Focal Chemical Stimulation of Cells with a MEMS Microfluidic Platform

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Focal delivery of chemicals at cellular and sub-cellular resolution provides a means of interfacing with the nervous system beyond electrical stimulation. A new microfluidic platform has been developed for focal delivery of chemicals to cells and tissue. For the first time, fluid intake as well as ejection and passive diffusion are possible. First results of real time focal chemical stimulation of cell cultures are presented.

The basic unit of the platform is a surface micromachined Parylene C microchannel (100 μm x 4 μm x 6 mm) perforated with a single central pore (10 or 20 μm diameter). The device has integrated platinum thermal flow sensors and SU-8 microfluidic interconnects at each end. The Parylene microchannel wall is 2 μm thick, supported by posts, and selectively reinforced with a 75 μm thick layer of SU-8. Custom packaging connects the platform to a gas-tight syringe and a syringe pump controls fluid flow in the microchannel.

Rat pheochromocytoma cells (PC12) were cultured on a device pre-treated with polyethyleneimine (PEI) to promote cell adhesion. Cells were loaded with fluo-4, a fluorescent Ca^{2+} indicator dye, and a pulse of a 10 mM bradykinin solution was delivered through the pore. Bradykinin induces a concentration-dependent release of intracellular Ca^{2+} stores, which was observed by fluorescence microscopy. Images were taken every 30 seconds for 18 minutes. Cells were identified and their individual brightness was measured on every image. All cells showed a fast increase and subsequent gradual decrease in brightness. Cells closest to the pore were the first to brighten and had the highest peak brightness. At larger distances from the pore cells brightened at later times and had lower peak brightness. This spectrum of bradykinin-induced responses demonstrates a decreasing bradykinin concentration with increasing distance from the pore. In a second test used to simulate tissue, PC12 cells were attached to a PEI-coated glass chip that was inverted and suspended 75 μm above the pore. Continuous delivery of ~30 mM Rhodamine B at a constant rate of 15 nL/min clearly showed a slow radial progression of Rhodamine uptake by the cells as a function of time.

Focal chemical delivery and stimulation from a microchannel-addressed pore has been demonstrated. This approach is scalable to a high density pore platform in which each pore is individually-addressed such that specific cell populations can be targeted. Integration of electrodes will enable a multi-modal neural interface.

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