Live-Cell Analysis Devices (LCAD) for Delivery and Sampling of Biomolecules

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Cell analysis and manipulation with significant implications in cell engineering and fundamental cell biology research require microfluidics devices capable of performing localized-electroporation induced delivery or sampling. We demonstrate a modular microfluidic chip, the live-cell analysis device (LCAD), in which the delivery and sampling functionalities are integrated in a single multilayer chip that utilizes localized electroporation to create pores in the cell membrane of cells seeded in an array of microwells.[1] The device architecture consists of several layers: a PDMS microfluidic channel layer used for cell seeding and introduction of media and reagents, an array of through-hole PDMS culture wells used to isolate small populations of cells, a nanochannel polycarbonate (PC) membrane for confining the electric field during pulse application, and a PDMS reaction-well layer used to load delivery reagents and isolate sampled molecules. To enhance the electroporation performance of high-porosity membranes, an additional gold electrode layer was introduced in the structure. To embed the metal electrodes in the LCAD, we developed an assembly protocol using self-assembled monolayer chemistries to reliably bond gold with PDMS.
We explored the design and experimental parameters and characterized their effect on system performance. By utilizing the LCAD, we demonstrated delivery of functional molecules at multiple-time-points and tracked their fluorescence. Moreover, we observed an enhancement in sampling with an improved well-to-well uniformity. Overall, the LCAD is a versatile platform with advantageous capabilities for analysis and manipulation of various cell types.

[1] C.A Patino, P. Mukherjee, E.J. Berns, E. Hakim Moully, L. Stan, M. Mrksich, H.D. Espinosa, *High-Throughput Microfluidics Platform for Intracellular Delivery and Sampling of Biomolecules from Live Cells*, ACS Nano **16**, 7937 (2022)