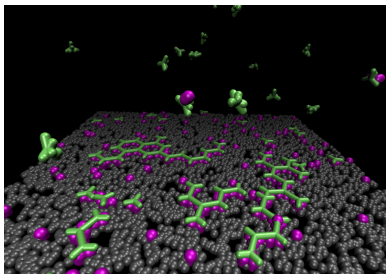
ASRC - City College of New York

Seminar in Biochemistry, Biophysics & Biodesign



Wednesday, November 3, 2021

12:00 – 1:00 PM

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Protein self-assembly at the right place and time

ABSTRACT Self-assembly of protein components is ubiquitous across biology, where these assemblies often must form at specific spatial locations within a cell to do work. In clathrin-mediated endocytosis (CME) and virion formation, for example, multiple protein types must localize to the cell's plasma membrane to ensure proper transport and communication in and out of cells. We develop theory and computational models, along with collaboration with experimental groups, to understand and predict how the success and dynamics of multi-protein self-assembly in pathways like CME can be controlled by stoichiometry, both active and stochastic driving forces, and membrane localization. We constructed a relatively simple theoretical model that quantifies how dimensional reduction (change in search space from 3D to 2D) can, on its own, provide a powerful driving force promoting assembly after membrane localization, thereby regulating the timing of assembly. We further showed how the membrane can also significantly accelerate assembly kinetics by orders of magnitude, largely dependent on the rate of arrival and adsorption to the membrane surface. Applying these ideas, along with new reaction-diffusion software NERDSS developed by our lab, we showed how nucleation and growth of clathrin proteins into hexagonal lattices on membranes can be sensitively tuned by the so-called adaptor proteins that link clathrin to the surface. Our model was validated to reproduce quantitatively in vitro fluorescence data tracking clathrin localization to membranes, and predicts regimes of assembly and spontaneous disassembly that are in close agreement with in vivo measurements. An essential role of many membrane-localized assemblies such as these are to remodel the membrane. We have therefore used continuum thin-film models to characterize how such proteins can drive membrane bending using mechanisms such as helix-insertion and scaffolding, with distinct energetic costs to each. These theoretical and computational approaches are general and can be applied to diverse biological systems, helping to understand how both hetero- and homo-subunit assemblies can be controlled to function within the nonequilibrium cell.

View this seminar live via Zoom at:

https://gc-cuny.zoom.us/j/4954048198?pwd=eVlkMFdHcjV6d3pkYzB4V2VtbHJGdz09

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