Title: Low complexity protein domain assembly mechanisms

Abstract: Proteins harboring low complexity amino acid sequences form organized and condensed assemblies functionally and pathologically in living cells. Assembly is driven by weak and transient molecular interactions that are well understood individually. However, multivalency is a key feature of low complexity protein domains and how these interactions collectively produce condensed assemblies in specific biological contexts is not well characterized. Our current efforts focus on condensation mechanisms involving β-strand mediated hydrogen bond interactions, which we investigate using solid state nuclear magnetic resonance, microscopy, and fluorescence spectroscopy. First, we aim to understand how dynamic and functional liquid droplets formed by the low complexity domains of RNA-binding proteins transition into rigid fibrillar hydrogels, a chemical process that underlies neurodegenerative disease pathology. Second, we aim to understand how functional liquid droplets are spatially localized in living cells though heterogeneous intermolecular interactions between low complexity protein domains of cell cytoskeleton proteins. Through these two avenues of research, we are forging an understanding of how low complexity protein domains drive the formation of condensed assemblies to achieve specific biological functions and how the assemblies are altered in disease.