Microfluidic Cell-Based Analysis

The focus of this project is the development of biomimetic microenvironments for improved cell culture and analysis. Microfluidic systems mimic the characteristic length dimensions and flow behaviors of in vivo capillary networks, exhibit similarly high surface area to volume ratios, and ultimately demonstrate great potential to modernize cell culture protocols that have remained largely unchanged for several decades. We have developed surface treatments that facilitate cellular attachment to and growth across various substrates, allowing us to merge our microfluidic fabrication expertise with cell culture protocols. We have also developed microelectronic strategies for immobilizing cells in discrete regions within the microenvironment. Focused by our collaborations with the National Institutes of Health (NIH), this work is directed toward mammalian neural cell culture due to the large health care impact of neurodegenerative disease and the profound difficulties in culturing neuronal cell populations. However, the strategies developed here are expected to become generic tools that are applicable to a wide variety of studies with various cell types.

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The purpose of this research is to develop strategies and tools for utilizing microfluidic systems for cellular analysis that improve conventional techniques through better environmental control while decreasing reagent consumption and analysis time. Neuronal cells are particularly fragile, are finicky about conditions under which they grow, and can be difficult to culture and study. We have developed two approaches for culturing healthy neuronal cells in specific patterns using microfluidic systems to guide their growth and proliferation. In the first approach, polyelectrolyte multilayer (PEM) surface coatings were deposited and patterned using microfluidics, and were utilized to render surfaces amenable to the direct surface attachment of mammalian neuronal cells and growth of neuronal projections. It was determined that neuronal cells grown on specific PEM coatings in a microfluidic environment were viable and healthy. Also, direct attachment of neuronal cell bodies to the treated surface was observed without any additional cellular supporting layers that are often needed in neuronal cell culture, as shown in Figure 1. Additionally, two different techniques, optical trapping and AC dielectrophoresis (DEP), were utilized to precisely position neural cells inside microfluidic systems for further study and manipulation as shown in Figure 2. When dielectrophoresis was combined with PEM surface treatment, rapid and persistent healthy neuronal cell arrays were produced.

Figure 1: ***Micropatterned PEMs on polydimethylsiloxane (PDMS) substrates. Monodispersed cell cultures are shown at two (A) and three (B) days after plating on a micropatterned surface. The bottom of each image as well as the 20 µm wide vertical line are PEMs-treated surfaces patterned using microfluidics. Cellular projections are confined along the narrow PEMs line (a) and by the edge of the PEMs surface treatment (b-c). Projections across the untreated PDMS surface were linear (d) and only extended between PEMs-treated regions.***

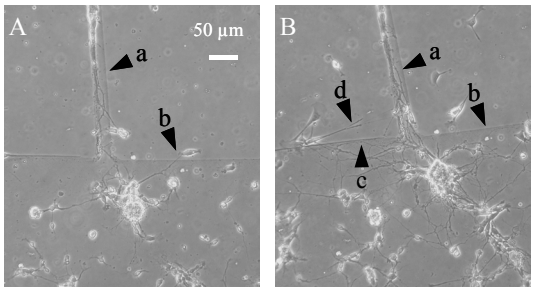
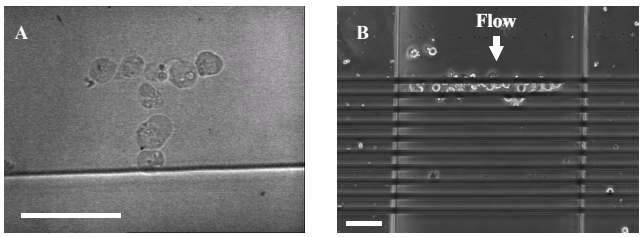


Figure 2: ***Optical (A) or dielectrophoretic (B) traps were used to immobilize cells in ordered arrays within the microenvironment. For optical trapping, suspended neural cells were manipulated individually several centimeters through stagnant microfluidic channels and positioned in an ordered "T" array. AC dielectrophoresis (DEP) immobilized neural cells from suspension as they flowed through the microfluidic network. Although all DEP electrodes (black lines) were energized, cells were effectively trapped with just the first few to generate a linear arrangement. Scale bars are 50 µm for both panels.***



The union of microfluidic systems with cell culture and analysis promises huge impacts in fundamental understandings of cellular mechanics, rapid screening of drug targets, and development of accurate models of *in vivo* systems for ADME/Tox (absorption, distribution, metabolism, excretion – toxicology) determinations.

Future Plans: While the strategies developed here will provide the framework for microfluidic cell-based analyses, this effort needs to grow to include various cellular systems as well as co-cultures of different cell types, long-term assays (days or weeks), and three-dimensional cultures in order to better support the medical and pharmaceutical communities in their efforts to make more rapid and precise measurements on cell populations.

Publication:

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