

Synthesis and Self-Assembly of Fully-Zwitterionic Triblock Copolymers

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ABSTRACT

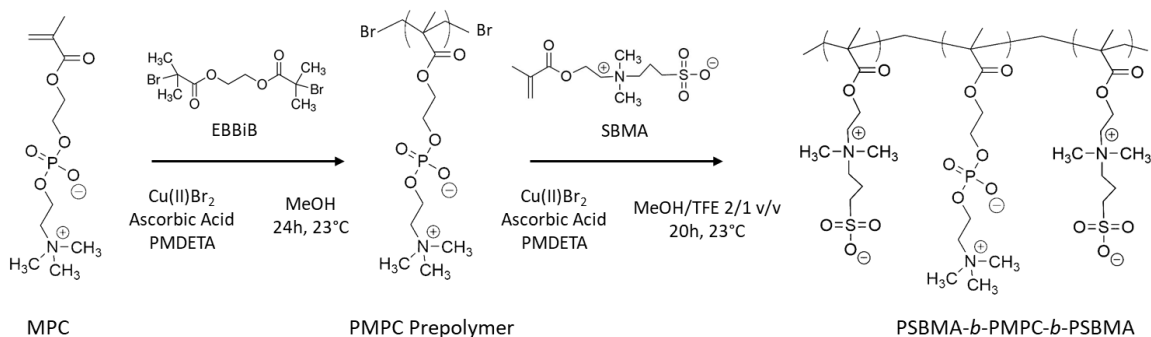
Zwitterionic polymers are a distinctive class of materials with unique physical and chemical properties. In this study, the synthesis of fully-zwitterionic ABA triblock copolymers was achieved by controlled radical polymerization using two different zwitterionic monomers, sulfobetaine methacrylate (SBMA) and 2-methacryloyloxyethyl phosphorylcholine (MPC). Due to the strong tendency of the sulfobetaine groups to aggregate, the fully-zwitterionic triblock copolymers demonstrated self-assembly, as well as salt and thermal responsiveness in solution.

Zwitterionic (ZI) functional groups, which contain an equal number of positively- and negatively-charged moieties while being overall charge neutral, typically possess large dipole moments (~ 20 D).¹ Through electrostatic forces, these groups can interact with ions, as well as promote strong self-associations.^{2,3} The large hydration capacity of ZI groups has led to the study of these materials for applications such as anti-fouling membranes and bio-inert implants or drug delivery systems.⁴⁻⁶ Polymerizable zwitterions have also been used to create hydrogels having large liquid contents and robust mechanical properties.^{7,8} Depending on the specific ZI group identity and the nature of the liquid medium, ZI self-association can be employed to form noncovalent, ZI dipole-dipole crosslinks that greatly enhance the strength of a gel polymer network.⁹⁻¹¹

The properties of each ZI functional group are highly dependent on the specific charged moieties present as well as the length of molecular spacing between them. Work by Shao *et al.* showed through molecular dynamics simulations that the extent of interaction between carboxybetaine (CB) or sulfobetaine (SB) zwitterions with alkali metal cations are very different, and that ZI self-aggregation depends on the relative difference in charge density between the positive and negative groups.¹²⁻¹⁴ Such reports demonstrate the importance of selecting a specific zwitterion for intended applications, however, few studies to date have examined the behaviors of materials containing more than a single type of ZI functional group.

In order to effectively exploit the different properties exhibited by specific ZI groups, one rational approach is to employ block copolymer architecture. Careful selection of monomers and block architecture can drive self-assembly, which allows for the formation of micelles, gel scaffolds, nanostructured thin films, and many other possibilities.^{15,16} For example, the Lodge group has pioneered the use of (non-ZI) ABA triblock copolymers as supporting scaffolds for ionic

liquid-based gel electrolytes, where copolymer self-assembly is driven by the combination of solvophobic end blocks and a solvophilic middle block.¹⁷ Historically, only a handful of ZI groups, paired with non-ZI blocks for contrast, have been incorporated into triblock copolymers.^{18,19} Ishihara and coworkers combined 2-methacryloyloxyethyl phosphorylcholine (MPC) as a middle block monomer with glycidyl methacrylate end groups to form ABA triblock copolymers for hydrogels with various biomedical applications.^{20,21} Poly(MPC), or PMPC, has also been employed as the A block material together with a poly(propylene oxide) middle block.²² To the best of our knowledge, however, there have not yet been any reports of *fully-ZI* ABA triblock copolymers, which presents an opportunity to utilize the properties of more than one ZI group to facilitate self-assembly and leverage the responsive nature of specific ZI groups.



Scheme 1. Synthesis scheme for PSBMA-*b*-PMPC-*b*-PSBMA by ARGET ATRP. After the first reaction, the prepolymer was washed and precipitated before addition of the end blocks.

In this study, we designed and synthesized fully-ZI ABA triblock copolymers using MPC as the middle block monomer and [2-(methacryloyloxy)ethyl]dimethyl-(3-sulfopropyl)ammonium hydroxide, also known as sulfobetaine methacrylate, (SBMA) as the monomer to construct the symmetrical end blocks. These two ZI monomers were selected because of their notably different

solubilities and self-association behaviors within various environments, including hydrophobic ionic liquids.²³ For the effective synthesis of block copolymers, controlled polymerizations, such as reversible addition-fragmentation chain transfer (RAFT) or atom transfer radical polymerization (ATRP), are utilized to create polymeric subunits with targeted molecular weights.²⁴ Here, the fully-ZI ABA triblock copolymer synthesis was realized in a two-step process via ARGET ATRP (see Supporting Information). As shown in Scheme 1, the PMPC prepolymer was synthesized using a bifunctional initiator, and then PSBMA was added at both ends to generate symmetrical ABA triblock copolymers.

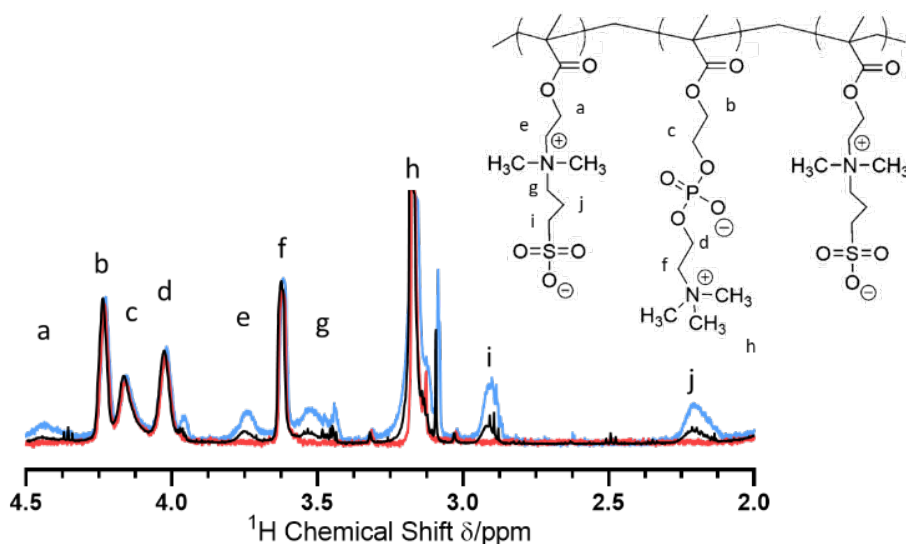


Figure 1. ¹H NMR spectra of the PMPC prepolymer (red) and two distinct PSBMA-*b*-PMPC-*b*-PSBMA triblock copolymers, one consisting of approximately 25 mol% PSBMA (black), and the other having 50 mol% PSBMA (blue). Peak assignments for both ZI functional groups are shown corresponding to the labels in the inset.

Two triblock copolymers were synthesized, each starting with the same PMPC prepolymer to which different lengths of PSBMA end blocks were then added. Chemical identification of the block copolymers was performed using ¹H NMR with peaks assigned according to the

literature.^{25,26} Figure 1 shows a portion of the ¹H NMR spectra obtained for both triblock copolymers as well as for the PMPC prepolymer (measured in D₂O). Peaks (a), (e), (i) and (j) are characteristic peaks of the SBMA sulfobetaine functional group, which clearly demonstrate successful incorporation of the PSBMA end blocks at two different PSBMA concentrations. Characteristic peaks for the methacrylate monomer vinyl protons located near 5.5 and 6 ppm are not visible (Figures S1 and S2), indicating that no unreacted monomer was present in the samples. By integrating the characteristic peaks for SBMA, it was estimated that the two triblock copolymers contained approximately 25 mol% and 50 mol% PSBMA, respectively. GPC measurements performed in 0.1M NaCl aqueous solution indicated peak broadening of both triblock samples compared to the PMPC prepolymer, likely due to strong attractive inter- and intramolecular interactions between sulfobetaine ZI groups (Figure S3). The peak broadening seen in the GPC traces supports the conclusion that PSBMA was properly added to the ends of the PMPC prepolymer; copolymer behavior in solvents of varying quality was further studied by dynamic light scattering (DLS), *vide infra*. Based on the GPC data for PMPC and the integrated ¹H NMR spectra, the two copolymers contained approximately 58 MPC units and either 20 or 58 repeat units of SBMA (25 mol% or 50 mol% SBMA, respectively).

Thermogravimetric analysis (TGA) demonstrated that the copolymers exhibit good thermal stability, up to approximately 200 °C, at typical scan rates (Figure S4). We were unable to identify glass transition temperature (*T_g*) values for each polymer subunit by conventional dynamic scanning calorimetry (DSC) measurements, which is likely due to both *T_g* values being close to the polymer degradation point.⁵ However, additional thermal analysis was conducted on the 25 mol% triblock copolymer sample by fast scanning calorimetry (FSC), which revealed two

distinct T_g values above 200 °C (Figure S5). The presence of two T_g values is characteristic of block copolymers, and suggests the self-assembly into distinct polymeric phases.

To study the self-assembly of our fully-ZI triblock copolymers, thin films (~15-30 nm) were prepared on silicon wafers by spin-coating from 2,2,2-trifluoroethanol (TFE). TFE was observed to be a good solvent for both the PMPC prepolymer as well as the ABA triblock copolymers. Figure 2 displays both the height (topography) and phase angle images that were captured via tapping-mode atomic force microscopy (AFM) of the three polymer films.

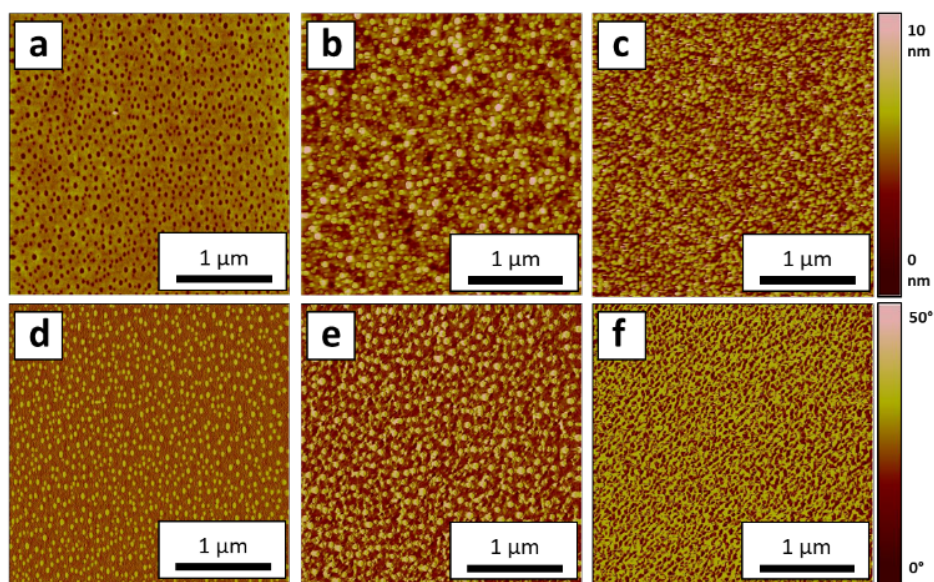


Figure 2. Tapping-mode AFM images of ZI polymer thin films (left to right): PMPC prepolymer, 25 mol% PSBMA triblock copolymer, and 50 mol% PSBMA triblock copolymer. Height data are displayed in panels (a), (b), and (c); corresponding phase angle data are shown below in panels (d), (e), and (f). All films were spun from TFE on silicon wafers and had thicknesses of ~15-30 nm. All images depict an area of 3 μm x 3 μm .

Figure 2(a) shows that the PMPC prepolymer film exhibited a relatively flat surface (root mean square roughness of 0.99 nm), which is consistent with the presence of a single-phase film

that is compatible with the substrate. The small pits that can be seen are attributed to a solvent evaporation effect, as the size and density of these pits was observed to vary as the spin-coating solvent quality was varied (data not shown). However, significant differences in the polymer film morphology were observed for the fully-ZI triblock copolymers due to the presence of PSBMA blocks. As shown in Figures 2(b) and 2(c), the addition of symmetrical PSBMA end blocks results in the formation of nanostructured assemblies that increase polymer film roughness (see also Figure S6). There is also a clear change in the feature size of these assemblies as the PSBMA concentration is increased from 25 mol% to 50 mol% within the triblock copolymer. We hypothesize that these nanostructures are a result of PSBMA end blocks aggregating due to their lower solubility in TFE compared to that of the PMPC middle block. The high contrast observed within the phase angle images, Figures 2(e) and 2(f), also supports the notion that the fully-ZI triblock copolymers can self-assemble into PSBMA- and PMPC-rich domains.

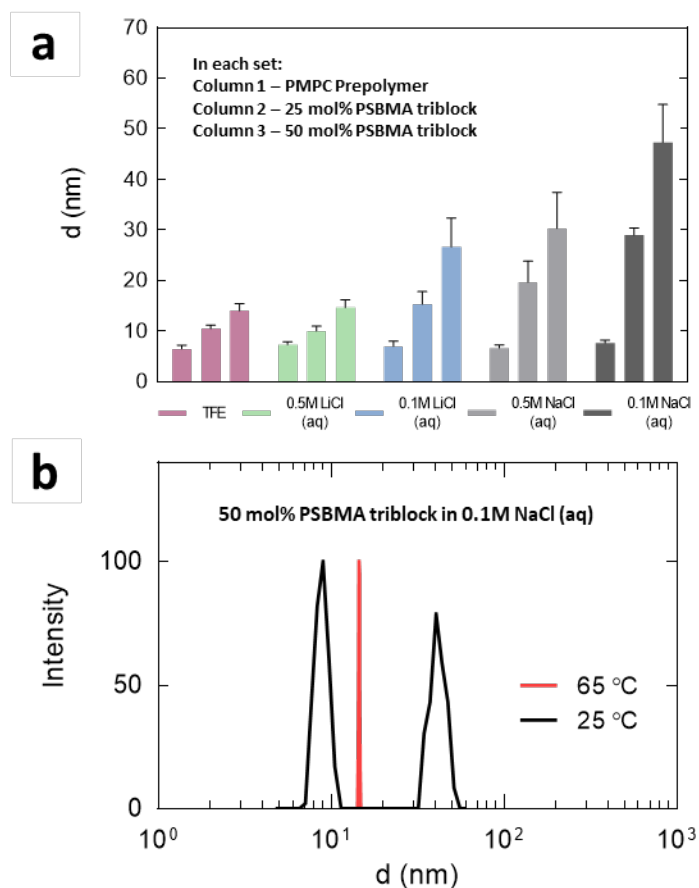


Figure 3. (a) DLS measurements of average particle size for polymer samples in different solvents. Within each grouping, column 1 represents the PMPC prepolymer, column 2 is the 25 mol% PSBMA triblock copolymer, and column 3 corresponds to the 50 mol% PSBMA triblock copolymer. (b) Comparison of DLS spectra recorded for the 50 mol% PSBMA triblock copolymer in 0.1M NaCl aqueous solution at two different temperatures: 25 °C (black) and 65 °C (red).

DLS experiments were conducted to highlight the importance of solvent quality on the aggregation behavior and salt-responsiveness of fully-ZI block copolymers in dilute solutions. Samples were prepared in aqueous solutions of either LiCl or NaCl (concentrations of 0.1M, 0.5M), as well as in neat TFE. From Figure 3(a), it can be seen that there were minimal differences in apparent particle size measured across the five different solutions of the PMPC prepolymer,

suggesting that, in all cases, PMPC is well-solvated and not aggregating. Meanwhile, there is a clear trend of increasing particle size observed with greater PSBMA content for the two triblock copolymers in each solvent. However, a notable variation in average particle size value depending on the particular solvent environment was observed for both ABA triblock copolymers, which suggests that the presence of PSBMA blocks led to greater self-aggregation behavior with decreasing solvent quality (*i.e.* from TFE to 0.1M NaCl_(aq)). While there is an apparent decrease in average particle size observed with increasing NaCl concentration, the presence of multiple peaks indicates that the copolymer remains only partially solvated. In comparison, the corresponding LiCl_(aq) solutions of the triblock copolymers yielded a lower average particle size, and, at the highest salt concentration tested (0.5M), a unimodal response was observed. Close agreement between the DLS sizes observed in TFE and 0.5M LiCl_(aq) suggests that in 0.5M LiCl aqueous solution, the triblock copolymers are indeed well-solvated.

DLS measurements were also used to probe the effect of solution temperature on the apparent triblock copolymer particle size. As seen in Figure 3(b), for the 50 mol% PSBMA triblock copolymer in 0.1M NaCl (which yielded the largest aggregates, Figure 3(a)), the spectra evolved from multimodal to unimodal as the solution temperature was increased from 25 °C to 65 °C. This also corresponded to a decrease in average particle size from ~50 nm to ~15 nm. At 65 °C, the solution is above the reported upper critical solution temperature (UCST) of PSBMA,^{27,28} which dramatically enhances triblock copolymer solubility and yields an apparent particle size comparable to that measured in TFE and the 0.5M LiCl_(aq) solution.

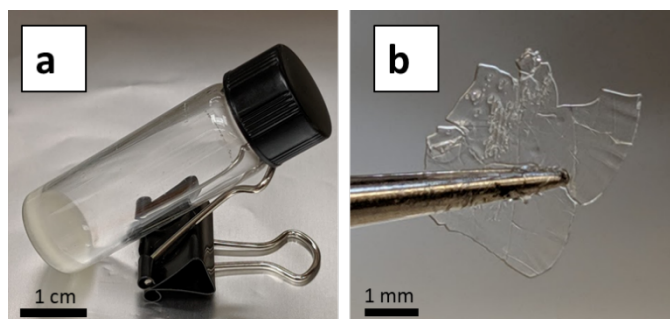


Figure 4. Photographs illustrating materials featuring fully-ZI ABA triblock copolymers. (a) Ionic liquid-rich gel electrolyte supported by a 25 mol% PSBMA triblock copolymer scaffold. (b) Solid polymer electrolyte thin film consisting of lithium bis(trifluoromethylsulfonyl)imide dispersed in the 50 mol% PSBMA triblock copolymer.

Due to the relative solubility difference of the sulfobetaine versus phosphorylcholine ZI functional groups within multiple environments, including the hydrophobic ionic liquid 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide (EMI TFSI),²³ the fully-ZI ABA triblock copolymers can self-assemble to form ionic liquid-rich gels (ionogels), as shown in Figure 4(a). Gelation is likely enabled by solvophobic PSBMA end block aggregates serving as noncovalent cross-links that are connected by the solvophilic PMPC middle block, in direct analogy to the non-ZI ABA triblock copolymer-supported ionogels reported by the Lodge group.²⁹ We observed that ionogels could be formed with EMI TFSI using 20 wt% of either fully-ZI triblock copolymers synthesized here, while the analogous PMPC prepolymer mixture did not form a gel (see Figure S7). The fully-ZI triblock copolymers also displayed good compatibility with the lithium salt LiTFSI, which suggests that these polymers featuring highly dipolar ZI side groups could be further explored for their use as solid polymer electrolyte (SPE) matrices. Figure 4(b) shows a thin film prepared by combining the 50 mol% PSBMA triblock copolymer in a 1:1 weight ratio with LiTFSI. The phosphorylcholine group of MPC has previously been shown to promote facile

lithium ion transport within ionogels,³⁰ while it is posited that the sulfobetaine group of SBMA drives copolymer self-assembly through the formation of ZI dipole-dipole physical crosslinks. The details of ion transport within the triblock-based electrolytes were not explored here; this study focused on the synthesis and self-assembly of these novel block copolymers. As demonstrated by the current thin film AFM images (Figure 2) and DLS measurements (Figure 3), fully-ZI triblock copolymers can indeed self-assemble due to the sufficiently different chemical natures of the two ZI blocks. Future experiments will be conducted to examine the effects of ZI group identity and block polymer architecture on polymer self-assembly in the presence of different ions.

In summary, we have successfully demonstrated the synthesis of fully-ZI ABA triblock copolymers comprising two distinct ZI monomer functionalities. Spontaneous copolymer self-assembly, which is driven by the different natures of the two ZI blocks, has been observed both for spin-coated polymer thin films and within aqueous solutions. We believe that these copolymers can find utility in several applications that leverage the chemical tunability of different ZI blocks, and, in future studies, we plan to explore their potential as electrolyte components for energy storage devices.

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/>.

Materials and methods, synthesis and characterization details, supplemental figures (PDF)

Acknowledgements

The authors thank Andrew Clark and Prof. Peggy Cebe at Tufts University for performing the fast scanning calorimetry measurements and associated analysis. This research was performed

with financial support from the Office of the Provost at Tufts University (Tufts Collaborates) and from the National Science Foundation (CBET-1802729).

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