Hydrogel-based actuators: possibilities and limitations

Leonid Ionov

Leibniz Institute of Polymer Research Dresden, Hohe Str. 6, D-01069 Dresden, Germany

The rapid development of microtechnology in recent times has increased the necessity for the development of devices, which are able to perform mechanical work on the micro- and macroscale. Among all kinds of actuators, the ones based on stimuli-responsive hydrogels, which are three-dimensional polymer networks strongly imbibed with water, deserve particular attention. This paper aims to provide a brief overview of stimuli-responsive hydrogel actuators with respect to their sensitivity to different stimuli, different kinds of deformation, the possibilities of generating different types of movement, as well as their applications.

Introduction

The rapid development of microtechnology (microelectronics, microfluidics, MEMS) in recent times has increased the necessity for the development of devices, which are able to perform mechanical work on the micro- and macroscale [1]. There are several approaches for the design of actuators based on the use of the piezoelectric effect, fluid flow, magnetic and electric fields. Among all kinds of actuators, the ones based on stimuli-responsive hydrogels deserve particular attention. Hydrogels are three-dimensional polymer networks strongly imbibed with water and the amount of water can approach up to 99 wt% of the hydrogel mass. Because of this property, hydrogels are able to considerably swell and shrink (>10 times in volume) when the amount of water in the polymer network changes, which may occur in response to different stimuli such as temperature (T), light, pH, ionic strength, among others. In this respect, the behavior of hydrogels mimics the hydromorphic movement of plants, where twisting and bending is provided by a change of the amount of water in the cells and tissues. Clearly, hydrogels are able to act in solely aqueous media that, on the one hand, limits their applications but, on the other hand, opens new perspectives for applications where other kinds of actuators are not desirable. For example, there are a variety of biodegradable and biocompatible stimuli-responsive hydrogels that allow the design of actuators for bioapplications. The character of deformation of inhomogeneous hydrogels can be far more complex and depends on many parameters such as the shape and size of the hydrogel, the character of distribution of inhomogenities and even whether the hydrogel is free-standing or lays on a substrate. This paper aims to provide a brief overview about stimuli-responsive hydrogel actuators with respect to their sensitivity to different stimuli, possibilities to generate different types of movement, as well as their applications. The paper does not aim to provide an overview of all papers in this broad field but rather to provide a complete picture of the possibilities and limitations of this fascinating field.

Stimuli

The swelling degree of hydrogels is defined by the balance of free energy for the network expansion, which depends on the cross-linking density, and the molar free energy of mixing, which depends on interactions between polymer chains and solvents as well as mixing entropy (Flory–Rehner Theory). While the cross-linking density of a hydrogel remains constant, the energetic and entropic components depend strongly on temperature, solvent quality, which in turn depends on temperature, pH, among others. Thus, by changing temperature and pH one can affect the swelling degree of hydrogels.

There are plenty of reports describing the fabrication of actuating hydrogel films with different stimuli-responsive properties For example, there are pH-responsive systems based on polyelectrolytes [2–11]; thermoresponsive systems based on polymers with low critical solution temperature (LCST) and upper critical solution temperature behavior [12–18]; solvent sensitive systems

E-mail address: ionov@ipfdd.de.

[6,8,19,20]; systems sensitive to electric signal [21–23], enzymes [24] and light, which are based on light-to-heat conversion [25–27], molecule isomerization of azobenzene fragments [28] and photo-deprotection of nitrobenzyl groups [29]. In all these cases, application and removal of stimuli lead to deformation and relaxation of a hydrogel, respectively. Very interesting actuation can be achieved using an oscillating Belousov–Zhabotinsky (BZ) redox reaction, which allows cyclical changes in shape of the hydrogel [30–32]. Such hydrogels consist of thermoresponsive poly(N-isopropylacrylamide) hydrogels with chemically linked ruthenium-based catalysts for the BZ reaction. BZ generates oscillations in the redox state of the catalyst that affects the LCST of thermoresponsive hydrogels leading to its oscillations. For example, using the BZ reaction Yoshida et al. [33] fabricated gels exhibiting autonomous peristaltic motion without external stimuli, prepared by copolymerizing temperature-responsive N-isopropylacrylamide with ruthenium tris(2,2′-bipyridine) (Ru(bpy)3) as a catalyst. In another approach, Maeda et al. fabricated a self-oscillating gel actuator without external stimuli by producing a gradient structure, which generates a pendulum motion by fixing one edge of the gel [34,35]. Such oscillating hydrogels can, for example, be used to direct particle transport [33] in the way that BZ reaction results in local swelling of the hydrogel changing with time. As a result, a moving wave of swollen hydrogel is formed. The wave provides peristaltic motion of the adsorbed microparticles.

The responsive properties of hydrogels with shape-memory effect are very interesting. These hydrogels, which contain nitrile groups, have patterned surfaces and are able to quickly bend or twist depending on the pattern when immersed in a solution of Zn salts. The deformed shape can be fixed in pure water. Immersion in Zn salts leads to a slow relaxation to the original state. This effect is based on simultaneous inhomogeneous shrinking and deformation of the hydrogel as well as a coupling (physical crosslinking) of nitrile groups by Zn^{2+} ions. In this case two nitrile groups are linked by one ion. The long-term exposure to Zn^{2+} ions leads to saturation of nitrile groups with Zn^{2+} ions and each nitrile group is bound to one Zn^{2+} ion. Therefore, the hydrogel keeps its shape after removal from a salty solution and slowly relaxes to its original shape when immersed in Zn^{2+} solution for a long time [36].

Thus, use of polymers with different responsive properties allows the design of hydrogels sensitive to various stimuli such as temperature, light, pH, among others, which can also be in the physiological range. Moreover, the design of self-oscillating hydrogel actuators is possible.

Types of deformation

Typically, changing conditions, such as temperature, pH and light, results in a homogeneous expansion or contraction of hydrogels in all directions (Fig. 1a). Complex deformation such as bending and twisting, as well as even more complex folding, is produced as a result of inhomogeneous expansion/shrinking, which occurs with different magnitudes in different directions [37,38]. The first possibility to achieve such deformations is by applying an inhomogeneous field, for example, a gradient of temperature or concentration, to homogeneous materials (Fig. 1b). In particular, it is known that a strip of an anionic hydrogel bends toward the cathode in an electric field [39]. Doi et al. [40] predicted that this bending behavior is governed by the concentration of the

dominant ions. Varghese and Arya have extended this theory and demonstrated that the same anionic hydrogel can be made to bend in two different directions by changing its crosslink density [41]. The second possibility to achieve bending is to use an inhomogeneous hydrogel, which consist of hydrogels with different swelling properties (Fig. 1c). For example, the bilayer hydrogel strip bends in the direction of the less expanding component that is similar to bimetal strip [42]. The third possibility to generate complex and extremely fast motion is to use snap-buckling deformation, which is similar to the motion of a Venus flytrap (Fig. 1d). This can be achieved using a hydrogel device with a doubly curved shape [43]. Anisotropic swelling of one side of such a doubly curved film results in a fast switching of the direction of curvature. In fact, among these four scenarios, the use of an inhomogeneous hydrogel (Fig. 1c) allows the design of actuators with the most complex trajectory of deformation that will be discussed in the next sections.

Effect of hydrogel shape on character of deformation

The shape of hydrogels plays a decisive role and defines the character of movement and final shape of deformed hydrogels. Among all kinds of shapes one can distinguish between two main groups: rods and layers.

Rods. Hu et al. were among the first to demonstrate reversible bending of stimuli-responsive polymer bilayer sticks, which consist of poly(N-isopropylacrylamide)-based polymers [46]. It was shown that when both the polymer forming bilayers are swollen, the bilayer is undeformed. Shrinking of one of the components leads to a bending of the rod that is similar to the behavior of bimetal strip. Later on, the possibility of bending in different directions was demonstrated on a hydrogel bilayer formed by polyacid and polybase [47]. At low pH the bilayer bends in the direction of the polyacid layer because this layer shrinks. The opposite scenario is observed at high pH. Similar to this work, Lahann et al. fabricated a smart polymer rod where a stimuli-responsive swellable polymer brush was grafted at one side. The rod bend and the radius of curvature are inversely proportional to the degree of swelling [48]. In fact all reports show that the bilayer rod bends in the direction on the nonswollen side.

Layers. Similar to rods, hydrogel layers bend in toward the less expanding component (Fig. 2a). The bending of the layer is however more complex than the bending of the rods. In fact, a rectangular hydrogel layer can bend either along its short or long sides, or along the diagonal. To address this question, Stoychev et al. investigated the bending/folding of rectangular stimuli-responsive hydrogel-based polymer bilayers with different aspect ratios and relative thicknesses placed on a substrate (Fig. 2b) [14,49]. It was found that the long-side folding dominates at high aspect ratios (ratio of length to width) when the width is comparable to the circumference of the formed tubes, which corresponds to a small actuation strain. Folding from all sides occurs when the width and length considerably exceed the deformed circumference. Moreover, it was found that the presence of the substrate plays a very important role by determining the direction of folding (Fig. 2b). In particular, the free-standing bilayer rolls along its short sides and scrolls are formed. By contrast, the bilayer which lies on the substrate rolls along its longer side and tubes are formed.
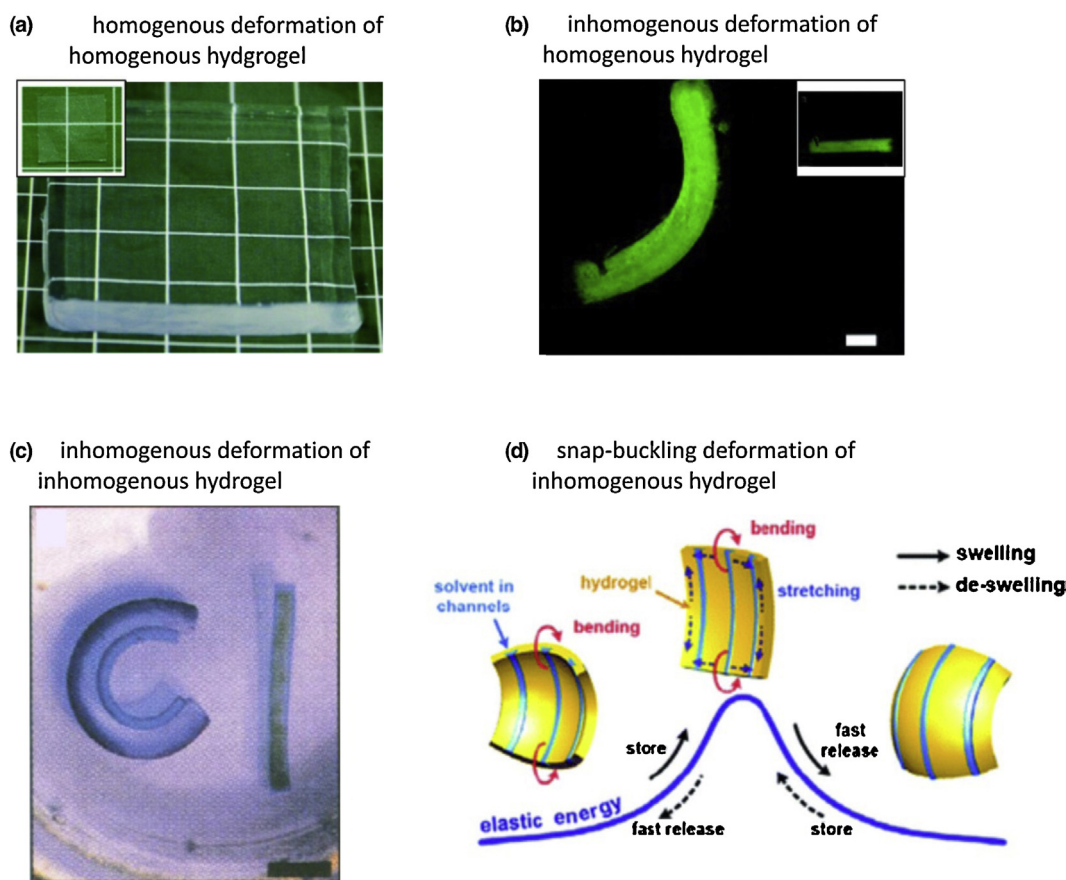
(a) homogenous deformation of homogenous hydrogel

(b) inhomogenous deformation of homogenous hydrogel

(c) inhomogenous deformation of inhomogenous hydrogel

(d) snap-buckling deformation of inhomogenous hydrogel

FIGURE 1

Different mechanisms of deformation of swelling of hydrogels: (a)–homogeneous swelling of homogeneous poly-(N,N-dimethylacrylamide)-based hydrogel (reprinted with permission of Ref. [44], Copyright (2011) American Chemical Society); (b) bending of homogeneous poly(sodium acrylate)-based hydrogel in the gradient of field (scale bar 1 mm, reprinted from Ref. [45], Copyright (2009) American Chemical Society); (c) bending of inhomogeneous poly(N-isopropylacrylamide)-based hydrogel bilayer (scale bar 5 mm, reprinted from Ref. [46], Copyright (1995) AAAS); (d) snap-buckling of polyethylene glycol-based hydrogel (reprinted from Ref. [43], Copyright (2010) Royal Society of Chemistry). Insets in (a) and (b) show the shapes before deformation.

The ratio of the bending curvature to the size of the film also plays a very important role. We demonstrated that star-like polymer films located on a water-impermeable substrate fold in one-step and leading to the formation of capsules if the bending curvature is large (Fig. 2c, left images). Folding of similar bilayers with a smaller bending curvature is more complex and occurs in a multistep manner (Fig. 2c, right images). In particular, homogeneous bilayer films can undergo sequential steps of folding by forming various 3D shapes with sharp hinges such as pyramid [50]. Step-by-step folding of different elements of self-folding films can also be achieved by local activation of selected areas of self-folding films by light [51].

Effect of structural inhomogeneity

It was observed that homogeneous hydrogels undergo a typically homogeneous change of the volume if there is no gradient of concentration or temperature. Applying a gradient of stimuli (temperature, pH, light, among others) to homogeneous hydrogels can lead to its bending [52]. Very recently it was demonstrated that one can achieve very complex deformation of homogeneous hydrogels using a local deposition of heavy metal ions in a charged hydrogel (ionoprinting). This method is based on applying electrodes to intrinsically homogeneous hydrogels. One of the electrodes is made of copper and the electrochemical reaction leads to the formation of

copper ions, which diffuse in the hydrogel and change their swelling properties. As a result the hydrogel bends, complex deformation (formation of hinges, bidirectional bending) is achieved using multiple electrodes [53].

Structural inhomogeneity plays a very important role and, along with the shape, defines character of deformation. This mechanism of controlling the character of deformation is implemented in nature (Fig. 3a,b,f,g,k,l). For example, pine cone scales and wheat awn are formed of two kinds of tissue [54–56]. In one of them cellulose fibers are oriented along the scale that allows bending (Fig. 3c,h). The orchid tree seedpod is also formed by two-layer structure, while the cellulose fibers in each layer are oriented at some angle with respect to each other that allows twisting (Fig. 3m) [57]. These, nature-inspired mechanisms of control of deformation were realized in the example of thermo-responsive hydrogels with incorporated magnetic plates, which are oriented in a specific direction during preparation of the hydrogel by a magnetic field. The magnetic plates play the role of cellulose fibers in plants. Similar to natural examples, hydrogels are able to bend and twist depending on orientation of magnetic plates (Fig. 3d,e,i,j,n,o).

In other reports, Hayward and Santangelo demonstrated that a patterned polymer film consisting of patches with different swelling
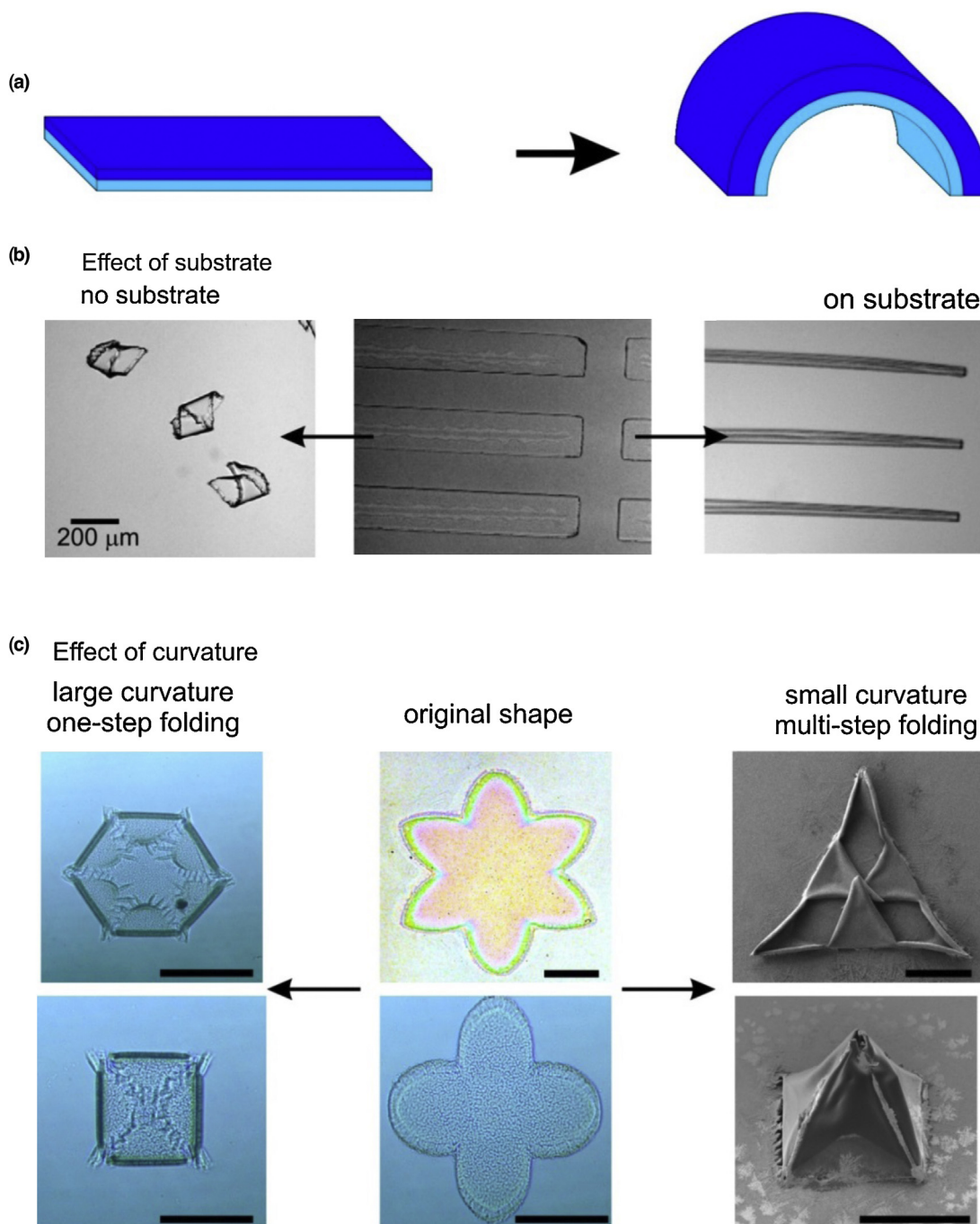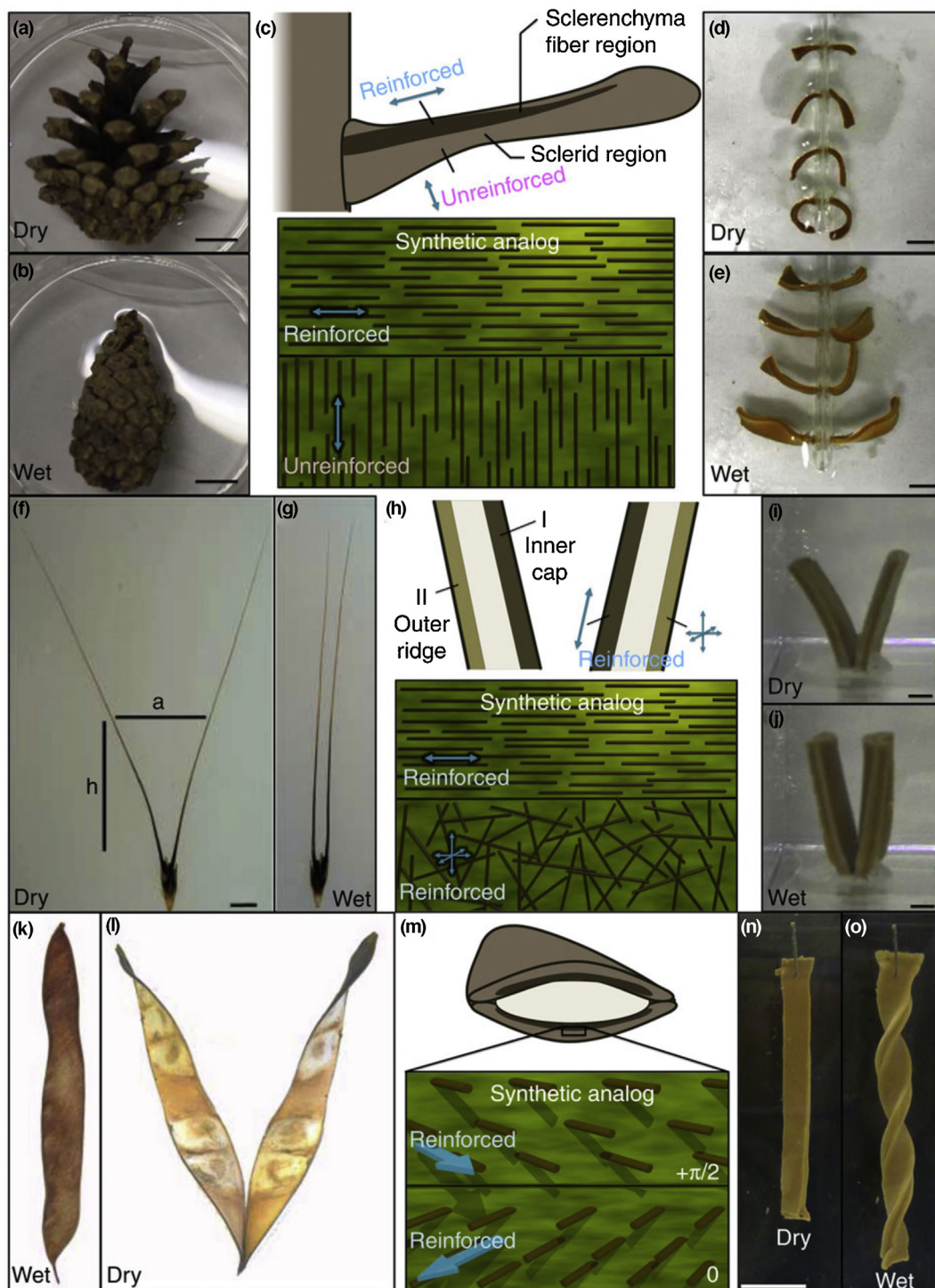
FIGURE 2

Different scenarios of deformation of bilayers based on poly(*N*-isopropylacrylamide)-based hydrogel (a) depending on the presence of substrate (b) and shape of the film (c). Scale bar is 200 μm (b – reprinted from Ref. [49], Copyright (2012) American Chemical Society, c – reprinted from Ref. [15], Copyright (2011) Royal Society of Chemistry and Ref. [50], Copyright (2013) Wiley-VCH Verlag GmbH & Co. KGaA). Scale bar is 200 μm.

degrees is able to fold in a very complex way and the character of folding depends on the pattern (Fig. 4a) [59,60]. When swollen in an aqueous medium, a film consisting of high- and one low-swelling stripes does not bend to the side of the less-swelling component, that is the case of 'classical', but rolls into a three-dimensional shape consisting of two nearly cylindrical regions connected by a transitional neck (Fig. 4b). Films with radial gradient of swelling properties, where the outer part swells more than the central part, fold in response to a change of temperature and form complex structures

(Fig. 4c). Kumacheva et al. investigated the folding of rectangular films formed by stripes of two or three polymers with different swelling properties [61,62]. Such films are unfolded when all polymers have the same swelling properties (either equally swollen or equally shrunk) and roll in different directions when polymers swell unequally.

Structural inhomogeneity can also be used for the generation of complex rod movement [63]. Similar to a bilayer, the birod bends in the direction of the less expanding component (Fig. 5a).

FIGURE 3

Deformation of natural actuators and synthetic actuators based on a poly(N-isopropylacrylamide)-based hydrogel with structural inhomogeneity. A conifer pinecone (a) dried out and (b) fully hydrated. (c) Cartoon schematic indicating the predominant orientation of cellulose fibers within a pinecone scale according to refs [54,55]. Synthetic pinecone scales constructed by orienting magnetic platelets in a similar bilayer structure within gelatin shown (d) as-prepared and (e) fully hydrated. A wheat awn system (f) dried out and (g) fully hydrated. Reprinted from Ref. [56] (reproduced with permission from AAAS). (h) Cartoon schematic indicating the predominant orientation of cellulose fibers within a wheat awn according to Ref. [56]. Synthetic wheat awn systems constructed by orienting magnetized alumina platelets in a similar bilayer structure within gelatin, shown (i) as-prepared and (j) fully hydrated. An orchid tree seedpod (k) hydrated and (l) dried out. Reprinted from Ref. [57] (reproduced with permission from AAAS). (m) Cartoon schematic indicating the predominant orientation of CMFs within the orchid tree seedpod according to Ref. [57]. Synthetic chiral seedpods constructed by orienting magnetic platelets in a similar bilayer structure within gelatin, shown (n) as-prepared and (o) fully hydrated. All scale bars are 1 cm. Whole image is reproduced with permission of Ref [58], Copyright (2013) Nature Publishing Group.
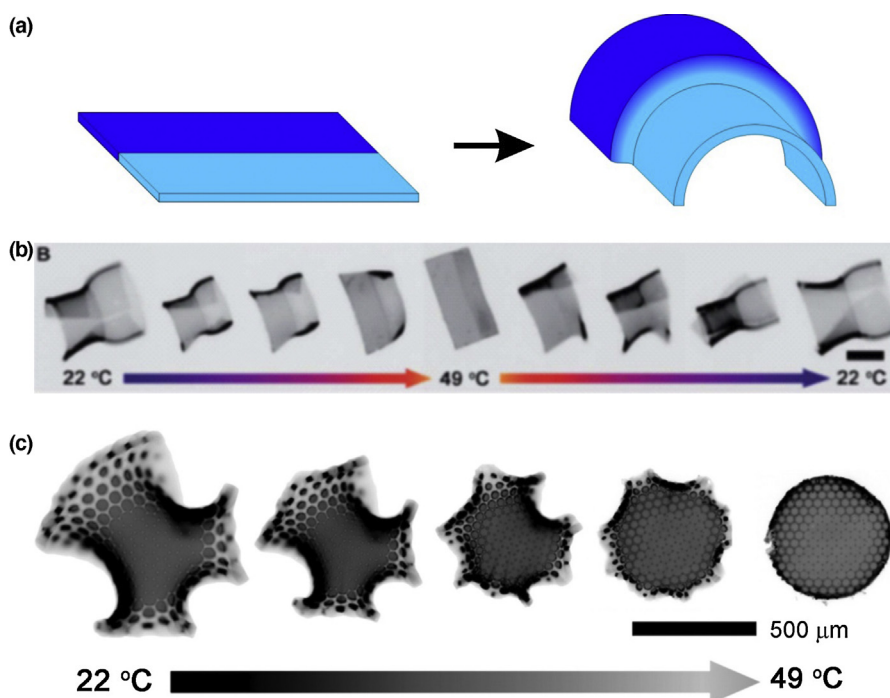
FIGURE 4

Temperature-responsive swelling of bistrips based on a poly(N-isopropylacrylamide)-based hydrogel: (a) scheme; (b) folding of simple shape; (c) folding of a complex shape with radial gradient of swelling properties. When the temperature of the aqueous medium is increased, the bistrip shrinks, unrolls, and finally recovers a flat shape by 50°C as the temperature is decreased [60]. Scale bar is 200 μm (reprinted from Ref. [60], Copyright (2012) Royal Society of Chemistry and Ref. [59], Copyright (2012) AAAS).

By making a sloped bilayer structure, the planar structure described in Fig. 5b can be bent along the y-axis as well as twisted around this axis when one of the layers is asymmetrically expanded in a specifically selected solvent. When the bilayer actuating device with triangular layers with respect to the y-axis is swollen, a helical-type actuating sensor can be formed. A double twisted helical photonic actuator can be formed as shown in Fig. 5c [19].

Applications

The reversible deformation of hydrogels can be used not only for the design of micromanipulators (artificial muscles) but also for a variety of applications such as sensors, optical devices with tunable focal length and color, control of liquid flow in microfluidic devices. Below are given some examples of application of actuating hydrogels.

Sensors. One possible kind of application of inhomogeneous hydrogels is sensors based on the detection of bending of inhomogeneous hydrogels (Fig. 6a) [1,64–67]. This can be realized using an atomic force microscopy (AFM) setup – AFM cantilevers are coated on one side with hydrogel and are able to bend depending on the swelling state of the hydrogel [64,65] In this way, pH- [64], temperature-, ion-sensitive [66,67] and biosensors [65] were
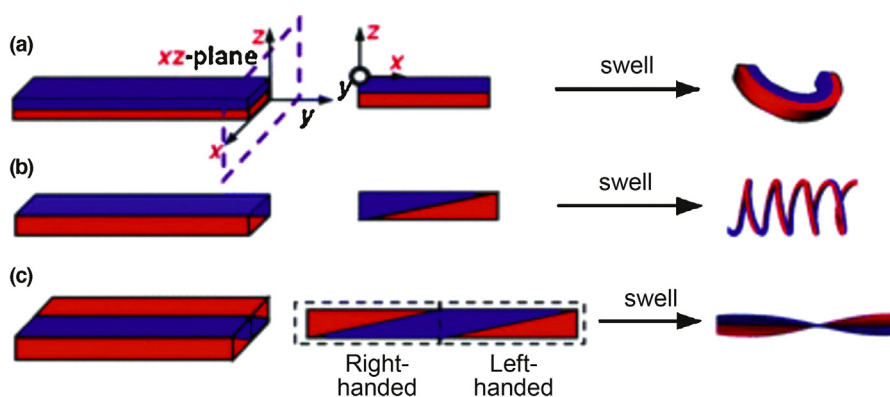
FIGURE 5

Schematic illustrations of deformation of inhomogeneous hydrogels (hydrogels where 'blue' and 'red' parts have different swelling properties): (a) bending, (b) polypeptide-type twisting, (c) DNA-type twisting actuators based on poly-(2-hydroxyethyl methacrylate)-based gels (reprinted from Ref. [19], Copyright (2011) Royal Society of Chemistry).
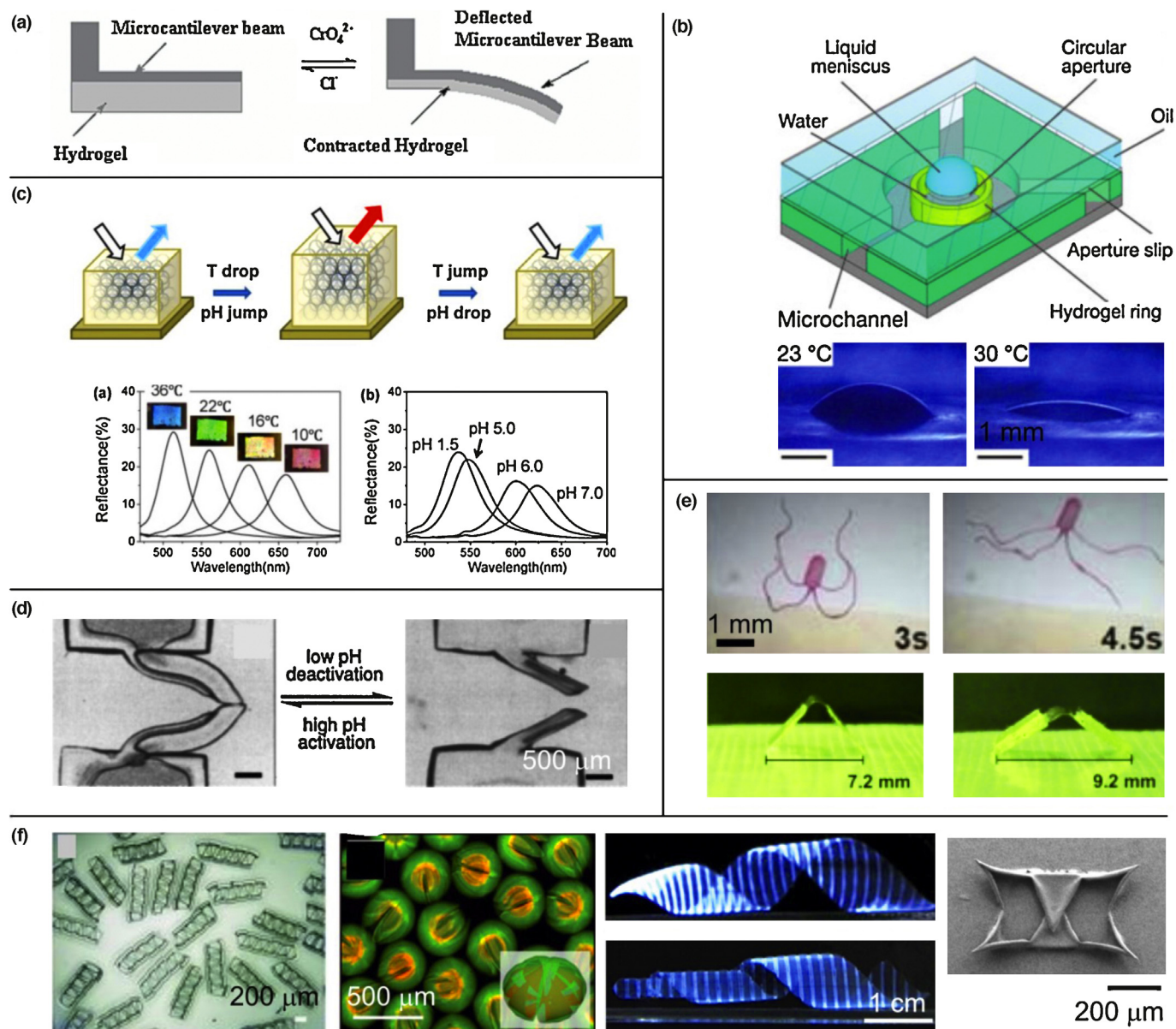
FIGURE 6

Examples of the application of hydrogels actuators: (a) cantilever sensor based on a polyacrylamide hydrogel, which bends when the environmental conditions are changed (reprinted from Ref. [67], Copyright (2003) American Chemical Society); (b) smart optical lenses with tunable focal length based on a poly(N-isopropylacrylamide)-based hydrogel (reprinted from Ref. [70], Copyright (2006) Nature Publishing Group); (c) materials with switchable coloration based on a poly(N-isopropylacrylamide)-based hydrogel (reprinted from Ref. [83], Copyright (2012) Elsevier); (d) smart valves for control of liquid flow based on poly-(2-hydroxyethyl methacrylate)-based hydrogel (reprinted from Ref. [77], Copyright (2001) American Institute of Physics); (e) swimmers based on a polyethylene glycol-based hydrogel and walkers based on a poly(acrylic acid)-poly(allylamine hydrochloride) hydrogel (reproduced from Refs. [84,85], Copyright (2011 and 2008) Wiley-VCH Verlag GmbH & Co. KGaA); (f) examples of 2D and 3D microfabricaiton using polyethylene glycon and poly(N-isopropylacrylamide)-based actuators (reproduced from Ref. [86], Copyright (2013) Wiley-VCH Verlag GmbH & Co. KGaA; Ref. [87], Copyright (2013) Wiley-VCH Verlag GmbH & Co. KGaA; Ref. [62], Copyright (2013) Nature Publishing Group; Ref. [50], Copyright (2013) Wiley-VCH Verlag GmbH & Co. KGaA).

developed. The advantage of this approach is simplicity: any AFM device can be used for sensing.

Optical devices. Stimuli-responsive hydrogel microparticles can be used as microlenses with a focal length that is tunable via external stimuli, which depends on the particle size and, as result, on the swelling degree [68,69]. In another possible scheme, the membrane separating water and oil is mounded on ring formed by macroscopic stimuli-responsive hydrogels (Fig. 6b) [70]. When exposed to an appropriate stimulus, the hydrogel ring underneath

the aperture responds by expanding or shrinking. This leads to a change in the volume of the water droplet located in the middle of the ring. The net volume change – the change in the volume enclosed by the ring and the change in water droplet volume – causes a change in the pressure difference across the water–oil interface that directly determines the geometry of the liquid meniscus.

A change of the volume of the hydrogel can be used for the design of materials with changing color. One way is although the

incorporation of gold or semiconductor nanoparticles in stimuli-responsive hydrogel particles [71,72]. In this case, the swelling and shrinking of hydrogel particles results in the change of aggregation/disaggregation of the incorporated nanoparticles that change their plasma resonance properties or fluorescence. Closely packed stimuli-responsive hydrogel microparticles provide another possibility for the design of photonic crystals with switchable optical properties (Fig. 6c) [73–76]. In this case spherical particles form densely packed arrays with periodicity defined by their size. The reversible swelling/shrinking of particles leads to change in the periodicity of the lattice that results in the change of the wavelength of transmitted and reflected light.

Microfluidic devices. Control of liquid flow in microfluidic devices is one of the potential applications of hydrogels actuators [77–81]. The simplest possibility is to use large hydrogel pieces which act as a smart valve (Fig. 6d). These valves allow the liquid to flow when the hydrogel is shrunk and closes the channel when swollen. Another possibility to control liquid flow is to use the bending of a hydrogel bilayer. Such a setup was realized by Yu et al. [77]. The valve consists of a bistrip formed by pH sensitive and pH-indifferent hydrogels. Back pressure closes the leaflets, thereby restricting backflow, whereas forward pressure opens the leaflets and allows fluid to pass. The valve activates and deactivates in response to solution pH due to the use of a pH-responsive hydrogel in the leaflets. At high pH, the valve is functional and at low pH the leaflets contract to close the valve. Therefore, the valve not only functions as a one-way check valve, but also provides the ability to call the valve into service when desired. Similar check valves were found in mammalian veins [82].

Walkers and swimmers. In fact, the bending of a hydrogel can easily be transformed to walking or swimming by applying cyclical stimuli (Fig. 6e). In 1992 Osada et al. reported the deformation of a polyelectrolyte hydrogel immersed in a surfactant solution causing swelling of the hydrogel [88]. The hydrogel bends toward the cathode that allows control over the direction of bending via the polarity of the applied voltage. Switching the polarity resulted in a change of the bending direction. Thus, the gel demonstrated bending and stretching upon cyclic change in the polarity of the applied voltage. The specific deformation of the hydrogel allowed its walking at a speed of 15 mm/min. Similar to this work, Sun et al. developed a macroscopical hydrogel-based actuating system, which is able to walk on a ratchet substrate. The system is based on the bending of a hydrophobic–hydrophilic bilayer in response to a change in humidity (Fig. 6e, lower panel) [84]. This bilayer actuator could drive a walking device carrying a load 120 times heavier than the actuator and to walk steadily on a ratchet substrate under periodic alternation of the relative humidity between 11 and 40%. This concept was further developed in later works. For example, Velev and Dickey demonstrated walking of electrically active hydrogel [89]. Bashir developed walkers by combining hydrogels cardiomyocytes forming together a bilayer structure which can walk [90].

Hydrogel-based actuators are also able to swim when their shape changes cyclically. Different shapes have been used to design hydrogel-based swimmers. Lee et al. used inhomogeneous deformation of hydrogels and fabricated pH-sensitive hydrogel actuators mimicking the shape and the swimming motion of octopus and sperm (homogeneous hydrogel in electric field) [85]. Such

aquabots are able to produce directional motion in response to a change of the electrochemical potential and can potentially be used for biomedical applications to sense and destroy certain microorganism. Smela et al. demonstrated more complex actuation on the example of conjugated polymer actuators formed by a bilayer consisting of polypyrrole and metal [91,92]. They showed that such bilayer actuators are able to capture and release particles [21,92].

3D microfabrication. In fact, most applications of actuating hydrogels are related to the generation of force or force momentum. By contrast, as it is shown above (Figs 2 and 4), the deformation of a hydrogel can also lead to a considerable change of shape: this is used for the design of complex 2D and 3D systems in an origami-inspired self-folding concept (Fig. 6f). In fact, utilization of the folding of hydrogels for the design of structured materials is highly attractive – it allows very simple, template-free fabrication of very complex repetitive 2D and 3D patterns [93–98], which can hardly be prepared using other very sophisticated methods, such as two-photon and interference photolithography. One of the advantages of self-folding hydrogels is the possibility of quick, reversible and reproducible fabrication of 3D hollow objects with controlled chemical properties and morphology of both the exterior and interior. There are many factors, which make hydrogel-based microfabrication particularly attractive [38,99,100]. First, there are a variety of polymers sensitive to different stimuli that allow the design of self-folding films, which are able to fold in response to various external signals. Second, there are many polymers changing their properties in physiological ranges of pH and temperature, as well as polymers sensitive to biochemical signals. Third, there are a variety of biocompatible and biodegradable polymers. These properties make polymer-based self-folding films very attractive for biotechnological applications. Fourth, polymers undergo considerable and reversible changes of volume that allow the design of systems with reversible folding. Fifth, fabrication of 3D structures with sizes ranging from hundreds of nanometers to centimeters is possible.

3D microfabrication using actuating hydrogels is particularly attractive for the design of scaffolds and the fabrication of 3D cellular constructs [101,102] that potentially allows the fabrication of 3D scaffolds for tissue engineering [86]. A very interesting application of self-folding hydrogels was recently demonstrated by Gracias et al. They used deformation of polymers to design 3D microfluidic systems [103]. Another application related to a change of shape of hydrogel structures is encapsulation and release. Cells were encapsulated in thermoresponsive poly(N-isopropylacrylamide)-based self-folding films upon cooling below 30°C and could be released from the film, which unfolds above 30°C. This encapsulation and release is completely reversible and could be repeated many times [14,15]. Very recently, fully biodegradable self-folding films, which consist of commercially available biodegradable polymers, were also used to encapsulate cells [104]. Self-rolled tubes obtained by rolling thermoresponsive bilayers with an additional layer of platinum is able to swim in a solution of hydrogen peroxide and the swimming can be activated/deactivated by change of the shape of the tube [105].

Stimuli-responsive surfaces. Very recently Aizenberg et al. demonstrated fascinating self-regulating oscillating hydrogel-based actuators [106]. In this study, arrays of PNIPAM pillars were

fabricated with a catalyst as a cap for each pillar. Intense exothermic reactions were localized at the tips of the pillars, also localizing the increased temperature in this region. Once the temperature reached the LCST, the rods bent into a region of liquid which was designed to contain no reactants, allowing the pillars to cool below the LCST. This caused the pillars to elongate once more and continue the cycle. Simulation results show that such an oscillation is stable at long times, and could thus continue so long as the supply of reagent continued.

Conclusions and outlooks

There are several advantages of hydrogel-based actuators. The first is the possibility of the design of actuators sensitive to different signals (pH, temperature, concentration, biosignals). Next, hydrogels undergo huge volume changes, which occur in relatively narrow ranges of changes of temperature, pH, and ionic strength. In spite of such big advantages, the use of hydrogel-based actuators is limited to aqueous solutions. Here, one must note that while water is really required for actuation, the design of hydrogel-based actuators acting in air conditions is possible. In this case, water molecules are adsorbed from air (humidity). It is clear that the volume expansion in air is much smaller and the response time is typically larger than in that in water. Another limitation of hydrogels is the dependence of the response time on the size which is related to slow diffusion of water molecules. The response time of hydrogels with the size of several cm can be as large as several hours. This problem can, however, be solved using porous hydrogels [45].

This review covered different possibilities toward the design of actuators using hydrogels, discussed different mechanisms of movement and gave an overview of their applications. In particular, the swelling of hydrogels can result in a variety of different deformation scenarios, from simple changes of the size, to bending and twisting, as well as multistep folding which is defined by the shape of hydrogels, their structural inhomogeneity, among others. This allows hydrogels to not only to perform mechanical work as 'artificial muscles' but also as sensors, active optical devices, smart valves for microfluidic devices, encapsulation of cells and in the design of biomaterials. One of the main advantages of hydrogel-based actuators over other types is the possible biocompatibility/ biodegradability that leaves an opens perspective for the design of resorbable actuators for *in vivo* applications. A very promising application of actuating self-folding hydrogels is 3D microstructuring. It was demonstrated that one can design various hollow structures using self-folding hydrogels such as tubes, capsules, cubes, pyramids, among others. Moreover, self-folding technology allows for very straightforward design of 3D structures with patterned walls that, for example, can hardly be achieved using interference- and two-photon lithography. Therefore, this technique opens possibilities for 3D patterning of cells and the design of scaffolds for tissue engineering.

Acknowledgement

References

[1] J.S. Randhawa, et al. Adv. Funct. Mater. 21 (2011) 2395–2410.
[2] V. Luchnikov, O. Sydorenko, M. Stamm, Adv. Mater. 17 (2005) 1177–1182.
[3] K. Kumar, et al. Chem. Mater. 21 (2009) 4282–4287.
[4] K. Kumar, et al. Eur. Polym. J. 44 (2008) 4115–4121.
[5] H.Y. He, J.J. Guan, J.L. Lee, J. Control. Release 110 (2006) 339–346.
[6] J.J. Guan, et al. J. Phys. Chem. B 109 (2005) 23134–23137.
[7] N. Bassik, et al. Polymer 51 (2010) 6093–6098.
[8] T.S. Kelby, M. Wang, W.T.S. Huck, Adv. Funct. Mater. 21 (2011) 652–657.
[9] S. Singamaneni, M.E. McConney, V.V. Tsukruk, Adv. Mater. 22 (2010) 1263–1268.
[10] S. Singamaneni, M.E. McConney, V.V. Tsukruk, ACS Nano 4 (2010) 2327–2337.
[11] T.S. Shim, et al. Angew. Chem. Int. Ed. 51 (2012) 1420–1423.
[12] J. Wang, et al. Biomed. Microdevices 7 (2005) 313–322.
[13] M.E. Harmon, M. Tang, C.W. Frank, Polymer 44 (2003) 4547–4556.
[14] S. Zakharchenko, et al. Soft Matter 6 (2010) 2633–2636.
[15] G. Stoychev, N. Puretskiy, L. Ionov, Soft Matter 7 (2011) 3277–3279.
[16] L.-W. Xia, et al. Nat. Commun. 4 (2013).
[17] A. Richter, G. Paschew, Adv. Mater. 21 (2009) 979–983.
[18] A.K. Agarwal, et al. Lab Chip 7 (2007) 310–315.
[19] K.-U. Jeong, et al. J. Mater. Chem. 21 (2011) 6824–6830.
[20] D.P. Holmes, et al. Soft Matter 7 (2011) 5188–5193.
[21] E. Smela, O. Inganas, I. Lundstrom, Science 268 (1995) 1735–1738.
[22] E.W.H. Jager, O. Inganas, I. Lundstrom, Science 288 (2000) 2335–2338.
[23] A.W. Feinberg, et al. Science 317 (2007) 1366–1370.
[24] N. Bassik, et al. J. Am. Chem. Soc. 132 (2010) 16314–16317.
[25] X. Zhang, et al. Nano Lett. 11 (2011) 3239–3244.
[26] Y. Liu, et al. Soft Matter 8 (2012) 1764–1770.
[27] J. Ryu, et al. Appl. Phys. Lett. 100 (2012) 161908.
[28] Y.L. Yu, M. Nakano, T. Ikeda, Nature 425 (2003) 145.
[29] P. Techawanitchai, et al. Soft Matter 8 (2012) 2844.
[30] D. Suzuki, et al. Soft Matter 8 (2012) 11447–11449.
[31] A.N. Zaikin, A.M. Zhabotinsky, Nature 225 (1970) 535–537.
[32] S. Maeda, et al. Int. J. Mol. Sci. 11 (2010) 52–66.
[33] Y. Murase, et al. Langmuir 25 (2008) 483–489. , http://dx.doi.org/10.1021/ la8029006.
[34] S. Maeda, et al. Macromol. Rapid Commun. 29 (2008) 401–405.
[35] S. Maeda, et al. Adv. Mater. 19 (2007) 3480–3484.
[36] T. Bai, et al. Soft Matter 8 (2012) 6846–6852.
[37] T.G. Leong, A.M. Zarafshar, D.H. Gracias, Small 6 (2010) 792–806.
[38] L. Ionov, Soft Matter 7 (2011) 6786–6791.
[39] T. Tanaka, et al. Science 218 (1982) 467–469.
[40] M. Doi, M. Matsumoto, Y. Hirose, Macromolecules 25 (1992) 5504–5511.
[41] H.L. Lim, et al. Adv. Funct. Mater. 21 (2011) 55–63.
[42] S. Timoshenko, J. Opt. Soc. Am. 11 (1925) 233–255.
[43] H. Lee, C. Xia, N.X. Fang, Soft Matter 6 (2010) 4342–4345.
[44] K. Haraguchi, K. Murata, T. Takehisa, Macromolecules 45 (2011) 385–391.
[45] M.L. O'Grady, P.-L. Kuo, K.K. Parker, ACS Appl. Mater. Interfaces 2 (2009) 343–346.
[46] Z.B. Hu, X.M. Zhang, Y. Li, Science 269 (1995) 525–527.
[47] P.D. Topham, et al. Macromolecules 40 (2007) 4393.
[48] S. Saha, et al. Angew. Chem. Int. Ed. 51 (2012) 660–665.
[49] G. Stoychev, et al. ACS Nano 6 (2012) 3925–3934.
[50] G. Stoychev, et al. Adv. Funct. Mater. 23 (2013) 2295–2300.
[51] K.E. Laflin, et al. Appl. Phys. Lett. 101 (2012) 131901.
[52] E. Wang, M.S. Desai, S.-W. Lee, Nano Lett. 13 (2013) 2826–2830.
[53] E. Palleau, et al. Nat. Commun. 4 (2013).
[54] E. Reyssat, L. Mahadevan, J. R. Soc. Interface 6 (2009) 951–957.
[55] C. Dawson, J.F.V. Vincent, A.-M. Rocca, Nature 390 (1997) 668.
[56] R. Elbaum, et al. Science 316 (2007) 884–886.
[57] S. Armon, et al. Science 333 (2011) 1726–1730.
[58] R.M. Erb, et al. Nat. Commun. 4 (2013) 1712.
[59] J. Kim, et al. Science 335 (2012) 1201–1205.
[60] J. Kim, et al. Soft Matter 8 (2012) 2375–2381.
[61] H. Thérien-Aubin, et al. J. Am. Chem. Soc. 135 (2013) pp 4834–4839.
[62] Z.L. Wu, et al. Nat. Commun. 4 (2013) 1586.
[63] S. Turcaud, et al. Int. J. Mater. Res. 102 (2011) 607–612.
[64] R. Bashir, et al. Appl. Phys. Lett. 81 (2002) 3091–3093.
[65] J.Z. Hilt, et al. Biomed. Microdevices 5 (2003) 177–184.
[66] K. Liu, H.F. Ji, Anal. Sci. 20 (2004) 9–11.
[67] Y. Zhang, et al. Anal. Chem. 75 (2003) 4773–4777.
[68] J.S. Kim, N. Singh, L.A. Lyon, Angew. Chem. Int. Ed. 45 (2006) 1446–1449.
[69] J. Kim, M.J. Serpe, L.A. Lyon, J. Am. Chem. Soc. 126 (2004) 9512–9513.
[70] L. Dong, et al. Nature 442 (2006) 551.
[71] I. Gorelikov, L.M. Field, E. Kumacheva, J. Am. Chem. Soc. 126 (2004) 15938–15939.
[72] M. Agrawal, et al. Langmuir 24 (2008) 9820–9824.

[73] K.-U. Jeong, et al. J. Mater. Chem. 19 (2009) 1956–1959.

[74] K. Ueno, et al. Adv. Mater. 19 (2007) 2807–2812.

[75] H. Fudouzi, Y. Xia, Adv. Mater. 15 (2003) 892–896.

[76] K. Matsubara, M. Watanabe, Y. Takeoka, Angew. Chem. Int. Ed. 46 (2007) 1688–1692.

[77] Q. Yu, et al. Appl. Phys. Lett. 78 (2001) 2589–2591.

[78] K.-F. Arndt, D. Kuckling, A. Richter, Polym. Adv. Technol. 11 (2000) 496–505.

[79] L. Dong, H. Jiang, Soft Matter 3 (2007) 1223–1230.

[80] D.J. Beebe, et al. Proc. Natl. Acad. Sci. U. S. A. 97 (2000) 13488–13493.

[81] D.T. Eddington, D.J. Beebe, Adv. Drug Deliv. Rev. 56 (2004) 199–210.

[82] L.A.F. Charles Goss, Gray's Anatomy, Lippincott Williams & Wilkins, Better World Books, Mishawaka, IN, U.S.A., 1985,   ISBN 10: 081210644X/ISBN 13: 9780812106442.

[83] J. Shin, S.G. Han, W. Lee, Sens. Actuators B: Chem. 168 (2012) 20–26.

[84] Y. Ma, et al. Angew. Chem. Int. Ed. 50 (2011) 6254–6257.

[85] G.H. Kwon, et al. Small 4 (2008) 2148–2153.

[86] M. Jamal, et al. Adv. Healthc. Mater. (2013), http://dx.doi.org/10.1002/adhm.201200458.

[87] T.S. Shim, et al. Angew. Chem. Int. Ed. 51 (2012) 1489.

[88] Y. Osada, H. Okuzaki, H. Hori, Nature 355 (1992) 242–244.

[89] D. Morales, et al. Soft Matter 10 (2014) 1337–1348.

[90] V. Chan, et al. Sci. Rep. 2 (2012) 857.

[91] E. Smela, Adv. Mater. 15 (2003) 481–494.

[92] E.W.H. Jager, E. Smela, O. Inganas, Science 290 (2000) 1540–1545.

[93] S. Yang, K. Khare, P.C. Lin, Adv. Funct. Mater. 20 (2010) 2550–2564.

[94] T.R. Hendricks, W. Wang, I. Lee, Soft Matter 6 (2010) 3701–3706.

[95] X. Chen, J. Yin, Soft Matter 6 (2010) 5667–5680.

[96] A. Schweikart, et al. Soft Matter 7 (2011) 4093–4100.

[97] A. Schweikart, A. Fery, Microchim. Acta 165 (2009) 249–263.

[98] J. Genzer, J. Groenewold, Soft Matter 2 (2006) 310–323.

[99] D.H. Gracias, Curr. Opin. Chem. Eng. 2 (2013) 112–119.

[100] C.L. Randall, E. Gultepe, D.H. Gracias, Trends Biotechnol. 30 (2012) 138–146.

[101] C.L. Randall, et al. Lab Chip 11 (2011) 127–131.

[102] M. Jamal, et al. Biomaterials 31 (2010) 1683–1690.

[103] M. Jamal, A.M. Zarafshar, D.H. Gracias, Nat. Commun. 2 (2011) 527.

[104] S. Zakharchenko, E. Sperling, L. Ionov, Biomacromolecules 12 (2011) 2211–2215.

[105] V. Magdanz, et al. Angew. Chem. Int. Ed. 126 (2014) 2711–2715.

[106] X. He, et al. Nature 487 (2012) 214–218.

RESEARCH: Review