In the News

catch the wave—
nanotechnology, the future is now

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Nanoscience and nanotechnology are shaping biomedical research worldwide. The initiative began with a symposium that took place at the National Institutes of Health (NIH) in 2000 and continued with the formation of the Nanotechnology Initiative (NNI) in 2001. Since then, nanotechnology has impacted many disciplines including materials science, electrical and computer engineering, medicine, and environmental science. Technological advancements fostered by this research are the development of advanced mass-storage devices, novel materials, efficient miniscule transistors and memory chips, gene and drug delivery nanoscale measurement apparatuses, energy-efficient solar cells, and air- and water-treatment systems. In April 2009, the IEEE Life Science Systems and Applications (LiSSA) Technical Committee in cooperation with NIH sponsored a workshop on nanomedicine to provide a forum where engineers and scientists can apply sophisticated nanotechnology to critical issues in health and medicine. Following is a synopsis of some of the state-of-the-art IEEE research in nanotechnology that will significantly impact the future of medicine and health care.

In recent years, there has been a surge of interdisciplinary collaborations among scientists, engineers, researchers, and medical practitioners focused on solving complex problems in medicine and related fields. These activities have resulted in the development of bioinspired silicon, neural prosthetics, image-processing systems, biosensors, and intravenous drug delivery devices that support diagnosis, treatment, and prevention of disease in patients. Supported by the NIH-wide Nanotechnology Task Force, the National Library of Medicine (NLM), and the National Institute of Biomedical Imaging and Bioengineering (NIBIB), and inspired by dialogue among several IEEE Societies and NIH institutions, the fourth IEEE–NIH LiSSA Workshop took place during the Nanoweek 2009 Conference held at NIH in Bethesda, Maryland.

The objective of this workshop was to create an environment in which engineers and scientists could discuss innovative technologies that support the application of nanotechnologies in medicine and health care. The workshop was inspired by NIH’s nanomedicine road map, which describes the importance of developing materials and devices in the size of molecules and atoms to support medical intervention. The expectation is that this workshop and collaborations stemming from it will support identification of cures to ailments such as cancer, degenerative bone and muscle disease, or damaged nerve cells.

Nanomedicine in Practice

One of the most exciting perspectives in the field of nanomedicine is the potential application of novel nanotechnology to medical science and practice. Nanomedicine involves medical diagnosis, monitoring, and treatment that take place at the level of single molecules or molecular assemblies where structure, control, homeostasis, and motility in living cells are observed. The research goal in this field is to improve prevention, diagnoses, and treatment of diseases in humans. Tools such as atomic force microscopy and biosensor arrays are used to understand cellular and molecular dynamics and are directly applied to the prevention and treatment of ailments such as cardiovascular diseases.

Several concepts were presented showing the application of nanotechnology in medicine. Among these was the use of diffusion tensor imaging (DTI) to study the growth and recurrence of glioblastoma multiforme (GBM). Studies of this nature have been found to be very important for the diagnosis and detection of recurrence of GBM after surgery [1].

Other practical concepts included the use of mass spectrometry imaging data to identify prostate cancer biomarkers. For this, a computational framework that uses matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) tissue imaging data was presented [2].

A molecular imaging concept that used multimodal optical imaging systems to image colon cancers was also discussed. This system combined optical coherence tomography (OCT) and fluorescence molecular imaging (DMI) to enable simultaneous imaging of tissue morphology and molecular information at high resolution [3].

The work presented at LiSSA can be leveraged to support many branches of medicine including oncology, neurology, cardiology, orthopedics, ophthalmology, radiology, pathology, and infectious diseases. It is expected to improve biological therapies such as vaccination, cell therapy, and gene therapy. In fact, some of this work can form the basis of the development of novel devices that support personalized medicine, novel drug delivery procedures, and surgery.

Nanotechnology Development

Nanotechnology development describes the infrastructure by which nanodevices, sensors, and processes are created. During LiSSA 2009, several such technologies were described, including the innovative concepts below.

The first concept involves the development of complementary metal oxide semiconductor (CMOS) technology that enables the fabrication of nanoscale devices. This technology, discussed by Ramachandran et al. [4], was used to fabricate 500-nm spaced metal electrodes that are capable of selectively capturing and detecting R2Bm protein molecules. This apparatus in cooperation with surface functionalization and protein–deoxyribonucleic acid (DNA) interaction allowed for specific binding
and direct current measurements that support electronic recognition of a number of biomarkers. The fabricated chip was referred to as the Proteonic Biochip. This chip was particularly interesting, because it used a current–voltage measurement to show a decrease in resistance between electrodes that exceeded two orders of magnitude when a linked protein was captured.

Another developmental technology of interest was described by Saito et al. [5]. The tools presented in the article allow for submicron perforations of substances within cell membranes by inducing local oxidations in the cell membrane. The authors applied the technique to the microinjection method and found that the injection of a functional dye, an antibody, and messenger ribonucleic acid (mRNA) to the cells was successfully achieved with 0% cell mortality. The cell responses were observed for a large number of cells.

Sunnie Xie shared research on the study of gene expression, active transport, and lipid metabolism using combinations of specific probes and advanced optical microscopy. The devices used in Xie’s research on living cells and organisms allowed for the quantitative probing of biochemical reactions in living cells, which supported detection and tracking of proteins with single-molecule precision. The researchers involved in this work were capable of detecting, imaging, and monitoring metabolites, which heretofore had been an unwieldy exercise.

A fourth novel concept presented during the workshop was on the fabrication of polyvalent therapeutic RNA nanoparticles, which was designed to support the delivery of siRNA, ribosomes, and drugs to targeted cells. The technology was designed to support innovative and radical cancer therapy. Shu et al. described their novel approach for the fabrication of polyvalent therapeutic pRNA nanoparticles [6]. The nanoparticles were specifically designed to deliver siRNA to cancer cells, with the objective of silencing targeted genes. Results of animal trials showed that this technique is highly efficient in preventing and treating cancer. The researchers felt that this technique will allow for long-term administration cancer therapy, without hampering the effects posed by mainstream broadcast drug delivery treatments.

**Systems and Application in Nanomedicine**

This research begins with the work by Chen and coworkers on using gold-based...
nanoparticles (GNPs) to support targeted cancer radiotherapy [7]. The premise is that successful treatment of cancer requires increasing the cytotoxicity of targeted tumor cells while reducing radiation exposure to normal cells. Nanotechnology was shown to be a promising method for achieving this result. The article focuses on the development and application of GNPs as radiosensitizers capable of targeting tumors and killing cancer cells. The authors designed glucose-capped GNPs that were able to specifically target cells of interest. Preliminary in vitro and in vivo results showed that the procedure was successful in increasing cell uptake and radiation cytotoxicity in the affected area.

In the work presented by Li et al. [1], a novel method of analyzing the recurrence pattern of GBM based on serial magnetic resonance imaging (MRI) was proposed. In this work, DTI is used to accomplish this analysis. The study supports monitoring the growth and recurrence of GBM. It is expected that this analysis can be used to support the diagnoses and detection of the recurrence of GBM after surgery. The findings of this research suggest that the combination of the quantitative measures of longitudinal, morphological, and diffusion pattern changes provides more accurate measures about the growth or recurrence of GBM. The proposed method has utility for both follow-up studies of GBM and clinical trials of various treatment methods.

In “HeartToGo: A Personalized Medicine Technology for Cardiovascular Disease Prevention and Detection,” Jin et al. [8] discussed a cell phone-based personalized medicine technology for managing cardiovascular disease. This technology was designed to continuously monitor and record ECG in real time and generate individualized cardiac health-summary reports that would identify abnormal CVD conditions at all hours of the day. The authors proposed an artificial neural network (ANN)-based technique that trained the phone to learn to adapt to its user’s physiological conditions based on clinical ECG data and specific medical information.

In contrast to other wireless communications, research involved investigation of the utility of wireless electricity (witricity) to medical sensors and implantable devices. The theoretical analyses were performed for several coupling scenarios of resonators, while in vitro experiments were conducted in open air through an agar phantom of the human head. The studies [9] showed that witricity had utility in providing wireless power to a variety of medical sensors and implanted devices.

**IEEE Societies in Nanomedicine**

To foster an atmosphere of open communication between the medical field and the engineering discipline, several IEEE Societies were invited to a brief research conducted by their members that had application to nanomedicine and health care.

The first of these was a briefing presented by Angela Hodge of the IEEE Circuits and Systems Society (CASS). Hodge shared an overview of the life sciences and biomedical research under investigation within the biomedical circuits and systems (BioCAS) technical committee, which was developed to support advancement in research and development of engineering technologies that contribute to biological and medical applications. This endeavor is inherently multidisciplinary and leverages expertise from a myriad of specialties including medicine, biology, chemistry, physics, engineering, and computer science.

Hodge stated that life sciences-related research by CASS members includes 1) biomedical instrumentation, 2) wearable systems, and 3) low-power circuits and sensors. This work has been the foundation of the CASS’s contributions to bioinspired silicon, neural networks, advanced prosthetics, and medical image processing. The conferences organized by the CASS participants broaden the knowledge of emerging areas of research that encompass the juxtaposition of life sciences and circuits and systems engineering.

Borenstein presented nanotechnology research under investigation by the IEEE Engineering in Medicine and Biology Society (EMBS). The presented research revolved around nanotopographic structures for applications in tissue engineering and regenerative medicine. Such structures occur naturally within the extracellular matrix of many tissues and influence a wide range of properties through mechanotransductive interactions. In Borenstein’s presentation, we observe innovative technological advances in nanoscale modification of substrates for tissue engineering and regenerative medicine. The work focused on the ways in which the presented studies would lead to application of patient care.

On behalf of the IEEE Lasers and Electro-Optics Society (LEOS), Ilev discussed the principles and novel approaches in nanobiophotonics for biomedical applications. He provided a comprehensive review of the state-of-the-art technology pursued by LEOS members. Specific attention was given to applications that involved spatial resolution below the 100-nm range.

Olivo-Marin presented bioimaging research currently under investigation by the IEEE Signal Processing Society (IEEE SPS). The author cited numerous advances in fluorescent probes, labeling techniques, and optical microscopy systems as being the cause of advancement in signal and image processing that supports biological and biomedicine research. The state of the art in image-processing methods and challenges were discussed, with significant attention being given to contributions in bioimaging.

**Best Paper Awards**

Four Best Paper Awards were given to participants in this year’s LiSSA workshop. In the student category, the award was given to Ramachandran et al. for the article on “Electronic Detection of Selective Proteins Using Nonantibody-Based CMOS Chip” [4]. Takshi et al. received the postdoctoral Best Paper Award for “Large-Scale High-Performance Cell Membrane Perforation, with Nanoimprinted Mass Producible Perforator” [5]. The overall Best Paper Awards were shared by Wei et al. and Shu et al. for their work on “Ligand-Function-alized Gold Nanorods as Theragnostic Agents” [10] and “Fabrication of Polyvalent Therapeutic RNA Nanoparticles for Specific Delivery of siRNA, Ribozyme and Drugs to Targeted Cells for Cancer Therapy” [6], respectively.
The Charles Desoer LiSSA Attendance Grant

The Charles Desoer LiSSA Attendance Grant was created to allow students exhibiting an interest in life science systems to attend the annual IEEE–NIH LiSSA Workshop. The grant was developed to aid in fostering research on stroke and to honor Prof. Charles A. Desoer, a victim of stroke, who is known for his education of circuit and system theorists. The grant sponsored one university student and two high-school students. Selection was made by a committee formed by the LiSSA workshop organizers.

The university student was selected based on a submitted publication, with preference being given to work on life science circuits and systems. Among the criteria were paper content, originality, significance, and quality of presentation. This year’s university winner was Priyanka Pachampettai Ramachandran. She received an attendance grant, a US$600 honorarium, and a certificate.

The high-school students were selected as a result of their involvement as NIH interns, with the preference being given to interns at NINDS. The applicants submitted a short essay describing their intern projects. Kefre Akpaete of Springbrook High School and Arwa Elbeshbishi of Poolesville High School were this year’s winners. Each received complimentary registration to attend LiSSA.

Supporting Collaborations

In summary, this workshop gave engineers and biomedical scientists the opportunity to exhibit and share state-of-the-art research while learning biological applications for these technologies. The event provided engineers and members of the health-care and medical communities an unique opportunity to identify areas of common research, with the hope that collaborations could be a natural by-product of the interaction.

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References


