Penn Program in Single Cell Biology

Single Cell Biology Symposium 2022

November 4, 2022, 1:00PM – 5:45PM
Arthur H. Rubenstein Auditorium
University of Pennsylvania

ABSTRACTS
Listed alphabetically by speakers' last name (underlined)

Looking under the hood: Establishing the framework for single cell data analysis
Junhyong Kim
Department of Biology, Department of Computer and Information Science, University of Pennsylvania

With the exponential growth of single cell biology, there has been a similar exponential growth of analysis methods. In this talk, I argue that while the availability of the new tools is important to the field, much of the methods are atheoretical and incremental. I show examples from simple first-step analyses in scRNA-seq data normalization and scATAC-seq peak quantification. I also discuss the need for a model of the single cell data, both in terms of kinds of noise and the kinds of patterns. I discuss a new method called "subspace clustering" that we have developed based on an explicit model of single cell variation. I argue that the most important need is the dissemination of fundamental knowledge to evaluate the plethora of methods.

Lattice light sheet microscopy – innovations, applications and future directions
Wesley R. Legant
Department of Biomedical Engineering and Pharmacology, University of North Carolina, Chapel Hill

Living specimens are both animate and three-dimensional. Lattice Light Sheet Microscopy (LLSM) utilizes optically structured beams to perform fast 3D imaging of dynamic processes in vivo with improved resolution and beam uniformity. I will provide an overview and characterization of different types of lattice lightsheet beams and their respective advantages and tradeoffs for live-cell imaging. I will also discuss our recent work developing lightsheet compatible microfluidic chips, AI-based instrument control algorithms, and single molecule imaging applications.

Looking under the hood of cells: from single molecule dynamics to whole cell organelle reconstructions
Jennifer Lippincott-Schwartz
Janelia Research Campus, HHMI, Ashburn, VA

Powerful new ways to image the internal structures and complex dynamics of cells are revolutionizing cell biology and bio-medical research. In this talk, I will focus on how emerging fluorescent technologies are increasing spatio-temporal resolution dramatically, permitting

simultaneous multispectral imaging of multiple cellular components. In addition, results will be discussed from whole cell milling using Focused Ion Beam Electron Microscopy (FIB-SEM), which reconstructs the entire cell volume at 4 voxel resolution. Using these tools, it is now possible to begin constructing an "organelle interactome", describing the interrelationships of different cellular organelles as they carry out critical functions. I will also present an additional tool, single particle tracking, describing how it can be used to characterize the dynamics of organelle contact sites and the behavior of tethering proteins. Together, the new tools are revealing new properties of organelles and their trafficking pathways, and how disruptions of their normal functions due to genetic mutations may contribute to important diseases.

Dissecting the repetitive genome's structure-function relationship in single cells

Jennifer E. Phillips-Cremins
Department of Genetics, Department of Bioengineering, University of Pennsylvania

The Cremins lab aims to understand how chromatin works through long-range physical folding mechanisms to encode neuronal specification and long-term synaptic plasticity in healthy and diseased neural circuits. We pursue a multi-disciplinary approach integrating data across biological scales in the brain, including molecular Chromosome-Conformation-Capture sequencing technologies, single-cell imaging, optogenetics, genome engineering, and induced pluripotent stem cell differentiation to neurons/organoids. Here, I will discuss our recent observations revealing BREACHes – Beacons of Repeat Expansion Anchored by Contacting Heterochromatin – in fragile X syndrome. Recently by engineering the repetitive genome in single cells, we observed BREACHes as Mb-scale H3K9me3 domains on autosomes encompassing severe chromatin misfolding in cis, long-range inter-chromosomal interactions, and instability of the repetitive genome.

Illuminating the biochemical activity architecture of the cell

Jin Zhang
Department of Pharmacology, Department of Chemistry & Biochemistry and Bioengineering, University of California, San Diego

The complexity and specificity of cellular processes require spatial microcompartmentation and dynamic modulation of the underlying biochemical activities, such as dynamic phosphorylation and dephosphorylation catalyzed by specific protein kinases and phosphatases, respectively. We hypothesize that cellular biochemical activities are spatially organized into an "activity architecture" and reorganization and restructuring of this activity architecture lead to disease. In this talk, I will introduce a series of genetically encoded fluorescent biosensors that we developed to achieve single cell analyses of biochemical activities, and then present a couple of studies where we combine single-cell imaging with targeted perturbations as well as biochemical and functional assays to probe the subcellular regulation of cAMP/PKA and ERK signaling pathways.