Biomaterial Interfaces
Room 117 - Session BI1-TuM

Characterization of Biological and Biomaterial Surfaces I

Moderators: Morgan Hawker, California State University, Fresno, **Sapun Parekh**, University of Texas at Austin

8:30am **BI1-TuM-3 Native Supported Lipid Bilayers: A Bioanalytical Tool to Study and Detect Viruses**, ***Marta Bally***, *H. Pace,* Umea University, Sweden **INVITED**

Cellular membranes are complex dynamic structures consisting of a lipid bilayer containing a multitude of biomolecules, including a variety of lipids, proteins and carbohydrates. Systematic investigations of biomolecular processes at the cell surface call for the development of bioanalytical platforms capable to recapitulate, in vitro and under well-controlled experimental conditions, this compositional complexity while maintaining the membrane´s basic physico-chemical properties (e.g. membrane fluidity). In this context, we present native supported lipid bilayers (nSLBs), two-dimensional fluid planar bilayers produced from purified cellular plasma membranes and mounted on a solid support as a promising tool. [1,2] These cell-free systems provide the compositional complexity of nature, yet they are free from metabolic feedback loops. They are a snapshot of the membrane's composition at the moment of cell lysis, providing hundreds of experiments with the exact same membrane composition. They further allow for optimal instrumental accessibility, being compatible with a broad range of surface-sensitive biosensing tools.

In our work, we take advantage of nSLBs to characterize virus- membrane interactions [2]. The combination of nSLBs with total internal reflection fluorescence microscopy allows us to quantitatively assess the attachment, detachment, and diffusion behavior of individual virus particles at the cell membrane and to address a variety of fundamental questions related to viral attachment and entry. Specifically, this experimental approach was used to (i) study how SARS-CoV-2 changes its interaction with the plasma membrane when evolving and mutating [3], (ii) investigate the role of a cellular factor in modulating HSV-1 interactions at the cell surface [4] and (iii) to study how different carbohydrate moieties modulate the dynamics of norovirus-membrane interactions [5].

Taken together, our research contributes to a better understanding of the mechanisms regulating the interaction between a virus and the surface of its host. Such insights will without a doubt facilitate the design of more efficient antiviral drugs or vaccines.

[1] Pace at al., Analytical Chemistry, **87(18)** (2015)

[2] Peerboom, N. et al., ACS Infect. Dis. **4 (6)**, (2018)

[3] Conca, D. et al., Biorxiv (2024), https://doi.org/10.1101/2024.01.10.574981

[4] Liu, L. et al., Biorxiv (2023) ¸https://doi.org/10.1101/2023.02.10.526562

[5] Pace, et al., In manuscript.

9:00am **BI1-TuM-5 Machine Learning-Enhanced Point of Care SERS Detection Of SARS-CoV2 Variants using Handheld Raman Spectrometer**, ***Sneha Senapati***, *J. Singh,* Indian Institute of Technology Delhi, India

The rapid evolution of SARS-CoV-2 and its emerging variants necessitates advanced diagnostic techniques for effective pandemic management. On-field detection of disease-causing pathogens is one of the primary health concerns. This study introduces a Machine Learning (ML)-enhanced surface-enhanced Raman scattering (SERS) methodology for the precise differentiation of distinct SARS-CoV-2 strains and sub-strains in clinical samples. Glancing angle deposition (GLAD), a physical vapor deposition technique, was utilized to create Ag nanorods (AgNR), which were then employed as extremely pure SERS substrates. The characterization of AgNR substrates were performed using FESEM, AFM, HRTEM, EDX, XRD, UV-Vis and contact angle. Our research targets the detection of four different strains of SARS-CoV2: Wildtype, Kappa, Delta, and Omicron, including their respective sub-strains (BA.1, BA.2, BA.5, and XBB). Using pristine AgNR arrays and a handheld Raman spectrometer, discernible spectral variations were observed. Despite the clarity in isolated cultured strains of viruses, clinical validation using nasopharyngeal swabs from positive samples presented complexities due to spectral overlaps. By harnessing the unique molecular vibrational patterns elucidated by Raman spectroscopy, SERS offers heightened sensitivity. But problems came up because of the small differences in spectral patterns between closely related SARS-CoV-2 variants found in clinical samples. To address this, machine learning (ML) algorithms were integrated to discern intricate patterns from SERS data, enhancing differentiation capabilities. Through the integration of gradient boost (GB) and support vector machine (SVM) models of ML within the SERS framework, our approach achieved an accuracy of 89% and 94%, respectively, in identifying targeted variants from nasal swabs of human patients. This integrated ML-SERS approach not only enhances detection efficacy but also offers cost-effective on-site detection capabilities and disease prediction ability. The demonstrated precision underscores the methodology's potential in future variant identification and pandemic surveillance.

9:15am **BI1-TuM-6 Nanoprobe X-Ray Fluorescence Analysis of Frozen-Hydrated Biological Samples - from 2D to 3D**, ***Axel Rosenhahn***, *C. Rumancev, L. Jusifagic, A. Gräfenstein,* Ruhr University Bochum, Germany

The accumulation of metals and the homeostasis of ions in biological cells and tissue is of fundamental relevance for a wide range of environmental, biological, and medical processes. Synchrotron-based nanoprobe X-ray fluorescence analysis provides a unique combination of metal analysis with high spatial resolution, a high penetration depth, and high sensitivity down to trace concentrations. In the last years we developed several endstations for the analysis of cryogenically prepared biological samples at the P06 beamline at Petra III. Cryopreservation is the gold standard if cells are meant to be analyzed in a preserved state that is as close as possible to their natural, hydrated state. In particular for highly soluble ions, such as potassium, cryopreservation is the only way to obtain accurate concentrations. The new technique has been used to analyze the stress response of cells to the presence of Huntingtin aggregates, which are currently hypothesized to be responsible for the consequences of the corresponding disease. Also, the intracellular distribution of different metal-based cytostatic compounds has been analyzed and compared to the cellular stress response as reflected by changes in the intracellular potassium level. In addition to the 2D imaging experiments, a new tomography setup has been developed that allows cross-sectional imaging of biological samples to image metal distributions. A novel self-absorption correction during the tomographic reconstruction has been implemented that compensates artefacts especially for light elements due to the limited photon-escape depth.

9:30am **BI1-TuM-7 Harnessing Plasmon-Enhanced Fluorescence for Ultrasensitive and Minimally-Invasive Bio-Diagnostics**, ***Srikanth Singamaneni***, Washington University in St. Louis **INVITED**

Detection, imaging, and quantification of low-abundant biomolecules within biological fluids, cells, and tissues is of fundamental importance but remains extremely challenging in biomedical research as well as clinical diagnostics.We have designed and synthesized an ultrabright fluorescent nanoconstruct, termed "plasmonic-fluor", as an "add-on" bio-label to dramatically improve the signal-to-noise ratio of a wide variety of existing fluorescence bioassays without altering or complicating the conventional assay workflow or read-out devices.We demonstrate that these novel nanoconstructs can be readily utilized in a broad range of bioanalytical methods, including fluorophore-linked immunosorbent assays, multiplexed bead-based immunoassays, lateral flow assays, immuno-microarrays, flow cytometry, and immunocytochemistry, to attain more than 1000-fold improvement in the limit-of-detection and dynamic range.Harnessing plasmonic-fluors, we also demonstrate minimally-invasive and ultrasensitive quantification of target protein biomarkers in interstitial fluid through microneedle-assisted *in vivo* sampling and subsequent on-needle analysis.With the microneedle patch, we demonstrate minimally-invasive evaluation of cocaine vaccine efficiency and longitudinal monitoring of inflammatory biomarker levels in mice.

Author Index

Bold page numbers indicate presenter