SEMS: RESEARCH PROJECT DESCRIPTION

1. Project Background and Description

Stretching the boundaries of bioelectrochemical imaging: Development of porous semiconducting electrodes for 3D live-cell photoelectrochemical imaging

We have been working with an AC-photocurrent imaging technique at electrolyte-insulator-semiconductor structures called light-addressable potentiometric sensors (LAPS), achieving a resolution of 800 nm. Recently, we have shown that electrolyte-semiconductor structures without an insulator are suitable for AC-photocurrent imaging of the local impedance and pH [1]. The AC-photocurrents at these structures feature redox currents caused by the oxidation of hydroxide ions in addition to the depletion layer charging currents observed in LAPS, resulting in a light-addressable electrochemical sensor (LAES) that is strongly sensitive to the negative surface charge of living cells [2]. We have tested a number of different semiconductor materials for this application to maximize sensitivity and biocompatibility. Promising preliminary results have been achieved with hematite and, more recently, with organic-inorganic hybrid materials.

Currently, LAES imaging is limited to the measurement in 2D cell culture. In this project, photosensitive organic-inorganic hybrid materials will be developed into porous scaffolds for 3D live cell photoelectrochemical imaging. This will allow application of LAES for functional, label-free imaging in 3D cell culture on organ-on-a-chip devices for the investigation of physiological cell signaling processes.

[1] De-Wen Zhang, Fan Wu, Steffi Krause, Analytical Chemistry, 89 (2017) 8129-8133, http://dx.doi.org/10.1021/acs.analchem.7b01898

[2] Fan Wu, Bo Zhou, Jian Wang, Muchun Zhong, Anirban Das, Michael Watkinson, Karin Hing, De-Wen Zhang*, and Steffi Krause*, Analytical Chemistry 91 (2019) 5896-5903; https://doi.org/10.1021/acs.analchem.9b00304

2. Project Scope

Objective 1. Development of a 2D flexible, light-addressable organic semiconductor electrode: The proposed architecture will be based on an inorganic-organic hybrid using known biocompatible semiconductor materials as a starting point, e.g. PEDOT:PSS as the organic phase. The substrate will be optimized for LAES sensitivity and spatial resolution by tuning the morphology of the organic semiconductor and using a two-photon effect for illumination. Induced pluripotent stem cell derived cardiomyocytes will be cultured on the sensor surfaces and imaged with photocurrent measurements.

Objective 2. Construction of 3D organic semiconductor/electrode architecture and cardiomyocyte culture: 3D organic semiconductor/electrode porous scaffolds will be constructed by ice templating with the optimal blend ratio from objective 1, followed by cell culture inside this 3D architecture. 3D imaging will be applied in the assessment of functional and structural features of 3D micro-topographic substrates and cultured engineered heart tissue. Using these techniques, dynamic changes to cells in 3D microenvironments can be non-destructively assessed repeatedly over time.

Objective 3. Investigation of physiological and pathological mechanisms of cardiomyocytes via 3D photoelectrochemical imaging: The heart is coordinated to contract in a concerted rhythm by a complex network of cardiomyocytes with electrical and mechanical coupling. During the cardiomyocyte contraction cycle an influx of sodium lead to the depolarization of the membrane, which then opens up voltage gated calcium channels. The calcium binds to ryanodine receptors, leading to further calcium release from the sarcoplasmic reticulum and sarcomeric contraction, followed by removal of the Ca^{2+} into the sarcoplasmic reticulum and out of the cell via the sodium-calcium exchanger pump. Contractile dysfunction arises as a consequence of disruption in the sequence of electro-mechanical coupling. Cardiomyocyte homeostasis and contractile function will be assessed by monitoring the ion transients (K^+, Ca^{2+}, Na^+), action potentials and simultaneous macroscale contractility.

3. Desired Skills from the Student

The student should have a strong background in chemistry or materials science. The student should be interested in gaining skills in photoelectrochemical imaging, materials characterization techniques such as XRD, AFM, SEM and XPS, cell and tissue culture, organ-on-chip-devices and the investigation of cell physiological processes.

4. Supervisory Team

Professor Steffi Krause is a Professor of Electroanalytical Systems and an expert in photoelectrochemical imaging and biosensors. https://www.sems.qmul.ac.uk/staff/s.krause

Dr Oliver Fenwick is a Royal Society University Research Fellow and an expert in developing materials for organic electronic and bioelectronic applications. https://www.sems.qmul.ac.uk/staff/o.fenwick

Dr Thomas Iskratsch is a Senior Lecturer in Bioengineering and an expert in cardiovascular mechanobiology. https://www.sems.qmul.ac.uk/staff/t.iskratsch