
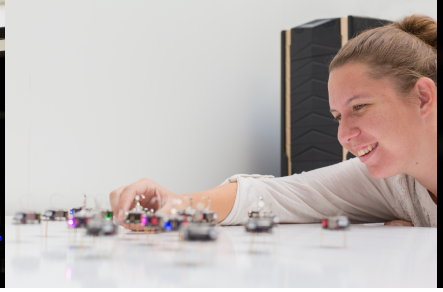


Physics colloquium

Force-sensitivity and Cooperativity Arising from Polymer Properties of Formins and other Intrinsically Disordered Molecules

Jun Allard
Department of Physics and Mathematics
University of California, Irvine

Date: **3/15/19**
Time: **10:30 AM**
Location: **COB2 170**

For more information contact
Jing Xu
jxu8@ucmerced.edu

Abstract: Proteins with intrinsically disordered regions, that lack a dominant structure, appear often in cell signaling and cell mechanics. In signaling, examples include the T cell receptor zeta chain. In mechanics, examples include the formin family that creates and elongates actin structures. Here, we develop models of intrinsically disordered regions with a simplified theta-solvent freely-jointed chain model coupled to idealized spherical binding enzymes. Many actin structures are nucleated and assembled by the formin family, including filopodia, focal adhesions, the cytokinetic ring and cell cortex. These structures respond to forces in distinct ways. Formins typically have profilin-actin binding sites embedded in disordered FH1 domains, hypothesized to diffusively explore space to rapidly capture actin monomers for delivery to the barbed end. Recent experiments demonstrate that formin-mediated polymerization accelerates when under tension. The acceleration has been attributed to modifying the state of the FH2 domain of formin. Intriguingly, the same acceleration is reported when tension is applied to the FH1 domains, ostensibly pulling monomers away from the barbed end. In this work we ask whether this behavior emerges from basic entropic polymer properties by simulating a model of formin-mediated actin polymerization. The binding of actin monomers to their specific sites on FH1 is entropically disfavored by the high disorder. We find that this penalty is attenuated when force is applied to the FH1 domain by revealing the binding site, increasing monomer capture efficiency. Overall polymerization rates can decrease or increase with increasing force, depending on the length of FH1 domain and location of binding site. Our results suggest that the widely varying FH1 lengths and binding site locations found in known formins could be used to differentially respond to force, depending on the actin structure being assembled. This nonlinear force response is part of a growing body of work demonstrating the emergence of nonlinear behavior, including cooperativity, anticooperativity, and sequentialization of enzymatic events, all arising from polymer properties alone.