

Monitoring of Cellular Spatiotemporal Dynamics via Machine Learning-Enhanced Electrical Impedance Spectroscopy

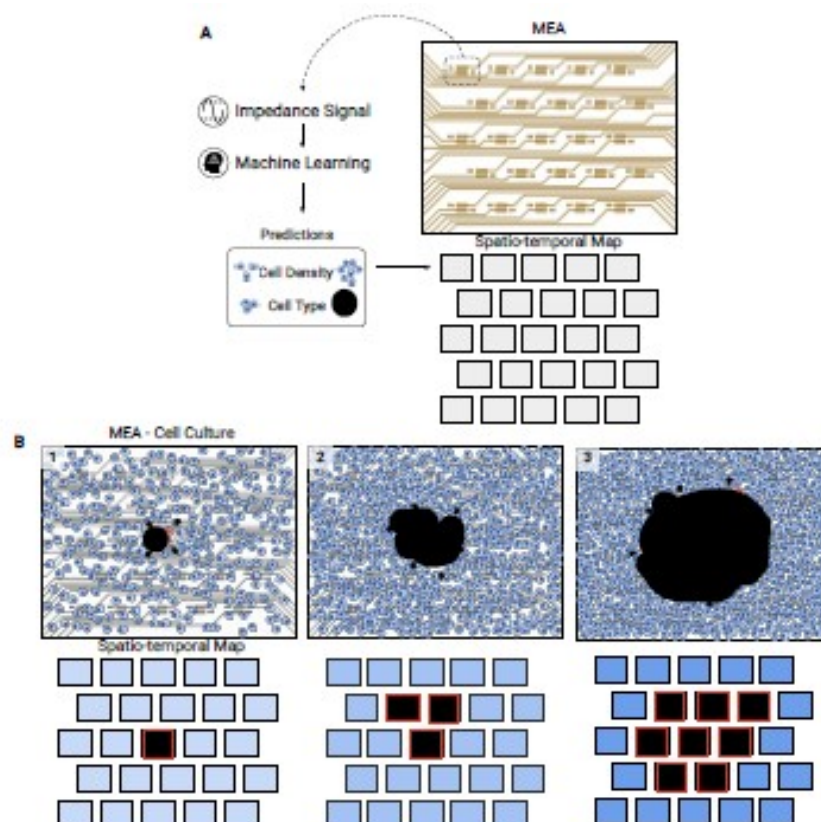
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Monitoring cellular spatiotemporal dynamics is essential for understanding a broad array of complex biological processes such as organ development during embryogenesis, cellular migration during wound healing, and cellular invasion during cancer progression. Using live-cell fluorescence microscopy to track cellular dynamics is often limited by dye-induced cytotoxicity and cellular photodamage. The goal of the present study is to demonstrate that a platform combining a microelectrode array (MEA), electrical impedance spectroscopy (EIS), and machine learning (ML), as schematically depicted in the figure below, enables real-time monitoring of cellular spatiotemporal dynamics in a noninvasive and label-free manner.

The platform is applied to normal and cancerous breast epithelial cells in either mono- or co-culture, correlating EIS measurements with cell growth parameters obtained from automated microscopy image analysis. An ML model is implemented to accurately predict the spatiotemporal evolution of cell density and size and to classify the different cell types based solely on EIS recordings. The technology is also shown to be capable of tracking pertinent biological processes including spatial heterogeneities in cell proliferation patterns and cell competition in co-culture.



Schematic of the methodology to non-invasively monitor cell spatiotemporal dynamics.

(A) An impedance signal is measured at each electrode pair position on the MEA. The signal is processed by a ML model to predict key parameters such as cell density, cell size, and cell type. The information is then used to construct a spatiotemporal map. (B) The system can monitor spatiotemporal patterns of cellular proliferation as well as competition between different cell types. Panels (1-3) correspond to different time points.