JMU Chemistry and Biochemistry Seminar
Friday, March 23, 2018
3:35pm in ISAT 159

Resolving cytosolic complex formation in living bacterial cells by 3D single-molecule tracking

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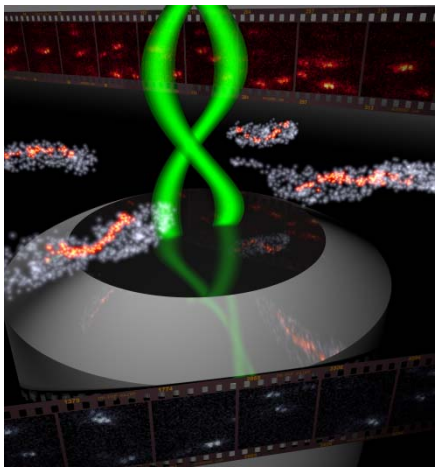
About a third of bacterial proteins are either transported across or integrated into the cell membranes, so that they can perform functions that are vital for bacterial survival in specific environmental niches. Directional transport of selected proteins often relies on large membrane-embedded biomolecular assemblies. For example, the dual membrane-spanning Type 3 Secretion System (T3SS) enables Gram-negative bacterial pathogens to inject so-called effector proteins directly into the cytosol of eukaryotic host cells – a virulence mechanism that currently results in more than 1 million human deaths per year. While the cocktail of injected effector proteins differs among pathogens, the structural proteins of T3SSs are highly conserved, making Type 3 secretion systems a prime target for the development of anti-virulence drugs that would provide valuable alternatives to broad-spectrum antibiotics in use today. Our research focuses on providing a more complete understanding of how membrane-embedded biomolecular assemblies, like the T3SS, are functionally regulated at the molecular level and how these assemblies ultimately enable bacterial survival and infection at the cellular level. To achieve this goal, we use a variety of state-of-the-art super-resolution imaging technologies, namely single-molecule localization microscopy and lattice-light sheet microscopy, which enable us to investigate molecular-level spatial and temporal phenomena inside living bacterial cells and cellular-level phenotypes within developing microbial communities.

In this talk, I will describe how shaping of light waves enables measurements of 2D and 3D motion trajectories of individual bacterial proteins at unprecedented resolution. These data allow us to resolve the distinct diffusive states of cytosolic proteins and determine the relative diffusive state abundances. Our results thus far indicate that structural T3SS proteins are capable of forming distinct oligomeric complexes in the bacterial cytosol. Some, but not all, of these complexes are dependent on the presence of other T3SS proteins and they change upon functional activation of type 3 secretion. Defining the cytosolic diffusion states of T3SS proteins that are directly associated with T3SS function opens a path towards describing the molecular basis of type 3 secretion in prominent bacterial pathogens.



Meet the Speaker, 2:15 – 3:00pm, Student Lounge, 3144