A microfluidics approach to probing filopodial development in neurons

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Key Research Aims and Goals

To investigate the effects of substrate-bound and diffusive guidance cues on the development of dendritic filopodia and spines.

Research Highlights and Results

- We are exploiting the unique properties of polydimethylsiloxane (PDMS) microfluidic devices towards studying early neuronal development. Recently, our group demonstrated the efficacy of solvent-extraction as a PDMS-treatment protocol that enables low-density cultures of primary hippocampal neurons. [[1], Fig. 1a].
- We have used flow manipulations in closed-channel microdevices to generate stable and instructive gradients of substrate-bound cues, such as laminin and poly-L-lysine (PLL), to allow precise control over neuron development and network formation. [[2], Fig. 1b].

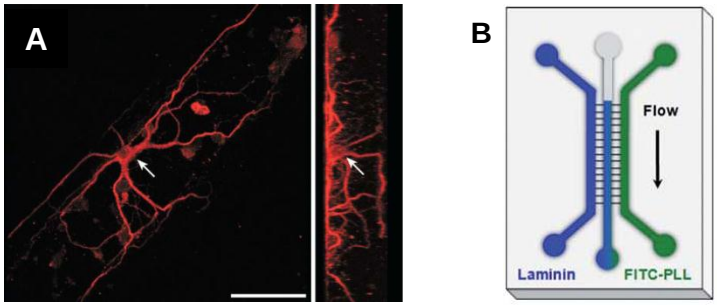

Fig 1 (a) Top-down and side views of a neuron in a microdevice at 8 days *in vitro* [1]. Cell body (arrows) and neurites are labeled with neuronal marker MAP2. Scale bar: 50 µm. (b) Schematic of device design used for generation of substrate gradients. Three primary channels, each 200 µm wide and 45 µm high, communicate through narrow interconnects.

Future Research Plans

- These neuron culture and gradient generation techniques will be used to compartmentalize neuronal dendrites into fluidically isolated channels, in order to selectively stimulate only certain regions of the cell, with a high degree of spatio-temporal control.
- This will enable us to study filopodial dynamics during early neuronal development. We will specifically investigate the effects of substrate-bound cues (e.g., laminin and PLL), diffusive cues (semaphorin3A), chemical stimulation (glutamate) and cell-cell contact and signaling.

[1] Millet L, Stewart M, Sweedler J, Nuzzo R, Gillette M (2007) Microfluidic devices for culturing primary mammalian neurons at low densities. Lab Chip 7, 987-994.
[2] Millet L, Stewart M, Nuzzo R, Gillette M (2010) Guiding neuron development with planar surface gradients of substrate cues deposited using microfluidic devices. Lab Chip 10, 1525-1535.