Self-Folding Thermo-Magnetically Responsive Soft Microgrippers

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ABSTRACT: Hydrogels such as poly(N-isopropylacrylamide-co-acrylic acid) (pNIPAM-AAc) can be photopatterned to create a wide range of actuable and self-folding microstructures. Mechanical motion is derived from the large and reversible swelling response of this cross-linked hydrogel in varying thermal or pH environments. This action is facilitated by their network structure and capacity for large strain. However, due to the low modulus of such hydrogels, they have limited gripping ability of relevance to surgical excision or robotic tasks such as pick-and-place. Using experiments and modeling, we design, fabricate, and characterize photopatterned, self-folding functional microgrippers that combine a swellable, photo-cross-linked pNIPAM-AAc soft-hydrogel with a nonswellable and stiff segmented polymer (polypoly(pentfluoropropene fumarate, PPF). We also show that we can embed iron oxide (Fe₃O₄) nanoparticles into the porous hydrogel layer, allowing the microgrippers to be responsive and remotely guided using magnetic fields. Using finite element models, we investigate the influence of the thickness and the modulus of both the hydrogel and stiff polymer layers on the self-folding characteristics of the microgrippers. Finally, we illustrate operation and functionality of these polymeric microgrippers for soft robotic and surgical applications.

KEYWORDS: smart materials, stimuli responsive materials, polypolypropylene fumarate, NIPAM, surgery, robotics

INTRODUCTION

The ability to grip and securely hold onto objects is a vital task in robotics, manufacturing, and surgery. Conventional robots are composed of stiff materials such as metals (aluminum, steel) and ceramics (silicon, silicon oxide) with their joints being actuated using electrical, pneumatic, or hydraulic signals. Soft robotics is an emerging, bioinspired field that promises to augment the capabilities of traditional hard robotics with polymeric modules that mimic biological actuators. As compared to their hard robotic counterparts, soft robotic structures have distinct advantages: they can be constructed using simple designs; be made lighter and inexpensive; be processed at low temperatures and in aqueous environments; and offer the possibility to mimic human functionality through their robotic functions.

Many previously described soft robotic actuators including those developed in the MEMS community are electrically or pneumatically driven. For example, the reversible electrochemical swelling of polypyrrole in a variety of bilayer, trilayer, and sandwiched configurations has been used to create a number of folding and actuating structures. More recently, a variety of pneumatically actuated robotic devices have been developed including a microhand for surgery, networks capable of intricate motion, and a universal gripper based on granular materials. While these devices offer significant advantages in terms of the control, speed, universality, and momentum, their need for tethers as well as electrical power or gas sources can increase their weight and complexity. This limits their applicability in small or confined spaces or during repetitive actuation over long time periods.

The use of stimuli responsive mechanisms provides an alternative to tethered actuation and offers the possibility for smart behaviors such as autonomous responses in specific environments. Many of these schemes employ hydrogels since these materials are able to swell significantly in response to a variety of stimuli such as temperature, light, or chemical reactions generating the energy and force to perform mechanical tasks. Hydrogel actuators can also be created...
using bigel strips composed of partially interpenetrated hydrogel networks with differing swelling properties. This concept was first demonstrated using bilayers of pNIPAM and acrylamide that had drastically different swelling behavior in response to temperature or aqueous environments.\textsuperscript{16} The use of stimuli responsive bilayers has recently been combined with photo-cross-linking approaches to create a range of microstructured actuators and self-folding devices.\textsuperscript{20,11,17--21}

In our previous work on self-folding microactuators, we have demonstrated a range of self-assembled, origami-inspired structures that spontaneously fold-up and actuate from two-dimensional patterns without the need for any wires or external controls.\textsuperscript{9,10,22--25} These structures utilized a variety of actuation forces derived by the minimization of surface tension; the release of residual stress triggered by light, enzymes, biochemicals, or temperature; and differential swelling based on pH or temperature changes. It is particularly noteworthy that previously created metallic microgrippers were autonomously actuated on introduction into the gastrointestinal tract of live pigs and used to biopsy tissue.\textsuperscript{24} In order to enhance biocompatibility and possibly endow biodegradability in such surgical applications and for robotics, we believe there is a pressing need to develop polymeric, origami-inspired, and stimuli responsive microgripper structures.\textsuperscript{9,22,25,26}

We have observed that one of the significant limitations of stimuli responsive hydrogel actuators is their low stiffness. For example, when we previously designed microgrippers composed of cross-linked pNIPAM-AAc alone, we observed that these grippers were very floppy and unable to securely grip onto beads which would often fall out of their grasp.\textsuperscript{26} In order to address this limitation, we previously introduced the concept of combining rigid polymer segments of a nonswellable polymer to increase the overall stiffness of the pNIPAM-AAc polymer.\textsuperscript{25} In this paper, we build on these earlier results to design, fabricate, and characterize mass-producible microgrippers capable of cell excision. We have incorporated nanoparticle doping and a sequential photolithographic approach to create large numbers of autonomous, polymer-hydrogel bilayer grippers. These grippers have numerous advantageous properties including the capability for magnetic direction, simultaneous actuation based on temperature, independent function, optical transparency, and gripping onto and isolating tissue. Over numerous cycles, the resulting grippers can fold completely in either direction on the basis of temperature and fold reversibly. We use finite element analysis to model the folding behavior of these soft robotic grippers to gain insight into the influence of important material and design considerations such as polymer thickness and modulus.

The characteristics, thermal responsiveness, and stiffness were chosen for the polymer materials of the grippers based on their relevance for biological applications. pNIPAM is a thermoresponsive hydrogel that undergoes a low critical solution temperature (LCST) above physiological temperature where the polymer becomes hydrophobic expelling water and losing 90% of its mass while below its LCST, the polymer is hydrophilic and absorbs water.\textsuperscript{27} The absorption and desorption of water in response to temperature serves as the actuation mechanism, and pNIPAM has been used extensively in drug delivery applications, cell culture, and tissue engineering applications.\textsuperscript{9,8--13}

We have addressed the issue of pNIPAM biocompatibility in a previous publication.\textsuperscript{25} Essentially, the backbone of pNIPAM hydrogels is not degradable although specific cross-linkers used to network the hydrogel can endow biodegradability.\textsuperscript{28,31} Therefore, a networked pNIPAM hydrogel can be created with tunable degradation rates based on cross-linker density and type. PPF, a material originally designed for filling bone defects and similar in tensile strength to trabecular bone,\textsuperscript{34,35} serves as a stiff and restrictive construct, mimicking phalanges in the human hand around which pNIPAM-AAc can contract or expand. The biodegradation products of PPF are propylene glycol and fumaric acid which are naturally expelled through the Krebs’s cycle.\textsuperscript{36}

Both PPF and pNIPAM are photopatternable and have been used previously in lithographic applications as well as to create therapeutic grippers or “theragrippers” in our own laboratory. By cross-linking, one can tune the physical and mechanical properties of the polymers without chemical modifications to the polymer backbone which can affect its biocompatibility.\textsuperscript{37}

The main advantage of photo-cross-linking over other cross-linking techniques is the ability to spatially and temporally control polymerization using photomasks and by varying the intensity of light. Further, a wide range of portable UV sources are available, and fast curing rates are achievable at room temperature. Photopatterned hydrogels can also be created over a wide range of sizes: we have previously created metallic microgrippers as small as a few hundred microns from tip to tip so that they can grip onto small sized cargo or pass through conventional catheters used in surgery.\textsuperscript{29} All that is needed is the optimization of spacing between grippers, spacing of the rigid segments, and thickness of the hydrogel and stiff segment layers.

Magnetic fields are biocompatible even at clinically relevant but high field strengths; therefore, they offer many attractive advantages over other propulsion and guidance schemes.\textsuperscript{38} Numerous examples of magnetically directed robotic devices have been developed for \textit{in vivo} applications including metallic microgrippers, microdrillers, modified bacteria, and microswimmers.\textsuperscript{21,22,38--40} Polymer microstructures can be made responsive to an electromagnetic field by incorporating magnetic nanoparticles within their network.\textsuperscript{21,41,42} In this work, we have directly incorporated magnetic nanoparticles into the pNIPAM-AAc trigger layer, allowing for remote direction while keeping the arms free to grip onto and/or isolate tissue at a desired location.

### MATERIALS AND METHODS

**Materials.** N-Isopropylacrylamide monomer (NIPAM, Scientific Polymer Products Inc.), poly-N-isopropylacrylamide (pNIPAM, MW 300 000, Scientific Polymer Products Inc.), N,N'-methylenbis-acrylamide (BIS, Sigma-Aldrich), n-butanol (Sigma-Aldrich), acrylic acid (AAC, Sigma-Aldrich), diethyl fumarate (DEF, Sigma-Aldrich), 80% hydrolyzed poly(vinyl alcohol) (PVA, MW 9–10 kDa, Sigma-Aldrich), iron(III) oxide (Sigma-Aldrich), Irgacure 2100 (Ciba), 1827 photore sist (Microchem), 351 developer (Microchem), and three inch silicon (Si) wafers (WRS) were used as we is without further modification.

**Synthesis of Polypropylene Fumarate (PPF).** PPF was synthesized by a previously published method\textsuperscript{43} and determined to have a MW of 804 Da and a polydispersity of 1.21.

**Synthesis of pNIPAM-AAc.** A NIPAM-AAc solution was prepared as described previously.\textsuperscript{27} Briefly, 3 g of NIPAM monomer, 0.4 g pNIPAM, and 0.18 g BIS were dissolved overnight in 7.5 mL of n-butanol under constant stirring at room temperature. To this solution, 0.3 mL of AAC was added followed by 0.1 g of Irgacure 2100. The resultant mixture was stirred until the additives had been completely incorporated.

**Profilometry.** Glass slides were repeatedly washed with acetone, methanol (MeOH), and isopropyl alcohol (IPA) after which they were...
Figure 1. Schematic diagram illustrating the reversible self-folding of soft microgrippers in response to temperature. The photopatterned microgrippers are composed of stiff PPF segments atop a pNIPAM-AAc layer. Above 36 °C, the pNIPAM-AAc layer excludes water and contracts which causes the grippers to first open and then close such that the PPF segments face outward. Below 36 °C, the pNIPAM-AAc absorbs water and swells which causes the microgripper to open and then close in the opposite direction such that the pNIPAM-AAc layer faces outward.
RESULTS AND DISCUSSION

Design and Fabrication of the Grippers. Our design is based on the combined use of stimuli responsive polymers such as pNIPAM-AAc with a degradable yet stiff polymer like PPF to increase rigidity of the actuator. Polymeric grippers were fabricated using sequential photolithography and fold into 3-D structures based on the swelling/deswelling through water absorption/desorption in response to temperature (Figure 1). The pNIPAM-AAc layer serves as a thermally responsive swelling hydrogel layer with a low shear modulus ($G_h = 162$ KPa) while the PPF layer serves as the nonswelling, restrictive layer with a much higher shear modulus ($G_n = 16$ MPa). Similar moduli values were previously reported for PPF mixed with ceramic materials showing compressive strengths ranging from 2 to 30 MPa.43

We used a serial photolithographic method to pattern the PPF/pNIPAM-AAc microgrippers (Figure 2, Supporting Information Figure 1). It is noteworthy that PPF is typically used in gram quantities for filling bone defects and photopatterning of this material is relatively new. Hence, it was necessary to develop methods to precisely control the thickness and lateral resolution of photopatterned PPF films. Specifically, we varied the spin coat speed, the UV intensity, and the spacing between PPF patterns to reliably mass produce well-structured microgrippers (details in Supporting Information Figure 1). We also note that since the PPF/DEF solution is much more viscous than the NIPAM-AAc solution, it is preferable to pattern the PPF/DEF solution first followed by NIPAM-AAc photopatterning. We observed that when patterned second, the PPF/DEF solution can dislodge the underlying patterned pNIPAM-AAc structures during spin coating. We also intentionally did not develop the PPF patterns before the addition of the NIPAM-AAc solution. It is noteworthy that delamination of bilayer actuators is a concern during reversible swelling and deswelling cycles. In our case, due to the material properties and processing, we observed sufficient adhesion between the two films, and we attribute it to two factors. First, the n-butanol in the NIPAM-AAc solution could partially develop the underlying PPF leading to polymer chain entanglement. Second, the reaction between the alkene functional groups of NIPAM, acrylic acid, DEF, and PPF could lead to improved adhesion at the interface.

Characterization of Gripper Folding. Once released from the wafer and equilibrated in solution, the polymeric structures were thermally responsive and could fold in both directions as shown in Figure 3A and in Supporting Information Movie 1 (am508621s_si_002). The literature LCST value for pNIPAM lies between 30 to 35 °C;27 however, it is known that the LCST can be altered by copolymerization of NIPAM with other monomers as in pNIPAM-AAc.31,44 We observed the self-folding transition temperature to be approximately 36 °C. We rationalize self-folding by noting that above this temperature pNIPAM-AAc is hydrophilic, the polymer collapses causing the gripper to close with the PPF segments on the outside of a closed gripper. Since the pNIPAM-AAc layer is opaque during polymer chain collapse, the transition can be readily observed under a microscope. As the temperature cools below 36 °C, the pNIPAM-AAc layer becomes clear and swells as it absorbs water causing it to open and then close in the opposite direction, now with the PPF segments on the inside of the gripper, as verified over 50 cycles.

We developed constitutive models for finite element simulation of the pNIPAM-AAc and PPF bilayer grippers (Supporting Information Figure 2) to study the influence of various design parameters on gripper folding and unfolding [Supporting Information Movies 2 and 3 (am508621s_si_003 and am508621s_si_004)]. The model was implemented into the open-source finite element code TAHOE (Sandia National Laboratories). As shown in Supporting Information Figure 2, the mesh was discretized using trilinear hexahedral elements, and a mesh convergence study was also performed to decide the mesh density. Self-folding results from the model are shown in Figure 3B as a function of temperature and the ratio of dry to swollen hydrogel weight ($\phi$); the ratio $\phi$ increases with increasing temperatures as water is expelled. The simulation model is based on the thermodynamic framework for equilibrium mechanics coupled with hydrogel swelling26 to describe the thermoresponsive behavior of the pNIPAM-AAc.
The free energy of the hydrogel is assumed to be the sum of a mechanical part, represented by a Neo-Hookean model for the entropy elasticity of the polymer network with Gaussian chain statistics and a component for the energy of mixing represented by the Flory–Huggins model. The Flory–Huggins parameter increases sigmoidally with temperature. The low-temperature and high-temperature values along with the transition temperature range were determined from the temperature-dependent swelling experiments described in the Materials and Methods section. The effect of diffusion through the micrometer-scale thick hydrogel layer was neglected, and we assumed the hydrogel was at equilibrium for each test temperature. A Neo-Hookean model was also applied to describe the mechanical behavior of the PPF layer. The shear modulus of the two layers was determined by dynamic mechanical analysis (DMA) described in the Materials and Methods section. Simulation snapshots in Figure 3B capture the opening and closing behavior of the grippers with the pNIPAM-AAc film on the inside of the grippers at high temperatures, and the trends agree with experimental data.

We also applied the model to investigate the effect of the gap between PPF segments, thickness, and modulus on the temperature-dependent folding configuration. Specifically, we varied the spacing between adjacent PPF segments on the gripper arms from 20 to 90 μm and found that this had a negligible effect. A smaller spacing between the rigid segments led to only slightly more folding. In contrast, both the thickness and modulus of the layers had a pronounced effect. In order to quantify the extent of folding as a function of these parameters, we plotted the ratio of the overall diameter of the grippers in the folded state ($D$) to the unfolded, flat diameter ($D_o$) while varying these parameters (Figure 4). A smaller value of ($D/D_o$) signifies greater folding. The thickness of PPF and pNIPAM-AAc was varied between half to twice the experimental thickness used, i.e., from 5 to 20 μm for PPF and 10 to 100 μm for pNIPAM-AAc (Figure 4A). The thickness of PPF ($t_p$) used in experiments was approximately 10 μm while the thickness of pNIPAM-AAc ($t_n$) used was approximately 34 μm when swollen. Increasing the PPF layer thickness results in a higher ($D/D_o$) ratio signifying lower folding which we attribute to a higher bending rigidity of the PPF. However, the effect of varying the thickness of the pNIPAM-AAc layer is more complicated. For example, when the thickness of pNIPAM-AAc
CONCLUSION

The goal of this study was to create and model stimuli responsive self-folding soft microgrippers composed of a continuous low modulus actuator layer of pNIPAM-AAc and stiff segments composed of PPF. pNIPAM-AAc was chosen as an appropriate actuator material based on its stimuli responsive properties and its method of actuation by swelling and deswelling in aqueous environments. We have validated the hypothesis that when this swellable soft hydrogel is combined with a nonswellable stiff polymer, it endows sufficient strength such that microgrippers structured in this manner are strong enough to excise cells from a tissue clamp. On the basis of the stiffness, biocompatibility, biodegradability, and photo-cross-linking of PPF we believe that this is an attractive material for photopatternable soft robotic actuators especially for medical applications. As we have shown, very thin but robust films of...
PPF can be created in any desired shape by spin coating and photopatterning.

Our results suggest that since these thermally responsive soft microgrippers actuate around physiological temperatures. The grippers could be stored in a cold solution, allowed to fold completely in one direction, and then deployed with a catheter to a desired location in the body. In the body, this self-folding transition would occur autonomously as the grippers equilibrate from a cold state to physiological temperatures as we achieved previously with metallic microgrippers.

The incorporation of magnetic particles into one or both of the polymeric layers allows the grippers to be remotely directed or retrieved. Since the grippers fold up compactly at both high and low temperatures, they are small enough to be deployed and retrieved using conventional catheters. Further, the compact initial shape would also reduce shear forces in the catheter during deployment. PPF is naturally hydrophobic as is pNIPAM-AAc when the temperature is above 36 °C, suggesting that cells could be grown onto the PPF for other biomedical applications. In cartilage engineering projects, PPF has been incubated in the presence of fetal calf serum to allow the cells to adhere.46,47 In addition to cell excision, these magnetic polymeric grippers could be directed and allowed to latch onto specific tissue locations to deliver therapeutics. This can be done by incorporating drugs into either the trigger layer or the structural layer as demonstrated previously.25

Finally, we have validated an important design approach for the enabling of relatively stiff stimuli responsive soft-tools by pairing a rigid polymer with a thermoresponsive hydrogel. From a bilayer design perspective, our modeling study shows that there is an optimal thickness ratio and modulus ratio of the active hydrogel layer and the stiff structural layer for the folding angle. Self-folding allows such actuators to respond to stimuli without the need for any wires, tethers, batteries, or power/gas sources. We envision that this approach could also be utilized with other photopatternable or printable biomaterials.48

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ABBREVIATIONS
pNIPAM-AAc, poly(N-isopropylacrylamide-co-acrylic acid)
PPF, polypropylene fumarate
LCST, low critical solution temperature
Si, silicon
DEF, diethyl fumarate
EtOH, ethanol
MeOH, methanol
Me H2O, deionized water
PVA, poly(vinyl alcohol)
UV, ultraviolet
FEM, finite element model
PBS, phosphate buffered saline
BIS, N,N-methylenebis-acrylamide
AAc, acrylic acid
ω, weight fraction of dry to swollen gel
Wswollen, weight of fully swollen sample
Wdry, weight of dry sample

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