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IEEE Seminar **IEEE Nanotechnology council UK & Ireland section**

4th August 2022 ***15:00 – 16:00 BST***

Title: Plasmonic Nanogap-enhanced Single-molecule Raman Spectroscopy: Towards Single-protein Raman Sequencing

Lecturer: Prof. Jian-An Huang

Abstract:

Proteins are the workhorses in biological systems that can be used to characterize cellular functions and progress of diseases as biomarkers. The fact that proteins cannot be amplified results in a serious lag of proteomics behind genomics and transcriptomics, hampering not only mechanistic studies but also clinical applications. The state-of-the-art single-molecule sequencing technologies towards protein sequencing include label-based fluorescence methods and label-free nanopore resistant pulse sensors. Compared to DNA, proteins are folded 3-dimentional structures and consist of 20 proteinogenic amino acids with different charges. These features limit these single-molecule sequencing methods to sequencing only single peptides, because they can detect 4 at maximum of the 20 proteinogenic amino acid residues comprising the primary sequence of a protein.

In this talk, I will present recent work in my group on a plasmonic nanogap sensor [1] that has demonstrated single-molecule Raman detection of all 20 proteinogenic amino acids [2]. In fact, each amino acid molecules have their own fingerprint Raman scattering signals that can be used for sequencing. But the Raman signals of single amino acids were too weak to be detected even by surface-enhanced Raman spectroscopy (SERS). In the tremendous amount of literature of SERS-based protein detections in past decades, the SERS spectra of proteins are mostly occupied by SERS signals of aromatic amino acids and backbones, while those of non-aromatic amino acids are invisible. By generating single plasmonic hot spot in the nanogap, our work demonstrated detecting single aromatic and non-aromatic amino acid residues within single peptides[3]. Our results suggest that the signal dominance due to large spatial occupancy of aromatic rings of the peptide sidechains can be overcome by the high localization of the single hot spot. Our works have paved a ground-breaking way to nanogap-enhanced Raman sequencing of single proteins.

Reference:

1 Huang, J.-A. *et al.* SERS discrimination of single DNA bases in single oligonucleotides by electro-plasmonic trapping. *Nature Communications* **10**, 5321 (2019). https://doi.org:10.1038/s41467-019-13242-x

2 Zhao, Y. Q., Iarossi, M., De Fazio, A. F., Huang, J. A. & De Angelis, F. Label-Free Optical Analysis of Biomolecules in Solid-State Nanopores: Toward Single-Molecule Protein Sequencing. *Acs Photonics* **9**, 730-742 (2022). https://doi.org:10.1021/acsphotonics.1c01825

3 Huang, J.-A. *et al.* Multiplexed Discrimination of Single Amino Acid Residues in Polypeptides in a Single SERS Hot Spot. *Angewandte Chemie International Edition* **59**, 11423-11431 (2020). https://doi.org:10.1002/anie.202000489

Bio: Jian-An Huang is an tenure-track assistant professor and a group leader of the Jianan lab of Nanophotonic Biosensors in University of Oulu. He received a Ph.D. degree on reproducible surface-enhanced Raman spectroscopy biosensors from City University of Hong Kong, and worked as a postdoctoral fellow on scanning near-field optical microscopy and low-dimentional semiconductor photodetectors at University of Hong Kong and then on plasmonic nanotechnologies at Italian Institute of Technology. His group combines plasmonic nanostructures (nanotube, nanopore, nanopillar) with molecular manipulation methods for single-cell, single-particle and single-molecule biosensing toward digital healthcare and personalized medicine.

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