ABSTRACT:

Utilization of biomacromolecules to engineer self-assembled materials that display target structure and function at the nanoscale is an active area of new materials research. Peptides that are short sequences of amino acids are excellent candidates for this purpose. Computational prediction of peptide sequences has further enabled faster screening and deterministic design of peptide-based biomaterials. In my dissertation defense, I will discuss my research findings on the utility of artificial peptides that were computationally designed to form coiled coils aka bundlemers. Short α-helical peptides tetramerize to form a bundlemers with a hydrophobic core and displaying side chains that are strategically chosen to drive their assembly under mild solution conditions.

Via a feedback cycle between experiments and sequence-optimization algorithms, I have tested multiple peptide designs for successful bundlemers formation. Specifically, small angle neutron scattering (SANS) measurements confirmed that all bundlemers are robust 2 nm x 4 nm cylinders. These bundlemers exhibit short-range attraction and long-range repulsion (SALR) interactions and their solution structure is uniquely impacted by sequence-specific surface-charge patterns, making bundlemers excellent globular-protein mimicking colloidal systems.

Taking advantage of their structural robustness, we have modified the bundlemers to incorporate thiol or maleimide groups at the N-termini that has yielded tetra-functional ‘monomers’. The decorated bundlemers are reacted via Thiol-Michael click reaction, resulting in end-to-end polymerization of bundlemers. Short linkers between bundlemers yield rigid rod-like polymers, whereas longer flexible linkers resulted in semi-rigid chain-like polymers, both having a cross-section of ≈ 2 nm (confirmed via SANS) and can be viewed under a Transmission Electron Microscope. The difference in inter-bundlemers dynamics within rigid rod-like versus semi-rigid chain-like polymers has been further corroborated by Neutron Spin Echo measurements.

Due to the step-growth polymerization kinetics of Thiol-Michael click reaction, the average length of rigid rod-like polymers is readily tunable. My SANS investigation into the inter-rod interactions has confirmed that the rigid rod-like polymers behave as polyelectrolytes in solution while also displaying a large intrinsic persistence length. Furthermore, lyotropic liquid crystal formation in concentrated solutions is dependent on constituent bundlemers design. Thus, the bundlemers-based rigid rod-like polymers are also excellent model systems to study sequence-driven structure-property relationships in proteinaceous 1D assemblies.