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Imaging of Polypeptoid Nanosheets with Atomic Scale Precision (In Honor of Ken Downing)

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The essential 2D crystalline nanostructure comprising synthetic polymers is single crystal that was observed in solution and in melt. The structure of polyethylene (PE) single crystal lamellae grown from solution was studied by using electron diffraction in landmark studies dating back to 1938[1]. Protein-based 2D crystalline membranes, such like purple membrane, were intensively investigated as early as 1975 by Handerson and Unwin[2]. It was later resolved at 3.5 Å resolution in Henderson, Baldwin, Downing, Lepault and Zemlin's co-authored work by applying crystal unbending protocols to the low-dose electron micrographs[3].

The resolution of structures resolved from radiation sensitive soft materials, in particular biomaterials, has been significantly improved in past 10 years due to the introduction of direct electron detectors and the development of novel image processing algorithms for cryo-EM imaging. Imaging synthetic soft materials with atomic resolution using electron microscopy is still challenging because synthetic soft materials are heterogeneous as compared to natural biomaterials.

We designed and synthesized a series of two amphiphilic diblock polypeptoids with the same hydrophilic poly(N-2-(2-(2-methoxyethoxy)ethoxy)ethylglycine) block (Nte) while different N-2-phenylethylglycine-based (Npe) hydrophobic blocks bearing hydrogen, bromine atoms as shown in Figure 1A and 1B. Our experiments were conducted on the crystalline nanosheets formed by self-assembly of these amphiphilic polypeptoid molecules in water. Low-dose cryo-electron microscopy micrographs were obtained from the frozen hydrated crystalline nanosheets. A combination of crystallographic (unbending protocol)[4, 5] and single particle methods [6], developed for cryo-electron microscopy of biological macromolecules, was used to obtain high resolution images of the crystalline nanosheets. As shown in Figure 1C and 1D, the parallel V-shaped and anti-parallel V-shaped motifs can be in the nanosheets formed by different polypeptoids. Figure 1E and 1F shows the FFTs of the corresponding averaged images in Figure 1E and 1F. Our approach is robust and enable direct visualization of the arrangement of bromine atoms in the crystalline polypeptoid nanosheets at 1.5 Å. It also enables the engineering of polypeptoid nanostructures with atomic scale precision [7].

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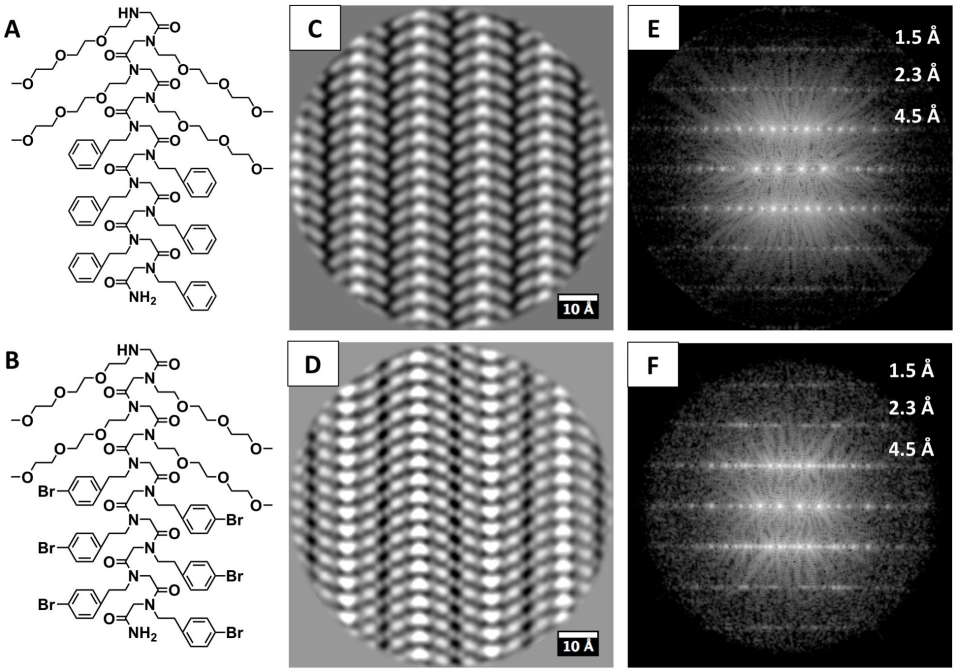

Figure 1. A. Chemical structures of amphiphilic diblock polypeptoid Nte_4-Npe_6. B. Chemical structures of amphiphilic diblock polypeptoid Nte_4-$NBrpe_6$. C. Averaged image of crystalline nanosheets formed by Nte_4-Npe_6. D. Averaged image of crystalline nanosheets formed by Nte_4-$NBrpe_6$. E. Fourier transform of averaged image in C. F. Fourier transform of averaged image in D.

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