
THE WEIZMANN INSTITUTE OF SCIENCE
FACULTY OF MATHEMATICS AND COMPUTER SCIENCE

Faculty Seminar

Room 155 ,Ziskind Building
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Representation, inference and design of multicellular systems

Abstract:

The past decade has witnessed the emergence of single-cell technologies that measure the expression level of genes at a single-cell resolution. These developments have revolutionized our understanding of the rich heterogeneity, structure, and dynamics of cellular populations, by probing the states of millions of cells, and their change under different conditions or over time. However, in standard experiments, information about the spatial context of cells, along with additional layers of information they encode about their location along dynamic processes (e.g. cell cycle or differentiation trajectories), is either lost or not explicitly accessible. This poses a fundamental problem for elucidating collective tissue function and mechanisms of cell-to-cell communication.

In this talk I will present computational approaches for addressing these challenges, by learning interpretable representations of structure, context and design principles for multicellular systems from single-cell information. I will first describe how the locations of cells in their tissue of origin and the resulting spatial gene expression can be probabilistically inferred from single-cell information by a generalized optimal-transport optimization framework, that can flexibly incorporate prior biological assumptions or knowledge derived from experiments. Inference in this case is based on an organization principle for spatial gene expression, namely a structural correspondence between distances of cells in expression and physical space, which we hypothesized and supported for different tissues. We used this framework to spatially reconstruct diverse tissues and organisms, including the fly embryo, mammalian intestinal epithelium and cerebellum, and further inferred spatially informative genes. Since cells encode multiple layers of information, in addition to their spatial context, I will also discuss several approaches for the disentanglement of single-cell gene expression into distinct biological processes, based on ideas rooted in random matrix theory and manifold learning. I will finally discuss how these results can be generalized to reveal principles underlying self-organization of cells into multicellular structures, setting the foundation for the computationally-directed design of cell-to-cell interactions optimized for specific tissue structure or function.