Using Microscopy and Generative Networks to Infer Novel Molecular Interactions

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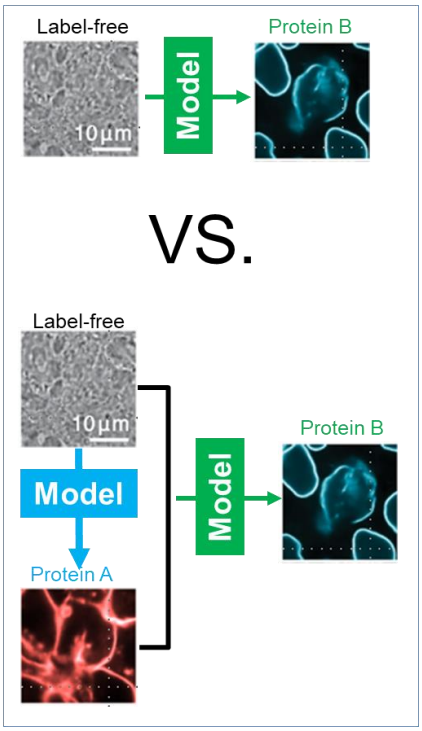

Cells are the fundamental unit of structure and function of all organisms. Proteins are the molecular machines that define the cell architecture, organization, and function. Microscopy is the only technology that allows us to see live cell behavior and to correlate cell function to protein quantity and location. Recent studies have demonstrated that label-free (without fluorescent stains for specific molecules) images contain information on the molecular organization within the cell by using machine learning-based generative approaches. The potential generation of such "virtual integrated cells" may overcome inherent limitations in optics and molecular biology that limits the number of proteins that can be concurrently images in a live cell. We propose to make the next big step by using matched fluorescent and label free images to predict (asymmetric) protein-protein interactions that will be used to identify novel molecular pathways that can be then verified experimentally. Interactions among different proteins is poorly characterized due to the difficulty in live imaging multiple different proteins in a cell. We propose here a proof-of-concept of a methodology that will enable predictive modeling of cell states and behavior, based on virtual predicted molecular organization and interactions from label free images. Such system-level understanding of molecular interactions will be a huge advance towards the "holy grail" of cell biology - an understanding of the cell as an integrated complex system.

Students taking part in this project: Katya Smoliansky, M.Sc. student, Department of Computer Science. Gil Baron, M.Sc. student, Department of Software and Information Systems Engineering.

Funded acknowledged publications:

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- Adar-Levor S, Nachmias D, Gal-Oz ST, Jahn YM, Peyrieras N, **Zaritsky A**, Birnbaum RY, Elia N. Cytokinetic abscission is part of the mid-blastula transition switch in early zebrafish embryogenesis. Preprint @bioRxiv: https://www.biorxiv.org/content/10.1101/2020.07.26.221515v1.
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- Riegman M, Sagie L, Galed C, Levin T, Steinberg N, Dixon SJ, Wiesner U, Bradbury MS, Niethammer P, **Zaritsky A**§, Overholtzer M§. Ferroptosis occurs through an osmotic mechanism and propagates independently of cell rupture. Nature Cell Biology 2020 (in press). § - co-corresponding authorship.
- Horev MB, Zabary Y, Zarka R, Sorrentino S, Medalia O, **Zaritsky A** and Geiger B. Differential dynamics of early stages of platelet adhesion and spreading on collagen IV- and fibrinogen-coated surfaces. F1000Research 2020, 9(ISF):449. DOI: https://doi.org/10.12688/f1000research.23598.1.