Biomaterial Interfaces Division
Room B117-119 - Session BI+AS+EM+NS+SE+TF-TuA

Functional Biomaterials II: Sensing and Diagnostics

Moderators: Joe Baio, Oregon State University, **Caitlin Howell**, University of Maine

2:20pm **BI+AS+EM+NS+SE+TF-TuA-1 AVS Nellie Yeoh Whetten Awardee Talk: Detection of SARS-CoV-2 using Surface-enhanced Raman Spectroscopy and Deep Learning Algorithms**, ***Yanjun Yang***[1], University of Georgia; *H. Li,* Chongqing University, China; *L. Jones, J. Murray, D. Luo, X. Chen, H. Naikare, Y. Mosley, R. Tripp,* University of Georgia; *B. Ai,* Chongqing University, China; *Y. Zhao,* University of Georgia

A rapid and cost-effective method to detect the infection of SARS-CoV-2 is crucial in the fight against *COVID-19* pandemic. This study presents three strategies to detect SARS-CoV-2 from human nasopharyngeal swab (HNS) specimens using a surface-enhanced Raman spectroscopy (SERS) sensor with deep learning algorithms. The first strategy is to use DNA probes modified silver nanorod array (AgNR) substrate to capture SARS-CoV-2 RNA. SERS spectra of HNS specimens have been collected after RNA hybridization, and a recurrent neural network (RNN)-based deep learning (DL) model is developed to classify positive and negative specimens. The overall classification accuracy was determined to be 98.9%. For the blind test of 72 specimens, the RNN model gave 97.2% accuracy in the prediction of the positive specimens, and 100% accuracy for the negative specimens. The second strategy is to use a human angiotensin-converting enzyme 2 protein (ACE2) functionalized SERS sensor to capture the intact viruses. Such a method can differentiate different virus variants, including SARS-CoV-2, SARS-CoV-2 B1, and CoV-NL63. A convolutional neural network (CNN) deep learning model for classification and regression has been developed to simultaneously classify and quantify the coronavirus variants based on SERS spectra, achieving a differentiation accuracy of > 99%. Finally, a direct SARS-CoV-2 detection on SiO_2 coated AgNR substrate is tested. SERS spectra of HNS specimens from 120 positive and 120 negative specimens are collected. The HNS specimens can be accurately distinguished as positive or negative with an overall 98.5% accuracy using an RNN-based deep learning model, and the corresponding Ct value can be predicted accurately by a subsequent RNN regression model. In addition, 99.04% accuracy is achieved for blind SARS-CoV-2 diagnosis for 104 clinical specimens. All the detections are accomplished in 25 min. These results indicate that the SERS sensors combined with appropriate DL algorithms could serve as a potential rapid and reliable point-of-care virus infection diagnostic platform.

2:40pm **BI+AS+EM+NS+SE+TF-TuA-2 Wafer-Scale Metallic Nanotube Arrays: Fabrication and Application**, ***Jinn P. Chu,*** National Taiwan University of Science and Technology, Taiwan

This presentation reports on the wafer-scale fabrication of metallic nanotube arrays (MeNTAs) with highly ordered periodicity. Various metals and alloys have been used to prepare MeNTAs via sputtering over a contact-hole array template created in the photoresist. We have used ferrous (stainless steel) and nonferrous (Cu-, Ni-, Al-, and Ti-based) alloys, as well as elemental metals (Cu, Ag, and Au), to form MeNTAs. The proposed nanotubes can be fabricated over a wide range of heights and diameters (from a few hundred nm to 20 µm) in various shapes, including tall cylinders and dishes. In addition, after combining with other nanomaterials (e.g., ZnO nanowires, graphene oxide, or Au nanoparticles), MeNTAs become nanohybrids suitable for many applications. These applications include thermal emitters, triboelectric nanogenerators, SERS-active biosensors, microfluidics, and anti-icing devices.

3:00pm **BI+AS+EM+NS+SE+TF-TuA-3 Low-Cost, Continuous Spectroscopic Monitoring of Chemical and Biological Contamination in Liquids**, ***Liza White***, *C. Howell,* University of Maine

Traditional UV-visible spectroscopic testing of liquids to assess contamination typically involves manual collection and measurement in a dedicated instrument at discreet time intervals. Here, we describe how low-cost, mass-produced diffraction gratings can be used to approach the functionality of traditional UV-visible spectroscopic readouts under continuous flow conditions. We designed and built a flow chamber setup that permitted uninterrupted monitoring of the diffraction pattern as water with different contaminants was passed over it. Various chemical dyes as well as biological contaminants such as bacteria and algae at varying concentrations in water were tested using standard LEDs as a light source. Information was extracted from the diffraction patterns by analyzing changes in the transmitted wavelengths as well as changes in scattering. Our results showed that the system permitted reasonable detection of each of the contaminants tested within a subset of the concentration range of a standard UV-vis instrument. Tests using the toxic dye methylene blue showed accurate detection well below the toxic limit (5 µg/mL), although the limit of detection for *E. coli* was higher at ~10^7 cells/mL. Our results demonstrate how mass-produced diffraction gratings can be used as low-cost detection systems for the continuous detection of contamination in liquids, opening the door for autonomous monitoring for a range of different applications.

3:20pm **BI+AS+EM+NS+SE+TF-TuA-4 Clickable Cerium Oxide Nanoparticles with Gadolinium Integration for Multimodal Micro- and Macroscopic Targeted Biomedical Imaging**, ***Anna du Rietz***, *C. Brommesson, K. Roberg, Z. Hu, K. Uvdal,* Linköping University, Sweden

Multimodal and easily modified nanoparticles enable targeted biomedical imaging at both the macro- and micro level. Computed tomography and magnetic resonance imaging are biomedical imaging techniques used daily in clinical practice all over the world. These non-invasive techniques can identify more medical conditions if contrast and sensitivity are increased. Commonly, targeted imaging is realized by conjugating biomolecular recognition elements such as antibodies to the contrast agent.

Herein, we present a clickable nanoparticle of our own design, consisting of a Cerium oxide nanoparticle core with integrated Gadolinium, coated with polyacrylic acid and functionalized with both a clickable moiety and a fluorophore. Click chemistry is a versatile toolbox of conjugation reactions that can be performed under gentle conditions enabling facile tailoring of the nanoparticles. Results from XRD and TEM studies clearly show that the cores are mono-crystalline and approximately 2 nm in diameter, the hydrodynamic radius of <5 nm is measured by DLS. The soft coat of the nanoparticles is characterized by IR spectroscopy as well as zeta potential measurements. We have verified the presence of azide-groups on the finished particles and the carboxylic groups of polyacrylic acid are firmly bound to the nanoparticle core. The nanoparticles have high colloidal stability even in physiological ionic strength environments with a zeta potential of -48 mV. We have proven direct anchoring of monoclonal antibody cetuximab to the nanoparticles enabling targeting of epidermal growth factor receptor, a common target in many cancer types. Fluorescence spectroscopy and relaxivity measurements were used to evaluate and optimize the properties for future imaging applications of tumors. The nanoparticles provide high MRI contrast with a T_1 relaxivity of 42 $s^{-1}mM^{-1}$ Gd, more than two times higher than currently used contrast agents. The finished antibody functionalized nanoparticles are efficiently purified using size exclusion chromatography, separating them from unbound nanoparticles and antibodies. Finally, the cellular uptake of the nanoparticles was evaluated using fluorescence microscopy as well as live/dead assays. We show that the nanoparticles are taken up by cell lines of head- and neck squamous cell carcinoma, in a lysosomal pattern. The nanoparticles are visualized at the nm scale inside the lysosomes using TEM. In conclusion, we have designed and synthesized a versatile nanoparticle with functionalized capping that enables facile fabrication of tailored nanoprobes for biomedical imaging.

4:20pm **BI+AS+EM+NS+SE+TF-TuA-7 Molecularly Imprinted Polymers (MIPs): Rising and Versatile Key Elements in Bioanalytics**, *J. Völkle, A. Feldner,* Center for Electrochemical Surface Technology, Wiener Neustadt, Austria; *P. Lieberzeit,* University of Vienna, Faculty for Chemistry, Department of Physical Chemistry, Vienna, Austria; ***Philipp Fruhmann***, Center for Electrochemical Surface Technology, Wiener Neustadt, Austria **INVITED**

Molecularly imprinted polymers (MIPs) are specific materials with tailored binding cavities complementary to a specific target molecule. Although the first example of artificial materials with molecular recognition were already described 80 years ago, they experienced a surge of popularity since the late 1990s due to improved synthetic methods and their great potential as recognition element in (biomimetic) sensors. MIPs can achieve similar selectivity and sensitivity as antibodies[1], while their robustness and stability is superior compared to biomolecules. They can also be used under non-physiological conditions, are suitable for long-term storage and accessed by scalable synthetic methods. These properties make them highly promising

[1] **AVS Nellie Yeoh Whetten Awardee**

candidates for a wide range of applications, from biomimetic receptor layers to nanomaterials or artificial antibodies.

Despite this versatility, their design and optimization towards a specific analyte is probably the most challenging task in the development of a sensor. In general, MIP based sensors either rely on electrochemical, mass sensitive or optical transducers and are commonly used as thin film or nanoparticle (nanoMIP). While there is a considerable amount of literature on electrochemical sensors with MIPs available, new developments such as the improvement of conductive MIPs[2], optimized epitope imprinting[3], or the development of novel synthetic techniques such as the solid-phase synthesis of nanoMIPs[4] are highly important for the further development of MIPs in sensing.

For this reason, this presentation will provide an overview about different MIP types, their synthesis, application, and challenges. Furthermore, their potential in future applications with be addressed to give a wholistic impression of the numerous possibilities of this versatile compound class.

References

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[2]Feldner, A., et al., Conductive Molecularly Imprinted Polymers (cMIPs): Rising and Versatile Key Elements in Chemical Sensing, *Submitted to Chemosensors (in Revision)*, **2023**

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#equal contribution

5:00pm **BI+AS+EM+NS+SE+TF-TuA-9 X-ray Fluorescence Analysis of Metal Containing Cytostatics in HeLa Cells using the Ultra-compact Cryo-vacuum Chamber µ-HORST***, **Lejla Jusufagic**, C. Rumancev, A. Rosenhahn, A. Steinbrück, N. Metzler-Nolte,* Ruhr-University Bochum, Germany

Synchrotron-based X-ray fluorescence spectroscopy (XRF) is an excellent method for investigating elemental distributions and metal concentrations in biological systems.[1-4] The method provides a high sensitivity down to the detection of trace elements with high spatial resolution and penetration depth.[3,4] We introduced an ultra-compact cryogenic vacuum chamber called "µ-HORST" at the P06 nanoprobe beamline at PETRA III, DESY to measure 2D-XRF elemental distribution maps and concentrations in cryogenically fixated cells treated with cytostatic metal complexes with varying ligand sphere.[1,2] The cells are grown on silicon nitride membranes and treated with a 10 µM solution of the metal complexes for different durations and all physiological processes were stopped by rapid cryo-fixation. Cryogenic fixation is a non-destructive method that keeps the cells as close as possible to their biologically hydrated state. The frozen cell samples can be transferred into the µ-HORST setup and maintained in a frozen state throughout the nano-XRF measurements. The acquired data show that the concentration of the metal complexes and their intracellular location can be correlated to the one of physiologically relevant ions such as potassium and zinc as well as associated changes in the metal homeostasis. The developed chamber can not only be used for the analysis of intracellular cytostatic metal complexes, but also to the accumulation of antimicrobial metal complexes or of anthropogenic metals in environmental samples.

References

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5:20pm **BI+AS+EM+NS+SE+TF-TuA-10 Hemocompatibility Analysis of Novel Bioinspired Coating***, **AnneMarie Hasbrook**, R. Faase, M. Hummel, J. Baio,* Oregon State University

Surface-induced thrombosis is a critical concern in medical device development. To minimize thrombosis, current extracorporeal circulation units require systemic anticoagulation. However, systemic anticoagulants can cause adverse effects such as thrombocytopenia, hypertriglyceridemia, and hyperkalemia. To address this issue, we combine the technology of polydopamine (PDA) functionalization with slippery liquid infused porous surfaces (SLIPS) to potentially enhance the biocompatibility of medical devices. PDA readily coats a wide variety of surfaces and can be functionalized with a thiolated fluoropolymer, via Michael Addition, to form a pseudo self-assembled monolayer (pSAM) which serves as the porous surface component of SLIPS. Liquid perfluorodecalin can then be added to complete the SLIPS coating. We hypothesized that the PDA SLIPS coating provides enhanced hemocompatibility due to its omniphobic properties and composition of compounds currently used in medical applications. Surface modifications were confirmed using contact angle and X-ray photoelectron spectroscopy (XPS) which revealed significant changes to the surface chemistry after the addition of each subsequent layer of PDA SLIPS. The coatings were evaluated for thrombogenicity via quantification of Factor XII (FXII) activation under static and dynamic settings, fibrin formation, platelet adhesion, and clot morphology. The PDA SLIPS coating activated 50% less FXII than glass and 100% more FXII than bovine serum albumin (BSA) coated substrates. PDA SLIPS had similar plasma clotting time to BSA and plasma clotted two times slower on PDA SLIPS than on glass. Platelet adhesion was increased two-fold on SLIPS compared to BSA and decreased two-fold on SLIPS compared to glass. PDA SLIPS had approximately 20% higher fiber diameter and 25% lower clot density than glass and was significantly different in fiber diameter and density than BSA.

5:40pm **BI+AS+EM+NS+SE+TF-TuA-11 Signal Enhancement for Gravimetric Biomimetic Detection – Conjugation of Molecularly Imprinted Polymer Nanoparticles to Metal Nanoparticles***, **Julia Völkle**,* CEST GmbH, University of Vienna, Austria*; A. Weiß, P. Lieberzeit,* University of Vienna, Austria*; P. Fruhmann,* CEST GmbH, Austria

Over the past decades, the field of biosensors and -diagnostics has been increasingly dominated by a growing demand for non-centralized point-of-care devices that do not rely on extensive laboratory infrastructure and trained personnel. Recently, the COVID-19 pandemic has emphasized the crucial role of such fast, reliable, and affordable diagnostic tools. Novel, tailor-made nanomaterials are considered a key component for tackling the upcoming challenges of miniaturization and cost-efficiency in the field of biosensing.

One emerging class of such biomimetic nanomaterials are molecularly imprinted polymer nanoparticles (nanoMIPs). nanoMIPs are artificial receptors that can mimic the highly selective binding capabilities of biological recognition units, such as antibodies and enzymes. Unlike their natural counterparts however, they are stable under a wide range of non-physiological conditions, suitable for long-term storage, and can be derived from a straightforward, rapid synthesis procedure without the need for cell culturing or animal experimentation. Thus, they are ideal candidates for the development of sensitive, robust and inexpensive bioanalogous sensors.

While impressive results regarding their high selectivity and low non-specific binding have been reported [1], nanoMIP-based gravimetric (quartz crystal microbalance, QCM) assays are restricted with regards to the achievable limit of detection by their comparatively low overall mass. This project therefore is focused on the synthesis of well-defined nanoMIP-metal nanoparticle (NP) conjugates, which would result in a larger change in mass upon binding of the recognition units to the QCM transducer. Moreover, conjugation to gold-NPs would allow the incorporation of nanoMIPs into other analytical techniques such as lateral flow devices (LFDs). Experiments therefore are focused on the incorporation of suitable functional groups for further conjugation into the nanoMIP polymer network, the surface functionalization of metal NPs with complementary linker moieties and a suitable coupling procedure. In the poster, nanoMIPs selective for various biologically relevant species are coupled to metal NPs and the performance of the conjugates in QCM-based detection is presented in detail and discussed.

[1] Park, et al. „Recent Advances of Point-of-Care Devices Integrated with Molecularly Imprinted Polymers-Based Biosensors: From Biomolecule Sensing Design to Intraoral Fluid Testing". Biosensors 12, Nr. 3 (22. Februar 2022): 136. https://doi.org/10.3390/bios12030136.

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