Microfluidic Brain Slice Chamber with Localized Injection Ports and Its Application to the Study of Cortical Spreading Depression

Yujie Tanye Tang\textsuperscript{a}, Héctor E. López-Valdés\textsuperscript{b}, KC Brennan\textsuperscript{b,d}, and Y. Sungtaek Ju\textsuperscript{a,c}.

\textsuperscript{a}Mechanical and Aerospace Engineering Department, \textsuperscript{b}Department of Neurology, \textsuperscript{c}Biomedical Engineering Interdepartmental Program, University of California at Los Angeles, CA, 90095, \textsuperscript{d}currently with Department of Neurology, University of Utah, Salt Lake City, UT 84108

Tel: +1-310-825-0985; E-mail:jusjt@seas.ucla.edu

Summary: We report a microfluidic chamber incorporating fluid ports with active suction to achieve localized chemical stimulation of brain slices. The chamber is used to investigate chemical thresholds for the induction of cortical spreading depression waves, which are implicated in migraine headache and traumatic brain injuries.

\textit{In vitro} experiments using brain slices have enabled systematic neuro-physiological and –pharmaceutical studies as brain slices retain neuronal connections and local anatomy while suppressing vascular activities. Perfusion chambers for brain slices integrated with microfabricated structures and microfluidic channels are attractive as they can improve the viability of slices and enable various sensing and stimulation modalities. Challenges remain, however, in precise and localized control of neuro-chemical micro-environments. Here, we report improvement in our previously reported microfluidic chamber\textsuperscript{1} for controlled local injection of soluble chemicals onto brain slice surfaces and its application to the study of cortical spreading depression.

The device (Fig. 1a) uses an array of PDMS (polydimethylsiloxane) micro-posts on the chamber bottom surface to maintain a steady flow of an artificial cerebrospinal fluid (ACSF) solution. Select posts are replaced with fluid ports, each consisting of one injection port surrounded by multiple suction ports. We applied the device to investigate the threshold concentration of relevant ions for the onset of cortical spreading depression (CSD) waves. CSD is implicated in migraine headache, stroke, and brain injury and has therefore been a subject of extensive study by the neuroscientific community. The initiation of CSD, however, is still incompletely understood. We chemically induce CSD in brain slices by locally injecting a potassium-rich ACSF solution and determine the threshold $K^+$ concentration for the initiation of CSD waves as a function of the fluid port size. Our preliminary results (Fig. 1c) suggest that the threshold concentration is a sensitive function of the size of chemical stimulation areas.

Our work establishes an experimental tool and systematic approaches to characterize brain slices under localized chemical stimulation and demonstrates how they can be used to improve our understanding of neurophysiological events and ultimately their effective mitigation.