Antagonistic Triblock Polymer Gels Powered by pH Oscillations

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Introduction. The search for an entirely synthetic molecular machine has been going on for many years.[1−5] Naturally occurring nanoscale machines found in cell biology operate by converting chemical energy into mechanical energy with very high efficiency while under isothermal conditions. A device that performs this type of energy conversion at the molecular level is commonly referred to as a *molecular motor*. The basis of such molecular motors is often a conformational change of a responsive macromolecule. In many of these biological systems, the macromolecule is also active in the transformation, where binding sites for the supplied chemical "fuel" facilitate the catalytic release of the stored chemical energy, resulting in a conformational change.[6] Simple passive conformational changes can also be used to make molecular motors based on stimulus-responsive units, such as a molecule that responds to, but does not take part in, the driving chemical reaction. This concept was first proposed by de Gennes[7] and realized by Howse et al.[8] In this example, the simple coil-to-globule transition[9] exhibited by a pH-responsive polyelectrolyte has been coupled with a pH-oscillating reaction to produce controlled volume pulsations that can exert an external force. An additional advantage conferred by using complementary polyelectrolyte pairs of polyacids and polybases is that devices fabricated from these two building blocks can be *bipolar*, such that one polymer exhibits a positive response while the other simultaneously exhibits a negative response. For example, one polymer may be swollen while the other is collapsed for a given solution pH, as depicted in Figure 1. In principle, judicious selection of the respective pK_a values of the responsive chemical group should enable a polyacid and a polybase to be used in tandem, equivalent to the antagonistic pairing common in mammalian muscle structures. This simple pairing works because, at low pH, both of the polyelectrolytes are protonated, so the polyacid is charge-neutral and the polybase exists as the protonated form of an amine, being a cationic polyelectrolyte. The charge density on the polybase chains induces both chain expansion and also mutual electrostatic repulsion between neighboring chains, whereas the neutral, hydrophobic polyacid chains remain in their collapsed conformation. At high pH, the polybase chains become deprotonated and collapse, whereas the polyacid chains ionize and hence expand as anionic polyelectrolytes.

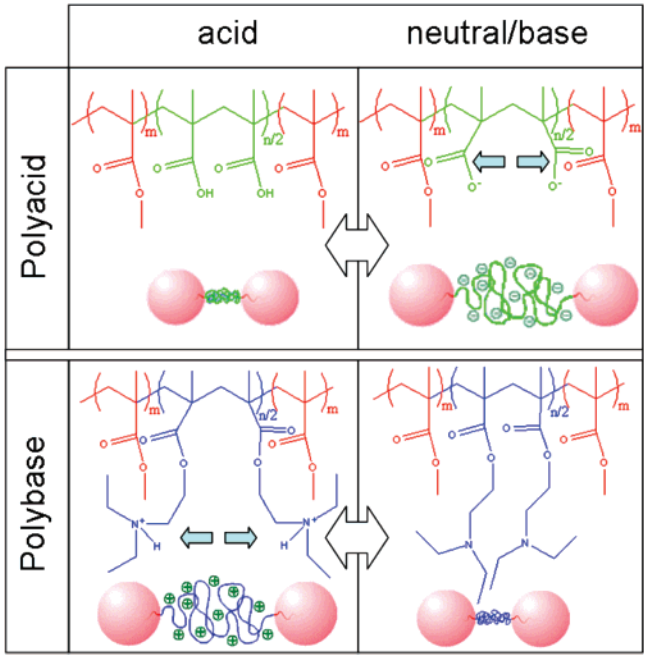

Figure 1. Schematic diagram representing the ionized and nonionized chemical structures and chain morphologies for the polyacid and polybase triblock copolymers under acidic and neutral/ basic conditions. The solid spheres represent the aggregated PMMA micro-domains.

To construct a realizable physical structure from these responsive polyelectrolytes, polybasic and polyacid hydrogels have been formed. Moreover, to ensure that these polymer gels remain intact during pH-induced oscillations, cross-links have been incorporated within the material. Although chemical cross-links can provide structural integrity, the approach inevitably introduces spatial inhomogeneities in cross-link density which lead to locally anisotropic expansion and contraction, creating mechanical stresses throughout the network.[10,11] Fibrous polymeric material can be used to accommodate such inhomogeneous stresses, which would otherwise lead to mechanical failure of the gel.[12,13] Another elegant approach to overcome this problem is to introduce self-assembling physical cross-links to create a responsive continuous polymer network with a homogeneous cross-link density distribution. Annealed physical cross-links allow isotropic expansion, thus minimizing the stress induced during volume transitions. One method to introduce such physical cross-links is to use block copolymer self-assembly to induce microphase separation.[14,15] This strategy requires at least two immiscible polymers that are covalently attached to one another in an A−B−A configuration, where B is the responsive block. When allowed to equilibrate by diffusion (during annealing), the block copolymer chains undergo microphase separation into distinct nanoscale domains of the individual blocks, while remaining chemically bound to each other. For a polymer of an A−B−A configuration, this results in the A groups situated in adjacent domains, spanned by the responsive midblock, B. More specifically, by controlling the composition of the symmetrical A−B−A triblock copolymer, one can generate physically cross-linked networks with a desired microstructure, such as lamellae, cylindrical rods or spheres,[16] representing 1, 2, and 3 dimensions of response, respectively.

Experimental Section. Materials. The polyacid hydrogel comprised of a poly(methyl methacrylate)-*block*-poly(methacrylic acid)-*block*-poly(methyl methacrylate) [PMMA$_{66}$-*b*-PMAA$_{996}$-*b*-PMMA$_{66}$] triblock copolymer, synthesized via anionic polymerization (M_n = 99 kg mol^{-1}, polydispersity [PD] = 1.03, PMMA volume fraction = 0.16)[17] and the polybase hydrogel comprised of a poly(methyl methacrylate)-*block*-poly(2-(diethyl-

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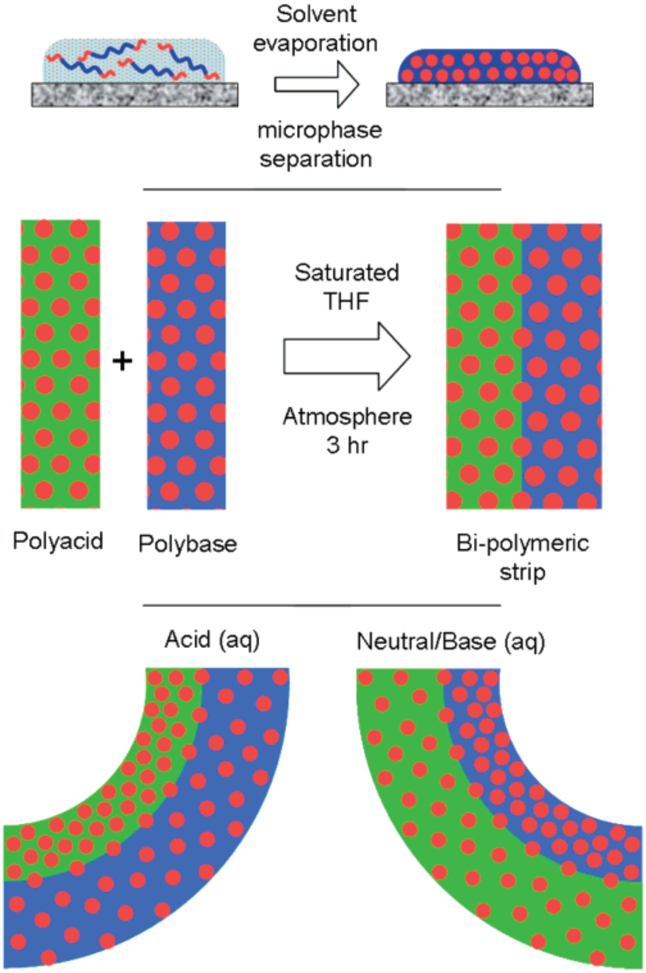

Figure 2. Schematic diagram of the annealing process for the fabrication of a "bipolymeric" strip and schematic depiction of the effect of varying the solution pH. The solid spheres represent the aggregated PMMA micro-domains.

amino)ethyl methacrylate)-*block*-poly(methyl methacrylate) [PMMA$_{273}$-*b*-PDEA$_{688}$-*b*-PMMA$_{273}$] triblock copolymer, synthesized via group transfer polymerization (M_n = 182 kg mol^{-1}, PD = 1.12, PMMA volume fraction = 0.17).[18]

Sample Preparation. A strip of the polyacid triblock copolymer was cast from a 25 wt % polymer in an acetone/methanol (25:75 vol/vol) solution onto a glass microscope slide to produce a dry gel film measuring 25 mm × 5 mm × 80 μm. The polybase was cast from THF to produce gel strips (5 mm × 1.5 mm × 80 μm) which were subsequently placed perpendicularly over the dried polyacid gel). The assembled structure was then placed into a saturated THF atmosphere for 3 h. Of the three polymeric components in our system (PMMA, PMAA, and PDEA) only the PMAA is insoluble in THF, and so the polyacid midblock remains glassy in this solvent-rich atmosphere. However, the PMMA end domains on the surface of the polyacid gel will become mobile and hence, given sufficient time, interdigitate with the mobile PMMA domains present at the surface of the polybase strip. This has the effect of generating physical cross-links between the two gel structures, physically binding them to each other (see Figure 2). Once annealed, a strip measuring approximately 2 mm × 1 mm × 160 μm was cut out, held between tweezers, and then subjected to pH oscillations using dibasic sodium phosphate/ citric acid buffers (Aldrich, 99%, pH 3.7 and pH 7.3), both with an ionic strength of 0.1 M. The buffers were periodically switched approximately every 2 min.

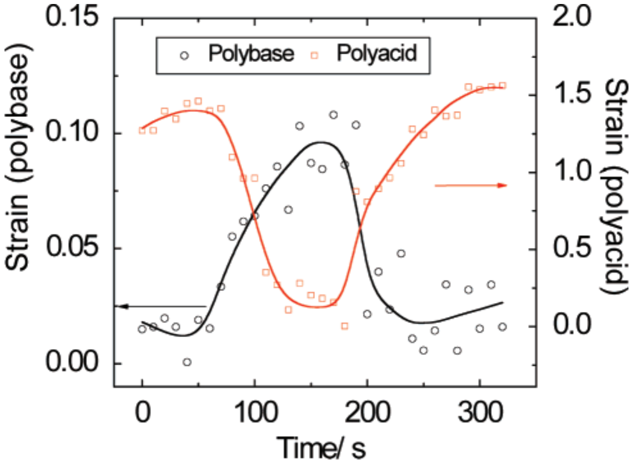

Figure 3. Strain data for the nonadhered, separate polyacid and polybase samples (measured after five complete oscillations).

Results and Discussion. To assess the suitability of the triblock polymers for their intended use as pH-responsive actuators, the individual pH-strain behavior of the polymers was first determined, where the strain is calculated by dividing the extension by the original dry length. The polymers were subjected to square wave oscillations in pH, from 3.7 to 7.3 (i.e., identical cycles to the pH trace created during the bipolymeric strip experiment) using a combination of phosphate and citrate buffer mixtures.[19] The strain behavior clearly demonstrates the antagonistic nature of the polybase and polyacid pH-response as the nature of their strains is clearly out of phase and similar in profile with respect to time (see Figure 3). It is also apparent that the pH-strain response of the polybase strip is significantly less than that observed for the polyacid strip. This is expected as the coil−globule transition of poly(methacrylic acid) is a substantial one and has been well documented over several decades.[20−25]

Aware of the dissimilarity in strains shown for the individual components, the bipolymeric strip was subjected to an identical pH cycle and the very end of the strip tracked by video microscopy (Figure 4a). The antagonistic behavior of the response from each hydrogel caused the bipolymeric strip to expand or contract according the pH environment it experienced. A movie showing the detailed displacement behavior of the bipolymeric gel piece is available as Supporting Information. Parts b and c of Figure 4 show the extremes of displacement for the basic/ neutral environment (expanded polyacid/contracted polybase) and the acidic environment (contracted polyacid/ expanded polybase), respectively. From this, we can clearly see the oscillatory motion resulting from the asymmetry in the strain behavior for the two materials. As the acid side expanded much more than the polybase, we generated a highly curved surface. When the conditions favored the expansion of the polybase a much smaller curvature of the bipolymeric strip in the opposite direction was observed. Figure 4a shows the displacement resulting from eight complete pH cycles, using video microscopy to track the spatial position of the tip of the gel. Initially we saw a small oscillation, both in degree of curvature and position from its anchoring point, as the dry strip swelled toward its fully expanded equilibrium structure. By the second oscillation the gel was fully swollen and showed reproducible mechanical oscillations. At low pH, the polyacid chains were collapsed (whereas the polybase chains were expanded) and the bipolymeric strip curled toward the polyacid. At neutral pH, the two polyelectrolytes switched conformation and the strip curled toward the polybase. As a result, the bipolymeric strip bends

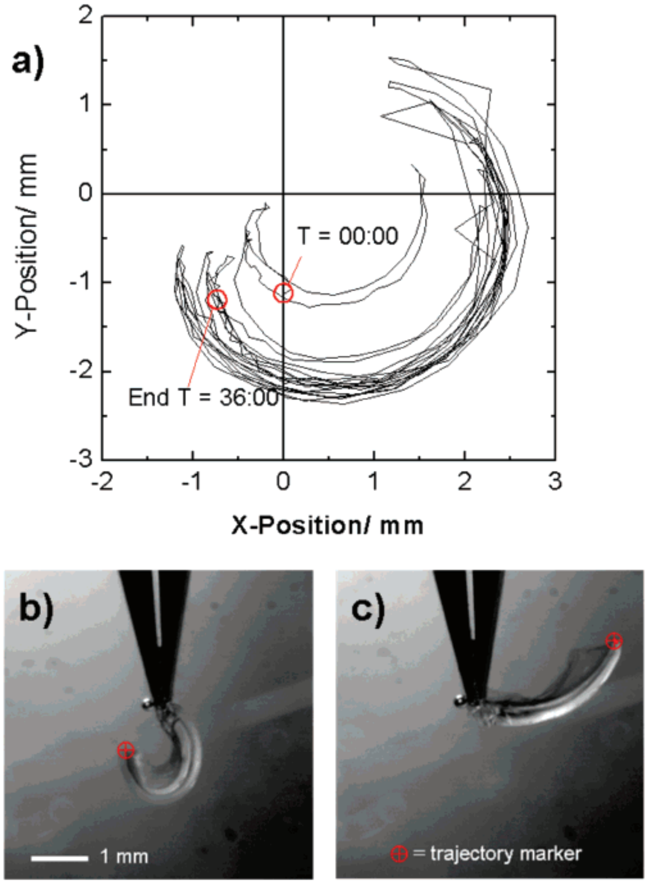

Figure 4. (a) Trajectory of the tip of the strip relative to its attachment position during eight pH oscillations, (b) microscopic image of the strip at pH 7.3 with expanded polyacid/collapsed polybase, and (c) microscopic image at pH 3.7 with collapsed polyacid/expanded polybase.

more than 90° (from its initial dry state) in both directions depending on the solution pH. The observed actuation clearly benefits from this antagonistic behavior showing curved surfaces at both extremes of its displacement. Further optimization of both the strain responses from each polymer and the judicious geometrical design would allow for each responsive layer to generate equivalent strains resulting in a more symmetrical motion, rather than motion predominately controlled by the response of the polyacid as seen here.

This work compares very favorably with an example of a polymer brush grafted to one side of an AFM cantilever. A pH responsive polymer brush has been used[26] to cause a 1.3 μm deflection of a ~100 μm cantilever. This is a much smaller strain (10^{-2}) than that described here which is approximately 2. Even for such a thin layer (20 nm), the response time is on the order of 30 s, illustrating the complex (and slow) response of polyelectrolytes.

Conclusions. In summary, we have created a pH-responsive lever, in which a small change in the individual polyacid or polybase gel length is transferred into a larger motion that curls up the gel. Moreover, this transfer of motion from a simple linear displacement into a curved displacement through the geometric design effectively increases the rate at which any displacement is generated. We have produced a robust, reversible, chemically driven mechanical actuator that has demonstrated its response over many pH oscillations. The affine nature of the triblock copolymers (demonstrated elsewhere for the polyacid[8] and the polybase[27]) indicates that this effect will also function at much smaller length scales, which is appropriate for a working biomimetic, soft nanotechnology device. This work demonstrates the potential applicability of such smart polymeric gels and suggests the fabrication of related molecular machines and devices based on the principles of soft nanotechnology.

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Supporting Information Available: A video clip (avi file) of the mechanical motion of the bipolymeric strip. This material is available free of charge via the Internet at http://pubs.acs.org.

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