Origins and consequences of translation-elongation kinetics on protein structure and function

Abstract: Protein folding research has been dominated by the assumption that thermodynamics determines protein structure and function. And that when the folding process is compromised in vivo the proteostasis machinery — chaperones, deaggregases, the proteasome — work to restore proteins to their soluble, functional form or degrade them to maintain the cellular pool of proteins in a quasi-equilibrium state. During the past decade, however, more and more proteins have been identified for which altering only their speed of synthesis alters their structure and function, the efficiency of the down-stream processes they take part in, and cellular phenotype. Indeed, evidence has emerged that evolutionary selection pressures have encoded translation-rate information into mRNA molecules to coordinate diverse co-translational processes. Thus, non-equilibrium physics can play a fundamental role in influencing nascent protein behavior, mRNA sequence evolution, and disease. In my talk I will discuss how our understanding of this phenomenon is being advanced by the application of theoretical tools from the physical sciences.

Biography: Ed O'Brien received his Bachelor's in Biochemistry and did his Ph.D. in Chemical Physics from University of Maryland College Park under Dave Thirumalai and co-advisor Bernie Brooks from the National Institutes of Health. He carried out post-doctoral research at University of Cambridge under Christopher Dobson and co-advisor Michele Vendruscolo. Ed has received a number of awards for his work including a Presidential Early Career Award in Science and Engineering, the American Chemical Society Junior Faculty Award in Computational Chemistry, NSF CAREER Award, NSF Postdoctoral Fellowship, EPSRC (UK) grant, BBSRC (UK) David Phillips Fellowship, and Royal Society (UK) Research Fellowship.