

Hydrogel-Based Artificial Muscles: Overview and Recent Progress

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Artificial muscles are promising as an intelligent material that can replace conventional power systems to reproduce the motion of a living organism. Among various building materials, hydrogels have great advantages as artificial muscles, such as responsiveness to a wide range of stimuli, large volume deformation, and sensitivity. However, conventional hydrogel actuators that generate only isotropic volume change in response to an external stimulus cannot be considered as artificial muscles because complex deformations are not possible. Instead, programmed complex deformations originated from a rationally designed anisotropic structure are desired in artificial muscles. Herein, recent approaches for constructing stimuli-responsive hydrogels with an anisotropic structure, thereby enabling a directional complex motion to mimic a muscle are reviewed. First, stimuli-responsive shape-deforming hydrogels as a main building matrix are categorized according to stimulating external signals. The representative methods for modulating the isotropic structure of a hydrogel into various anisotropic structures, such as multilayer structure, linearly oriented structure, and patterned structure are discussed. Finally, the recent strategies to achieve muscle-like motion of hydrogels by combining stimuli responsiveness and anisotropic structures for translation from elementary contraction and expansion to programmed deformations, such as multidirectional bending, directionally amplified deformation, and compositive programmed motion, are covered.

1. Introduction


Conventional power systems, such as combustion engines, are widely used in various devices; however, reproducing the motion of a living organism has several limitations, such as difficulties in miniaturization and compelled continuous operations.^[1] An artificial muscle refers to a device that can reproduce the motion of a living organism by reversible contraction and expansion of materials in response to a specific stimuli, which is similar to muscles

responding to a neural signal.^[2] Artificial muscles have been developed using various materials, such as polymer fiber,^[3,4] elastomer,^[5,6] and shape-memory alloy.^[7,8] Depending on the materials that form the artificial muscle, desired characteristics, such as a large output force and fast response speed, can be achieved. However, there are several disadvantages as well, such as inadequate scale of deformation and poor biocompatibility.

Hydrogels are 3D polymer chain networks that contain a large amount of water and possess distinct advantages and potential over other material candidates for artificial muscles. Abundant water enables the exchange of solute between the hydrogel network and external solvent and diffusion in the network.^[9] In addition, based on well-studied manufacturing methods, properties, and modification strategies, hydrogels have tunable physicochemical characteristics. Generally, they have tissue-like softness and good biocompatibility, that make them a promising material in diverse biomedical applications.^[10] As an actuator, responsiveness to various stimuli, such as temperature, pH, light, electric

field, and specific chemical and molecules, can be imparted to them^[11,12] for generating large volume deformations.^[2] In addition, hydrogels can sufficiently endure large deformations because of their flexibility. Furthermore, most stimuli-responsive hydrogels have responsiveness for ambient stimuli with considerable sensitivity, which is an important feature as intelligent materials to compose artificial muscles.^[12,13] However, hydrogels usually exhibit a homogeneous isotropic structure,^[14] thus, only simple isotropic contraction and expansion are possible.^[15]

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Furthermore, the actuation characteristics of most actuators strongly depend on the internal structure of materials; thus, rational structure designing is required for advanced applications.^[16] The correlation between structure and actuation characteristics is frequently observed in nature. For example, skeletal muscles exhibit very efficient anisotropic contraction because of their highly aligned anisotropic structure.^[17] Similarly, anisotropic structures have many advantages, such as complex deformation and efficiency to hydrogel actuators. Therefore, structure modulation has become a crucial step for developing hydrogel-based artificial muscles.

To design a hydrogel-based artificial muscle that reversibly produces programmed complex motions, both stimuli responsiveness and anisotropic structure are necessary. Accordingly, we will review shape-deforming hydrogels as stimuli-responsive building materials for artificial muscles; their structure-modulation methods to prepare anisotropic structures; and hydrogel-based artificial muscles facilitating reversible, complex deformations and motions. The history and previous developments described by several reports will be reviewed,^[2,15,16,18] such as example of stimuli-responsive functional components and their operation mechanism, conventional methods for anisotropic hydrogel manufacturing, and hydrogel-based artificial muscle generating typical complex motion. Furthermore, we will focus more on the recent reports based on novel approaches for building a muscle-like hydrogel.

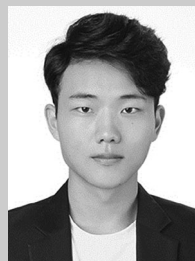
The scope of this Review is hydrogel-based systems that generate reversible complex mechanical motion and work. Because some hydrogel actuators only generate simple expansion and contraction motion or irreversible collapse of the network and those are not included in our focus. By using the terminology “artificial muscle,” we intended to provide an intuitive grasp for the scope of this Review.

2. Stimuli-Responsive Shape-Deforming Hydrogels

Stimuli-responsive shape-deforming hydrogels have been extensively applied in various fields, such as controlled drug-delivery systems,^[12] flow control in microfluidic devices,^[19,20] and sensors.^[21] Generally, their shape-deforming property provides the fundamental contraction and expansion motions. The mechanisms and representative examples of the major category of stimuli-responsive shape-deforming hydrogels are briefly described in the following sections (Figure 1).

2.1. Temperature-Responsive Hydrogels

Generally, temperature-responsive hydrogels are classified into lower critical solution temperature (LCST) hydrogel and upper critical solution temperature (UCST) hydrogel (Figure 1A). LCST hydrogels swell or shrink at temperatures below or above the LCST. In contrast, UCST hydrogels, which is a relatively rare category, shrink or swell at temperatures below or above the UCST. This temperature responsiveness is mainly because of the temperature-dependent change in the number of hydrogen bonds formed between the polymer chains or between the solvent and polymer chains. Hydrogen bonding can be dissociated



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or formed by temperature increase or decrease, and the change in the number of hydrogel bonds affects the extent of molecular interactions between the polymer chains or between the solvent and polymers.^[2,18]

In LCST hydrogels, the hydrogen bonds are formed mainly between the polymer and water at a lower temperature. When the temperature increases above the LCST, the dissociation of hydrogen bonding between hydrophilic polymer chain and water occurs, which causes the dehydration of polymer chains and the enhancement of hydrophobic interaction between the polymer chains. Therefore, the hydrogel shrinks at temperatures above the LCST. For example, poly(*N*-isopropylacrylamide) (PNIPAM)-based hydrogels, which are the most extensively studied temperature-responsive hydrogel, swells under the LCST (25–32 °C) because of the intense hydrogen bonding between the water molecule and amide group of the polymer network. Above the LCST, the dissociation of the hydrogen bond causes weakening of water imbibing; thus, hydrophobic interaction between the isopropyl groups of the polymer network becomes dominant and the hydrogel shrinks. A significant advantage of an LCST hydrogel is that the LCST can be adjusted easily by altering the ratio between the hydrophilic and hydrophobic groups. For example, the LCST can be increased by adding more hydrophilic monomers.^[18] Among the LCST hydrogels, poly(*N,N*-diethylacrylamide) and poly(ethylene oxide)-poly(propylene oxide) block copolymer-based hydrogels are widely used in the biomedical field because their LCSTs are close to body temperature.^[12]

In contrast, in a UCST hydrogel, hydrogen bonds are mainly formed between the polymers. In this case, the dissociation of

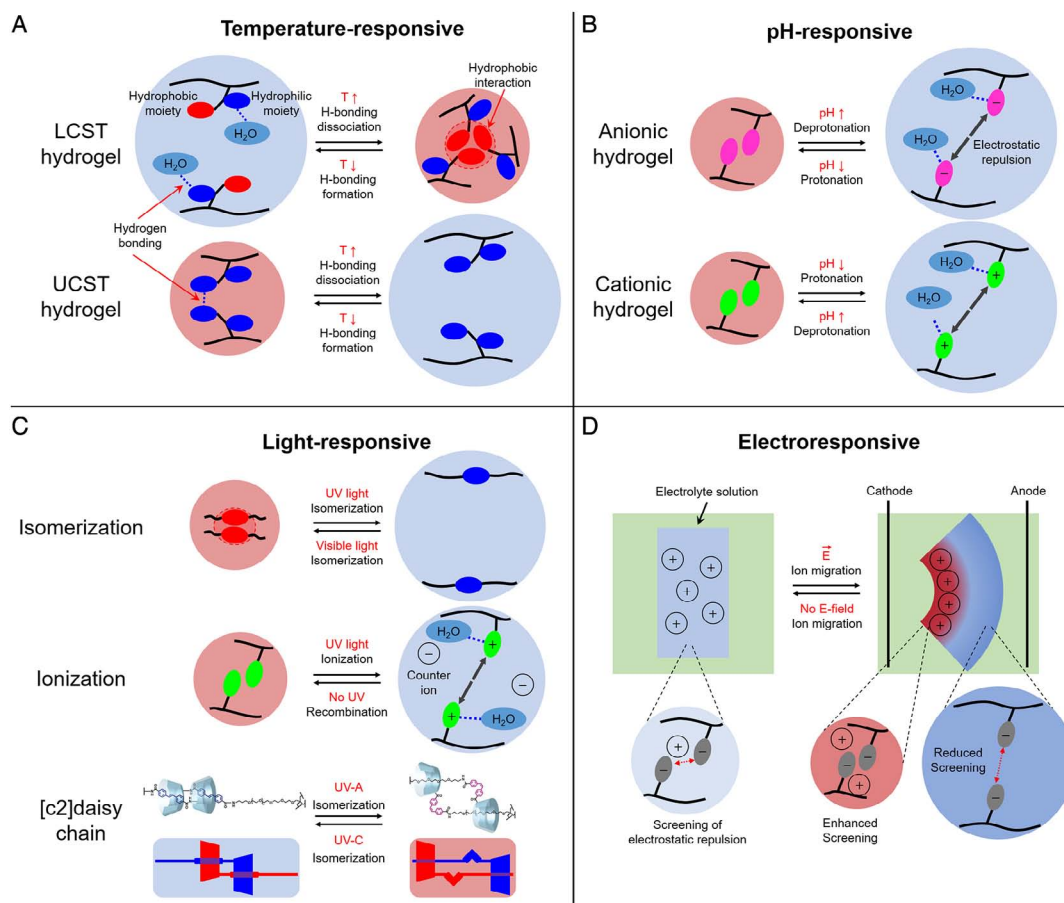


Figure 1. Major mechanisms of A) temperature-responsive, B) pH-responsive, C) light-responsive, and D) electroresponsive shape-deforming hydrogels. C) Adapted with permission.^[22] Copyright 2018, American Chemical Society.

hydrogen bonding at the elevated temperature causes weakening of polymer–polymer interaction; thus, the hydrogel swells. For example, as poly(*N*-acryloyl glycinamide) has the primary amide group at the end of the side chain and one amide group in the middle of the side chains form hydrogen bonding between the polymer chains under the UCST, the hydrogel shrinks. Above the UCST, the hydrogel swells with the dissociation of the hydrogen bond and the decrement of the cross-linking density.

2.2. pH-Responsive Hydrogels

pH-responsive hydrogels contain ionizable functional groups and are classified into anionic and cationic hydrogels depending on the ionic form of the functional group (Figure 1B). Anionic and cationic hydrogels swell at the high and low pH values, respectively. Their swelling occurs with the increment in the osmotic pressure caused by the ionization of the functional group, which causes an increment in the polymer chain hydrophilicity and generation of counter ions.^[18] Simultaneously, electrostatic repulsion between the charged ionic groups also contribute to swelling.^[11] In an anionic/cationic hydrogel, the neutral ionizable functional groups are ionized by deprotonation/protonation at a pH value above/below their pKa. The

hydrogels can shrink with the neutralization of ionized functional groups by adjusting the pH value of the solvent. Poly(acrylic acid)-based hydrogels are a well-known type of anionic hydrogel that have carboxyl groups as the ionizable functional group. Above or around pH 4.25, pKa of an acrylic acid, the carboxyl group is deprotonated, and it becomes negatively charged, thereby resulting in swelling of the hydrogel. Representative types of cationic hydrogel are chitosan-based hydrogels that have primary amine groups as the ionizable functional group. Below pH 6.5, the pKa of a chitosan, the amine group is protonated, and it becomes positively charged, thereby resulting in swelling of the hydrogel.

2.3. Light-Responsive Hydrogels

A conventional method of preparing light-responsive hydrogels using the light stimuli to indirectly induce the deformation of hydrogels that are prepared based on the temperature- or pH-sensitive hydrogel as the mother matrix. For example, light irradiation can trigger the deformation of temperature-sensitive hydrogels that contains photothermal materials, such as gold nanoparticle (AuNP)^[23] and chlorophyllin.^[24] For pH-responsive hydrogels that contains light-responsive ionizable functional

groups, irradiation induces the release of proton or hydroxyl ions from light-responsive ionizable groups, resulting in pH alteration and subsequent deformation of the pH-sensitive hydrogel.^[25]

Light can be also used as a direct stimulus for shape-deformation of a hydrogel. In this case, light responsiveness is generally achieved by adding photoreactive materials into the polymer network. Under light irradiation, photoreactive moiety undergoes reversible changes, such as isomerization and ionization (Figure 1C). Those changes cause variation in the properties of the hydrogel that causes shape deformation. For example, azobenzene is a representative photoreactive functional group that isomerizes in responses to light irradiation.^[26] The hydrophobic interaction between the *trans*-azobenzene groups tethered on the main polymer chains causes shrinkage the hydrogel. Under ultraviolet (UV) light irradiation, isomerization to *cis*-azobenzene occurs and hydrogel swells because of the dissociation of the hydrophobic azobenzene assembly.^[27] The reverse isomerization reaction from *cis*- to *trans*-form and subsequent contraction of the hydrogel can be induced by visible light irradiation. A triphenylmethane leuco derivative is another well-known material with ionizable characteristic under UV irradiation.^[28] When they are incorporated into hydrogels, the reversible ionization causes reversible shape deformation, which is similar to that in pH-responsive hydrogels.

Recently, a molecular muscle, which is a category of shape-deforming system, has gained a significant attention because of their highly controlled actuation mechanism.^[29,30] For example, a interlocked chains based on inclusion complex, called [c2]daisy chain,^[31,32] consisting of α -cyclodextrin (α CD), *trans*-stilbene (Sti), and polyethylene glycol (PEG), have the ability to exhibit muscle-like unidirectional contraction and expansion.^[22] As UV light induces reversible isomerization of *trans*-Sti and *cis*-Sti, the formation and dissociation of α CD-*trans*-Sti can be controlled.^[33] Under UV-A irradiation, the α CD separated from *cis*-Sti glides along the PEG chain connected to *cis*-Sti, so that the length of the chain is shortened. By the irradiation of UV-C, the inclusion complex is reformed due to the recovered *trans*-Sti, leading to lengthened chains. Therefore, light-responsive unidirectional contraction/expansion of interlocked chains can be achieved. By incorporating molecular muscles into a polymer network of a hydrogel, their microscopic motion becomes upsized to the macroscopic level, and stimuli-responsive shape-deforming hydrogels with beneficial characteristics are obtained. The hydrogel actuator prepared by incorporating a [c2]daisy chain overcame the previous limitations, such as slow speed of the motion and difficulty in scale-up to the macroscopic level.^[26] Unlike the general actuation mechanism of hydrogel actuators, which depends on the absorption and desorption of water, this system is characterized by the contraction and expansion of the hydrogel because of the mechanical deformation of the [c2]daisy chain. Therefore, the hydrogel actuator cross-linked with a [c2]daisy chain retains the shape-deforming ability even in a dry state.

2.4. Electroresponsive Hydrogels

Similar to indirect deformation triggering of light, electric stimuli can induce change in temperature-, pH-, or redox-responsive deformation of hydrogels. For example, an electric field can

induce temperature increment and resultant deformation of a temperature-responsive hydrogel via Joule heating or dielectric heating. In addition, the generation of hydroxyl ion and the resultant increment of the pH value through electrochemical reaction around cathode can stimulate the deformation of pH-responsive hydrogels.^[34] In other cases, the deformation of a redox-responsive hydrogel can be triggered electrochemically.^[35]

The mechanism of direct electroresponsiveness of a hydrogel is relatively complicated as compared with other responsiveness. Generally, polyelectrolytes are adopted because they have immobile charged groups on the polymer network and mobile counter ions that respond to the electric field.^[36] When the electric field is applied to the hydrogel, charged groups are attracted toward the oppositely charged electrode, and the resulting stress is exerted on the polymer network.^[37] Simultaneously, mobile counterions are dragged toward the other electrode. There are several explanations for the effects of this dragging. One is that ions migrate out with dragging water molecules, which is called as electro-osmosis. Another is that ions are trapped in the hydrogel rather than escaping, and a concentration gradient is formed (Figure 1D). For example, in the hydrogel with negatively charged chains, applying electric potential induces the accumulation of positive ions in hydrogel close to the cathode. This ion-enriched side shrinks because of the enhancement of screening of electrostatic repulsion between the negatively charged groups on the polymer network. In contrast, ion-depleted side swells because of relatively higher electrostatic repulsion between polymer chains. Shape deformations are caused by the combination of several mechanisms including those described earlier.^[38]

Most electrically induced deformations are intrinsically anisotropic because of the vector characteristic of an electric field, which is different from the isotropic deformations derived from temperature- and pH-responsive hydrogels described earlier. The deformation mechanism and behavior depend on the characteristics of the hydrogel, and on various operating conditions, such as contact of the electrode with the hydrogel and presence of electrolytes in the solvent.^[36–38] To fabricate electroresponsive hydrogels, several natural and synthetic polyelectrolytes, such as hyaluronic acid, chondroitin sulfate, partially hydrolyzed polyacrylamide (PAM), and poly(2-acrylamido-2-methyl propane sulfonic acid), are used.^[15,36]

2.5. Hydrogels with Responsiveness for Other Stimuli

Based on the widely studied characteristics and manufacturing methods, numerous types of stimuli can be used to stimulate the shape deforming of hydrogels. Responsiveness to a wide range of stimuli, in addition to that described earlier, pressure,^[39,40] redox change,^[41,42] specific ion,^[43,44] and several biorelevant molecules including glucose,^[45,46] antigen,^[47] and enzyme,^[48–50] is one of the greatest advantages of hydrogel actuators.

3. Anisotropic Hydrogels

The microscopic structures of most hydrogels are isotropic because they are generally fabricated by the polymerization of monomers, which are homogeneously dispersed in an aqueous

media.^[14] Therefore, the macroscopic contraction and expansion of the stimuli-responsive hydrogels that are derived from the degree of hydration are also isotropic. To facilitate a complex anisotropic motion in an artificial muscle, which is difficult to realize with an isotropic hydrogel, the anisotropic microscopic and/or macroscopic structure of hydrogels are in demand. In particular, biological applications significantly demand anisotropic hydrogels because most biological tissues have anisotropic hierarchical structures and resultant functionalities. Accordingly, methods used for manufacturing anisotropic hydrogels have been widely studied. In the following section, the structure

directing strategies used for preparing anisotropic hydrogels and their applications are described (Figure 2).

3.1. Multilayer Structure

Multilayer-structured hydrogels are composed of macroscopic multiple layers that exhibit different characteristics, such as mechanical and chemical properties, and play specialized roles (Figure 2A). Their multifunctionality with different properties that depend on the layers can facilitate various applications, such as controlled drug delivery^[52–54] and biomimetic scaffold.^[55,56]

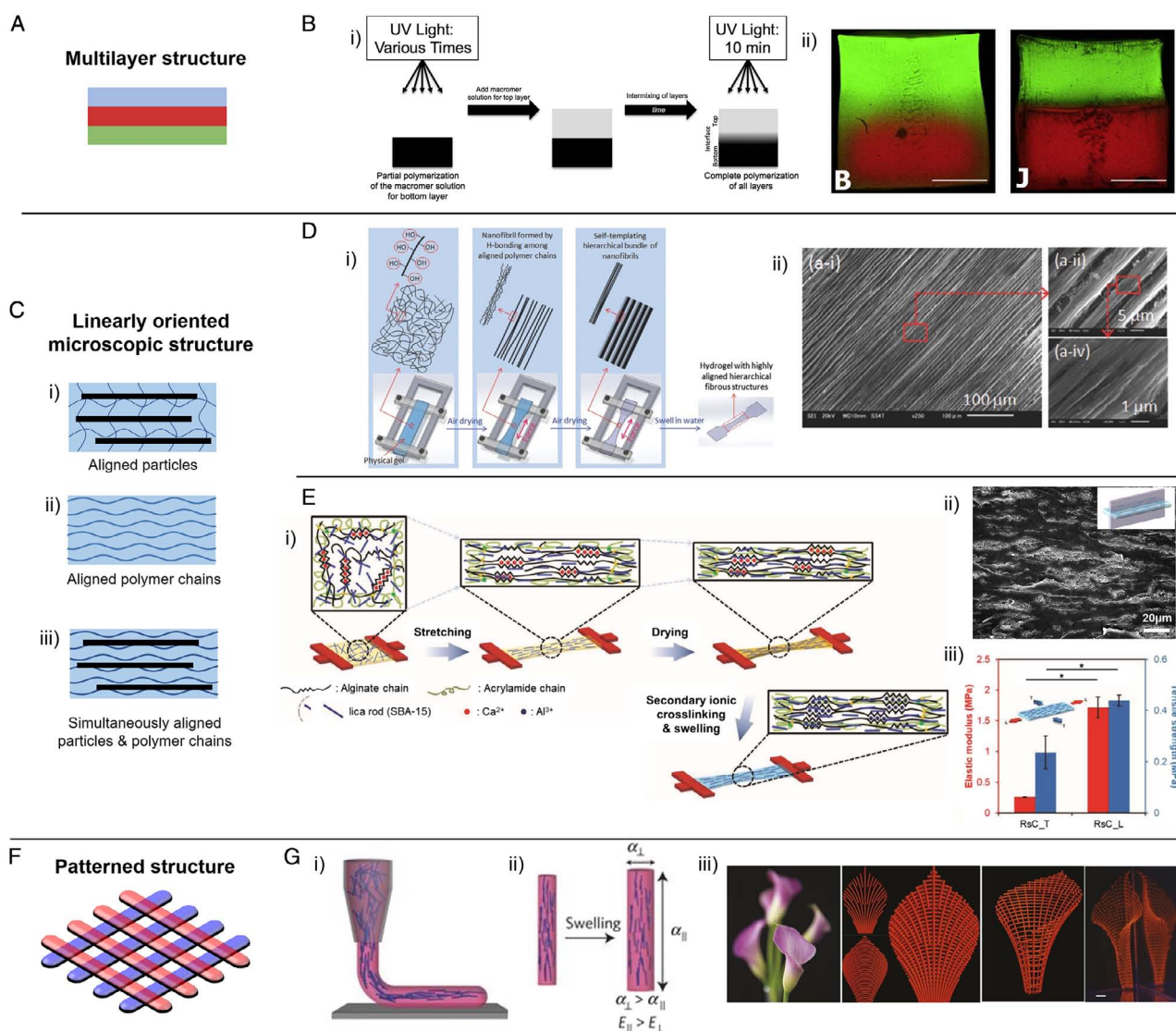


Figure 2. Various anisotropic structures in hydrogel and fabrication methods. A) Multilayer structure. B) i) Manufacturing process of a multilayer hydrogel and ii) interface thickness change depending on degree of prepolymerization of bottom layer. C) Linearly oriented microscopic structure. D) i) DCC method used to produce a hierarchically oriented polymer network structure and ii) scanning electron microscope (SEM) images of a DCC-applied alginate hydrogel. E) i) Remodeling and subsequent drying and cross-linking (RsDC) process to prepare Alg/PAM hydrogel embedded with aligned inorganic filler, ii) SEM images of longitudinal cross section of resultant hydrogel, and iii) its anisotropic mechanical property. F) Patterned structure. G) i) Process of 4D printing of hydrogel, ii) swelling behavior of printed hydrogel filament), and iii) conversion of a 3D surface to print path, simulated curvature, and printed curvature. B) Adapted with permission.^[56] Copyright 2015, Elsevier Ltd. D) Adapted with permission.^[81] Copyright 2018, Wiley-VCH. E) Adapted with permission.^[69] Copyright 2019, Wiley-VCH. G) Adapted with permission.^[51] Copyright 2016, Springer Nature.

The most general approach to prepare a multilayer hydrogel is the repetition of precursor solution casting and gelation.^[56,57] The precursor solution contains monomer or polymer chains, and cross-linking agents such as cross-linker, initiator, and accelerator. After the solution spread flatways, gelation is conducted with certain cues such as UV irradiation to obtain hydrogel layer (Figure 2B-i). Additional layers can be synthesized by repeating aforementioned process. Because the poured solution permeates into the network of lower layer, a superimposed network is formed around the interface and synthesized layers are well attached. The thickness of the superimposed network can be controlled by adjusting the gelation starting time of the upper layer or degree of gelation of the lower layer. The longer the time between the solution pouring and the gelation starting time, the more time the solution can penetrate into the lower layer, so the superimposed layer becomes thicker with delaying the start of gelation. If the lower layer is not fully gelled, the added solution is mixed with the precursor solution of the lower layer that has not yet been gelled (Figure 2B-ii).^[57] The gelation of the partially gelled lower layer and the interface is completed with the gelation of the upper layer. Therefore, low degree of gelation of the lower layer leads to a thicker superimposed network. The resultant multilayer structured hydrogels are composed of parallel flat layers.

Radially multilayered hydrogel with core-shell onion-like structure can be also obtained in two opposite ways, outward and inward.^[58] The outward way refers to omnidirectional growth of the layers on a core.^[59] To allow omnidirectional growth, the dip-coating method is used, whereas the monomers and cross-linking agents are separately contained in the substrate and solution. For example, a permeable core is first immersed into the initiator solution to load the initiator on the surface of the core. A shell grows on the core after the subsequent immersion of the core into a solution that contains the monomers and cross-linking agents. By repeating the immersion process into the initiator and monomer/cross-linking agent solutions, outer shells can be sequentially formed. The inward way requires a bulk precursor gel as the starting macroscopic hydrogel, which can be shrunk and cross-linked further.^[60] When the precursor gel is dipped into a solution that can induce cross-linking and shrinking, the surface of the precursor gel becomes a compartmented outer layer. Subsequent repetitive dipping causes the formation of inner layers while the solution permeates through the outer layers. For example, a non-neutralized alcohol gel can be neutralized and shrunk in the NaOH solution. When the non-neutralized alcohol gel is immersed into the NaOH solution and taken out before being fully neutralized, the neutralized outer domain become a shell because the region shrinks and is separated from core by shrinking. If the precursor gel with the first layer undergoes the same procedure, the outmost region of the non-neutralized core becomes the second layer.

3.2. Linearly Oriented Microscopic Structure

The multilayer structure described earlier forms a macroscopically anisotropic hydrogel. In contrast, the microscopically anisotropic structure hydrogel can be directed via linear orientation of the internal polymer chain network and/or incorporated particle (Figure 2C). The linearly oriented structure can exhibit

macroscopically anisotropic properties, which can be used for amplifying specific properties of the hydrogel in the oriented direction. For example, the mechanical properties of an isotropic hydrogel can be highly amplified in a certain direction by modulating the structure of the hydrogel into the linearly oriented structure.^[61] A linearly oriented structure can facilitate several valuable applications, such as anisotropic cell culture scaffold^[62,63] and anisotropic mass transport.^[64,65]

Hydrogels with linearly oriented structures are mostly manufactured by inducing a temporarily aligned structure and subsequently fixing the aligned structure.^[14] The temporary structure can be induced by directly aligning a polymer network (Figure 2C-i) or aligning the particles after incorporating the particles that have a high aspect ratio (Figure 2C-ii) or simultaneous alignment of both (Figure 2C-iii). Directional stimuli, such as mechanical forces or vector fields, are used for aligning. Mechanical forces include shear,^[62,66–68] tensile,^[61,69,70] and compressive force;^[71] and vector fields include electric field,^[72–74] magnetic field,^[75–78] and ion flux.^[79] To induce alignment using a vector field, the incorporated particle or polymer chain should have corresponding responsiveness to the field. Fixation of induced temporary structures can be conducted by polymerization or cross-linking of components. In addition to the sequential alignment and fixation, the oriented structured hydrogels can be manufactured by making hydrogel on an oriented template. In particular, 3D templates, such as directionally grown crystal^[80,81] and oriented scaffold,^[65] could be used to prepare the oriented structured hydrogels. A typical method is ice crystal templating,^[81] which is conducted by growing directional ice crystal in a precursor solution. The ice crystal can be easily eliminated after polymerization; thus, this method is commonly used for obtaining oriented void channels.

Among the aforementioned methods, the method of mechanical force-induced polymer network alignment followed by fixation is an effective and straightforward approach to manufacture a linearly oriented structured hydrogel.^[69–71,82] The advantage of this method is its applicability on a preformed hydrogel to transform the microscopic structure. However, this method has an intrinsic limitation that its application is limited to only those gels that have high toughness. A recent approach, called drying in confined condition (DCC), extended the applicability of this method to brittle physical hydrogels (Figure 2D-i).^[82] Instead of directly exerting a mechanical force, polymer network alignment was induced by drying with fixing both ends in the longitudinal direction. Shrinkage occurs during drying in the direction perpendicular to the longitudinal direction; however, the contraction in the longitudinal direction is inhibited, and the resultant force is exerted in the longitudinal direction. The contraction decreases the distance between the polymer chains, and the exerted force aligns the polymer network. The highly aligned and closely packed chains allow dense cross-linking between polymer chains via hydrogen bonding. The resultant structure can be maintained even after reswelling because of dense cross-linking. When the hydrogel was dried and reswelled without fixing the two ends, the resultant structure was homogeneous, whereas the DCC process produced an extremely aligned hierarchical structure (Figure 2D-ii).

In a very recent study, the drying-induced polymer network rearrangement was combined with a typical mechanical

force-induced polymer network alignment method called remodeling and subsequent cross-linking (RsC) to increase the degree of anisotropy (Figure 2E-i).^[70] The RsC process was previously introduced for transforming the preformed alginate/polyacrylamide (Alg/PAM) double network hydrogel into a linearly aligned hydrogel.^[61] The Alg/PAM hydrogel is stretched unidirectionally to align and closely pack the polymer chains. The Alg/PAM hydrogel is highly stretchable; thus, sufficiently high degree of alignment can be achieved by exerting high degree of stretching. The induced temporary anisotropic structure is fixed by immersing the hydrogel into a multivalent cationic solution that cross-links the alginate chains. Then, the anisotropic hydrogel is obtained through the formation of dense secondary cross-linking. When drying step is additionally added after RsC process (called RsDC process) of Alg/PAM hydrogel incorporated with high-aspect-ratio mesoporous silica microrods, unidirectional stretching along with the subsequent drying highly align both polymer network and incorporated silica rod (Figure 2E-ii).^[70] The resulting anisotropic composite hydrogel fixed by subsequent cross-linking exhibit high structural (Figure 2E-ii) and mechanical (Figure 2E-iii) anisotropy with greatly enhanced modulus, strength, and toughness, which is reminiscent of the hierarchically linear collagen structure of tendon and ligament.

3.3. Patterned Structure

Patterned structure refers to a rationally designed complex structure using elaborate techniques, such as photolithography and 3D printing. In a patterned structure, multilayer, linearly oriented, or other anisotropic structures are included or sometimes coexist. For example, a multilayer structure can be obtained by UV irradiation with a stripe-patterned photomask,^[83] and a typical grid structure along with a combination of multiple oriented layers can be produced by 3D printing (Figure 2F). The significance of a patterned structure is precisely locating and assembling the desired polymer network and structure. Patterned structures are preferred in applications that require sophisticated structures, such as artificial organs, because of their exquisiteness in making the desired structure and consequential functionalities.^[84]

In patterned hydrogel fabrication, one promising strategy is templating. For example, well-ordered linearly aligned micro-channel structure could be obtained by fabricating hydrogel on a silicon wafer with corresponding aligned pattern.^[85] In next, photolithography is generally used to achieve selective photopolymerization, and occasionally used to achieve local photodegradation. For photopolymerization, the patterns can be created in two ways. First, by preparing a bulk gel containing the precursor of the gel to be patterned and then inducing photopolymerization to form an additional patterned network.^[86] Then, the interpenetrating pattern network is formed. Second, by preparing a mold-like patterned gel and filling residual interspace by another gel.^[87] In this case, the superposed domain becomes larger as the start of later polymerization is delayed. For photodegradation, a photodegradable bulk hydrogel is first prepared and then patterned by photolithography.^[88] 3D hydrogel printing is mostly performed by the direct ink writing (DIW) technique.^[89] DIW is a relatively simple 3D printing technique, which is conducted by

ink extrusion and hardening. The ink should be a fluid that can be extruded through a nozzle and should be able to rapidly harden to retain the structure after deposition. Therefore, acrylate polymers are preferred that can be free-radical polymerized under UV irradiation or heating.^[89]

Hydrogel 3D printing is a suitable technique for manufacturing complex shape; however, there is a lack of viscosity, polymerization speed, and cross-linking density to create an overhanging or hollow architecture.^[89] To achieve such architecture, postdeformation approach is required. One representative approach called 4D printing is shown in Figure 2G.^[51] The main component of the ink is acrylamide monomer, which becomes a swellable polymer matrix by photopolymerization and cellulose fibril that has high aspect ratio. During extrusion, nanofibrils are aligned in longitudinal direction by shear force (Figure 2G-i) After printing completes, photopolymerization of acrylamide monomer is started by UV irradiation. A printed hydrogel has anisotropic stiffness and causes higher swelling ratio in transverse direction than longitudinal direction because of the aligned fibrils (Figure 2G-ii). By making a double-layer-structured hydrogel using the oriented layer and swell it, the complex 3D structure can be achieved, which cannot be produced by a single 3D-printing process. In this study, a model is developed to predict the resultant curvature from the print path and to convert a target 3D surface to the print path. Based on the model, a rationally designed nature inspired 3D structure can be produced by controlling parameters that include local curvature and dimension of the structure (Figure 2G-iii).

4. Hydrogel-Based Artificial Muscles

To date, the two major points to be considered when manufacturing hydrogel-based artificial muscles are discussed. First one is stimuli-responsive polymer components, such as certain polymers and functional materials, which determine responsiveness, extent and speed of motion, and available operation conditions of the artificial muscle. The other one is the anisotropic structure of the hydrogel that could convert isotropic contraction and expansion to the desired complex and efficient motion such as bending motion, directionally amplified motion, and composite programmed motion. In this section, strategy to prepare hydrogel-based artificial muscles that generate those programmed motion with several examples is discussed. The structure dominantly determines the motion; thus, relationship between the type of motion and category of anisotropic structure will be provided.

4.1. Bending Motion

In artificial muscles, the most general type of motion is bending motion that generate substantial displacement from tiny contraction or expansion.^[14] As arm bends and straightens along with the contraction of biceps and triceps muscle of arm, respectively, artificial muscles composed of multiple layers that have different responsiveness and can generate bending motion toward relatively shrinking layer (Figure 3A). There are several categories of a system according to the type of incorporated layers. A unimorph system is most simple one that contains a responsive layer

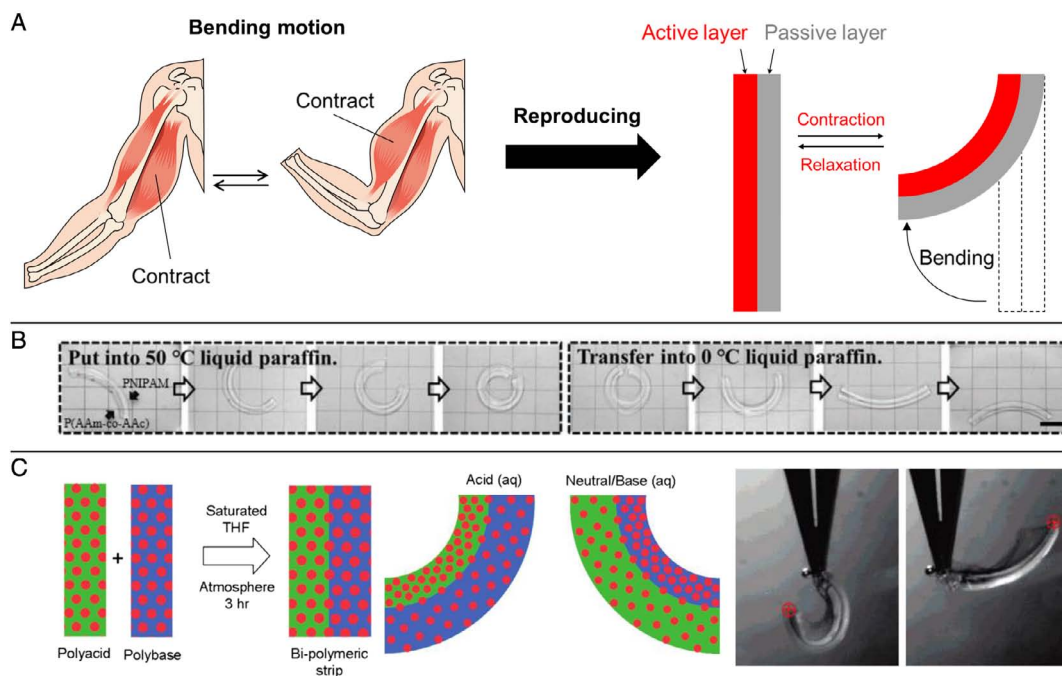


Figure 3. Hydrogel-based artificial muscle for bending motion. A) Bending and straightening motions of arm and reproduction of the motions in hydrogel-based artificial muscles. B) Example of bending motion of hydrogel-based artificial muscle with unimorph bilayer structure. C) Example of bending motion of hydrogel-based artificial muscle with bimorph bilayer structure. B) Adapted with permission.^[90] Copyright 2019, Wiley-VCH. C) Adapted with permission.^[92] Copyright 2007, American Chemical Society.

and nonresponsive layer, called active and passive layers, respectively. If the active layer contracts, bending motion occurs toward active layer, and conversely, if active layer expand, bending motion occurs toward passive layer (Figure 3B).^[90] When an active layer, which can contract and expand in response to multiple stimuli, is adopted, bending motion can occur in both directions.^[91] For example, when an active layer that contracts in acidic condition and expand in high-salt concentration is prepared with passive layer, the artificial muscle will be bent toward active layer in acidic condition and toward the passive layer in a concentrated salt solution. Although the active layer generates stimuli-responsive deformation, the passive layer contributes to motion by elastic energy. During bending, passive layer store elastic energy that exert in the direction opposite to bending direction but weaker than the deformation energy of active layer. During recovery, reverse deformation energy of active layer and stored elastic energy of the passive layer exert in identical direction. A bimorph system consists of two active layers that inversely respond to specific stimuli. As one active layer contract, the other active layer expands, creating efficient bending motion toward the contracting active layer. For example, an artificial muscle that consist of anionic and cationic pH-responsive hydrogel layers can be bent toward anionic layer in acidic condition and toward cationic layer in neutral and basic conditions (Figure 3C).^[92] In contrast to a unimorph system, the deformation energy of both layers always exert in same direction due to inverse responsiveness of two layers. Consequently, the motion is relatively efficient than unimorph.

4.2. Directionally Amplified Deformation

Unidirectional contraction and expansion of muscle fiber can be reproduced by amplifying the deformation of artificial muscle in a specific direction (Figure 4A). For example, a hydrogel manufactured by the formation of the PNIPAM network within void channels of the PEG scaffold displayed greater deformation in the direction perpendicular to the direction of alignment than the direction of alignment. (Figure 4B).^[93] Directionally amplified deformation can be induced by generating anisotropic dimension or anisotropic stiffness. When artificial muscles prepared in an anisotropic dimension (filaments or beams) deform isotropically, a larger amount of deformation occurs in the longitudinal direction; however, the aspect ratio does not change. For example, if a hydrogel filament, which has a 10:1 aspect ratio, expands isotropically; the length increases ten times more than the thickness. For artificial muscles with anisotropic stiffness, the following principle works. The stiffness indicates the degree of resistance against deformation; thus, contraction and expansion of stimuli-responsive hydrogels are hindered by the stiffness of the hydrogel. In most linearly oriented structured hydrogel, stiffness is higher in oriented direction than in the direction perpendicular to the oriented direction.^[14] As a result, more deformation occurs in the direction perpendicular to the oriented direction and less deformation occurs in the oriented direction. The principles of increasing stiffness are different in several oriented structures manufactured by oriented fibril,^[51] void channel,^[93] plates,^[73,75,94] and so on; however, the aforementioned principle can be applied generally.

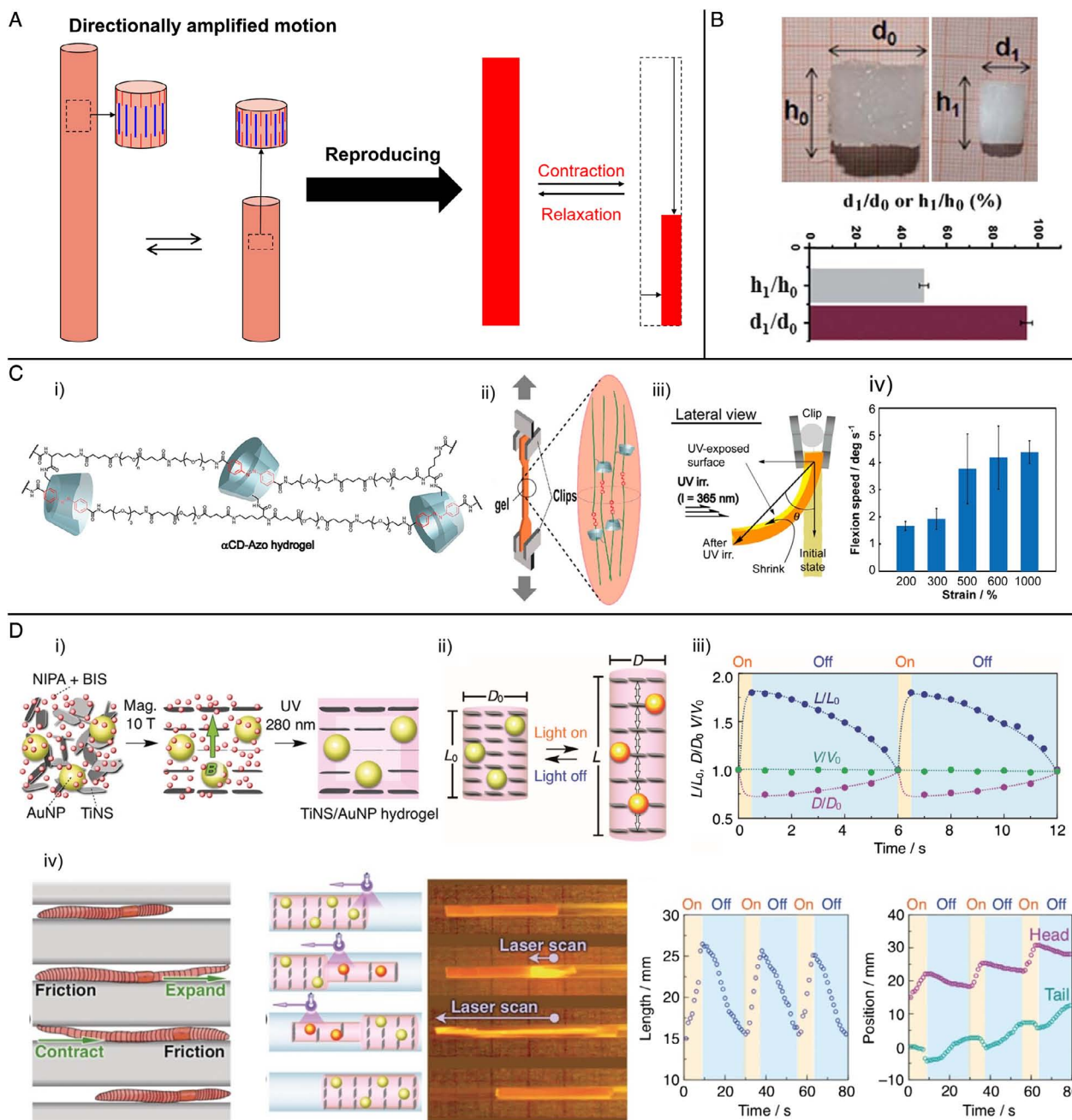


Figure 4. Hydrogel-based artificial muscle for directionally amplified motion. A) Contraction and relaxation of muscle fiber and reproduction of the motion in hydrogel-based artificial muscles. B) Example of directionally amplified motion of hydrogel-based artificial muscle. C) i) Molecular structure of a hydrogel cross-linked with [2]rotaxane, ii) alignment of molecular muscles and polymer chains induced by mechanical stretching, iii) an experimental setup to measure the actuation performance, and iv) flexion speed change depending on prestretched strain. D) i) Components and fabrication process of hydrogel-based artificial muscle containing TiNSs and AuNPs in temperature-responsive polymer network, ii) actuation of the artificial muscle in response to light irradiation, iii) deformation rate depending on time, and iv) the earthworm-like peristaltic crawling motion of the AuNPs containing artificial muscle in a capillary. B) Adapted with permission.^[93] Copyright 2012, The Royal Society of Chemistry. C) Adapted with permission.^[95] Copyright 2018, American Chemical Society. D) Adapted with permission.^[23] Copyright 2018, Wiley-VCH.

Although the principle that anisotropic stiffness inducing anisotropic deformation is generally valid, there are exceptional examples obeying other principles according to the characteristics of polymer network or incorporated particle. Following two examples show artificial muscles which deform more in stiffer

direction. It is also worth noting that their unique actuation mechanisms allow them to be operated in open air. In an example shown in Figure 4C, deformation is amplified in the oriented direction by the alignment of the polymer network. A molecular muscle called [2]rotaxane similar to [c2]daisy chain shown in

Figure 1C can result higher toughness when incorporated into a hydrogel network.^[95] The molecular muscle is composed of α CD, Azo, and PEG chain (Figure 4C-i) and can generate unidirectional contraction and expansion in respond to UV light irradiation. When a hydrogel cross-linked with [2]rotaxane is stretched, molecular muscles and polymer chains are aligned in stretched direction (Figure 4C-ii). The hydrogel has adequate flexibility; thus, components can be aligned in high degree with stretching over ten times. After fixing aligned structure by drying, the actuation performance is measured, as shown in Figure 4C-iii. The contraction of the exposed layer causes bending motion because the UV light is irradiated on one face. Furthermore, microscopic unidirectional contraction occurs in the longitudinal direction of the molecular muscle; thus, the flexion speed increases proportionally with the degree of orientation (Figure 4C-iv). This example showed intuitive but rare anisotropic actuation that brings about efficient deformation in an oriented direction by aligning the polymer network. The motion of the artificial muscle originated from the motion of the molecular muscle instead of migration of the solvent; thus, operation in air conditions is possible.

The example shown in Figure 4D also shows exceptional system and results. A hydrogel-based artificial muscle is prepared from a mixture of temperature-responsive PNIPAM network, oriented titanate nanosheet (TiNS) by magnetic field, and AuNP via subsequent photopolymerization (Figure 4D-i).^[23] Due to the photothermal effect of AuNPs, response of the hydrogel can be stimulated by near-infrared (NIR) light irradiation. When temperature increases above LCST of PNIPAM network, polymer network becomes dehydrated and release huge amount of water molecules that enhance the electrostatic repulsion between TiNSs.^[96] As a result, the hydrogel lengthens in the direction perpendicular to the TiNS plane (Figure 4D-ii). When the light is turned off, the hydrogel shortens with the rehydration of the polymer network and decrease in electrostatic repulsion between TiNSs. The actuation mechanism does not depend on absorption and desorption of solvent; thus, the artificial muscle can be operated in open air, and the deformation is isovolumetric and rapid (Figure 4D-iii). A noteworthy point is the use of photothermal effect of AuNPs that enables rapid facile, and even remote heating of the hydrogel, resulting in the rapid actuation of hydrogel (Figure 4D-iii). The photothermal heating-induced lengthening speed of PNIPAM/TiNS system became almost double compared with alternative immersion into hot and cold water baths. This high response speed may allow a practical manipulation of temperature-responsive hydrogel-based artificial muscles. As AuNPs have a good dispersity in water and compatible with various hydrogel systems, earlier approach possibly can be adopted to improve the response speed of temperature-responsive hydrogel-based artificial muscle. In addition, the deformation is an isovolumetric change; thus, the diameter of the hydrogel changes inversely with the change in length. Once scanning NIR laser over the hydrogel located in a capillary, earthworm-like peristaltic crawling motion is produced (Figure 4D-iv).

4.3. Compositive Programmed Motion

To perform various works, living organisms handle their body parts compositively by actuate corresponding muscles.

For example, to pick up an object, fingers should be bent proper degree and direction. In the same manner, to achieve compositive programmed motion in artificial muscles, elementary, and complex deformations, such as aforementioned bending and directionally amplified motion, should be combined appropriately (Figure 5A). For example, various compositive motions can be produced by assembling hydrogel blocks which can generate bending motion by immersing in a poor solvent.^[97] Because of the anisotropic structure of hydrogel with parallelly ordered lamella networks, the contraction of polymer network causes bending motion of the hydrogel. In addition, the self-healing property of the hydrogel makes the assembly of the hydrogel blocks possible. Consequently, compositive motion of the integrated hydrogel is achieved.

Using patterning techniques, stimuli-responsive building materials and anisotropic structures can precisely be arranged in designed manner, and delicate compositive programmed motions can be produced. Alignment hydrogel fibers that compose active layer make possible the amplification of deformation in specific direction and control the direction of bending motion. Patterning techniques allow the precise alignment of hydrogel fiber resulting in corresponding bending direction control. Bending in multiple directions is also possible by combining multiple layers that possess responsiveness to different stimuli and aligned different directions.^[83,86] Among the patterning techniques, 3D printing is one of the promising method (Figure 5B-i).^[83,86,98] By printing aligned active layers in orthogonally crossed pattern, a four-arm gripper was manufactured (Figure 5B-ii).^[98]

Precise arrangement of active and passive networks in designed pattern makes the reversible transition between 2D sheet and various complex 3D architectures possible.^[86,87,99,101] For example, reversible folding and unfolding between the planar figure of a cube or tetrahedron and corresponding polyhedron was achieved by printing planar figure using polymer inks with different responsiveness (Figure 5C). Actuation of selectively deposited active layer causes local bending/recovery and consequential folding/unfolding of the planar figure to corresponding polyhedron. In another example, reversible transition between a sheet and surface with periodic curvature was achieved by patterning active and passive regions periodically. Local internal stress is generated from the mismatch of deformation, and the sheet is buckled to relieve the stress. A wide range of deformation and resultant geometry can be programmed by applying various responsive polymer, pattern, and external conditions. As an another example, a micropatterned hydrogel fabricated using a micropatterned template also can be adopted for achieving a complex 3D motion (Figure 5D).^[85,102,103] Photolithography allows tailored patterns from linearly aligned microchannel to complex combination of them. Molded pattern and corresponding compositive motions result in biomimetic complicated morphology and inside out flipping motion.

Aforementioned patterning techniques make precise control of structure possible, but sometimes quite intricate equipment and process are required. In fact, along with elaborate production, the convenience of manufacturing also should be considered. A novel approach demonstrated the reversible printing of bending sites (Figure 5E-i).^[100] Ion deposition, called ionoprinting, generate local metal ion-rich site on the

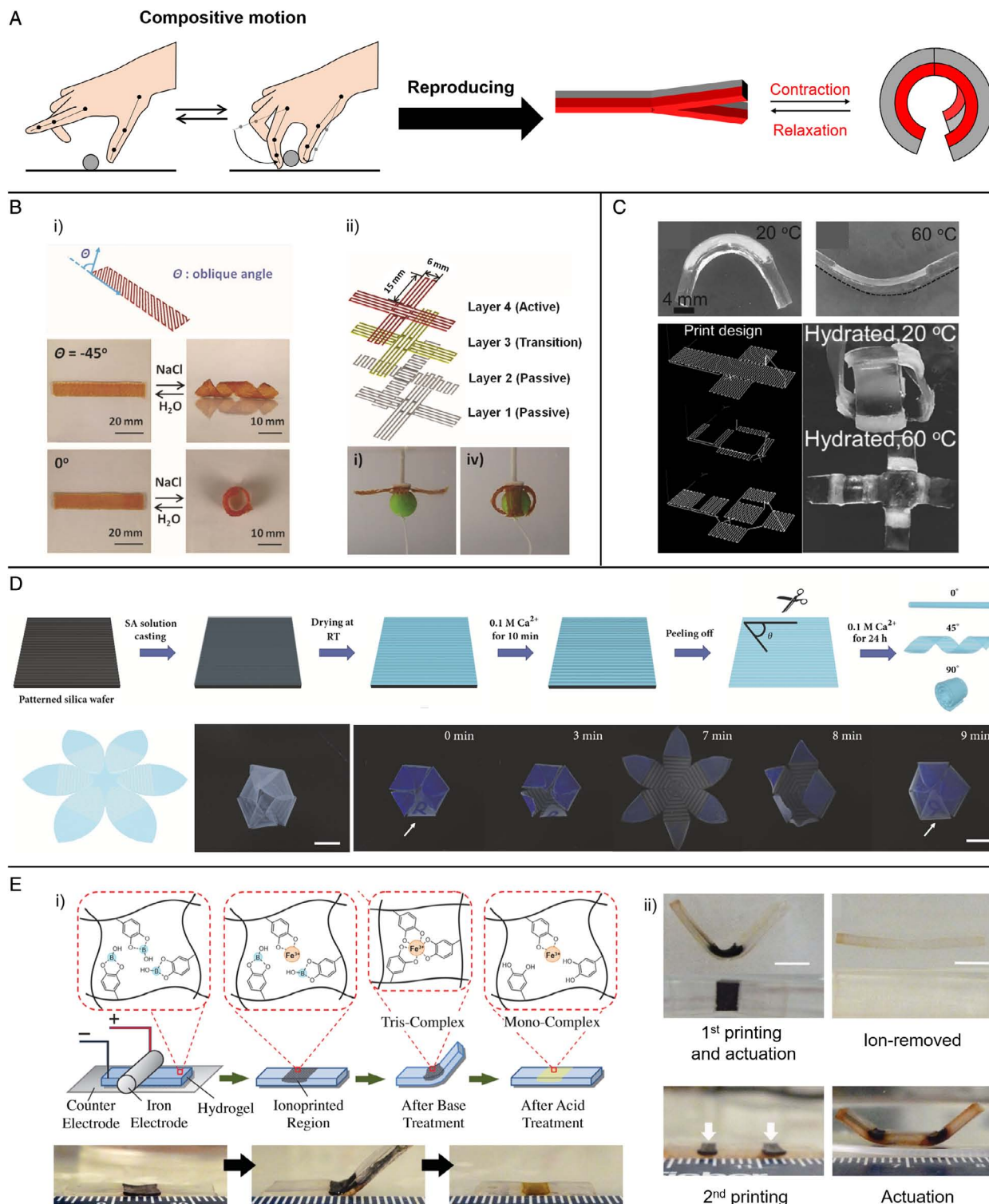


Figure 5. Hydrogel-based artificial muscle for programmed compositive motion. A) Picking up motion of living organism and reproduction of the motion in hydrogel-based artificial muscle. B) i) Controlling of the bending angle by preparing linearly oriented structure via 3D printing, and ii) a four-arm gripper manufactured by aligning a hydrogel fiber parallel to the desired bending direction via 3D printing. C) Reversible folding and unfolding between planar figures of cube and cube achieved by printing active layers on the folding position of a planar figure. D) Fabrication process of hydrogel-based artificial muscle by templating method and patterned structure with corresponding deformations. E) i) Ionprinting on dopamine-containing hydrogel and actuation mechanism, ii) ion removal and second printing. B) Adapted with permission.^[98] Copyright 2018, Wiley-VCH. C) Adapted with permission.^[99] Copyright 2016, Wiley-VCH. D) Adapted under a Creative Commons Attribution License (CC BY 4.0).^[85] Copyright 2019, The Authors, published by AAAS. E) Adapted with permission.^[100] Copyright 2014, Wiley-VCH.

dopamine-containing hydrogel. Because catechol groups can form a coordination complex with a metal ion, ionprinted site can have a relatively high cross-linking density in basic condition. Generated stress from cross-linking density difference makes the hydrogel bend. By exposing the bent hydrogel to an acidic environment, the cross-linking subsequently dissociated, and the hydrogel straightened. The deposited ion can be removed by ethylenediaminetetraacetic acid solution treatment, and another pattern can be printed on the ion-removed hydrogel (Figure 5E-ii). Programmed compositive motion to various 3D shapes can simply be achieved by printing a designed pattern on the hydrogel.

Including earlier examples, progress in hydrogel patterning techniques and analyses of correlation between patterned structure and consequential architecture will enable much more complex architecture and resultant advanced applications.

4.4. Applications of Hydrogel-Based Artificial Muscles

As biological muscles allow reversible mechanical motion and work to living organisms, hydrogel-based artificial muscles are adopted to provide reversible mechanical motion and work in various applications where the benefits of hydrogels can be utilized effectively such as soft gripper and locomotor.

The most fundamental application is a device that pushes or lift an object.^[35,104] Actuators that generate simple contraction and expansion motion also can provide such work, but bending motion or directionally amplified motion is needed for high efficiency in most cases. A typical application is components in a pipe or microfluidic device such as hydrogel valve^[19,105,106] and sorter (Figure 6A).^[107] The operation can be divided in two types: actuation upon the demand and actuation in response to the environmental stimuli. The former allows on-demand flow control, so it can provide controllability to the user. The latter simultaneously provide sensing capability, so preferred in autonomous flow control.^[19]

By designing and constructing appropriate structures, brilliant and diverse applications are possible. For example, utilizing the transparency of the hydrogel, the smart lens was manufactured by two hydrogel networks, chitosan and cellulose/carboxymethylcellulose, that possess opposite swelling/deswelling behavior in response to pH change (Figure 6B).^[108,112] Due to stimuli-responsiveness and suitably designed structure, the smart lens displayed tunable focal length, which is beneficial functionality observed in human lens. In spite of harsh condition, pH = 1, considerable focal length range, broader than a human lens, was achieved.

Another typical application is a gripper composed of multiple finger-like bending strips.^[113–119] There was an interesting research that demonstrated transparent and rapid hydrogel gripper that successfully captures live goldfish without giving a damage to the fish due to its softness, which is practically meaningful performance (Figure 6C).^[109] It is noteworthy that successful and harmless capturing which is originated from balanced mechanical property. The softness, although is an advantage of hydrogel but cause shortcomings when used as an actuator, was well utilized.

Next, although still remained in the proof-of-concept stage, hydrogel locomotors, also called walker, based on hydrogel-based

artificial muscle were reported.^[110,120–122] Some hydrogel locomotors could restrictively be operated on the surface which have specific geometry.^[120,121] However, well-designed novel systems presented locomotion on flat surface (Figure 6D),^[110,122] and unprecedented earthworm-like motion in capillary (Figure 5E).^[23]

Finally, mechanical motion is used to provide an on-off switchable capability for other functionalities. For example, the bilayer hydrogel composed of temperature-responsive shape-deforming hydrogel and pH-responsive color-tunable hydrogel was demonstrated (Figure 6E).^[111] When the closed flower-like hydrogel without a fluorescent signal is heated, it is opened, and the fluorescent inner layer is exposed. The emission from inner layer can be enhanced by lowering pH. The reverse actuation, closure of hydrogel, and decrease in fluorescent signal, can be conducted by cooling the hydrogel. This research may provide an important strategy and idea for the integration of different systems and functionalities to produce synergistic performance.

Including aforementioned examples, several researches demonstrated considerable performance and applications of hydrogel-based artificial muscles.^[15,113,123–129] Although hydrogels have shortcomings in mechanical performance, there are several differentiated advantages and corresponding promising applications. In addition, hydrogels are relatively easy to the construction of a composite system, so coupling with other systems such as another functional hydrogel and nanomaterials would be a favorable strategy to improve performances. Incorporating functional nanomaterials is a promising approach to be investigated in the future. Biological applications, including work-providing exoskeletons and implantable artificial muscle, may be potential applications.^[123] Although biocompatibility, primary advantage of hydrogels makes them promising material for biological applications, plenty of issues such as biodegradability, delivery of stimuli, integration into human body, and lifetime should be addressed for practical application, especially in vivo application.

5. Conclusions

Nowadays, the extensive information required for designing a hydrogel-based artificial muscle is available. Specific materials, structures, and manufacturing methods should be sorted out considering the desired characteristics, such as operating condition, response rate, mechanical properties, and output force. Until now, overview and examples of stimuli-responsive shape-deforming hydrogels, anisotropic hydrogel manufacturing methods, strategy to translate to complex deformations from isotropic deformations are described. Those contents probably provide brief guide for the sorting out.

Because the typical characteristics of hydrogel-based artificial muscles can serve as advantages in certain fields, there are several applications wherein they can be practically used and provide proper performance. However, sometimes the typical characteristics serve as weaknesses that prevent the use of hydrogels irrespective of their advantages. Recently, some of those weaknesses are partially overcome, but further improvements are still needed for broader application. Furthermore, to surpass the proof-of-concept stage and move ahead to practical use, several additional functionalities are also required. They are as follows:

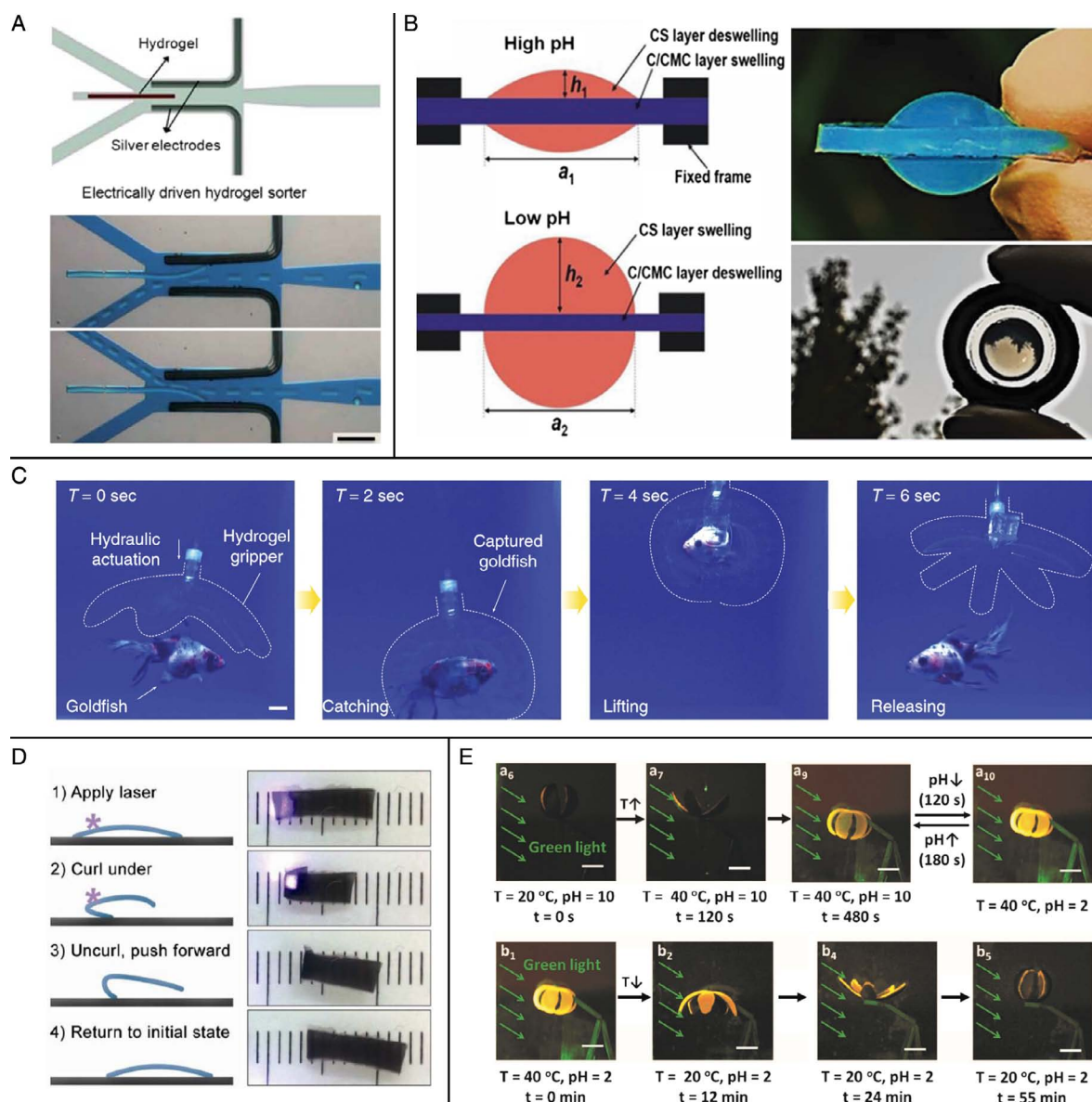


Figure 6. Applications of hydrogel-based artificial muscles. A) A sorter in microfluidic device. B) A hydrogel lens with tunable focal length. C) A camouflaged hydrogel gripper. D) A hydrogel locomotor presenting walking motion on flat surface. E) A bilayer hydrogel actuator presenting synergistic performance of mechanical motion and fluorescent emission. A) Adapted with permission.^[107] Copyright 2010, The Royal Society of Chemistry. B) Adapted with permission.^[108] Copyright 2017, The Royal Society of Chemistry. C) Adapted with permission.^[109] Copyright 2017, Springer Nature. D) Adapted with permission.^[110] Copyright 2013, American Chemical Society. E) Adapted with permission.^[111] Copyright 2017, Wiley-VCH.

1) The high water contents, which are the source of many advantages of hydrogels, are also the cause of many disadvantages. Low solid contents lead to mechanical weakness and low concentration of functional components. Thus, as artificial muscles, the network is easy to break, response rate is low, and output force is weak. The ideal way to increase the output force and response speed might be to increase the driving force of the actuation. There are several approaches such as increasing the concentration of functional moiety, increasing the intensity of stimuli, and incorporating nanomaterials to provide driving force, which has been generally applied.^[22,23,95,96,98,110] Recently, 3D-printed

hydrogel-based gripper demonstrated substantial output force, over 100 times the weight of the actuator, which was comparable with elastomer-based actuator.^[98] The considerable output force is originated from good mechanical property of the composite hydrogel. As the printed composite hydrogel was composed of very thin fiber, the response speed was not much slower. In another research, a rapid response speed, elongated by 180% within 0.5 s, was reported based on the novel system that contains nanosheets to provide driving force.^[23] In addition, some additional functionalities, such as self-healing property, need to be considered to overcome fragile nature and short

lifetime; 2) For most systems, operation conditions surrounded by external solvents are necessary for water exchange that leads to expansion and contraction, and for delivery of solvent-mediated stimuli, such as pH. Even if the actuation mechanism and stimuli delivery are independent of the external solvent, an external solvent is needed to prevent drying. In other words, operation condition of hydrogel-based artificial muscles is limited. Recently, novel hydrogel-based artificial muscles with unique actuation mechanisms that do not require external solvent demonstrated considerable performance and extended narrow operation conditions of hydrogel-based artificial muscles to the open-air and dry conditions.^[23,96] For practical use under the open-air condition with a considerable lifetime, the ways to prevent drying such as coating and backing layers are necessary; 3) Because uptake and release of external solvent are not that fast, and the required time for solvent permeation is increased with the volume increasing, typical solvent-mediated actuation mechanisms make response speed slow and limit scale-up. For this issue, sophisticated manufacturing methods such as 3D printing can provide improvement. For example, in a 3D-printed gripper, the output force was improved by increasing the number of active layers without decreasing the response speed.^[98] The reason is that 3D-printed layers are the collection of thin filaments, so large surface area and resultant good accessibility make response speed constant even in relatively bulky size.

In operating hydrogel-based artificial muscles, the issue of delivery of stimuli is as important as the properties of the hydrogel. For practical and general applications, rapid and facile delivery of stimuli is needed. One of the promising approaches is incorporating nanomaterials. For example, heating can be conducted by light irradiation by incorporating photothermal nanomaterials such as reduced graphene oxide nanosheets^[110] and AuNPs.^[23] In addition, beneficial functionalities of nanomaterials such as good conductivity of reduced graphene oxide nanosheets^[110] can effectively assist the delivery of stimuli. Those modifications may allow practical stimuli delivery and performance improvement, especially in response speed.

Including the aforementioned weaknesses, numerous challenges are still remaining, but, considering the advantages and potentialities of hydrogels, further studies to develop advanced hydrogel-based artificial muscle will be indispensable and valuable researches.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

anisotropic structures, artificial muscles, hydrogels, hydrogel actuators, stimuli-responsive hydrogels

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