ChemComm

Sequence Isomeric Giant Surfactants with Distinct Self-Assembly in Solution

Journal:	*ChemComm*
Manuscript ID	CC-COM-11-2018-009207.R1
Article Type:	Communication

ChemComm

COMMUNICATION

Sequence Isomeric Giant Surfactants with Distinct Self-Assembly in Solution

Wei Zhang,[a] Wenpeng Shan,[a] Shuailin Zhang,[a] Yuchu Liu,[a] Hao Su,[b] Jiancheng Luo,[a] Yanfeng Xia,[a] Tao, Li,[c] Chrys Wesdemiotis,[a,d] Tianbo Liu,[a] Honggang Cui,[b] Yiwen Li,[e*] Stephen Z.D. Cheng [a,f*]

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

We have designed and synthesized a pair of sequence isomeric giant surfactants based on polystyrene (PS) and polyhedral oligomeric silsesquioxane (POSS) nanoparticles. Although those two macromolecules possess identical compositions as "sequence isomers", the distinctly arranged POSS sequence leads to different molecular packing conformation, and further induce distinguished self-assembly behaviors in DMF/water solutions.

Design and synthesis of sequence-defined macromolecules has attracted a lot of attentions in recent years and still remains to be very challenging. In the synthetic aspect, quite a few elegant approaches have been developed.[1-9] For instance, Meier et al. developed a method to synthesize sequence-controlled oligomers through the Passerini three-component reaction.[10] Lutz and co-workers synthesized sequence-coded polymers with >10k Dalton molecular masses based on the phosphoramidite coupling reaction.[11, 12] Zhang's group achieved sequence-controlled polymers by using furan-protected maleimide as a latent monomer.[13] Although sequence has been well known to be one of the key molecular parameters to determine the structures and properties in biomacromolecules, such as peptides, peptoids and nucleic acid,[14-18] there are only limited amount of works regarding to the sequence effect on synthetic macromolecules.[19-22] Johnson et al. very recently demonstrated that the stereochemical sequence could dictate unimolecular diblock copolymer assembly in the bulk.[23] Our group has developed sequence-controlled "giant molecules", which are precisely defined macromolecules in terms of stereochemistry, composition, sequence, topology and molecular mass built on molecular nanoparticles (MNP) such as polyhedral oligomeric silsesquioxane (POSS) nanoparticles.[24-26] By using POSS nanoparticles as macromonomers, the sequence effect of giant molecules can be amplified, and versatile distinct phase structures, including unconventional Frank-Kasper A15, sigma and dodecagonal quasicrystal structures, have been obtained from the sequence isomers in the solid state.[24, 27] It could also be interesting to investigate the sequence effect of synthetic macromolecules on their self-assembly behaviors in solution or thin film states.

In another aspect, the solution self-assembly behaviors of giant surfactants have been widely investigated in our group.[28-30] Giant surfactants are a kind of precisely defined amphiphilic macromolecules composed of MNP heads and polymer tails. These giant surfactants capture the essential feature of small molecular surfactants while possess much larger sizes.[28] They are thus bridging the gap between traditional amphiphilic block copolymers and small molecular surfactants. Several macromolecular parameters, such as the molecular composition and topology, have been demonstrated to play important roles in the self-assemble behaviors of giant surfactants in solution.[30-33] To further advance our understanding, how does the sequence, as another molecular parameter, affect the solution assembly of giant surfactants remains to be explored. In this letter, we have prepared a pair of polystyrene (PS) and POSS-based "sequence isomers" PS-$(BPOSS)_2$(APOSS) and PS-(APOSS)$(BPOSS)_2$ (denoted as PS-BBA and PS-ABB, where B represents BPOSS with seven isobutyl groups at corners of the POSS core, and A represents APOSS with seven carboxylic acid groups at corners of the POSS core) to explore the effect of sequence in giant surfactants.

[a.] Department of Polymer Science, College of Polymer Science and Polymer Engineering, The University of Akron, Akron, Ohio, 44325-3909, United States
[b.] Department of Chemical and Biomolecular Engineering, The Johns Hopkins University, Baltimore, MD 21218, United States
[c.] Department of Chemistry, The University of Akron, Akron, Ohio 44325-3601, United States
[d.] X-ray Science Division, Advanced Photon Source, Argonne National Laboratory, Argonne, Illinois, 60439, United States; Department of Chemistry and Biochemistry Northern Illinois University, DeKalb, IL 60115, United States
[e.] College of Polymer Science and Engineering, State Key Laboratory of Polymer Materials Engineering, Sichuan University, Chengdu, 610065, China
[f.] South China Advanced Institute for Soft Matter Science and Technology, South China University of Technology, Guangzhou, China, 510640

† Footnotes relating to the title and/or authors should appear here.
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

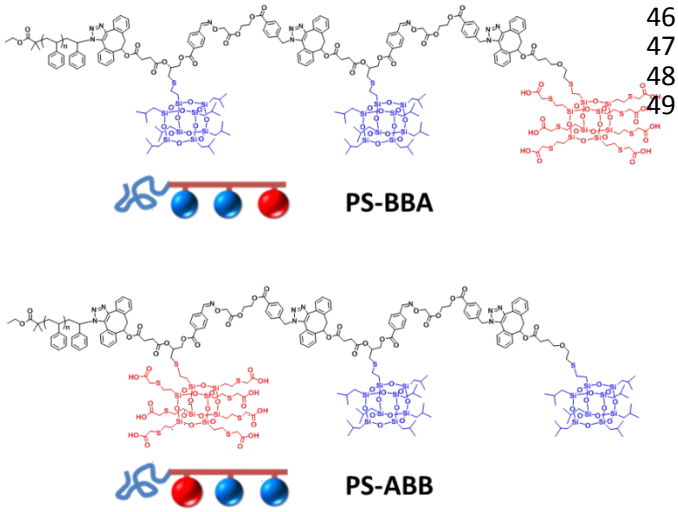


Figure 1. Molecular structures of PS-ABB and PS-BBA.

The polymer-POSS conjugates are synthesized through iteratively performed strain-promoted alkyne cycloadditions (SPAAC) and oxime ligations as we previously reported.[8] Their molecular structures are shown in Figure 1. The detailed synthetic route is listed in the Supporting Information. The building blocks such as DIBO-B-CHO, DIBO-V-CHO, DIBO-B, DIBO-V and the "click adaptor" were prepared as previously described.[8, 27] An azido terminated polystyrene (PS-N_3) with molecular weight of 2k is used as the starting material. Then, two BPOSSs are installed onto the polymer chain-end through two reaction cycles of SPAAC and oxime ligations, followed by attaching one more VPOSS, which has seven vinyl groups at each corner and is the precursor of APOSS. As the POSS NPs are attached onto the polymer chains, in the ^{1}H NMR spectra, the characteristic signals from BPOSS (δ 1.8-1.9 ppm for -C<u>H</u>$(CH_3)_2$) and VPOSS (δ 5.8-6.2 ppm for -C<u>H</u>=C<u>H_2</u>) appear clearly as shown in Figure S1a, and the GPC curves exhibit clear shift toward low retention time, indicating the increase of molecular weight (Figure S1b). Furthermore, matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mass spectrum also shows consistent molecular weight compared to the calculated molecular weight with a single distribution with distance of 104 Da., which corresponds to a styrene repeat unit (Figure S1c). Finally, VPOSS is converted into APOSS via thiol-ene click reaction[34] to afford PS-BBA (Scheme S2). Its "sequence isomer" PS-ABB can be synthesized in a similar way but just with the incorporation of VPOSS or BPOSS in a different step (Scheme S3). Due to the same chemical composition, these two macromolecules show almost identical NMR, GPC and MALDI-TOF spectra (Figures S2-S5).

In the solution assembly study, dimethylformamide (DMF) was used as the common solvent for both the hydrophilic and hydrophobic parts to dissolve the materials at different initial concentrations, water was then added very slowly into the system as we previously described for PS-$(APOSS)_n$ samples.[29, 31] In order to directly compare the influence of sequence issue on these two giant molecules, we used exactly identical conditions to prepare the micellar samples, including initial concentrations of 0.1 wt%, 0.4 wt% and 1 wt%, respectively. It was observed in the transmission electron microscopy (TEM) results that PS-BBA can only form spherical aggregates at different initial concentrations in the experiment (Figures 2a-2c). However, it is very interesting to note that the "sequence isomer" PS-ABB shows different assembly morphologies. For example, at a low concentration (0.1 wt%), it also forms spherical assemblies (Figure 2d). As the initial concentration increases to 0.4 wt%, it becomes cylindrical assemblies (Figure 2e). Further increase the initial concentration to 1 wt%, it could form a kind of ribbon-like assemblies instead of traditional vesicular structures as show in Figure 2f.

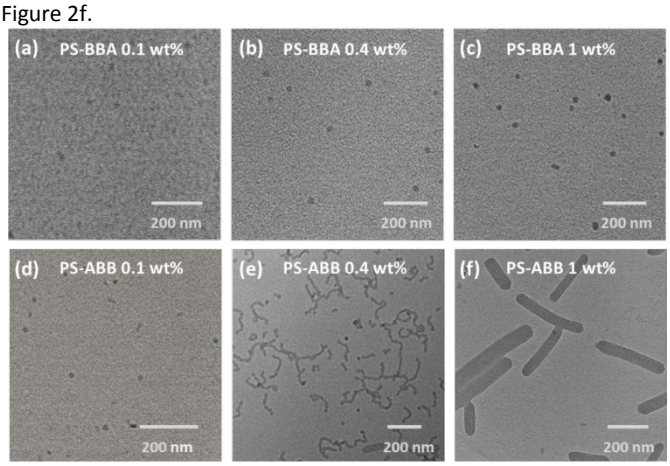


Figure 2. TEM images of the assembled structures of PS-BBA (a-c) and PS-ABB (d-f) at initial concentration of 0.1 wt%, 0.4 wt% and 1 wt%, respectively.

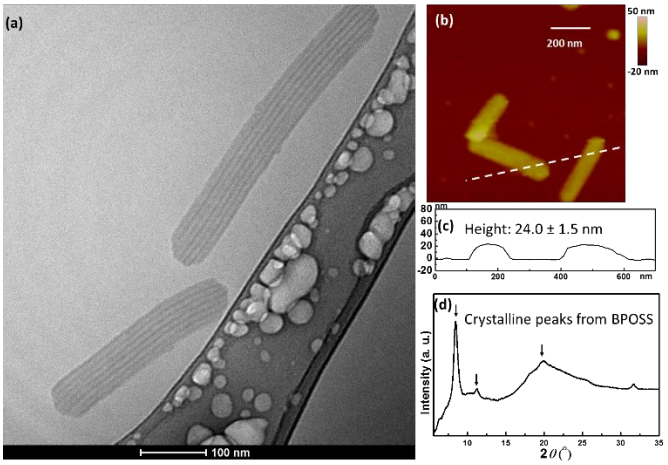


Figure 3. Characterizations of the ribbon-like structure of PS-ABB. (a) cryo-TEM image; (b) AFM image and (c) height profile (d) wide angle X-ray diffraction.

By looking at the ribbon-like assemblies in details, phase separated lamellar structures exist with spacing of about 10 nm. The ribbon-like structure is further confirmed by Cryo-TEM to exclude the drying effects (Figure 3a). The lengths of the ribbon-like assemblies are several hundreds of nanometers with widths around 70-100 nm from the TEM results. The thickness of the ribbon-like assemblies is measured to be about 25 nm using atomic force microscope (AFM) (Figures 3b and 3c).

The concept of packing parameter (p) established in self-assembly of small molecular surfactant system also can be applied to evaluate giant surfactants.[29-31] It is defined as $p = V/(a \times l)$, where V, l and a are the volume and length of the hydrophobic tail, and the cross-section area of the hydrophilic head group, respectively.[35] Three regions of the p values, $p < 0.33$, $0.33 < p < 0.5$, and $p > 0.5$, usually indicate spherical micelles, cylindrical micelles and vesicles/lamellae, respectively. Our previous work has demonstrated that the initial concentration of giant surfactant is one of the criteria in determining the final assembled structure via the degree of ionization of carboxylic acid groups on APOSS, which decreases as

the initial concentration increases.[30] This results in the reduction of effective head size and cross-section area of the surfactant, finally leading to the increase of p.[31]

For these two sequence isomeric giant surfactants, the volume of the hydrophobic part (V) is identical and can be estimated to be 5.6 nm^3 by the following calculation:

$$V = V_B + V_{PS} = \frac{M_B}{N_A \rho_B} + \frac{M_{PS}}{N_A \rho_{PS}} ,$$

where V_B and V_{PS} are the volume of the BPOSS and PS parts respectively; M_B = 1.6 kg/mol (for simplification we include the linker as well) and M_{PS} = 2 kg/mol are the molecular mass of the BPOSS and PS parts, respectively; ρ_B = 1.1 g/cm^3 and ρ_{PS} = 1.04 g/cm^3 are their densities;[36] and N_A is the Avogadro constant.

Polymer tails in giant surfactant has been previously found to be highly stretched especially for low molecular weight, which is different from most traditional amphiphilic block copolymers.[29] So, for simplified qualitative analysis of the difference in self-assembly trending, the contour length of polystyrene tail (l_{PS}) in this work can be estimated about 5 nm by $l = 0.154n\sin(109.5^o/2)$, where n = 40 (two carbons per repeat unit). The length of BPOSS part with the linkers (l_B) is also about 5 nm. When we assume no ionization condition, the smallest cross-section area of APOSS (a_A) can be estimated to be 1.8 nm^2 according to the its diameter of about 1.5 nm. In the self-assembly of PS-BBA, the hydrophobic BPOSS and PS are on the same side of APOSS and thus, they could stay together in the hydrophobic core. This molecule resembles a "one-head one tail" giant surfactant. As the initial concentration increase, the degree of ionization of carboxylic acids on APOSS decreases, which leads in the decrease of effective head size and a_A,[31] so that p becomes larger. Note that p reaches the maximum possible value by assuming no ionization of APOSS and the polar head becomes the smallest volume. It could be calculated to be $p_{max} \approx 0.31$ via the formula $p_{PS\text{-}BBA} = V/[a\times(l_{PS} + l_B)]$. Therefore, the macromolecule would only adapt to a cone-shape conformation and form spheres with any initial concentration of PS-BBA. At the same time, the cone-angle may decrease due to the smaller heads thus more molecules will assemble into one sphere as the concentration increases. This is evidenced from the light scattering experiments in Figure S5 that the size of the spheres increases with the initial concentrations. Notably, the assumption of using contour length of PS in the calculation is also supported by analyzing the spherical micelles of PS-BBA with initial concentration of 0.1% as an example. By subtracting the size of APOSS and the length of BPOSS part with linkers from the measured micelle size of about 11 nm, the calculated length of PS part is about 4.5 nm, which is closed to its fully stretched length.

While for the other sequence isomer PS-ABB, the hydrophobic PS and BPOSS are phase separated by APOSS. In order to avoid the hydrophobic moieties to direct contact with water, the molecule has to adapt to a folded conformation so that both the PS and BPOSS could stay in the hydrophobic core phase. This makes PS-ABB to resemble a "one head two heterogeneous tails" giant surfactant, in which one tail is PS and another tail is two BPOSSs. The two bulky "parallel" linked tails of PS-ABB will make its assembly behavior very different from its sequence isomer PS-BBA. The maximum possible p value can be calculated to be $p_{max} \approx 0.62$ based on the similar calculation (See SI). Therefore, PS-ABB has higher tendency to form non-spherical assemblies such as cylindrical micelles or vesicles, especially at higher concentrations. When the concentration is relatively high at 1 wt%, we speculate that $p > 0.5$ and the it should be in the "vesicle/lamellae region", in which giant surfactants usually forms vesicles.[28] However, in this case, the PS-ABB molecules alternatively form the nanoribbon-like assemblies containing lamellar structure within the ribbons. It is known that BPOSS is a crystalline moiety.[37-39] When the molecule is in or close to a "vesicle/lamellae region", crystallization with high enthalpy may act as the driving force to form unconventional structures.[40] In current case, we speculate that BPOSS may have crystalized, so that a straight lamellar structure is preferred instead of vesicles. According to literature and the above experiments, the freeze-dried self-assemblies of these giant surfactant in solution as shown in Figure 4a could represent their true solution state.[29] So, we perform wide angle X-ray diffraction (WAXD) of the freeze-dried PS-ABB assembled nanoribbon-like structure. In Figure 3d, it clearly shows the diffraction peaks attributed to crystalline BPOSS,[38, 41] which supports our speculation. As the concentration decreases, a_A increases and p decreases. For 0.4 wt%, p value may decrease to below 0.5, thereby, worm-like cylindrical assemblies are observed. At the lowest concentration of 0.1%, p may further decrease to be below 0.33, the assembled structures thus become spheres. In these two cases, due to the formation of curvature structures, BPOSSs are not crystallized, which is confirmed by the WAXD spectra of the corresponding freeze-dried samples as shown in Figure S9. Therefore, a possible model summary of the self-assembly behaviors of these two sequential isomers is proposed in Figure 4.

In addition to different self-assembly behaviors in solution, PS-ABB and PS-BBA also show differences in the bulk state. PS-ABB can also form a lamellar structure after thermal annealing (Figure S10a), but only a disorder structure can be observed in PS-BBA sample (Figure S10b).

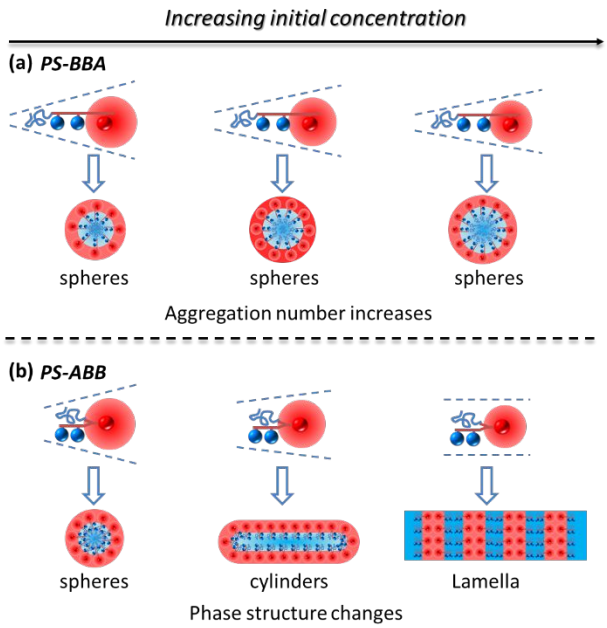


Figure 4. Proposed models for the illustration of the different assembly process for the sequential isomer: (a) PS-BBA and (b) PS-ABB. The blue ball represents BPOSS and the red ball represents APOSS. The red corona around the red ball indicates the partially ionized APOSS, which could become smaller when the initiate concentration increases

To conclude, we have designed and synthesized two giant surfactants with exactly the same composition but different sequences, PS-ABB and PS-BBA. The distinct nanoparticle sequences in giant molecules could lead to different macromolecular conformations, which could further affect their separate self-assembly behaviors in DMF/water solution. The conjugate of PS-BBA, which resembles a "one head one tail" giant surfactant, can only

form spherical assemblies. While the conjugate of PS-ABB, which resembles a "one head two heterogeneous tail" giant surfactant, can form spheres, cylinders or a nanoribbon-like structure in response to different initial concentrations. With the growing field of sequence-controlled oligomer/polymer chemistry, these results further support the importance of sequence-control in synthetic macromolecules, which can have dramatic impacts on the self-assembled structures and macromolecular properties.

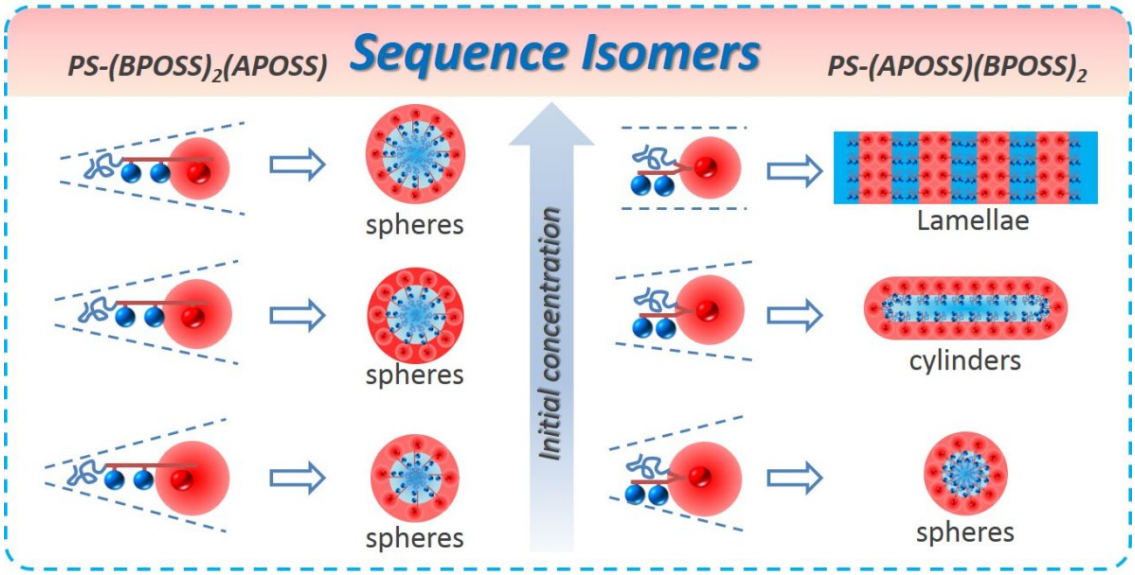
This work was supported by NSF (DMR-1408872, CHE-1808116) and NSFC (51603133). This research used resources of the Advanced Photon Source, a U.S. Department of Energy (DOE) Office of Science User Facility operated for the DOE Office of Science by Argonne National Laboratory under Contract No. DE-AC02-06CH11357.

Conflicts of interest

There are no conflicts to declare

Notes and references

1. M. L. McKee, P. J. Milnes, J. Bath, E. Stulz, A. J. Turberfield and R. K. O'Reilly, *Angew. Chem. Int. Ed.*, 2010, **49**, 7948-7951.
2. M. Porel and C. A. Alabi, *J. Am. Chem. Soc.*, 2014, **136**, 13162-13165.
3. Y.-H. Wu, J. Zhang, F.-S. Du and Z.-C. Li, *ACS Macro Lett.*, 2017, **6**, 1398-1403.
4. A. Anastasaki, B. Oschmann, J. Willenbacher, A. Melker, M. H. C. Van Son, N. P. Truong, M. W. Schulze, E. H. Discekici, A. J. McGrath, T. P. Davis, C. M. Bates and C. J. Hawker, *Angew. Chem. Int. Ed.*, 2017, **56**, 14483-14487.
5. S. Martens, J. Van den Begin, A. Madder, F. E. Du Prez and P. Espeel, *J. Am. Chem. Soc.*, 2016, **138**, 14182-14185.
6. Y. Hibi, M. Ouchi and M. Sawamoto, *Nat. Commun.*, 2016, **7**, 11064.
7. W. Xi, S. Pattanayak, C. Wang, B. Fairbanks, T. Gong, J. Wagner, C. J. Kloxin and C. N. Bowman, *Angew. Chem. Int. Ed.*, 2015, **54**, 14462-14467.
8. W. Zhang, M. Huang, H. Su, S. Zhang, K. Yue, X.-H. Dong, X. Li, H. Liu, S. Zhang, C. Wesdemiotis, B. Lotz, W.-B. Zhang, Y. Li and S. Z. D. Cheng, *ACS Cent. Sci.*, 2016, **2**, 48-54.
9. D. Debnath, J. A. Baughman, S. Datta, R. A. Weiss and C. Pugh, *Macromolecules*, 2018, **51**, 7951-7963.
10. S. C. Solleder and M. A. R. Meier, *Angew. Chem. Int. Ed.*, 2014, **53**, 711-714.
11. A. Al Ouahabi, L. Charles and J.-F. Lutz, *J. Am. Chem. Soc.*, 2015, **137**, 5629-5635.
12. A. A. Ouahabi, M. Kotera, L. Charles and J.-F. Lutz, *ACS Macro Lett.*, 2015, 1077-1080.
13. Y. Ji, L. Zhang, X. Gu, W. Zhang, N. Zhou, Z. Zhang and X. Zhu, *Angew. Chem. Int. Ed.*, 2017, **56**, 2328-2333.
14. J.-F. Lutz, M. Ouchi, D. R. Liu and M. Sawamoto, *Science*, 2013, **341**, 1238149.
15. J. Sun, A. A. Teran, X. Liao, N. P. Balsara and R. N. Zuckermann, *J. Am. Chem. Soc.*, 2013, **135**, 14119-14124.
16. C. Leng, H. G. Buss, R. A. Segalman and Z. Chen, *Langmuir*, 2015, **31**, 9306-9311.
17. Y. Suzuki, G. Cardone, D. Restrepo, P. D. Zavattieri, T. S. Baker and F. A. Tezcan, *Nature*, 2016, **533**, 369-373.
18. R. V. Thaner, Y. Kim, T. I. N. G. Li, R. J. Macfarlane, S. T. Nguyen, M. Olvera de la Cruz and C. A. Mirkin, *Nano Lett.*, 2015, **15**, 5545-5551.
19. C. Laure, D. Karamessini, O. Milenkovic, L. Charles and J.-F. Lutz, *Angew. Chem. Int. Ed.*, 2016, **55**, 10722-10725.
20. J.-F. Lutz, J.-M. Lehn, E. W. Meijer and K. Matyjaszewski, *Nat. Rev. Mater.*, 2016, **1**, 16024.
21. M. Porel, D. N. Thornlow, N. N. Phan and C. A. Alabi, *Nat. Chem.*, 2016, **8**, 590-596.
22. J. Li, R. M. Stayshich and T. Y. Meyer, *J. Am. Chem. Soc.*, 2011, **133**, 6910-6913.
23. M. R. Golder, Y. Jiang, P. E. Teichen, H. V. T. Nguyen, W. Wang, N. Milos, S. A. Freedman, A. P. Willard and J. A. Johnson, *J. Am. Chem. Soc.*, 2018, **140**, 1596-1599.
24. W. Zhang, X. Lu, J. Mao, C.-H. Hsu, G. Mu, M. Huang, Q. Guo, H. Liu, C. Wesdemiotis, T. Li, W.-B. Zhang, Y. Li and S. Z. D. Cheng, *Angew. Chem. Int. Ed.*, 2017, **56**, 15014-15019.
25. W.-B. Zhang, X. Yu, C.-L. Wang, H.-J. Sun, I. F. Hsieh, Y. Li, X.-H. Dong, K. Yue, R. Van Horn and S. Z. D. Cheng, *Macromolecules*, 2014, **47**, 1221-1239.
26. K. Yue, M. Huang, R. L. Marson, J. He, J. Huang, Z. Zhou, J. Wang, C. Liu, X. Yan, K. Wu, Z. Guo, H. Liu, W. Zhang, P. Ni, C. Wesdemiotis, W.-B. Zhang, S. C. Glotzer and S. Z. D. Cheng, *Proc. Natl. Acad. Sci. U.S.A.*, 2016, **113**, 14195-14200.
27. W. Zhang, S. Zhang, Q. Guo, X. Lu, Y. Liu, J. Mao, C. Wesdemiotis, T. Li, Y. Li and S. Z. D. Cheng, *ACS Macro Lett.*, 2018, **7**, 635-640.
28. X. Yu, Y. Li, X.-H. Dong, K. Yue, Z. Lin, X. Feng, M. Huang, W.-B. Zhang and S. Z. D. Cheng, *J. Polym. Sci., Part B: Polym. Phys.*, 2014, **52**, 1309-1325.
29. X. Yu, S. Zhong, X. Li, Y. Tu, S. Yang, R. M. Van Horn, C. Ni, D. J. Pochan, R. P. Quirk, C. Wesdemiotis, W.-B. Zhang and S. Z. D. Cheng, *J. Am. Chem. Soc.*, 2010, **132**, 16741-16744.
30. X. Yu, W.-B. Zhang, K. Yue, X. Li, H. Liu, Y. Xin, C.-L. Wang, C. Wesdemiotis and S. Z. D. Cheng, *J. Am. Chem. Soc.*, 2012, **134**, 7780-7787.
31. Y. Chu, W. Zhang, X. Lu, G. Mu, B. Zhang, Y. Li, S. Z. D. Cheng and T. Liu, *Chem. Commun.*, 2016, **52**, 8687-8690.
32. W. Zhang, Y. Chu, G. Mu, S. A. Eghtesadi, Y. Liu, Z. Zhou, X. Lu, M. A. Kashfipour, R. S. Lillard, K. Yue, T. Liu and S. Z. D. Cheng, *Macromolecules*, 2017, **50**, 5042-5050.
33. S. A. Eghtesadi, M. A. Kashfipour, X. Sun, W. Zhang, R. S. Lillard, S. Z. D. Cheng and T. Liu, *Nanoscale*, 2018, **10**, 1411-1419.
34. Y. Li, X.-H. Dong, Y. Zou, Z. Wang, K. Yue, M. Huang, H. Liu, X. Feng, Z. Lin, W. Zhang, W.-B. Zhang and S. Z. D. Cheng, *Polymer*, 2017, **125**, 303-329.
35. R. Nagarajan, *Langmuir*, 2002, **18**, 31-38.
36. K. Wu, M. Huang, K. Yue, C. Liu, Z. Lin, H. Liu, W. Zhang, C.-H. Hsu, A.-C. Shi, W.-B. Zhang and S. Z. D. Cheng, *Macromolecules*, 2014, **47**, 4622-4633.
37. L. Cui, J. P. Collet, G. Xu and L. Zhu, *Chem. Mater.*, 2006, **18**, 3503-3512.
38. M. Huang, C.-H. Hsu, J. Wang, S. Mei, X. Dong, Y. Li, M. Li, H. Liu, W. Zhang, T. Aida, W.-B. Zhang, K. Yue and S. Z. D. Cheng, *Science*, 2015, **348**, 424-428.
39. H. Liu, J. Luo, W. Shan, D. Guo, J. Wang, C.-H. Hsu, M. Huang, W. Zhang, B. Lotz, W.-B. Zhang, T. Liu, K. Yue and S. Z. D. Cheng, *ACS Nano*, 2016, **10**, 6585-6596.
40. J. Zhang, L.-Q. Wang, H. Wang and K. Tu, *Biomacromolecules*, 2006, **7**, 2492-2500.
41. A. J. Waddon and E. B. Coughlin, *Chem. Mater.*, 2003, **15**, 4555-4561.



Two sequence isomeric giant surfactants exhibit distinguished self-assembly behaviors, which is mandated by different molecular packing conformation induced by molecular sequence.