Microfluidics and real-time behavioral analysis: Tools for screening drugs, toxins, and pathogens

Abstract

Microfluidics refers to the manipulation and analysis of small amounts of fluid within physical structures of micrometer dimensions. This interdisciplinary field has been widely accepted for studying biological processes, chemical reactions, drug screening, and lab-on-chip diagnostics. Notable benefits of microfluidic systems, compared to macro-scale platforms, include low cost of reagents, faster screening, improved data resolution, higher information content, and automated sample preparation and handling.

Here, we leverage the advantages of microfluidics with real-time imaging to characterize behavioral traits of microorganisms, particularly the non-parasitic *C. elegans*. Different physical and chemical microenvironments are created on-chip to test their adaptability to applied stress and subsequent recovery. In contrast to testing human subjects, this model organism provides a simpler biological system with ease of standard lab culture and gene manipulation.

The talk will start with a survey of microfluidic systems for whole-animal screening – capturing single worms, exposing them to chemical stimuli, and imaging neuronal or pharyngeal signals. Next, we describe our work on quantifying behavior of free-moving worms and role of specific genes in manipulating this behavior. Specifically, we discuss platforms to differentiate locomotion patterns in sinusoidal channels and assess the resistance to toxins and pharmacological drugs. Through behavioral and RNA-interference assays, we showed the genetic underpinning of cyanide resistance. An algorithmic search approach is employed to find an optimal combination of four drugs with better efficacy than each individual drug. Besides chemical screening, our technique is extended towards studying the behavior of plant-parasitic worms. A microfluidic platform is built for growing multiple *Arabidopsis* plants in parallel and observing root infection over several days.

Our developed tools are aimed to be simple in operation/handling, reliable and robust, information rich, portable for easy transport, and requiring minimal human intervention. Several aspects of this work have been successfully adopted by our collaborators to study different biologically-driven hypotheses. To summarize, there are identifiable problems in plant and animal biology, with significant social and economic importance, that could be addressed by engineers across various disciplines, particularly in system design, automation, and large-scale data analysis.