IMS Associates Program
Annual Meeting
May 22, 2008

All AM activities in IMS 20

9:00 - 9:15 Welcome – Ed Kurz

9:15 - 9:55 "Toward Smart Interfaces for Biomaterials" Jon Goldberg, Director of the Center for Biomaterials, University of Connecticut Health Center

With disease, trauma and particularly an aging population, there is a growing need for replacement of a wide range of tissues. Until about 15 years ago biomaterials were designed as inert, distinct replacements, and this is how current treatment is still delivered. However, recent advances in materials design and cell biology have lead to *smart interfaces* where functionalized biomaterial surfaces interact with and control cellular response. Stem cells are playing an increasingly important role, but many materials-related challenges and opportunities remain in this new era of regenerative medicine.

9:55 -10:20 "Miniaturized, Implantable Biosensor for Glucose Monitoring" Fotios Papadimitrakopoulos, Nanomaterials Optoelectronics Laboratory, Polymer Program, Professor, Department of Chemistry, Associate Director of the Institute of Materials Science

The development of glucose and other metabolic biosensors is an area of intense research with application in diabetes, obesity and metabolic monitoring in general. At the University of Connecticut we are developing a totally implantable glucose biosensor, with current dimensions of 0.5 diameter X 5 mm length. Major obstacles to the development of implantable biosensors are their oxygen dependence and their *in vivo* stability, and a noted gradual loss of function *in vivo.* While the oxygen dependence of the sensors has been attributed to the large offset between the glucose and oxygen levels in the subcutaneous tissue, the *in vivo* instability has been attributed to a number of factors including, tissue trauma and biofouling.

The tissue reactions include inflammation and eventual fibrosis encapsulation that cause an initial edema at the site, followed by fibrous encapsulation and loss of blood and therefore analyte supply. To overcome this we have been developing a biocompatible "smart" coating that releases drugs and growth factors to counter the inflammation and fibrous encapsulation and encourage neo-angiogenesis. Recently, we have reported, in a series of the development and *in vivo* evaluation of a composite coating for implantable devices, based on physically cross-linked poly(vinyl alcohol) (PVA) hydrogels containing dexamethasone-loaded poly(lactic-co-glycolic acid) (PLGA) microspheres, that controls both the acute and chronic phases of inflammation over a 1-month period. These composite coatings successfully deliver tissue response modifiers (TRM) such as dexamethasone and vascular endothelial growth factor (VEGF) at the implant site providing a sustained anti-inflammatory effect and neo-angiogenesis for a one month period using a rat model. We are currently extending this to a three month life-time and have successfully prevented inflammation and fibrous encapsulation for 90 days in rats. These biocompatible coatings will facilitate development and commercialization of our implantable biosensor.

Another major problem associated with the development of totally implantable, enzymatic glucose sensors is the lack of linearity in the hyperglycemic region and the lack of sensitivity in the hypoglycemic region. This is a consequence of the large imbalance between the glucose and oxygen levels in the blood and plasma, which causes the sensor enzymatic reaction to be oxygen limited. We have developed techniques to overcome these limitations through the fabrication of highly tunable layer by layer (LBL) assembled outer membranes. The sensitivity and linearity of these sensors were further improved by using the 'periodically biased amperometry' technique for testing the sensors. The technique involves the application of bias voltage for a very short duration at regular intervals of time. Under the optimum conditions, these glucose sensors exhibited linearity extending into the hyperglycemic regions compared to the traditional control enzymatic sensor which only functioned in a linear fashion up to 10mM. In addition, our newly development amperometric method enabled a 2-fold increase in the magnitude of the measured current at the hypoglycemic range.

10:20 - 10:40 Break

10:40 – 11:05 "The Influence Of Wound Healing Drugs On The Nano-Mechanical Properties Of Individual Cells", Bryan Huey, Assistant Professor; Chemical, Materials and Biomolecular Engineering Department

The UConn NanoMeasurements Lab has recently installed a unique combination of the widely applied optical technique of 3-D fluorescence microscopy and deconvolution along with with the high force sensitivity and spatial resolution of atomic force microscopy (AFM). These complimentary methods allow novel simultaneous optical and topographic, mechanical, and/or or electronic measurements of structures, including living cells.

In this study, the elasticity of living HaCaT (human epithelial) cells was monitored in vitro, both with and without exposure to epidermal growth factor (EGF). It was found that the HaCaT cells exhibited an increase in both size and elasticity with increasing length of exposure to 25 ng/mL EGF. Additionally, results applicable to more general cell-AFM studies were obtained, including optically characterizing fixed cell dimensions during concurrent AFM measurements.

Fixed MH-S cells (mouse lung macrophages) transfected with GAP-43 GFP to identify the cell membrane were separately found to deform by up to 50% when imaged with the AFM as compared to their 3D optically derived height. These results suggest that 3-D optics provide a more accurate measure of cell height than AFM imaging. Force measurements performed on living MH-S cells also reveal extensive cell deformation with relatively small applied forces (7nN or less) as well as the viscoelasticity of living MH-S cells. This unique combination of techniques, AFM with 3D optics, therefore provides novel insight into the optical and mechanical properties of individual cells.

11:05-11:30 “Hydrophobically Associating Hydrogels for Ocular Drug Delivery”, Tom Seery; Associate Professor, Chemistry;
Director of the Polymer Program

11:30 - 11:55 “Composite Materials for Orthopedic Applications”, Montgomery Shaw, A.T. DiBenedetto Distinguished Professor; Chemical, Materials and Biomolecular Engineering Department, Polymer Program

Of importance to orthopedic procedures are repair materials that can carry significant loads without excessive deformation. In addition, these materials need to be biocompatible, biosorbable, and conducive to the replacement of the repair material with native bone. To meet these requirements, we have designed composites using two biocompatible/biosorbable polymers, poly(L-lactic acid) (L-PLA) and polycaprolactone (PCL), with the latter filled in a carefully designed fashion with nano needles of hydroxyapatite (HA). Discussed in this talk are the design and processing challenges and solutions for achieving high while maintaining enough toughness to make robust devices.

Co-investigators: Dr. James Olson (Teleflex Medical), Prof. Mei Wei
Students: Lyndon F. Charles, Fei Peng, Shih-Po Sun.

All PM activities in Jorgensen Gallery
12:00-1:00 Lunch

1:00 -1:15 Status of the Associates Program – Ed Kurz

1:15- 1:45 “Non-Biological Materials Applications of DNA”, Jeff Stuart, Associate Research Professor, IMS

Molecules of biological origin, including proteins and DNA, are gaining recognition as having potential as active elements in a wide variety of technologies, from sensors to microelectronics to optical memories. This burgeoning field is quickly becoming ubiquitous with examples of how natural materials can help solve problems in a more facile and efficient manner than conventional technologies, particularly in the field of nanotechnology. DNA is one such example, of a biological material with unique materials properties that are not easily duplicated in conventional materials which can be exploited for applications quite separate from native biological function; possibilities include sensors, active and passive filter elements, optical materials, and conducting polymers. These applications are independent of DNA's role as a genetic material, but are derived entirely from its inherent non-natural materials properties.

2:00 Tour of IMS