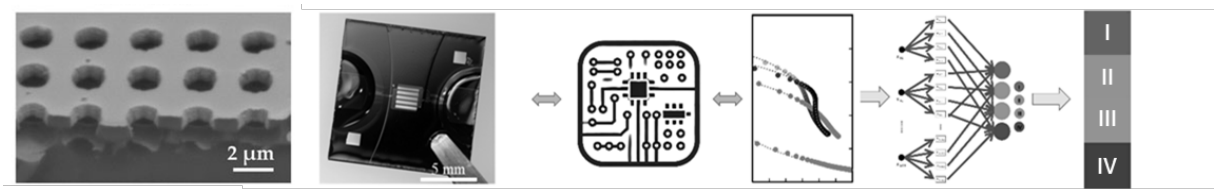
Smart Membrane: An On-Chip Cell Sensor for Monitoring Barrier Tissue Supported by an Artificial Neural Network

Bo Tang[1,2]; V. Krajka[1,2]; M. Liu[3]; W. Zhao[1]; S. Reichl[2,4]; A. Dietzel[1,2]

[1]Institute of Microtechnology, Technische Universität Brauschweig, Brauschweig (Germany)
[2]Center of Pharmaceutical Engineering (PVZ), Technische Universität Braunschweig, Braunschweig (Germany)
[3]Institute of Pharmaceutical Technology and Biopharmaceutics, Technische Universität Braunschweig, Braunschweig (Germany)
[4]German Research Center for Artificial Intelligence (DFKI), Kaiserslautern (Germany)
b.tang@tu-braunschweig.de, v.krajka@tu-braunschweig.de

The conventional transepithelial electrical resistance (TEER) technique only yields a single value for assessing cell layers and often requires off-incubator microscopy to reveal further details. Here, we present an electrical cell sensor platform that uses a smart nanoporous membrane for continuous electrical cell-substrate impedance sensing (ECIS). The device features an ultrathin, ultra-low-stress 700 nm Si_xN_y membrane that is monolithically integrated at the wafer-level into an organ on chip system which is sealed with a glass lid (Fig. 1) [1]. Coplanar electrodes interface with custom electronics for impedance measurement under sinusoidal excitation.
Human umbilical vein endothelial cells (HUVECs) were seeded and monitored via impedance spectra, which were corroborated by bright-field and fluorescence microscopy. Nyquist plots captured distinct stages of cell development. We trained a 1D convolutional neural network (Conv1d) to classify the phases of adhesion, spreading, monolayer formation, and barrier maturation. Model validation was achieved through pharmacological perturbation using PN159 and BAC, with >95% confidence in detecting reversible and irreversible barrier disruption. We benchmarked our sensor against conventional immunostaining for tight junction markers and demonstrated substantially higher sensitivity, enabling real-time and non-invasive detection of barrier dynamics.
To contextualize the impedance data, the ECIS spectra and phase descriptions were vectorized using OpenAI's semantic embeddings. A secondary Conv1d then projected both sets of data into a shared latent space, enabling a large language model (LLM) to generate descriptive interpretations of cell states directly from the ECIS data.
This approach allows for the non-invasive and automated monitoring of barrier dynamics in barrier-on-chip systems, eliminating the need for microscopy and endpoint assays. Integrating LLMs also supports intelligent, automated experimental reporting. We envisage its wide applicability in organ-on-chip platforms for real-time physiological and pathological studies.



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References:

[1] B.Tang., S. Bendas, V. Krajka, et al., *Frontiers in Sensors* 3 (2022)