

Integrated and scalable molecular brain mapping

Jae Cho

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Abstract

Understanding the brain requires integrative knowledge of its cellular-, network-, and system-level architectures. Existing volume imaging techniques have proven the potential to provide such information, but the lack of technology to label large volumes for visualization has limited their utility. Here, we address this challenge by developing technologies -- stochastic electrotransport and SWITCH -- to extend multiplexed labeling methods to larger volumes. Stochastic electrotransport selectively expedites transport of molecular probes into the tissue without damaging it. SWITCH synchronizes the labeling reaction to achieve consistent and uniform labeling. These technologies are demonstrated by successfully visualizing several molecular markers in adult mouse brain tissues, which have been previously infeasible in time and cost.

Although our focus is on neuroscience, the concepts and methods described in this thesis are quite general. Stochastic electrotransport will be applicable to any nonlinear transport problems, and SWITCH will be applicable to any problem requiring synchronization of reaction kinetics across long distances. Additionally, the tools and techniques developed for imaging, image processing, and image analysis will be useful for any large-scale imaging pipeline.

Thesis Supervisor: Kwanghun Chung

Title: Samuel A. Goldblith Career Development Assistant Professor of Chemical Engineering