PHYSICAL SEMINAR

Visualizing Bacterial Physiology at High Resolution using Single-Molecule Tracking and Lattice-Light Sheet Microscopy

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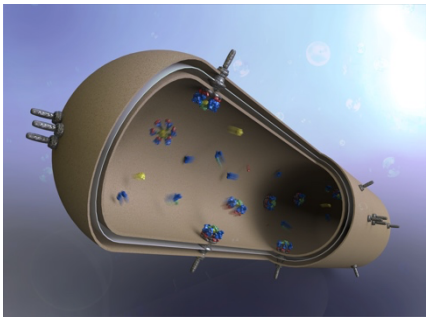
Host: Prof. Randy Goldsmith

Our lab develops new imaging approaches for visualizing bacterial physiology in relevant contexts: We use live-cell single-molecule localization microscopy and lattice-light sheet microscopy to access 3D spatial and temporal information with high resolution. At molecular and cellular length scales, our research focuses on understanding how Gram-negative bacterial pathogens assemble and regulate the Type 3 Secretion System (T3SS) – a 7 MDa multi-protein complex that spans two, and sometimes three cellular membranes. The T3SS is used by prominent bacterial pathogens to inject effector proteins into the cytosol of eukaryotic host cells. At cellular and super-cellular length scales, our research focuses on visualizing the behaviors of individual bacteria inside tissue-like microbial communities. Microbial communities have substantial impacts on physiological and pathophysiological processes in higher living organisms. We are primarily interested in host-microbe interfaces in the human gut.



In the first part of my talk, I will describe how single-molecule localization and tracking microscopy in different genetic backgrounds provides a path towards understanding the molecular assembly mechanism(s) that contribute to type 3 secretion in living cells. Through computational aberration correction and numerical modeling, we determine the 3D subcellular localization and diffusive states of individual, fluorescently labeled T3SS proteins. Our results indicate that T3SS proteins pre-assemble into freely diffusing cytosolic complexes prior to binding to the membrane-spanning multi-protein complex. Determining to what extent cytosolic proteins assemble with each other in living cells provides key insights into the dynamic regulatory network that controls type 3 secretion.

In the second part of my talk, I will describe how lattice light-sheet microscopy enables non-invasive 3D imaging of microbial communities at single-cell resolution. Analyzing the resulting 3D images using a combination of computer vision and machine learning approaches enables multi-cell tracking of cell motions, cell morphologies, and cellular gene expression over time. Our goal is to apply these new imaging and image analysis approaches to understand the emerging functional capabilities of microbial communities in terms of the behavioral phenotypes of individual cells. Such knowledge can help inform new strategies for controlling microbial community growth and harness the metabolic potential of the microbial world in new biotechnological applications.

DATE: TUESDAY, APRIL 26TH, 2022

TIME: 11:00 AM – 1435 Learning Studio, North Tower

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