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Supramolecular Peptide Composite Assemblies: Mimicking Biological Form and Function in Synthetic Systems

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Microtubules (MTs) are dynamic, multifunctional biomaterials that facilitate a range of complex biological process in cells ranging from regulation of cell morphology to separation of chromosomes during cell division to directing the intracellular transport of molecular cargo.[1] The remarkable precision, versatility, and dynamic nature of these non-equilibrium structures has motivated our desire to mimic their structure and function in synthetic materials. Here, I will identify a number of the key attributes responsible for MT form and function, and describe our efforts to merge computation and experiment to design, synthesize, and study a family of self-assembling peptides intended to mimic MTs.

MTs are self-assembled biological filaments assembled from tightly bound heterodimers of α and β tubulin. These dimers assemble head-to-tail into protofilaments that associate laterally into closed sheets forming the characteristic tubular morphology of the MTs. These tubules are approximately 25 nm in diameter and can be many micrometers long, though the length of the MTs is subject to their dynamic assembly and disassembly within a cell (dynamic instability). Ultimately, both the initial assembly and dynamic instability of MTs are governed by complex electrostatic and hydrogen bonding interactions between tubulin heterodimers and other functional biomolecules within the cell. These interactions allow biology to effectively program MT form and function to meet the dynamic and evolving needs of a cell.

From a synthetic materials perspective, we aim to create simplified peptide or composite peptide molecules capable of similar programmable functional assembly that could similarly be used to facilitate dynamic or adaptable organization of nanomaterials. To guide the design and facilitate understanding of these peptide systems, we utilize a combination of density functional theory (DFT) and self-consistent field theory (SCFT) that can reveal simplified or distilled molecular characteristics needed in an artificial MT scheme. These computational studies have provided insight into the necessary molecular geometries, peptide compositions, and even targeted intermolecular interactions built into our MT-mimetic designs. In particular here, I will describe a collection of simulation-inspired peptides in which we demonstrate that molecular shape, electrostatic interactions, hydrogen bonding, and solvent interactions influence peptide self assembly into sheets, fibers, ribbons, vesicles and tubules (Figure 1).[2,3] Moreover, we show that by creating hybrid or composite compositions containing multiple functionalities, it is possible to control molecular self-assembly through interactions with secondary molecules. For example, select bola-peptide compositions are shown to undergo unique self-assembly in collaboration with the surfactant sodium dodecylsulfate, creating a composite structure that is resistant to enzymatic degradation. In another example, molecules comprising self assembling peptides, such as diphenylalanine, and boronic acid form ribbon-structures whose reversible self-assembly is mediated by binding of polysaccharides to the boronic acids. Just as in the natural MT system, the self-assembly (and disassembly) in these hybrid systems is regulated by molecular shape, electrostatic and hydrogen bonding interactions, and the programmable response of these molecules to chemical stimuli.

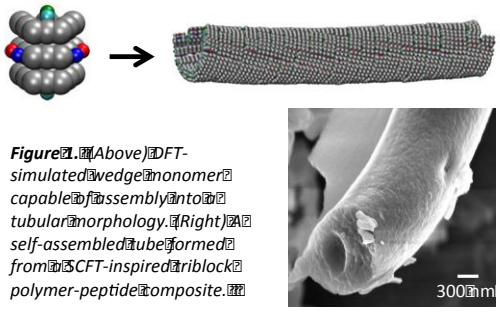

Figure 1. *(Above) DFT-simulated wedge monomer capable of assembly into a tubular morphology. (Right) A self-assembled tube formed from a SCFT-inspired triblock polymer-peptide composite.*

Continued development of these hybrid, composite peptide systems is aimed at developing a new class of biomimetic molecular materials which mimic not only the form, but also the underlying function of some of Nature's most compelling supramolecular creations.

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