Biomaterial Interfaces Division
Room Hall B - Session BI-TuP

Biomaterial Interfaces Division Poster Session
Moderator: Joe Baio, Oregon State University

BI-TuP3 Stimuli-responsive Thin Films made from Highly Methoxylated Citrus Pectin, ***Zeinab Veisi,*** *N. Alcantar, R. Toomey,* University of South Florida

We have used high-methoxyl citrus pectin polysaccharides to fabricate ultra-thin responsive coatings to be potentially implemented as elements of stimuli-responsive systems with diverse applications in drug delivery, tissue engineering, biomedicine, and etc.

Pectin is composed of a backbone chain structure of D-galacturonic acid units linked by α-1,4-glycosidic bonds. The carboxyl groups present in a polygalacturonic acid chain may exist as charged carboxyl acid groups or esterified with methyl groups. The ratio of methyl esters per total number of carboxyl groups is defined as the degree of esterification (DE). Low-methoxyl pectin (DE<50%) can be cross-linked in the presence of divalent ions such as Ca^{2+} ions. High-methoxyl pectin exhibits weak affinity for Ca^{2+} cations due to the lower charged carboxyl group content challenging their Ca^{2+}-induced cross-linking.

Herein, thin coatings of high-methoxyl citrus pectin were fabricated as surface-attached hydrogel networks by spin-casting solutions of pectin onto a solid surface followed by Ca^{2+} induced crosslinking. The cross-linking was performed by introducing the cross-linker (Ca^{2+}) in a poor solvent for pectin to eliminate water in the cross-linking process. Cross-linking the coatings in a non-solvent ensures that the coatings remain intact by preventing dilution of the pectin chains. However, the Ca^{2+} ions freely diffused into and cross-linked the pectin to form robust coatings. Using this strategy, pectins with up to 70% esterification were cross-linked. Generally, high-methoxyl pectins do not cross-link in the presence of calcium unless at high pectin concentrations.

The coatings prepared in this manner demonstrated a volume-phase transition induced by temperature. The responses of coatings were assessed by characterizing their swelling behaviors using ellipsometry and ATR-FTIR to provide insights into the nature of the transition. Our findings show that at temperatures below approximately 35 ˚C, the coatings were hydrophilic. At higher temperatures, the coatings expelled water and collapsed giving rise to distinctive de-swelling profiles. The hydrophilic/hydrophobic transition was driven by dehydration of methoxyl groups whereas water remained bound to the carboxylate groups. It was also observed that the response of the coatings can be tuned by adjusting temperature, degree of cross-linking, and pH of the surroundings to induce a desired response. Our finds show that thin films of the high-methoxyl pectin polysaccharides can be employed for establishing responsive surfaces with tunable responses suitable for the pharmaceutical and biotechnology industries.

BI-TuP4 Fluorescent DNA Nanosphere Barcdoe System by Rolling Circle Amplification for Tumor Cells Detection, *SW. Han,* ***JongBum Lee,*** University of Seoul, Republic of Korea

Nucleic acid-based nanotechnologies have been developed with the base pairing property and applied to numerous bioengineering fields of study. As a novel engineering material, DNA has been used to fabricate nanostructures from simple 2D structures to complex 3D structures. With this development of DNA nanoarchitecture, enzymatic replication technique has been also attracted as a new strategy for building nucleic acid-based nanostructures. Here, DNA nanosphere (DNANS) is fabricated by rolling circle amplification (RCA) and coated with antibodies for target cells detection. DNANS can be applied as a barcode system which can distinguish the tumor cells by recognizing tumor-specific protein. As a proof of concept, the capability for target detection of DNANS barcode system was demonstrated. This target-specific antibody-coated DNANS suggests a new route for the simple and selective recognition of cancer cells.

BI-TuP7 Vapor-Deposited Porous Polymers for the Fabrication of Giant Lipid Vesicles, ***Nareh Movsesian,*** *M.T. Matthew Tittensor, G. Dianat, N.M. Malmstadt, M. Gupta,* University of Southern California

Giant unilamellar vesicles (GUVs) are cell-sized biomimetic model membranes useful for examining membrane properties and building artificial cells. Hydrogel-assisted rehydration is an emerging technique to form GUVs under physiological conditions at high yields circumventing the shortcomings of traditional techniques such as electroformation and gentle hydration. Herein we present porous negatively charged poly (methacrylic acid-co-ethylene glycol diacrylate) *(xPMAA)*membranes fabricated using an unconventional solvent-free initiated chemical vapor deposition (iCVD) technique and utilized as hydrogel substrates for vesicle formation. Physicochemical properties of the hydrogel substrates such as morphology and crosslinking density are controlled by iCVD process parameters. Zwitterionic and charged lipid mixtures are applied on hydrogel membranes as thin lipid films and subsequently swollen in an aqueous hydration buffer. Here we show that vesicle yield and size are controlled by the morphology, the density, and the charge of the polymer. Our findings show that high hydrogel porosity and reduced electrostatic interactions between the polymer and the lipid are preferred for vesicle formation.

BI-TuP8 Developing a pH Responsive Hydrogel for the Encapsulation of Poly(ethylene glycol) 3350, ***Phuong Anh Nguyen***[1], *B. Matheson, D. Cuylear, H.E. Canavan,* University of New Mexico

Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States. The most reliable screening method of CRC is a colonoscopy which requires a 4-Liter poly(ethylene glycol) electrolyte lavage solution (PEG-ELS) for preparation. Two in five patients are non-compliant to their colonoscopy schedules, with many patients who abstain reporting refusal due to significant discomfort associated with this preparation. Furthermore, there are distinct gender differences in the tolerance of PEG-ELS in male and female populations. We hypothesize the differences in clinic are a result of cytotoxicity effects of PEG. PEG is approved by the FDA for use in medical devices, and has been recognized for many years as a biocompatible/bioinert polymer but few studies have truly studied the short-term and long-term effects of high concentrations of PEG on multiple cell lines. We have developed a pH responsive hydrogel to control the release of PEG – reducing adverse effects associated with colonoscopy preparations. The hydrogels have been characterized using NMR, FTIR, and XPS to ensure chemical identity, rheometry to assess the stiffness/robustness of the hydrogels in varying environments, and SEM and other techniques to confirm uniformity of size. Biocompatibility testing of exposure to increasing PEG concentrations over a period of 3 hours, 6 hours, 12 hours, 24 hours, and 48 hours shows PEG is biocompatible to mammalian cell lines in low concentrations, and in fact, increases their growth and viability. At higher concentrations, however, PEG is cytotoxic to cells. Although it would be difficult to get to toxic levels of PEG in the body in a single dose, current uses of PEG should be re-evaluated due to possible adverse cumulative effects due to the cytotoxicity effects seen *in vitro.* Further directions of this work will evaluate the pH responsiveness of our hydrogel formulation to deliver PEG *in vitro* and *in vivo,* and assessment of the cellular response to the hydrogels using mammalian cells specific to the gastrointestinal system of humans, as well as imaging analysis to envision their penetration.

BI-TuP9 Hemocompatibility of the Endexo™ Fluoro-oligomeric Surface, ***Bill Theilacker,*** Medtronic*; J. Ho, J. Swenor,* Interface Biologics*; M.F. Wolf, J.L. Kalscheue, S. Thinamany,* Medtronic*; S. Ubl,* medtronic

Blood represents one of the most complex biochemical systems in living organisms. As a result, the design of medical device materials is often tailored to reduce platelet adhesion and activation, protein adsorption, and thrombus formation. With roughly 50% or more of Medtronic products contacting vascular tissue, medical device materials that show evidence of biocompatibility with blood (aka 'hemocompatibility') are of high interest. The Endexo™ surface treatment from Interface Biologics is asserted to show improved hemocompatibility through the action of low molecular weight fluoro-oligomeric additives that bloom to the surface and reduce or inhibit blood platelet activation and procoagulant protein formation. Incorporating Endexo technology into materials is straightforward and does not change the mechanical or functional properties of the underlying medical device.

Through a collaborative effort, we examined the IBI fluoro-oligomeric additive added to a common copolyester base polymer used in blood-contact applications and evaluated the platelet and coagulation protein activating capacity. Tritan™ polyester (Eastman) was formulated with several different concentrations of Endexo™ fluoro-oligomeric additive. The surface chemistry of the samples was characterized by Scanning Electron Microscopy (SEM), X-ray photoelectron spectroscopy (XPS), and Time-of-Flight Secondary Ion Mass Spectrometry (TOF-SIMS). An in vitro vacuum test tube model developed at Medtronic was employed to asses

[1] **National Student Award Finalist**

hemocompatibility. Complete blood count analysis, platelet activation (via ELISA immunoassay for platelet plasma protein βTG), and coagulation protein formation (via ELISA immunoassay for the thrombin coagulation protein indicator TAT) was evaluated in the exposed blood.

The Endexo™ surface modifying agent appeared to show improved interaction with blood platelets. Similar favorable performance as assessed by TAT and βTG indicators of hemocompatibility may suggest a viable avenue for incremental improvement in the hemocompatibility of blood contacting devices and device materials. Surface analysis results show the Endexo formulated materials are modified with F-rich chemistry with no change in surface morphology. Medical devices that show improved performance in *in vitro* studies of hemocompatibility have potential to show improved performance in the *in vivo* clinical setting.

BI-TuP10 High Performance Dopamine Sensor Based on Field-Effect Transistor (FET) with H uman Dopamine Receptor Integrated-Multidimensional Conducting Polymer Nanofiber, ***Jinyeong Kim***, *S.J. Park,* Korea Research Institute of Bioscience and Biotechnology (KRIBB), Republic of Korea

Dopamine (DA) has been studied in the field of nervous and cardiovascular systems. Abnormal levels of dopamine is an indicator of neurological disorders, resulting in Alzheimer's and Parkinson's diseases. Therefore, dopamine is a clinically useful diagnostic sign and requires a novel approach with high sensitivity, selectivity and a rapid response. Various sensors have been developed, such as high-performance liquid chromatography (HPLC), mass spectroscopy, and spectrophotometry. However, they are limited by their high cost, low sensitivity, and variable label response.

The field-effect transistor (FET) has been used in the development of diagnosis for several decades. It is gated by changes of charge carrier density in the channel induced by the binding of target molecules, leading to high-performance biosensors. In addition, the FET platform has attracted due to their low cost, easy operation, fast response, label-free operation, parallel sensing as well as high sensitivity.

In this article, we introduced a high performance dopamine sensor based on FET assay. Multidimensional carboxylated poly(3,4-ethylenedioxythiophene) (MCPEDOT) NFs membrane was utilized as the conductive channel of sensor in the FET system. Interestingly, it provided high performance sensing due to enhanced interaction from high surface area and gate-potential modulators. Moreover, hDRD1, G protein-coupled receptors (GPCRs) as the recognition elements, was first expressed in Escherichia coli and modified with the surface of MCPEDOT NFs, leading to high selectivity. As a results, the hDRD1−MCPEDOT NF-based FET exhibits a rapid real-time response (<2 s) with high dopamine selectivity and sensitivity performance (approximately 100 fM).

BI-TuP11 Detection of B-type Natriuretic Peptide in Human Serum Based on Flexible Biosensors and Data Analysis Methodology, ***Xinruo Yi***, *A. Khalaf, R. Gunasekeran, M.H. Yun, M. Akcakaya,* University of Pittsburgh*; Y.Z. Zhang, S. Marc, N. Petroni,* UPMC

The demand on using biosensor during clinical diagnosis to detect the heart failure (HF) becomes increasing at market. B-type natriuretic peptide (BNP), as we know, is a hormone in response to stretching resulting from increased ventricular blood volume. The detection of BNP plays an important role in HF and various diagnosing cardiovascular diseases. Hence, it is important to alarm abnormal BNP levels and to monitor BNP changes appropriate to the diagnostic ranges for an HF event. In particular, BNP levels in human blood range from < 100 ng/l for normal humans to 101 ~ 1000 ng/l for HF patients. Finding BNP level will help the physician make decisions on whether the patient should be admitted to hospital or discharged.

We present a simple, high yield, low-cost and label-free method based on a two-dimensional (2-D) flexible polyaniline (PANI) biosensor along with ultra-sensitivity and specificity for biomarker detection. The 2-D PANI film which was chemically synthesized in a facile and controllable way had high surface-to-volume (S/V) ratios and showed good semiconducting properties. In order to prepare our biosensor, first, we performed surface modification using 1-ethyl-3-(3-dimethyaminopropyl) carbodiimide (EDC), and N-hydroxysuccinimde (NHS) to fix the monoclonal antibodies onto the 2-D PANI film. Second, the 2-D PANI film was treated by using non-target protein like bovine serum albumin (BSA) to block the free sites on the surface and further avoid getting noise signals. After that, our label-free biosensor for the detection of BNP is ready for the test. The detection of BNP in real human blood becomes complicated by the precipitation of red blood cells which will bind with the BNP antibody and block them to get the position of BNP antibody near biosensor surface. Instead, serum samples from patients with heart failure, obtained directly from the University of Pittsburgh Medical Center (UPMC) after separating the red blood cells from the whole blood by centrifugation, were tested.

In this work, we did the mixed blind test with two healthy samples (healthy sample) and two patient samples (with high BNP concentration). In addition, we used various approaches including electrical analysis, standard deviation method, principle component analysis (PCA), quadratic discriminant analysis (QDA) and linear discriminant analysis (LDA) to successfully identify these blind samples, which could be used to determine whether the patient has HF or not.

BI-TuP12 Characterizing Hetero-oligomer of Amyloid-beta and Alpha-synuclein with Bio-AFM, ***Eun Ji Shin***, *J.W. Park,* Pohang University of Science and Technology, Republic of Korea

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are neurodegenerative diseases resulting in progressive degeneration or death of neuron cells. These are associated with the aggregation of peptides, 'amyloid-beta (Aβ)' and 'alpha-synuclein (α-syn)'. It is believed that Aβ and α-syn oligomers are intermediates in the fibril formation, and both oligomers and fibrils are primarily responsible for the pathogenesis. Further study showed that rate of the oligomerization (or aggregation) increases when Aβ and α-syn co-exist, and the co-existence causes the diseases even worse. It is very likely that hetero-oligomers could be formed, but presence and structure of the hetero-oligomers have not been elucidated.

Herein, we employed atomic force spectroscopy with a liquid cell to characterize the hetero-oligomers generated in vitro. For comparison, homo-oligomers were prepared separately. In particular, antibodies recognizing N-terminal of Aβ and N-terminal of α-syn were conjugated at AFM probes, and the specific interaction between the antibodies and surface of the oligomers was followed. After adsorbing the oligomers on mica surface, a tip tethering Aβ antibody was used to get high resolution force maps of a target oligomer, and subsequently another tip tethering α-syn antibody was brought to the same target for the examination. The overlaid map revealed that specific unbinding events with respect to two different antibodies were observed within an oligomer, and it holds for all sizes under investigation. Because homo-oligomers were not observed at all, it can be said that formation of hetero-oligomers is strongly favored. It is intriguing to note that the percentage of recognizing pixels for α-syn increases in comparison with the α-syn homo-oligomer, suggesting a different mode of aggregation for the hetero-oligomerization. We believe that such structural information helps to understand the relationship between the misfolded proteins and the pathogenesis in brain.

BI-TuP13 Creation of de novo Nucleic Acid Binding Disordered Proteins using the Thermally Responsive Behavior of Elastin-like Polypeptides, ***Telmo Diez***, *G.P. Lopez, N.J. Carroll,* University of New Mexico

Intrinsically disordered proteins (IDPs) are dynamic polypeptides used by eukaryotic cells in cell signaling, transcription, and chromatin remodeling functions are frequently employed in packaging and un-packaging of nucleic acids (NAs). Elastin-like polypeptides (ELPs) are biosynthetic biopolymers that have similar structural features to natural IDPs. Importantly, ELPs condense to form coacervates above a lower critical solution temperature (LCST). In this research, we focus on the combination of thermally responsive ELPs with natural nucleic acid binding domains to create promising responsive engineered protein constructs. In this study, we show how an ELP comprising nine positive charges from eight lysine interspersed within the chain is capable of interacting with NAs above its LCST. We characterize the amount of DNA captured by ELP and we use microfluidics to form aqueous microdroplets containing the ELP and fluorescent DNA to visualize DNA capture within ELP coacervate spheres via fluorescence microscopy. We characterize the thermodynamic binodal phase boundary (i.e. in the temperature-concentration dependent phase diagram) of the ELP[Office3] [#_msocom_3] /NA mixture to resolve the ELP volume fraction within the coacervate to predict the optimal temperature to maximize DNA capture. Finally, we combined this ELP with smaller RRM and RGG domains that bind nucleic acids found in natural FUS protein, a common NA binding protein that plays a role in genomic integrity.[Office4] [#_msocom_4] RRM is a 70 amino acid domain found to bind promiscuously to nucleic acids, and RGG is a 100 amino acid long domain rich on arginine and glycine found to be essential in the RRM interactions with nucleic acids. These studies have implications for, and yield insights into, the tailoring of engineered protein constructs that bind nucleic acids with predictable behavior and controlled release that could have many applications in gene therapy and other areas of bionanotechnology.

Author Index

Bold page numbers indicate presenter