Biomaterial Interfaces Division
Room 101B - Session BI+AS+IPF+NS-TuA

IoT Session: Biofabrication, Bioanalytics, Biosensors and Diagnostics

Moderators: Graham Leggett, University of Sheffield, UK, Tobias Weidner, Aarhus University, Denmark

2:20pm **BI+AS+IPF+NS-TuA-1 Functionalization of Silica Materials *via* Click Reaction of Surface Silanol Groups with Vinyl Sulfones*, Fang Cheng, H Wang, W He, B Sun, J Qu,*** Dalian University of Technology, China

Silica-based materials are widely used in the fields of catalysis, chromatography, biomaterials, biosensing and drug delivery due to their earth abundance and low cost. Success of these applications mostly relies on the functionalization of silica surfaces, among which covalent binding of organic molecules is preferred. Common strategies for the covalent functionalization of silica materials involve either silane treatments or Si-H reactions. Each has its share of limitations, with the former suffering from self-polymerization and multilayer modifications, and the latter being sensitive to moisture and oxygen. Herein, we proposed the 'click' reaction of silanol groups with vinyl sulfones, which enables a new and simple strategy for functionalization of silica materials. For the first time, the 'click' concept was extended to silanol groups that are abundant on the surface of silica materials, using compounds bearing vinyl sulfone groups. By simply immersing silica materials in vinyl sulfone solutions at 60℃, functionalization could be achieved in hours in the presence of catalysts. The chemical stability of vinyl sulfones and mild reaction conditions make this strategy advantageous than silane treatments and Si-H reactions. We demonstrated that silica materials with sizes ranging from microscale to macroscale could all be functionalized. Using compounds bearing multiple vinyl sulfone groups, silica materials can be further functionalized with varies of biomolecules due to the versatile reactivity of vinyl sulfone group towards thiol, amino and alcohols. Furthermore, the stability of resulting Si-O-C bond can be tuned by the properties of the vinyl sulfone compounds (e.g., hydrophobicity and surface density) as well as the environmental factors (e.g., solvents, pH and temperature). Increase in the hydrophobicity and functionalization density of the vinyl sulfone compounds could increase the stability of Si-O-C bonds. Contrast to the high stability in organic solvents, degradation of Si-O-C bond can be realized in aqueous solutions, which can be accelerated by addition of acid or base. This is rarely observed with bonds produced based of silane treatments and Si-H reactions. It could broaden the biomedical applications of functionalized silica, for example, to provide tailored release of drugs or proteins from silica surface.

2:40pm **BI+AS+IPF+NS-TuA-2 Organosilica pH Nanosensors Applied to Realtime Metabolite Monitoring*, Kye Robinson,*** Monash University, Australia*; K Thurecht,* University of Queensland, Australia*; S Corrie,* Monash University, Australia

Continuous monitoring of biomarkers in biological environments is a key challenge for the development of biosensors capable of providing real-time feedback[1]. These sensors promise to aid in the treatment of diseases with a highly dynamic nature however current technologies remain scarce[1]. Nanoparticle based "optodes" have emerged as sensitive and tuneable biosensors, using chromo/ionophores to generate analyte-specific changes in fluorescence spectra in a dynamic and reversible manner. Currently this type of sensor suffers from limitations including leaching of reagents from the nanoparticles over time, combined with poor colloidal stability and resistance to fouling in biological fluids.

An organosilica core-shell pH sensitive nanoparticle containing a mixture of covalently incorporated pH-sensitive (shell) and pH-insensitive (core) fluorescent dyes has been developed. This platform demonstrates good long term stability (80 days), fast response time (<100 ms) and resistance to fouling in biological conditions[2]. This presentation will describe the modification of these pH sensing particles towards the production of a lactate responsive particle for sensing through coupling with lactate dehydrogenase. Here we will present our latest results focussed on enzyme encapsulation in addition to modulation of shell parameters including thickness and degree of crosslinking in order to tune response kinetics for application in biological tissues.

[1] Corrie, S. R. et al., Analyst, **2015**, 140, 4350-4364

[2] Robinson, K. J. et al., ACS Sensors, **2018**

3:00pm **BI+AS+IPF+NS-TuA-3 Impact of Different Receptor Binding Modes on Surface Morphology and Electrochemical Properties of PNA-based Sensing Platforms*, Johannes Daniel Bartl,*** Walter Schottky Institut (WSI) and Physics Department, Technische Universität München, Germany*; P Scarbolo,* Dipartimento Politecnico di Ingegneria e Architettura (DPIA), Università degli Studi di Udine, Italy*; S Gremmo, G Rziga, M Stutzmann,* Walter Schottky Institut (WSI) and Physics Department, Technische Universität München, Germany*; M Tornow,* Molecular Electronics Group and Department of Electrical and Computer Engineering, Technische Universität München, Germany*; L Selmi,* Dipartimento di Ingegneria "Enzo Ferrari" (DIEF), Università di Modena e Reggio Emilia, Italy*; A Cattani-Scholz,* Walter Schottky Institut (WSI) and Physics Department, Technische Universität München, Germany

Silicon-based field-effect devices have been widely studied for label-free DNA detection in recent years. These devices rely on the detection of changes in the electrical surface potential during the DNA recognition event and thus require a reliable and selective immobilization of charged biomolecules on the device surface [1]. The preparation of self-assembled monolayers of phosphonic acids (SAMPs) on metal oxide surfaces is an efficient approach to generate well-defined organic interfaces with a high density of receptor binding sites close to the sensing surface [2,3]. In this work, we report the functionalization and characterization of silicon/silicon nitride surfaces with different types of peptide nucleic acid (PNA), a synthetic analogue to DNA [4].

Differently modified PNA molecules are covalently immobilized on the underlying SAMPs either in a multidentate or monodentate fashion to investigate the effect of different binding modes on receptor density and morphology important for PNA-DNA hybridization. Multidentate immobilization of the bioreceptors *via* C_6-SH attachment groups at the *γ*-points along the PNA backbone provides a rigid, lying configuration on the device surface (PNA 1), whereas a monodentate immobilization by Cys-capped PNA molecules (PNA 2) results in more flexible and more accessible receptor binding sites. Our results indicate that the presented functionalization scheme can be successfully applied to produce morphologically and electrochemically different PNA bioreceptor binding sites on silicon/silicon nitride surfaces. Consequently, a well-chosen modification of the PNA backbone is a valid approach to influence the sensing properties of surface-immobilized PNA bioreceptors, which might provide an additional parameter to further tune and tailor the sensing capabilities of PNA-based biosensing devices.

[1] Ingebrandt S. and Offenhausser A., *Phys. Status Solidi A* **203** (2006), 3399–3411.

[2] Chaki N. K. and Vijayamohanan K., *Biosens. & Bioelectron*. **17** (2002), 112.

[3] Stutzmann M., Garrido J. A., Eickhoff M. and Brandt M. S., *Phys. Status Solidi A* **203** (2006), 3424–3437.

[4] Nielsen P. E. and Egholm M. (ed.), Peptide Nucleic Acids, Horizon Scientific Press (1999).

3:20pm **BI+AS+IPF+NS-TuA-4 Biosensor for Detection of Gasotransmitter from Living Cells Employing Silver Nanorods Array*, Shashank Gahlaut, C Sharan, J Singh,*** Indian Institute of Technology Delhi, India

The detection of endogenous gases including H_2S is of immense interest nowadays as it opens the way to predict some diseases as well as an early stage diagnosis. These three gasotransmitter (H_2S, NO and CO) gaseous molecules transfer the information and give the signal for mainly cardiovascular diseases Therefore, its detection has crucial importance in bio-medical science. Here, we demonstrate H_2S detection from living cells using silver nanorods arrays fabricated by glancing angle deposition method. Colorimetric and wettability properties of silver nanorods are being observed for the gaseous detection. We use the model organism *E.coli* to demonstrate the feasibility of the method for the determination of live and resistant strains of the bacteria. For the human cell, we have used Hela cell line for the same. For the simplicity and feasibility of the technique, Android based mobile app has been developed for the colorimetric detection. Data obtained in this study show the potency of the system to identify live/dead bacteria with or without antibiotic treatment and compared with the time-consuming standard plating method, it a simple and cost-effective method for the estimation of living and resistant microorganism. The performance of AgNRs as H_2S gas sensor is investigated by its sensing ability of 5 ppm of gas with an exposure time of only 30 s. It has potential application in the area of antimicrobial resistance and bio-medical healthcare.

4:20pm **BI+AS+IPF+NS-TuA-7 Conversion of Human Stem Cells into Insulin Producing Cells Through 2D Platforms for Enhanced in-vitro Insulin Production**, *S Vishwakarma, A Khan,* Central Laboratory for Stem Cell Research and Translational Medicine, Centre for Liver Research and Diagnostics, Deccan College of Medical Sciences, India*; **Marshal Dhayal,*** IIT (BHU), Varanasi, India

Transplantation of whole pancreas/cadaveric islets is the most commonly acceptable treatment option for uncontrolled diabetes. However, the wider clinical applicability of these approaches is limited due to unavailability of donors and continuous need for the administration of immunosuppressant. Here we report a new strategy for efficient in-vitro trans-differentiation of human-hepatic progenitor cells (hHPCs) into insulin producing cells (iPCs) on biologically compatible micro-chips of 2D platforms. The physiological function of transdifferentiated hHPCs confirmed the activation of intracellular Ca^{++} signaling and activation of pancreatic transcription factors (pTFs) which triggers the insulin exocytosis during hyperglycemic challenge. The iPCs on these micro-chips showed upregulated expression of master regulator Pdx-1, β-cell specific marker Nkx-6.1 and more importantly C-peptide similar to human pancreatic b-cells during hyperglycemic challenge. These platforms may provide long-term survival and function of iPCs which could be better technology for developing effective therapeutic options for the management of diabetic.

4:40pm **BI+AS+IPF+NS-TuA-8 Polyzwitterion-modified Nanoparticles for Selective Antibody Separation**, *F Cheng, C Zhu, **Wei He**, B Sun, J Qu,* Dalian University of Technology, China

Antibody separation is a key biopharmaceutical process, which requires high specificity and efficiency in isolating the biomacromolecule from a complex biological fluid. Development of the separation adsorbent benefits diagnostics and therapeutics, such as point-of-care testing, treatment of cancer and autoimmune disease. In the process of antibody separation, Protein A chromatography is a commonly employed adsorbent, which could obtain antibody in high purity from serum or ascites. In the process-scale purification and therapeutic plasma exchange, safety issues, e.g. leakage and instability of the immobilized Protein A, and cross-contamination during regeneration, are overwhelmed in biopharmaceutics. An alternative approach to Protein A chromatography is using synthetic ligand, molecular weight of which is commonly less than 200 Da. The main advantages of synthetic ligand are well-controlled chemical structure, low cost, ease in clean-in-place, and repeatable regeneration capability in harsh conditions. However, it is a challenge to adsorb antibody in a highly selective manner from a complex biological fluid, which consists a variety of proteins with a broad range of concentrations.

Herein, we report a facile method to develop a quick separation adsorbent, which adsorbs antibody from a complex biological fluid with a high specificity. Two types of zwitterionic polymer-modified magnetic nanoparticles (NPs) are fabricated by conjugating pSBMA onto PEI-precoated NPs via either one-step method (1S NPs) or two-step method (2S NPs). For both methods, divinyl sulfone is used as linker molecule. Although 1S NPs were capable of resisting both IgG and BSA, 2S NPs exhibited specificity toward IgG adsorption in complex biological fluids, e.g. mixture of serums and IgG. The moderate interactions (Kd ~1.2 μM) between IgG and 2S NPs are three orders of magnitude lower than IgG binding with Protein A (Kd 10nM) . Through complementary characterizations and analyses, we rationalize that the surface developed herein with IgG specificity contains two key components: polyzwitterions with short chain length and sulfone groups with high density.

5:00pm **BI+AS+IPF+NS-TuA-9 Orienting Proteins on Surfaces with Site-specific Bioorthgonal Ligations**, ***Riley Bednar**, R Mehl,* Department of Biochemistry and Biophysics, Oregon State University

The functionalization of material surfaces with proteins is of great importance to a number of technologies, from industrial processes to biomedical diagnostics. However, while it has been proposed that orientation may be important to the function of such biomaterials, efforts to study such roles are hampered by a lack of rapid, quantitative, and orientation-specific immobilization techniques which will reduce non-specific fouling, and allow substoichiometric attachment of proteins onto surfaces in an orientation-controlled manner. Here, Carbonic Anydrase II (HCA)—a 30 kDA, monomeric metalloenzyme which catalyzes the interconversion of carbon dioxide to bicarbonate—is immobilized onto strained *trans*-cyclooctene (sTCO)-functionalized magnetic resin in an orientation-specific manner via bioorthogonal ligation with a site-specifically installed tetrazine-containing amino acid (Tet2.0).

5:20pm **BI+AS+IPF+NS-TuA-10 High-throughput Study of the Role of Spatial Organization on the Activity of Surface-Bound Enzymes**, ***Nourin Alsharif**,* Boston University*; T Lawton, J Uzarski,* Natick Soldier Research, Development and Engineering Center*; K Brown,* Boston University

Many of the exceptional properties of natural materials (e.g. fracture toughness of bones, strength to weight ratio of bamboo) can be attributed to their structural hierarchy, which originates, in part, from the nanoscale organization of the enzymes that synthesize these materials. In order to best utilize such enzymes *ex vivo* to grow engineered biomaterials, the role of this multiscale organization must be understood. Here, we report a novel strategy for studying the activity of arrangements of enzymes within a multifunctional material in a high throughput manner. In particular, we use top-down patterning techniques in conjunction with small molecule self-assembly to designate enzyme-binding regions amidst a non-binding, hydrophobic background. Key to this experimental scheme is the parallel nature of both the fabrication and the characterization processes that enable the efficient study of many geometric parameters of the enzyme-binding features. These parameters include, (1) feature size, (2) density of enzyme within each feature, and (3) distance between features. This level of control can in principle allow us to separate effects of reaction kinetics and substrate diffusion. Two strategies have been explored for the immobilization of enzymes including click chemistry to non-natural amino acids and binding to poly-histidine affinity tags. Top-down lithography and enzyme assembly were verified using a variety of surface characterization techniques including atomic force microscopy, X-ray photoelectron spectroscopy, infrared spectroscopy, spectroscopic ellipsometry, and contact angle goniometry. Initially, this high throughput paradigm is used to develop a fluorimetric assay to quantify the activity of surface-bound enzymes as a function of their spatial organization. Together with the widespread utilization of high throughput techniques in synthetic biology, the ability to study spatial organization in a rapid fashion is expected to dramatically improve *ex vivo* applications of enzymes.

5:40pm **BI+AS+IPF+NS-TuA-11 Fabrication of Amino acid Contained Poly-lactic Acid Nanofibers by Electrospinning**, *C Li,* National Yang Ming University, Taiwan, Republic of China*; J Hsieh,* Ming Chi University of Technology, Taiwan, Republic of China*; **P.H. Lin,*** National Yang Ming University, Taiwan, Republic of China

Polylactic acid (PLA, $[C_3H_4O_2]_n$, CAS 26161-42-2) is a biodegradable and thermoplastic polymer. PLA is naturally produced and can be extracted from many plants such as sugarcane, cornstarch or cassava roots. Typical industrial production processes for PLA are direct condensation of lactic acid monomers (~100°C - 160°C) and ring-opening polymerization of lactide with metal catalysts. For applications in bulk forms, PLA can be produced by extrusion, casting, injection molding and spin coating or even 3d printing.

In cell and tissue engineering applications, amino acids are essential ingredients for cell-tissue culture, implants/replacements, drugs and treatment tests. There are twenty amino acids appearing in human genetic codes by triplet codons and usually categorized according to their polarity, acidity/basicity.

In this study, we fabricate nanofibers by electrospinning on a spin-coated PLA film. This specially designed combination of PLA films and nanofibers is meant to have enduring interfacial adhesion between the two for biomedical applications such as implants. Both PLA nanofibers and films are mixed with selected amino acids. Five amino acids were chosen: tryptophan (Trp,), methionine (Met,), serine (Ser,), glutamate (Glu,) and arginine (Arg,). The selection is based on the different electrical polarity of each amino acid. The electrical polarity has profound effects on the solubility, pH acidity of amino acids in water and many other associated biochemical functions. These amino acids are representatives of certain biochemical features for potentially different influences in our applications for cell culture.

The electrospinning process is controlled by several parameters such as the voltage of power supply, feeding velocity of polymer solution through the syringe pump, electrical field strength and distance to the collection plate of nanofibers. Different combinations of these parameters are studied to determine an optimal control for fiber formation. Properties of and microstructures of deposited films and nanofibers are investigated as following: thickness and deposition rate by surface profilometer; microstructures by Fourier transform infrared spectrometer (FTIR); surface morphology by scanning electron microscope (SEM); optical properties by UV-Visible-IR spectrometer and wettability by the contact angle.

Author Index

Bold page numbers indicate presenter