Combinatorial Discovery of Biomimetic Atomically-Defined Soft Nanomaterials

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Scientific Thrust Area: Biological Nanostructures

Research Achievement: A defining characteristic of most biomacromolecules is that they have precise 3-dimensional structures and very sophisticated functions, such as molecular recognition and catalysis. And yet the underlying architecture of protein and nucleic acid structure is relatively simple: a linear polymer chain of specific monomer sequence. We aim to apply the rules that govern the folding of these chains toward the construction of a new class of atomically-defined non-natural soft nanomaterials.

Peptoids are a novel class of non-natural biopolymer based on an N-substituted glycine backbone that are ideally suited for nanomaterials research[1] (Figure 1). This bio-inspired material has many unique properties that bridge the gap between proteins and bulk polymers[2]. Like proteins, they are a sequence-specific heteropolymer, capable of folding into specific shapes[3,4] and exhibiting potent biological activities[5]; and like bulk polymers they are chemically and biologically stable and relatively cheap to make. Peptoids are efficiently assembled via automated solid-phase synthesis from hundreds of chemically diverse building blocks[6], allowing the rapid generation of huge combinatorial libraries[7,8]. This provides an ideal platform to discover nanostructured materials capable of protein-like structure and function.

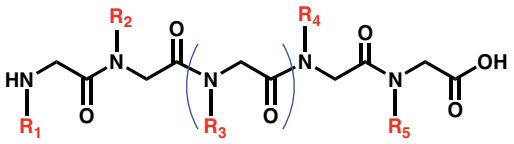

Figure 1. Peptoids are a sequence-specific bio-inspired polymer based on an N-substituted glycine backbone.

We will demonstrate that peptoids can be used to design precisely-structured nanomaterials. Because peptoids lack hydrogen bond donors and chiral centers in their backbone, simple designs emphasizing periodic hydrophobic and electrostatic interactions can be rapidly evaluated. We have designed a combinatorial library of amphiphilic peptoid 36mers of specific sequence, and discovered sequences that self assemble into extremely thin crystalline sheets in aqueous solution with no template. The sheets are only 3 nm thick, and yet extend in two dimensions up to hundreds of microns (Figure 2), creating one of the thinnest two-dimensional organic crystalline materials known. These materials have been characterized by fluorescence microscopy, atomic force microscopy, electron microscopy and x-ray diffraction, as well as their kinetics of formation and thermodynamic stabilities. The ability to spontaneously assemble two-dimensional crystalline materials in solution could have tremendous potential to enable the bottom-up fabrication of optical and electronic devices, template the patterning of inorganic or biological materials, or serve as biological membrane mimetics.

Future Work: In the short term, we plan to investigate the sequence and structural requirements of the peptoid chains to understand exactly what is necessary to form stable sheets. We plan to further engineer the sheet-forming interactions to create even more stable and more highly crystalline sheets. The ultimate goal is to create materials with atomically-precise control over the location of each atom in the material. Because the peptoid chemistry allows precise sequence control over every monomer, we can then begin to create tailored functional sheet structures.

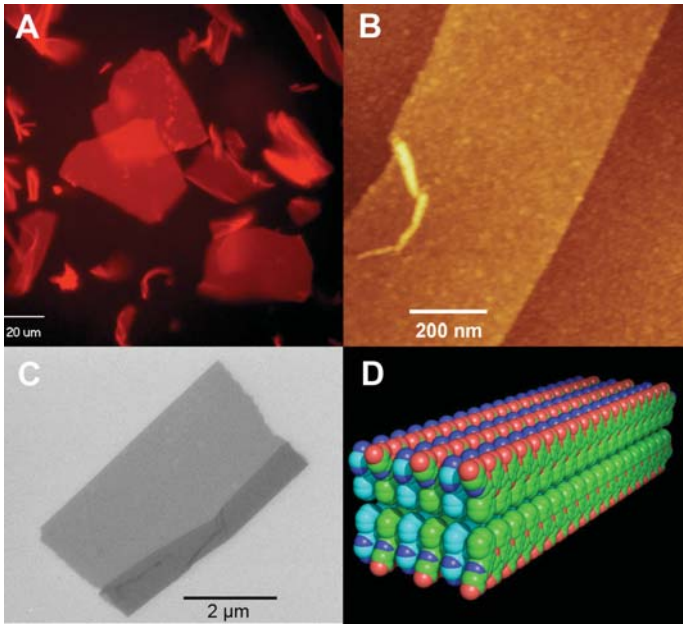

Figure 2. (A) Fluorescence microscopy image of sheets floating in aqueous solution stained with Nile Red, (B) AFM image of a single sheet, (C) SEM image of an isolated sheet, (D) molecular model showing proposed peptoid bilayer structure.

Our longer-term goals are to study the transport of ions and small organic molecules across the sheets, and to display proteins, peptides, small molecules, inorganic nanocrystals, cells and combinatorial libraries of ligands on the surface of the sheets. The freely-soluble 2D sheet motif can serve as a structural platform to segregate compartments or present attached materials in a soluble but highly correlated manner that should find a wide variety of applications.

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