Biomaterial Interfaces Division
Room On Demand - Session BI-Contributed On Demand
Biomaterial Interfaces Contributed On Demand Session

BI-Contributed On Demand-1 A Mussel Inspired Catechol Polymer: Is It Sticky?*, **Laura Mears**, J. Appenroth, M. Valtiner,* Vienna University of Technology, Austria

Mussel foot proteins are an inspiring material for adhesives that can work in challenging, saline environments. There has been a focus on the high concentration of L-DOPA within the proteins believed to be the source of strong adhesion. The nature of catechols in general provides for both interactions of the aromatic group and the hydroxyl groups for hydrogen bonding with surfaces. The carboxylic acid groups on amino acids like L-DOPA make these molecules particularly sensitive to the pH of the environment, which the mussel appears to exploit to regulate their adhesive interaction. The catechols are also active electrochemically, expanding the methods that can be used to control their interactions.

Here, we will present work on a catechol based polymer. The adhesive properties have been tested using the surface forces apparatus, a force sensitive technique, which uses multiple beam interferometry to track the confined thickness of the material. The polymer was confined between various surfaces in order understand its adhesion, also in a range of electrolyte environments (salt concentration, pH etc.) to mimic real world conditions. The results will be put into the context with the performance of biocompatible adhesives, with a particular view to medical and biomedical engineering applications that present these challenging saline environments in the real world.

BI-Contributed On Demand-4 Fast, Accurate Blood Analysis Algorithm for X-Ray Fluorescence on Homogeneous Thin Solid Films of Microliter-sized Whole Blood Droplets*, T. Balasooriya, W. Peng, N. Suresh, A. Gurijala, S. Khanna, A. Chow, M. Sahal,* Arizona State University*; S. Ram,* Yale University*; S. Narayan,* University of Pennsylvania*; Y. Pershad,* Stanford University*; E. Culbertson,* Ronald Reagan UCLA Medical Center*; R. Culbertson, N. Herbots,* Arizona State University*; V. Desai, **Aarush Thinakaran**,* MicroDrop Diagnostics, LLC

Whole blood diagnostics use High-Performance Liquid Chromatography (HPLC), requiring hours to days for analysis of 2-10 mL blood volumes. Small volume, fast blood tests, e.g. glucose monitors, yield results in seconds but are limited to a single blood component.

Fast, accurate whole blood tests are necessary for medical practices, ER, OR, ICU/NICU, etc. to monitor patient status for electrolytes, and many other conditions.

This work tests a radical new approach to not only reduce blood volumes drawn but also to yield faster and highly accurate whole blood diagnostics for several elements. Super/hyper-hydrophilic coatings HemaDrop™ can rapidly solidify µL drops into planar Homogenous Thin Solid Films (HTSFs)[1,2]in minutes. HTSFs can be formed by applying blood drops on a strip coated with HemaDrop with metered calibration and analyzed by XRF or other solid state methods. XRF data collection takes minutes compared to HPLC, counting X-Rays at a high data rate instead of hours-long microfluidics of blood in porous ceramic columns. XRF analysis software is not accurate enough for medical standards, which requires relative error <10%. XRF analysis software typically uses an all peaks fitting algorithm while searching fits with 117 of the 118 elements of theperiodic table.

Most XRF software fits the whole spectra with polynomials, yielding false positives for detection, and significant error (> 50%) due to background distortion around small signals from trace elements, which are of key importance in blood diagnostics. Finally, XRF emission lines, being neither Gaussians nor Lorentzians, are ill-suited for curve fitting. To improve speed, accuracy and reliability of XRF on blood HTSFs, a new algorithm, "Fast, Accurate Blood Analysis by XRF" (FABAX), is coded as an app, "Fast, Hand-Held Analysis by XRF"(FHAX) . FABAX computes a Riemann sum of counts across the full signal width for each tagged element and subtracts a trapezoidal sum computed from background noise levels left and right of the signal, instead of a potentially poor or error-laden fit.

FABAX interfaces with handheld XRF analyzers or desktop XRF units via smartphone, to generate fast, accurate, reliable blood diagnostics. Small footprint, handheld XRF units combined with a smartphone are suited to space limitations typical of medical settings. Crammed OR's, crowded ER patient triage stations, or refugee camps can use it quickly and accurately to determine blood electrolytes and metal in mg/dL, using the built-in triple calibration, from one 10 µL blood drop.

[1]N. Herbots, et al. (2019). MRS Advances. 1-25. 10.1557/adv.2019.398.

[2]N. Herbots, et al, US & Intl. Pat. Pend. (2016-20)

BI-Contributed On Demand-10 Surface Analysis of Alum Adjuvant for Vaccine Development and Delivery*, G. Guerrini,* University of Siena LAMMB (Biotechnology and Molecular Microbiology Lab), Italy*; J. Banuls Ciscar,* European Commission, Joint Research Centre, Italy*; F. Fumagalli,* European Commission, Joint Research Centre, Italy*; J. Ponti, L. Calzolai,* European Commission, Joint Research Centre, Italy*; D. Medaglini,* University of Siena, LAMMB (Biotechnology and Molecular Microbiology Laboratory), Italy*; **Giacomo Ceccone**,* European Commission, Joint Research Centre, Italy

The worldwide pandemic crisis caused by the COVID 19 virus strongly impact almost all human activities. In absence of a specific pharmaceutical products and vaccine, virologists and medical experts agree that the only way to fight and reduce the risk of infection is to maintain the physical distance while tracing the positives cases and impose quarantine in places where the infecting parameter R_0increases above 1. However, this type of measures impacts dramatically the economic situation and the research to find a vaccine has become extremely urgent.

The development of vaccine is not an easy task especially when pure antigens are employed for reducing vaccine immunogenicity. This requires the use of adjuvants to optimize vaccine effects whilst maintaining its safety.

Adjuvants based on Aluminium salts are amongst the most used because of its high safety profile, whilst its mechanisms of actions still remain unclear.[1,2,3]

In this work we present a detailed surface analysis by means of X-ray Photoemission Spectroscopy (XPS and Time of Flight Secondary Ion Mass Spectrometry (ToF-SIMS) of a polymeric platform to be used for vaccine development and delivery. This platform consisted in Al containing polymer substrate prepared in two different formulations, namely micro-Alum and nano-Alum. The effectiveness of the Alum-platform was tested against ovalbumin protein.

Both XPS and ToF-SIMS were able to deliver information about the interaction of the ovalbumin and the substrate. In particular, results indicate that, independently of the substrate formulation (micro or nano), a ratio of Alum/OVA of 3:1 was required to reach saturation, confirmed on sample superrnatant by SDS-PAGE gel, where the 3:1 ratio is the first in which OVA protein could be detected.

Moreover, Circular dichroism analysis on Al:OVA complexes shown a conformational change of the protein secondary structure upon adjuvant binding

References

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BI-Contributed On Demand-13 Design for X-ray Fluorescence, X-ray Photoelectron Spectroscopy, and Ion Beam Analysis of Blood Drops solidified as Homogeneous Thin Films for Fast, Small Volume, Accurate Diagnostics*, N. Suresh, A. Gurijala, S. Khanna, A. Chow, W. Peng, T. Balasooriya,* MicroDrop Diagnostics, LLC*; M. Sahal,* Arizona State University*; L. Puglisi,* SiO2 Innovates, LLC*; E. Culbertson,* MicroDrop Diagnostics, LLC*; N. Herbots,* Arizona State University*; A. Thinakaran, **Ashwin Suresh**,* MicroDrop Diagnostics, LLC

Analysis in the liquid phase for blood diagnostics requires 2-10 mL volumes to reach the medical accuracy standard, relative errors < 10%.

Assessing/monitoring patients requires fast diagnostics for blood such as electrolyte (Na, Mg, K, Cl, Fe), O2 levels, total proteins, CO2, metals (e.g. Pb), and radio-nuclides (e.g, Co^{60}). Tests may need repeating hourly or daily in ICUs. But drawing mLs of blood results in Hospital-Acquired Anemia for

premature infants in NICU, patients in ICU and the chronically ill. Small blood volume diagnostics (SBVD) is key to improve care.

A rapid SBVD thin film device, InnovaStrip™[1-4], has been designed to process µL-sized blood drops into uniform, uncoagulated, thin solid films for analysis the solid state rather than liquid, via hyper-hydrophilic coatings, called 'HemaDrop™ WB'[1-4]. Super-hydrophilic coatings 'called HemaDrop™ P'[1-5] can also separate plasma and serum for more detailed diagnostics.

HemaDrop™ coated InnovaStrip devices are designed to solidify µL-blood drops into Homogeneous Thin Solid Films (HTSFs) rapidly and consistently by absorbing in less than 5 minutes the aqueous component of whole blood in a temperature range of 18-25°C and relative humidity ranging from 25-50%.

Ion Beam Analysis (IBA) and X-Ray Fluorescence (XRF) of whole blood and plasma HTSF can yield accurate Na, K, Mg, Ca, Cl and Fe composition with relative errors < 10% in less than 20 min from blood drop collection to diagnosis[5].

InnovaStrip™ consists of Al-clad substrates coated with HemaDrop™ with wells for drop collection into HTSF, and calibrated solutions HTSF for conversion of a/o into mg/dL.

Based on IBA, XRF and XPS compositions from different depths, the thickness of blood HTSF, HemaDrop coatings and metal cladding are optimized for reproducibility and accuracy to medical standards < 10%.

HTSF uniformity is measured via optical microscopy and XPS. XPS probes HTSF composition to within an escape depth of 5 nm. XRF is fast, compact and portable, and conducted in air, ideal for SVBD in the ER, OR, MD office, field hospital or crisis area.

IBA and XRF reach < 2-3% relative error, and are reproducible to ≤10% using InnovaStrip™ µL-sized whole blood drops and blood plasma can be uniformly solidified into thin solid films and analyzed in the solid state in air and in vacuo for composition. The advantages of SVBD in the solid state include speed, accuracy, ease of storage, reduced risk of contamination, while maintaining accuracy.

[1-4]N. Herbots, N. Suresh et al. US & Intl. Pat. pend (2016-20).

[5]N. Herbots, N. Suresh, et al. (2019).MRS Adv.. 1-25. 10.1557/adv.2019.398.

BI-Contributed On Demand-16 Mussel Foot Adhesion: A Fundamental Perspective on Factors Governing Strong Underwater Adhesion*, J. Appenroth, L. Mears, P. Bilotto, A. Imre, H. Cheng,* ***Markus Valtiner,*** Vienna University of Technology, Austria

Tuning interfacial electrochemistry is central to the principle of the strong underwater adhesive of mussels. In this contribution we critically discuss recent progress in the field, and we discuss how interfacial electrochemistry can vary interfacial forces by a concerted tuning of surface charging, hydration forces and tuning of the interfacial ion concentration.

Specifically, we will show electrochemical signatures of a large number of different catechol functionalities and show how catechol chemistry can be utilized for cross-linking musselfoot mimicking polymers. Further, we will show how the electrochemical oxidation of catechols can steer the interfacial ion concentrations by a variation of the pH value, and hence surface charging. We can correlate this with interfacial interaction forces measured by AFM and the surface forces apparatus.

In this view we will discuss paths into further understanding and utilizing redox-proteins and derived polymers for enhancing underwater adhesion in a complex salt environment.

BI-Contributed On Demand-19 Hand-Held X-ray Fluorescence (XRF) Analysis for Fast, Accurate, Comprehensive Small Volume Blood Diagnostics using Blood Drops Rapidly Solidified into Homogeneous Thin Solid Films*,* ***Thilina Balasooriya****, W. Peng, N. Suresh, A. Gurijala, M. Sahal,* Arizona State University*; S. Narayan,* University of Pennsylvania*; Y. Pershad,* Stanford University*; E. Culbertson,* UCLA Medical Center*; R. Culbertson, N. Herbots,* Arizona State University

Over 4 billion Blood Diagnostics (BD) tests are performed annually worldwide. Current diagnostics uses High-Performance Liquid Chromatography (HPLC). HPLC requires hours to days for results and uses 2-10 mL of blood. Drawing tens of mL of blood for multiple tests leads to hospital-acquired anemia at a rate of 74% in the chronically ill. Faster and more comprehensive whole blood tests are needed in ERs, ORs, and ICUs to diagnose incoming patients immediately for dehydration, anemia, etc.

This work investigates a new approach via a new hand-held device design - called InnovaStrip™ - to greatly reduce blood volumes for BD. InnovaStrip™ yields *simultaneously* more accurate and *comprehensive* BD for electrolytes (Na, Mg, Ca, Cl, K, Ca), metals (Fe, Cu, Se, I), toxins (As, Cd, Hg, Pb), and radio-nuclides (^{87}Sr, ^{131}I, ^{235}U, ^{239} Pu) and aims to diagnose presenting conditions at intake with one *single initial* Small Volume Blood Diagnostics (SVBD) test, instead of several, within minutes.

InnovaStrip™ includes three components: (1) low-cost blood drop collection strips, (2) a hand-held X-Ray Fluorescence (XRF) analyzer and (3) an innovative SVBD algorithm, '*Fast Accurate Blood Analysis*, or FABA™, deployed via an app, '*Fast Hand-held Analysis for XRF*', or FHAX™. The blood collection strips, made of off-the-shelf components, are coated with a new Hyper-Hydrophilic coating, 'HH HemaDrop™'. These coatings rapidly planarize and solidify µLs of blood into Homogenous Thin Solid Films (HTSFs) in minutes. The collection strips include three HSTFs of pre-solidified calibration solutions for rapid conversion of XRF relative concentrations into medical units of mg/dL for BD. Besides XRF, other solid-state analyses such as Ion Beam Analysis via compact ion sources like ^{241}Am can be incorporated in the analyzer.

The medical 'gold' standard for SVBD - such as blood glucose monitors - requires relative errors ≤ +/-10%, in other words, less than 10% false negatives or positives. Current XRF analysis commercial software is not accurate for trace elements such as blood electrolytes. They have poor background fitting, yield false positives/negatives, and yield large errors (> 50%) for trace elements quantitation. Instead, FABA™ computes fast, direct Riemann sums of counts for raw signals of selected elements *only* and subtracts the *actual* background, and is optimized for each specific element, instead of using an all-encompassing curve fit. FABA then interfaces with handheld XRF analyzers via the FABA App to generate accurate BD results. ORs, ERs, refugee camps, and other medical settings can use InnovaStrip™ to quickly and accurately diagnose initial patient status for blood electrolytes and iron – thus hydration and anemia – from one single 10 µL blood drop.

BI-Contributed On Demand-22 GCIB-ToF-SIMS Imaging for Lipid Imaging in Planaria*,* ***Lara Gamble****, D. Graham,* University of Washington, Seattle*; C. Anderton, D. Velickovic,* Pacific Northwest National Laboratory*; T. Angerer,* University of Washington, Seattle

Lipids not only make up the structure of cells walls, they have also been recognized as key players in cell signaling and disease. Information on their location and their changing distribution under different conditions can result in a better understanding of individual lipid species contributions to changes in phenotype. In order to map the lipidomic landscape in planarian worms, longitudinal sections of planaria were analyzed with imaging time-of-flight secondary ion mass spectrometry (ToF-SIMS). The data contained in the resulting images were analyzed with multivariate analysis (MVA) in order to identify chemically unique areas in scores images as well as the mass spectrometry (MS) signals (peaks) associated with those areas in loading plots. By comparing light microscopy images of the sections and MS/MVA scores-images, we were able to identify several organ structures in the sections: brain (CNS), intestines, pharynges (different to other planarian species, *Phagocata gracilis* has multiple small pharynges instead of one central pharynx), testes, and several parts of the male reproductive system. Subsequently, we were able to identify unique lipid species present in each organ system. The lipid assignments, respective fragment identities, and their locations from ToF-SIMS analysis were confirmed via LC-MS/MS on lipid extracts and ultra-high mass resolution MALDI-MS imaging. It was found that for many lipid species, the fragmentation patterns within ToF-SIMS spectra match those seen in MS/MS. These data show that the semi-destructive nature of ToF-SIMS can be utilized to enable more confident molecular annotation by providing intact molecular species and their fragments simultaneously.

BI-Contributed On Demand-25 Studying the Aggregation Effect of Microbes on Mineral Oxide and Synthetic Soil Using ToF–SIMS*,* ***Yuchen Zhang****, X. Yu, J. Son,* Pacific Northwest National Laboratory*; Q. Huang, W. Chen,* Huazhong Agricultural University, China

The colonization of bacteria and the subsequent formation of biofilms on mineral surfaces play a key role in soil aggregation and organic processing. Therefore, characterization and understanding of the biofilm interactions with soil components are important in deepening our knowledge in the

biosphere and rhizosphere. In this work, *Shewanella* MR-1 was used as the model bacteria biofilm due to its known traits in soil chemistry and microbiology. A mixture of silica, alumina, and iron oxide was used as the model soil system. A microfluidic chamber was developed to culture biofilms using soft lithography and polydimethylsiloxane. The infrastructure of the microchamber was largely based on the system for analysis at the liquid vacuum interface, or SALVI. Specifically, a clean silicon (Si) wafer was included as the main substrate for biofilm attachment in the microfluidic chamber for fast prototyping and bacteria screening. When the mature biofilm formed in the micro channel, the soil component was mixed to the growth media (TSB without dextrose) and used as nutrients to support the biofilm's growth. The effluent was collected periodically after 0, 4, 8, 12, 16, 24 and 48 hours (hr.) to follow the evolution of the mineral and microbial interactions. Samples were desalinized and deposited onto the Si wafer prior to using time-of-flight secondary ion mass spectrometry (ToF-SIMS) for further analysis. ToF-SIMS is a sensitive surface technique and it offers submicrometer spatial mapping of molecular species of importance in metabolic processes compared to other mass spectrometry techniques. Our initial results show that a significant transition point of compositional changes occurs between 4 and 8 hr. In addition, new peaks such as fatty acids and lipid fragments appear in the biofilms and the mineral oxide mixture compared with controls of bacteria biofilms and planktonic cells, respectively. Interestingly, clusters of organic fragment peaks appear frequently in the high mass range, i.e., $m/z > 500$, after interacting the biofilm and minerals, suggesting the formation of new extracellular polymeric substance (EPS). We postulate that these high mass peaks are lipids, proteins or polysaccharide components. Peak identification is in progress. Additionally, the formation of these new substances may be related to biomineralization process as a result of the interaction of the biofilm and soil mineral components. Integration of the microfluidics and ToF-SIMS provides a new approach to study the interaction between biofilm and soil simulant, taking advantage of the ToF-SIMS high resolution mass spectral analysis and the ability of following the living bacteria behavior inherent of microfluidics with sensitivity and selectivity. Our new findings provide new insights into the role of biofilms in soil aggregation that occurs at the microbe-mineral interface.

BI-Contributed On Demand-28 Toward Custom Degradation of Silk-Based Biomaterials: Tailoring the Surface Chemistry of Silk Fibroin via Plasma-Based Strategies*, **Morgan Hawker**,* California State University, Fresno

Naturally-derived, degradable polymers offer tremendous potential to the field of biomaterials. Indeed, the presence of degradable devices in pre-clinical/clinical trials and on the market has expanded considerably over the past decade, spanning a variety of applications from stents to suturing. Degradable devices are designed to perform their intended function for a set time, after which they break down into harmless byproducts. These byproducts are then absorbed by the body, mitigating the need for secondary removal surgery. Notably, degradable polymeric devices are typically designed for a specific application and, thus, exhibit fixed degradation kinetics. Furthermore, prior attempts to control naturally-derived polymer degradation used methods that altered the polymer's bulk mechanical properties (e.g., physical cross-linking), which can hinder the device function due to mechanical mismatch between the device and its surrounding biological environment. There is a critical need to develop a fabrication technology that results in polymeric devices with programmable degradation rates - without altering their bulk mechanical properties - for deployment over a range of intended applications.

This talk will highlight recent efforts to develop a radio-frequency plasma copolymerization approach with the potential to modulate the degradation of naturally-derived polymer materials. In this work, silk fibroin (SF) was used as a model polymer system. Naturally-derived polymers like SF are known to degrade via surface-mediated enzymatic hydrolysis, so surface properties are paramount in controlling polymer construct/enzyme interactions. As such, the objective of this work was to prepare SF films with variable surface properties. SF films were first dropcasted using established methods, and films were subjected to plasma treatment to customize their surface chemistries/wettabilities. Plasma feedgas composition was tuned using two unique precursors: 100% acrylic acid (to produce thin films with polar functional groups on the SF surface), 100% pentane (to produce thin films with non-polar functional groups on the SF surface), and mixed precursor conditions (to create SF surfaces with intermediate wettabilities). Plasma parameters were optimized for each individual precursor, as well as for copolymerization. Contact angle goniometry was utilized to evaluate the wettability of all plasma-modified and control SF films. Findings demonstrated that surface wettability depends not only on feedgas composition, but also on applied plasma power. Collectively, this plasma copolymerization strategy is a promising method to customize naturally-derived polymer degradation.

BI-Contributed On Demand-31 Using Transferrable Graphene-Based Membranes for Spatial and Temporal Control of Cell Cultures*, **Keith Whitener**, D. Haridas, W. Lee,* US Naval Research Laboratory*; S. Yoseph,* Howard University*; C. So, J. Robinson,* US Naval Research Laboratory

Exerting spatial and temporal control over cell populations is a powerful capability which offers the promise of manipulating and interrogating living systems for use in advanced biological engineering such as bottom-up tissue engineering. To this end, we have developed techniques for reversibly transferring graphene-based thin film materials in a biocompatible way. Using single-layer hydrogenated graphene as well as partially reduced graphene oxide as mechanical support layers, we can deposit spatially patterned materials such as metallic electrical contacts, molecules with biochemical activity, and polymers, and transfer them to arbitrary surfaces using simple water delamination. We found that incorporating a thin gelatin layer onto the film mitigates cytotoxicity and cytolysis associated with graphene-based materials and enables transfer of materials-patterned thin films to mesenchymal stem cells without sacrificing viability. In addition, the low melting point of gelatin enables facile removal of these thin films. Simple and fast fabrication, deposition, and removal of patterned materials on cells allows for spatial as well as temporal control over external stimulus delivery to those cells. We also found that the partially reduced graphene oxide thin films are impermeable to most molecules, and we are exploiting this property along with transferrable photolithography to construct cell masks for spatially patterned biomolecule delivery and cell cocultures.

BI-Contributed On Demand-34 Polymeric Thin Films Designed to Direct *Pseudomonas aeruginosa* Iron Scavenging, Biofilm Growth, and Pathogenicity*, **Trevor Donadt**, Y. Wu, J. Lang, S. Li, R. Yang,* Cornell University

Ample biointerfacial materials research has focused on biocidal or antifouling outcomes, yet some microbes can be utilized for advantageous qualities when allowed to colonize a surface under appropriate conditions. A critical bottleneck has formed in the design and deployment of functional yet safe microbes due to a small selection of materials that have been used to both support growth and program microbial function without genetic manipulation. Our approach to programming microbial function involves the use of initiated chemical vapor deposition (iCVD) to design polymer thin film coatings with properties that control the behavior of exposed bacteria. The present work examines iCVD-generated polymer thin films that behave cooperatively in iron scavenging by *Pseudomonas aeruginosa* and change the expression of siderophores and biofilm formation by cells cultured on these films, resulting in reduced virulence. The material characterized herein sets the stage for future work on tunable biointerfaces that influence microbial activity exclusively through surface phenomena without reliance on soluble elements.

BI-Contributed On Demand-37 Hydrogen Peroxide Detection Using Modified Electrochemical Electrodes for the Intestinal Environment*, **Santiago Botasini**, D. Jesner, J. Stine, R. Ghodssi,* University of Maryland

Electrochemical hydrogen peroxide (H_2O_2) sensors have been extensively researched using enzymatic and non-enzymatic approaches. The last one is most promising as they not suffer from enzyme denaturalization. However, their application in real environments is limited due to matrix interference. In particular, H_2O_2 and other reactive oxygen species (ROS) have been linked to bacterial recognition responses and autophagy within the human gastrointestinal tract (GIT), and are related to inflammasome activation. In the gut, high concentrations have also been correlated with the presence of epithelium inflammation. This could be due to circumstantial internal illness but could also be indicative of a degradation of mucosal permeability, which has been hypothesized as the primary cause of several chronic autoimmune pathologies, such as Crohn's disease, type-I diabetes, and food allergies.

This work presents the modification and characterization of an electrochemical H_2O_2 sensor to measure physiological concentrations in the human gut. Different electrochemical modifications have been explored, including the addition of Nafion®, to mitigate the fouling effect, and carbon nanotubes to improve the electron transfer. Copper, ceria, platinum, and silver metals, are compared as catalyzers for the H_2O_2 reduction. Sensor performance was evaluated with cyclic voltammetry and amperometric measurements using a benchtop potentiostat, as well as a portable potentiostat, AD5941 front-end development kit (Analog Devices), to

validate the feasibility for miniaturization into a potential smart capsule device. The results showed that, although copper coverings provide better sensitivity, platinum electrodes with a Nafion® coating was observed the better approach for sensing H_2O_2, in terms of simplicity, reproducibility and reliability for prolonged experiments. Changes in the pH produce negligible changes on the sensor performance. Additionally, a limit of detection of 25 µmol L^{-1} and a mean recovery of ca. 90% was observed when on the sensor was immersed in artificial intestinal fluid.

BI-Contributed On Demand-40 Electrochemical Activation of CNT-coated Carbon Fiber Microelectrodes for Serotonin Sensing*, **Jinjing Han**, S. Botasini, A. Chapin, R. Ghodssi,* University of Maryland, College Park

Serotonin (5-hydroxytryptamine, 5-HT) is a key neurotransmitter in the brain, contributing to the pathophysiology of mental health disorders, such as anxiety and depression. 5-HT measurement *in vivo* requires real-time measurement techniques with high sensitivity because of its low concentration. For decades, carbon fiber (CF) based electrochemical sensors have been the predominant detection method for 5-HT in biological samples due to their fast response time, wide linear response, and low cost. Therefore, further improvements towards high-sensitivity carbon fiber microelectrode (CFMEs) for electrochemical 5-HT detection are required for *in vivo* monitoring.

Here, we combine two surface modification methods to the CFME: 1) coating with Nafion/carbon nanotubes (CNTs) and 2) applying an electrochemical pretreatment. First, CNTs dispersed by Nafion in isopropanol (IPA) were dip-coated onto a bare CF (Nafion-CNT@CF). Then, electrochemical pretreatment was performed by immersing the coated CFME in phosphate-buffered saline (PBS) and applying two triangular waveforms sequentially: an oxidation waveform (0 V to +2.5 V) followed by a reduction waveform (0 V to -1.5 V) (Nafion-CNT/EC@CFs). The CNT coating dramatically increases the electrode specific area, which is further increased by electrochemical pretreatment via an electrochemical etching effect. Both surface coating and electrochemical pretreatment increase surface area and surface roughness to form additional binding sites, resulting in higher sensitivity to 5-HT.

Initially, the electrode performance was characterized in 10 µM of 5-HT in PBS using cyclic voltammetry (CV) at 1 V/s scan rate. A well-defined oxidation peak was observed at 0.45 V (Fig. S1) with oxidation peak currents (Ipa) of 0.32 µA and 1.25 µA for Nafion-CNT@CF and Nafion-CNT/EC@CF, respectively. No oxidation peak was detected for the bare CF electrode. The Nafion-CNT/EC@CF showed a **3.9-fold increase** in current response to 5-HT compared to the Nafion-CNT@CF. Further characterization of the Nafion-CNT/EC@CF was conducted at various concentrations between 0.1 – 1 µM (Fig. S2). The Nafion-CNT/EC@CF exhibited a linear range (up to 1 µM, R^2=0.9744) with a sensitivity, determined using the slope of the linear region, of 0.19 µA/µM. The limit of detection (LOD) is calculated to be 370 nM. The combination of an additive surface coating and subtractive electrochemical pretreatment synergically increased the surface area for 5–HT binding events. The surface modified CFMEs provide a sensitive and label-free method to directly detect 5-HT electrochemically in real time, enabling the potential for sub-micromolar detection of 5-HT in biological samples.

BI-Contributed On Demand-43 Grafting-to of Biomimetic Bottlebrush Polymer*, L. Navarro, D. French, T. Shah, **Stefan Zauscher**,* Duke University

Specifically-adsorbed bottlebrush coatings are found in nature as brush-like glycoproteins that decorate biointerfaces and provide anti-fouling, lubrication, or wear-protection. While protein-bottlebrush hybrids are promising proteoglycan mimics, many challenges still exist to robustly produce such polymers. We briefly report on a novel modular approach we have developed to synthesize protein-brush hybrids by copper-catalyzed azide-alkyne cycloaddition. Furthermore, the use of such proteoglycan mimics is still limited because of the current lack of understanding of their adsorption behavior and surface conformation. Here we thus describe the adsorption behavior of PEG-based, biotinylated bottlebrushes with different backbone and bristle lengths to streptavidin model surfaces in PBS. We used QCM, LSPR, and AFM, to elucidate how bottlebrush dimensions impact their adsorption kinetics, surface conformation, mechanical properties, and anti-fouling properties. We found that the adsorption behavior is characterized by three kinetic regimes: (I) a transport-limited regime, (II) a pause, and (III) a penetration-limited regime. We also found that bristle length more dramatically affects brush properties than backbone length. Specifically, larger bottlebrush dimensions lead to reduced molar adsorption, retarded kinetics, weaker anti-fouling, and softer brush coatings. WE believe that our findings aid the rational design of biomimetic bottlebrush coatings for a broad range of biomedical applications.

BI-Contributed On Demand-46 Design and Synthesis of Multifunctional Nucleotide Analogue Delivery Vehicles to Combat Cancer*, Y. Yang, S. Deshpande, A. Chilkoti, **Stefan Zauscher**,* Duke University

The use of DNA as a polymeric building material transcends its function in biology and is exciting in bionanotechnology for applications ranging from biosensing, to diagnostics, and to targeted drug delivery. Our research is motivated by the complexity and low yield of syntheses of current aptamer-targeted nanoparticle drug carriers that are typically carried out by multi-step chemical conjugation of aptamer and drug to a carrier. Here, we demonstrate a highly efficient in situ enzymatic polymerization strategy that “grows” a polynucleotide drug segment and a self-assembly segment from an aptamer “initiator.” Specifically, we exploit the ability of a template-independent DNA polymerase —terminal deoxynucleotidyl transferase (TdT)— to catalyze the polymerization of 2’-deoxyribonucleoside 5’-triphosphates (dNTP, monomer) from the 3’-hydroxyl group of an oligodeoxyribonucleotide (initiator). We found that the reaction kinetics follows a “living” chain-growth polycondensation mechanism and that like in “living” polymerizations, the molecular weight of the final product is determined by the starting molar ratio of monomer to initiator. Our synthesis approach can incorporate a wide range of unnatural dNTPs into the growing chain, such as, hydrophobic fluorescent dNTP and 5-fluoro-2'-deoxyuridine (FdUTP), a nucleotide analog of the anticancer drug 5-fluorouracil (5-FU). This “one-pot” enzymatic reaction approach offers a new, dramatically simplified and innovative route for the synthesis of nuclease-resistant, multifunctional block- copolymers which can self-assemble into size-optimized micellar structures for drug delivery applications.

BI-Contributed On Demand-52 Structure Determination of Surface Bound Proteins: Are We There Yet?*, **David Castner**,* University of Washington

Controlling how proteins are immobilized is essential for optimizing the performance of *in vitro* protein-binding devices. Comprehensive analysis of surface immobilized proteins provides the level of detail about the immobilization process and the structure of the immobilized biomolecules needed to develop and optimize these devices. In particular, surface analysis methods such as x-ray photoelectron spectroscopy (XPS), time-of-flight secondary ion mass spectrometry (ToF-SIMS), sum frequency generation (SFG) vibrational spectroscopy, surface plasmon resonance (SPR) biosensing and quartz crystal microbalance with dissipation (QCM-D), when combined with Monte Carlo (MC) and molecular dynamics (MD) computation methods, provide a powerful method for obtaining information about the attachment, type, orientation, conformation and spatial distribution of surface immobilized proteins. Although much progress has been made in characterizing surface bound proteins over the past 40 years, the ability to provide atomic level structural information is still lacking, especially for large proteins. In recent years the combination of new computational and experimental methods has been used to obtained detailed characterization of model peptides and small proteins. In particular, Protein G B1, an immunoglobulin (IgG) antibody-binding domain of Protein G, has proven to be an excellent small protein for developing and expanding our ability to characterize the structure of surface bound proteins. Using protein engineering methods to site selectively introduce cysteine into the Protein G B1 structure provides a method for controlling its orientation on well-defined surfaces. Multi-technique characterization coupled with biological reactivity measurements were used to show the effect of Protein G B1 orientation on IgG antibody binding. The challenge now is to extend this approach to larger and more complex proteins. Another challenge is developing computation methods that can predict the structure of surface bound proteins. Also, it is important to continue to advance our ability to characterize protein structure under biologically relevant conditions such the 3D structures found in aqueous based environments. Sum-frequency scattering (SFS) spectroscopy is one method well suited for these measurements.

BI-Contributed On Demand-55 Chemical Changes On, and Through, The Bacterial Envelope in *E. coli* Mutants Exhibiting Impaired Plasmid Transfer Identified Using Time-of-Flight Secondary Ion Mass Spectrometry*, Kelly Dimovska Nilsson,* University of Gothenburg, Sweden*; M. Palm,* University of Gothenburg, Sweden, Centre for Antibiotic Resistance Research, University of Gothenburg, Sweden*; J. Hood, J. Sheriff,* School of Engineering, Newcastle University, UK*; A. Farewell,* Department of Chemistry and Molecular Biology, University of Gothenburg, Sweden, Centre for Antibiotic Resistance Research, University of Gothenburg, Sweden*; J. Fletcher,* University of Gothenburg, Sweden

Antibiotic resistance causes 25 000 deaths every year. The rate of the spread and the threat that antibiotic resistance pose on a global scale makes this a field of great interest for research. Transfer of plasmids (mobile DNA) between bacterial cells through conjugation is one of the major contributors to the spread of antibiotic resistance. A larger understanding of the mechanisms behind this process and how to possibly hinder it could help to quench the development observed around the world. In this study, the changes in lipid composition in the cell membrane of three mutated E. coli strains were analysed using a J105 - *3D Chemical Imager*.

Using a J105 (Ionoptika Ltd, UK), an unconventional, time-of-flight secondary ion mass spectrometry (ToF-SIMS) instrument coupled to a 40 keV CO_2 gas cluster ion beam (GCIB) allowed analysis of the outer membrane of mutated *E. coli* previously identified as having impaired plasmid transfer capability, related to the spread of antibiotic resistance, and how the lipid composition changed in the membrane due to the mutations. The sub-set of mutants were selected as the mutations were expected to result in changes in the bacterial envelope composition, through the deletion of genes encoding for FabF, DapF and Lpp, where the surface sensitivity of ToF-SIMS can be most useful. Analysis of arrays of spotted bacteria allowed changes in the lipid composition of the bacteria to be elucidated using multivariate analysis and confirmed through imaging of individual ion signals.

Significant changes in chemical composition were observed, including a surprising loss of cyclopropanated fatty acids in the *fabF* mutant where FabF is associated with the elongation of FA(16:1) to FA(18:1) and not cyclopropane formation. The ability of the GCIB to generate increased higher mass signals from biological samples allowed intact lipid A (*m/z* 1796) to be detected on the bacteriaand, despite a 40 keV impact energy, depth profiled through the bacterial envelope along with other high mass ions including *m/z* 2428, attributed to ECA_{CYC}, that was only observed below the surface of the bacteria and was notably absent in the depth profile of the Lpp mutant.

The analysis provides new insights into the action of the specific pathways targeted in this study and paves the way for whole new avenues for the characterization of intact molecules within the bacterial envelope.

BI-Contributed On Demand-58 Novel Bio-Inspired Urinary Catheter Reduces Protein Deposition and Incidence of Catheter-Associated Urinary Tract Infections*, Marissa Andersen,* University of Notre Dame*; J. Fong,* University of Maine*; A. LaBella, A. Molesan,* University of Notre Dame*; C. Howell ,* University of Maine*; A. Flores-Mireles,* University of Notre Dame

Urinary catheterization is a common procedure in healthcare facilities and catheter placement predisposes patients to the development of catheter-associated urinary tract infections (CAUTI), the most common nosocomial infection. Their treatment has become a high priority due to the rise of uropathogens' antibiotic resistance. Efforts have focused on development of vaccines, immunotherapies, and antimicrobial coated-catheter materials; the latter having shown promise *in vitro*, however in clinical trials, they are unsuccessful or yield mixed results. In humans and mice, we have shown that in response to urinary catheterization fibrinogen (Fg), a host protein, is released, deposited and accumulated on catheters. This allows Fg to serve as a scaffold for microbial colonization leading to an increase in initial pathogen binding to catheter surfaces as shown in previous studies. Deposited Fg may also hinder the release or availability of antimicrobials on coated-catheters and may also prevent direct contact with pathogens. This phenomenon could partly explain why antimicrobial-coated catheters show antibacterial effects *in vitro* but not *in vivo*. Therefore, we hypothesized that reducing Fg deposition will prevent uropathogen colonization of the catheter, a critical step for establishing infection and thus reducing the establishment of CAUTI. Our approach utilized infusing silicone catheters with liquid silicone to create a slippery surface which prevents protein deposition. With this material we found a significant reduction in Fg and uropathogen colonization on these modified catheters *in vitro.* Additionally, this modification showed a decrease not only in 91.2% of deposited host proteins on the catheter but also the burden of a group of six uropathogens during CAUTI, which correlated with the reduction of Fg deposition *in vivo.* Together, our findings suggest that anti-protein fouling urinary catheters may provide an effective antibiotic-sparing therapy against CAUTI.

BI-Contributed On Demand-61 Deconvolution of 3D OrbiSIMS Biological Datasets *via* Comprehensive Molecular Formula Prediction*, A. Kotowska, M. Edney, **David Scurr**,* University of Nottingham, UK

Modern mass spectrometry (MS) techniques produce a wealth of complex data-sets with a significant bottleneck in their analysis, this is especially so with biological samples. Existing analytical software has been successfully developed in LC/GC-MS and FT-ICR MS, some of which combines a molecular formula prediction with visualization of MS data through plotting of double bond equivalence (DBE) versus carbon number[1] (where DBE relates elemental composition to unsaturation in a molecule). This is typically an unused method in SIMS data analysis owing to the highly fragmented nature of the secondary ions and relatively few molecular ions being available. Datasets such as those acquired from the 3D OrbiSIMS utilising the gas cluster ion beam and OrbiTrap™ analysis modes provide high mass resolved spectra including many molecular secondary ions. As such these data-sets are amenable to this analytical approach. In this series of work molecular formula prediction and data visualization has been demonstrated to effectively deconvolute complex biological data-sets in a manner which is unachievable using established approaches to SIMS analysis, such as targeted compound searching and/or untargeted methods including multivariate data analysis (MVA).

In this work we have developed software for formula prediction and data visualization, successfully applying it to 3D OrbiSIMS data acquired from frozen hydrated human skin tissue, human serum samples and freeze dried cultured cells. In the 3D OrbiSIMS analysis of human skin samples this approach has enabled the discrimination of chemical species present within skin including fatty acids, lipids, N-acyl ethanolamines, sterols, ceramides, glycerides (mono, di and tri) and amino acids. The software also allows for the illustration of the respective depth profiles for each species identified which can be used to rationalise their identity through their presence or absence within specific physiological layers. The chemically filtered data-sets are available for subsequent analysis using techniques such as MVA. Analysis of human serum samples showed that proteins and lipids were easily distinguished and 1,477 lipid peaks were automatically assigned and classified in the serum with the selection of protein related secondary ions having the potential to act as a filtering stage during protein identification using 3D OrbiSIMS[2]. Furthermore, in the analysis of cultured cells, amino acids, fatty acids, lipids, metabolites and sample substrate can also be readily separated and identified using this approach.

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BI-Contributed On Demand-64 Immiscible Liquid-Coated Filters Resist Biofouling*, **Justin Hardcastle**, D. Regan, C. Fong,* University of Maine*; R. Shah, S. Hung, A. Cihanoglu, J. Schiffman,* University of Massachusetts Amherst*; C. Howell,* University of Maine

During the purification of water and air, biofouling is an ongoing issue that leads to flow decay, and current chemical and physical cleaning methods for fouled filters can lead to filter degradation over time. In addition to being porous throughout, commonly used filters such as polytetrafluoroethylene (PTFE) and polyvinylidene fluoride (PVDF) often have a textured surface that promotes the adhesion of bacteria and other contaminants. In this work, we present bio-inspired liquid-coated filters as a new approach to creating filters that resist fouling. Liquid-coated filters were created by immobilizing a water immiscible liquid on the surface of commercially available synthetic filters. For water filtration tests, 0.45 µm pore diameter PTFE and PVDF filters were coated with omniphobic perfluoropolyether liquids. We measured the continuity of the surface liquid layer by testing how easily a water droplet could begin to move the surface, as well as the anti-adhesion properties of the surface liquid layer through quantifying the speed of a droplet's movement at a static angle of inclination. The results indicate that the PTFE membranes sustained a more consistent functional liquid layer, with an approximately 75% lower sliding

angle and 70% faster droplet movement at a fixed angle, than the PVDF. Dead-end pure water permeability (PWP) experiments conducted at an applied pressure of 1.5 bar indicated that liquid-coated PVDF membranes had a statistically equivalent PWP of 2827 ± 323 L/m^2-h-bar, for over 10 cycles of use. For aerosol filtration, we tested the efficiency in capturing and releasing aerosolized *Escherichia coli* using liquid-coated commercial PTFE and HEPA filters. We determined that bacteria trapped on the liquid-coated filters could be removed with increased efficiency compared to bare controls. The use of liquid-coated materials in water and air purification applications opens new doors for the creation of a biointerface that resists adhesion in dynamic environments.

BI-Contributed On Demand-67 A Graphene-Based Platform for Investigation of Protein Assembly by Infrared Nanospectroscopy*, **Xiao Zhao**, D. Li,* Lawrence Berkeley National Laboratory (LBNL), China*; Y. Lu,* Lawrence Berkeley National Laboratory (LBNL), Taiwan*; P. Ashby, M. Salmeron,* Lawrence Berkeley National Laboratory (LBNL)

The nanoscale structures and dynamical processes of proteins have been extensively studied by various imaging techniques such as electron microscopy and atomic force microscopy (AFM) in liquid. However, these imaging techniques can damage or perturbate the samples and do not provide chemically identification. This prevents a direct monitoring of structural and chemical evolution under physiological conditions. Herein, we demonstrate a new nondestructive platform that enables nanoscale Infrared (IR) spectroscopy for S-layer protein at graphene-aqueous solution interface by combining graphene liquid cell and Fourier Transform Infrared Nanospectroscopy (nano-FTIR). Single layer graphene separating the assembly solution and the tip minimize the sample damage and tip contamination. The protein structural evolution during and after assembling process is monitored by recording the amide I and II vibration bands, which provides unique and complimentary information to the AFM morphology in liquid. Our platform opens up broad opportunities for *operando* study of soft materials or nanostructures (enzyme, membrane protein, virus, and plastic material) in their realistic condition and under external stimuli.

BI-Contributed On Demand-70 Analysis of Intact Proteins in the 3d Orbisims*, **Anna Kotowska**, G. Trindade, P. Williams, J. Aylott,* University of Nottingham, UK*; A. Shard,* National Physical Laboratory (NPL), UK*; M. Alexander, D. Scurr,* University of Nottingham, UK

The identification of proteins at surfaces has applications in studying biosensors used in the biotechnological field and cell interactions with biomaterials [1][2]. Secondary ion mass spectrometry (SIMS) is a surface analysis technique with lateral resolution below 200 nm and has been applied for the characterisation of protein functionalized surfaces. However, intense protein fragmentation by the primary ion beam results in only limited information about protein identity, conformation or orientation by statistical analysis of single amino acid ion intensities. The use of large gas cluster ion beams (GCIB) as analysis beams has allowed for more information to be derived from peptide samples (up to 3kDa) in SIMS by detection of multi amino acid fragments [3]. However, these distinct ions have not previously been identified for proteins.

Here we use the 3D OrbiSIMS (HybridSIMS, IONTOF GmbH) [4], combining an argon GCIB primary ion beam and the Q Exactive™analyzer to identify proteins directly from a surface. In sixteen example proteins in a range of sizes from 6 kDa (insulin) to 272 kDa (fibronectin), up to 12-membered amino acid sequences were detected and assigned using the *de novo* sequencing approach. The multi amino acid fragments were assigned with confidence due to the high mass accuracy (<2 ppm) and the MS/MS capability of the instrument. This illustrates the potential to identify proteins adsorbed on the surface and utilise the 3D OrbiSIMS in characterising interactions of proteins with materials used in tissue engineering and medical devices.

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BI-Contributed On Demand-73 Cell Instructive Materials for Next Generation Medical Devices: Microtopography Opportunities*, **Morgan Alexander**,* The University of Nottingham, UK

The range of biomaterials found in the clinic today are dominated by materials that have been chosen largely on the basis of their availability and mechanical properties. It would be desirable to design our way forward from this situation to new and better biomaterials chosen for positive interactions with surrounding cells and tissues. Unfortunately, our understanding of the interface between most materials and biology is poor. Only in isolated cases is there a good understanding of cell-material interactions and fewer still where material-tissue interactions are well characterised and understood.

This paucity of information on the mechanism of biomaterial interactions within the body acts as a roadblock to rational design. Consequently, we have taken a high throughput screening approach to discover new bio-instructive polymers from large chemical libraries of synthetic monomers presented as micro arrays. [1,2,3] This approach is akin to engineering serendipitous discovery and will be exemplified using examples that have been taken from the lab all the way to the clinic.

The latest work combining from this bio-instructive materials area micro topography combined with bio-instructive polymer chemistries including the TopoChip[4,5], ChemoTopoChip [6] and the ArchiChips [unpublished] will be highlighted in this talk.

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BI-Contributed On Demand-76 Physical Virology of SARS-CoV-2 Uptake and Adhesion*, S. Kumar,* University of Texas at Austin*; A. Paul,* University of Texas at Austin, Chalmers University of Technology, Sweden*; N. Nehra, D. Wang, A. Nisar, **Sapun H. Parekh**,* University of Texas at Austin

The SARS-CoV-2 novel coronavirus disease has caused a global pandemic disease that has spread globally to more than160 countries, disrupting global health and costing trillions in economic damage in the process. SARS-CoV-2 infects host cells primarily by binding Angiotensin-Converting Enzyme 2 (ACE-2) surface receptor via its Spike (S) protein. Substantial efforts have gone into sequencing the virus and understanding its biochemistry, but remarkably little is known about the biophysics of the virus or its entry process into cells. The virus infection data reveal some interesting physical trends: 1) global data on SARS-CoV-2 indicates improved stability of the virus at lower temperatures, 2) there is a higher infectious risk for older people – with more fibrotic (stiffer) lungs, and 3) the particle exhibits very different lifetimes on different surfaces. From a

physical perspective, SARS-CoV-2 is a ~ 100 nm polymer particle with a lipid envelope and protein shell, and its S protein binds to a cell receptor causing internalization. In this sense, it is no different than a typical polymer nanoparticle that biomaterial scientists have been working with for years. Here investigate the SARS-CoV-2 virus from a physical science perspective using viral mimic particles: S protein coated nanospheres and S protein containing pseudo-typed viruses. We report adhesion strengths for different surfaces and study viral uptake into lung airway cells as a function of different host temperatures and the stiffness of underlying “lung” tissue matrix. We find that physical variables affect uptake, and our results suggest viral infection is indeed elevated for stiffer lungs, similar to what is seen in the clinic. We also compare results from the nanosphere and pseudo-type virus systems and in an effort to highlight where our physical approach falls short and where it is appropriate. We hope this work not only provides a better understanding on how physical factors influence viral transmission and pathogenicity but also demonstrates the opportunities of taking a physical science to virology.

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