Development of Model Neural Prostheses with Integrated Microfluidics for Drug Delivery

CNF Project # 1214-04
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Abstract:

A number of chronic brain diseases are increasingly being treated by the implantation of electrically active probes into specific brain regions. Our goal is to develop more tissue compatible miniaturized probes improving probe function and controlling any adverse effects of probe implantation [1].

Optimization of tissue compatibility requires locally delivered drug therapy that can be altered as a function of time after implantation. We are exploring two approaches: short-term delivery immediately after implantation via time-release from drug-containing polymers, and long-term administration via microfluidics [2]. Advantages of microfluidics are that the drug cocktail can be changed from outside the body, and that the local tissue drug concentration can be maintained at biologically active and controlled levels. Preliminary studies using microfluidic channels with multiple outlets on probes designed for implantation into the cortex of rat brains showed that the diffusion of small molecules from the outlet was faster than the diffusion-driven molecular transport along the channel. This resulted in a pulse of drug release followed by a rapid decrease in injected drug concentration.

Two approaches are being evaluated to maintain drug injection over time. The first is to pressure inject the drug solution using the original dead-ended channels [2]. A second approach is to use lower pressure to circulate flow through microfluidic channels such that diffusion through the outlets is the primary delivery mechanism. The continually circulating flow constantly supplies fresh solution at a constant concentration to the outlets. This is expected to maintain tissue drug concentration using low-pressures with reservoirs external to the tissue being treated. The drug concentration at the outlets can also be maintained at any desired concentration thereby maintaining tissue drug level concentrations.

Model neural probes were fabricated using a DRIE process [2] on both sides of silicon substrate to form the implant. Surface micromachining [3,4] were integrated with bulk subtractive techniques to create free standing, three dimensional silicon structures with integrated microfluidics [5].

Summary:

The successful use of brain implants to treat chronic diseases requires stable two-way electrical communication between neurons, the electrically communicating cells of the brain, and the implant. This level of biocompatibility can likely only be achieved with continuous pharmacologic intervention that is changed as a function of time. Thus, incorporating drug delivery systems into our brain implants is critical. The U-channel design has advantages in terms of changing the drug regime and for delivering controlled high concentrations of drug.

References:


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Figure 1, above: The U-Channel device will allow fluid to be passively cycled through the implanted section of the microfluidic channels. Diluted fluid will evaporate out of the exit port as higher concentration fluid is drawn through the inlet. Material in the implanted region of the channel will remain at a relatively high concentration resulting in a constant diffusion source.

Figure 2, right: Scanning electron micrographs of U-Channel probes fabricated using conventional surface micromachining and Deep Reactive Ion Etching. Alkali Hydroxide etching was used to make channels deeper and facilitate both active and passive cycling of fluid through the devices during implantation.