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Towards Holistic Imaging and Phenotyping of Intact Biological Systems

Abstract:

Holistic measurement of diverse functional, anatomical, and molecular traits that span multiple levels, from molecules to cells to an entire system, remains a major challenge in biology. In this talk, I will introduce a series of technologies including CLARITY, SWITCH, MAP (Magnified Analysis of Proteome), and stochastic electrotransport that enable proteomic and structural imaging for scalable, integrated, high-dimensional phenotyping of both animal tissues and human clinical samples. SWITCH enables over twenty rounds of relabeling of a single tissue with precise co-registration of multiple datasets by synchronizing key chemical reactions in tissue processing. With SWITCH, we demonstrated combinatorial protein expression profiling and high-dimensional quantitative analysis of the human cortex. MAP enables scalable superresolution proteomic imaging of large scale tissues by expanding intact organs four fold linearly while preserving their 3D proteome, nanoscopic architecture, and intercellular connectivity. Using MAP, we demonstrated molecular imaging of subcellular architectures and accurate tracing of densely packed neural projections. To speed up the labeling process in CLARITY, SWITCH, and MAP, we developed a novel electrokinetic method termed stochastic electrotransport, which enables immunolabeling of whole mouse brains within 1-3 days. We hope these new technologies to accelerate the phase of discovery in a broad range of biomedical research.