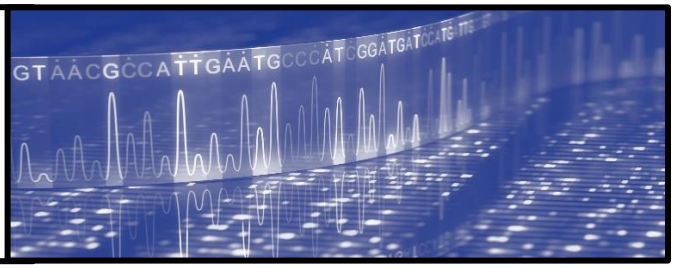
Yale Center for Biomedical Data Science



CBDS Seminar Series

"Computational tools for multimodal analysis of single cell trajectories"

Nir Yosef, PhD ~ Associate Professor, Dept. EECS & Center for Computational Biology at UC Berkeley

Single-cell RNA-sequencing has emerged as a popular modality for dissecting temporal processes such as tissue development and cellular differentiation. Current efforts in the field now go beyond mRNA and provide additional types of information for every cell, which may further enhance these studies. In this talk, I will survey our efforts to develop computational tools that can leverage two such data types. The first data type I will discuss is protein abundance – this is enabled by Total-Seq or CITE-Seq, a method which estimates the abundance of dozens of proteins on a cell's membrane in addition to its transcriptome. We have designed a method, *Total-VI*, that learns a joint representation of a cell's state from paired mRNA and protein measurements while capturing uncertainty and propagating it to a range of tasks (e.g., batch correction, subpopulation identification, differential expression). I will demonstrate the utility of Total-VI in the context of an ongoing study of T cell lineage specification in the thymus. The second data type I will cover is traceable genetic alterations – this approach uses CRISPR/Cas9 to introduce heritable marks to cells, enabling the reconstruction of cellular lineages. I will discuss a suite of tools (*Cassiopeia*) we have designed to help build such lineages, while tackling hurdles such as missing data and the need for scalability. I will conclude by briefly presenting a third method (*HotSpot*) designed for a joint analysis of transcriptome and CRISPR/Cas9- based lineage information, and its application to characterizing heritable gene programs during embryogenesis.

Nir Yosef received his Ph.D. in Computer Science from Tel Aviv University and then proceeded to postdoctoral training at the Broad Institute, where he worked on transcriptional regulation of T cell differentiation. Nir joined the faculty at UC Berkeley in 2014, where he is currently an Associate Professor of Computer Science and a core member at the Center of Computational Biology. He is also an associate member of the Ragon Institute of MGH, MIT and Harvard and a Chan Zuckerberg Biohub investigator. The Yosef lab is developing data- centric methods for studying how changes in transcription are associated with various phenotypes in the immune system. In that capacity, the lab is developing and applying computational tools that leverage single cell genomics data, with the goal of better understanding the factors that contribute to variability between cells, (e.g, metabolism, chromatin structure), and their broader implications (e.g., in autoimmunity). A second area of research is method development for studying regulatory regions in the genome, based on chromatin profiles and massively parallel reporter assays.

Wednesday, March 4, 2020
4:00 – 5:00 p.m. Seminar
Brady Auditorium