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Monitoring Cellular Spatiotemporal Dynamics through Machine Learning-Enhanced Multi-Electrode Impedance Spectroscopy

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Our research aims to understand the dynamic spatiotemporal organization of cell mixtures—a critical factor influencing tissue development, tissue regeneration, size control, and cancer progression [1]. Traditional techniques, notably live-cell fluorescence microscopy, present limitations such as cell dye toxicity and exposure to photo damage. To address this, we propose a cost-effective and label-free alternative utilizing a micro-electrode array (MEA) and impedance spectroscopy (IS) to monitor different cell types in space and time.

Impedance spectroscopy (IS), a technique established in material studies, is now finding its place in biomedical applications [2]. Cellular membrane properties and conductivity changes contribute to distinct impedance signals as a cell population develops [3]. Our platform is the first to offer spatial and temporal monitoring with a wide-frequency range, advancing prior work on impedance spectroscopy in cell cultures.

The sensing platform is microfabricated to create a 25-electrode pair array, isolated and coated for optimal cellular adhesion. We conduct measurements on healthy (MCF10A) and cancerous (MCF7) breast epithelial cells, initially seeded in single-cell monolayers and later in co-culture formations. Our experimental design involves seeding cells on the device, capturing images, and correlating impedance measurements. Machine learning algorithms assist in deciphering the electrical characteristics of impedance signals, while image segmentation software evaluates cellular confluency and density.

The results demonstrate robust relationships between impedance signals and cell density and confluency values. We observe differences in the healthy and cancerous growth dynamics as well as monolayer formation. We train machine learning models to facilitate the monitoring of these changes and provide rapid cell density estimations. Furthermore, we successfully classify different cell types, highlighting the technology's ability to discern healthy from cancerous cell lines. Our ongoing studies include co-culture experiments, where mixed cellular populations undergo spatial and temporal monitoring, allowing us to explore the dynamics of cancer progression using the developed sensing technology.

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[2] Stupin, D. D., Kuzina, E. A., Abelit, A. A et al. (2021). *ACS Biomaterials Science & Engineering* 7, 1962-1986. doi.org/10.1021/acsbiomaterials.0c01570

[3] Voiculescu, I., Li, F., and Nordin, A. N. (2021). *IEEE Sensors Council* 21, 5612–5627. doi.org/10.1109/JSEN.2020.3041708