and applied research because microorganisms are deeply involved in the transformation of metals and metalloids in the environment. In particular, the recent observation that toxic tellurite can be precipitated either inside or outside the cells being used as electron sink to support bacterial growth, opens new perspectives for both microbial physiologists and biotechnologists. As promising nanomaterials, tellurium based nanoparticles show unique electronic and optical properties due to quantum confinement effects to be used in the area of chemistry, electronics, medicine and environmental biotechnologies.

Ueno, S. (2012). "Studies on magnetism and bioelectromagnetics for 45 years: from magnetic analog memory to human brain stimulation and imaging." Bioelectromagnetics **33**(1): 3-22.

Forty-five years of studies on magnetism and bioelectromagnetics, in our laboratory, are presented. This article is prepared for the d'Arsonval Award Lecture. After a short introduction of our early work on magnetic analog memory, we review and discuss the following topics: (1) Magnetic nerve stimulation and localized transcranial magnetic stimulation (TMS) of the human brain by figure-eight coils; (2) Measurements of weak magnetic fields generated from the brain by superconducting quantum interference device (SQUID) systems, called magnetoencephalography (MEG), and its application in functional brain studies; (3) New methods of magnetic resonance imaging (MRI) for the imaging of impedance of the brain, called impedance MRI, and the imaging of neuronal current activities in the brain, called current MRI; (4) Cancer therapy and other medical treatments by pulsed magnetic fields; (5) Effects of static magnetic fields and magnetic control of cell orientation and cell growth; and (6) Effects of radio frequency magnetic fields and control of iron ion release and uptake from and into ferritins, iron cage proteins. These bioelectromagnetic studies have opened new horizons in magnetism and medicine, in particular for brain research and treatment of ailments such as depression, Parkinson's, and Alzheimer's diseases.

Umarov, G. R., et al. (1999). "[Effect of electrostatic field on bacteria E. coli]." Aviakosm Ekolog Med **33**(1): 61-62.

On the basis of the quantum mechanical theory of phase transitions and chemical reactions developed by the authors it is shown that the mentioned processes are controlled by the definite active centers. The electrostatic fields (without electric current included) are capable of changing the degree of activity and structure of these centers and so are capable of controlling the results of processes under study. The reported experimental studies performed on the living objects validate this hypothesis. It was concluded that electrostatic fields (natural and technogenic) exert some action on life activity of the organisms and therefore it is necessary to provide the proper optimal conditions for the life activity in the inhabited spacecraft. For this purpose the special equipment is proposed by the authors.

Uthamacumaran, A. (2017). "A biophysical approach to cancer dynamics: Quantum chaos and energy turbulence." Biosystems **156-157**: 1-22.

Cancer is a term used to define a collective set of rapidly evolving cells with immortalized replication, altered epimetabolomes and patterns of longevity. Identifying a common signaling cascade to target all cancers has been a major obstacle in medicine. A quantum dynamic framework has been established to explain mutation theory, biological energy landscapes, cell communication patterns and the cancer interactome under the influence of quantum chaos. Quantum tunneling in mutagenesis, vacuum energy field dynamics, and cytoskeletal networks in tumor morphogenesis have revealed the applicability for description of cancer dynamics, which is discussed with a brief account of endogenous hallucinogens, bioelectromagnetism and water fluctuations. A holistic model of mathematical oncology has been provided to identify key signaling pathways required for the phenotypic reprogramming of cancer through an epigenetic landscape. The paper will also serve as a mathematical guide to understand the cancer interactome by interlinking theoretical and experimental oncology. A multi-dimensional model of quantum evolution by adaptive selection has been established for cancer biology.

Utkin, Y. N. (2017). "Modern trends in animal venom research - omics and nanomaterials." World J Biol Chem **8**(1): 4-12.

Animal venom research is a specialized investigation field, in which a number of different methods are used and this array is constantly expanding. Thus, recently emerged omics and nanotechnologies have already been successfully

applied to venom research. Animal venoms have been studied for quite a long time. The traditional reductionist approach has been to isolate individual toxins and then study their structure and function. Unfortunately, the characterization of the venom as a whole system and its multiple effects on an entire organism were not possible until recent times. The development of new methods in mass spectrometry and sequencing have allowed such characterizations of venom, encompassing the identification of new toxins present in venoms at extremely low concentrations to changes in metabolism of prey organisms after envenomation. In particular, this type of comprehensive research has become possible due to the development of the various omics technologies: Proteomics, peptidomics, transcriptomics, genomics and metabolomics. As in other research fields, these omics technologies ushered in a revolution for venom studies, which is now entering the era of big data. Nanotechnology is a very new branch of technology and developing at an extremely rapid pace. It has found application in many spheres and has not bypassed the venom studies. Nanomaterials are quite promising in medicine, and most studies combining venoms and nanomaterials are dedicated to medical applications. Conjugates of nanoparticles with venom components have been proposed for use as drugs or diagnostics. For example, nanoparticles conjugated with chlorotoxin - a toxin in scorpion venom, which has been shown to bind specifically to glioma cells - are considered as potential glioma-targeted drugs, and conjugates of neurotoxins with fluorescent semiconductor nanoparticles or quantum dots may be used to detect endogenous targets expressed in live cells. The data on application of omics and nanotechnologies in venom research are systematized concisely in this paper.

Utkin, Y. N. (2018). "Brain and Quantum Dots: Benefits of Nanotechnology for Healthy and Diseased Brain." Cent Nerv Syst Agents Med Chem **18**(3): 193-205.

INTRODUCTION: The brain is the most complicated organ in a vertebrate's organism. In a human, it contains about two hundred billions of neurons and non-neuronal cells. To understand the mechanisms of the brain functions is the great challenge for the researchers. Much is already done on this way; however, it remains a lot to do still, and to get deeper knowledge, new approaches should be developed. One of this is to use benefits that nanotechnology brings in this area. Nanotechnology opens up unique opportunities, not only for material science research, but also for biology, medicine, and many other disciplines. There are several kinds of nanoparticles that can be applied in brain studies, Quantum Dots (QD) being so far most often used. QD are semiconductor light emitting nanocrystals with nanometer-sized structures of unique optical properties. They have bright fluorescence, are resistant to bleaching and able of emitting fluorescent light of different wavelengths. These properties make QD perfect tools for visualization of brain structures and mechanisms underlying its functions. Due to unique QD properties, even single molecules under study can be observed. Moreover QDs can be used for brain-targeted drug delivery. CONCLUSION: In this review, the application of quantum dots for the brain research is considered and benefits that it can bring are discussed.

Valet, G., et al. (2004). "Cytomics--new technologies: towards a human cytome project." Cytometry A **59**(2): 167-171.

BACKGROUND: Molecular cell systems research (cytomics) aims at the understanding of the molecular architecture and functionality of cell systems (cytomes) by single-cell analysis in combination with exhaustive bioinformatic knowledge extraction. In this way, loss of information as a consequence of molecular averaging by cell or tissue homogenisation is avoided. PROGRESS: The cytomics concept has been significantly advanced by a multitude of current developments. Amongst them are confocal and laser scanning microscopy, multiphoton fluorescence excitation, spectral imaging, fluorescence resonance energy transfer (FRET), fast imaging in flow, optical stretching in flow, and miniaturised flow and image cytometry within laboratories on a chip or laser microdissection, as well as the use of bead arrays. In addition, biomolecular analysis techniques like tyramide signal amplification, single-cell polymerase chain reaction (PCR), and the labelling of biomolecules by quantum dots, magnetic nanobeads, or aptamers open new horizons of sensitivity and molecular specificity at the single-cell level. Data sieving or data mining of the vast amounts of collected multiparameter data for exhaustive multilevel bioinformatic knowledge extraction avoids the inadvertent loss of information from unknown molecular relations being inaccessible to an a priori hypothesis. CHALLENGE: It seems important to address the challenge of a human cytome project using hypothesis-driven molecular information collection from disease associated cell systems, supplemented by systematic and exhaustive knowledge extraction. This will allow the description of the molecular setup of normal and abnormal cell systems within a relational knowledge system, permitting the standardised discrimination of abnormal cell states in disease. As one of the consequences, individualised predictions of further disease course in patients (predictive medicine by cytomics) by characteristic discriminatory data patterns will permit individualised

therapies, identification of new pharmaceutical targets, and establishment of a standardised framework of relevant molecular alterations in disease. This special issue of Cytometry, on new technologies in cytomics, focuses on prominent examples of this presently fast-moving scientific field, and represents one of the preconditions for the formulation of a human cytome project.

Valiev, M., et al. (2009). "Interactions of Cl- and OH radical in aqueous solution." J Phys Chem A **113**(31): 8823-8825.

There is a considerable controversy surrounding the nature of the Cl-/OH complex in aqueous solution, which appears as a byproduct of the irradiation of salt solutions in nuclear reactor operation, radioactive waste storage, medicine, and environmental problems. In this work, we report results of combined quantum mechanical molecular mechanics calculations of ground-state free-energy surfaces and absorption spectrum through the CCSDT level of theory that are consistent with the experimental data and suggest that hemibonded HOCl- species may indeed exist in bulk aqueous solution.

Vandervelde, T. E. and S. Krishna (2010). "Progress and prospects for quantum dots in a well infrared photodetectors." J Nanosci Nanotechnol **10**(3): 1450-1460.

Over the past fifteen years, there has been significant interest in developing intersubband quantum dot (QD) detectors for the mid-(MWIR) and long-wave infrared (LWIR) regimes. This class of detectors is generally referred to as quantum dot infrared photodetectors, or QDIPs. At present, one of the leading technologies is that of the quantum dots-in-a-well infrared photodetector, called a DWELL-IP or just a DWELL detector. The DWELL name comes from the active region's structure, which consists of a layer of quantum dots imbedded in (or in some cases grown on) a quantum well. This dot/well combination is similarly surrounded by a barrier material. Here, we identify the major players and their contributions to the evolution of the DWELL-IP. While this dot/well/barrier material combination originally consisted of InAs/InGaAs/GaAs, the materials used has widened in recent years. This paper reviews the progress to date for this quickly advancing field. Some of these advancements have come from the additional focus that has been brought to bear on the physical understanding and experimental mechanics of the structure itself. Explorations into the multi-spectral nature of these detectors have also created unique applications for these detectors. This type of QDIP is now becoming the dominant detector of its class and is quickly heading for parity with quantum well infrared photodetectors (QWIPs) that are presently commercially dominant. Given the potential utility of the infrared spectrum for applications in medicine, military, industrial, and academic fields the DWELL-IPs potential to be an inexpensive, versatile, multi-spectral, infrared detector indicates it has a bright future.

Vatansever, F. and M. R. Hamblin (2016). "Surface-initiated ring-opening metathesis polymerization (SI-ROMP) to attach a tethered organic corona onto CdSe/ZnS core/shell quantum dots." J Nanopart Res **18**(10).

Core-shell CdSe/ZnS quantum dots (QDs) are useful as tunable photostable fluorophores for multiple applications in industry, biology, and medicine. However, to achieve the optimum optical properties, the surface of the QDs must be passivated to remove charged sites that might bind extraneous substances and allow aggregation. Here we describe a method of growing an organic polymer corona onto the QD surface using the bottom-up approach of surface-initiated ring-opening metathesis polymerization (SI-ROMP) with Grubbs catalyst. CdSe/ZnS QDs were first coated with mercaptopropionic acid by displacing the original trioctylphosphine oxide layer, and then reacted with 7-octenyl dimethyl chlorosilane. The resulting octenyl double bonds allowed the attachment of ruthenium alkylidene groups as a catalyst. A subsequent metathesis reaction with strained bicyclic monomers (norbornene-dicarbonyl chloride (NDC), and a mixture of NDC and norbornenylethylisobutyl-polyhedral oligomeric silsesquioxane (norbornoPOSS)) allowed the construction of tethered organic homo-polymer or co-polymer layers onto the QD. Compounds were characterized by FT-IR, 1H-NMR, X-ray photoelectron spectroscopy, differential scanning calorimetry, and transmission electron microscopy. Atomic force microscopy showed that the coated QDs were separate and non-aggregated with a range of diameter of 48-53 nm.

Walach, H. and M. Loef (2015). "Using a matrix-analytical approach to synthesizing evidence solved incompatibility problem in the hierarchy of evidence." J Clin Epidemiol **68**(11): 1251-1260.

OBJECTIVES: The hierarchy of evidence presupposes linearity and additivity of effects, as well as commutativity of knowledge structures. It thereby implicitly assumes a classical theoretical model. STUDY DESIGN AND SETTING: This is an argumentative article that uses theoretical analysis based on pertinent literature and known facts to examine the standard view of methodology. RESULTS: We show that the assumptions of the hierarchical model are wrong. The knowledge

structures gained by various types of studies are not sequentially indifferent, that is, do not commute. External validity and internal validity are at least partially incompatible concepts. Therefore, one needs a different theoretical structure, typical of quantum-type theories, to model this situation. The consequence of this situation is that the implicit assumptions of the hierarchical model are wrong, if generalized to the concept of evidence in total. CONCLUSION: The problem can be solved by using a matrix-analytical approach to synthesizing evidence. Here, research methods that produce different types of evidence that complement each other are synthesized to yield the full knowledge. We show by an example how this might work. We conclude that the hierarchical model should be complemented by a broader reasoning in methodology.

Walkey, C., et al. (2009). "Application of semiconductor and metal nanostructures in biology and medicine." Hematology Am Soc Hematol Educ Program: 701-707.

Advances in nanotechnology research have led to the creation of new generation of contrast agents, therapeutics, and delivery systems. These applications are expected to significantly improve the diagnosis and treatment of a variety of diseases. Two nanotechnologies-semiconductor and metallic nanostructures-are the most advanced in this young field and have been extensively investigated for clinical use. These nanostructures are currently the "model" for the developments of many novel nanostructures. This review describes their chemical design, tunable properties, and utility in medicine. Furthermore, we will describe the current understanding of their toxicity, which could be barriers to their use for human.

Wang, B., et al. (2016). "Molecular Simulations Bring New Insights into Protoporphyrinogen IX Oxidase/Protoporphyrinogen IX Interaction Modes." Mol Inform **35**(10): 476-482.

Protoporphyrinogen IX oxidase (PPO, EC 1.3.3.4) catalyzes the oxidation of protoporphyrinogen IX (protogen IX) to protoporphyrin IX (proto IX) in the haem/chlorophyll biosynthetic pathway. Although extensive studies of PPO have already afforded many insights into its biological function and its significance to agriculture and medicine, details of the enzymatic mechanism as well as the nature of the specific amino acids involved in substrate binding still remain largely unknown due to the lack of structural information about protogen IX binding to PPO. In this study, we carried out a detailed and systematic investigation on the binding mode of protogen IX in the Nicotiana tabacum PPO (mtPPO) by performing a computational docking followed by molecular simulations, quantum mechanics calculations, and an integrated analysis. The proposed binding mode was consistent with experimental studies, and several potential key residues that have not been investigated in previous studies, such as Thr70, Arg233, Ser235, Ser474 and Lys477, were identified. In addition, we compared the binding modes of protogen IX in mtPPO and Homo sapiens PPO, and found their differences. Considering the low sequence identity and the differences of biochemical properties among the PPOs from various species, the investigation could provide a valuable basis for the design of PPO inhibitors with high potency and species-selectivity.

Wang, D., et al. (2014). "Computational design of two-photon fluorescent probes for intracellular free zinc ions." J Phys Chem B **118**(34): 10101-10110.

Two-photon fluorescence probes used in two-photon fluorescence microscopy (TPM) can achieve intact tissue imaging without destruction. Therefore, for a long time, TPM has been an important tool in biology and medicine. In this background via a quantum chemical method, a series of zinc ion probe molecules using N,N-di(2-picolyl)ethylenediamine (DPEN) as the recognition group were studied, which are based on the photoinduced electron transfer (PET) mechanism. The fact that the one-photon absorption peak is almost unchanged and the fluorescence emission intensity increased significantly upon coordination with a zinc ion reveals that these probes can be PET fluorescent bioimaging reagents. And it is predicted that when the chemically modified probe molecule is incorporated with Zn(2+), the two-photon absorption (TPA) cross-section (deltamax) will greatly increase and the TPA peak will be in the near-infrared region. The molecules after changing the fluorophore become more suitable for probing Zn(2+) in vivo, and a modification at the end of the fluorophore can fine-tune the fluorescence and TPA properties. The detailed investigations will provide a theoretical basis for synthesizing new zinc-ion-responsive two-photon fluorescent probes.

Winter, R. L., et al. (2018). "Growth and function of equine endothelial colony forming cells labeled with semiconductor quantum dots." BMC Vet Res **14**(1): 247.

BACKGROUND: Endothelial progenitor cells (EPCs) contribute to neovascularization and vascular repair in vivo and are attractive for clinical use in ischemic disease. Tracking of stem and progenitor cells is essential to determine engraftment after administration. Semiconductor quantum dots (QD) are promising for cell labeling due to their ease of uptake by many cell lines and their continued presence after many cell generations. The purpose of this study was to

evaluate function and growth of equine EPCs after QD labeling. Additionally, this study evaluated the duration of QD label retention and mechanisms of QD label loss. RESULTS: Endothelial colony forming cells (ECFCs) from adult horses (N = 3) were employed for this study, with QD labeled and unlabeled ECFCs tested from each horse. Cell proliferation of ECFCs labeled with QD at 20 nM was quantified by comparing the number of cell doublings per day (NCD) and the population doubling time (PDT) in labeled and unlabeled cells. Function of labeled and unlabeled ECFCs was assessed by comparing uptake of acetylated low-density lipoprotein (DiO-Ac-LDL) and tubule formation on growth factor containing matrix. Cell proliferation was not impacted by QD labeling; both NCD (p = 0. 95) and PDT (P = 0. 91) did not differ between unlabeled and QD labeled cells. Function of ECFCs assessed by DiO-Ac-LDL and tubule formation was also not different between unlabeled and QD labeled cells (P = 0. 33 and P = 0. 52, respectively). ECFCs retained their QD labeling over 7 passages with both 5 nM and 20 nM label concentrations. Reduction in label intensity was observed over time, and the mechanism was determined to be cell division. CONCLUSIONS: Equine ECFCs are effectively labeled with QD, and QD concentrations up to 20 nM do not affect cell growth or function. QD label loss is a result of cell division. The use of QD labeling with equine EPCs may be an ideal way to track engraftment of EPCs for in vivo applications.

Winter, R. L., et al. (2020). "Cell engraftment, vascularization, and inflammation after treatment of equine distal limb wounds with endothelial colony forming cells encapsulated within hydrogel microspheres." BMC Vet Res **16**(1): 43.

BACKGROUND: Endothelial colony forming cells (ECFCs) may be useful therapeutically in conditions with poor blood supply, such as distal limb wounds in the horse. Encapsulation of ECFCs into injectable hydrogel microspheres may ensure cell survival and cell localization to improve neovascularization and healing. Autologous ECFCs were isolated from 6 horses, labeled with quantum nanodots (QD), and a subset were encapsulated in poly(ethylene) glycol fibrinogen microspheres (PEG-Fb MS). Full-thickness dermal wounds were created on each distal limb and injected with empty PEG-Fb MS, serum, ECFCs, or ECFCs encapsulated into PEG- Fb MS (ECFC/MS). Analysis included wound surface area (WSA), granulation tissue scoring (GS), thermography, collagen density staining, and immunohistochemical staining for endothelial and inflammatory cells. The purpose of this study was to track cell location and evaluate wound vascularization and inflammatory response after injection of ECFC/MS or naked ECFCs in equine distal limb wounds. RESULTS: ECFCs were found near and within newly formed blood vessels up to 3 weeks after injection. ECFC and ECFC/MS groups had the greatest blood vessel quantity at week 1 in the wound periphery. Wounds treated with ECFCs and ECFC/MS had the lowest density of neutrophils and macrophages at week 4. There were no significant effects of ECFC or ECFC/MS treatment on other measured parameters. CONCLUSIONS: Injection of microsphere encapsulated ECFCs was practical for clinical use and well-tolerated. The positive ECFC treatment effects on blood vessel density and wound inflammation warrant further investigation.

Wise, K. and M. Brasuel (2011). "The current state of engineered nanomaterials in consumer goods and waste streams: the need to develop nanoproperty-quantifiable sensors for monitoring engineered nanomaterials." Nanotechnol Sci Appl **4**: 73-86.

As nanomaterials are harnessed for medicine and other technological advances, an understanding of the toxicology of these new materials is required to inform our use. This toxicological knowledge will be required to establish the medical and environmental regulations required to protect consumers and those involved in nanomaterial manufacturing. Nanoparticles of titanium oxide, carbon nanotubes, semiconductor quantum dots, gold, and silver represent a high percentage of the nanotechnology currently available or currently poised to reach consumers. For these nanoparticles, this review aims to identify current applications, the current methods used for characterization and quantification, current environmental concentrations (if known), and an introduction to the toxicology research. Continued development of analytical tools for the characterization and quantification of nanomaterials in complex environmental and biological samples will be required for our understanding of the toxicology and environmental impact of nanomaterials. Nearly all materials exhibit toxicity at a high enough concentration. Robust, rapid, and cost effective analytical techniques will be required to determine current background levels of anthropogenic, accidental, and engineered nanoparticles in air, water, and soil. The impact of the growing number of engineered nanoparticles used in consumer goods and medical applications can then be estimated. This will allow toxicological profiles relevant to the demonstrated or predicted environmental concentrations to be determined.

Woinska, M., et al. (2016). "Hydrogen atoms can be located accurately and precisely by x-ray crystallography." Sci Adv **2**(5): e1600192.

Precise and accurate structural information on hydrogen atoms is crucial to the study of energies of interactions important for crystal engineering, materials science, medicine, and pharmacy, and to the estimation of physical and chemical properties in solids. However, hydrogen atoms only scatter x-radiation weakly, so x-rays have not been used routinely to locate them accurately. Textbooks and teaching classes still emphasize that hydrogen atoms cannot be located with x-rays close to heavy elements; instead, neutron diffraction is needed. We show that, contrary to widespread expectation, hydrogen atoms can be located very accurately using x-ray diffraction, yielding bond lengths involving hydrogen atoms (A-H) that are in agreement with results from neutron diffraction mostly within a single standard deviation. The precision of the determination is also comparable between x-ray and neutron diffraction results. This has been achieved at resolutions as low as 0.8 A using Hirshfeld atom refinement (HAR). We have applied HAR to 81 crystal structures of organic molecules and compared the A-H bond lengths with those from neutron measurements for A-H bonds sorted into bonds of the same class. We further show in a selection of inorganic compounds that hydrogen atoms can be located in bridging positions and close to heavy transition metals accurately and precisely. We anticipate that, in the future, conventional x-radiation sources at in-house diffractometers can be used routinely for locating hydrogen atoms in small molecules accurately instead of large-scale facilities such as spallation sources or nuclear reactors.

Wojnarowska, Z., et al. (2011). "Nanoscale domains with nematic order in supercooled vitamin-A acetate: molecular dynamics studies." Phys Rev E Stat Nonlin Soft Matter Phys **83**(5 Pt 1): 051502.

Vitamin-A acetate is one of the most versatile vitamins. It is applied in medicine because of its antioxidative properties, in tumor therapy because of its cytostatic activity, and in cosmetics because of its nutritional additives. Herein, using broadband dielectric spectroscopy, the molecular dynamics of supercooled and glassy vitamin-A acetate was investigated. It was shown that dielectric measurements carried out at ambient and elevated pressures reveal a number of relaxation processes associated with different types of molecular motions: alpha, delta, and nu processes-observed above the glass transition temperature and the next two modes: beta and gamma identified in the glassy state. The occurrence of the delta mode in the dielectric spectrum may imply the existence of nanoscale domains with nematic order. This hypothesis is further checked by atomic force microscopy measurements. Finally, we have determined the value of the glass transition temperature (T(g)) as well as the steepness index (m(P)) at various T-P conditions.

Wolnicka-Glubisz, A., et al. (2009). "Peroxidation of lipids in liposomal membranes of different composition photosensitized by chlorpromazine." Photochem Photobiol Sci **8**(2): 241-247.

Chlorpromazine (CPZ), a phenothiazine derivative, is a neuroleptic drug widely used in medicine because of its tranquilizing and antipsychotic properties. CPZ often causes side effects including cutaneous photosensitization and ocular damage. It was suggested that reactive oxygen species, including singlet oxygen, might play an important role in its phototoxicity. In this work, we studied effects of cholesterol and saturation of fatty acid phospholipids on peroxidation of liposomal lipids induced by UVA irradiation in the presence of chlorpromazine by measuring lipid hydroperoxides using HPLC-EC(Hg) and the iodometric assay. Our study shows that the CPZ-photosensitized peroxidation of lipids is modified by cholesterol and the type of phospholipids present in the liposomes. Thus in liposomes made of the unsaturated 1-palmitoyl-2-oleoyl-phosphatidylcholine (POPC), chlorpromazine photosensitized strong peroxidation of lipids, which was mainly due to generation of singlet oxygen. In such liposomes, CPZ-photosensitized peroxidation of lipids was decreased, in a dose-dependent manner, by addition of cholesterol. On the other hand, in liposomes made of dimyristoyl-phosphatidylcholine (DMPC) and cholesterol peroxidation of lipids was 5 fold slower, while generation of singlet oxygen was reduced over 20 fold. Importantly, cholesterol had no effect on lipid peroxidation in POPC and DMPC liposomes induced by other photosensitizers such as Rose Bengal and merocyanine 540. We postulate that the effect of cholesterol on peroxidation of lipids in liposomal membranes, photosensitized by chlorpromazine, is mostly due to the cholesterol-dependent modulation of CPZ partition in such membranes, which dramatically lowers the efficiency of the photoexcited CPZ to generate singlet oxygen.

Yong, K. T., et al. (2013). "Nanotoxicity assessment of quantum dots: from cellular to primate studies." Chem Soc Rev **42**(3): 1236-1250.

Tremendous research efforts have been devoted to fabricating high quality quantum dots (QDs) for applications in biology and medicine. Much of this research was pursued with an ultimate goal of using QDs in clinical applications. However, a great deal of concern has been voiced about the potential hazards of QDs due to their heavy-metal content. Many studies have demonstrated toxicity of various QDs in cell culture studies. However, in a smaller number of

studies using small animal models (mice and rats), no abnormal behaviour or tissue damage was noticed over periods of months after the systemic administration of QDs. Nevertheless, the correlation of these results with the potential for negative effects of QD on humans remains unclear. Many urgent questions must be answered before the QDs community moves into the clinical research phase. This review provides an overview of the toxicity assessment of QDs, ranging from cell culture studies to animal models and discusses their findings. Guidelines for using various nonhuman primate models for QD toxicity studies are highlighted. This review article is intended to promote the awareness of current developments of QD applications in biology, the potential toxicity of QDs, and approaches to minimizing toxicity.

Young, R. W. (1988). "Solar radiation and age-related macular degeneration." Surv Ophthalmol **32**(4): 252-269.

Age-related macular degeneration (AMD) involves a progressive impairment of the outer layers in the center of the retina. Experimental studies have demonstrated that bright light preferentially damages precisely the region that degenerates in AMD. The evidence that solar radiation is responsible for some of the deteriorative changes that lead to AMD is examined in this review. In the primate eye, the high-energy portion of the solar spectrum is most hazardous to retinal molecules, with damaging effects increasing as photon energy rises. This action spectrum is explicable by the quantum laws which describe the interaction of radiation with matter. High-energy visible and ultraviolet photons can produce molecular damage by a photochemical mechanism. The lesion is exacerbated by oxygen, which initiates free-radical chain reactions (photodynamic effects). Melanin exerts a protective effect against damage from sunlight. In the human retina, documented lesions from solar radiation range from the acute effects of sun-gazing to injuries resulting from prolonged periods of exposure in brightly illuminated environments. The damage occurs in the same region that degenerates in AMD. A cataractous lens and ocular melanin both protect the retina against AMD, as predicted by the radiation hypothesis. Identification of an environmental factor that evidently plays a role in the etiology of AMD provides the basis for a program of preventive medicine.

Yu, G. T., et al. (2019). "Molecular Targeting Nanoprobes with Non-Overlap Emission in the Second Near-Infrared Window for in Vivo Two-Color Colocalization of Immune Cells." ACS Nano **13**(11): 12830-12839.

Monitoring specific immune cells in vivo will provide significant information for improving the therapeutic effect of immunotherapy. Herein, the in vivo two-color fluorescence molecular imaging of an important immune cell, myeloid-derived suppressor cell (MDSC), was realized by using quantum dot (QD)-based nanoprobes with non-overlap emission in the second near-infrared window (NIR-II, 1000-1700 nm). NIR-IIa and NIR-IIb QDs were conjugated with two MDSC-specific antibodies, respectively, and targeted the in vivo MDSCs together. Due to the suppressed photon scattering and diminished autofluorescence in the NIR-II window, the distribution of MDSCs in different organs and tissues was clearly revealed in a non-invasive way by the colocalization of two-color fluorescence from nanoprobes. The high-resolution imaging further confirmed the exact distribution of MDSCs in tumor immune microenvironment (TIME). Our results demonstrated that NIR-II fluorescence nanoprobes with molecular targeting ability provided a powerful tool for monitoring the dynamic change of immune cell populations in TIME in vivo, thus guiding the choice of clinical medicine and evaluating the therapeutic effect.

Yu, W., et al. (2019). "Simultaneous determination of curcumin, tetrahydrocurcumin, quercetin, and paeoniflorin by UHPLC-MS/MS in rat plasma and its application to a pharmacokinetic study." J Pharm Biomed Anal **172**: 58-66.

Curcumin (CUR) is a bioactive compound present in many composite prescriptions of traditional Chinese medicine together with quercetin (QR) and paeoniflorin (PF). Little is known about the influence of QR and PF on the absorption and metabolism of CUR when the three compounds are orally co-administered. In this study, a rapid, sensitive, and reliable ultra-high-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) method was developed and validated for the simultaneous determination of CUR, tetrahydrocurcumin (THC), QR, and PF in rat plasma by using tinidazole as the internal standard (IS). A liquid-liquid extraction method with ethyl acetate was used to pre-treat the plasma samples. Chromatographic separation was conducted on a C18 column with isocratic elution using acetonitrile and 0.1% formic acid water solution (80:20, v/v) as the mobile phase at the flow rate of 0.3 mL/min. A TSQ Quantum Access Max API mass spectrometer equipped with electrospray ionisation (ESI) source in selection reaction monitoring (SRM) mode was employed to determine transitions of m/z 369.0 --> 176.9, 373.1 --> 137.0, 303.0 --> 228.9, 478.9 --> 120.9, 248.1 --> 121.0 for CUR, THC, QR, PF, and IS, respectively. The selectivity, precision, accuracy, extraction recovery, matrix effect, and

stability of the method were validated. This developed and validated method was successfully applied in the pharmacokinetic study of CUR, THC, QR, and PF in rats. The effects of QR and PF on the pharmacokinetics of CUR and its metabolite, THC, were evaluated in the plasma of Sprague-Dawley rats that were orally co-administered CUR, QR, and PF. The results showed that the combined use of QR, PF, and CUR has a possible influence on the metabolism and excretion of CUR. Our work provides a fundamental method for the rapid simultaneous determination of CUR, THC, QR, and PF in rat plasma. Furthermore, this study will provide a basic method for the analysis of pharmacokinetic interaction of CUR, QR, and PF and offer a scientific basis for a possible combination therapy with the three compounds.

Yu, X., et al. (2020). "Fluorescent Properties of Morin in Aqueous Solution: A Conversion from Aggregation Causing Quenching (ACQ) to Aggregation Induced Emission Enhancement (AIEE) by Polyethyleneimine Assembly." Macromol Rapid Commun **41**(14): e2000198.

Unlike normal conversion from aggregation caused quenching (ACQ) to aggregation induced emission enhancement (AIEE) by introducing aromatic rotors tuning aggregation modes, in this study, it is achieved through a supramolecular assembly with polymer. Thus, it provides an easy approach for the inhibition of unwanted H-aggregation between luminogens. As a kind of flavonoid, morin has shown great potential in therapeutics. However, its poor solubility and weak emission in aqueous solution greatly limit its bioapplications. When morin is dissolved in aqueous solution, the presence of 30 x 10(-6) m polyethyleneimine (PEI) induces significant emission enhancement and bathochromic shift. Consequently, the quantum yield (QY) of 24.5% is either achieved by assembling with PEI, versus 0.76% of its ACQ state composed of H-aggregation in aqueous solution. Particularly, the in-depth mechanism studies reveal that it is the assembly with PEI that disassociates the H-aggregation in aqueous solution and further restricts the stretching and/or rotation of morin, which eventually reduce the nonradiative decays and enhance the emission. Therefore, the present study reports a unique phenomenon of AIEE effects on morin. Particularly the in-depth investigation on intrinsic mechanisms will highlight and greatly expand the development of more luminogens from traditional Chinese herbals.

Yu, X. W., et al. (2017). "Research on Ratio of Dosage of Drugs in Traditional Chinese Prescriptions by Data Mining." Stud Health Technol Inform **245**: 653-656.

Maximizing the effectiveness of prescriptions and minimizing adverse effects of drugs is a key component of the health care of patients. In the practice of traditional Chinese medicine (TCM), it is important to provide clinicians a reference for dosing of prescribed drugs. The traditional Cheng-Church biclustering algorithm (CC) is optimized and the data of TCM prescription dose is analyzed by using the optimization algorithm. Based on an analysis of 212 prescriptions related to TCM treatment of kidney diseases, the study generated 87 prescription dose quantum matrices and each sub-matrix represents the referential value of the doses of drugs in different recipes. The optimized CC algorithm can effectively eliminate the interference of zero in the original dose matrix of TCM prescriptions and avoid zero appearing in output sub-matrix. This results in the ability to effectively analyze the reference value of drugs in different prescriptions related to kidney diseases, so as to provide valuable reference for clinicians to use drugs rationally.

Zrazhevskiy, P., et al. (2010). "Designing multifunctional quantum dots for bioimaging, detection, and drug delivery." Chem Soc Rev **39**(11): 4326-4354.

The emerging field of bionanotechnology aims at revolutionizing biomedical research and clinical practice via introduction of nanoparticle-based tools, expanding capabilities of existing investigative, diagnostic, and therapeutic techniques as well as creating novel instruments and approaches for addressing challenges faced by medicine. Quantum dots (QDs), semiconductor nanoparticles with unique photo-physical properties, have become one of the dominant classes of imaging probes as well as universal platforms for engineering of multifunctional nanodevices. Possessing versatile surface chemistry and superior optical features, QDs have found initial use in a variety of in vitro and in vivo applications. However, careful engineering of QD probes guided by application-specific design criteria is becoming increasingly important for successful transition of this technology from proof-of-concept studies towards real-life clinical applications. This review outlines the major design principles and criteria, from general ones to application-specific, governing the engineering of novel QD probes satisfying the increasing demands and requirements of nanomedicine and discusses the future directions of QD-focused bionanotechnology research (critical review, 201 references).

Zuo, Y., et al. (2018). "Silica Nanoparticles with Up-conversion Fluorescence Based on Triplet-Triplet Annihilation Mechanism for Specific Recognition of Apoptosis Cells." Anal Chem **90**(24): 14602-14609.

Discrimination of live and apoptotic cells is a crucial task in the research of pharmacology, biology, pathology, and medicine science. Recently, up-conversion (UC) luminescent materials have appealed much attention due to their unique ability to convert low energy excitation photons to high energy ones. However, UC fluorescence has not been employed in the field of discrimination of live and apoptotic cells. We present a facile and costless Stober method to fabricate robust silica nanoparticles (SiO2 UCNPs) exhibiting several merits, such as narrow size distribution and UC luminescence. SiO2 UCNPs could discriminate live and apoptosis cells by taking advantage of the unique surface property of SiO2 UCNPs for the first time. This work is also the first demonstration of the use of single photon excited UC fluorescence derived from nanoparticles for biological recognition of a specific type of cells.

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