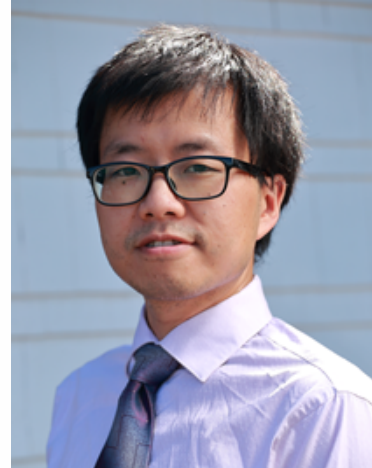## Xiaoyin Chen, PhD

Visiting Assistant Investigator
Allen Institute for Brain Science

Monday, October 31, 2022
1:00 p.m.
Traylor 709

Faculty host: Justus Kebschull

Unraveling the Modular Organization of the Cortex by In Situ Sequencing

Abstract: The cerebral cortex is composed of many areas that are distinct in cytoarchitecture, connectivity, and neuronal activity. This specialization allows cortical areas to function distinctly and flexibly in behaving animals to support cognition and behaviors. How such specialization is achieved at the cell type level, however, remains unclear. Addressing this question systematically is challenging, because neuronal connectivity and gene expression is highly diverse both within and across cortical areas. We aim to solve this question using in situ sequencing-based approaches. We previously developed BARseq, which uses in situ sequencing of RNA barcodes to map long-range projections and associate projections with gene expression at cellular resolution. Because BARseq is high throughput and low cost, it can be applied at a brain-wide scale to investigate neuronal types and their connectivity across cortical areas. As a first step, we used BARseq to interrogate the spatial distribution of neuronal types across the whole cortex. We sequenced the mRNAs of 107 cell type marker genes in 1.2 million cells across a mouse forebrain hemisphere. Our data recapitulated transcriptomically defined cell types found in previous comprehensive single-cell RNAseq datasets, and the complement of cell types in each cortical area is highly distinct. Surprisingly, the composition of cell types reveals a hierarchical and modular organization of cortical areas that is consistent with connectivity-based modules found in previous studies. Our findings thus provide a unified view of the cortex based on gene expression and connectivity, and pave a foundation for resolving the cell type connectivity across cortical areas in future studies.

Bio: Xiaoyin is an Assistant Investigator at the Allen Institute for Brain Science. Xiaoyin's team is developing and applying sequencing-based neuroanatomical approaches to understand the wiring logic of neuronal types across development and species. Xiaoyin obtained his B.S in biology in Tsinghua University in Beijing, China. He then moved to New York City and did his Ph.D training with Dr. Martin Chalfie at Columbia University, where he studied mechanosensation in the nematode C. elegans. Xiaoyin then joined Tony Zador's lab at Cold Spring Harbor Laboratory as a postdoc. In Tony's lab, Xiaoyin developed BARseq, a sequencing-based neuroanatomical technique with cellular resolution and unparalleled throughput. Xiaoyin was awarded the Kavli Institute Award for Distinguished Research in Neuroscience for his PhD thesis work. He was a Simons Collaboration on the Global Brain fellow and an O'Neil fellow during his postdoc work. He received a Discovery award from the Department of Defense Peer Reviewed Medical Research Program and an NIH Director's New Innovator Award. His work in developing BARseq was featured by the NIH Director's Blog, BRAIN Initiative Alliance, and various news media including Nature, Spectrum, Technology Networks, etc.