Biomaterial Interfaces Division
Room 101B - Session BI-ThM

Biomolecules and Biophysics at Interfaces

Moderator: Joe Baio, Oregon State University

8:00am **BI-ThM1 Bioinspired Adaptive Reconfigurable Material Systems based on Smart Hydrogels**, ***Ximin He***, University of California, Los Angeles **INVITED**

From the cellular level up to the body system level, living organisms cooperatively sense to adapt to or self-regulate the local environment, and can also harvest energy from the environment to keep alive and perform various functionalities. These graceful capabilities arise from the chemo-mechanical actions that transform the molecular configuration changes to micro/macroscopic mechanical motions, in response to environmental cues. Inspired by these unique adaptive abilities, we have developed a series of adaptive material systems, which are based on stimuli-responsive hydrogels capable of adaptively reconfiguration. This presentation will introduce three novel functionalities that this broad-based platform has demonstrated, including ultrafast optical sensing of chemical and biological species and autonomous regulating of local conditions. Living organisms ubiquitously display colors that adapt to environmental changes, relying on the soft layer of cells or proteins. Inspired by this strategy, we created a simple and universal adaptive color platform based on a hydrogel interferometer (*Adv. Mater.* 2018). Such interference colors provide a visual and quantifiable means of revealing rich environmental metrics. The single material-based platform has advantages of remarkable color uniformity, fast response, high robustness, and facile fabrication. Its versatility has been demonstrated by diverse applications: a volatile-vapor sensor with highly accurate quantitative detection, a colorimetric sensor array for multi-analyte recognition, breath-controlled information encryption, and a colorimetric humidity indicator. Portable and easy-to-use sensing systems are demonstrated with smartphone-based colorimetric analysis. Second, based on this platform, we further realized a novel function - fully autonomous separation of target molecules from a mixture fluid such as wastewater or biofluid.

8:40am **BI-ThM3 Importance of a In Depth Characterisation for the Design of Functional Gold Nanoparticles for Bioapplications**, *R. Capomaccio, I. Ojea-Jimenez, D. Mehn, P. Colpo, D. Gilliland,* European Commission - Joint Research Centre, Italy*; R. Hussain, G. Siligardi,* Diamond Light Source Diamond House, Harwell Science and Innovation Campus, UK*; L. Calzolai,* ***Giacomo Ceccone***, European Commission - Joint Research Centre, Italy

The design and fabrication of functionalized nanoparticles (NPs) are of great interest in biotechnology and biomedicine, especially for diagnostic and therapeutic applications.[1] However, at the moment the challenges related to the characterization of complex, multi-functional nanoparticles are still hampering the development of advanced bio-nano-materials.[2,3] In particular the interaction of NPs with protein has been the subject of many investigations in the last years and although important advances were made, several important issues (e.g. thermodynamic constants, protein structure changes) are still not completely understood.[4-6]

In this work, the interaction of gold nanoparticles (AuNPs) with human serum albumin (HSA) has been investigated as model system. First a simple method to determine the structure and morphology of the AuNPs-HSA complexes will be described.[7] Then the interaction of HSA with a model system consisting of AuNPs functionalized with two differentially-terminated poly(ethylene oxide) ligands, providing both "stealth" properties and protein-binding capabilities to the nanoparticles have been investigated. In particular, the purpose of this study was to: i) monitor and quantify the ratios of ligand molecules per nanoparticle; ii) determine the effect of coating density on non-specific protein adsorption; iii) to assess the number and structure of the covalently-bound proteins. For this a combination of techniques, including Centrifugal Liquid Sedimentation, Dynamic Light Scattering, Flow Field Flow Fractionation, Transmission Electron Microscopy, Circular Dichroism, XPS and ToF-SIMS have been employed to compare complementary outcomes from typical and orthogonal techniques used on nanoparticle characterisation.[8]

[1] S. Chen, et al., Nanomedicine: Nanotechnology, Biology, and Medicine, 2016, **12**, 269

[2] D. Grainger, D. Castner, Adv. Mater., 2008, **20**, 867

[3] S. Laera et al, *Nano Lett.*, 2011,***11*(10),**4480

[4] G Y Tonga, et al., Adv. Mater. 2014, **26**, 359

[5] D Walczyk, et al., J. AM. CHEM. SOC. 2010, **132**, 5761

[6] S. Winzen, et al., Nanoscale, 2015, 7, 2992

[7] R. Capomaccio, et al., Nanoscale, 2015, **7**, 17653

[8] I. Ojea-Jimenez, et a., Nanoscale 2018 (in print)

9:00am **BI-ThM4 A Model Membrane Microsystem for Measurement of the Kinetics of Transmembrane Proton Transport**, *J.P. Madsen, A. Johnson, M.L. Cartron, N.C. Hunter, S.P. Armes,* ***Graham Leggett***, University of Sheffield, UK

Binary brush structures consisting of poly(cysteine methacrylate) (PCysMA) "corrals" enclosed within poly(oligoethylene glycol methyl ether methacrylate) (POEGMA) "walls" are fabricated simply and efficiently using a two-step photochemical process. First, the C-Cl bonds of 4-(chloromethyl)phenylsilane monolayers are selectively converted into carboxylic acid groups by patterned exposure to UV light through a mask and POEGMA is grown from unmodified chlorinated regions by surface-initiated atom-transfer radical polymerization (ATRP). Incorporation of a ratiometric fluorescent pH indicator, Nile Blue 2-(methacryloyloxy)ethyl carbamate (NBC), into the polymer brushes facilitates assessment of local changes in pH using a confocal laser scanning microscope with spectral resolution capability. Moreover, the dye label acts as a radical spin trap, enabling removal of halogen end-groups from the brushes via *in situ* dye addition during the polymerisation process. Second, an initiator is attached to the carboxylic acid-functionalised regions formed by UV photolysis in the patterning step, enabling growth of PCysMA brushes by ATRP. Transfer of the system to THF, a poor solvent for PCysMA, causes collapse of the PCysMA brushes. At the interface between the collapsed brush and solvent, selective derivatisation of amine groups is achieved by reaction with excess glutaraldehyde, facilitating attachment of aminobutyl(nitrile triacetic acid) (NTA). The PCysMA brush collapse is reversed on transfer to water, leaving it fully expanded but only functionalized at the brush-water interface. Following complexation of NTA with Ni^{2+}, attachment of histidine-tagged proteorhodopsin and lipid deposition, light-activated transport of protons into the brush structure is demonstrated by measuring the ratiometric response of NBC in the POEGMA walls.

9:20am **BI-ThM5 Theranostics Gold Nanoparticles for Brain Cancer Applications**, *I. Naletova, L.M. Cucci, F. D'Angeli, C.D. Anfuso, G. Lupo,* University of Catania, Italy*; A. Magrì,* National Council of Research (CNR), Italy*; C. Satriano,* University of Catania, Italy*;* ***Diego La Mendola***, University of Pisa, Italy

In this work, hybrid assemblies of plasmonic gold nanoparticles (AuNPs) and peptides mimicking the putative cell binding domain of angiogenin protein (60-68 sequence)[1] were investigated in their interaction with artificial membranes of supported lipid bilayers (SLBs) and cellular membranes of cancer cell lines. In particular, the response of glioblastoma cell line (A172), as model of the most aggressive cancer that begins within the brain[2], and neurons obtained by differentiated neuroblastoma cell line

(SHSY5Y), as 'normal cells', was scrutinized. The influence of copper, which is a pivotal co-player of cellular homeostasis in both physiological and pathological angiogenesis, was investigated in parallel with the gold nanoparticles functionalized with a fluorescent derivative of Ang(60-68) peptide. Control experiments using the non-fluorescent peptide analogous immobilized onto the AuNPs either by physisorption (Ang(60-68)) or chemisorption (Ang(60-68)Cys) were also included. The hybrid peptide/AuNP/copper systems were characterized by means of UV-visible, AFM and CD, to address the plasmonic changes, the nanoparticle coverage and conformational features at the hybrid biointerface. Lateral diffusion measurements on SLBs after their interaction with the peptide-functionalised AuNPs pointed to a stronger membrane interaction in comparison with the uncoated nanoparticles. Cell viability and proliferation assays indicated significant differences, in the presence or absence of copper, for the two cell lines. Cell imaging by confocal microscopy evidenced dynamic processes modulated in a synergic way by the different components (peptide, gold nanoparticle, copper) of the hybrid nanoplatforms at the level of the cell membrane (cytoskeleton features observed by actin staining) as well as at the sub-cellular compartments (copper-binding proteins).

[1] Cucci LM, Munzone A, Naletova I, Magrì A, La Mendola D, Satriano C. *Biointerphases*. 2018;13(3):03C401.

[2] Bleeker FE, Molenaar RJ, Leenstra S. Recent advances in the molecular understanding of glioblastoma.*J Neurooncol.* 2012;108(1):11-27.

11:00am **BI-ThM10 Non-equilibrium Thermodynamic Model for DNA at Nanochannel Junctions***, **Saroj Dangi,*** North Carolina State University

DNA, often studied as a polymer molecule, extends along the axis of confining channel if the size of channel is less than the radius of gyration of the molecule. Extended molecule can be manipulated for wide range of applications such as DNA sorting, gene mapping, single molecule experiment, and fundamental polymer physics experiment. The optimization and advancement of these nanofluidic applications necessitates the understanding of physics behind the confinement of DNA in nanochannel. So far, most of the studies have considered linear and uniform channels. However, many nanofluidic applications such as sorting, single molecule experiment require complex manipulation of DNA in branched channels with junctions. Dynamics response of DNA in such nanofluidic networks with junctions and asymmetric channels is relatively unknown. We studied the transport of DNA in a nanofluidic device made up of series of nanochannel junctions with asymmetric channel size. Here we present a non-equilibrium thermodynamic model for a nanochannel junction with asymmetry in channel size. We show that the transport direction of DNA in the device can be tuned locally by altering the confinement free energy of DNA or the flow potential in nanochannels. Using our model, we show that the motion of DNA in branched nanofluidic networks can be predicted stochastically.

11:20am **BI-ThM11 Dipeptide Nanocontainers Immobilised on Graphene Nanoplatforms for Drug-delivery Applications***, V.C.L. Caruso,* University of Catania, Italy*; G. Trapani,* University of Catania and Scuola Superiore di Catania, Italy*; L.M. Cucci, I. Naletova,* University of Catania, Italy*; D. La Mendola,* University of Pisa, Italy*; **Cristina Satriano,*** University of Catania, Italy

Graphene oxide (GO) nanosheets, owing to their high surface-to-volume ratio and the richness of oxygen-containing moieties (including carboxyl, hydroxyls and epoxide groups) represent ideal 2D nanoplatforms for drug delivery applications [1]. The integration of GO with homo-aromatic dipeptides, which are able to self-assemble into ordered structures such as nanotubes and nanowires [2], may offer unique potentialities at the biointerface because of the increased biocompatibility of the hybrid system and, remarkably, for the capability to load/protect a cargo into the peptide nanocontainers. Moreover, metal ions can influence/drive the peptide self-assembling process as well as to induce additional properties of the hybrid system (e.g., antibacterial and angiogenic properties in the case of Cu^{2+}ions [3]).

In this work, the hydrophobic dipeptides Phe-Phe (FF) and Tyr-Tyr (YY) were grown in the presence of graphene oxide (GO) and copper ions, to fabricate hybrid peptide-GO-metal nanoassemblies with multifaceted features.

The nanoassemblies were scrutinised spectroscopically (UV-visible, fluorescence and circular dichroism) and microscopically (atomic force microscopy and confocal microscopy). Quartz crystal microbalance with dissipation monitoring (QCM-D) was used for real-time acoustic sensing of the interaction of the hybrid nanoplatforms with supported lipid bilayers, used as model cell membranes. Promising results of cellular uptake in neuroblastoma cells were measured by confocal microscopy for the assemblies loaded with the anticancer drug doxorubicine.

[1] Consiglio, G., Di Pietro, P., D'Urso, L., Forte, G., Grasso, G., Sgarlata, C., ... & Satriano, C. (2017). Surface tailoring of polyacrylate-grafted graphene oxide for controlled interactions at the biointerface. *Journal of colloid and interface science*, *506*, 532-542.

[2] Reches, M., & Gazit, E. (2003). Casting metal nanowires within discrete self-assembled peptide nanotubes. *Science*, *300*(5619), 625-627.

[3] Yu, L., Jin, G., Ouyang, L., Wang, D., Qiao, Y., & Liu, X. (2016). Antibacterial activity, osteogenic and angiogenic behaviors of copper-bearing titanium synthesized by PIII&D. *Journal of Materials Chemistry B*, *4*(7), 1296-1309.

11:40am **BI-ThM12 Seriatim Operando STM and FTIR Study of Phospholipid Membrane Phase Transition Driven by Electrochemical Potential Control***, **Taro Yamada,*** RIKEN, Japan*; S. Matsunaga, H. Shimizu,* The University of Tokyo*; T. Kobayashi,* RIKEN, Japan*; M. Kawai,* The University of Tokyo

Phospholipid (1,2-dialkanoyl-sn-glycero-3-phosphocholine, DHPC for alkyl=C_6H_{13}, DDPC for $C_{10}H_{21}$) monolayers were prepared on 1-octanethiol-terminated gold surface, as a model of biological cell membrane, and nano-scopically observed by electrochemical scanning tunneling microscopy (EC-STM) and internal multiple reflection Fourier-transformed infrared absorption spectroscopy (FTIR) within aqueous electrolytic solutions. This dual-technique in situ operando observation revealed structural changeover of the phospholipid membrane according to the applied electrode potential. In 0.05 M NH_4ClO_4 solution (pH 7.0) at 0 V vs RHE, DHPC monolayer was a fluidic monolayer along the underlying thiol monolayer, with mobile chasms through which underlying vacancy islands of the substrate were frequently seen.by application of -0.2 V, the monolayer was slowly converted into solid striped structure. This is designated as "hemimicellar aggregation" [1] with a periodicity of 4.3 nm, and observed also for DDPC. By returning the substrate potential, the lipid monolayers restored fluidic phase. This transition was reversible and repeatable. By application of +0.2 V the fluidic feature was maintained despite a slight increase of monolayer height. When the potential was swept from +0.2 V to -0.2 V, elliptic agglomerates with an average diameter of 13 nm was observed. After this, the hemimicellar aggregation was never observed by any kind of potential cycling. This irreversible change of phase coincided with the seriatim FTIR observation, using deuterium-labelled DHPC molecules. The initial change of fluidic to hemimicellar did not exhibit drastic change in IR spectra, except a reversible splitting of the P-O stretching in the region of 1200-1300 cm-1. After application of +0.2V DHPC with the head-group choline part ($-C_2D_4N^+(CD_3)_3$) was lost as a surface IR signal. This is an evidence for irreversible dissociation of DHPC into choline and phosphatidyl acid. The elliptic grains correspond to the phosphaticyl acid, differently agglomerated from that of intact DHPC hemimicelles. The potential shift of this amplitude is similar to the membrane potential of real cells. It is seen that phospholipid molecules, the robust solid component of cell membrane, can be easily involved chemical reactions under such membrane potential by the aid of membrane proteins for example. This series of experiment also demonstrates the applicability of seriatim surface observation techniques such as IR spectroscopy in addition to STM, which does not always distinguish the molecular species and detect chemical reactions.

[1] J. Am. Chem. Soc. 126 (2004) 12276.

12:00pm **BI-ThM13 Mitochondria Localized Polymerization for New Cancer Therapy***, **Ja-Hyoung Ryu,*** Ulsan Natioanl Institute of Science and Technology, Republic of Korea

Recently, targeting mitochondria, the vital organelle for cell survival, as it plays a central role in energy production and apoptotic pathways, has been recognized as an efficient strategy in different therapeutic techniques by disturbing the normal function. Specifically, the conjugation of drug to triphenylphosphonium (TPP), a lipophilic cation, enables its accumulation into the mitochondria of cancer cells more than ~10 times greater than into normal cells as the mitochondrial membrane potentials (~ -220 mV) of cancer cells exhibits more negative charge than that of normal cells (~ -160 mV). The conjugation of TPP with bioactive molecules (e.g. small molecules and peptides) thus would provide a promise approach to target and disrupt the mitochondria of cancer cells, enhancing the efficacy of cancer chemotherapy. Recently, we reported that the supramolecular polymerization of dipeptide inside the mitochondria induced the dysfunction of mitochondria by disrupting the membrane, resulting in the

selective apoptosis of cancer cells. Due to the more negative mitochondria membrane potentials in cancer cells compared to normal cells, the TPP-conjugated molecules highly accumulated in the cancer cells and induced the self-assembled structures.

In addition, we describe a mitochondria-targeting biomineralization system that favorably can induce silicification and consequent apoptosis of various cancer cells. The biomineralization system features triphenylphosphonium (TPP) and triethoxysilane (mineralization monomer). The TPP enabled its accumulation into the mitochondria of cancer cells more than 7 times, compared with normal cell. Very intriguingly, the silicification of the triethoxysilane moiety to form biomierals in cancerous mitochondria results in apoptosis thorough mitochondria dysfunction, while there is no toxic effect into normal cell at the same concentration. Furthermore, this system efficiently inhibits the tumor growth of the mouse xenograft cancer model, which is very interesting and efficient anti-cancer therapy with simple molecular design. These results provide a new insight into the use of the mitochondrial targeting molecules for the regulation of cellular functions and a therapeutic approach

Author Index

Bold page numbers indicate presenter