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Review Article

A mini-review on bio-inspired polymer self-assembly: single-component and interactive polymer systems

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Biology demonstrates meticulous ways to control biomaterials self-assemble into ordered and disordered structures to carry out necessary bioprocesses. Empowering the synthetic polymers to self-assemble like biomaterials is a hallmark of polymer physics studies. Unlike protein engineering, polymer science demystifies self-assembly by purposely embedding particular functional groups into the backbone of the polymer while isolating others. The polymer field has now entered an era of advancing materials design by mimicking nature to a very large extend. For example, we can make sequence-specific polymers to study highly ordered mesostructures similar to studying proteins, and use charged polymers to study liquid–liquid phase separation as in membraneless organelles. This mini-review summarizes recent advances in studying self-assembly using bio-inspired strategies on single-component and multi-component systems. Sequence-defined techniques are used to make on-demand hybrid materials to isolate the effects of chirality and chemistry in synthetic block copolymer self-assembly. In the meantime, sequence patterning leads to more hierarchical assemblies comprised of only hydrophobic and hydrophilic comonomers. The second half of the review discusses complex coacervates formed as a result of the associative charge interactions of oppositely charged polyelectrolytes. The tunable phase behavior and viscoelasticity are unique in studying liquid macrophase separation because the slow polymer relaxation comes primarily from charge interactions. Studies of bio-inspired polymer self-assembly significantly impact how we optimize user-defined materials on a molecular level.

Introduction

Biomaterials have a lot to teach us how to control polymer self-assembly. Biological macromolecules are encoded with information to form intrinsically ordered and disordered regions to carry out a plethora of functionalities necessary for bioprocesses [1,2]. Encoding synthetic materials with information opens opportunities to guide polymer self-assembly for hierarchical organization and compartmentalization that only biopolymers were capable of before [3]. Multiple intra- and inter-molecular interactions (e.g. hydrophobicity, electrostatics, sterics, and hydrogen bonding) contribute simultaneously to the ultimate shape of the polymer. Isolating these intertwined factors is meaningful but challenging for the polymer community when developing fundamental understandings of controlling polymer self-assembly. In return, wisdom gained from artificial polymer systems could potentially be applied to explain malfunctions of biomaterials due to loss of desired structures. Where biology and polymers meet inspires tremendous innovations for materials to have nature's ability to form structured complexes with advanced performance.

Seeking molecular control over bulk polymer assembly has been a longstanding quest in polymer and biology studies. How much power do we need in our synthetic polymer systems to make them work like biological macromolecules? What control handles have been given to us to tune artificial

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soft materials to make more meaningful polymers [4]? The increasing number of publications on 'bio-inspired polymers self-assembly' (111k as of August 2022, Web of Science!) indeed tracks the vigorous activities of embedding nature's capability into synthetic polymers. In this mini-review article, challenges and recent advances in controlling self-assembly will be elaborated. Self-assembly will be discussed in (1) single-component systems to study the phase junction in block copolymers and to investigate hierarchical mesostructures formation [5,6], and (2) multi-component systems in the context of complex coacervation, which is a charge-driven liquid–liquid phase separation phenomenon [7] (Figure 1).

Self-assembly in a sequence-controlled, single-component system

Self-assembly in a single-component polymer system is a common phenomenon in biological systems. Decoupling the intertwined factors contributing to the ultimate chain shape requires precise control of polymer chemical structure as subtle changes in chemistry might smear the bulk polymer properties. In contrast with traditional random copolymerization methods, sequence-defined polymer platforms provide a great handle to make on-demand polymers with precise control over chain comonomer composition, patterning, and chain length distribution [8]. There are a few well-established sequence-defined polymerizations, such as precise macromonomer approaches and interactive chain growth, and a wide variety of polymer backbones, such as the biomimetic polypeptoid/peptides, hybrid, and modified monomers, available for forming self-assemblies on a broad length scale [9–12].

Among sequence-controlled polymerization methods, polypeptoids are one of the most convenient to make with excellent yield and monodispersity [6], thus being widely used to develop fundamental understandings of polymer physics on self-assembly otherwise hard to achieve with traditional random copolymerization techniques. The fully robotic polypeptoid synthesis method grows polymer chains on a solid substrate and continues adding half-monomers cyclically with (1) an acylation step of a halogenated carboxylic acid in the presence of a coupling agent and (2) a displacement step with a primary amine. Functional monomers are directly incorporated into the polypeptoid backbones by forming an amide bond, which also avoids stereochemistry or hydrogen bonding as in other sequence-defined polymer platforms. Having tremendous flexibility in chemistry, to

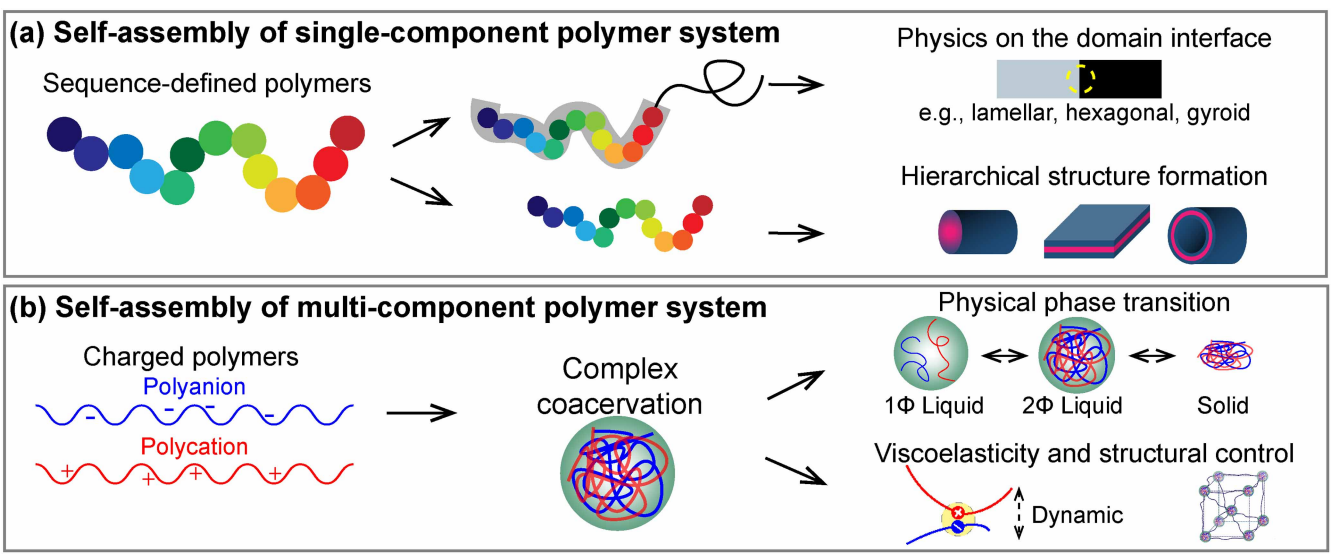

Figure 1. A schematic overview of the topics covered in this review, including (a) single-component and (b) the multi-component polymer systems.

In the single-component systems, hybrid polymers will be discussed to demonstrate the steric effects between domains in self-assembled block copolymers. The role of sequences will be elucidated in controlling hierarchical structures formation. In the multi-component system, complex coacervation as a classic macro-ionic phase separation phenomenon will be discussed in terms of phase behavior, viscoelasticity, and hierarchical structures formation.

date polypeptoids have been used to study the effects of local chain stiffness, hydrophobicity/hydrophilicity, patterning, chain lengths, and defects in bulk polymer properties, including self-assembly.

Polypeptoids are designed as a controllable segment to control block copolymer assembly. When chemically incompatible segments are covalently bonded together to form a block copolymer, phase separation occurs to form domains rich of either polymer as demixing minimizes entropy. Guiding polymer micro-phase separation into complex structures, such as lamellae, gyroids, and hexagonal cylinder packing was a game changer and created opportunities to extend polymer uses on much smaller scales, such as membranes for nanofiltration [13] and directed self-assembly for nanopatterning [14]. The Segalman group systematically embedded helices in hybrid diblock copolymers to learn the chain steric limitations in forming complex structures [15]. Helices are peculiar structures found in biological macromolecules to stiffen chains. Helical and stiff polypeptoid block was synthesized with chiral side groups, whereas the coiled and flexible polypeptoid block was with racemic side groups [15–18] (Figure 2a). Other than helicity, both polypeptoids were chemically identical. In dilute solutions, helical polypeptoids have smaller statistical segment lengths than flexible ones, but similar insensitivity to solvent qualities. This suggests that the polypeptoids have stronger self-steric constraints than polymer–solvent interactions in determining chain conformation [16]. To further demonstrate the effect of a stiffer block, helical polypeptoids were clicked to a poly(n-butyl acrylate) (PnBA, coil) to form a diblock copolymer (Figure 2b) [15]. The domain size of a hexagonal cylinder packing structure increased, and a lower order-disorder transition temperature was found, both attributing to extensive chain stretching near the block junction and negative packing interactions at the cylinder center. Similarly, an interfacial helical segment in a polystyrene (PS, coil)-polypeptoid diblock copolymer shifted the self-assembly window towards less organized conformation, showing that chain flexibility is important for more organized nanostructures (Figure 2c) [17]. Furthermore, in the lamellae phase window, helicity lowered the disorder temperature without negatively impacting the domain size (Figure 2d) [18]. A minor enthalpic penalty and a significant entropic gain were captured as a result of interfacial chain stretching. Without changing the overall polymer chemistry, polypeptoids demonstrated that a stiffened segment leads to intensified chain stretching in the block junctions that disfavors block copolymer self-assembly into more ordered nanostructures.

Monomer sequence can also tune self-assembled lamellar structures demonstrated by a hybrid diblock copolymer, PS-polypeptoid (Figure 2e) [19,20]. The polypeptoid block containing non-compatibilizing units formed lamellae with the most distinct phase boundary. The presence of compatibilizing units in the polypeptoids segment increased interfacial widths and interfacial mixing [20]. Simulation based on self-consistent field theory supported the hypothesis of chain conformational change caused by localizing compatible comonomers at the domain interface [19]. These exciting findings demonstrate fascinating fine-tuning methods to smear phase boundaries while minimizing mixing efforts to compatibilize blocks in one single polymer molecule. Moving on, reversed studies to look for minimal required chirality and compatibilizing units will be of interest to the biology and biomedicine community to design sensors that detect cellular aggregates formed as a result of protein misfolding or denaturing due to sequencing mistakes.

More hierarchical two-dimensional and three-dimensional structures can be achieved by combining hydrophobic and hydrophilic side groups in alternating or diblock sequences, such as nanofibers [21–23], nanotubes [23–25], and nanosheets [26–33] (Figure 3). Hydrophobic (e.g. aromatic, halogenated aromatic, and aliphatic) and hydrophilic (e.g. carboxylic and amine) side groups are used to tailor the amphiphilicity of the polypeptoids to form nanostructures freely in solution or assisted by a substrate [21,31,32]. The strong hydrophobic interactions (π–π stacking) are a typical self-assembly driving force. To form a hydrophobic core in bilayer nanosheets, experiments and simulation showed evidence of amide bond rotation from trans- (coiled) to *cis*-conformation to facilitate dense polymer packing in alternating residual sequences [34,35] (Figure 3a). An interesting report showed that three units were the onset for polypeptoids to self-assemble into ordered nanosheets and nanofibers: two phenyl and one amine side groups [22]. Intriguingly, the molecular orientation in a nanosheet crystalline was visualized by a cryogenic electron microgram which provided information of precise chain stacking on an atomic level for the first time [29]! The tolerance of hydrophobic packing was investigated by chemically modifying the phenyl side groups in different positions to examine for nanosheet formation [27] and stability [26]. Aromatic side groups with two carbon spacers (phenethyl side group) appeared to favor nanosheets formation potentially due to greater rotational flexibility required for lateral and planar π interactions. Setting up the molecules with appropriate degrees of freedom for sufficient intra- and interpolymeric interactions hydrophobically and electrostatically is important in controlling ordered structures formation as applied materials. A study on encapsulating proteins and oxide nanoparticles into multilayered

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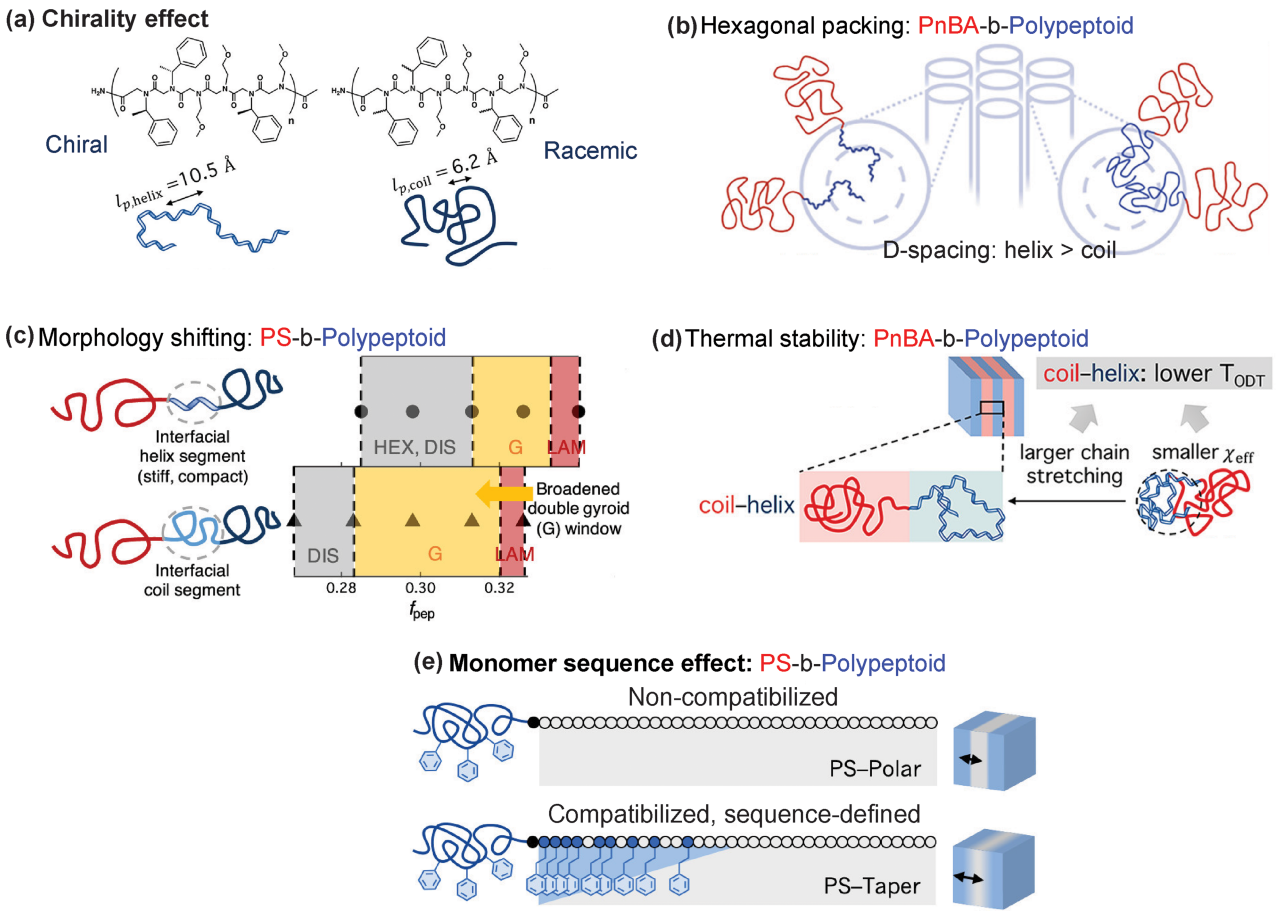

Figure 2. Demonstration of how side group chirality and monomer sequence affect block copolymer bulk self-assembly.

(**a**) Chemical structures of helical polypeptoids formed with chiral side groups and coiled polypeptoids formed with racemic side groups. The helical persistence length was a correlation distance along the helical contour, while the coiled persistence length was along the polymer chain contour, suggesting that helices made the polypeptoids segment more locally stiff in chain conformation while the chain remained overall flexible. Adapted with permission from ref. [18]; copyright © 2019 American Chemical Society. (**b**) Illustration of poly(n-butyl acrylate) (PnBA)-b-polypeptoids forming hexagonally packed cylinders, where helical polypeptoids block increased D-spacing due to unfavorable packing conditions due to chain stretching. Adapted with permission from ref. [15]; copyright © 2018 American Chemical Society. (**c**) Demonstration of polystyrene (PS)-b-polypeptoid self-assembled into different nanostructures and a helical interfacial segment shifted the self-assembly window towards a more significant polypeptoids volume fraction with narrower gyroids region. Adapted with permission from ref. [17]; copyright © 2021 American Chemical Society. (**d**) Representation of PnBA-b-polypeptoids self-assembled into lamellae structures with lower thermal stability against disordering, indicating unfavorable chain stretching in forming lamellae morphology. Adapted with permission from ref. [18]; copyright © 2019 American Chemical Society. (**e**) Schematic PS-b-polypeptoid diblock copolymer with non-compatibilized and compatibilized polypeptoid segments to form lamellae structures with widening intermixing regions. Adapted with permission from ref. [19]; copyright © 2020 American Chemical Society.

polypeptoid nanosheets [31] shows a promising future for using self-assembled polymers as scaffolds, functional membranes, and drug delivery vehicles.

Self-assembled nanotubes can be formed from blocky co-polypeptoid structures with one or more nonpolar segments [23–25,36,37]. The ordering of the nonpolar groups was shown to start with spheres, then a lipid-like bi-layer, followed by rolling into a single-walled tube with excellent chemical stability and mechanical strength (Figure 3b) [25]. Nonpolar block size is proportionally scaled to the tube diameter and wall thickness. A three-arm polypeptoids design demonstrated the transition from nanotubes to nanofibers by replacing the aromatic side groups with aliphatic ones and reducing the number of polar side groups [23]. Aromatic side groups with only one carbon spacer (benzyl side group) dominated reports on polypeptoid nanotubes. Surprisingly, one report showed single-wall nanotube formation from diblock copolypeptoids prepared with linear polar and

nonpolar side groups in tiles using only van der Waal interactions (Figure 3) [24]. The diameter of the nanotubes proportionally scales with the size of blocks, indicating a good control handle for tube formation. The sequence-defined platform is a great tool to advance studies of polymer self-assembly by fine-tuning specific parts of the sequence without disrupting the rest of the molecule, providing precise structure-property correlations otherwise difficult to achieve.

Polypeptoids have great potentials to embed more functionalities to target real-life problems. It will be curious to investigate the minimal changes in structures and sequence required to migrate hierarchical structures from one to another. Defect tolerance would also be an attractive direction to look into as we have a powerful tool to plant mistakes on a monomer level that could be useful in a wide range of applications. For example, we can develop diseases related models to see how discontinuous hydrophobic residuals would affect hydrophobic core formation as in biological bilayer structures. Another approach will be to explore the targeted disassembly of the sheets and tubes as protective encapsulation scaffolds to release hydrophobic drugs. All of the forementioned applications will rely on building a more fundamental understanding of structure-processing-property relations with sequence-defined polymers.

Self-assembly induced by electrostatic in a multi-component system

A cell is a crowded place full of charged macromolecules interacting with soft frictions in water so learning to take advantage of the electrostatic interactions to drive self-assembly becomes beneficial. About 100 years ago, Oparin [38] and Haldane [39] theorized almost simultaneously that life might have started in a simple soup rich in large molecules in the primitive ocean (similar to the idea of membraneless organelles). Even though the linkage between the physical material condensation and biology remained unestablished, the idea of a stable liquid–liquid phase separation driven by supramolecular interactions attracted lots of investigations in soft materials design. Bungenberg de Jong and Kruyt used the term 'coacervates' for the polymer-rich phase in liquid–liquid phase separation, a colloidal assembly between oppositely charged polyelectrolytes [40,41]. Ever since the 1920s, research in coacervates and their formation mechanism has covered the span of almost all categories in charged polymer science. And coacervation also facilitated new developments in encapsulation and drug delivery methods [42,43], food and personal care products [44,45], and compartmentalization [46–48]. Understanding the unique charge-driven phase behavior has become the key to studying complex coacervates and polymer chain dynamics [49–51].

With low surface tension and abundant charge interactions [52], complex coacervates have a long history of being used to encapsulate cargos, e.g. proteins/polypeptides [53–57], DNA/RNA [58], water-soluble cargos [59–61], and biomedicine [62,63]. The non-ionic hydrophobic backbone and aromatic side groups are strong promoters for cargo loading because the polymer-cargo π–π interactions resist swelling in the coacervates phase [60,61]. However, highly ionic environments can destroy the coacervation equilibrium due to having no entropic gain from crowding small molecules in a polymer-rich phase. Coacervate microencapsulation leads to developing encapsulation scaffolds for molecules of a wide variety of hydrophobicity as well as target delivery vehicles that are sensitive to environmental changes, such as salt and local pH.

The solid intractable polyelectrolyte complexes (PECs) and liquid coacervates were studied separately for a long time and the transition has only recently been discovered. Solid PECs exhibit tremendous potentials in thin film science [64–67] because of their great encapsulation and self-healing capability, as well as pH and salt sensitivity [68–71]. And PECs demonstrated unexpected moisture-dominating polymer relaxation and toughening even in the absence of salt [72–75]. Recently, the Schlenoff group showed the phase transition continuum from solid to liquid complex coacervates using a canonical pair of polyelectrolytes, poly(4-styrene sulfonate sodium salt) (PSS) and poly(diallyldimethyl ammonium chloride) (PDADMAC) in the presence of potassium bromide (KBr) [49] (Figure 4a). Neutron scattering confirmed that the chain conformation was flexible (Gaussian polymer) in coacervates, supported by the decreasing radius of gyration due to the abundance of salt and water as opposed to solids [76]. In particular, the Perry group used rheological methods to probe the polymer network change as a result of the physical transition from solid PECs to liquid coacervates [77]. A frequency-invariant crossover point in the normalized complex moduli was identified as an 'diphasic' salt concentration that separated a gel-like network with ionic crosslinkers and a flexible polymer network with dynamic ionic bonds (Figure 4b). This solid-to-liquid transition opens a new processing window of using complex coacervates thanks to the special salt-plasticizing nature of PECs. There are a few special features of

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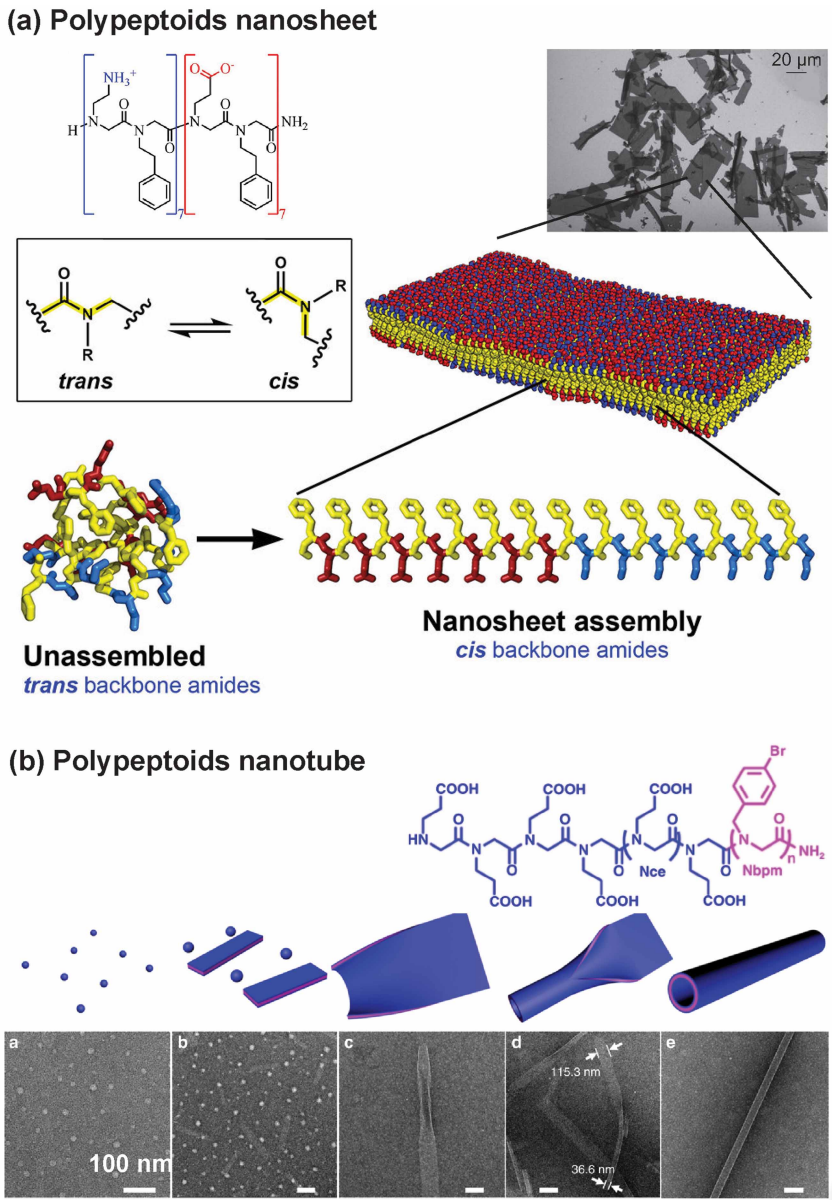

Figure 3. Demonstration of how polypeptoids of different hydrophobic and hydrophilic monomer arrangements can lead to self-assembled into (a) nanosheet and (b) nanotubes.

(**a**) Polypeptoids have a conformational change while densely packed into a lipid-like bilayer nanosheet structure. Adapted with permission from [35]; copyright © 2018 American Chemical Society. (**b**) The polypeptoids nanotubes formed over time and evolved from spheres with a hydrophobic core, bilayer sheet, and a tube. Adapted with permission from [25]; copyright © 2018 Springer Nature publishing group.

the thermodynamically stable, macro-ionic coacervate phase, for example, net charge neutrality [78] and time-dependent mixing kinetics to reach equilibrium [79]. Whereas PECs can have overcompensating polymer components [80,81] and kinetically trap polymers while forming a precipitate. Harnessing the liquid nature of complex coacervates, nanofabrication of films [82,83] and fibers [84–86] with a fully water-based method in one step was enabled, leading to the invention of more environmentally friendly precursor solutions.

Controlling coacervation, or the liquid–liquid phase separation behavior, is key to studying the coacervate self-assembly. Having hundreds of polyelectrolytes coacervated, the significant role of the polymer backbone chemistry is demonstrated in detail [87,88] (Figure 5a). In general, greater molecular weight [50,84,89], more

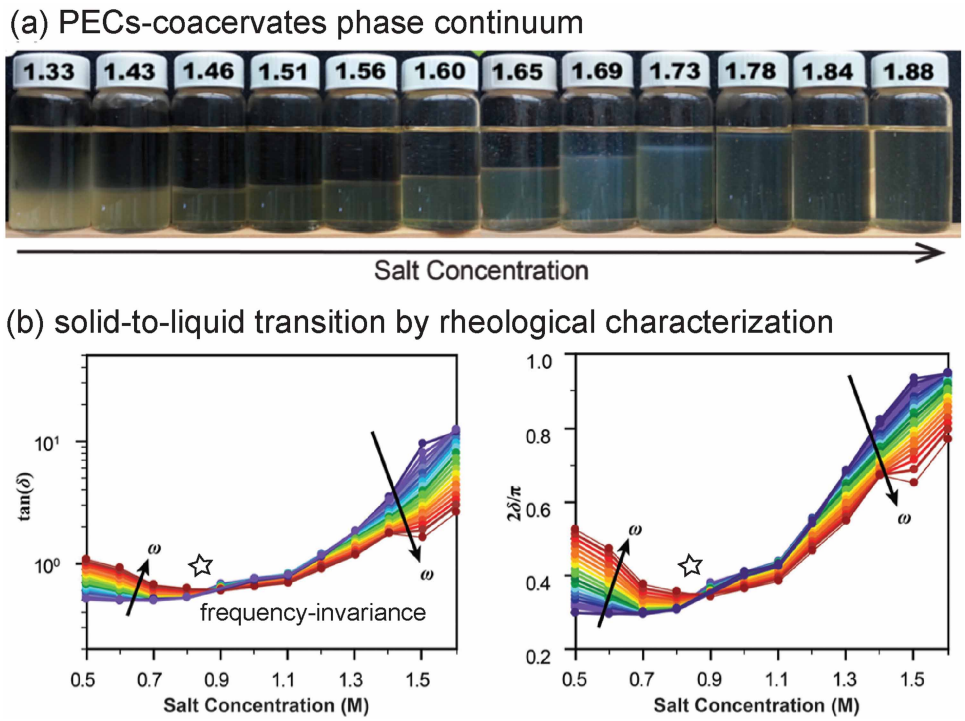

Figure 4. The reversible phase transition continuum of polyelectrolytes complexation between liquid to solid physical states.

(**a**) A digital photograph of the poly(4-styrene sulfonate sodium salt) (PSS) and poly(diallyldimethyl ammonium chloride) (PDADMAC) complex coacervates prepared in increasing salt concentrations. The numbers at the cap of each vial were the as-prepared KBr concentration. Adapted with permission from ref. [49]; copyright © 2014 American Chemical Society. Further permissions related to the material excerpted should be directed to the ACS. (**b**) Plots of tan(δ) and the normalized phase angle 2δ/π on the PSS/PDADMAC complexes and coacervates as a function of as-prepared salt concentration. Data were shown for oscillation frequencies from 1–100 rad/s indicated by the arrows. The star highlighted a frequency-invariant point marking the transition between solid-to-liquid in complexes. Adapted with permission from ref. [77]; copyright © 2017 Royal Society of Chemistry.

hydrophobic backbones [90–93], and charge densities [94,95] enhance coacervates/PECs salt resistance; and small protonated amines and aromatic sulfonate bind strongly [96]. In addition, sequence-defined polypeptides provided insights into weak polyelectrolytes coacervation to combat precipitation as a result of strong hydrogen-bonding. The interplay between chirality, charge density [92,93] patterning [97–101], and hydrophobicity (π-interactions) has been examined. In particular, having a racemic polypeptide component, a small segment of homochiral units and alternating chiral unit patterning contribute positively to liquid coacervates formation because hydrogen bonding was disrupted. Intriguingly, the different surface tensions of coacervate droplets were shown to facilitate the formation of hierarchically organized, multiphasic coacervate droplets with up to three compartments [102] (Figure 5b). This finding provides a prototypical scenario for biological condensates in primitive ocean and membraneless compartmentalization while bridging polymer chemistry and biophysics.

Modulating charge and neutral blocks (i.e. di-block, terminal, and centered) of polyelectrolyte was shown to control the formation of different hierarchical structures in the coacervate phase (Figure 5a). While bulk coacervates have been the mainstream in studies, lamellar [104], micelles [105,106], hexagonal cylinder packing [107], and crosslinked gels network (including body-centered cubic structure) [108–110] are achieved via chemically modifying the backbone chemistry of the polyelectrolytes and tuning the polymer/salt volume fraction. Among others, lamellae should be the easiest to develop as the two blocks of have extremely low compatibility (i.e. large χ, Flory-Huggins interaction parameter) thus a phase separation is entropically favored. However, although theory and simulations provided excellent predictions of forming lamellae structure by capturing the

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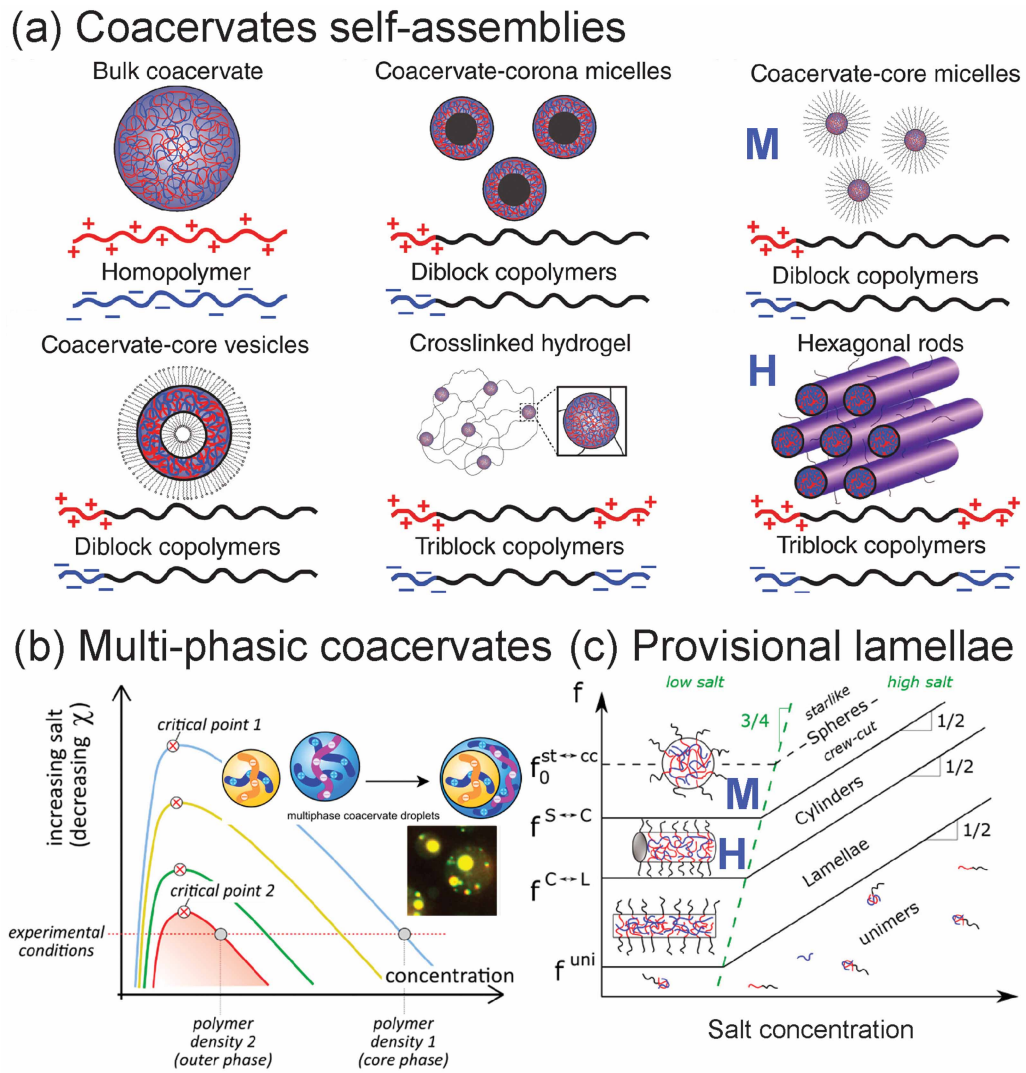

Figure 5. Schematic of the interactive complex coacervates self-assemblies formed with various oppositely charged homo- and copolyelectrolyte structures.

(**a**) Schematic presentation of the structure of complex coacervates to form bulk, micellar, gel, and hexagonally packed cylindrical morphologies in solution. Adapted with permission from ref. [62]; copyright © 2016 John Wiley and Sons publishing groups. (**b**) Multiphasic coacervates coexist in a single droplet with different surface tensions, indicating stable liquid–liquid coacervates phase separation across other polymer systems in a single incident. Adapted with permission from ref. [102]; copyright © 2020 American Chemical Society. (**c**) A simulation diagram showing the combinations of polymer ionization in diblock polyelectrolytes and salt concentration for possible lamellae formation in complex coacervates. Adapted with permission from ref. [103]; copyright © 2018 American Chemical Society.

intense polymer-salt-water interplay, lamellae is experimentally the hardest to form in coacervation (Figure 5c) [103,111,112]. It is difficult to make polyelectrolytes with a perfect polarity balance between hydrophobic, hydrophilic, and ionic segments that entropically favors lamella. Moving on, I believe the electrostatic-driven self-assembly will inspire more work to leverage charges to compatibilize traditionally incompatible polymers [113], intensify chain interactions, and stabilize polymers chemically and temporarily, enabling on-demand polymer chain morphology changes in an applied materials perspective.

A more comprehensive understanding of the dynamic molecular interactions inside complex coacervates has been developed by joint efforts of experiments and simulation tools. Multiple complex parameters, such as charged site connectivity, polymer compatibility, and the water network have been taken into account for

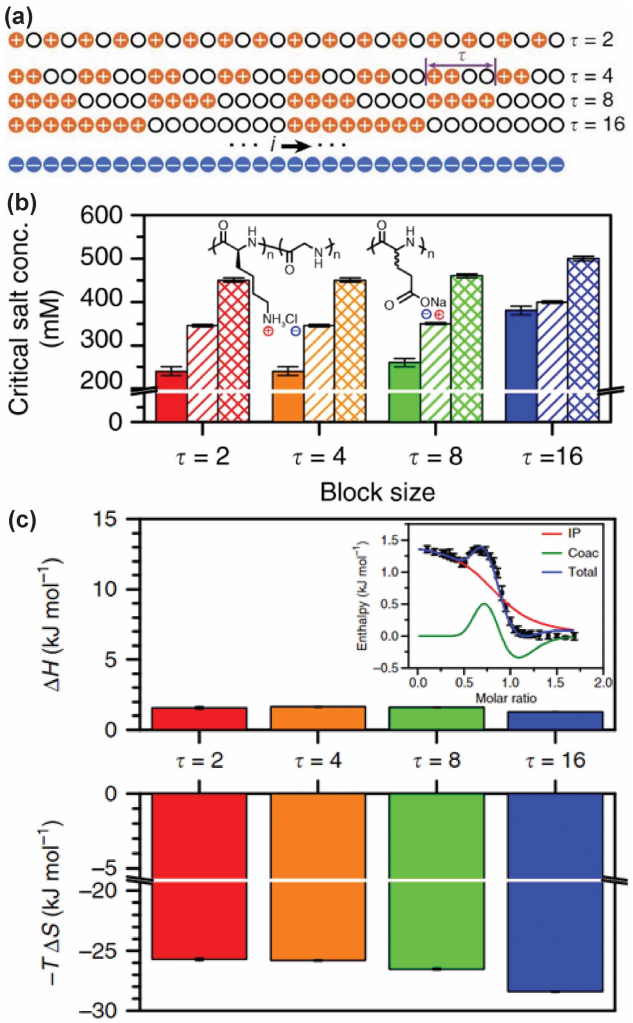

Figure 6. Schematic demonstration of the structures of sequence-defined polycations with increasing charge and neutral block size using polypeptides to form coacervates with fully charged polyanions.

(**a**) The block size τ indicated each repeat unit in the polycation. The polyanion was fully charged and stoichiometrically mixed to form coacervates. (**b**) Salt resistance increased as τ increased for each combination. (**c**) Different block sizes barely made a difference in enthalpy. At the same time, the entropic gain increased for larger block sizes, suggesting that coacervation was entropy-driven and larger block sizes had more significant entropic gain. Adapted from ref. [118]; copyright © 2017 Springer Nature publishing group.

physical accuracy [114,115]. Contribution to free energy upon complexation came primarily from the entropy due to the release of counter-ions and water restructuring [116–119]. Sequence-defined polypeptides showed a more significant entropic gain from coacervating the pairs with a larger block of neutral monomers and a greater salt resistance (Figure 6) [118]. The larger repeat unit size led to a more compact structures as lower probability of counterion and water aggregating near neutral segments, as well as a more significant excluded volume effect. Greater activation energy and longer time are required to shift the consecutively paired charges all at the same time [91,117–120]. It is worth mentioning that effects of charge connectivity and polymer excluded volume were neglected in traditional models but captured by the Sing group who used a polymer reference interaction site model (PRISM)-based model. Combining sequence-specific polymer materials and simulation works, a much more comprehensive description of complex coacervation will be readily developed in the foreseeable future.

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Complex coacervates are viscoelastic materials because ionic pairs constantly form and break between oppositely charged polymers in water [121–123]. This unique chain interactions lead to the viscoelastic nature of complex coacervates, differentiating coacervates from traditional polymer solutions whose rheological property was predominantly determined by polymer topology, concentration, and chain length [124]. In other words, as the classic sticky Rouse Model suggests, the ionic bonds create an interactive ionic network with friction points between polymers to slow down chain relaxation. A characteristic relaxation time parameter is commonly referred to describe how liquid-like or solid-like of a coacervate [124–127]. Similar to controlling the phase behavior of coacervation, slower chain relaxation was found in systems with more hydrophobic backbones [91], decreasing dielectric constant in the solvent background [122,128], greater temperature, and less ionic environments [129,130]. Coacervates are also linear viscoelastic materials, meaning their dynamic moduli are self-similar and could be superposed to reveal a governing behavior by shift factors, such as temperature, pH, solution dielectric constant, salt/polymer concentration [121–123,127,129]. The capability to manipulate the interactions in complex coacervates significantly impacts how coacervates can be designed as interactive material platform for uses in a wide range of applications. With the versatile handles given to tune the charge interactions in water, future work to embed functionalities to complex coacervate materials will benefit a lot from the fundamental theories developed so far, for example, making a semiconductive film via coacervation [131].

One last topic that fascinated me was the studies on water dynamics in the complex coacervates network. Water molecules, taking over 80 wt% of coacervates, are a critical but often times overlooked factor in coacervation studies because capturing water dynamics is difficult. A lot of the studies indicate how water restructures by simply stating swelling or anti-swelling the coacervates phase. Work by the Han group fascinated me by showing the dynamic hydrophobicity-induced dehydration process in coacervation using a custom-made instrument [132,133]. They also showed that water diffusivity was high near the polymer network probed by spin labels, indicative of a highly interactive polymer-water network [134–136]! Work to investigate the role of water and its interactions with polymer, salt, and counterions will be interesting and enriching our knowledge of a much more dynamic network that surrounds and reshapes the polymer network.

Conclusion

Nature demonstrated excellent skillsets in making spontaneous self-assembly happen in water. This review paper discusses how sequence and charge, two of the most impactful drivers in biomaterial self-assembly can be used to build fundamental understandings of synthetic polymer self-assembly. In particular, bio-inspired sequence-specific polymers provide an extremely well-controlled method to make user-defined molecules, offering a handle to directly and precisely correlate polymer chemistry and performance on a molecular level. Charge-driven self-assembly in multi-polymer network opens opportunities to modulate polymer interactions in water, allowing for a fully water-based material platform in applied sciences. Building on the well-established science of bio-inspired polymers, engineering applied materials will be enlightened in fields, such as energy conversion, nanolithography, and biomedicine.

Summary

- Bio-inspired strategies pave the paths toward designing functional polymer materials with biomaterial's strengths of self-directed assembly, bringing tremendous impacts in fundamental biophysics and smart materials design.
- The power of controlling polymer sequence drives rapid development of understanding sequence patterning and chain steric effects in copolymer self-assembly.
- The viscoelastic and dynamic chain interactions in forming liquid complex coacervates provide new insights into charge-driven self-assemblies related to membraneless organelles/or biological condensates.

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Competing Interests

The author declares that there are no competing interests associated with this manuscript.

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Abbreviations

PDADMAC, poly(diallyldimethyl ammonium chloride); PECs, polyelectrolyte complexes; PSS, poly(4-styrene sulfonate sodium salt); PnBA, poly(n-butyl acrylate).

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