

Cite this: Soft Matter, 2012, 8, 3747

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Block-copolymer-like supramolecules confined in nanolamellae†

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Received 5th January 2012, Accepted 8th February 2012

DOI: 10.1039/c2sm00035k

This paper describes the development of a new concept in supramolecular assembly of existing functional polypeptides to form diblock-like molecular clusters through complementary hydrogenbonding interactions, providing a potential route toward design and fabrication of block copolymer-like supramolecular materials.

The design of supramolecular polymers utilizing well-defined hydrogen-bonding interactions has received intensive attention and the desire to use functional small-molecule building blocks through non-covalent interactions of functional molecules has led to the advent of supramolecular materials chemistry. This area of science is primarily focused on the design of functional units capable of ordering into multi-leveled structures by the static self-assembly process.2 Multiple hydrogen bonding interactions used in supramolecular systems are moderately strong and highly directional. These supramolecules possess desirable properties such as thermo-reversibility and responsiveness to external stimuli including pH, solvent polarity, temperature, and concentration³⁻⁵ and also improved thermal and mechanical stabilities as compared with single-hydrogenbonding systems.3

Polyhedral oligomeric silsesquioxane (POSS) with a general structure of (RSiO_{3/2})₈ shows several important features, including the cubic siloxane cage and the distribution of the eight pendant arms from the cube in a three dimensional arrangement. POSS derivatives comprise a family of molecularly precise, near-isotropic molecules that have diameters ranging from 1 to 3 nm, depending on the number of silicon atoms in the central cage and the nature of its peripheral substituent group. 6-12 Over the past decade, POSS molecules have attracted considerable interest as "self-healing" hightemperature nanocomposites and space-survivable coatings, 13,14 lowk dielectric materials, 15 and as templates for the preparation of nanostructural materials such as liquid crystalline polymers,16 catalysts, 17 dendrimers, 18 and multi-arm star polymers. 19-21

Polypeptides are biological macromolecules that are composed of amino acids. A typical polypeptide is composed of different amino acids in different proportion and combination. The conformational studies of model polypeptides are important for making steps toward the biological characteristic of more complex proteins. ²² Generally, the secondary structure of peptide chains plays a crucial role in the

formation of the well-defined tertiary structure of proteins.²³ The knowledge of the primary structure of the peptide chains is also critical for many biochemical and biophysical studies. The α-helix to coil transition in polypeptides with the thermodynamic driving forces was described by Schellman^{24,25} almost 50 years ago. From a synthetic point of view, the most well-known example is poly(γ-benzyl-Lglutamate) (PBLG) that has been employed as a model rigid-rod polymer^{26,27} in bulk and solution states, ²⁸ providing its unique behavior such as thermotropic liquid crystalline ordering, 29,30 thermo-reversible gelation, 31,32 etc. In addition, the synthesized PBLG has both α -helix and β-sheet secondary structures stabilized by intra- and intermolecular hydrogen bonds, 33 which is the most studied secondary motif due to its high frequency in natural proteins.

In our previous study, we combined the well-defined macromolecular architectures of polyhedral oligomeric silsesquioxane (POSS) and PBLG to generate polymeric building blocks having distinct 3-D shapes for the self-assembly of supramolecular structures.34 Furthermore, we also reported that the hydrogen bonding interactions of POSS-based supramolecular macromers can be used in an orthogonal fashion to expand their application in proton exchange membranes. 35,36 There remain many aspects of forming block copolymer-like clusters transferred from binding and recognition events in fundamental research into non-covalent systems. In this study, we devised a strategy of synthesizing an aminophenyl functional initiator containing a uracil (U) unit and then converted it through a ring-opening polymerization (ROP) to a well-defined polymer (U-PBLG). We prepared a POSS macromer containing multi-functional diamidopyridine units (MD-POSS) through a click reaction of propargyl-functional POSS with azide modified diamidopyridine compounds. The U-PBLG is expected to interact with its complementary MD-POSS to form self-assembly ordered structures of the complementary uracil-diaminopyridine (U-DAP) pairing. In addition, the periodic spacing of fabricated secondary cholesteric nano-lamellar morphology can also be controlled by varying the mixing ratio of U-PBLG/MD-POSS blends to tailor the surface activity of the nanolamellae for specific requirements and applications. Herein, we investigated these blends including peptide conformations and functional interactions.

Syntheses and molecular recognition properties of MD-POSS and U-PBLG

A new nanoparticle MD-POSS was synthesized through a click reaction between propargyl-functional POSS with azide modified

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† Electronic supplementary information (ESI) available. See DOI: 10.1039/c2sm00035k

DAP compounds as a hydrogen bonding segment (Scheme 1). MDPOSS was recovered in high yield (83%) after direct filtration and washed with cold diethyl ether. Its molecular weight ($M_{\rm w}=6853~{\rm g}~{\rm mol}^{-1}$) matches well as a POSS derivative containing ten DAP groups which is consistent with the structure of the molecule presented in the ESI†. Subsequently, U-PBLG was synthesized *via* ring opening polymerization using γ -benzyl-L-glutamate as a monomer and uracilinitiator(9), with the resulting U-PBLG exhibiting acceptable PDI (1.21), and *ca.* 30 repeat units, as determined by GPC and ¹H NMR (see ESI†). To further understand secondary structures of U-PBLG between α -helix and β -sheet conformations, it seems likely that the presence of a terminal uracil moiety induces only α -helical conformation in U-PBLG.²⁸ (Detailed conformational analyses are described in ESI†.)

Molecular recognition is an interesting phenomenon that can result in various morphological changes.37 The U-PBLG forms complexes with MD-POSS through complementary U-DAP hydrogen bonding and has the capabilities for forming well-ordered structures through bottom-up assembly of U-PBLG/MD-POSS complexes and the assembly behavior of these complexes was investigated using ¹H NMR titration and circular dichroism (CD) spectra. The U-PBLG/MD-POSS mixture was dissolved in CDCl₃ at 25 °C to calculate the association constant (K_a) of the U–DAP complex where the chemical shift of the amide proton of uracil in the complex U-PBLG/MD-POSS was monitored to give a value of K_a of 114.07 M⁻¹ from Benesi-Hildebrand plots (Fig. S8†). This observed K_a value is significantly lower than the theoretical value of 800 M⁻¹(Fig. 1A),³⁸ implying that only a fraction of the MD-POSS can complex with U-PBLG because the uracil group located at the polymer chain end results in lower probabilities of collisions between DAP and U groups. Therefore, we speculate that the observed low K_a is due to a higher fraction of the DAP-DAP interaction and thus dilutes the influence of the strong DAP-U interaction. To further investigate the self-assembly behavior, CD spectra were measured using various blend ratios of U-PBLG/MD-POSS in THF at 25 °C (Fig. 1B). The incorporation of MD-POSS into U-PBLG led to a red shift from 222 nm to 232 nm, whereas control octaisobutyl-POSS/U-PBLG remained unchanged without wavelength shift. This observation indicates that the red-shifts of U55D and U73D are due to the aggregation³⁹ and the DAP-U complex forms highly stable hydrogen-bonded complexes in THF. It is worthy to note that strong hydrogen-bond-induced helical aggregations of synthetic polypeptides are quite rare, although its DAP-U complex is not completely extended. Both ¹H NMR and CD spectra indicate that

Scheme 1 Synthesis of MD-POSS and U-PBLG.

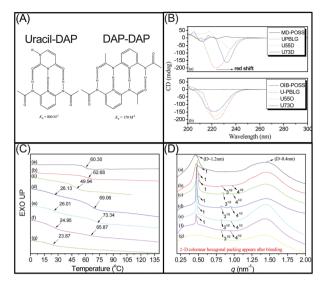


Fig. 1 (A) K_a values of hydrogen bonding pairs between uracil–DAP and DAP–DAP functional groups. (B) CD spectra of (a) MD–POSS/U–PBLG and (b) OIB–POSS/U–PBLG blends in THF. (C) DSC of (a) MD–POSS, (b) U19D, (c) U37D, (d) U55D, (e) U73D, (f) U91D and (g) U–PBLG. (D) WAXS of MD–POSS/U–PBLG blends (a) U–PBLG, (b) U91D, (c) U73D, (d) U55D, (e) U37D, (f) U19D and (g) MD–POSS.

the U-PBLG/MD-POSS interaction occurs through strong cooperative hydrogen bonding between U-PBLG and MD-POSS, resulting in highly special conformational changes in the solution state even though the structural incompatibilities are present between the POSS and polypeptide nanoclusters.

Self-assembly of U-PBLG/MD-POSS in the bulk state

Since U-PBLG and MD-POSS are able to form a star-like copolymer structure, the self-assembly of these complexes in the bulk state was investigated using differential scanning calorimetry (DSC). Fig. 1C displays DSC traces for various U-PBLG/MD-POSS complexes. The glass transition temperatures (T_g) of pure U-PBLG and MD-POSS are at 24 °C and 60 °C, respectively. For the U37D complex, there is one $T_{\rm g}$ at 50 °C, implying that the highly complementary hydrogen bonding interaction benefits the formation of a miscible blend. However, further increasing the U-PBLG content in the U-PBLG/MD-POSS blend (U55D, U73D and U91D) results in two $T_{\rm g}$ s (Fig. 1C) due to the repulsion between PLBG and POSS domains facilitated by DAP-U interaction. On the other hand, the intrinsic nanoscale phase separation is related to the hydrogen bonding and morphological difference between hydrophilic (PBLG) and hydrophobic (POSS) segments. Supramolecular interaction effects on phase separation are intriguing and rarely observed in the past. This leads us to investigate the microstructures of these complexes in more detail through WAXS and TEM characterization.

Fig. 1D displays WAXS patterns of U–PBLG/MD–POSS complexes. U–PBLG shows two amorphous halos with a *d*-spacing of 1.2 and 0.4 nm, corresponding to the distances between the plane of hexagonally packed PBLG rods and helical pitch sizes, respectively. Surprisingly, these U–PBLG/MD–POSS complexes exhibit an obvious shift and a slight decrease in signal half-high-width in their amorphous intensity at high values of *q* (0.47 nm⁻¹), indicative of

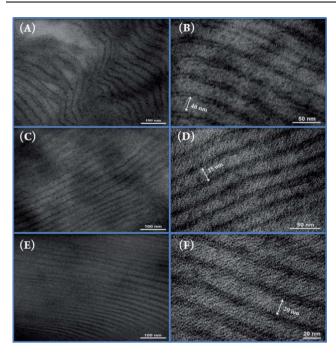
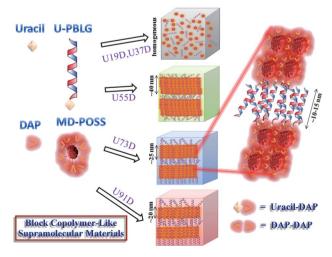


Fig. 2 TEM images of (A) U55D, (C) U73D and (E) U91D and enlargements of (B) U55D, (D) U73D and (F) U91D.

specific structures with a relatively regular structure. In addition, U–PBLG/MD–POSS complexes display strong positions at $1:3^{1/2}:4^{1/2}$, corresponding to the distance between the planes of hexagonally packed PBLG rods. Previous studies indicated that the short-chain PBLG (DP = 30) in solid state cannot assemble to form the cholesteric liquid crystalline and ordered large-scale secondary cholesteric twisting structures. Therefore, the U–DAP interaction must play a critical role in facilitating the formation of the specific twisted microstructures.

To directly observe the microstructure of the U-PBLG/MD-POSS complexes, TEM measurements were carried out (Fig. 2). TEM results showed the random coil structures for U19D and U37D (in Fig. S10†), indicative of amorphous morphologies with a well-dispersed POSS. On the other hand, it also revealed that the highly complementary hydrogen bonding was present within the U-PBLG/



Scheme 2 Morphology of MD-POSS/U-PBLG blends.

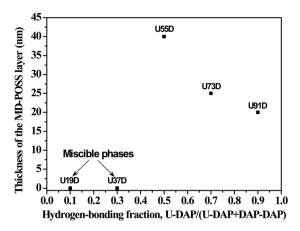


Fig. 3 Thickness of the MD-POSS *versus* hydrogen-bonding fraction as measured by TEM.

MD-POSS complex and resulted in a miscible phase. For the U55D, U73D and U91D blends, well-ordered lamellar structures can be observed as shown in Fig. 2. The dark regions correspond to the U-PBLG phase while the bright regions are attributed to the MD-POSS phase. In addition, all the complexes possess lamellar structures with a U-PBLG phase of 10-15 nm. In the case of the U55D complex, the TEM micrograph shows that the distance between MD-POSS phases is ca. 40 nm. On the other hand, the U73D and U91D complexes possess a relatively small distance between MD-POSS phases (ca. 20–30 nm). According to the above, the increase in the fraction of the MD-POSS within the blends leads to change in the distance between MD-POSS phases due to the assembled MD-POSS through DAP-DAP interaction (Scheme 2 and Fig. 3). Through appropriate design of compositions of the U-PBLG/MD-POSS complexes, the *d*-spacing of the cholesteric lamella morphology can be controlled, enabling us to tailor the surface activity of the nanolamellae for specific requirements and applications.

Conclusions

In summary, U–PBLG/MD–POSS complexes were prepared exhibiting ordered cholesteric lamellar structures. The *d*-spacing between MD–POSS phases can be controlled by varying the component ratio of the complexes, which has rarely been observed previously. This U–PBLG/MD–POSS supramolecular system is the first organic/inorganic supermolecule possessing diblock copolymer-like morphological properties as a result of complementary interactions and provides a potential route toward design and fabrication of block copolymer-like supramolecular materials.

Acknowledgements

We thank Prof. Kung-Hwa Wei's research group for their help with the TEM experiment. This study was supported financially by the National Science Council, Taiwan (contract no. NSC 99-2120-M-009-008).

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