San Antonio Nanotechnology Forum (SANTF)

Third Annual Conference

November 16, 2016

Exploring Issues and Frontiers of Nanotechnology

SUMMARY REPORT

San Antonio Nanotechnology Forum (SANTF) successfully organized the Third Annual Conference on November 16, 2016. The themes of this year's conference were in the general areas of Biotoxicity, Biocompatibility, and Biomedical Applications of Nanotechnology and Nanomaterials.

Following introductions by the meeting organizers, the keynote address was given by Dr. Beena Koshy, Assistant Vice Chancellor for Innovation and Industry Relations of the University of Texas System. Dr. Koshy stressed the ubiquitous and expanding role of nanotechnology in modern life, and also noted that nanotechnology has become an important economic driver, underlying its importance in the academic, industrial, and medical sectors.

The next four sessions were broadly organized into various topical areas and consisted of platform presentations.

Session I: Medical Applications of Nanotechnology: Session Chair: Dr. Randolph Glickman, UTHSCSA

Talk 1. "Nanotoxicity: What Are the Best Approaches for Characterization, Exposure, Dosimetry and Cell Models?", presented by Dr. Saber Hussain, of the Molecular Bioeffects Division of the Air Force Research Laboratory at Wright Patterson AFB, Ohio. Dr. Hussain outlined a program for studying and characterizing toxicity and biocompatibility of nanomaterials. He touched on the transformative nature of nanotech, while emphasizing the importance of toxicity testing early in the development phase of a nanotech research project – rather than as an afterthought. Such testing programs should also include environmental health and occupational safety aspects. Dr. Hussain outlined major topics to be addressed in the biosafety research:

1) Fundamental interactions of nanomaterials with biological and physical processes
2) The effect of size, morphology, and material composition on overall toxicity
3) Long-term effects of sub-lethal exposures
4) Development of predictive models for operational use of specific materials, which can support safety standards

Dr. Hussain then went on to outline his current research. Using *in vitro* models to study nanoparticle interactions with cells, the relation of nanoparticle physicochemical properties with the ability of particles to coat, adhere, and accumulate in cellular organelles has been studied. In general, smaller particles are more toxic. Positively charged particles are more toxic than are negatively charged ones; and the ability to affect mitochondrial membrane potential is highly toxic. The use of CTAB to prevent particle aggregation is a continuing problem, as toxicity remains even after repeated washing of particles. Particle shape also plays a role, with rod- and fibershaped particles having greater toxicity compared to spherical particles. There is an indication that the fractal dimension of the particle is related to their toxicity.

Because nanoparticles can enter biological systems by many routes, it is difficult to carry out accurate dosimetry, and thus there is a need for the development of realistic exposure paradigms. Current safety standards are not generally applicable to nanomaterials. Recommendations for improving standards include the use of more realistic exposure models, more physiological relevant models, and the use of engineered tissue models, e.g., 3D tissue cultures, for pre-*in vivo* tests, with the ultimate goal development of a simulated "human-on-a-chip" model for toxicity testing.

Talk 2. "Gold nanoparticle-assisted laser therapy for enhancement of antibiotic efficacy in methicillin-resistant Staphylococcus aureus biofilms", presented by Dr. Dickson Kirui, Naval Medical Research Unit, San Antonio. A major motivation for this research is the need to address the public health challenge of antibiotic-resistant infectious organisms, such as methicillin-resistant *Staph. aureus* (MRSA). In support of this need, the finding that up to 50% of wound isolates are drug-resistant has been reported by the military. The approach described in this talk examined a non-drug-based therapeutic approach for bacterial infection control. Laser therapy, using targeted gold nanoparticles (AuNP), was designed to direct photothermal and photoacoustic (shock wave) effects at bacterial biofilms to disrupt them and destroy the organisms. The AuNP were targeted to the *Staph. aureus* with antibodies that recognized surface antigens on the bacteria. The efficacy for disrupting biofilms was proportional to the number of AuNP bound to the targets and the number of laser pulses delivered. While laser therapy alone was effective at removing the biofilm matrix, the combined effect of laser and gentamycin (an antibiotic) led to a 4 log reduction in bacterial viability. Another advantage of the combined laser+antibiotic approach is that lower doses of antibiotic can be used to achieve an effective therapy, thereby reducing the likelihood of developing drug-resistance in the target bacteria.

Talk 3. "Nanoparticle-Mediated Laser Surgery for Cancer Treatment: Mathematical Modeling and Experiments", presented by Dr. Yusheng Feng, of the Dept. of Mechanical Engineering, UTSA. The general approach described was the development of a model to optimize tumor treatment(s). Nanoparticles can be used to delineate the tumor borders, both for imaging purposes and for mediating effective therapy. With appropriate imaging, the extent of the tumor, and its internal characteristics, e.g., the degree to which it is hypoxic, can be determined. The presence of the nanoparticles can also provide selective absorption of the laser energy in the vicinity of the tumor, thus enhancing laser-induced thermotherapy. To model the transfer of heat into the tumor, and thus optimize the therapy, Pennes' heat transfer equation was used. Fundamental quantities are incorporated into this classic equation, e.g., entropy, mass, thermal coefficient, energy deposition, blood flow, to model realistically the tissue response to the laser thermotherapy; however, the introduction of nanoparticles perturbs tissue properties, especially if they selectively absorb the laser energy. Thus, the model must be adapted to account for the nanoparticle effects. The particular tissue model used in this study was prostate cancer. The heterogeneity of the prostate tissue, such as the presence of blood vessels, must also be accounted by the model. In practical use, a real-time estimate of tissue temperature during the administration of the laser therapy can be provided by magnetic resonance imaging/thermography. Such an approach can yield an indication of optimal and sub-optimal temperature treatment zones in the target tissue, and the laser application can be adjusted accordingly. With the introduction of nanoparticles into this treatment model, the effect of the laser and the treatment zone can be enhanced.

Session II. Advances in Nanotechnology in Engineering and Biomedical Applications. Session Chair: Dr. Qiaoying Zhou (Joy), Ph.D. Northwest Vista College.

Talk 1. "Defect-engineered nanocarbons for electrochemical energy storage", presented by Dr. A.M. Rao, Dept. of Physics and Astronomy, Clemson University, SC. A continuing challenge is the storage of renewable energy for use during non-producing times, such as at night or when there is insufficient wind. While batteries are widely used for this purpose, they have drawbacks. An alternative technology is the use of supercapacitors, which can tolerate high charge and discharge rates. Supercapacitors have high specific power (W/kg), but low specific energy (Wh/kg), compared to batteries or fuel cells which have high specific energy but low specific power. Dr. Rao discussed the quest to increase the specific energy of supercapacitors without excessively reducing the specific power. With regard to electrochemical double-layer capacitors (EDLC), a practical goal has been to increase the lifetime of the device while also decreasing their lifetime cost. Carbon electrolyte, a porous material, is widely used in these devices, but the nonuniformity of the pores in the material adversely affects the availability of ions. In addition, the use of binder materials leads to an increase in the internal resistance of the device and decreases its efficiency. New carbon materials are sought to overcome these limitations. Allotropes offer one approach, which may consist of diamond, graphite, C_{60} single wall nanotubes (SWNT), or graphene (basically, an open end nanotube of carbon, 1 molecule thick). Another approach is that of multiwall nanotubes (MWNT), in which well-aligned nanotubes provide excellent paths for current carriers. The challenge is to grow MWNT on current collectors without use of binder materials, in a scaleable manufacturing process. Such processes include the use of a moving substrate, e.g., Al foil, in a chemical vapor deposition oven at ~600° C, or in a spray-coating process. Graphene sheets can also be enhanced by defects produced by Ar laser exposures, creating additional paths for current carriers. N-doped graphene is proving to be suitable for high power storage applications.

Talk 2. "Ordered Gold Nanorod Assembly: From Modeling to DNA Biochip Application", presented by Dr. Zhong Mei, Dept. of Biomedical Engineering, UTSA. In conventional approaches for biomedical nanotech-based sensors, the surface plasmon resonance (SPR) of a nanoparticle is sensitive to changes in local refractive index due to the presence of biological macromolecules. If fluorescence signaling is possible, then the detection sensitivity may increase to the nano-and in some cases the picomolar range. Optimizing the assembly of nanoparticle-based sensor is a challenge; one approach to this is through controlled assembly of AuNPs. This class of nanoparticle offers stability, the possibility to form complex structures, and tunability for particular wavelengths especially in the NIR. Vertical organization of the structure yields regular and predictable electric fields, supporting enhanced fluorescence properties. Gold rods are attractive for this type of organization because they can self-assemble on a patterned substrate, e.g., in a hex-packing pattern for a predictable electric field. In general, fluorophore enhancement is highly dependent on (1) the measurement distance from the AuNP, due to the Förster energy transfer mechanism. This was clearly demonstrated with a fluorophore coupled to the AuNP by an oligonucleotide of varying lengths. (2) The size and shape of the AuNP (rods in particular) due to different localized SPR (LSPR); enhancement occurs when LSPSR has maximal overlap with the fluorophore excitation-emission wavelengths. A hypothetical application of this nanoparticle configuration is for specific DNA detection. The AuNP is conjugated to a single strand DNA with a fluorophore quenched by the AuNP. Binding of a complementary DNA strand causes the sensor DNA strand to unfold and/or extend, which moves the fluorophore away from the AuNP, thus releasing the fluorescence signal. The configuration of such a biochip was illustrated. If DNA sensors with different specificities are spatially separated on the biochip, then multiplexed detection is possible. An application for such a biochip is the detection of specific short nucleotide polymorphisms (SNPs).

Talk 4. "Magnetoelectric Nanorobot for Biomedical Applications", presented by Soutik Betal, Department of Electrical Engineering, UTSA. The development of "molecular machines" was described in this presentation. Molecular-scale devices can exploit alternating electromagnetic fields for propulsion. Such devices could assume arbitrary configurations and have diverse functions. Motion can also be conferred to biological cells by a related approach. Cells are loaded with magnetic nanoparticles by electroporation, and then the cells may be moved and manipulated without physical contact through the use of external magnetic fields. Applications involving the movement and placement of cells in specific locations, e.g., for therapeutic purposes, or for targeting individual cells, were described in the presentation.

Session III. Advances in Nanotechnology in Engineering and Biomedical Applications: Session Chair: Dr. Bharathi Subramaniasiva, Northwest Vista College.

Talk 1. "Science and Technology of a Novel Biocompatible/Corrosion Resistant Ultrananocrystalline Diamond Coating (UNCD®) and Application to the Development and Commercialization of a New Generation of Medical Devices", presented by Dr. Orlando Auciello, Bioengineering Department, Univ. of Texas at Dallas. Dr. Auciello described the development of the UNCD coating. The initial process used C_{60} and H_2 along with high temperature to grow the coating; however, while this process successfully produced the coating, it proved not to be scaleable. By modifying the process to be carried out under 99% Ar gas and $^{12}CH_4$ plasmas, improved seeding and deposition was achieved with electrodeposition. The process yields a diamond-like surface coating, which has excellent biocompatibility. It is also electrically conductive, water resistant, and corrosion resistant. One of the applications for this material is a "photo-optic chip" to be used as a retinal prosthetic device, which is coated with the UNCD expressly for its inertness. The chip is placed outside of the eye itself, with electrical leads inserted into the retina to stimulate the neurons there. This chip has been successful in animal models and is awaiting FDA approval for human tests. Other medical implants are undergoing development using the UNCD for its excellent biocompatibility and durability. The material also integrates well into bones, which will aid the development of orthopedic devices.

Talk 2. "Applications of microfluidics and chip technology to measure picoampere currents in single cells", presented by Dr. Thomas Knott of Cytocentrics, San Antonio. Dr. Knott described the development of the Cytocentrics single cell patch clamping system for measuring ion channel currents, which can be used in drug discovery, cardiac pharmacology, drug safety investigations, and monitoring the cellular effects of candidate drugs. He noted that nanotechnology can be used to measure and manipulate ion channels in cell membranes. This work is being done in collaboration with the Center for Innovation in Drug Discovery (CIDD) at the Univ. Texas Health Science Center at San Antonio. Dr. Knott also discussed another aspect of nanotoxicology, in that nanoparticles, such as AuNP, can block hERG channels in cardiac tissue. While this can be a toxic action, it can also be exploited for therapeutic use; ion channels are targets for more than 10% of drugs currently being developed. The Cytocentrics microfluidics device captures a cell with 2 suction channels, and then a dual channel patch channel establishes a gigohm seal with the cell membrane. At present, the system only produces an "outside-in" patch. The current passing through channels located within the seal region is thus measured. Drugs and agents can be applied to the cell and the effect on channel conductance quantitatively measured, which provides the ability to determine the drug action with considerable sensitivity and selectivity.

Talk 3. "Nanofluid Morphology Effects in Interfacial Transfer Processes", presented by Dr. Drew Johnson of the Dept. of Civil & Environmental Engineering, UTSA. Dr. Johnson characterized the general topic of his talk as "Nanoparticle Brownian Motion". He noted that classical theories of Brownian motion didn't seem to apply to the behavior of nanoparticles in a fluid. To begin to understand the movement of nanoparticles, Dr. Johnson's team began by examining NaCl diffusion across semipermeable membranes. Then, they applied a similar approach to nanoparticle diffusion, using etched polycarbonate membranes with cylindrical pores; however, with this model system they did not observe enhanced mass transfer. They found that in a gas-liquid transfer scheme, increasing the volume-fraction of Si nanoparticles actually decreased O_2 diffusion, an observation that was unexpected. Enhanced heat transfer was observed in this model, a finding that could be explained by formation of aggregates, thus increasing particle interactions that act as highly-conducting paths. While nanoparticle Brownian motion cannot explain enhanced mass transfer effects; an effective medium theory can describe nanofluid transfer properties.

Talk 4. "Engineered Metastructures for Tailoring Plasmon-Mediated Effects on Molecular Adsorption and Spatial Chirality", Dr. Michael Miller, Southwest Research Institute, San Antonio. Metamaterials' properties derive from their constituent units, while conventional materials' properties derive from their inherent atoms and molecular structure. Metamaterials can be designed to exhibit arbitrary properties, e.g., negative refractive index and antennas with elements much shorter than their effective wavelengths. Dr. Miller discussed the formation and tuning of surface plasmons. Metallic materials exhibit group oscillations of the electron clouds (a gas). The size and structure of the material define the resonant frequency and shape of the plasmon. Note that nanoscale plasmons lie in the near infrared (NIR) and have been exploited for numerous applications, such as surface enhanced Raman scattering (SERS). Dr. Miller's work has demonstrated plasmon-mediated catalysis for dissociative pathways without the need for an external field. He also explored chirality in a theoretical model using helical SiO "nanosprings" as a substrate in an external field. In an ortho field, dipoles formed and in a para field multipoles formed. Raman scattering was attenuated in the ortho mode, and intensified in the para mode.

Session IV. Education and Safety Training in Nanotechnology: Session Chair: Dr. Vasiliki (Vicky) Zorbas Poenitzsch, Department of Materials Engineering, Southwest Research Institute.

Talk 1. "Training and Education in Advanced Materials at NW Vista College", presented by Dr. Bharathi Subramaniasiva, NW Vista College. The former nanotechnology program at NW Vista was recently reformulated and renamed the Advanced Materials Program, to signify that broader scope of the program. This also reflects the growth of nanotechnology and materials science in industry and academics that is driving the requirement for a workforce with the need for skills at a variety of levels to suit the particular requirements. Dr. Subramaniasiva then went on to describe the challenges and objectives of this new program.

Talk 2. "Nanomaterial versus Nanotechnologies: Scale-up Limitations and Challenges in Topical Formulations", presented by Dr. Elishalom Yechiel of Elsom Research Col, San Antonio. Dr. Yechiel gave an interesting -- and challenging – discussion of the surprising complexity of reducing compounds to nanoparticles for better delivery of compounds through topical administration. He stressed the importance of arriving at consensus definitions of nanosizing, nanomaterials, and nanotechnology, in order to achieve consistent results across industries. He gave an interesting historical perspective by describing methods from antiquity for producing very small particles. It has long been known that the medicinal properties are affected by the particle size of a drug agent. As examples of widely diverging approaches to nanoscale materials, he suggested that mitochondrial ATPase could be considered as a nano-machine. Tools specific for a particular application must be developed along with the nano-applications. Scaling-up of the application could be divergent: that is, the scale-up could follow *Centralization*, which would produce one gigantic machine, or, it could follow *Replication*, in which a large number of tiny machines would be produced. Finally, Dr. Yechiel discussed the emerging regulatory climate for nanomaterials. As one (possible over) reaction to perceived threats of nanomaterials, he cited the approach by the International Center for Technology Assessment (ICTA), which supports further extension of government oversight of nanomaterials, such as the requirement to report the use of all nanoscale materials to the EPA. How this will play out under the new Administration is anyone's guess at this moment. However, one can find plenty of examples embedded in our society, such as social memes, internet conspiracy theories, science fiction that reveal the existence of public concern and even fear of nanotech. Dr. Yechiel concluded by questioning if scientists and technologists are sufficiently involved in the development of safety standards for nanotechnology, as well as the education of the public about nanotechnology.

Talk 3. "Current Skillsets for Working in Nano-Safety", presented by Dr. Dominick E. Fazarro, University of Texas at Tyler, Tyler, TX. The National Nanotech Coordinating Office (NNNC) has stressed the pervasiveness of nanotech and its economic importance. Dr. Fazarro noted that, notwithstanding the increasing importance of nanotech, the human element is often inadequately considered, especially when handling novel materials. As also noted by Dr. Hussain earlier, Dr. Fazarro stated that safety is too often an afterthought, rather than an essential part of the development and implementation of a new nanomaterial. Early incorporation of safety procedures and training is essential to prevent major accidents occurring in the workplace. Dr. Fazarro then described networks existing in Texas that support and provide safety education and training in nanomaterials and advanced materials. These include programs at Rice University, Texas State University, Univ. of Texas at Tyler, and programs supported by an OSHA/Susan Harwood Grant. The program that Dr. Fazarro has helped to develop is organized into 7 major topic modules. The skill sets that are stressed in the program include chemical safety, materials science, industrial engineering, and related topics. There is also a program available for in-house training that generally relies on NIOSH-provided materials. The general action plan is to be proactive and not reactive to nanosafety.

Posters, Panel Discussion and Meeting Wrap-up.

Following these platform presentations, each of the students presenting posters at the meeting were given 2 minutes at the podium to present an overview of their research. A lively discussion of the challenges and emerging commercial applications of nanotechnology was conducted by a panel consisting of Dr. Auciello, UT Dallas, Dr. Fazarro, UT Tyler, Christine Burke, Director of the Commercialization & Technology Transfer Office, UTSA, and Tom Long, Exec. VP of Business Recruitment, SA Economic Development Foundation, San Antonio. The panel discussion was chaired and conducted by Dr. Kathryn Mayer, Department of Physics and Astronomy, UTSA.

Finally, a meeting wrap-up was given by Dr. Randolph Glickman (UT Health Science Center SA), who categorized the significance and impact of the various presentations into three overall categories: BioMedical, Materials, and Educational. The range represented by the topics covered represent very well the increasing impact of nanotechnology and nanomaterials in a wide swath of contemporary life: industrial, medical, scientific/technical, military, and consumer sectors are all experiencing the impact of novel materials being deployed in the nanoscale. Along with realizing the benefits of nanotechnology, society must also address the various challenges presented by nanotechnology, especially those relating to safety and human factors.

Dr. Jaclyn Shaw, Director for Research Support, Office of the Vice President for Research Support, UTSA presented the Certificates of Participation and gift bags to the student presenters and Panel members.

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Meeting Report, submitted by Dr. Randolph D. Glickman, Dept. of Ophthalmology, UTHSCSA and updated by Dr. Madhav Rao Govindaraju.