

TEM Investigations of Peptoid Structures

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The potential for chemical diversity of peptoid polymers was immediately apparent upon their development [1]. Appreciation for their structural diversity has been developing more slowly. We have used EM imaging and electron diffraction to study some of these novel structures.

Peptoids are similar to peptides in having the same carbon-nitrogen backbone. The differences derive from the fact that peptoid sidechains are attached to the nitrogen, rather than carbon as in peptides. With no resultant mechanism for forming the hydrogen bonds that stabilize helical structures in proteins, the expectations for secondary structures in peptoids are much more limited than in proteins. However the range of peptoid side chains is vastly greater than the 20 natural amino acids, which has led to a wide variety of self-assembling peptoid aggregates and ordered arrays. In recent years, a wide variety of peptoid polymers have been shown to be crystalline in the solid state. Inspired by successes and limitations of conventional polymer chemistry in developing membranes suitable for applications such as fuel cells and batteries, we have investigated use of the peptoid backbone as a scaffold for constructing membranes with better control of composition and properties. The overall goal is to obtain membranes with enhanced mechanical and electrical properties, starting from our current understanding of polymers such as polystyrene and polyethylene. Many membranes have been formed with derivatives of these as diblock copolymers containing hydrophilic and hydrophobic blocks. We have synthesized various polypeptoids with corresponding diblock motifs, taking advantage of the sequence specificity of peptoids.

One of the first membrane-forming peptoids we looked at is based on alkyl/ethyleneoxy sidechain blocks. A surprise upon visualizing this material by cryo-EM was the appearance of tubes with a prominent 2.4-nm axial repeat that corresponds to the distance expected between backbones [2]. Figure 1 shows the chemical structure and an image of this material. A model for a single-layered structure was proposed (Fig. 1C), based on the idea that the molecules assemble as tiles in a highly ordered structure. Variants of this material also form thin, apparently monolayer sheets, from which we have obtained high resolution images and which show electron diffraction spots to at least 0.2 nm in addition to the 2.4 nm repeat (Fig. 1D). It appears that in the sheets the side chains run roughly perpendicular to the plane of the sheet, but we do not yet have an atomic model that accounts for all features in the diffraction patterns. Higher resolution imaging should lead to development of an accurate model.

The most widely studied electrolyte membranes are based on sulfonated polymers such as Nafion. However, most sulfonic acid-based membranes are poor proton transporters, since very little water is retained at the high temperatures required for operation. Phosphonated polymers are attractive systems because they exhibit efficient proton transport under low water uptake conditions [3]. We have used cryo-EM to characterize sequence-defined phosphonated peptoid diblock copolymers (Fig. 2A). This material forms self-supporting sheets with a honeycomb type of phase separation when dried from the solvent on lacey films (Fig. 2B), and forms vesicles when mixed with water (Fig. 2C). The vesicle

images are similar in appearance to cryo-EM images of lipid vesicles, although the ease of manipulation of peptoid chemistry allows great variety in defining the vesicle wall thickness (in this case about twice the typical lipid film thickness) and surface properties. The structural diversity seen with these materials reflects the range of possibilities for developing peptoid-based membranes with specific properties.

References:

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[4] Funding for this work was provided by the Soft Matter Electron Microscopy Program, supported by the Office of Science, Office of Basic Energy Science, U.S. Department of Energy, under contract no. DE-AC02-05CH11231.

Figure 1. A peptoid comprising blocks each having 18 alkyl or ethyleneoxy sidechains (A) self-assembles into hollow tubes. The tubes, imaged by cryo-EM (B), are seen on edge and on end, and have a prominent axial repeat spacing of 2.4 nm, corresponding to the spacing between backbones in the atomic model proposed in (C) [2]. Crystalline sheets are also found in this material, and are the predominant aggregate with the corresponding peptoid having 9 repeats of each sidechain. Electron diffraction of a stack of four of these crystals shows spots corresponding to the 2.4 nm repeat as well as spacings around 0.45 nm corresponding to sidechain spacings, as well as higher orders to at least 0.2 nm.

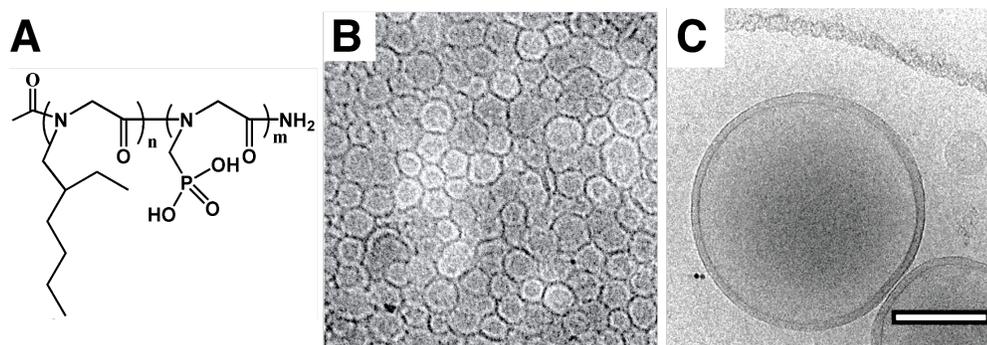
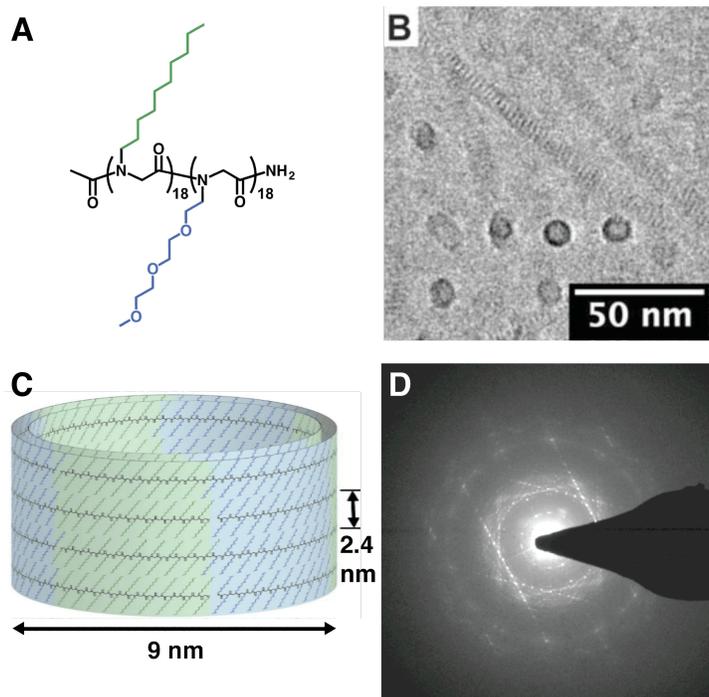


Figure 2. The phosphonated peptoid poly-*N*-(2-ethyl)hexylglycine-*block*-poly-*N*-phosphonomethylglycine (A), with $n=m=18$, assembles into a continuous, phase-separated film over holes in a lacey film, as seen by cryo-EM (B). When mixed into water, it forms vesicles (C) similar in appearance to lipid vesicles imaged by cryo-EM. Scale bar = 100 nm.