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Next-gen biomimetic actuators: bilayer hydrogel evolution in the 21st century and its advancements from a post-2020 perspective

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Bilayer hydrogel actuators, composed of two hydrogel sheets exhibiting distinct swelling rates or ratios, have emerged as a promising class of smart materials. Their asymmetrical responsive properties enable controllable deformations, including bending and buckling. Recently, these smart materials have garnered significant attention for their versatile applications, playing crucial roles as manipulators or grippers, walkers and swimmers, and biomimetic devices. This perspective serves as a celebratory piece, illuminating the evolutionary journey of these smart materials and delving into their recent advancements post-2020. It provides readers with a focused spotlight on the current state-of-the-art materials, offering insights into their capabilities and projecting potential expansion avenues in the near future.

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1. Introduction

Hydrogel actuators, characterized by programmable shape deformations responsive to external stimuli, represent a frontier in materials science with transformative potential across a myriad of applications.^{1–4} Their ability to undergo substantial changes in volume and shape has propelled them into the spotlight, revolutionizing fields such as soft robotics, biomedical engineering, and materials science.

The evolution of hydrogel technology in biomedical applications has been marked by a shift from traditional rigid actuators to the remarkable versatility offered by hydrogels. These three-dimensional polymeric networks, highly hydrated and capable of retaining large amounts of water, are distinguished by their biocompatibility, permeability, and unique responsiveness to environmental triggers.^{5–7} As a result, hydrogel-based actuators have found applications in wearable devices, nanomechanical tools, biocompatible medical devices, transparent ionic conductors, and micro-biorobots.^{5–11} The design principles of hydrogel actuators vary, encompassing both homogeneous expansion/contraction with special structures and inhomogeneous structures with distinct swelling/shrinkage degrees in different directions.¹² Anisotropic hydrogels, which exhibit inhomogeneous structures, have emerged as promising candidates due to their superior operability and controllability. Among them, bilayer hydrogels stand out, capable of intricate 2D and 3D shape transformations under external stimuli.^{13,14} These bilayer

hydrogel actuators achieve planar-to-3D shape transitions by modulating local concentrations and/or cross-linking densities in the two layers.¹⁴

While hydrogel actuators have successfully responded to various stimuli such as temperature, pH, solvent, light, and electric fields,^{5–14} the quest for multifunctional actuators capable of responding to multiple stimuli remains a compelling challenge.¹⁵ Drawing inspiration from animal tissues and organs, researchers aim to develop hydrogel actuators with the ability to camouflage through color change in response to environmental stimuli. Despite progress, only a few hydrogel actuators with integrated multi-stimuli responsive shape morphing and color-changing properties have been reported.^{16–18} Challenges persist in achieving precise control over bidirectional motions with tunable amplitude, limiting their application in complex environments such as underwater scenarios.^{19,20}

This comprehensive review embarks on a detailed exploration of bilayer-based hydrogel actuators, providing insights into their intricate designs, fabrication techniques, and diverse applications. The journey begins with an in-depth analysis of responsive hydrogels and their biomimetic designs, unraveling the multifaceted nature of hydrogel actuators and their crucial roles in drug delivery, soft robotics, and biomedical engineering. Navigating through this dynamic landscape, the review addresses challenges, presents case studies highlighting successful applications, and peers into the future to uncover exciting prospects. The aim is to shed light on recent advancements in these smart bilayer-based actuators, offering a succinct update on developments and outlining potential avenues for expansion and growth in this field.

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2. Biomimicry in material science and translating it to hydrogel actuators

Biomimicry, stemming from the Greek words “bios” (life) and “mimesis” (to imitate), represents a compelling approach in materials science, transcending conventional design principles. This method takes a unique journey through the annals of evolution, spanning millions of years, to glean insights from nature’s intricate designs and systems.²¹ At its essence, biomimicry acts as a catalyst for innovation, employing the emulation of biological strategies to craft solutions that are inventive and sustainable. This departure from tradition not only yields materials that are efficient and resilient but also deepens our understanding of the intricate mechanisms governing the natural world.^{22,23} The spectrum of biomimetic materials unfolds across diverse applications, showcasing its versatility. Structural materials, inspired by the adhesive capabilities of gecko feet, give rise to micro-structured adhesives, providing robotics with climbing and gripping capabilities.^{24–26} Functional materials, replicating the lotus effect, result in super-hydrophobic surfaces, introducing self-cleaning materials for textiles and buildings. Smart materials, drawing from mussel adhesive proteins, find application in medical adhesives, wound closure, and underwater bonding, demonstrating the inherent adaptability of biomimetic approaches.^{27–29}

In nature, various organisms such as the octopus, jellyfish, Venus flytrap, and mimosa exhibit remarkable abilities in movement, predation, reproduction, and other activities through stimulus-responsive soft actuation.¹⁰ Inspired by these intriguing phenomena, considerable efforts have been made to develop artificial responsive hydrogel actuators, including artificial muscles, smart actuators, and soft robots. Hydrogels, characterized by highly cross-linked hydrophilic networks and a high water content, serve as biologically inspired materials for such endeavors (Fig. 1A).^{10,28} By modifying their chemistry, structure, and function, it becomes feasible to engineer artificial soft actuators that respond to stimuli. However, typical hydrogels often suffer from brittleness due to uneven distribution of networks and cross-links, limiting their practical applications in actuators subjected to mechanical loading. To address this challenge, it has become imperative to design toughening and energy dissipation processes to enhance the strength, fracture, and fatigue resistance of hydrogels, enabling them to sustain practical actuation akin to natural organisms.¹⁰

Moreover, hydrogel actuators can be designed to achieve complex shape changes and movement processes through rational responsive design. Therefore, tough and responsive hydrogels are highly sought after due to their chemical and structural diversity. These hydrogels not only exhibit excellent flexibility and biocompatibility but also demonstrate the ability to adapt to complex environments by quickly responding to external stimuli.²⁹

In the realm of materials science research and practical applications, conventional stimuli-responsive hydrogel actua-

tors composed of simple polymer molecular structures often exhibit various deficiencies such as weak mechanical properties, slow response, and poor environmental tolerance. In contrast, natural hydrogels found in biological tissues possess outstanding mechanical performance owing to their multi-component and multiscale hierarchical structures.¹⁰ For instance, pinecones exhibit high toughness modulus and strength values. Inspired by such extreme mechanical properties of soft tissues, many tough hydrogel actuators with remarkable mechanical properties have been developed. These advancements have paved the way for the design and processing of mechanically robust tough hydrogels, thereby expanding their functional applications in soft actuators.

The construction of reversible non-covalent bonds (sacrificial bonds), such as hydrogen bonds, electrostatic interactions, coordination bonds, supramolecular recognition, and hydrophobic associations, plays a crucial role in developing toughness in hydrogels.¹⁰ These bonds effectively enhance the mechanical properties of hydrogels by consuming and dissipating a large amount of energy during breaking. Moreover, these reversible non-covalent bonds can endow hydrogels with self-healing properties. Based on this construction principle, various tough hydrogels have been developed, including double network hydrogels, slide-ring hydrogels, nanoparticle-reinforced hydrogels, nanocomposite hydrogels, and micelle-crosslinked hydrogels.^{24–29}

Furthermore, responsiveness can be achieved by further chemical design or modification of the hydrogel network structure, enabling hydrogels to undergo changes in volume or shape to achieve soft actuation when exposed to environmental stimuli such as temperature, pH, light, magnetic field, electric field, and redox reactions. The research on flexible, intelligent devices based on responsive hydrogels and actuation behaviors has recently gained widespread attention. However, efficiently combining responsiveness and toughening mechanisms to develop tough responsive hydrogels that withstand repetitive loads remains a critical step in practical applications. Typical construction methods include integrating hydrogels with different properties on the same device, constructing precise and controllable property distribution in a single hydrogel, and achieving programmed deformation or movement when subjected to external stimuli.

The application of biomimicry to hydrogel actuators is underpinned by several compelling rationales that collectively enhance their design and functionality. Foremost, biomimicry facilitates the harnessing of nature’s precision, exemplified in the delicate movements of muscles and the adaptive responses of biological tissues to environmental stimuli.³⁰ This precision becomes a guiding principle for the replication of intricate mechanisms in hydrogel actuators, elevating their design to achieve enhanced performance. Moreover, the rationale extends to optimizing functionality and efficiency. Evolution has meticulously fine-tuned biological structures to achieve optimal functionality while minimizing energy expenditure. By mimicking these evolutionarily honed structures in the design of hydrogel actuators, we not only enhance their efficiency but



also imbue them with heightened responsiveness and adaptability, thus optimizing their overall performance (Fig. 1B).^{30–32}

A crucial aspect of biomimicry's application to hydrogel actuators lies in environmental resilience. The emulation of nature's inherently sustainable solutions in hydrogel design aligns seamlessly with the principles of green chemistry. This approach results in the creation of materials that exhibit reduced ecological impact, offering a more environmentally friendly alternative in the realm of materials science.³² The versatility and adaptability intrinsic to natural systems, meticulously explored through biomimicry, become key drivers for expanding the applications of hydrogel actuators. By implementing these features derived from nature, hydrogel actuators can transcend their conventional uses and find utility across a spectrum of applications, ranging from the intricacies of soft robotics to the frontiers of biomedical devices.³³ We also believe that biomimicry serves as a wellspring of inspiration

for multifunctionality in hydrogel actuators. Nature frequently presents solutions that serve multiple purposes, and the study and emulation of these multifunctional systems inspire the creation of hydrogel actuators capable of responding to diverse stimuli. This aspiration mirrors the inherent complexity observed in biological tissues, presenting a pathway for the development of advanced hydrogel actuators with multifaceted functionalities. Table 1 provides a comprehensive comparison of various actuators based on key performance metrics such as energy density, elongation, pressure, and response time, offering valuable insights into their suitability for different applications.

In a culmination of inspiration, biomimicry guides researchers toward multifunctionality in hydrogel actuators. Nature's penchant for multifaceted solutions becomes a guiding light, inspiring the creation of hydrogel actuators capable of responding to a spectrum of stimuli. This aspira-

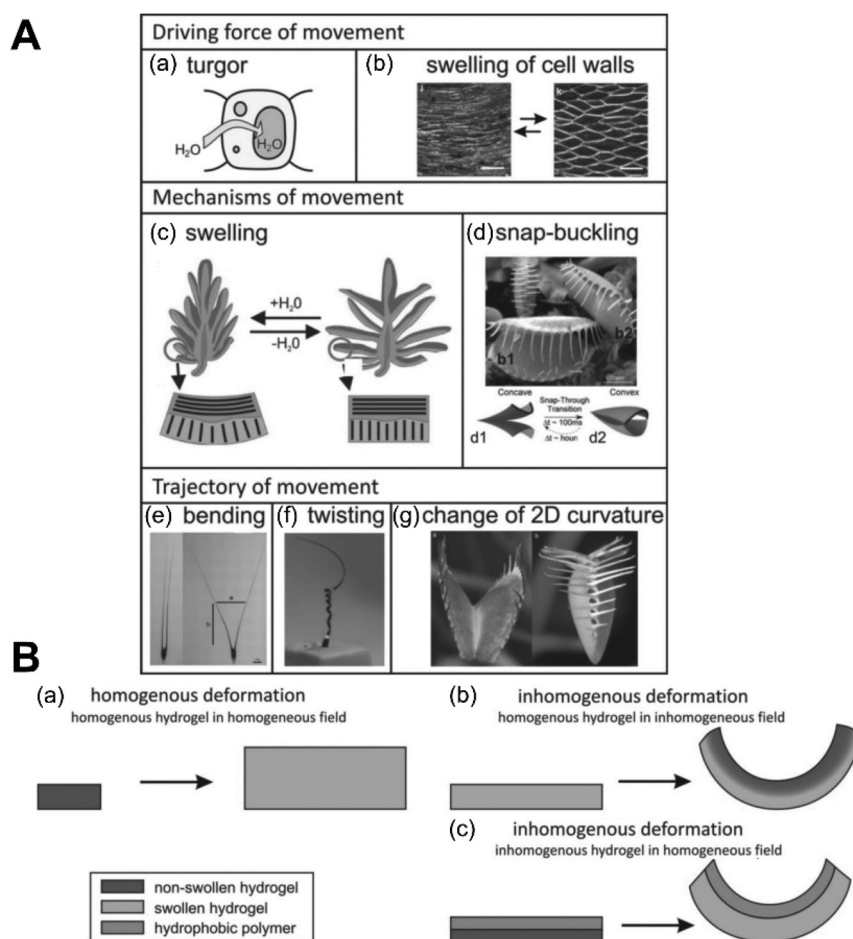


Fig. 1 (A) Examining examples of reversible movements in plants provides valuable insights into the dynamic responses driven by distinct forces, mechanisms, and trajectories. Firstly, the driving forces of turgor pressure (a) and swelling of cell walls (b) underscore the multifaceted nature of plant biomechanics. Turgor pressure relies on the controlled pressure of cell contents, while the swelling of cell walls involves the expansion of cellular components. In terms of mechanisms, swelling (c) and snap-buckling (d) contribute significantly to these reversible movements in plants. Swelling, a fundamental process, entails the expansion of cellular components, while snap-buckling represents a sudden structural transition that plays a role in achieving reversible deformations. The trajectories of these movements add another layer of complexity to plant biomechanics. Bending (e), twisting (f), and changes in two-dimensional (2D) curvature (g) showcase the diverse ways in which plants adapt and respond to external stimuli, demonstrating their inherent flexibility and resilience. (B) Translating the biomimetic concept to bilayers, reprinted with permission from ref. 31, copyright reserved Wiley 2013.



Table 1 Comparison of actuator performance metrics³¹

Actuator	Energy density (J cm ⁻³)	Elongation (%)	Pressure (MPa)	Response time (ms)
Solenoids	0.025	50	0.1	5
Piezo-actuators	0.05	0.2	110	0.5
Magnetostrictive	0.025	0.2	70	0.4
Shape-memory alloy	10	8	900	300
Hydrogels	0.35	90	4	300
Electrochemical	0.14	50	25	16
Muscle	0.59	70	1.18	0.03

tion mirrors the profound complexity observed in biological tissues, propelling biomimicry in materials science to open up avenues for innovation, sustainability, and a deeper connection with the natural world. In essence, biomimicry emerges not just as a methodology but as a profound exploration, unraveling the secrets of nature to inform and elevate the creations of human ingenuity.

3. Anisotropic hydrogel actuators: a biomimetic approach

Polymeric hydrogel actuators operate through the uptake and release of water, and their isotropic structures traditionally limited them to simple homogeneous swelling/shrinking responses under uniform stimuli.³⁴ To overcome this limitation and broaden their applications, the field has progressed towards achieving complex deformations and movements.^{1,34,35} Two primary approaches have emerged: firstly, imposing nonuniform external stimuli such as electric fields or localized light irradiation onto isotropic hydrogels, and secondly, fabricating internal anisotropic hydrogels. Given the challenges in precisely applying nonuniform external stimuli, the focus has shifted towards the fabrication of anisotropic structures, marking a significant stride in biomimetic engineering. Anisotropic hydrogel actuators, inspired by the intricate structures observed in nature, represent a paradigm shift in biomimicry, offering tailored functionalities by introducing directional variations in their properties. The relevance of anisotropic hydrogels to biomimicry lies in their ability to replicate nuanced and directional responses akin to those found in biological tissues and organisms.¹

The design principles of anisotropic hydrogel actuators draw deeply from nature's blueprint, where materials exhibit varying properties in different directions, enabling precise and controlled movements. Anisotropic hydrogels incorporate these directional variations in their composition or structure, facilitating biomimetic responses and the development of actuators capable of emulating intricate and purposeful movements observed in living organisms. A critical exploration involves comparing anisotropic and isotropic hydrogel actuators. Isotropic hydrogels maintain uniform properties in all directions, while anisotropic counterparts deviate from hom-

ogeneity by displaying distinct characteristics based on the direction of measurement. This divergence enables anisotropic hydrogel actuators to perform with enhanced specificity and adaptability, closely mirroring dynamic responses seen in biological systems. A comparative analysis reveals the distinct advantages and applications unique to anisotropic designs.

Over the past few decades, PNIPAM has garnered significant attention due to its thermo-responsive behavior within a biomedical relevant temperature range. This synthetic thermo-responsive polymer, derived from the acrylamide monomer *N*-isopropylacrylamide (NIPAAm), comprises amide and propyl groups. Its thermal behavior in aqueous media involves a phase transition from a hydrophilic state to a hydrophobic one upon heating above its lower critical solution temperature (LCST). Below the LCST, PNIPAM absorbs water and swells, while exceeding the LCST causes the PNIPAM network to collapse and precipitate (Fig. 2).³⁶

In the hydrated state below the LCST, water molecules form hydrogen bonds with the carbonyl group, accepting two hydrogen bonds, while the nitrogen atom of the amide group donates one hydrogen bond. Upon exceeding the LCST, rearrangement of intramolecular hydrogen bonds occurs, resulting in a reduction in the number of hydrogen bonds between PNIPAM and water and the formation of intra-chain hydrogen bonds.^{37–39} This leads to the collapsed network of PNIPAM chains (Fig. 2). However, the precise mechanism by which PNIPAM self-assembles in water above the LCST remains incompletely understood. Another explanation posits that the enthalpy gain of water molecules associated *via* hydrogen bonds with the amide groups of the polymer becomes smaller than the counter effect of the entropic gain of the system with water being dissociated when above the LCST of the hydrogel. Additionally, computer simulations have suggested a substantial decrease in the solvent-accessible surface area and a decrease in the torsional energy of the isopropyl groups during this thermal transition.^{37–39}

Additionally, the LCST of PNIPAM exhibits a correlation with its molecular weight, presenting variability among smaller polymers due to the presence of hydrophilic or hydrophobic end groups. The introduction of copolymerization with other monomers further offers a versatile method to manipulate the LCST. Typically, incorporating more hydrophilic monomers tends to increase the LCST, while integrating more hydrophobic monomers tends to decrease it. This nuanced control over the LCST enables tailored adjustments to suit specific application requirements.³⁹

Furthermore, in water/organic solvent mixtures, the LCST is contingent upon the volume fraction and type of the co-solvent. Generally, an increase in the volume fraction of the organic solvent leads to a decrease in the LCST. However, beyond a certain volume ratio, the LCST may begin to increase. This phenomenon arises from a competition for water molecules between PNIPAM chains and co-solvent molecules, illustrating the intricate interplay between molecular interactions within the hydrogel matrix.³⁹ Moreover, copolymerization with other monomers not only tunes the LCST but also serves as a



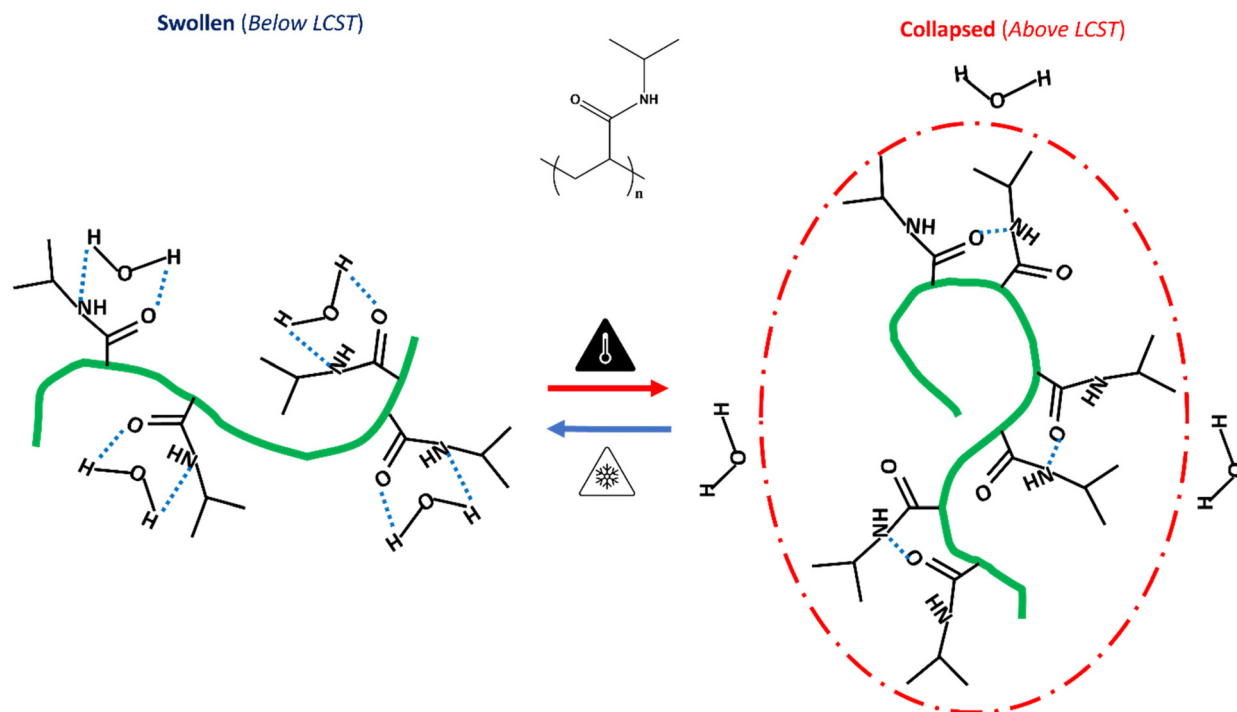


Fig. 2 Schematic representation of water swelling and de-swelling mechanisms of PNIPAM chains, induced by lower critical solution temperature (LCST) temperature changes, and hydrogen bonding formations.

strategy to enhance the mechanical properties and biodegradability of PNIPAM-based hydrogels. By incorporating various monomers with different properties, such as hydrophilicity or hydrophobicity, the overall performance of the hydrogel can be tailored to meet specific application demands. This versatility in structure–property relationships of the polymer sparks considerable debate and exploration in the development of hydrogels, paving the way for innovative advancements in the field.³⁹

However, the deswelling and swelling rate of PNIPAM-based hydrogel actuators often face limitations due to the slow diffusion rate of water molecules. Enhancing the actuating speed of such hydrogels becomes imperative for expanding their application in thermos-responsive hydrogel systems.^{37,41} Studies indicate that altering the size and arrangement of micropores within the hydrogel can improve the actuating speed. For instance, introducing sodium alginate microcapsules as a pore template has shown promise in reducing swelling balance time. Yet, challenges arise in maintaining a balance between actuation speed and strength, as increased actuation speed tends to weaken the hydrogel. Expanding more on this domain, in the realm of hydrogel actuators, those responsive to near-infrared stimuli demonstrate significant potential in various applications, including valves, soft robotics, organization, and grippers. The incorporation of 2D nanomaterials, such as $\text{Ti}_3\text{C}_2\text{T}_x$ -MXenes, into hydrogel frameworks proves to be a novel approach for fabricating shape-programmable soft actuators. MXenes, with their unique properties, are introduced into hydrogel systems to create multi-

functional composite hydrogels with excellent performance. Anisotropic hydrogel actuators, created through the integration of MXenes and hydrogels, exhibit rapid photo-responsive behavior and high actuation strength.

Drawing inspiration from the pulvinus of *Mimosa pudica*, the researchers developed $\text{Ti}_3\text{C}_2\text{T}_x$ -MXene-based nanocomposite hydrogels with ordered orientation. This innovative approach yielded a PNIPAM/MXene directional hydrogel (PMD) characterized by rapid photo-responsive deswelling rates under light irradiation. In comparison to isotropic hydrogels, the anisotropic hydrogel exhibited notably accelerated deswelling kinetics. Remarkably, within just 20 seconds in water at 40 °C, the PMD hydrogel achieved a deswelling rate of 0.4, significantly outpacing its isotropic counterpart (Fig. 3).³⁸ Upon temperature elevation, an initial formation of a dense outermost layer of collapsed PNIPAM hydrogel network occurred during the early stages of deswelling. This outer layer effectively hindered outward water flux from the hydrogel matrix. However, due to the presence of oriented structures within the hydrogel, water molecules could be released from the polymer pores under the influence of capillary force. Notably, the presence of these oriented pores inside the hydrogel impeded or potentially prevented the formation of the dense outermost layer as the hydrogel network collapsed during deswelling. Consequently, water could continuously discharge from the hydrogel's interior.³⁸

Of particular significance, the anisotropic hydrogel exhibited superior performance compared to its isotropic counterpart. This observation underscores the unique advantages of



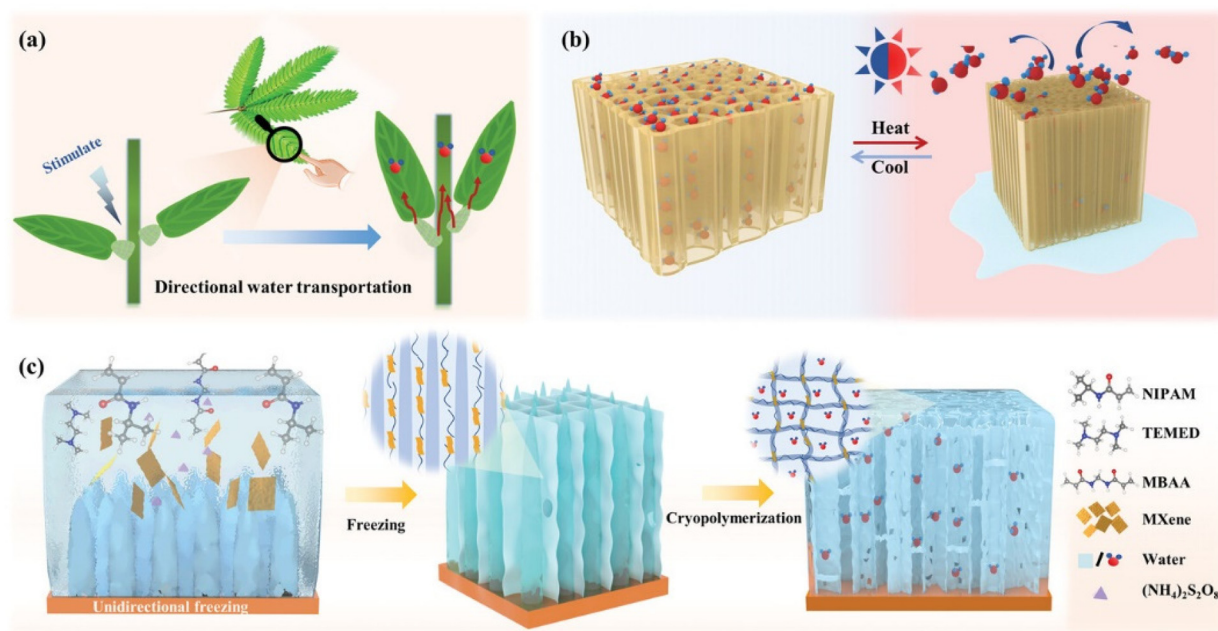


Fig. 3 Diagram (a) illustrates the closure of a leaf induced by the stimulation and contraction of the mimosa leaf pulvinus. In diagram (b), the process of deformation for a hydrogel actuator with rapid deformation is depicted. Lastly, diagram (c) provides a schematic representation of the synthesis process of the hydrogel, reprinted with permission from ref. 38, copyright reserved Wiley 2023.

PMD hydrogels with anisotropic structures, suggesting promising prospects for their utilization in various applications.³⁸ Notably, these hydrogels exhibit high actuation strength, lifting 40 times their weight loads (Fig. 3). The applications of PMD hydrogels extend to soft robots, valves, and remote-controlled devices, showcasing their potential as intelligent soft actuators with rapid responsiveness and robust actuation strength.

Utilizing the rapid shrinkage capability of the PMD hydrogel under near-infrared (NIR) light irradiation, a photo-responsive actuator was ingeniously fabricated. This actuator exhibited local responsiveness to NIR light stimulation (808 nm, 0.9 W cm⁻²), enabling the bending deformation of the entire actuator, thus achieving programmable bending of the PMD hydrogel (Fig. 3).³⁸ The MXene content and thickness of the hydrogel were meticulously regulated to independently control the degree of deformation. Notably, PMD hydrogels with higher MXene content exhibited faster contraction under NIR irradiation. Consequently, hydrogel strips with elevated MXene content folded more rapidly, resulting in higher folding angles at the same irradiation time. The optimal bending speed was observed at a moderate MXene concentration of 1 mg mL⁻¹. However, PMD hydrogels with higher Ti₃C₂T_x contents, such as 5 mg mL⁻¹, demonstrated a notable decline in performance. This decline may be attributed to the increased interaction between PNIPAM and excess Ti₃C₂T_x nanosheets, which hindered the movement of polymer chains during the phase transition of the hydrogel (Fig. 3).³⁸

The aforementioned example serves as a glimpse into the evolving landscape of biomimicry and anisotropic actuators.

However, our vision extends beyond this illustration, as we foresee that a deeper exploration of anisotropic hydrogel actuators within the biomimicry framework has the potential to unveil a vast realm of possibilities for innovative engineering. Understanding and replicating design principles inspired by natural structures provide a foundation for developing hydrogel actuators capable of nuanced and directional responses. Comparative analysis with isotropic counterparts highlights the unique advantages of anisotropic hydrogel actuators, emphasizing their potential in applications ranging from soft robotics to biomedical devices.

4. Traversing the evolution of bilayer-based biomimetic anisotropic hydrogel actuators post-2020

In the expansive domain of hydrogel actuators, the fundamental significance of structure in dictating properties and, by extension, potential applications are a universally acknowledged principle. Anisotropic structures, characterized by directional variations, stand as the cornerstone for propelling the development of hydrogel actuators. A spectrum of anisotropic structures, spanning from bilayer configurations to gradient, patterned, and oriented structures, has been subject to exploration, aiming to instigate intricate deformations and shape transformations. Existing literature reviews, while contributing to the understanding of the overall growth and evolution of biomimetic anisotropic hydrogels, often fall short in



Table 2 Detailed comparison of different anisotropic structures, highlighting their respective advantages and disadvantages

Type of anisotropic structures	Advantages	Disadvantages
Bilayer hydrogels	<ul style="list-style-type: none"> • Bilayer hydrogels offer simple yet effective structures for achieving controllable deformations such as bending and buckling. • They capitalize on asymmetrical responsive properties, providing directional control over shape changes. • The layer-by-layer assembly allows for precise tuning of properties by adjusting the composition or thickness of each layer. 	<ul style="list-style-type: none"> • Bilayer hydrogels typically exhibit limited shape transformations beyond bending, restricting their versatility in certain applications. • Achieving complex 3D shapes may require additional manipulation or integration with other techniques.
Gradient structures	<ul style="list-style-type: none"> • Gradient hydrogels enable complex shape deformations by exploiting variations in polymer chain distribution or filler concentration. • They offer the potential for sophisticated shape changes beyond simple bending, such as twisting or curving. • Gradient hydrogels can be tailored to respond to multiple stimuli, expanding their functionality. 	<ul style="list-style-type: none"> • Fabricating gradient structures may require specialized techniques such as electrophoresis or nanoparticle migration, adding complexity to the manufacturing process. • Achieving precise control over gradient distribution throughout the hydrogel may be challenging.
Patterned structures	<ul style="list-style-type: none"> • Patterned hydrogels provide predefined regions of differential swelling or responsiveness, enabling programmable shape changes. • They offer a high degree of control over the resulting deformations, allowing for the creation of intricate 3D shapes. • Photolithography techniques offer scalability and reproducibility in fabricating patterned hydrogels. 	<ul style="list-style-type: none"> • The fabrication of patterned hydrogels may require specialized equipment and expertise, potentially limiting accessibility. • Achieving uniformity and consistency in patterned structures across large areas can be challenging.
Oriented structures	<ul style="list-style-type: none"> • Oriented hydrogels leverage directional alignment of nanofillers to induce anisotropic swelling behavior, leading to tailored shape transformations. • They mimic natural structures found in plants, offering inspiration for biomimetic designs. • Techniques such as shear force alignment or magnetic field orientation provide precise control over the orientation of nanofillers. 	<ul style="list-style-type: none"> • Fabricating oriented structures may require specialized processing techniques and materials, potentially increasing manufacturing complexity. • Achieving uniform alignment of nanofillers throughout thick hydrogel samples may be challenging.

spotlighting recent developments. This narrative seeks to act as a bridge, addressing the gap and shedding light on the latest advancements in the realm of bilayer-based biomimetic anisotropic hydrogels post-2020. Table 2 presents a detailed comparison of different anisotropic structures, highlighting their respective advantages and disadvantages.

In the nascent stages of research on anisotropic hydrogels, the primary focus was on overcoming the inherent challenges posed by the highly solvated environment of hydrogels.⁷ Early investigations were driven by the desire to replicate the intricate structures found in natural tissues and organs. One of the pioneering breakthroughs came from Mredha *et al.*, who introduced a bio-inspired method for fabricating anisotropic hydrogels with hierarchical fibrous structures akin to tendons and ligaments.⁷ This marked a pivotal moment as it demonstrated that complex, biomimetic structures could indeed be achieved in synthetic hydrogels.¹⁵

Building upon this foundation, subsequent research efforts saw a surge in the development of innovative fabrication techniques. A notable advancement was the introduction of a self-welding-based approach to create multilayer anisotropic hydrogels, mirroring the hierarchical organization observed in compact bone. This method not only showcased the versatility of synthetic hydrogel engineering but also hinted at the potential for mimicking diverse natural structures with precision and control.¹⁶

The exploration then expanded into the realm of tubular structures, with researchers successfully fabricating anisotropic tubular hydrogels resembling the intricate microarchitecture of blood vessels. This achievement represented a significant leap forward, as it not only allowed for the replication of complex biological structures but also opened up new avenues for applications in tissue engineering and regenerative medicine.¹⁷

These early successes served as catalysts for further innovation and collaboration within the scientific community. Researchers from diverse backgrounds converged to explore novel fabrication methods, molecular design strategies, and applications of biomimetic anisotropic hydrogels. The transition from initial proof-of-concept studies to more sophisticated methodologies underscored the evolving interests and capabilities within this dynamic field, laying the groundwork for a new era of biomimetic materials research with far-reaching implications across various disciplines.

Bilayer structures, a prominent archetype, involve the assembly of two hydrogel sheets with distinct swelling rates or ratios. Strategies such as layer-by-layer polymerization and reversible switches, such as host-guest interactions, enable the construction of bilayer hydrogel actuators.¹ The layer-by-layer polymerization technique has emerged as a widely employed strategy in the fabrication of hydrogel actuators characterized by bilayer structures.¹ In this method, the monomer solution



of the second layer permeates slightly into the first layer during the preparation process, resulting in the formation of an interpenetrating network at the interface. This interconnecting layer acts as a junction, tightly binding the two layers together. A notable example of this approach is evident in the work of Chu and colleagues, who successfully developed a series of temperature-controlled manipulators using poly(*N*-isopropylacrylamide) (PNIPAM)-clay nanocomposite hydrogels. Through meticulous adjustments in the thickness ratio of the two hydrogel layers, each containing different clay contents, the thermoresponsive bending direction and degree of the hydrogel actuators could be precisely tuned.^{35,40} This demonstrated a fine level of control over the bilayer structure, influencing the responsiveness of the resulting hydrogel actuators. Similarly, Yoon and collaborators have contributed to this field by presenting a static-motion bilayer hydrogel actuator. This bilayer structure comprises an active layer, PNIPAM-*graft*-methylcellulose (PNIPAM-*g*-MC), characterized by a substantial thermal hysteresis, and a passive layer composed of polyacrylamide (PAAm).^{40,41} This dynamic combination provides a platform for achieving controlled deformations in response to external stimuli. Notably, the integration of magnetic nanoparticles with a photothermal effect in this bilayer actuator introduces a dimension of versatility. This innovative addition empowers the hydrogel actuator to undergo static bending upon exposure to light irradiation. The incorporation of magnetic nanoparticles enhances the overall functionality, paving the way for responsive behaviors dictated by external cues such as light. This integration showcases the potential for expanding the scope of bilayer hydrogel actuators and their applications, exemplifying the synergistic effects achievable through thoughtful combinations of materials and stimuli.

Over the years, the realm of developing bilayer-based biomimetic anisotropic hydrogels has evolved, and post 2020, we see a number of research that focus on using additive manufacturing as the processing tool. Three-dimensional (3D) printing technologies have emerged as a transformative tool for crafting soft actuators using diverse raw materials and achieving preprogrammed patterns. However, the intricate nature of this process necessitates precise adjustments to printing parameters, particularly filament diameter and overall structure, to attain optimal results.

Conventionally, biomimetic actuators are crafted using two-dimensional (2D) strategies. However, the transition to 3D printing opens new frontiers, offering precise control over composition, morphology, and the incorporation of intricate patterns and hollow structures. Notably, PNIPAM-based hydrogel actuators, while widely used, have faced challenges in compatibility with 3D printing conditions. Addressing this, a pioneering strategy introduces the fabrication of a thermoresponsive gelatin methacryloyl (GelMA)-poly(*N*-isopropylacrylamide) (PNIPAM) hydrogel, named the “GN” hydrogel. This composite hydrogel, serving as the active layer, exhibits temperature-dependent changes in swelling ratios. The bilayer hydrogel, incorporating GelMA as the passive layer, undergoes corresponding curvatures. This innovative approach not only

overcomes traditional constraints but also explores the untapped potential of 3D printing technologies in the realm of biomimetic actuators.⁴²

When investigating the structure–property relationships of these polymers, it was observed that the composition of GelMA and NIPAM exerted a significant influence on various hydrogel properties. Specifically, hydrogels with higher NIPAM content and lower GelMA content demonstrated greater swelling and temperature-dependent swelling. This phenomenon may be attributed to the relaxation state of GelMA chains and the enhanced water absorption facilitated by the hydrophilic amide groups of NIPAM. This finding was further corroborated by differential scanning calorimetry (DSC) measurements, which revealed a slight increase in the phase transition temperature (PTT) of the GN hydrogel compared to regular PNIPAM hydrogels, due to the introduction of hydrophilic GelMA chains. The elevated PTT can be ascribed to the increased enthalpy of hydrogen bond dissociation resulting from the presence of GelMA chains in the GN system.

The thermoresponsive behavior of PNIPAM-based hydrogels, characterized by a transition between hydrophobic and hydrophilic states above and below the PTT respectively, has been extensively documented in the literature. This behavior aligns with the observations made in this study and provides a theoretical framework for understanding the hydrogel's response to temperature variations. Furthermore, small-angle X-ray scattering (SAXS) analysis provided valuable insights into the nanostructure of the cross-linked hydrogel network, revealing temperature-dependent morphological changes in the GN hydrogel. The formation of mesoglobules and the subsequent change in chain conformation observed in this study supported the thermoresponsive phase transition of the hydrogel, which serves as the underlying mechanism driving the actuation process. This structural understanding not only enhances the comprehension of the hydrogel's behavior but also provides a basis for optimizing its performance in various applications.

Expanding on their results and the actuation process, the methodology employed for fabricating and actuating GN-GelMA bilayer hydrogels is elucidated in Fig. 4(I)A. The optimization process for the GelMA concentration in the passive layer involved assessing the curvature change of the bilayer hydrogel during bending between 37 and 25 °C, as depicted in Fig. 4(I)B. Notably, a larger curvature change was observed with a passive layer composed of 4.5 wt% GelMA. While the curvature changes among passive layers of 6, 7.5, and 9 wt% GelMA showed no significant difference, the 4.5 wt% GelMA hydrogel exhibited a relatively low storage modulus of 0.2 kPa. Among these, the hydrogel composed of 7.5 wt% GelMA demonstrated a balanced mechanical strength of 2.4 kPa. Consequently, the 7.5 wt% GelMA hydrogel, serving as the passive layer alongside the GN2 hydrogel as the active layer, was selected for bilayer hydrogel actuator preparation. The actuator with a bilayer thickness ratio of 1:1 achieved the maximum curvature difference between the heating and cooling processes. The optimized bilayer hydrogel exhibited a



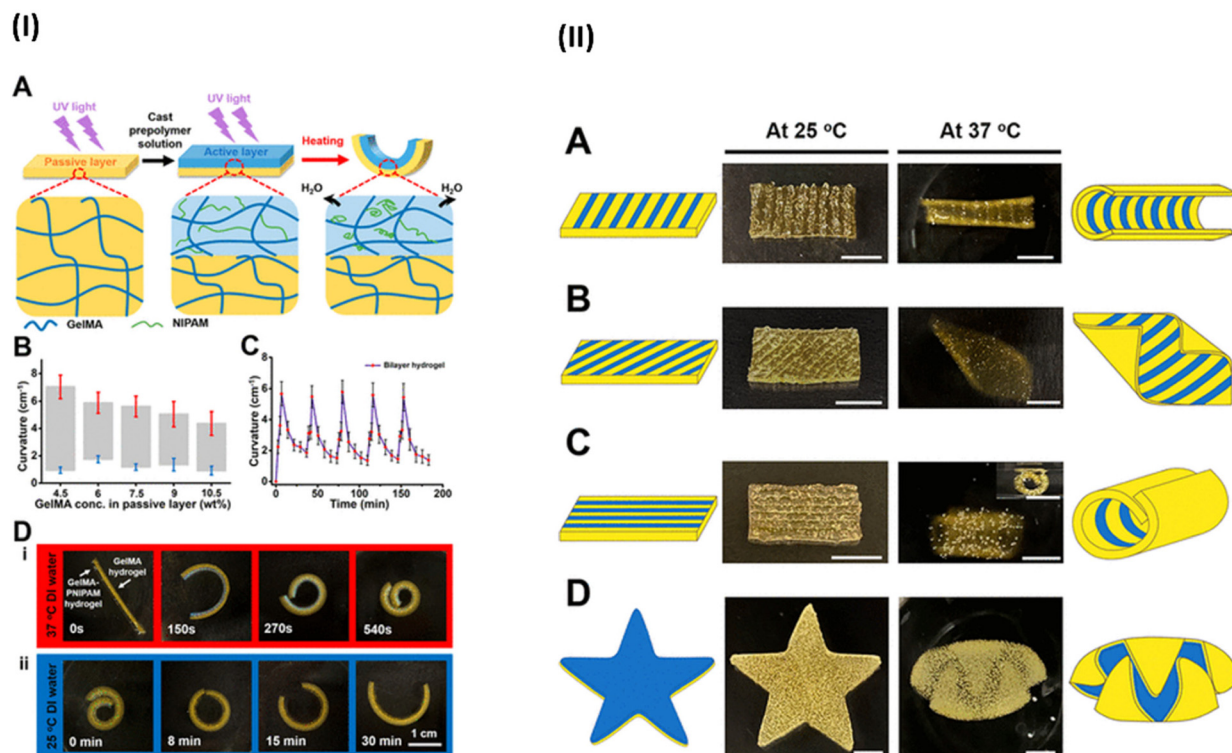


Fig. 4 (I) Illustration and characterization of bilayer hydrogels. (A) The depiction and analysis of bilayer hydrogels. (A) The bilayer hydrogel was crafted, comprising a GelMA passive layer and a GelMA–PNIPAM (GN) active layer. When the temperature surpasses the phase transition temperature, PNIPAM chains aggregate, leading to the collapse of the network and inducing a bending motion in the bilayer hydrogel. (B) The curvature range observed in 25 or 37 °C water for bilayer hydrogels, with the passive layer composed of GelMA at varying concentrations. (C) Cyclical testing of the curvature change in the optimized bilayer hydrogel in water between 25 and 37 °C, where the passive layer consisted of a 7.5 wt% GelMA hydrogel. (D) Depicted images showcasing the bending process of the optimized bilayer hydrogel, with the passive layer dyed using curcumin (scale bar = 1 cm). (i) The bilayer hydrogel bent toward the active layer, photographed in 37 °C water. (ii) The bilayer hydrogel was transferred to 25 °C water, unbent, and photographed in the water. (II) The transformation of hydrogel actuators in response to a shift from 25 °C air to 37 °C water is illustrated in the provided schematics and photographic images. In these representations, the GelMA–PNIPAM layer is visually denoted by blue stripes, while the GelMA layer is depicted as the yellow base. The GelMA layer is highlighted by staining it with curcumin in the photographic images. The actuation processes for different patterned hydrogel actuators are presented below: (A) actuation of the hydrogel with orthogonally aligned stripes on the top side. (B) Actuation of the hydrogel with diagonally aligned stripes on the top side. The side view of the actuated hydrogel is provided as an inset beside the top view image. (C) Actuation of the star-like bilayer hydrogel. All scale bars in the images are set at 1 cm. The images were captured in environments of 25 °C air and 37 °C water. The presented hydrogel actuators exhibit distinct shape deformations based on the specific patterns and orientations of GelMA–PNIPAM layers, showcasing the responsive and programmable nature of these biomimetic structures, reprinted with permission from ref. 42, copyright reserved American Chemical Society 2023.

curvature of approximately 1.3 cm^{-1} at 25 °C and 5.5 cm^{-1} at 37 °C. The corresponding scanning electron microscopy (SEM) image of the optimized bilayer hydrogel is presented in Fig. 4 (I)B, showcasing pore sizes of approximately 59 μm for the GN layer and 93 μm for the GelMA layer.

To assess the reversibility of the bilayer hydrogel, it underwent cyclic bending processes between 37 and 25 °C water for several cycles. As shown in Fig. 3c, the curvature during the bending process proved to be repeatable for five consecutive cycles. Actuation images, depicted in Fig. 4(I)D, illustrate the dynamic behavior of the bilayer hydrogel strip when immersed in 37 °C water. The strip bent toward the active layer, turning white due to the presence of PNIPAM. Upon relocation to 25 °C water, the reverse process unfolded, with the hydrogel partially recovering and reaching equilibrium after approxi-

mately 30 minutes. The versatility of the thermoresponsive GelMA–PNIPAM bilayer hydrogel actuators was demonstrated through various patterned designs, showcasing diverse actuation behaviors when immersed in 37 °C water. Fig. 4(II)A displays a hydrogel actuator with orthogonal GelMA–PNIPAM stripes, resulting in a deformed semicircular shape. In Fig. 4 (II)B, the hydrogel with diagonal stripes forms an arched shape, following the curvature of the stripes. The actuation behavior of the hydrogel with parallel stripes along the longer side of GelMA is presented in Fig. 4(II)C, revealing substantial folding and transforming the hydrogel into a helix shape. Lastly, Fig. 4(II)D showcases a bilayer hydrogel with a star-shaped pattern, where the arms of the star bend when immersed in 37 °C water, culminating in their convergence.

On a similar context, Wu *et al.* developed a novel light-responsive hydrogel is introduced, featuring a robust polypyrrole (PPy) coating on a copoly(isopropylacrylamide-4-benzoylphenyl acrylate) [P(NIPAM-ABP)] electrospun matrix.⁴³ This study draws inspiration from the hierarchical structure of whale baleen, renowned for its ultrahigh strength, to develop a novel high-strength hydrogel – the polypyrrole (PPy)-coated electrospun nanofiber-oriented copoly(*N*-isopropylacrylamide-4-benzoylphenyl acrylate) [P(NIPAM-ABP)] hydrogel, referred to as PPy-P(NIPAM-ABP) hydrogel. This innovative hydrogel, achieved through a straightforward process of coating PPy onto P(NIPAM-ABP) hydrogel nanofibers *via in situ* polymerization of pyrroles, exhibits remarkable mechanical strength and programmable light-responsive biomimetic actuation.⁴³ The key features of the PPy-P(NIPAM-ABP) hydrogel are multifaceted. Firstly, the dense PPy outer coating effectively reduces stress concentration, resulting in a significant enhancement of mechanical performance, with tensile strength escalating from 1.21 to 5.12 MPa. Secondly, the PPy coating endows the hydrogel with high-efficiency photothermal conversion, enabling exceptional light-responsive actuation. Thirdly, the porous structure of PPy-P(NIPAM-ABP) hydrogel nanofibers accelerates the speed of light-responsive actuation due to its high specific surface area. To harness these advantageous properties, the study introduces an anisotropic robust bi-hydrogel actuator, termed the PCPP bi-hydrogel, by bonding a polyethylene glycol diacrylate-cellulose nanofiber (PEGDA-CNF) composite hydrogel membrane onto the PPy-P(NIPAM-ABP) hydrogel layer through interfacial UV-polymerization of PEGDA monomers. The resulting PCPP bi-hydrogel actuator demonstrates both ultrafast and powerful light-responsive deformation, a testament to its potential applications in remotely controlled biomimetic actuators.

Noteworthy is the capability of the PCPP bi-hydrogel actuator to offer programmable complex deformations, attributed to the anisotropic structure of regularly oriented P(NIPAM-ABP) nanofibers. The actuator exhibits impressive characteristics, including powerful gripping capacity (up to 100 times its self-weight), ultrafast folding at $1285.71^{\circ} \text{ s}^{-1}$, rapid bending at $32.73^{\circ} \text{ s}^{-1}$, and swift bending recovery at $434.36^{\circ} \text{ s}^{-1}$. Furthermore, the PCPP bi-hydrogel actuator demonstrates synergistic functions, emulating the child's sit-up and the starfish's continuous crawling movement.

Importantly, the study achieved the fabrication of a starfish-mimetic actuating device utilizing the PCPP bi-hydrogel actuator. This innovative device exhibits the integration of rapid light-responsive complex actuations and swift recovery speeds, as depicted in Fig. 5. Resembling the natural starfish found in the ocean, this artificial “starfish” demonstrated remarkable capabilities, showcasing the synchronized bending of its five “legs” in under 1 second upon area laser irradiation (5.0 W power, 15.0 mm spot diameter). Equally noteworthy is its rapid return to the original shape in less than 1 second after the laser is withdrawn.

This research introduces a pioneering remotely controlled light-responsive hydrogel actuator with unparalleled force,

speed, and programmability. The findings hold significant implications for inspiring the design and fabrication of innovative soft biomimetic actuating materials and systems, particularly in the realm of remote-controlled, light-responsive devices with multifaceted capabilities.

Expanding more on this real, in recent years, there has been a notable trend in hydrogel research, where researchers are increasingly combining multiple techniques to design intricate anisotropic structures with enhanced complexity and control.⁴⁴ Moreover, the exploration of remotely controlled shape-changing hydrogels in response to various stimuli, including magnetic, electric, and light stimuli, has gained prominence. These shape-changing hydrogels offer ultrafast and precisely programmable actuations, finding applications in soft micro-actuators/robots, drug-controlled release systems, intelligent valves, and other emerging fields.⁴⁵

However, despite the advancements in intelligent hydrogels, most of them typically exhibit a singular intelligent function, limiting their biomimetic capabilities. In nature, many organisms, such as starfish, octopuses, and chameleons, possess the remarkable ability to change both color and shape.⁴⁶ These creatures can seamlessly combine these two functions when necessary, enabling them to capture prey, protect themselves, and convey signals effectively. While some researchers have successfully explored intelligent hydrogels achieving color-changing and shape-changing bi-functional synergy, integrating these two intelligent functions to create bi-functional synergistic biomimetic devices is still in its early stages. The design of such devices poses significant challenges but holds immense potential to broaden the applications of intelligent hydrogels.^{43,46,47}

To elucidate more on the drawbacks and to bridge the gap, Jiang *et al.* introduces an innovative approach by exploring an anisotropic bi-layer hydrogel. This hydrogel combines a pH-responsive rhodamine-B (RhB) functionalized fluorescent hydrogel (RFH) layer and a photothermal-responsive shape-changing poly(*N*-isopropylacrylamide) (PNIPAM) hydrogel layer infused with melanin (MPH).⁴⁸ The resulting bi-layer hydrogel exhibits fluorescent color-changing and shape-changing bi-functional synergy, offering fast and complex actuations under 808 nm irradiation of near-infrared (NIR) light. The melanin-composited temperature-responsive PNIPAM hydrogel, with its high efficiency of photothermal conversion, and the anisotropic structure of the bi-layer hydrogel contribute to its remarkable performance. Moreover, the incorporation of melanin notably improved the mechanical properties of the hydrogel, as evidenced by rheological experiments. The storage modulus (G') and loss modulus (G'') of MPH were significantly higher than those of the PNIPAM hydrogel across the entire frequency range ($0.1\text{--}100 \text{ rad s}^{-1}$) at 20°C . Moreover, rheological experiments conducted at different temperatures (20°C and 40°C) revealed temperature-dependent changes in the mechanical behavior of the MPH hydrogel. Specifically, at 40°C , both G' and G'' decreased significantly compared to those at 20°C , indicating that external temperature variations can influence the deformability and performance of the hydro-



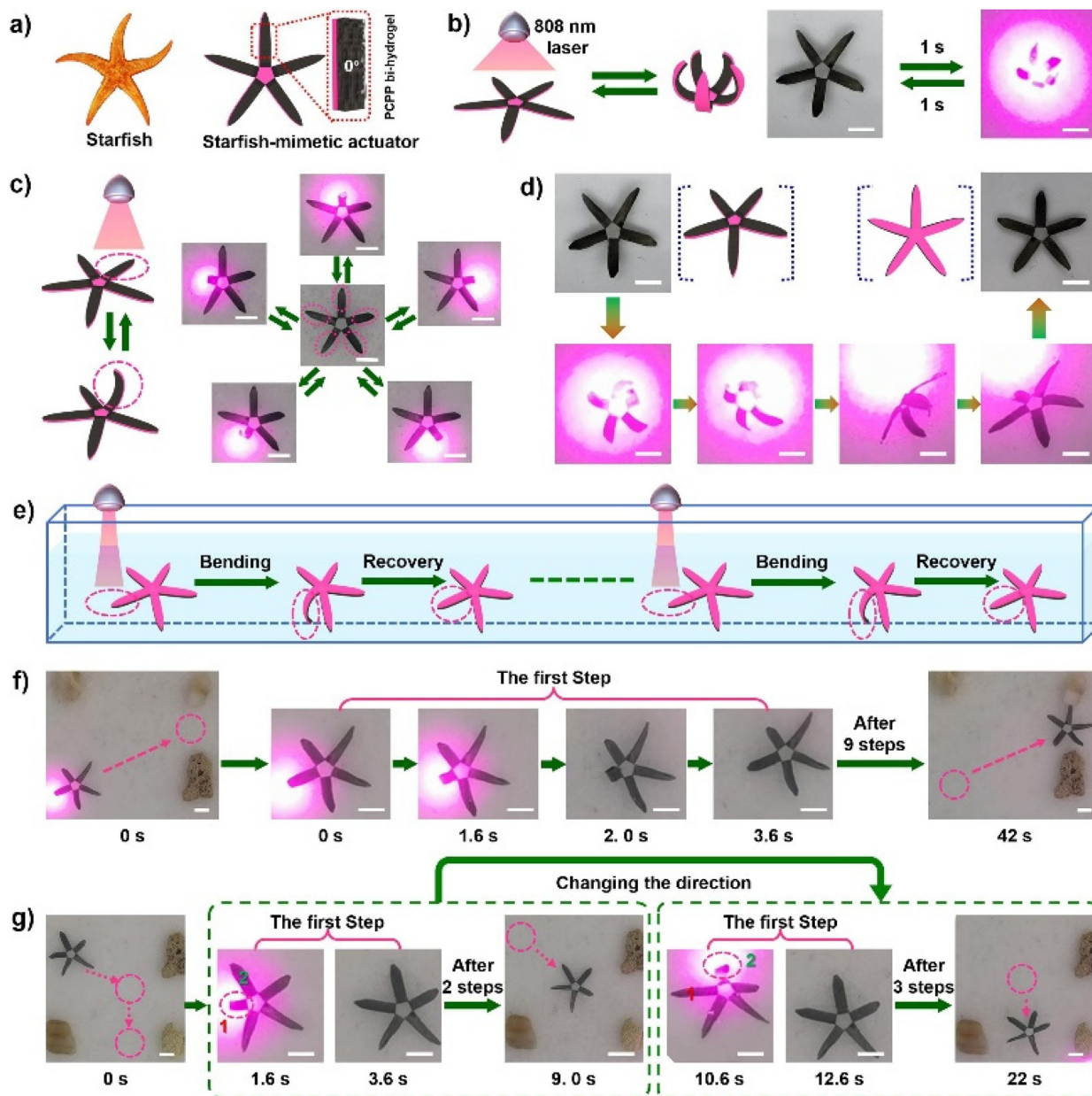


Fig. 5 The starfish-mimetic actuating device, employing the PCPP bi-hydrogel, showcases a remarkable synergy of fast light-responsive complex deformation and rapid recovery under 808 nm laser irradiation. (a) The anisotropic structure of the starfish-mimetic actuating device is depicted, highlighting the strategic arrangement that enables its unique actuation capabilities. (b) Demonstrating the efficacy of the device, Fig. 6b captures the synchronized upward bendings of the legs on the "starfish" under the influence of 5.0 W laser power and a 15.0 mm spot diameter. This emphasizes the swift and coordinated response of the hydrogel to the external stimulus. (c) One-by-one bendings of the "starfish legs" under more controlled conditions, utilizing 1.0 W of power and a 5.0 mm spot diameter. This fine-tuned actuation illustrates the precision achievable in the device's movements. (d) The turning-over process of the "starfish", employing 5.0 W of laser power and a 15.0 mm spot diameter. This process involves a dynamic reorientation of the device, facilitated by the non-uniform irradiation on the hydrogel. (e) An illustration captures the concept of the continuous crawling movement of the "starfish", providing a visual narrative of the hydrogel's ability to navigate and adapt to its environment. (f) Depicting the continuous forward crawling movement of the "starfish" under 2.5 W of laser power and a 5.0 mm spot diameter. This showcases the sustained progression of the hydrogel on a rough surface, mimicking the crawling behavior. (g) The "starfish", displaying its crawling movement in different directions. With 2.5 W of laser power and a 5.0 mm spot diameter, the hydrogel adeptly changes its course, emphasizing the device's versatility in responding to controlled stimuli. All experiments were conducted in 10 °C water, and the scale bars in all figures are 5.0 mm, providing a standardized reference for the observed behaviors of the starfish-mimetic actuating device, reprinted with permission from ref. 43, copyright reserved Elsevier 2023.



gel. Additionally, the RhB-functionalized fluorescent hydrogel layer enables rapid pH-responsive fluorescent color changes, seamlessly integrated with NIR-responsive shape changes.

Utilizing the near-infrared (NIR)-responsive complex shape change and the pH-responsive fluorescent color change of the developed bi-layer hydrogel, a series of biomimetic devices have been ingeniously designed (Fig. 6). In typical dark conditions, conventional stimuli-responsive hydrogels remain

imperceptible. However, the unique features of this bi-layer hydrogel enable the creation of a biomimetic “gripper”, capable of exhibiting fluorescent color for real-time tracking even in the dark within an aqueous solution at pH = 3 (Fig. 6a). Upon NIR light irradiation, the melanin-added poly (*N*-isopropylacrylamide) (MPH) layer experiences heating, prompting immediate bending of the bi-layer hydrogel. Consequently, the biomimetic “gripper” tightly grabs an object

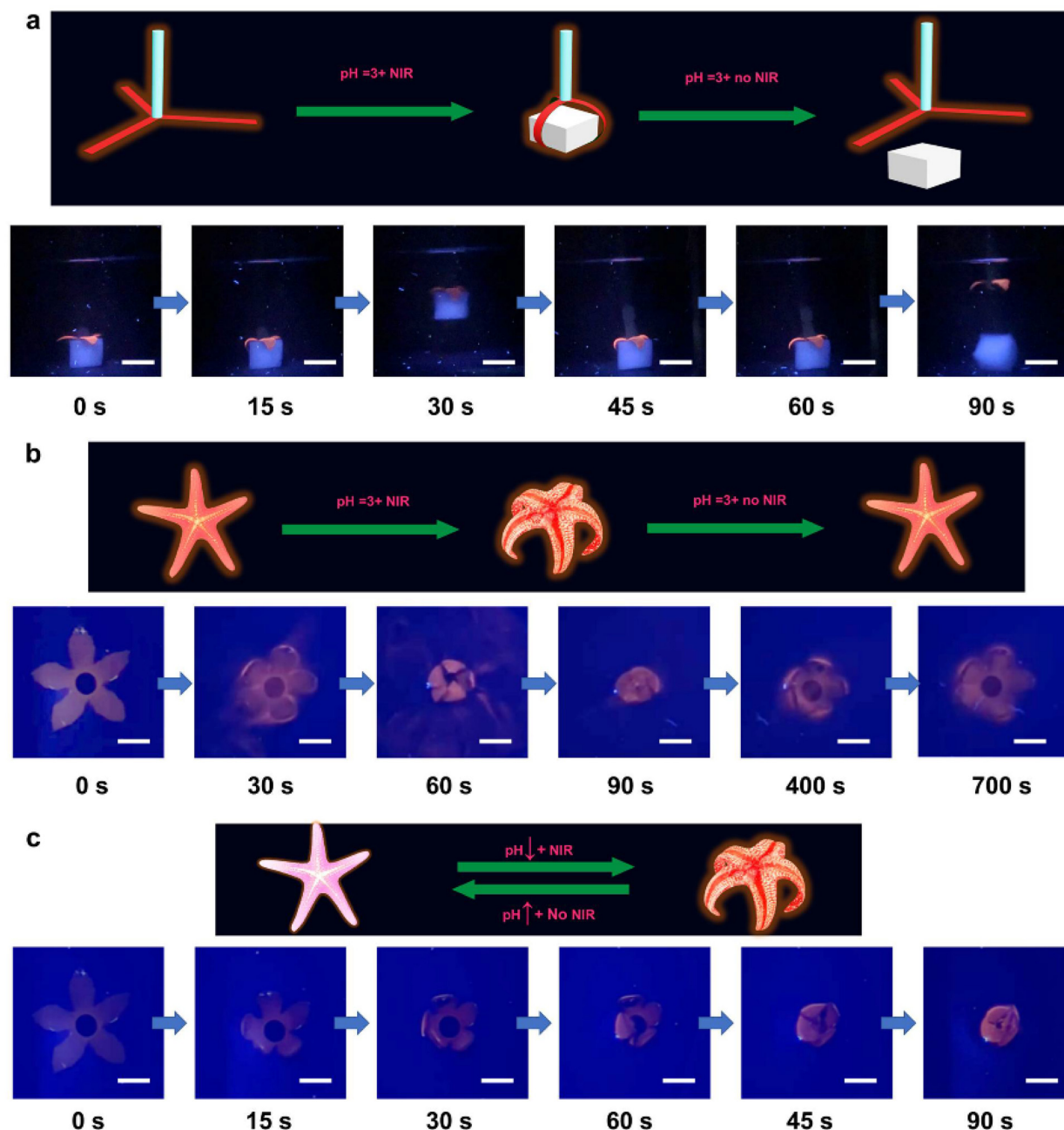


Fig. 6 The monitoring sequence of the biomimetic “gripper” in low-light conditions is detailed in (a), revealing its capacity for real-time tracking even in the absence of external illumination. In (b), a similar tracing process is presented, illustrating the movements and transformations of the biomimetic “starfish” in complete darkness. The figure (c) depicts the simultaneous color-changing and shape-changing progression of the biomimetic “starfish” under the influence of near-infrared (NIR) light and a pH shift from 10 to 3. All measurements are provided with a scale bar set at 5 mm, ensuring clarity in observing these biomimetic processes, reprinted with permission from ref. 48, copyright reserved MDPI 2023.



and releases it at a specific location without NIR light irradiation. All these gripping and releasing processes are distinctly traceable in complete darkness.

Additionally, a biomimetic “starfish” has been conceptualized based on the capabilities of this bi-layer hydrogel (Fig. 6b and c). Similar to the biomimetic “gripper”, the shape-changing actions of this biomimetic “starfish” are easily observable even in dark conditions (Fig. 6b). When immersed in an acidic solution with pH = 3, the fluorescence of the rhodamine-B (RhB) functionalized fluorescent hydrogel (RFH) layer becomes prominent. However, due to the obstructed MPH layer, the bi-layer hydrogel remains inconspicuous. Under the area irradiation of NIR light (5.2 W cm^{-2} intensity of an 808 nm laser lamp), the biomimetic “starfish” initiates movement, and the actuation behavior is meticulously recorded in the dark. As the “tentacles” of the biomimetic “starfish” gradually curve, the biomimetic entity exhibits vibrant fluorescence. Subsequent removal of the NIR light results in the bionic starfish gradually reverting to their initial state. Crucially, akin to natural starfish, this biomimetic “starfish” has the remarkable ability to simultaneously alter its color and shape (Fig. 6c). By synchronously NIR-irradiating it and changing the pH from 10 to 3, the “starfish” curls its body, revealing an increasingly intense fluorescent orange color. In essence, this biomimetic “starfish” achieves a remarkable bi-functional synergy, providing both color-changing and shape-changing capabilities.

The research provides a pathway to comprehend that this bi-layer hydrogel can be harnessed for the design of various biomimetic devices, showcasing the actuation process even in darkness for real-time tracking. The ability to mimic starfish, changing color and shape synchronously, exemplifies the high-level biomimetic capabilities of this bi-functional synergistic hydrogel actuator. This work paves the way for the development of novel biomimetic materials and systems, showcasing the potential of bi-layer hydrogels with color-changing and shape-changing bi-functional synergy in advanced biomimetic devices.

Circumscribing these developments, we find that in recent years, there has been a notable focus on advancing the fabrica-

tion of sophisticated actuators, including the emulation of microstructures resembling skeletal muscle.^{49,50} The skeletal muscle, hailed as nature’s most efficient actuator, possesses an extraordinary amalgamation of mechanical properties, featuring high strength, fatigue resistance, and precisely coordinated contraction and relaxation movements. This exceptional performance is intricately linked to the presence of highly oriented fibrous structures within the muscle tissue. The recognition of the pivotal role played by these aligned fibrous structures in natural muscles serves as a guiding principle for achieving outstanding mechanical characteristics in synthetic materials. Despite the acknowledged importance of these features, successfully replicating muscle-like aligned fibrous structures in hydrogel actuators has remained a challenging feat within the realm of scientific exploration. This scarcity highlights the formidable obstacles in reproducing the intricate architecture and mechanical prowess inherent in natural muscles when developing synthetic hydrogel systems.⁵¹

To counter the above drawback, Dr Wang’s research team introduces a groundbreaking design concept to create hydrogel actuators with a muscle-like aligned microfibrillar architecture. Overcoming the historical trade-off between shape-changing speed and mechanical properties, the researchers employ thermoinduced phase separation and mechanical alignment techniques.⁵² The approach involves engineering a thermo-responsive polymer with metal-phenolic complexes to generate macroporous thermogels through an irreversible thermal sol-gel transition. Subsequent stretching alignment at an elevated temperature produces muscle-like oriented microfibrillar architecture, resulting in anisotropic hydrogels with bundled networks. This aligned microfibrillar morphology imparts ultrafast shape-changing speed and excellent mechanical properties, marking a significant advancement in responsive hydrogel actuators (Fig. 7).

The molecular design approach adopted in this study aimed to induce the irreversibility of sol-gel thermal phase transition, ultimately yielding a thermogel with enhanced properties. This was achieved through the engineering of a thermoresponsive polymer featuring a rationally designed

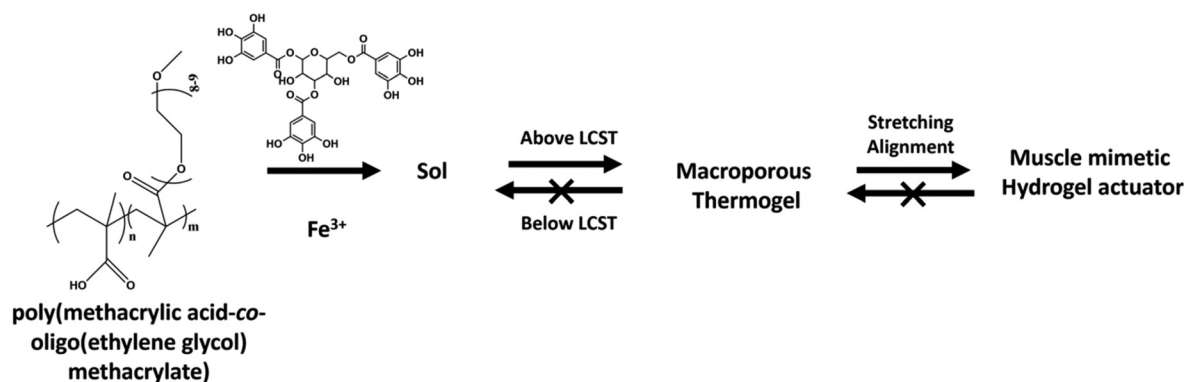


Fig. 7 Schematic representation of the design of hydrogel actuators based on a combination of thermoinduced phase separation and mechanical alignment.



supramolecular motif. Upon reaching the LCST, the thermo-responsive polymer chains underwent a phase transition and aggregated into bundle structures, leading to gelation. Subsequently, the introduction of supramolecular cross-links effectively concentrated, thereby increasing noncovalent cross-linking densities within the bundled network (Fig. 7). The dynamic nature of the engineered supramolecular motifs facilitated the exchange of cross-linkers and rearrangement of network topology at elevated temperatures, enabling the formation of anisotropic hydrogels with oriented bundle structures through mechanical stretching alignment. This anisotropic muscle-like structure was anticipated to impart improved mechanical properties and actuation performance to the final hydrogels.

Prior to designing the supramolecular motifs, poly(methacrylic acid-*co*-oligo(ethylene glycol)methacrylate) (poly(MAA-*co*-OEGMA)) was synthesized as the thermoresponsive polymer *via* one-pot free-radical polymerization. The COOH groups within this polymer were capable of forming strong noncovalent complexes with various hydrogen-bond donors and metal ions. Furthermore, the acid-ether hydrogen bonds formed between the OEGMA side chains and the PMAA allowed for the tailoring of mechanical properties and LCST over a wide range by controlling the compositions. The copolymer composition was intentionally adjusted to ensure a balance between efficient acid-ether hydrogen-bonded complex formation and good water solubility. Subsequently, tannic acid (TA), rich in pyrogallol and catechol groups, was introduced to the concentrated aqueous solutions of poly(MAA-*co*-OEGMA) to formulate a ternary complex. The incorporation of Fe³⁺ ions further enhanced the stability of the formed physical networks by forming metal-phenolic complexes with TA. This resulted in the formation of a homogeneous ternary complex solution dissolved in water, characterized by multiple hydrogen bonding and coordination complexes, thus paving the way for the development of robust anisotropic hydrogels with superior properties.

The anisotropic hydrogels exhibit remarkable mechanical strength, toughness, and fatigue resistance. The high degree of porosity allows for ultrafast reversible thermoactuation within 1 second, addressing the longstanding challenge of simultaneously enhancing shape-changing speed and mechanical properties in hydrogels. This can be further visualized from Fig. 8, whereupon heating from 25 to 50 °C, the muscle-like hydrogel demonstrates an anisotropic shrinkage of 48.2% along the stretched direction within 1 second. The hydrogel strip recovers to 91% of its original length after 2 seconds of cooling, showcasing impressive shape memory. Even after repeated cycles, the material maintains its anisotropic shrinkage capability, lifting a clamp 100 times heavier than its weight with an 18% contraction strain.

Beyond these advancements, the design concept enables the fabrication of diverse biomimetic geometries and actuation modes. Reprogramming the hydrogel's starting geometry allows for the creation of complex biomimetic shapes, including helices, spirals, and mimicking the movements of crea-

tures like birds and snakes. This research introduces new possibilities for intelligent hydrogel actuators in fields such as soft robotics, artificial muscles, and biomimetic devices.

Recently, there have been efforts to translate biological systems into actuators. In the pursuit of innovative material design, the incorporation of a lipid bilayer structure reminiscent of natural cell membranes with a hydrophobic fatty acid inner layer and a hydrophilic zwitterionic surface layer has sparked interest.⁵³ This architectural arrangement imparts cell membranes with elasticity, bendability, and fluidity. Recently, there has been a growing fascination with structures akin to hydrogel-organogel and hydrogel-elastomer hybrids.^{54–57} Unlike hydrogels, organogels and elastomers boast impressive mechanical properties, hydrophobicity, and responsiveness to organic solvents. The combination of these disparate materials can yield a binary asymmetric structure with complementary effects. However, effectively combining the hydrophilic and hydrophobic phases to create a robust interface has proven challenging, prompting numerous investigations to address this issue.

Various methods have been explored to achieve this combination. One approach involves the direct copolymerization of two immiscible phases, such as hydrophilic and hydrophobic components, with bonding occurring at the diffusion layer of the interface.⁵⁸ However, this method results in an exceptionally thin diffusion layer, leading to weak interfacial strength due to significant polarization differences between the two phases. Another common method entails pretreating the elastomer with benzophenone, activating the surface, and then inducing covalent cross-links between preshaped hydrogels and preformed elastomers.⁵⁹ Liu *et al.* introduced a double bond onto the hydrogel surface, copolymerizing it with organogel monomers to obtain hydrogel-organogel hybrids.⁶⁰ While these methods show promise, they are often limited by the type of hydrogels and involve intricate preparation processes. Advancing this field, Suo *et al.* utilized special silane coupling agents to modify both elastomer and hydrogel precursors, bonding the two layers with siloxane bonds. However, preventing the condensation of silane coupling agents, especially in wet environments, remains a challenge. Additionally, the condensation reactions throughout the entire gel and the presence of surfactants may result in uncontrollable changes in physicochemical properties.⁶¹

In this context, a novel and versatile method has been developed for fabricating hydrogel-organogel bilayer films with robust interfaces. This method involves introducing nanoparticles modified with double bonds into the immiscible solution of hydrogel and organogel precursors, strategically positioned at the interface.⁵⁸ Through a “one-pot” copolymerization process, bilayer structures are formed, with hydrogel-organogel phases intricately bonded by abundant covalent interlinks. Notably, a new zwitterionic polymer, poly(3-(1-(4-vinylbenzyl)-1*H*-imidazol-3-ium-3-yl)propane-1-sulfonate) (polyVBIPS), exhibiting strong antipolyelectrolyte salt-responsive and thermoresponsive properties, is designed for the hydrogel layer. The resultant bilayer film demonstrates rapid



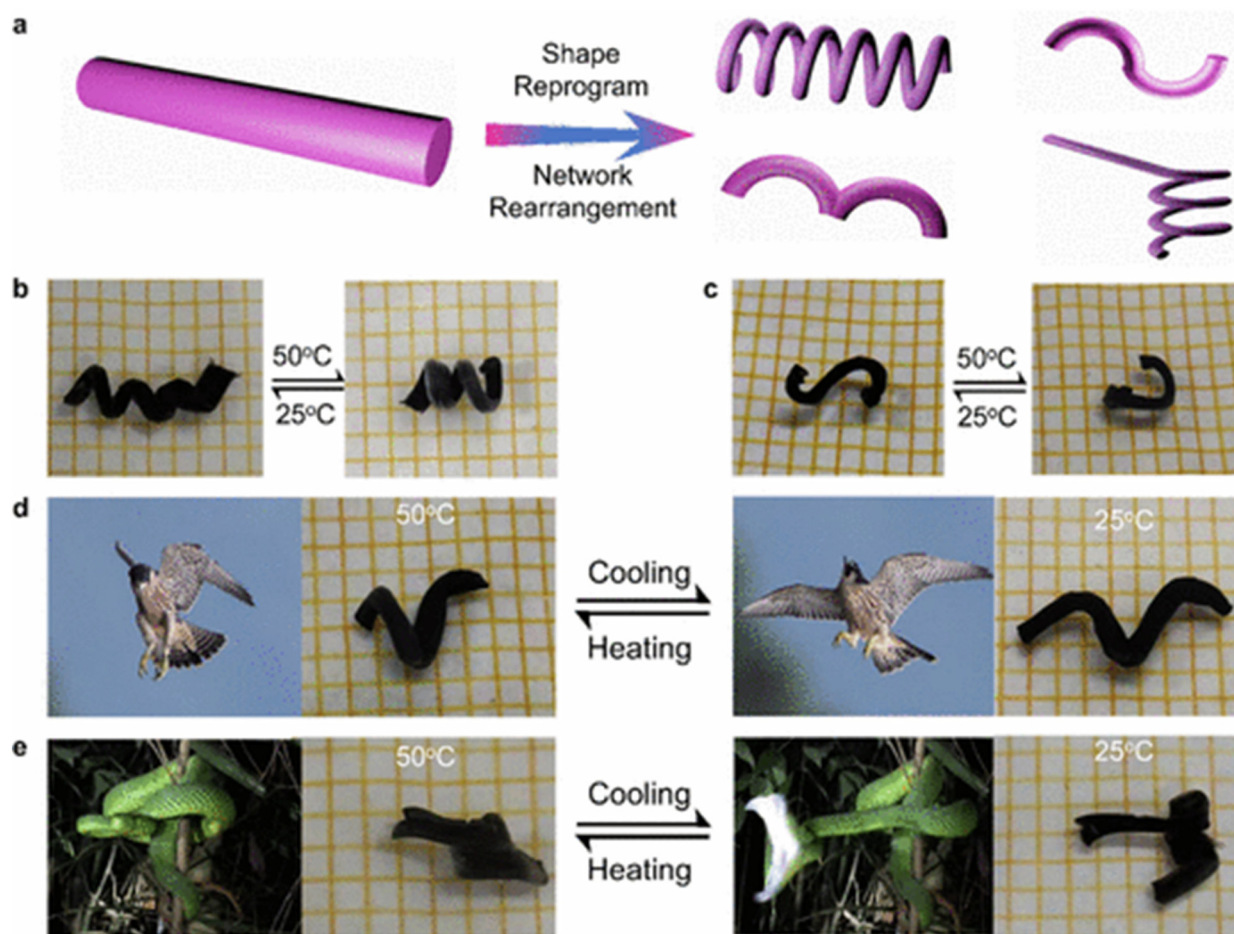


Fig. 8 Reconfigured spiral, helical, and biomimetic actuators achieved through network rearrangement. (a) The shape re-programmability of anisotropic hydrogels is schematically depicted, utilizing the dynamic nature of supramolecular cross-linked networks to facilitate network rearrangement. (b) Photographic sequence illustrating the reversible transformation between unwinding and winding, and (c) the disappearance and reappearance of the “S”-shaped spiral actuator. (d and e) By adjusting the temperature of aqueous media, reprogrammed anisotropic hydrogels successfully imitate the flying bird (d) and striking snake (e), reprinted with permission from ref. 52, copyright reserved American Chemical Society 2021.

and reversible bending behaviors attributed to the salt-/temperature-response of polyelectrolytes and the organic solvent response of the organogel. Importantly, the actuated properties, including bending degree, direction, and rate, can be precisely regulated by altering salt concentration/type, temperature, organic solvent types, and thickness.⁵⁸

The mechanical properties of the integrated hydro/organogel were thoroughly characterized due to their significant impact on actuation performance. Initially, the tensile properties of the polyVBIPS-SiO₂-polyBA bilayer film with various crosslinkers were evaluated. Pure polyVBIPS hydrogels exhibited relatively low tensile stress (0.075 MPa) and tensile strain (64.4%), while polyBA organogels displayed comparatively higher tensile stress (0.195 MPa) and tensile strain (134.5%). Upon integration of the hydrogel with the organogel, a notable enhancement in the tensile stress of the bilayer film was observed. Specifically, as the MBAA content increased from 1 wt% to 2 wt%, the tensile stress of the bilayer film significantly rose from 0.65 to 0.93 MPa, accompanied by a decrease in tensile strain from 88.5% to 50.9%. This increase in MBAA

content led to the formation of more compact networks with increased strength but concurrently restricted the mobility of polymer chains, thereby reducing toughness.⁵⁸

Additionally, a comparison of the tensile strength of polyVBIPS-SiO₂-polyBA bilayers with different MPS-SiO₂ content and a constant MBAA content of 1.5 wt% was conducted. Bilayer integration with low MPS-SiO₂ (0.05 wt%) content exhibited a tensile stress of 0.5 MPa, similar to the polyVBIPS-polyBA bilayer film, with a tensile strain of only 39.4%. Increasing the MPS-SiO₂ amount to 0.1 and 0.2 wt% resulted in a rise in tensile stress to 0.85 and 0.94 MPa, respectively, accompanied by increases in tensile strain to 59.7% and 45.9%. These findings indicate excellent tensile properties, suggesting effective integration of MPS-SiO₂ into the two pure gels. However, further increasing the MPS-SiO₂ content to 0.3 wt% led to a relatively lower tensile stress (0.84 MPa), likely due to the diminished interface strength induced by excess nanoparticles at the interface.⁵⁸

An interesting question to probe is where can apply these actuators? Oil leakage in seawater has emerged as a pressing



environmental issue, posing a severe threat to marine ecosystems. The effective recovery of oil from oil/water mixtures presents a significant challenge.^{58,62} Leveraging the exceptional seawater absorption properties of polyVBIPS and the water resistance and oxidation resistance of polyBA, a novel solution is proposed in the form of a polyVBIPS-SiO₂-polyBA bilayer pipe. This innovative design incorporates a polyVBIPS hydrogel as the inner wall and a polyBA organogel as the outer wall. The primary objective is to facilitate the purification of seawater-containing oil during transportation.

The seawater absorption capabilities of polyVBIPS and the insulation and protection provided by polyBA organogel are critical components of the proposed bilayer pipe's functionality. Fig. 9a illustrates the assessment of wettability, where a 0.53 M NaCl solution (similar to the NaCl concentration in seawater) was used. The contact angle on the hydrogel surface decreased rapidly within 400 s, indicating the quick absorption of seawater. In contrast, the organogel surface maintained a stable contact angle, demonstrating its effective insulation and protective qualities. The seamless pipe, sealed through a secondary gelation method as depicted in Fig. 8b, ensures the integrity of both inner and outer walls.⁵⁸

To mimic real oil transportation, a machine oil/seawater mixture (with equal masses of machine oil and seawater at 0.8 g each, and dyed seawater using rhodamine B) was injected into the bilayer pipe, followed by slight vibrations (Fig. 9c). After 30 minutes, upon removing the mixture from the pipe (iii of Fig. 8d), it was observed that the dyed seawater was nearly entirely absorbed by the inner wall (polyVBIPS hydrogel). Importantly, less than 1 wt% of the colorless machine oil remained in the pipe. Notably, the swelling of the polyVBIPS hydrogel (inner wall) can be reversed by treating it with a Na₂SO₄ solution, allowing for the recovery of its original state.⁵⁸ This innovative polyVBIPS-SiO₂-polyBA bilayer pipe demonstrates the promising potential for addressing oil contamination in seawater, offering an effective and sustainable solution to mitigate the impact of oil leakage on marine environments. This study presents a highly promising approach for crafting asymmetric structures of hydrogel-organogel, thereby broadening their potential applications in diverse fields, including but not limited to actuators.

While there has been considerable research focused on bilayer hydrogel actuators primarily capable of bending shape deformations, recent efforts have sought to expand the appli-

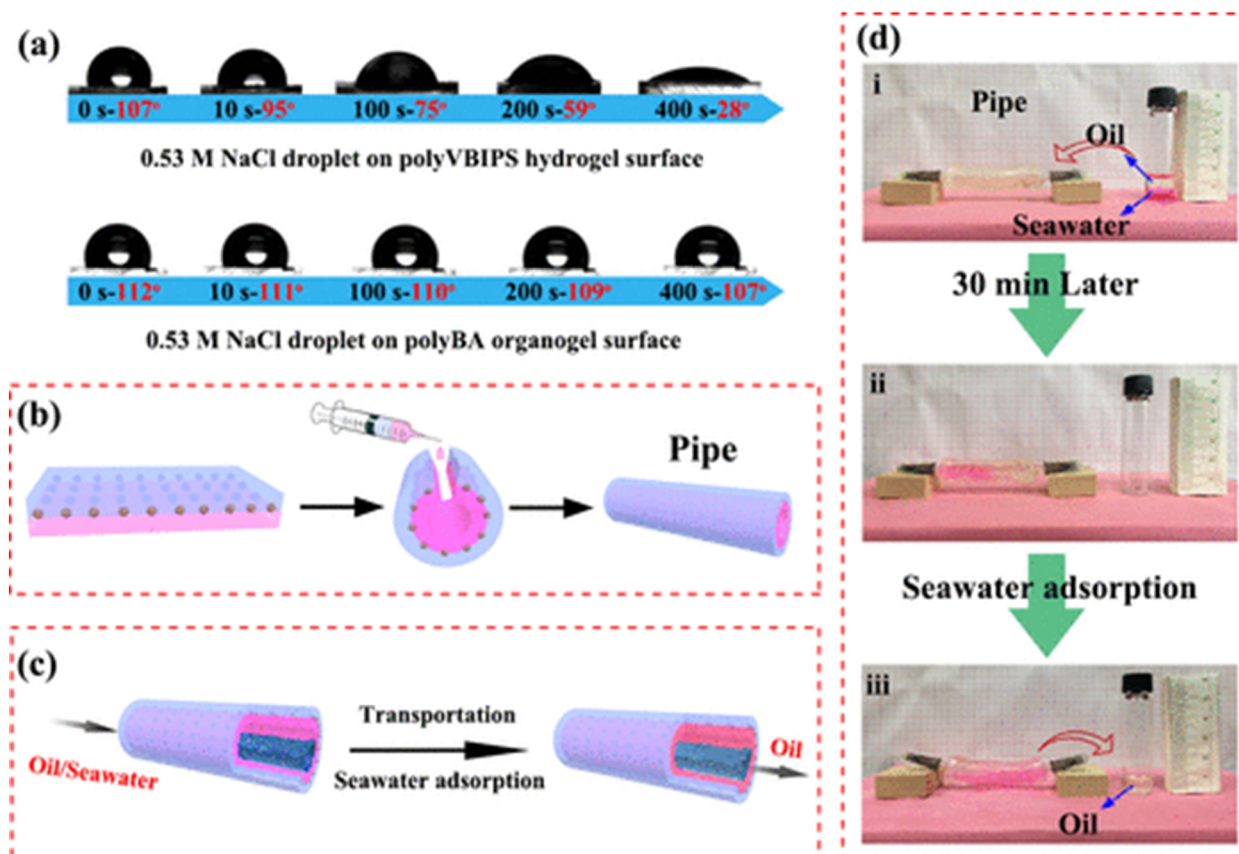


Fig. 9 Development of a bilayer pipe for the separation of oil and water using polyVBIPS-SiO₂-polyBA. (a) Monitoring the changes in contact angle values on the surfaces of polyVBIPS hydrogel and polyBA organogel. Illustration of (b) the manufacturing process of the polyVBIPS-SiO₂-polyBA bilayer pipe and (c) the oil/water separation mechanism during transportation. (d) Experimental validation showcasing the application of the polyVBIPS-SiO₂-polyBA bilayer pipe in purifying oil through the absorption of seawater, reprinted with permission from ref. 58, copyright reserved American Chemical Society 2020.



cation scope of these smart materials.⁶³ Researchers are exploring hydrogel actuators with diverse inhomogeneous structures, searching for alternative ways to enhance and develop these intelligent materials. This shift in focus indicates a growing interest in unlocking new functionalities and applications beyond the conventional bending behaviors associated with bilayer hydrogel actuators.

In this theme, gradient structures, characterized by variations in polymer chain distribution or fillers, provide avenues for intricate shape deformations. Incorporating stimuli-responsive nanoparticles or adjusting the cross-linking density through innovative techniques, such as electrophoresis or ion transfer printing, results in hydrogel actuators with programmable shaping behaviors. Gradient porous elastic hydrogels, achieved through heterobifunctional cross-linkers, showcase rapid thermoresponsive folding/unfolding performances and illustrate the versatility of gradient structures.^{64,65}

However, current reports on gradient structures necessitate intricate programming methods involving external field driving forces, resulting in a costly and complicated process for programming composite multistructures.⁶⁶ To address this challenge, Dr Fu's research group proposed an innovative, cost-effective structural programming strategy for developing a bilayer-co-gradient structure. This unique multiple asymmetric

structure involves a bilayer structure embedded within a gradient structure. Importantly, the construction method introduced by the researchers does not entail additional preparation steps, providing a simplified approach (Fig. 10I). The process involves overlaying a poly(acrylic acid-2-(dimethylamino)-ethyl methacrylate) (P(AA-DMAEMA)) layer (PAD layer), known for its robust swelling capacity, onto a poly(hydroxyethyl methacrylate-2-(dimethylamino)-ethyl methacrylate) (P(HEMA-DMAEMA)) layer (PHD layer) with a weaker swelling capacity. Through the casting method, the gradient structure of the PAD layer is self-assembled based on gradient radical polymerization, initiated by the natural gradient-dissolved oxygen, eliminating the need for complex external field driving forces. Simultaneously, the interpenetrating network layer, formed by the infiltration behavior of the PAD prepolymer solution, firmly locks the gradient structure into the bilayer structure. The resulting asymmetric bilayer structure, complemented by the embedded gradient structure, empowers the hydrogel to exhibit exceptional stimulus-responsive shape deformation and programmability based on temperature and pH. Furthermore, the researchers demonstrated the functionality of a four-armed hydrogel gripper assembled from the prepared anisotropic hydrogel, showcasing grasping behavior. This designed structure is anticipated to pave the way for inno-

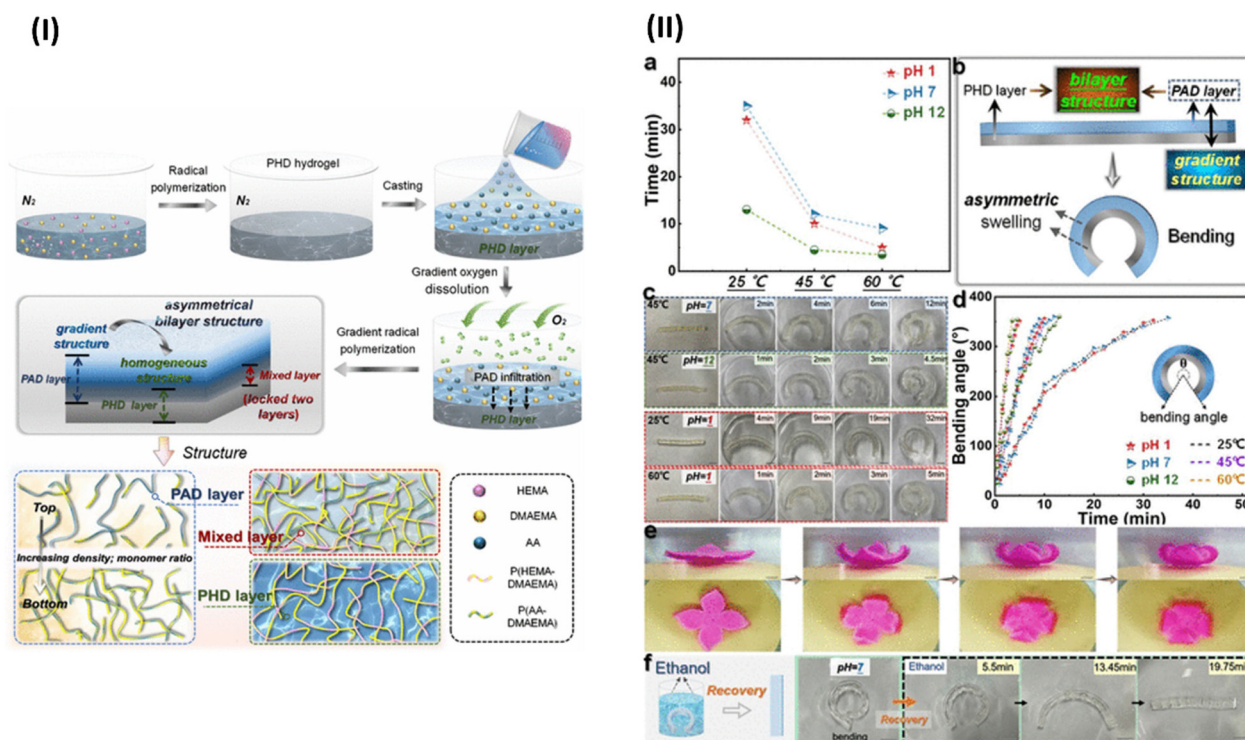


Fig. 10 (I) Schematic of preparing the PAD/PHD hydrogel (II). (a) Time taken for PAD4/PHD to achieve maximum bending angle under varying conditions (pH and temperature). (b) Illustration depicting the mechanism of deformation. (c) Visual representation of deformation behaviors of PAD4/PHD under diverse conditions. (d) Changes in bending angle over time for PAD4/PHD under different conditions (pH and temperature). (e) Observing the shape deformation of the PAD4/PHD hydrogel flower in alkaline conditions (60 °C). (f) Recovery process of PAD4/PHD, exhibiting swelling under neutral conditions in ethanol. The scale bars represent 10 mm, reprinted with permission from ref. 66, copyright reserved American Chemical Society 2023.

vative advancements in the structural programming of smart actuators.⁶⁶

To explore macroscopic deformation patterns based on anisotropic swelling, the bending behaviors of the fabricated bilayer hydrogel under diverse conditions, varying pH and temperature, were examined. The ease with which PAD4/PHD hydrogels bent into circular shapes at different temperatures under pH 1, pH 7, and pH 12 conditions was observed in Fig. 10-IIa, highlighting their superior bending capacity. The complete bending process from a regular rectangular hydrogel strip to a circular shape under pH 1, 7, and 12 conditions at 60 °C took only 5, 9, and 3.5 minutes, respectively. This exceptional bending property was attributed to the asymmetric swelling induced by the synergistic effect of the bilayer structure of the hydrogel and the embedded gradient structure of the PAD4 layer (Fig. 10-IIb). The proposed synergistic effect was corroborated by the difference in bending time between PAD4/PHD hydrogels with a single bilayer structure and those embedded with a gradient structure.⁶⁶

Interestingly, the bending speed of PAD4/PHD was fastest at pH 12 and slowest at pH 7 at the same temperature. At 45 °C, the time taken to bend into a circular shape at pH 7 was

2.7 times longer than at pH 12 (Fig. 10-IIc). These results indicated a remarkable pH sensitivity in the deformation behavior of PAD4/PHD hydrogels. This unique pH sensitivity was attributed to the asymmetric swelling behaviors being influenced by pH changes in different mediums. Additionally, the bending behavior demonstrated distinct thermosensitivity, with the bending time dramatically decreasing with increasing temperatures at the same pH. For instance, the time taken by the PAD4/PHD hydrogel to bend into a ring shape at 25 °C was almost 6.5 times longer than at 60 °C under acidic conditions.⁶⁶ This acceleration was due to the thermal motion intensifying the asymmetric swelling behavior, resulting in a faster bending speed.

Another aspect of an actuator, as we discussed earlier, is the precise control of the material. To precisely control the deformation behavior, a bending kinetic test was conducted concerning the component ratio (AA-to-DMAEMA ratio). Fig. 10-IId illustrates the quantified variation process of the PAD4/PHD hydrogel in terms of time and the corresponding bending angle. The pattern observed between bending speed and the AA-DMAEMA ratio provided an avenue for targeted hydrogel preparation and precise control of the bending

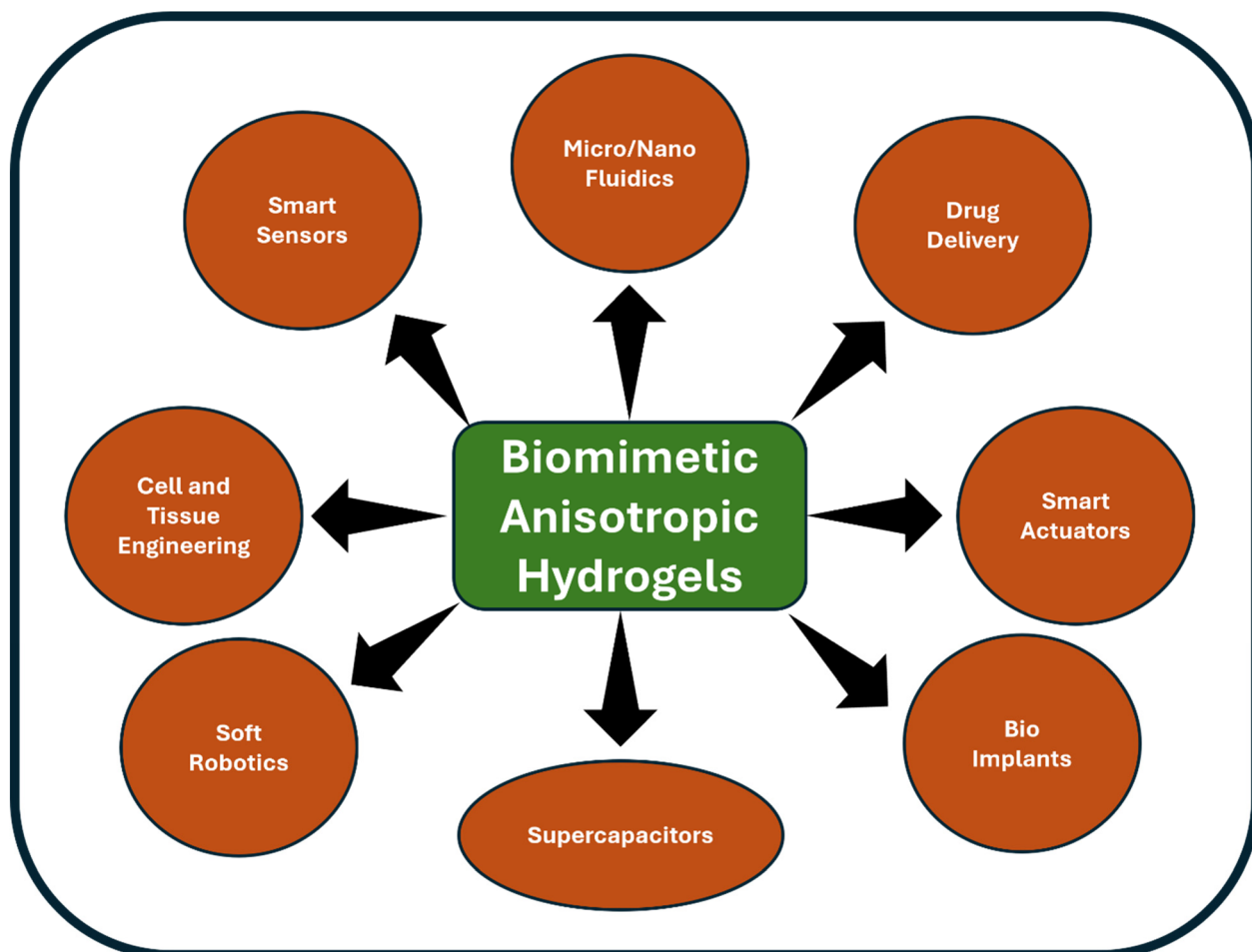
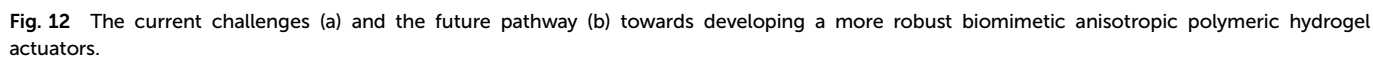


Fig. 11 Potential future directions include the areas of application for biomimetic anisotropic actuators.





Beyond these, innovative approaches like building block assembly and 3D printing further diversify anisotropic structures, promising unlimited possibilities for hydrogel actuators. Utilizing molecular switches or robust interactions, building blocks can assemble into hydrogel architectures with reversible shape transformations. The advent of 3D printing technologies allows the design and construction of stimuli-responsive hydrogels with diverse shapes, paving the way for novel developments in polymeric hydrogel actuators.

Despite these commendable accomplishments, challenges and opportunities persist in the field of hydrogel actuators (Fig. 12). Precise control over shape deformation performance remains a priority, and emerging techniques such as digital printing and 3D printing offer promising avenues for constructing well-defined anisotropic structures, enhancing the control of actuating behaviors. The evolution of multi stimuli-responsive hydrogel actuators is also essential to achieve programmed multistep deformation behaviours.¹ We also believe that the construction of hydrogel actuators with rapid responsiveness is imperative. By reducing their size to microscale or nanoscale, these actuators not only demonstrate quick responsiveness but also exhibit excellent stability compared to traditional polymeric micelles or vesicles. This attribute holds promise for applications in the biological field. Additionally, considerations regarding generated power and energy transfer efficiency between external energy sources and mechanical energy become crucial for practical applications. In addressing these challenges

and seizing the outlined opportunities, the field of hydrogel actuators is poised for continued growth and innovation.

Despite the challenges in the field of hydrogel actuators, the future holds promising developments, particularly with the rise of DNA-based actuators. While various DNA hydrogel-based structures have been explored for biosensing and biomedical applications, the focus is now shifting towards responsive DNA hydrogel-based actuating devices capable of switchable macroscopic shape deformations. Previous studies have demonstrated systems with either minor shape deformations or unidirectional deformations. However, to address the practical applications in biosensing and biomedicine, there is a critical need to design and construct DNA hydrogel-based actuating systems that not only exhibit substantial shape deformations but also showcase excellent reversibility at high speeds in response to specific stimuli.⁶³

This shift towards DNA-based actuators signifies a potential breakthrough, leveraging the unique properties of DNA, such as sequence and function programmability, precise assembly capacity, molecular recognition, and responsiveness to various stimuli. The exploration of responsive DNA hydrogels, which involve the crosslinking of DNA strands or polymer chains to form 3D networks, offers a versatile platform for achieving controlled and switchable mechanical properties.⁶⁷ These properties can be triggered by a range of external stimuli, including temperature, pH, metal ions, nucleic acid strands, biomolecules, light, or enzymes. Future advancements in DNA-based hydrogel actuators are anticipated to open new avenues for intelligent and responsive systems, contributing significantly to the fields of biosensing and biomedicine. The ability to achieve both substantial shape deformations and rapid reversibility will enhance the practical applicability of these actuators, paving the way for innovative and efficient solutions in various biomedical and technological applications.

An emerging avenue poised for significant growth in the field is the fabrication of thermoresponsive bilayer asymmetric hydrogel actuators, representing a major leap forward in the construction of biomimetic shape-morphing systems.^{68–70} Traditional techniques for creating thermoresponsive hydrogel actuators have typically involved the direct polymerization of pre-crosslinked precursors, a method that poses challenges in introducing the material gradients or structural anisotropy essential for achieving shape-morphing capabilities. However, recent scientific innovations, coupled with advanced processing tools, have paved the way for groundbreaking approaches. One such innovative approach gaining traction is 4D printing, distinguished by its technical precision, flexibility, and programmable stimuli-responsiveness. This cutting-edge method streamlines the fabrication process, allowing for the adjustment of size and layer compositions to create material gradients or structural anisotropy through 3D printing.⁵⁹ This breakthrough is expected to revolutionize the development of intelligent shape-morphing actuators, offering unprecedented control over their design and functionality.

Furthermore, the use of light as a wireless and spatially precise remote control has emerged as a powerful tool for

inducing the deformation of thermoresponsive hydrogel actuators through photothermal conversion. Recent advancements in photothermal agents, including natural plant-derived materials, have demonstrated superior light-harvesting abilities in the red and near-infrared (NIR) regions, making them valuable components for achieving photothermal conversion. Notably, nanothylakoid, a plant-derived material, mimics the photosynthetic process, showcasing promising absorption properties in the red and NIR regions. Integrating such natural plant-derived photothermal materials with 4D printing holds tremendous potential for advancing biomimetic hydrogel actuators to new heights of sophistication and efficiency.⁶⁷

In the coming years, we anticipate the emergence of novel fabrication routes that will contribute significantly to the development of smart structures. One promising avenue is the exploration of patterned structures, drawing inspiration from nature's intricate designs. Certain plant structures, for example, exhibit fascinating shape transitions upon dehydration, and replicating such patterns could open new possibilities for hydrogel actuators. Photolithography stands out as a powerful tool in this regard, enabling the creation of hydrogel sheets with chemically distinct regions. This approach facilitates preprogrammed large 3D shape transitions, mimicking the intricate behaviors observed in nature. Introducing visible patterns, such as those achieved through UV-reduction of graphene oxide, adds another layer of complexity, providing hydrogel actuators with multiresponsive 3D complex deformations. This expansion of capabilities enhances the versatility and potential applications of hydrogel actuators.

Another avenue of exploration involves oriented structures, taking inspiration from natural phenomena like pinecones. The fabrication of oriented structures often entails aligning nanofillers within hydrogel matrices through shear force or magnetic fields. Utilizing viscoelastic solutions containing cellulose nanofibrils or unilamellar titanate nanosheets results in hydrogel actuators with asymmetric swelling behaviors. This asymmetry enables the generation of complex 3D morphologies and unidirectional procession, mimicking the behavior of natural systems. Directional freezing is another technique contributing to the creation of oriented void channels within hydrogels, further enhancing their anisotropic structure. These advancements in fabrication techniques are poised to open up new frontiers in the design and functionality of smart structures, providing innovative solutions for diverse applications.

Addressing the aforementioned challenges in the field of hydrogel actuators necessitates collaborative efforts from interdisciplinary experts with diverse backgrounds. The multifaceted nature of these challenges requires insights from researchers with expertise in polymer science, materials engineering, robotics, biology, and other relevant fields. By fostering a collaborative environment, researchers can pool their knowledge and skills to overcome the existing hurdles and drive innovations in the development of biomimetic anisotropic polymeric hydrogel actuators. The interdisciplinary approach is crucial for gaining a comprehensive understanding of the



complex interactions and requirements involved in designing advanced hydrogel actuators. For instance, experts in materials science can contribute insights into developing hydrogels with enhanced mechanical properties, while robotics specialists can offer perspectives on the practical applications and integration of these actuators into functional systems. Similarly, input from biologists may be essential for achieving a closer mimicry of natural systems, ensuring that hydrogel actuators not only perform effectively but also align with biological principles.

As researchers from different disciplines collaborate, there is a strong belief that the field of biomimetic anisotropic polymeric hydrogel actuators will witness vigorous development in the near future. This collaborative synergy is expected to lead to breakthroughs in the design, fabrication, and application of hydrogel actuators, unlocking new possibilities for smart and adaptive materials in various fields.

Conflicts of interest

All individuals listed as authors qualify as authors and have approved the submitted version. Their work is original and is not under consideration by any other journal. They have permission to reproduce any previously published material.

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