Single Cell Apoptosis Monitoring with SPRm Impedance

Electrochemical impedance spectroscopy (EIS) technique consists in introducing a perturbation into the sample by means of an AC voltage to an electrode and detecting its current response. This technique is commonly used in material science for corrosion studies but its use in biological applications have grown rapidly and this technique is now used to monitor cell adhesion, growth, differentiation and death.[1]

Despite the power of EIS, it lacks to provide spatial information which is essential to study the structure of the cells. SPR microscopy (SPRm) Impedance is a technology that provides high spatial resolution via SPR imaging while also measuring EIS. It is based on the fact that plasmon excitation at the surface of a metal film is sensitive to the surface change of the film. As shown in Fig 1, an oscillating (AC) potential is applied to the gold coated sensor film (WE) via a potentiostat and the potential of the sensor surface is controlled with respect to a reference electrode (RE) and a counter electrode (CE). The detector provides the SPR image and the impedance image maps local variations in the dielectric and conductive properties which in turn reflect changes in the cellular structure.[2]

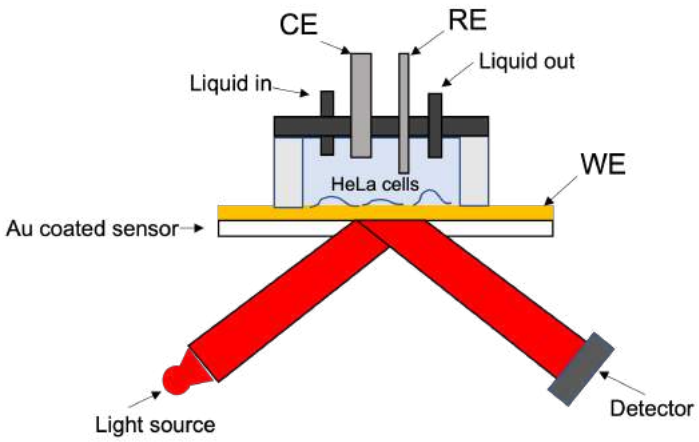

Fig 1 Schematic illustration of SPRm Impedance

Researchers at Arizona State University used this SPRm Impedance configuration to record a sequence of apoptotic events in SiHa cells by the treatment with MG132 (molecule that inhibits the proteosome) and TRAIL (tumor necrosis factor-related apoptosis inducing ligand).[3] Exposure to these chemicals induced cellular shrinking, fragmentation, formation of blebs at the plasma membrane and finally, the disintegration of the cells into several membrane-bound apoptotic bodies. Fig 2 shows the simultaneous bright field (a), SPRm (b) and Impedance (c) images of the cells at time 0, 30 min and 75 min after apoptosis treatment. The SPRm image shows a decrease of signal near the center of the cell, reflecting detachment from the surface.

The impedance image shows a rapid change in the nucleus region as well, however, the bright field image does not indicate the apoptosis process.

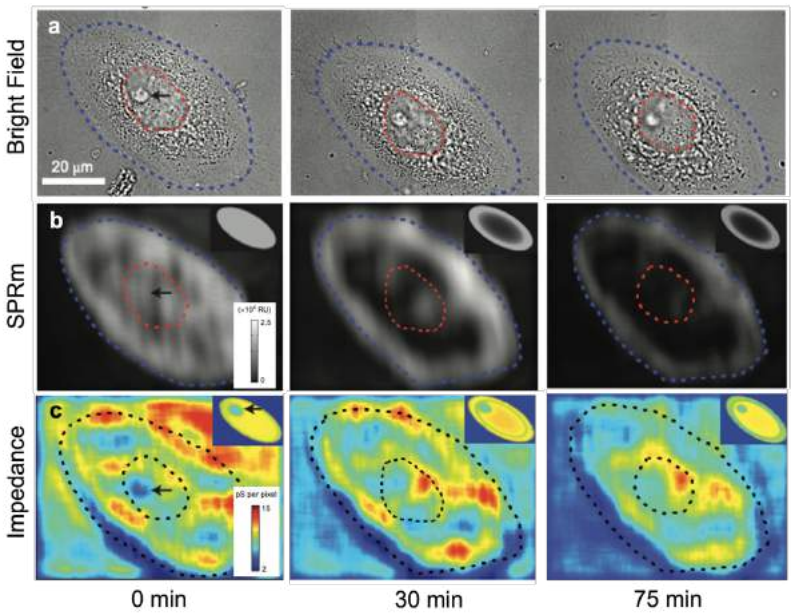

Fig 2 Bright field (a), SPRm (b) and impedance (c) images of a single SiHa cell after apoptosis treatment. Outer dashed circles outline the cell and inner dashed circles indicate the cell nucleus. Insets in b and c show simulated SPRm and impedance images.

This study was extended to compare the responses of different cells on the same chip. It was noted that the impedance responses of the cells decrease over time, but they occur at different rates, reflecting heterogeneity of cell apoptosis. Decreases of the impedance and SPRm signal of the cells are mainly due to the cell detachment from the sensor surface.

SPRm Impedance is a label-free with high spatial and temporal resolutions which provides the sub-cellular responses due to local conductivity and dielectric responses on individual cells. In addition to this cellular application, SPRm Impedance has been used to study electroporation, a process that has been used to introduce DNA and drugs into cells[3] and to detect ligand binding kinetics of GPCRs with a self-assembled virion-oscillator microarray detection.[4]

[1] Katarzyna Krukiewicz, Electrochemistry Communications 2020, 116, 106742
[2] Biosensing Instrument Technical note 107 Basic Principles of SPRm Impedance
[3] Wei Wang et al, Nat Chem 2011, 3, 249–255
[4] Guangzhong Ma et al, J Am Chem Soc. 2018 Sep 12;140(36):11495-11501