Solution and Surface Methods for Quantifying Coiled Coil Interactions

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Monday, August 31st, 2026, at 8:30 AM (EDT)
Colburn Lab, Room 366 | Zoom: https://udel.zoom.us/j/91296626455 | Password: bndl_dlvo

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Peptides and proteins exhibit precise arrangement and control over nanostructure with excellent monodispersity, in a way that conventional nanoparticles cannot replicate. Over the last three decades, the design rules of protein tertiary and quaternary structures have become clear and enabled the creation of synthetic peptides that mimic the behavior of isotropic and anisotropic nanoparticles. Additionally, while existing colloids with anisotropic surface patches typically exhibit only like-patch or inverse-patch attractions, peptides and proteins exhibit molecular specificity over the patterning of surfaces with hydrophilic/hydrophobic groups (like-patch attraction), as well as positive/negative charge patches (inverse-patch attraction) present on the same surface. By applying the lens of colloidal theory to these highly tunable nanoparticles, an important longstanding gap between larger colloidal particles and their comparison to proteins can be bridged.

In this dissertation, a series of peptides that spontaneously self-assemble into antiparallel, tetrameric coiled coils, termed bundlemers, was used as the basis for studying interparticle interactions both in bulk solutions and at solid surfaces. Owing to the site-specific modifications enabled by the amino-acid sequence control of structure, studies examining interparticle interaction anisotropy and probing of interactions at specific geometries were carried out. Light and X-ray scattering were used to examine the effect of charge patch presence and localization on colloidal stability versus soluble aggregate formation, as well as the formation or inhibition of liquid-crystalline phases. Bundlemers with high surface charge density behaved as predicted by isotropic interaction potentials, like the DLVO potential, when electrostatic interactions were longer range at low ionic strengths; however, many sequences and solubilizing conditions showed assembly in cases where simple isotropic models would not predict this. These deviations were attributed to the anisotropic distribution of hydrophobic and charged groups, which under conventional isotropic models were assumed to be uniform across the nanoparticle surface.

To demonstrate the role of localized anisotropic interactions, site-specific modifications were made to alter the surfaces thereby changing their interparticle interactions. Unlike typical proteins, the robust assembly of the bundlemer allows for solvent-exposed amino acids to be substituted freely without altering the overall structural conformation. From a combination of all-atom simulations, scattering measurement, and microscopy (where applicable), these site-specific modifications revealed that modifications made near the termini of the nanoparticle

disproportionately changed the solution behavior, as they alter the ability of short-range hydrophobic interactions to contribute to the interparticle interaction potential. This was demonstrated particularly clearly by way of the recently developed analytical framework for a generalized osmotic virial coefficient, $B_{22}(q)$, which captures net interparticle interaction as a function of interparticle separation distance.

Site-specific modifications were also used to enable orientation-specific immobilization of the bundlemer to surfaces. Modification of the bundlemer N-termini with cysteine enabled a surface-confined grafting-from synthesis strategy, in which sequential covalent addition of bundlemer to the surface of gold nanoparticles produced quantized, multilayer bundlemer brushes with well-defined thickness at each growth step, offering a route toward the arbitrary patterning of 1D bundlemer architectures. N-terminal cysteines were also used to immobilize the bundlemer for experiments examining the mechanical response of bundlemer particles under an applied external load. These measurements represent the first direct rupture force measurements of tetrameric coiled coils in the literature and showed the reinforcement of coiled-coil strength by increasing the oligomerization state relative to dimeric coiled coils.

Together, these studies of bundlemer materials design and anisotropic interactions will inform the design of subsequent hierarchical and hybrid materials using the bundlemer as a predictable model building block.