

Stimuli responsive self-folding using thin polymer films

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The ability to manipulate the curvature of thin films in response to a specific stimulus such as light, heat, pH, electric fields or chemicals can be utilized to create a variety of smart three dimensional (3D) materials. Because of the high structural and chemical variability of polymers that can be created by synthetic approaches, thin films composed of polymers are especially useful in creating a wide range of stimuli-responsive structures. Moreover, since polymer thin films can be patterned by a number of planar techniques such as photolithography, molding, or imprinting, a variety of precisely patterned 2D precursors can be used to fold-up functional structures such as tubular, spherical and polyhedral capsules, biomimetic actuators and even microsurgical tools. This article reviews recent advances and highlights future challenges.

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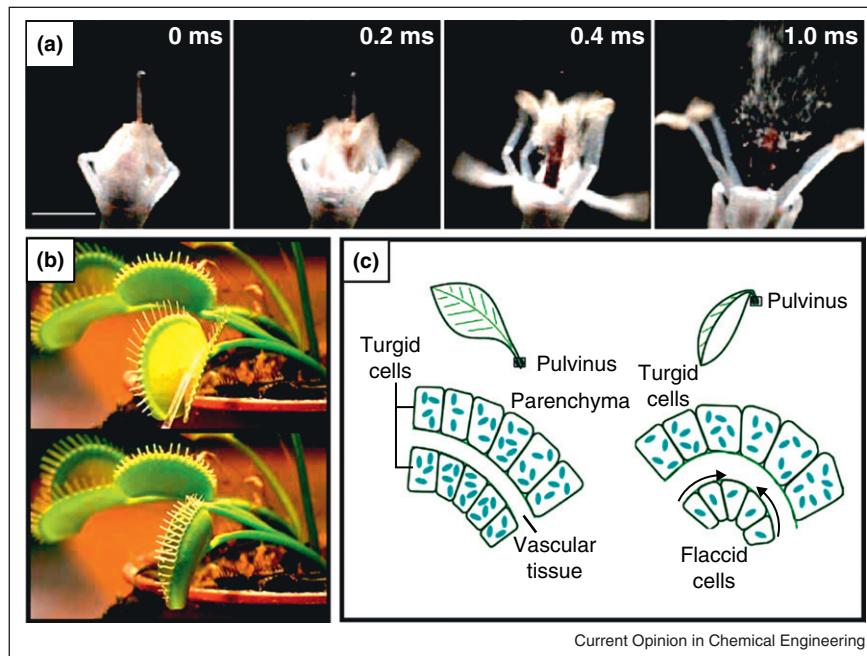
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Introduction

Stimuli responsive materials are expected to play an important role in the creation of multi-functional, smart, reconfigurable, mechanized, and biomimetic structures at a variety of length scales [1**]. Self-folding broadly refers to a class of self-assembly systems in which structures curve or fold-up either spontaneously or in response to a stimulus. In the perfect sense of the term, self-folding materials are composed of multiple interconnected units that fold up without any active human control. Self-folding of biomolecules such as proteins is an essential feature of the internal machinery of a cell and a variety of supramolecular and origami inspired strategies have been developed to create synthetic stimuli responsive self-folding molecular structures ranging from self-folding cavitands [2,3] to foldamers [4,5] to DNA boxes [6]. Folding in these systems is typically mediated by relatively weak interactions such as hydrogen bonds which can be broken or formed. Additional design principles

such as the control of steric interactions and molecular rigidity are also important in these systems and some attempts have been made to mimic these design principles in meso-scale assembly with polymer linked blocks interacting via capillary forces [7–9]. It has also recently become clear that the manipulation of strain in patterned thin films can cause them to fold-up on length scales ranging from the nano to the macro, and with a variety of materials including metals, semiconductors, and polymers [10**,11*,12,13,14**,15*,16,17*,18**,19]. However, in many of these studies, the patterned thin films roll or fold-up spontaneously on release from the substrate, which typically occurs during dissolution a sacrificial layer. In order to enable stimuli responsive self-folding structures using thin films, it is necessary to arrest their spontaneous curvature and activate folding or unfolding only in response to a specific stimulus, which is readily achieved by driving chemical, structural, or mechanical property changes in polymers.

The need for stimuli responsive self-folding thin film structures is evident on both an intellectual and technological level. On an intellectual level, controlled folding is widely observed in nature, especially in plants, and is often the result of stimuli responsive changes in the turgor pressure of specialized cells (Figure 1) [20,21*]. Plants do not contain muscles and must rely on relatively simple mechanisms to enable motion which is often also essential to their survival. Seemingly simple yet important functions such as the dispersal of pollen require advanced engineering tasks of separating the particles and releasing them with low terminal velocities so that they stay afloat and are carried over large distances. Remarkably, plant motion can be achieved at very high speeds and in response to a variety of stimuli. For example, it has been reported that pollen can be catapulted from the Bunchberry flower when its petals open within 0.5 ms while accelerating up to $2200 \times g$ (Figure 1A) [22]. Interestingly, the researchers uncovered mechanistic details of the motion by noting that these flowers opened even when the stamen was treated with a metabolic inhibitor sodium azide, but could not open when their turgor pressure was reduced by osmotic dehydration with sucrose. Likewise, mechanically stimuli responsive carnivorous plants such as the Venus Fly Trap can snap shut in about 0.1 s and it has been suggested that changes in shape, curvature and volume of cells and buckling of the leaves drive rapid closure (Figure 1B) [23–25]. It has also been observed that the Venus Fly Trap closes in response to electrical stimulation alone and that the mechanical stimulation is pH dependent, suggesting that a range of environmental stimuli could modulate actuation [26].

Figure 1

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Stimuli responsive actuation in plants. (a) Bunchberry flower opening, recorded on video at 10 000 frames/s. Time elapsed is indicated. First frame shows a closed flower with four petals fused at the tip, restraining the stamens. Blur represents the distance moved in 0.1 ms. Scale bar, 1 mm. Reprinted by permission from Macmillan Publishers Ltd. from Ref. [22], © 2005. (b) The Venus Fly Trap in its open and closed states. Reprinted by permission from Macmillan Publishers Ltd. from Ref. [24], © 2005. (c) Bending response of a leaf (top) to the deswelling-induced bending of the pulvinus (bottom). Reprinted from Ref. [49] with permission from John Wiley and Sons, © 2011.

On the technological front, there is a need to create stimuli responsive self-folding structures to enable smart functional materials and actuators. Moreover, one of the big open challenges in materials engineering is the pressing need to facilitate structures that can open and close at small size scales which can be challenging to achieve especially off-chip and in an untethered manner. Examples of such structures include smart microcapsules for targeted drug delivery, mobile elements for micro-robotics, artificial cilia and smart valves for lab-on-a-chip applications, active pores in separation membranes and untethered microsurgical tools. Also, human engineering relies heavily on the use of electricity or pneumatics as a source of energy for actuators, and the ability to trigger actuation by alternate means such as by using chemicals could provide added functionality and even enable biomimetic or autonomous functions [27[•],28^{••}]. While some stimuli responsive actuators can be created with conventional shape memory polymers [29[•]], they can be challenging to pattern using lithographic methods and their shapes often require pre-programming, both of which can restrict miniaturization. Moreover, the design focus in these materials is on manipulating the molecular architecture and chain flexibility which can be realized in response to only a limited number of stimuli.

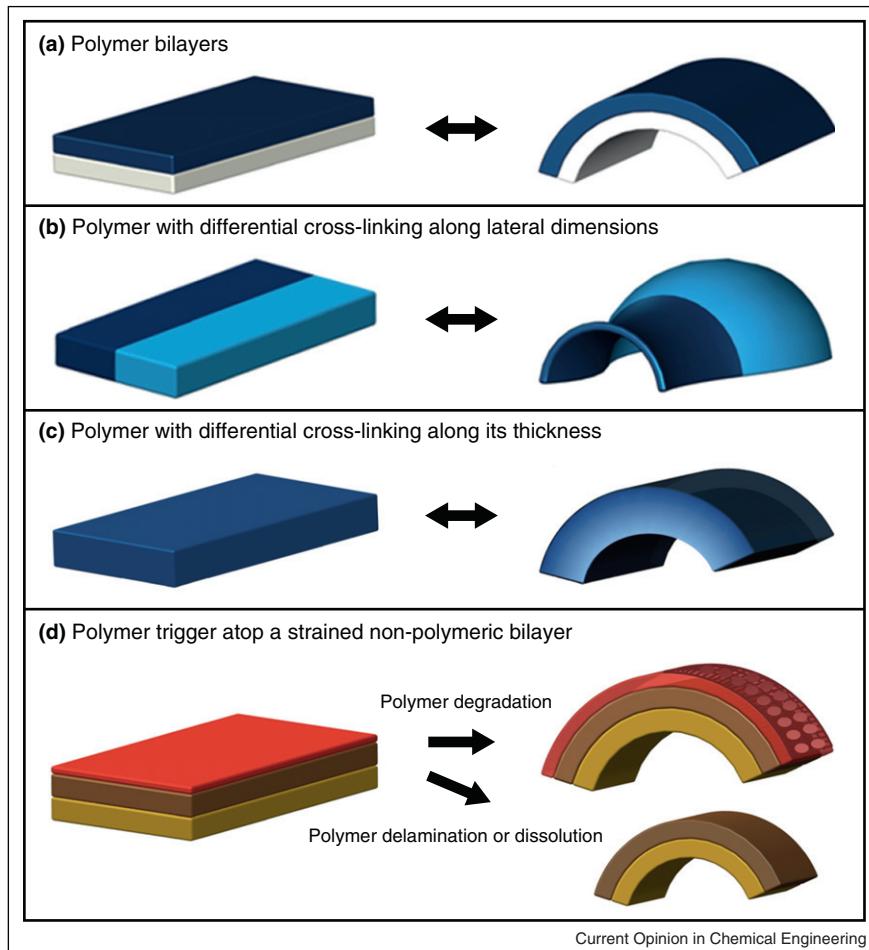
Design principles

In order to create a self-folding structure using thin films, it is necessary to engineer differential stress either along its thickness or lateral dimensions so that a bending moment is generated. An illustration of a proposed schematic for the bending response of a leaf (Figure 1C) suggests that even a differentially swelling well-adhered bilayer would cause bending, and this is indeed the case. The important thin film design principles that are compatible with photopatterning and can be utilized to create stimuli responsive self-folding polymeric materials are schematically illustrated in Figure 2.

Polymer bilayers

A straightforward strategy to create a stimuli responsive self-folding structure is to utilize bilayers wherein either one or both layers are polymers (Figure 2A). Curving or bending is achieved when one of the polymer layers contracts or swells more than the other, in response to a specific stimulus. Actuators based on bilayer bending can be traced back to the bimetallic strip, an invention generally credited to the British clockmaker John Harrison who in the mid 1700s created riveted strips composed of sheet brass and steel which curved owing to differences in thermal expansion coefficients and compensated for

Figure 2

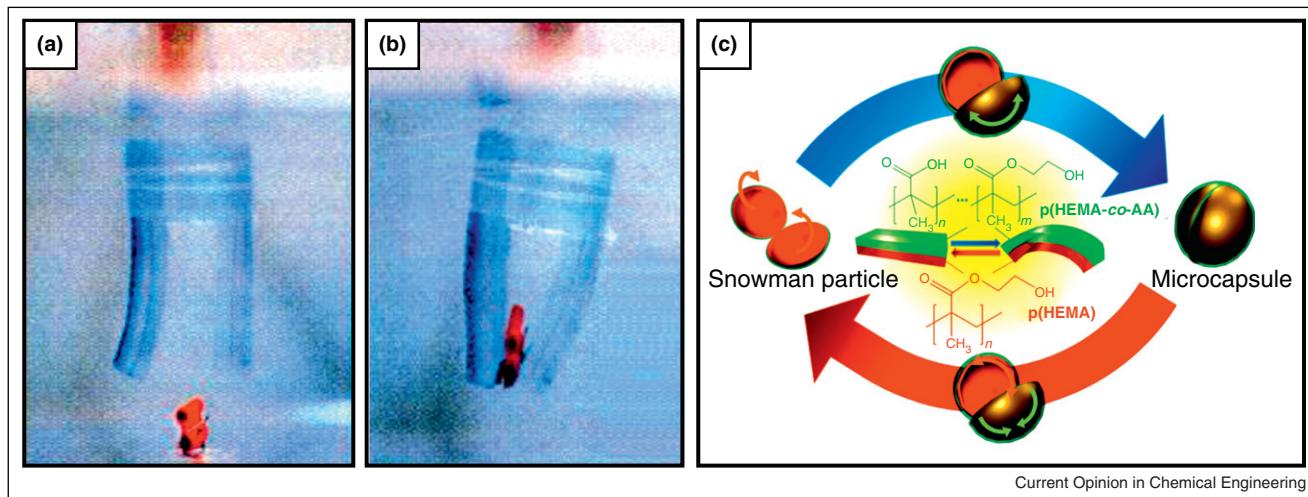


Schematic illustration showing four important strategies to enable stimuli responsive structures using thin polymer films.

temperature changes [30]. As noted by Timoshenko, in the absence of external forces, and when the thickness of each metallic film is the same, the curvature is directly proportional to the difference in elongation of the two films and inversely proportional to the thickness of the bilayer [31]. As compared to metals, polymers and especially hydrogels can undergo significantly larger volume changes and additionally respond to a variety of stimuli. Further, recent developments in the patterning of these soft materials using lithographic, molding, and imprinting approaches have advanced significantly allowing them to be structured with microscale precision. Hence, polymer-constituted bilayer structures provide a relatively facile and attractive means to enable stimuli-responsive materials. Early work on controlled folding was demonstrated with polypyrrole-gold bilayers [32•]; these polymer based bilayer actuators enabled significantly larger deformations and required lower actuation voltages as compared to piezoceramics. In addition to bilayers, alternate layered configurations have been realized for such

electromechanical actuators or so called artificial muscles; these approaches include ionic polymers sandwiched between metallic electrodes and trilayered films [33,34•]. While such ionic polymer actuators can indeed provide controlled folding, they typically require an electrical power source as well as an electrode connection to the bilayer, which can restrict off-chip actuation, maneuverability, and miniaturization.

In order to design structures that fold in response to non-electrical and tether-free stimuli, alternate polymers and hydrogels must be utilized. Macroscopic modulation of hydrogels was first described in the context of a bigel strip composed of N-isopropylacrylamide (NIPAM) [35] and acrylamide (PAAM) which bent in response to variations in acetone concentration or temperature [36••]. The authors reported flat sheet to tube transitions and utilized this bigel strategy to create a hand shaped device that closed at 35 °C and opened at room temperature (22 °C) (Figure 3A). In the last

Figure 3

Stimuli responsive materials based on differentially swelling polymer bilayers. **(a and b)** A gel 'hand' made from two bigel strips tied together at one end with a spacer. (a) At 22 °C, the 'fingers' are open and the red object is released. (b) At 35 °C, the 'fingers' are closed and the object is caught. Reprinted from Ref. [36] with permission from AAAS, © 1995. **(c)** Reversible structural transformation of a hydrogel bilayer, one consisting of p(HEMA-co-AA) and the second consisting of p(HEMA), depending on pH. Reprinted from Ref. [42] with permission from John Wiley and Sons, © 2012.

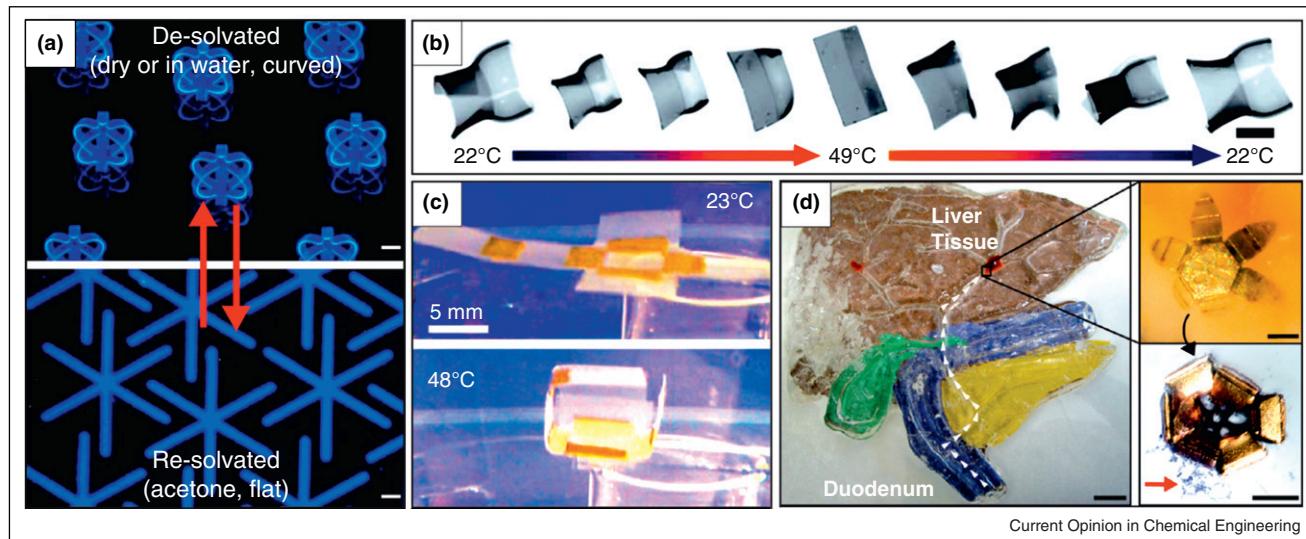
decade, the bilayer concept has been combined with a range of photo and soft-lithographic patterning approaches to create a variety of self-assembling microstructures. For example, Guan *et al.* created pH responsive self-folding microstructures composed of soft-lithographically patterned bilayers of poly(methacrylic acid) (PMAA) and poly (EGDMA). The two layers adhered well and while PMAA is a pH responsive hydrogel, poly(EGDMA) is strongly cross-linked with a relatively low swelling ratio [37]. The dissimilar swelling of polymer bilayers in different solvents was used by Luchnikov *et al.* to create solvent responsive rolled-up microstructures [38]. They utilized polystyrene (PS) which is hydrophobic and poly (4-vinylpyridine) (P4VP) which is less hydrophobic; the bilayer rolled up on immersion in aqueous acidic media (such as 0.01–0.1% hydrofluoric acid). They attribute this bilayer curving to swelling of P4VP layer on protonation and consequent electrostatic repulsion with minimal swelling of the PS layer [39].

In order to create photolithographically patterned hydrogel actuators, my own laboratory has photocrosslinked NIPAM derivatives atop other polymers such as PEGDA to form pH and ionic strength responsive hinged hydrogel actuators that were shaped like leaves [40]. Thermally responsive pNIPAM/polycaprolactone capsules have been developed by Stoychev *et al.* and used to encapsulate yeast cells [41]. Photolithographically patterned snowman shaped hydrogel bilayers composed of poly(HEMA-co-AA) and poly(HEMA) were used to

create reversibly pH-responsive microcapsules owing to swelling of poly(HEMA-co-AA) under basic conditions (Figure 3B) [42]. These and other examples of the use of polymer bilayers to enable folding, wrinkling and stimuli-responsive actuation for applications in drug delivery or the creation of biomimetic structures suggest that this technique is becoming well established [17,43–48]. A noteworthy point is that the implementation of the bilayer actuation concept requires good adhesion between the two layers; if the adhesion is poor, the layers will delaminate during differential swelling or contraction. Adhesion can be improved by coating the second polymer layer on a partially cured first layer, adding copolymers or cross-linkers at the interface, or by utilizing surface grafting or surface polymerization methods; the latter has been demonstrated in the case of self-folding Au-polymer brush bilayers [49].

Cross-linked polymer films with spatial heterogeneities

The concept of manipulating differential strain in a bilayer to drive stimuli responsive folding can be extended to a single chemically constituted polymer or gel by creating gradients or spatial heterogeneities within the film. Such heterogeneities can be generated by photocrosslinking variable concentrations of monomers or crosslinkers, doping with optically absorbent or photoactive molecules, and/or exposure to different intensities of ultraviolet light using optical filters or photomasks. Heterogeneities can either be created along lateral dimensions (Figure 2B) or along the

Figure 4

Schemes for enabling stimuli responsive self-folding based on spatial heterogeneity and polymer triggers. **(a)** Fluorescence images of an array of flower-shaped structures that (top) reversibly curved on de-solvation and (bottom) flattened on resolvation. Scale bars are 100 μm . Reprinted from Ref. [51**] with permission from Macmillan Publishers Ltd., © 2011. **(b)** Temperature responsive swelling of hydrogel bistrips. Reprinted from Ref. [53] with permission from the Royal Society of Chemistry, © 2012. **(c)** Folding of a cube based on SWNT-pNIPAM/LDPE bilayer actuators by thermal actuation at 48 °C in water. Reprinted from Ref. [54] with permission from the American Chemical Society, © 2011. **(d)** External biopsy in a model of the human biliary system using enzymatically responsive microgrippers. Reprinted from Ref. [58] with permission from the American Chemical Society, © 2010.

thickness (Figure 2C) [35,50*,51**,52]. For example, Klein *et al.* first described novel buckling or wrinkling of heterogeneous NIPAM discs on immersion in a hot bath [50*]. The heterogeneity was achieved by programmable mixing of different monomer concentrations and injection into a Hele-Shaw cell. Our own laboratory has shown that it is possible to create cross-linking gradients along the thickness of a widely utilized photo-sensitive hydrophobic epoxy SU8 owing to its strong molecular absorbance at low ultraviolet wavelengths [51**]. By the use of photomasks and on conditioning such SU8 films, a variety of stimuli responsive structures such as arrays of flower-like structures (Figure 4A) or metamaterial sheets were created. Metamaterials are periodic materials, often composed of heterogeneous components with a large refractive index contrast, thus featuring novel electromagnetic properties. In our studies, the contrast was achieved by patterning metallic resonators on a polymeric substrate, and the metamaterial sheets crumpled or flattened out on solvent exchange which induced solvation and desolvation of the films, and consequently reversible self-folding at differentially cross-linked hinges. The ability to create stimuli-responsive metamaterials offers the possibility for the realization of adaptive optical and electromagnetic coatings. Kim *et al.* have shown that differentially cross-linked NIPAM bistrips with lateral swelling heterogeneities show interesting thermally responsive shape transformations (Figure 4B) [52,53], which could

potentially be utilized to create novel stimuli-responsive structures. Spatial heterogeneities can also be achieved by doping NIPAM with carbon nanotubes (CNTs) which were used to realize thermal stimuli responsive NIPAM/LDPE bilayer folding (Figure 4C) and offer the possibility for optically responsive folding owing to the strong absorption of the CNTs in the near infrared [54]. It is noteworthy that optically responsive polymeric bending and folding can also be achieved by the inclusion of photoactive molecules such as azobenzene [55] or photo-induced stress relaxation [56].

Polymer triggers atop strained non-polymeric bilayers

As evident from our previous discussion, it is relatively straightforward to create polymeric and hydrogel actuators that respond to temperature, pH, electric and optical signals. However, it still remains challenging to create actuators that respond to selective biochemicals such as enzymes. Moreover, in some applications such as micro-surgery, there is a need to create stiff and sharp actuators that are strong enough to incise or excise tissue; hence it is often necessary to utilize inorganic components. Because of the wide range of polymers that can be synthesized to degrade in response to specific chemicals, polymers can be utilized as triggers atop pre-stressed inorganic bilayers such as those composed of heteroepitaxially strained semiconductors or residually stressed metals. A polymer layer can be photopatterned atop a strained bilayer and as

long as it is well adherent and stiff enough, it will arrest spontaneous self-folding of the underlying bilayer and can also render the folding stimuli responsive. Only in response to an appropriate stimulus, which can be a specific chemical that causes softening, degradation, dissolution or delamination of the polymer trigger, the energy in the underlying strained bilayer can be released causing it to actuate (Figure 2D) [57^{**}]; the one limitation is that such self-folding is typically irreversible. Nevertheless this one-way triggered actuation can provide significant functionality with high speed, sensitivity and selectivity. For example, we have fabricated polymer triggered self-folding structures in complex shapes such as multi-hinged grippers that can close within seconds to minutes and with a strong enough force to excise tissue. It is also noteworthy that the appropriate choice of polymer such as gelatin or carboxymethyl cellulose caused the grippers to close with high specificity to proteases or cellulases respectively [58]. Since the hinges within these thin film multilayered self-folding devices effectively function both as sensors and actuators, one can fabricate biosensing microactuators or microtools using this approach [59]. These structures can display smart and autonomous behaviors and do not require any batteries, wires or tethers (Figure 4D) [27,58,60,61]. In fact, we used thermally responsive so called μ -grippers to perform biopsies *in vivo* [62^{*}]. These μ -grippers remained flat when stored on ice, and folded within ten minutes on insertion into the live animal. They were used to retrieve tissue samples from the bile duct, a hard to reach place in the body, thus demonstrating the applicability of these devices in minimally invasive diagnostics.

Conclusions

The emerging field of stimuli responsive self-folding allows for the creation of smart three dimensional structures. Reversible folding has been achieved with electric and optical signals, pH, ionic strength and solvent exchange while predominantly one-way triggered actuation has been achieved in response to a range of biochemical stimuli. To create biochemically responsive reversible self-folding structures, it would be necessary to utilize thin bi-layers or bi-strips composed of novel polymers such as glucose [63] or antigen responsive [64] gels. In doing so, it may be possible to create a range of biosensing actuators to enable autonomous functions and biomimetic behaviors. Additionally, while such stimuli responsive structures have been demonstrated at the molecular and the 100 μm to 1 cm length scales, the intermediate 0.1 to 1 μm scale remains relatively unexplored, mainly owing to challenges in patterning polymers and hydrogels with these dimensions. It is noteworthy that self-folding methods work at these size scales and 100 nm scaled metallic self-folding polyhedra have already been achieved, [65] but similarly sized stimuli responsive polymeric self-folding structures have yet to be demonstrated. Additional developments in the

micro and nanopatterning of thin polymer films such as using direct-write [66] or imprint [67] techniques could enable these advances. It is noteworthy that surface forces have also been applied to curve and self-fold polymeric thin films [68^{*},69^{*}] and so called capillary origami has been demonstrated and can even be controlled using electric fields [70]. However, the capillarity driven reversible self-folding of micro and nanostructures in response to chemical stimuli would require the manipulation of capillary forces such as with surfactants, and this could prove challenging.

It is important to note that chemical engineers have an important role to play in the design and implementation of such stimuli-responsive self-folding materials. The diffusion and reaction rates of chemical stimuli interacting with the polymer chains within these thin films determine the time scale of actuation. For example, in our enzymatically triggered microgrippers, actuation is achieved when proteases diffuse through the gelatin trigger layer and cause chain scission within it, the overall kinetics of which ultimately determines the time scale of folding. Further, even equilibrium models for estimating and optimizing the swelling based bending of hydrogel bilayers require one to account for the free energy of mixing which provides the mechanical energy required for actuation. Hence, an overall optimization of transport, thermodynamic and kinetic parameters alongside molecular characteristics such as polymer chain length, steric side groups, extent of cross-linking and microstructural variables such as cross-link gradients, lateral geometry, and thickness is required to design self-folding materials that respond to different stimuli with large forces and high sensitivity, selectivity and speed. Clearly, much future work is needed, but it is fair to say that recent advances in stimuli responsive self-folding have achieved significant strides and already offer glimpses of smart and autonomous materials and devices that can be realized using these approaches.

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