Synthesis of Variable-Length Coiled Coil Peptides as Functional Building Blocks for Hierarchical Materials

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Zoom: https://udel.zoom.us/j/93529402059, Password: peptide

Proteins play vital roles in life by providing structural and dynamic properties that underpin essential biological functions. These properties, including structural rigidity, temperature sensitivity, and pH responsiveness, are highly desirable in material systems to create functional materials. One approach to capture these properties is to incorporate peptides that mimic the structural domains of proteins responsible for these dynamic properties into materials. However, the potential application of peptides as functional building blocks for material design extends beyond biomimicry, especially considering the possibilities offered by computationally designed peptides. This thesis explores the use of computationally designed coiled coil-forming peptides as functional building blocks for hierarchical material design. This involved characterizing a new series of coiled coils and using those peptides as building blocks for purely peptidic and hybrid peptide materials.

A novel series of computationally designed tetrameric coiled coil-forming peptides were used to explore how peptide length affects coiled coil stability. These peptides were synthesized, and their secondary structure was characterized, leading to the establishment of design rules dictating the necessary peptide length for tetrameric coiled coil formation. Furthermore, the shortest stable sequence was utilized as a model system to examine how solution conditions influence coiled coil stability. The addition of various monovalent salts increased the stability of the coiled coil. Moreover, the coiled coil remained stable over a pH range of 4 to 11, showcasing the robustness of this sequence. As such, this coiled coil peptide was integrated as a physical

cross-linker in a hydrogel that responds to changes in temperature and strain, allowing for injection via a syringe.

To enhance the functionality of these new sequences and broaden the scope of similar computationally designed peptides, a truncation of an extremely stable coiled coil-forming peptide was synthesized. Although too short to independently form a coiled coil, this truncated sequence contained the functional elements required for coiled coil formation. By incorporating click-reactive groups at the N-terminus of the truncated sequence, the sequences could be linked together, resulting in the assembly of rigid-rod polymers by stabilizing a coiled coil structure. This presents a new polymerization mechanism for these rigid-rod polymers, relying on physical assembly rather than chemical linkage, as previously documented. Furthermore, the ability of truncated sequences to create functional materials significantly broadens the potential functionality of the computationally designed coiled coils described in this thesis.

A novel class of hybrid material was synthesized by incorporating metal-organic polyhedral (MOP) into peptides, resulting in hybrid peptide-inorganic materials. Initially, the MOP was functionalized with "click" functional groups by synthesizing and coupling "click" functional anhydrides. This modified MOP was then linked to various peptides, resulting in a water-soluble pH-responsive MOP that selectively precipitated from solution under acidic pH conditions. To enhance the biocompatibility of these MOP materials, it was necessary to impart water solubility to the traditionally insoluble MOP. A stepwise conjugation approach was developed to attach ethylene glycol and maleimide to the MOP as a post-synthetic modification, yielding a "click" functional water-soluble MOP. This modified cage was then conjugated to a coiled coil peptide in water, forming nanosheets with a thickness equivalent to a single coiled coil. The materials developed in this study offer a diverse range of building blocks that are robust enough to support various modifications and conjugations. These advancements hold potential in applications such as 3D printing, drug delivery, and selective membrane separations, inspiring new avenues of research and development.