AUTOMATED MICROFLUIDIC PLATFORMS TO FACILITATE NERVE DEGENERATION STUDIES WITH C. ELEGANS

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With its well-characterized genome, simple anatomy, and vast array of uses in molecular biology, the roundworm, *Caenorhabditis elegans* (*C. elegans*) is a well-established model organism in neurobiology. Concurrently, neurodegenerative diseases are some the most devastating and least understood ailments in modern medicine, making high-throughput approaches to understand their fundamental mechanisms imperative to developing new therapies. The worm's physical length-scales and simple genetics make it an ideal in vivo tool for high-throughput screening platforms. Concurrently, microfluidic technology has been used to make devices that manipulate these animals in a multitude of fashions to study various biological phenomena.

With these considerations in mind, we have developed microfluidic platforms to facilitate optical interrogation of neurodegenerative and neuroregenerative phenomena in *C. elegans* for large-scale screens. First, we developed a multiwell format device with 16 on-chip reservoirs to house and quickly deliver distinct worm populations to any liquid-format imaging platform. The system achieved unprecedented delivery speeds, avoided any population cross-contamination, and maintained animal viability. We then expanded this platform into a 64-well device that acted as a modular plug and play system for

simple manipulation by conventional high-throughput liquid handling systems. The chip could be manipulated in the same fashion as a multiwell plate and interfaced with a novel pneumatic gasket system to achieve delivery speeds that were two-fold faster than those attained on the 16-well device.

In addition, we worked to develop a potential optical interrogation platform that could be fed populations of worms by the aforementioned delivery systems. This microfluidic chip consisted of an array of parallel traps to house individual worms over long durations. In this system, one could perform time-lapse studies of nerve regeneration following cuts to single axons mediated by a femtosecond pulse laser. Specifically, the platform was designed for regeneration studies in the *C. elegans* PQR neuron.