Catalyst: Size Distribution in Self-Assembly Matters

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Introduction

At the undergraduate level, it is taught that a lack of precision and homogeneity in chemistry is an indication of improper synthesis and purification and is frowned upon (and rightfully so). However, polymer chemistry, which has become a powerhouse of syntheses for new and functional materials, almost never achieves the purity and precision that one sees in, e.g., drug syntheses (to the dismay of those undergraduates). Some of the most powerful synthetic protocols in large-scale polymer preparation yield chains with "narrow dispersities," and increasing the number of components to prepare copolymers adds to the complexity of the chain distribution, now also in terms of composition. Efforts to prepare perfectly uniformly sized and sequence-defined copolymers has been at the epicenter of many research efforts, mainly aimed at mimicking the properties of their naturally occurring counterparts (e.g., proteins) in the transportation of information, directed self-assembly, catalysis, etc.[1] There has been a lot of speculation throughout the years regarding the significance of polymer dispersity in terms of molecular-weight distribution and heterogeneity. This Catalysis article aims to capture the essence of recent research efforts on the subject and set the challenge for future works in the field.

Often misused as a single qualitative measure, polymer dispersity (i.e., M_w/M_n, often referred to as the polydispersity index [PDI] but denoted per IUPAC regulations as molecular-weight distribution or dispersity [$Đ_M$])[2] describes the variation of the sizes of the individual polymer chains within a sample and is often considered a measure of inconsistency of the size of polymer chains in a mixture and an indicator of (lack of) control during the polymerization process. Inherent limitations in the control (or even elimination) of dispersity in polymer synthesis are well described in a recent review.[3] Although here we focus on dispersity in terms of molecular-weight distribution and compositional drift, we note that other forms of dispersities (such as stereochemical or architectural, e.g., through cyclization, back biting, or chain transfer) are imaginable, and all of these can dramatically alter the effective volume of the polymer and thus the self-assembling properties of the copolymer.

When it comes to the self-assembly of block copolymers, a wealth of literature addresses the formation of highly ordered structures, either in solution or in bulk, as a function of the macromolecular characteristics of the copolymer. Extrapolating from the Flory-Huggins equation regarding polymer miscibility, it is generally accepted that the chain length (referred to as N) and the (im)miscibility of the respective blocks (namely the χ parameter) in a medium (which can be a selective solvent) or the counterpart block of the copolymer dictate the phase behavior of the copolymer as a function of the volume fractions of the respective components. It is often suggested in the literature that disparity in the chain length will vary N and thus drastically broaden the χN compound that effectively describes the boundaries of each phase. Similarly, deviating the sequence of the copolymer building blocks, e.g., through a gradient transition of the two blocks around the junction, affects the χ parameter by effectively diluting the (otherwise) immiscible blocks with a compatibilizing component. Although these factors point toward the need for precise compositions and uniform sizes in order to achieve highly ordered and well-defined self-assembled structures, recent reports have shown that this might not be the case, and the hitherto perceived drawback of dispersity in polymer systems could be a desired characteristic for optimal self-assembled structures in the future.

The polymer science community is now well equipped with a wealth of techniques that enable researchers to harness the composition, molecular weight, and size distribution of synthetic copolymers. Nonetheless, high precision does not always correlate with optimal properties, especially with regard to applications that call for polymers with high molecular-weight distributions as a result of their improved processability. Furthermore, many reports in the literature describe the self-assembly of disperse copolymers into well-defined ordered structures. This leaves a lingering question: how monodisperse should a polymer be to result in predictable self-assemblies?

In Bulk

When it comes to the self-assembly of block copolymers in bulk, theoretical studies have shown that dispersity of one of the blocks skews the phase diagram. Although the interfacial energy is not dispersity dependent, the domain spacing of the resulting structure is. This can be ascribed to the fact that dispersity reduces the stretching energy of polymer chains. Furthermore, the stability of the interface is compromised as a result of the presence of lower-molecular-weight blocks. As a consequence, the phase diagram is shifted toward the disperse polymer block, and the order-disorder transitions shift to higher χN values. Indeed, it has since been experimentally shown that disperse blocks are influenced by the lower-molecular-weight chains and appear to occupy smaller volumes, which effectively induces curvature of the interface toward the disperse domain. Although a handful of such reports can be found in the literature (readers are encouraged to refer to the aforementioned reviews for more details), there might just be more to dispersity than just deviation from the average molecular weight.

One easy way to introduce compositional and size distribution is through blending otherwise uniform copolymers. The overarching conclusion of variations of this approach described in the literature is that greater variation results in larger phase domains (ultimately macrophase separation), an effect that can be conveniently exploited to tune the domain spacing of periodic structures. Nonetheless, it is impossible to extrapolate the phase behavior of *any* copolymer blend from the existing literature, and this is one of the main challenges of the self-assembly of disperse copolymers.

So far, dispersity has been assessed as a one-dimensional interpretation of the polymer size distribution, but Fors and co-workers' reports focus on depicting the molecular-weight distribution with regard to its skewness (Figure 1). By determining the domain spacings of block copolymers consisting of a poly(styrene) and a poly(methyl methacrylate) block, whereby the dispersity of the former was varied both in absolute value and in the shape of the molecular-weight distribution,[4] the authors showed that the otherwise identical block copolymers self-assembled into lamellae with significantly different domain spacings depending on the skewness of the molecular-weight distribution. This difference was ascribed to the fact that the copolymers were dominatingly high- or low-molecular-weight chains, thus suggesting that dispersity alone is not a sufficient measure for characterizing the macromolecular properties of copolymers because it does not mirror the skewness of the distribution, which can ultimately dictate the self-assembly characteristics in bulk. We note that the overall dispersity of the studied copolymers was below 1.3, so according to measures of controlled radical polymerizations, the polymers had narrow molecular-weight distributions.
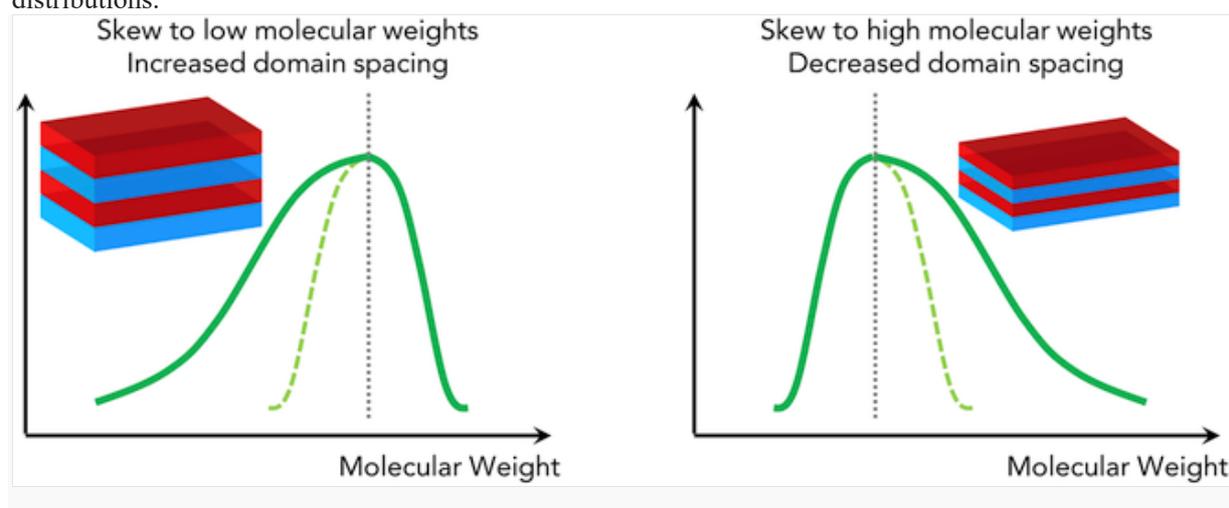

Figure 1 Skewness Matters: As reported by Fors and co-workers, polymers with similar dispersities and molecular weights self-assemble into lamellae with different domain spacings. Skewness to high molecular weights results in smaller domain spacings than those of their counterparts with skewness to low molecular weights.

Molecular-weight distribution might just be the tip of the iceberg. Although a large body of literature covers various aspects of block copolymers with respect to their chemical composition, molecular weight, dispersity, thermal properties, etc., it is often noted that the complexity of a multi-component system that can self-assemble drastically increases with an increasing number of components, and new morphologies can also arise. A phase diagram for a triblock copolymer, for example, is dependent not only on the relative volume fractions of the components but also on the order in which these are present along the chain.

Current efforts are aimed at understanding the effect of the sequence of building blocks on the self-assembly properties of the constituting copolymer. Perhaps the most interesting such work is that of Cheng and co-workers, who prepared "giant" monomers to create oligomeric sequences that were shown to self-assemble.[5]They effectively introduced an "alphabet" consisting of the various "letters" (i.e., building blocks) and demonstrated that by changing the order of the building blocks, not only could they form different "words" (i.e., oligomers) on a molecular level, but the way the "words" assembled also vastly changed, pointing to a meaningful relationship between sequence and self-assembly in bulk. Nonetheless, the effect of dispersity could be lost because the building blocks are so large. In some cases, the obtained structures were ascribed to the relative volume fractions of the components given that different sequences were found to result in the same structures, inasmuch as the mole ratios were the same.

Although compositional drift is hard to define, especially for larger polymer chains, molecular dynamics simulations to investigate the self-assembly properties of tapered copolymers—i.e., polymers whose composition gradually changes along the chain within a given region—point to a predictable behavior.[6] Unsurprisingly, copolymers with a completely statistical monomer sequence exhibit different self-assembly properties than copolymers with sharp block definitions. Furthermore, copolymers with less defined sequences result in assemblies with smaller domains, in line with the findings of similar studies on copolymers with molecular-weight dispersities (as opposed to composition). To that extent, the effect of monomer sequence on the polymer properties and self-assembly structural characteristics can be simplified through the study of a diblock, a tapered, and an inverse-tapered copolymer.[7] The latter exhibits dramatically different thermal properties and interfacial roughness than the diblock copolymer; however, the domain spacing is surprisingly comparable.

In Solution

The effect of dispersity of block copolymers on their ability to self-assemble in selective solvents was investigated in the seminal work of Eisenberg and co-workers.[8] Assessing a set of copolymers for which the dispersity of one block was varied (i.e., from ca. 1.00 up to ca. 2.00), they reported an effect on the size of the self-assembled structures obtained: increasing the dispersity of the hydrophilic block was shown to result in larger vesicles formations, which was attributed to the arrangement of the differently sized chains in a fashion that favors increased curvatures and thus smaller particles. Furthermore, various block dispersities also showed morphological differentiation because mixtures of chain lengths were able to accommodate more chains to aggregate. Similar to the findings of disperse block copolymers self-assembling in bulk, the core chain stretching dominates the total free energy of the aggregate, and thus a morphological change occurs.

A different study of the effect of dispersity on the self-assembly of polymers in solution involved poly(sodium acrylate-*b*-styrene) block copolymers of varying dispersities as stabilizers in the emulsion polymerization of styrene.[9] With increasing dispersity, the aggregation number of the assemblies, as well as the surface tension, increased. Interestingly, the critical micellization concentration of the copolymer and the size distribution of the particles were consistent over the range of dispersities studied.

Another systematic approach involved studying the ability of narrowly disperse amphiphilic block copolymers (compared with disperse copolymers of similar compositions) to self-assemble in water.[10]Interestingly, both types of copolymers resulted in similarly sized well-defined aggregates, and the size and aggregation number were dependent only on relative compositions and the degree of polymerization. Although these findings stray from earlier conclusions, we note that the copolymers in this study exhibited low glass transition temperatures, so their ability to "shuffle" and re-arrange is more favorable. Indeed, this observation points to the fact that the self-assembly of copolymers in bulk or in solution involves a wide range of parameters that drastically affect the resulting morphology and its characteristics. To our knowledge, there are limited examples of block copolymers whereby all blocks have high dispersities; indeed, most reports focus on a narrowly distributed block connected with a disperse one.

Applications and Implications

The implications of dispersity and inhomogeneity for potential applications of copolymers vary. DNA molecules are characterized by uniform and precise compositions that dictate subsequent functions (e.g., protein synthesis), and as much as one misplaced building block can imbalance a whole organism (such as in the case of sickle cell disease), thus pointing toward the importance of precise macromolecular

sequences. On the other hand, the functions of enzymes are often mimicked by self-assembled block-type copolymers (i.e., with some dispersity) that bear a catalytic moiety: the core of the assembly affords the confinement and hydrophobicity that is often considered key in enzymatic catalysis, albeit lacking in efficiency and substrate selectivity. In this case, the function is achieved despite the disperse nature of the macromolecule. Drug delivery is another potential application for well-defined self-assembled copolymers. The complexity of such systems makes it difficult to gauge the effect of dispersity; however, considering the scenario where a moiety present on the polymer chains (e.g., a binding ligand) is responsible for the affinity of the assembly to a target (e.g., to a cancer cell), inconsistency in the location and amount of the moiety among chains would drastically vary the affinity across the assembled nanostructures and, consequently, the drug dosage delivery.

In the absence of solvent, the effect of phase separation is aimed at equally delicate functions. Considering, for example, the optical properties of a self-assembled structure, diversity of the domain size (which, as discussed earlier, is related to size and composition homogeneity) results in fading reflectance intensity, increasing loss of the constructive interference, and thus loss of the structural coloration. Given that such structures are employed in light-manipulating applications—e.g., reflective coatings, lenses, and "smart" colorants, some of which are commercially available—the effect of dispersity is imminent and of broad significance.

The use of synthetic sequence-defined polymers for information storage has emerged as a potential application, and its feasibility has been demonstrated. Although dispersity and inhomogeneity among the macromolecules will surely compromise the information readout, it is not impossible to imagine the importance of the median composition that could be correctly interpreted through appropriate statistical analysis. Is it more favorable to ensure uniformity and definition at the expense of strenuous syntheses or optimize the analytical methods that can account for inhomogeneities? Once the applicability of sequence-controlled polymers gains momentum, such questions will surely be answered.

Conclusions

Here, we note some advances that have investigated the effect of dispersity and the importance of building-block sequence on the self-assembly of these copolymers, and we draw different conclusions when comparing self-assembly in bulk with that in solution. In bulk, dispersity as a one-dimensional value largely affects the volume fraction of the respective building blocks and thus alters the phase diagram of the copolymer. Moreover, the shape of the polymer size distribution further influences the dimensions of the periodic structure. With regard to the building-block sequence, it is apparent that there is still a lot of ground to cover in order to generalize and understand the governing principles given that the χ parameter might not be adequately precise for predicting the self-assembly behavior of multi-component and/or sequence-defined copolymers.

The morphology of polymer self-assemblies in solution appears to be less sensitive to greater dispersities than the morphology in bulk. Given that the reported size of the assembled structures is largely consistent, the only occasion where a change in the morphology has been observed is for dispersities ranging from 1.0 to 2.0, a much greater variation than that of the studies in bulk. One could assume that in solution, the solvent and its miscibility with the copolymer components dominate and compensate for variations in the molecular weight of the copolymer, at least within a reasonable margin. With the relatively recent development of sequence-controlled polymers, a systematic investigation of the effect of variations in the composition of a copolymer with respect to the characteristics of its self-assembly in solution has yet to be reported.

With the development of techniques that allow great precision in the synthesis of polymers of defined molecular weight and composition, it is exciting to see how this new generation of materials will alter the field of self-assembly and the consequent properties and applications. This short article points to existing literature on the topic but also suggests some future challenges, such as investigating the self-assembly of diblock copolymers by varying the dispersity of both blocks (in bulk and in solution); experimentally decoupling size and composition dispersity in the self-assembly of copolymers, particularly with respect to the precision required (sequence controlled versus sequence defined); systematically showing the ability of disperse copolymers to "shuffle" into ordered structures with respect to their mobility (glass transition, plasticization effects, etc.); and evaluating the directed self-assembly of disperse copolymers in solution.

Acknowledgments

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