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Bio-Inspired Design of Submerged Hydrogel-Actuated Polymer Microstructures Operating in Response to pH Change

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Responsive and reversibly actuating surfaces have attracted significant attention recently due to their promising applications as dynamic materials^[1] that may enable microfluidic mixing,^[2] particle propulsion and fluid transport,^[3] capture and release systems,^[4] and antifouling.^[5] Analogs in nature serve as inspiration for the design of such advanced adaptive materials systems—microorganisms use flagella for propulsion,^[6] cilia line the human respiratory tract to sweep mucus from the lungs and prevent bacterial accumulation,^[7] and echinoderms use pedicellariae for body cleaning and food capture.^[8] Significant characteristics of these biological systems include functionality in a fluidic environment, controllable actuation direction or pattern, and the ability to translate chemical signals or stimulus into mechanical motion. Researchers have taken various approaches to fabricating biomimetic actuators, among which are biomorph actuators made using Micro Electromechanical Systems (MEMS) technology,^[9] magnetically actuated poly(dimethylsiloxane) (PDMS) structures,^[10] and artificial cilia or actuators made from responsive gel.^[11, 12] However, most fabricated actuators, such as MEMS or magnetically-actuated PDMS posts, must be driven by an external force or field and are not responsive to chemical stimuli. Actuating structures that have been made from responsive hydrogel are

either low aspect ratio and their motion is not patternable,^[11] or the movement is

irreversible.^[12] Microscale actuation systems which exhibit reversible chemo-mechanical response and control of actuation direction or pattern have proven difficult to achieve.

Inspired by biological actuators, which can be broadly interpreted as composites consisting of an active “muscle” component coupled with a passive “bone” structure, we recently developed a hybrid actuation system in which a crosslinked acrylamide-based hydrogel, acting as an analog to muscle, drives the movement of embedded silicon^[13,14] or polymer^[15] microposts, serving as analogs to skeletal elements. Actuation was achieved by the swelling and contraction of the humidity-responsive gel upon hydration/drying. Actuation direction was controlled by modulating the hydrogel thickness; since thicker hydrogel exhibits a greater absolute change in volume than thin hydrogel, the forces exerted on the structures—and thus their actuation direction—can be patterned.

However, a humidity responsive system will not function in the fluidic environment required for many applications such as propulsion, cargo transport, or microfluidics, and it is difficult to pattern uni-directional actuation of posts over large areas due to their lack of preferred bending direction. To enable the actuators to function in various environments, it is possible to alter the chemistry of the hydrogel muscle to make it shrink or swell while submerged in response to a range of stimuli including light,^[16] temperature,^[17] biomolecules (e.g. glucose),^[18] or pH.^[19] To gain additional control over bending orientation, beyond what is achievable by topographically patterned hydrogel, we can utilize principles of symmetry breaking found in nature—such as the asymmetric distribution of growing actin filaments allowing for uni-directional cellular motion^[20] or the oval cross-sections of cilia on the bodies of fish and amphibians enabling sensing of anisotropic flow fields^[21,22]—and design asymmetric actuators which support anisotropically shaped structures that may limit motion to only desired directions. We present here a novel bio-inspired surface operating in a fluidic environment for which reversible actuation of embedded skeletal elements is generated by the

chemo-mechanical response of a pH-sensitive hydrogel over large areas with controlled patterns and direction of actuation.

Copolymerization of weakly ionizing monomers, such as acrylic acid, vinylpyridine, maleic acid, etc., with acrylamide renders the hydrogel sensitive to pH change.^[23-25] We chose acrylic acid (AAc) as the weakly acidic segment in acrylamide (AAm)-based hydrogel to prepare a random copolymer network, poly(AAc-*co*-AAm). The presence of AAc ($pK_{a,AAc} = 4.25$) lends the hydrogel its pH responsiveness, as the swelling volume correlates with the degree of ionization of the hydrogel network.^[26] At $pH > 4.25$, the AAc is ionized, which leaves the hydrogel polymer backbone with a net charge (**Figure 1a**). Dissociated hydrogen ions remain in the hydrogel to balance this negative charge which in turn causes increased osmotic pressure, ultimately leading to water infiltration and hydrogel swelling. At $pH < 4.25$, the acrylate is protonated, the osmotic pressure is decreased, water is expelled, and the hydrogel contracts. We used this volume-phase transition of the pH-responsive hydrogel to drive the actuation of embedded microstructures (**Figure 1b**).

To test this hydrogel for the capability of generating pH-responsive actuation, we embedded microposts (diameter = 1.5 μm , height = 10 μm , square array with pitch = 8 μm) made of glycidyl methacrylate (GMA)-modified UV-curable epoxy in a uniform poly(AAc-*co*-AAm) hydrogel film made by placing a flat piece of epoxy over the sample surface during hydrogel polymerization and crosslinking (**Figure 1c**). We added a strong acid and a strong base successively to the solution in which the sample was submerged and observed actuation of the embedded structures between bent and upright states (**Figure 2a**). Actuation was fast, taking place in only fractions of a second, indicating that the system was quickly overwhelmed by hydronium or hydroxide causing rapid contracting or swelling of the thin layer of hydrogel. Hydrogel contraction (at $pH < 4.25$) puts the embedded microstructures under high strain which deforms and bends them from their upright equilibrium configuration. The structures are restored to their original equilibrium configuration and stand upright when

the strain is removed by swelling the hydrogel (at pH > 4.25) (Figure 1b). Therefore, the pH change of the surrounding fluid is reversibly transduced to the bending/unbending actuation of the microstructures. The observations made from this example of pH-responsive hydrogel-driven actuation hold true for all variations of actuator structures and hydrogel morphologies we describe here.

The use of a flat contact or confining surface to create a uniform film of hydrogel causes the microposts to bend uni-directionally, but only within small domains often less than 10 mm² (Figure 2a). These small domains can be explained by the fact that symmetrical microposts have no preferred bending orientation, making their actuation direction sensitive to small and local anisotropies in hydrogel thickness which may arise from the fabrication procedure or from one structural element bending and locally inducing a change in hydrogel profile.^[27] Since many applications involving actuation, such as flow generation or particle propulsion, may require coordinated and uni-directional movement over a significantly larger area, we redesigned the microstructures to be asymmetric, thereby biasing the bending in certain directions even while embedded in a flat, unpatterned hydrogel film. We fabricated arrays of microfins (length = 10 μm, width = 1.2 μm, height = 11 μm, pitch = 10 μm perpendicular to the length and 5 μm parallel to the length) and used them in place of the microposts. Large areas of uni-directional actuation, on the order of several cm², often limited only by sample size, were observed (**Figure 2b**, movie in Supporting Information). The bending stiffness of these microfins perpendicular to the long axis of the fin is significantly (~70 times) smaller than that along the long axis of the fin. Therefore, the structure itself strongly favors bending in only two opposite directions along a single axis. We were able to discriminate between these two possibilities and further control the one-directional actuation by using slightly tilted microfins or by shadow exposure of UV light to the hydrogel precursor layer on the microfin structures. Such asymmetric actuator structures demonstrate the importance of symmetry in providing for, or limiting, favored directions of actuation. Similar

fin structures, with their inclination to uni-directional actuation, may enable the system to be adapted for materials or applications in which directional motion is essential.

In order to gain insight into the mechanisms of actuation and how the responsive volume change of the hydrogel is coupled to the movement of the structures, we needed to be able to control and slowly alter the local pH of the solution. It is difficult to precisely manipulate local pH by direct addition of acid or base to the sample in solution; the system is quickly overwhelmed with hydronium or hydroxide ions, and the details of the actuation process are challenging to visualize, not to mention the difficulties in reproducibility and variable diffusion. Using electrochemically-generated pH gradients instead enabled us to change the pH of the solution predictably, reproducibly and accurately within a narrow range of pH. Such reversible pH gradients were produced in solution by applying a voltage to partially-submerged electrodes. Electrolysis of water produced hydronium and hydroxide ions at the anode and cathode respectively, and their subsequent migration toward the opposite electrode generated a stable pH gradient.^[28] We cycled the pH (dozens of times or more) simply by switching the polarity of the applied DC voltage to reverse the pH gradient direction. Typically, Pt electrodes separated by 3 cm with applied voltage of 15 V at room temperature resulted in the reversal of local pH between the electrodes within a few minutes. The phase transition of the poly(AAc-co-AAm) hydrogel occurs at pH = 4.25 and only small changes in pH around this point are needed for actuation. Therefore, we adjusted the initial pH of the electrolyte solution to 4, so that the center of the pH gradient was shifted close to $pK_{a,AAc}$ to reduce the amount of hydronium and hydroxide ions that must be produced in order to vary the pH of the solution in the region of the sample around 4.25 and to trigger actuation.^[28]

Using this method, we examined microposts movement both in an unpatterned, flat hydrogel film and in a patterned hydrogel layer with a honeycomb topography that induces micro-floret actuation of the embedded microstructures.^[15] Representative results are shown

in **Figure 3**. With electrochemically-generated pH gradients, the pH change is slow enough that the volume-phase transition of the hydrogel took place over a few seconds and the details of the actuation could be easily recorded (movies in Supporting Information). We observed the differences in the rates of actuation corresponding to either contraction or expansion of the hydrogel; there is a sharp and relatively fast actuation transition upon contraction, while actuation is slow and gradual upon swelling. Swelling time for the hydrogel was increased to about a minute, while contraction time was increased to approximately 5 seconds. This behavior correlates very well with general hydrogel theory and experiment: the kinetics of pH-responsive hydrogel volume change depend on a variety of factors including ion exchange rate, solvent diffusion rate, gel thickness, and crosslinking density, and the net result is that swelling and contraction are asymmetric processes, where swelling is slower than contraction.^[23] The actuated polymer microstructures in essence function as a self-reporting system for the hydrogel dynamics, visualizing and amplifying important features of the differences in the rates of the swelling and deswelling cycles. We have also shown that the actuation rate is highly tunable, from actuation taking place in fractions of a second up to a minute, depending on the methods of pH change and applied electric field, as well as the thickness and profile of the gel layer that moves the structures. We believe that this resultant spatiotemporal difference in the actuation rate and mode may be advantageous for biomimetic cilia or fins, as an asymmetric beating motion at a tunable rate is necessary to generate flow or directional movement.^[3,29,30]

Detailed modeling of forces and chemo-mechanical factors contributing to the patterned actuation of differently shaped polymer microstructures driven by a pH-responsive hydrogel is currently underway. However, simple estimates of the magnitude of force required to bend these polymer microposts can be made from previously published results that modeled bending of similarly-structured silicon posts (8 μm tall with an aspect ratio of 10) embedded in a humidity-responsive hydrogel.^[13] Such surface-attached silicon posts required

a force of $F_{Si} \sim 100 \mu\text{N}$ to bend and therefore the force F_{poly} required to bend polymer microposts by the pH-responsive gel is on the order of $1 \mu\text{N}$:

$F_{poly}/F_{Si} \sim (E_{poly}/E_{Si}) * (h_{Si}/h_{poly})^3 * (r_{poly}/r_{Si})^4$. The model can be further simplified by considering the structures, which are not surface-attached but suspended in the hydrogel, and in that case the deflection angle (α) of the structures can be estimated from the swelling ratio of the hydrogel: $\cos\alpha = v_c/v_s$, where v_c and v_s are the volumes of the hydrogel in contracted and swollen states respectively.^[13] For the pH-responsive hydrogel, for which we have determined the swelling ratio of ~ 5 - 10 , α is estimated to be up to $\sim 80^\circ$.

Toward the potential application in microfluidics, we are also interested in how these pH-sensitive actuators respond to abrupt spatial changes in pH, where both acidic and basic conditions exist within a micrometer-length scale over the sample surface, and particularly whether the actuation is spatially patternable. Microfluidics has recently emerged as a powerful tool for “lab-on-a-chip” applications ranging from sample analysis, flow sensors, and cell manipulation and sorting, to chemical synthesis and monitoring,^[31] in part because of unique fluidic phenomena that occur on the microscale, such as laminar flow. Not only does incorporation of these hybrid actuating surfaces with microfluidics open the doors to future integration with microfluidic devices, but it allows us to take advantage of laminar flow to precisely control the placement of acid and base over the sample. We therefore created microfluidic systems in which the bottom surface of the channels was made of a hybrid actuation system (**Figure 4a**). **Figure 4b** shows an example of such a design, using a microfin actuating surface: the laminar flow of acid and base allows for spatial control of actuation down to the micron scale. The actuation response is highly localized: the gel contracts and the microfins bend only in areas over which acid is flowing, while neighboring microfins subjected to base remain upright (movie, Supporting Information). The transition from bent to upright at the interface of the acid and base streams is sharp and only a few microns wide. While microfluidics provides a way to spatially control the actuation, the actuators themselves

could also serve as a sensitive self-reporting system in a device allowing for easy visualization of pH changes.

In conclusion, we have developed a novel chemo-mechanical hybrid actuation system that enables pH-responsive reversible motion in liquid. Inspired by biological actuators, the system is a composite of passive structural skeletal elements put in motion by a poly(AAc-co-AAm) hydrogel muscle that swells and contracts in response to chemical signals. We have successfully demonstrated the patternable actuation of polymer microposts controlled by structured hydrogel layer, as well as the uni-directional actuation of asymmetric microfins over a large area. The dynamics and mechanism of actuation were studied using electrochemically-generated pH gradients that allow us to visualize the hydrogel volume-phase transition and how this translates to movements of the microstructures. We also integrated these actuators with microfluidics and observed that the actuation can be spatially patterned using laminar flows. The variations in actuation methods, microstructures, and hydrogel morphologies we demonstrate here lay the foundation for an expanse of possibilities with such a hydrogel-driven adaptive actuation system optimized for fluidic environments.

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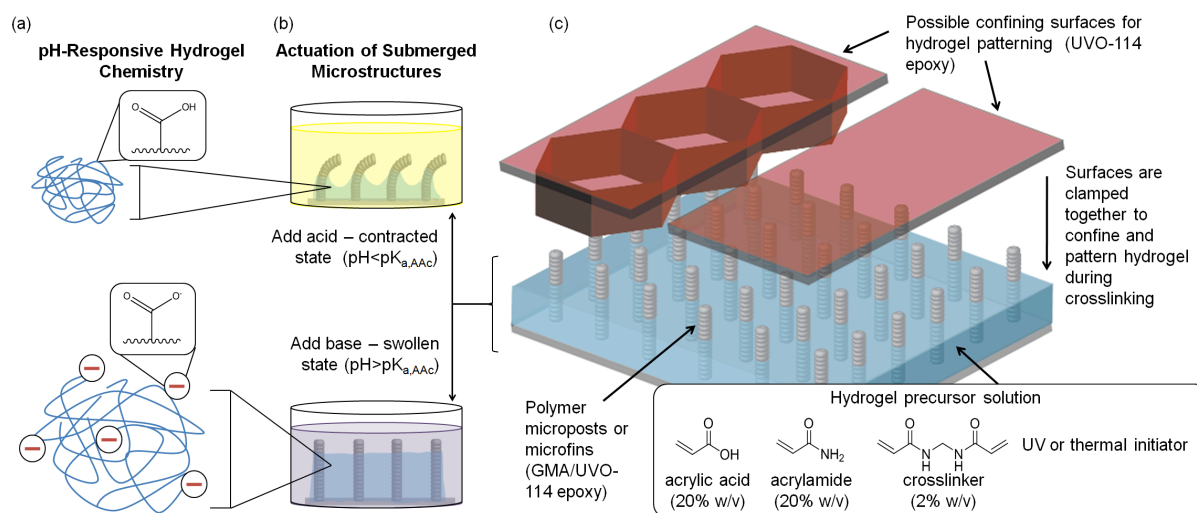


Figure 1. Schematics of the experimental set-up. (a) Hydrogel response to pH. (b) Actuation of microstructures embedded in a hydrogel submerged in aqueous solution colored with bromophenol blue indicator. (c) Overview of the fabrication of pH-responsive hydrogel-embedded polymer microstructures with topographically-patterned hydrogel. The confining surface can have any arbitrary pattern.

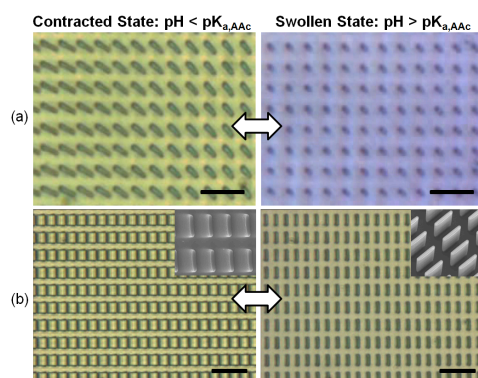


Figure 2. Optical microscope images of microposts (a) and microfins (b) after addition of acid (left) and base (right). The color arises from bromophenol blue indicator. (Inset: SEM images of microfins bent in hydrogel and microfins without hydrogel.) Scale bar = 20 μm . See Supporting Information for movies

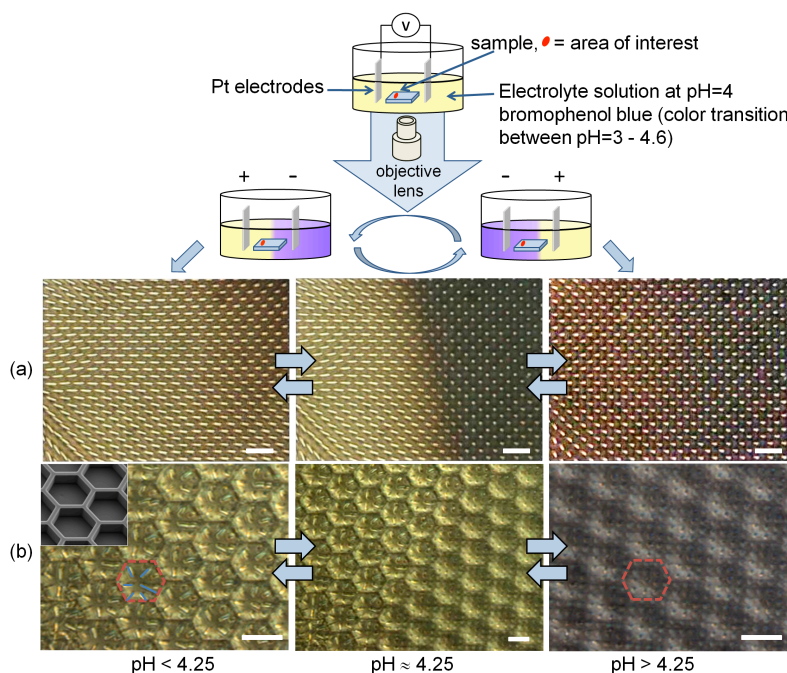


Figure 3. Schematics and optical microscope images of pH-responsive actuation using electrochemically-generated pH gradients. (a) Directional actuation using flat confinement, (b) Opening-microfret actuation made by confinement using a honeycomb-patterned surface. Left panels: bent microposts (contracted hydrogel). Middle panels: transition state (volume-phase transition of the hydrogel); note sharp boundary between the bent and the upright posts. Right panels: upright microposts (swollen hydrogel). Electric fields of ca. ± 0.5 V/mm were

used. Note that the color transition of the indicator does not exactly match the pH volume-phase transition of the hydrogel. Scale bar = 20 μ m. See Supporting Information for movies.

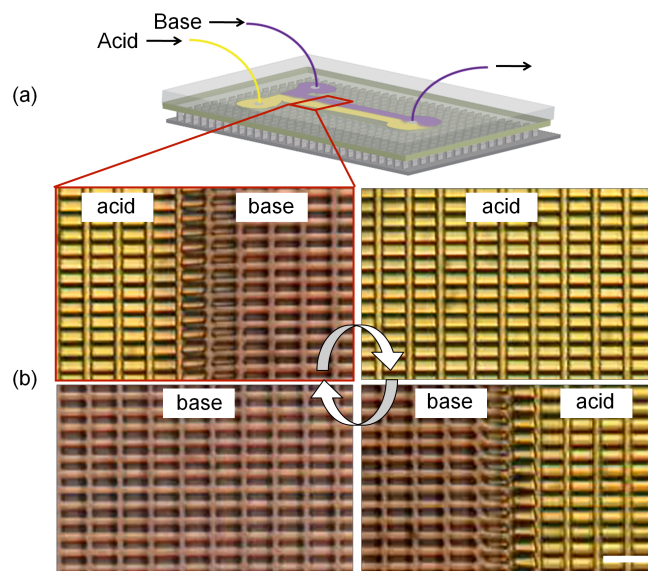


Figure 4. pH-actuated microstructures in microfluidic channels. (a) Schematic of the experimental set-up. (b) Optical microscope images of microfins within a microfluidic channel and demonstration of spatially controlled actuation using laminar flows of acid and base. As indicated, the images correspond to setups in which acid was supplied in the left channel and base in the right channel; acid in both channels; base in both channels; base in the left channel and acid in the right channel, correspondingly. The color arises from bromophenol blue indicator. See Supporting Information for the movie. Scale bar = 20 μ m. Flow is from top to bottom of the images.

The table of contents entry

A bio-inspired hybrid materials system has been developed by utilizing pH-responsive, poly(acrylic acid-*co*-acrylamide) hydrogel as the “muscle” that dynamically and reversibly actuates the embedded microposts and microfins while the sample is submerged. The system is designed to provide uniform directional bending actuation over a large area and integrated with electrochemical and microfluidic cells.

Keyword: Stimuli-responsive materials

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