

High content label free assessment of single cell dynamics based on electrically modulated microscopy assays

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Whether bacterial or mammalian, quantitation of single cell dynamics is a prerequisite for challenging cell based biosensing applications, ranging from identification of cell persisters to assessment of cytopathic effects.

We present a multimodal, label free, high spatial resolution and low temporal noise functional imaging instrument enabling high resolution optical and electrical impedance mapping - the latter beyond the limitations of standard electrode-based technologies (surface or scanning ones). It exploits the electrical modulation of the refractive index of a tailored (sensing) interfaces, via an externally applied AC voltage to provide label free contrast of the local impedances and surface charge densities. This enables high content label free assessment of single cells capable to provide electrical, morphological and structural properties of relevant cellular structures dynamics. As recently demonstrated, the concept can be integrated with quantitative phase microscopy [1] or reflected light microscopy [2] and grounds an even wider range of electrically-modulated optical assays for measuring the electric field locally, and achieve electro-optical maps with high spatial and temporal resolutions.

We demonstrate high resolution electro-optical mapping of biosystems and biointerfaces for analyzing at single cell level, both eukaryotic and prokaryotic (bacterial) cells. In particular, the use of the label free, real time features of the reflected-light microscopy of the cellular structures in the vicinity of an electrified interface is thoroughly addressed with assessment of the dynamic cell response to model stimulus (a last resort antibiotic) as a case study.

The virtues and challenges of the novel opto-electrochemical method as an enabling tool to monitor intracellular trafficking and impedance contrasts in living cells are highlighted, together with proof of concepts of bacterial assessment and cytopathic effect evaluation of relevance for viral infection.

The unique detection characteristics of this so called DynaScope are essential for applications in the fields of cell signalling, drug screening and hazard evaluation.

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1. Polonschii C., *et al.*, High resolution impedance mapping using electrically-activated quantitative phase imaging, *LSA* (2021) 10:20 www.nature.com/articles/s41377-020-00461-x
2. Munteanu R.E., *et al.*, “High spatial resolution electrochemical biosensing using reflected light microscopy”, *Scientific Reports* (2019), 9:15196