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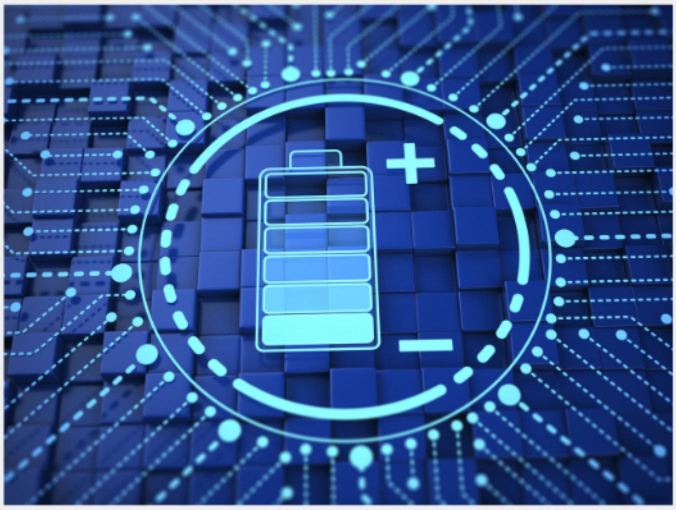

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4D Printing of Hydrogels: A Review

Mathilde Champeau, Daniel Alves Heinze, Thiago Nunes Viana, Edcarlos Rodrigues de Souza, Anne Cristine Chinellato, and Silvia Titotto**

3D printing permits the construction of objects by layer-by-layer deposition of material, resulting in precise control of the dimensions and properties of complex printed structures. Although 3D printing fabricates inanimate objects, the emerging technology of 4D printing allows for animated structures that change their shape, function, or properties over time when exposed to specific external stimuli after fabrication. Among the materials used in 4D printing, hydrogels have attracted growing interest due to the availability of various smart hydrogels. The reversible shape-morphing in 4D printed hydrogel structures is driven by a stress mismatch arising from the different swelling degrees in the parts of the structure upon application of a stimulus. This review provides the state-of-the-art of 4D printing of hydrogels from the materials perspective. First, the main 3D printing technologies employed are briefly depicted, and, for each one, the required physico-chemical properties of the precursor material. Then, the hydrogels that have been printed are described, including stimuli-responsive hydrogels, non-responsive hydrogels that are sensitive to solvent absorption/desorption, and multimaterial structures that are totally hydrogel-based. Finally, the current and future applications of this technology are presented, and the requisites and avenues of improvement in terms of material properties are discussed.

1. Introduction

The main characteristics of additive manufacturing (AM) techniques relate to the layer-by-layer construction nature, which literally adds manufacturing material via layers previously drawn up by computer-aided design (CAD). It leads to a wide design spectrum, precision, and versatility for fabrication of complex structures, in which the geometry of the constructs, the spatial distribution of the materials, and thus the properties of the whole structure are precisely programmed and controlled.[1] It also decreases the number of processing steps when compared to other common manufacturing processes that result in high costs when customized blueprints are needed.

Conventional 3D printing produces static objects.[2] While technologies to produce inanimate 3D objects have continued evolving mainly fed by academia motivation and industry partnerships, some researchers started to move forward to 4D printing to assess the impact derived from responsive objects that could actually respond to environmental stimuli after fabrication (print completion and cure) as a function of time[3–8] via alteration of shape, function, properties,[7] and/or proper displacement.[5] Not all stimulus-responsive components are able to experiment intended transformation when exposed to optimum stimulus because 4D printing requires a set interaction mechanism to plan out the series of shape-shifting behaviors when triggered by the stimulus under an appropriate amount of time.[8] The 4D printing general concept relies predominantly on the following factors—the AM process, types of stimulus-responsive material, stimuli, interaction mechanism, and mathematical modeling, usually undertaken in conjunction with geometric programming using CAD and finite-element analysis (FEA).[8]

Several authors had already mentioned correlation between biologically inspired engineering and advancements in additive manufacturing,[9,10] but Skylar Tibbits pioneered the 4D printing field by performing several conceptual tests at the MIT since 2011[6,11] and introduced its main concepts in his TED talk conference in 2013[12] by anticipating relationships between self-assembly and self-evolving systems found in nature and additive manufacturing blueprints. In physics, 4D, meaning the four common dimensions, refers to 3D space, which adds the dimension of time. In 4D printing, the fourth dimension arises from the ability of the printed structure to change its shape and/or functionality along time when exposed to a given environmental stimulus, during its post-printed lifetime.[4,13–16] 4D printing pioneers opened up the 4D printing field relating it to stimuli via passive energy, meaning that the system should not be imbedded with other sources of energy that could calibrate the amount of energy flown to the system such as electric power.[17] Recently, other research groups started to also consider the possibility of using mixed energy source, including active energy that can be applied locally.[17] Another important

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factor is the ability to self-revert to the original programmed status over a certain period of time in case of stimuli alteration and to withstand responsiveness, although in some cases even partial reversion cycles substantially alter the response and the properties of the material.[18] However, it is expected that the response and reversion processes may not happen in an equal length of time,[19] as several examples found in botany and invertebrate sea life.

Besides shape memory polymers, hydrogels are the other class of polymers that has found application in 4D printing.[16,20–22] Hydrogels are 3D hydrophilic polymer networks that are capable of absorbing a large amount of water without dissolving due to the presence of crosslinking between chains.[23] Even if the definition of 4D printing of hydrogels involves a change of shape and/or functionality of the printed structure along time, the studies have mainly focused on the creation of shape-morphing devices. Smart or stimuli-responsive hydrogels are so-called since their physical or chemical properties can be changed in a controlled fashion when submitted to a specific external stimulus such as temperature, pH, ion concentration, electric field, magnetic field.[24] For various smart hydrogels, the stimulus produces a swelling change. This characteristic has been explored by several authors to generate shape transformations in hydrogel sheets produced with conventional techniques for many years[25] and have appeared to be materials of choice for 4D printing. Non-responsive hydrogels have also been used as composite matrices in which a particle accounts for the responsiveness to a specific stimulus,[5,26] and in combination with other non-responsive hydrogels in multimaterial structures that can hydrate/dehydrate.[27,28] In every case, the change must entail a swelling mismatch in the structure to induce the shape morphing, so controlling the local material composition and structure as well as the spatial arrangement during printing can lead to complex and programmed movements.

First, the 3D printing technologies that have been employed to date in 4D printing (light-based and extrusion-based) are briefly depicted, as well as the required characteristics of the precursor materials adapted to each technique, and the effect of the precursor composition and printing parameters on the properties of the printed object. Then, the hydrogels that have been 4D-printed are described: smart hydrogels are classified by stimulus. Non-responsive printed hydrogels that respond by swelling/deswelling are also reported, as well as multimaterial structures that are totally hydrogel-based and the composites composed of a matrix of hydrogel are also reviewed. Nevertheless, multimaterials systems that are not totally composed of hydrogels are out of the scope of this review. Finally, the current and potential future applications of this technology are described, in addition to some improvement avenues in terms of materials properties for each application that is provided.

2. Printing Technologies and Materials Requirements

Most additive manufacturing processes can support 4D printing if the printed material, also called precursor material, is compatible with the printer.[8,29] The printing process is preceded by the generation of a virtual model of the geometry to be printed, that is drawn up by CAD. This model is then translated to the printer software, and this translation process is highly dependent on the printing technique, since the geometry to be produced is combined with the characteristics of the machine and with processing parameters. Here is presented a brief overview of the two main techniques that have been used up to now in 4D printing of hydrogels, light-based and extrusion-based techniques, as well as the printing parameters that can be adjusted. The characteristics of the precursor solution/gel required for each technique is also described. The inkjet technique that deposits a precursor material drop-by-drop has been employed at the early beginning of the 4D printing of hydrogel, but for having been barely used, it is not included in this work.[6,7]

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Silvia Titotto is the founder and principal investigator of the 4D Printing and Biomimetics-4DB research group. She holds a Ph.D. from Politecnico di Torino in technological innovation and a Ph.D. from the University of São Paulo in design and architecture. She is a tenured associate professor at the Federal University of ABC and holds a permanent professorship at the Graduate Program in engineering and management of innovation. She was a visiting professor at the University of Bologna, Technical University of Silesia, Technical University of Riga, and University of Freiburg. Her research interests are biomimetics, additive manufacturing, and programmable materials.

2.1. Light-Based Printing Techniques

2.1.1. Printer Features and Operation

Light-based printing techniques use photopolymerization to promote the conversion of the monomers present in a precursor

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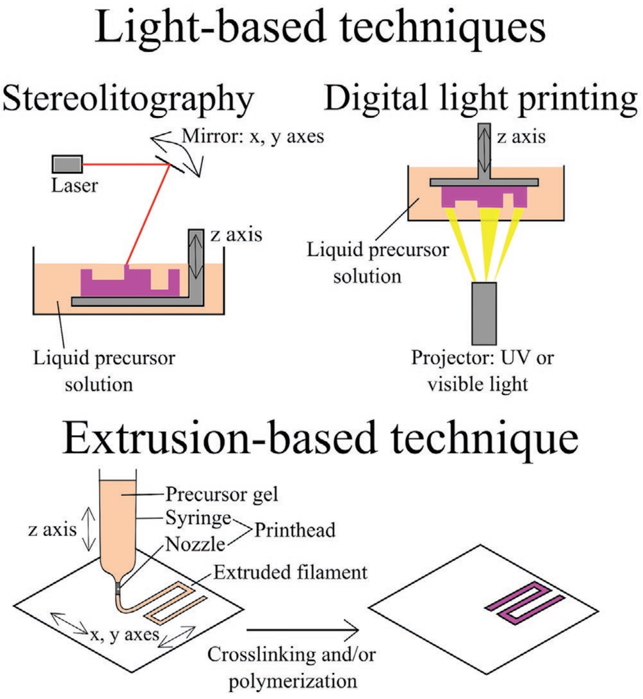

Figure 1. Light-based and extrusion-based printing techniques commonly used in 4D printing of hydrogels.

solution contained in a tank into a cured hydrogel network. A solution layer is exposed to a radiation beam. When the polymerization process of this layer is completed, it is moved vertically to allow the formation of a new layer, which will again be exposed to radiation. Regarding how to radiate the precursor solution, there are two main variants: stereolithography (SLA) that uses a laser to produce a spot-promoting beam,[30] and digital light processing (DLP), which uses a projector to illuminate a specific area,[31] as shown in **Figure 1**.

In the SLA technique, a laser is focused on the precursor solution and the polymerization and crosslinking of monomers occurs at the focus point. The movement of the mirror permits to scan the solution with the laser, where the hydrogel should form. The machine structure (mirrors, handling systems), together with the material characteristics (such as swelling and shrinkage[32,33]), will define the resolution obtained in printing.[34,35] By controlling the exposure time and the intensity of the laser, the characteristics of the polymerized and crosslinked hydrogel in the printed layer can be locally controlled. Therefore, recent work has focused on the study of polymerization kinetics, evaluating the response of the precursor gel to the time of exposure, intensity and depth of cure, in order to obtain printed hydrogels with more robust mechanical properties, produced with faster printing times and better resolution control.[36] The formulation of precursor gels for light-based printing is further explained in Section 2.1.2

In DLP, a projector illuminates the area of the printed layer that should be photopolymerized, which is divided into pixels (smallest unit of area that can be illuminated). Choosing which pixels are illuminated defines the shape of the part to be printed on each layer. The resolution depends on the pixel size and of the z-axis motion system and also on material characteristics, as explored by Han et al., who evaluated the effect of light intensity, layer thickness and adhesion.[37] Regarding the material, polymerization kinetics also plays a role in the resolution. While vertical movements control the polymerization depth, the grayscale is focused on the xy-plane. It is a strategy where the intensity of the light varies in a set of pixels, obtaining a grayscale and therefore avoiding abrupt transitions in the properties of the material in terms of monomer conversion and degree of crosslinking.[28]

2.1.2. Formulation of the Precursor Solution

In light-based printing techniques, a liquid precursor solution, also called photo-curable resin, is used. The solution is composed of a photoinitiator, a photoabsorber, a crosslinker, and a monomer[35,37] or a pre-polymer (polyethylene glycol diacrylate, poly(propylene glycol) dimethacrylate, etc.)[27,38] that can be polymerized and/or crosslinked via free-radical transfer. The photoinitiator absorbs laser light to form radical species that initiate polymerization. Then, monomers or pre-polymers are incorporated into the polymeric network in the region irradiated by the laser spot. Spatial control of light intensity and time of light exposure allow local control of the monomer conversion and crosslinking density, influencing local swelling.[28] The swelling mismatch arises from a density variation, which is possible to obtain from a single precursor solution composition as higher light intensity and longer time of exposure result in higher density of the hydrogel network and lower swelling.

Commercial resins are available, but for a better control of the properties of the printed hydrogel, specific formulations can be developed. The photoinitiator should be selected to accommodate the wavelength of the light source. In DLP, UV-light is generally used but visible light is a safer alternative.[28] Any monomer that is polymerized through free-radical polymerization can be used (*N*-isopropylacrylamide[37] or acrylates such as hydroxyethyl acrylate, hydroxyethyl methacrylate,[28] or acrylic acid[39]), and mixtures of monomers can be interesting possibilities to modulate swelling properties.[19,28,37] For example, the incorporation of 2 wt% of the ionic monomer 3-sulfopropyl methacrylate potassium salt (SPMA) and 5 wt% of aliphatic urethane diacrylate allowed an increase in swelling and a larger stress generation in a copolymer of methacrylates.[19] In another study, 11 wt% of 2,2′-(ethylenedioxy)diethanethiol (EDDET) was added to poly(propylene glycol) dimethacrylate (PPGDMA) resin to reduce the glass transition temperature and the rubbery modulus of crosslinked PPGDMA,[38] which resulted in a higher bending curvature of a bilayer sheet made of PPGDMA as one of the layers. Increasing the monomer concentration and/or the ratio of crosslinker to monomer tend to decrease the swelling degree of the final hydrogel.[37] In order to control the light penetration depth, photoabsorbers can be added to the precursor solution.[38,39] These organic molecules increase the light absorption and accentuate the structural gradient obtained in the z-axis, increasing the control of z resolution.

Considering that the rates of polymerization and photocrosslinking are dependent on the above-mentioned composition of the precursor solution, the light intensity and time of exposure must be adapted every time the formulation is

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modified. A pre-study is necessary to correlate the printing parameters with the network density and its consequent swelling, in order to precisely control the shape-morphing of the printed part.

2.2. Extrusion-Based Printing Technique

2.2.1. Printer Features and Operation

In extrusion-based techniques, the precursor gel, also called ink, is conditioned in a refillable printhead, which comprises a syringe equipped with a nozzle (Figure 1). The deposition operation that consists in the extrusion of a filament can be done either with the aid of compressed air[40,41] or with the use of an electromechanical system.[42,43] The precursor gel is deposited on a platform and either the platform or the printhead moves to control the spatial deposition of the layer in the horizontal plan (*x*, *y* plan in Figure 1). The movement of the printhead generally controls the deposition along the vertical axis (*z*-axis in Figure 1).

Machines with multiple printheads are available, allowing multiple materials to be deposited simultaneously.[43,44] The quality and diameter of the deposited filament are adjusted by the velocity of the moving parts (printhead or platform) of the equipment, by the flow rate of material, and the internal diameter of the nozzle.[44–46] The material and chemical treatment of the platform impacts the wetting properties and consequently influence the thickness of each layer.[47]

Beyond the properties of the precursor gel described in Section 2.2.2 and the printing parameters, the resolution of the printed part is also dependent on intrinsic parameters of the machinery (headstock positioning system, motors characteristics, control of air pressure, encoders).[48]

After the deposition step, post-treatment can be necessary to obtain the final chemical composition in the hydrogel construct, such as promoting the crosslinking of polymeric chains or polymerizing monomers present in the precursor gel composition.[47,49–51] For that reason, the precursor gel and the hydrogel are distinguished and correspond to the extruded material and the material in the final 4D structure, respectively.

Challenges in extrusion printing include polymerization kinetics, because if the kinetics are too slow, there may be problems in keeping the printed form dimensionally stable. Another difficulty is that the precursor gel can eventually cause the extrusion nozzles to clog, resulting in the deposition of material with less accuracy[52] and resolution. The resolution of the technique has been reported to be in the range of 100–150 µm,[52,53] but can be improved by reducing the deposition rate and the nozzle diameter.[54]

Furthermore, the development of the precursor gel is a challenge itself, as it needs specific properties in order to obtain good resolution of the printed form, which is further discussed in Section 2.2.2.

2.2.2. Rheological Requirements of the Precursor Gel

For the use of hydrogels in 3D/4D printing through extrusion-based printing, one of the main characteristics that need to be understood is the printability of the precursor gel. Printability, in this case, is not only related to the behavior of the material when being sheared in the nozzle of the printer, but also to its performance and stability after being printed.[49,55] As stated by Kim et al.,[56] three main properties need to be fulfilled to obtain a stable hydrogel for 3D printing. The first one is relatively high viscosity; the second is strong shear-thinning behavior, and the third is crosslinking mechanisms.[56] Gao et al.[55] complement that viscosity alone is not a determining factor in the stability of precursor gel after printing. Instead, it is important to understand the viscoelastic relationship between loss modulus (G″) and storage modulus (G′) of the material, called tan δ (G″/G′). Small values of tan δ represent a material with a predominant G′ value, that is, a solid-like behavior, resulting in a stable hydrogel.[55] Thus, it is extremely important to understand and optimize the rheological behavior of the material when developing a precursor gel for 4D printing, which can be a challenging task.[49] Exploring further these printability aspects, precursor gel requirements can be categorized into two main parts. The first one is the behavior of the gel during extrusion, called extrudability, and the second one is its behavior after being printed, denoted by shape fidelity. **Figure 2** summarizes the main variables for the extrudability and shape-fidelity, and related rheological tests to characterize a precursor gel for extrusion-based printing.

Extrudability: Extrudability is related to the stress needed to print the precursor gel through the nozzle.[55] In general, it is expected a gel with higher viscosity, for better stability and to avoid the formation of tension-driven droplets during extrusion.[57] The overall viscosity of a precursor gel can be controlled mainly by two aspects of its composition: its polymer concentration and the molecular weight of the polymer.[57] Increasing these parameters results in higher overall viscosity.[50,58] While high viscosity is important to avoid dripping and for the stability of the printed form, higher viscosities can result in difficulties during printing.[55] Thus, inks should present shear-thinning behavior, to increase its extrudability. This behavior is defined as a decrease in viscosity as a function of shear rate, that is, for higher shear rates, as when it is being sheared through the nozzle, the hydrogel will show smaller values of viscosity. This behavior occurs as the structure of the material reorganizes itself during extrusion, facilitating the flux of material. However, when it is no longer being sheared, the structure should recover, showing higher viscosity values.[59–61] Precursor gels naturally exhibit shear-thinning behavior, as they are composed of polymers, whose chains align during shearing. However, it is possible to enhance this behavior in precursor gels by adding specific particles (graphene oxide, nanofibrillated cellulose, laponite, etc.) to its composition, which increases the zero shear rate viscosity of the material, without increasing as much the viscosity at high shear rates.[46,49,58,62]

Another important aspect of the printability of a gel is its recovery time. As the material goes through the nozzle and its viscosity reduces, it needs to quickly recover after being extruded. The recovery time is related to how fast the material viscosity recovers after being extruded.[58]

Shape Fidelity: The second important rheological aspect to be discussed for extrusion-based printing is shape fidelity. During printing, several layers are deposited one over the other,

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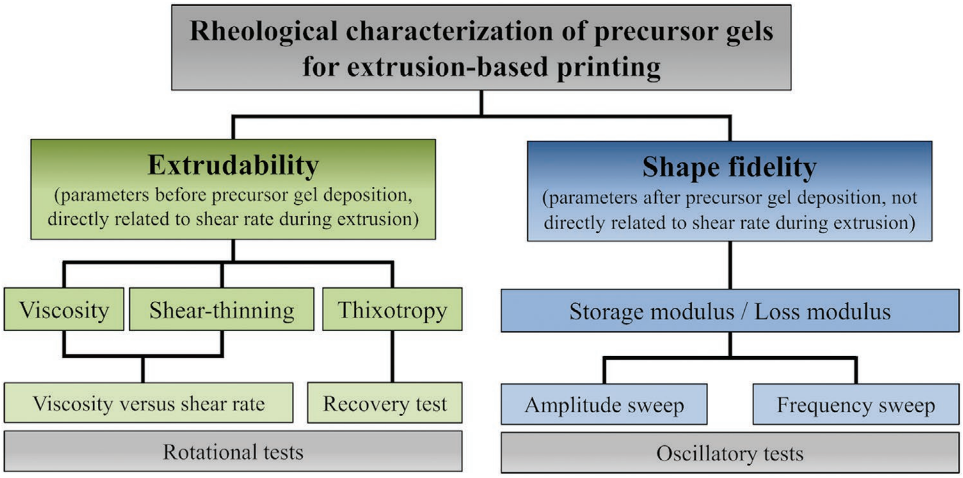

Figure 2. Summary of tests for rheological characterization of precursor gels based on key variables for extrusion-based printing.

which can cause the structure to collapse and lose its form. In addition, poor rheological properties leads to an inconstant printing filament diameter and to a flow of the material after being extruded, resulting in a larger width and smaller height of the printed shape. These problems can be diminished by controlling the viscoelasticity of the hydrogel, via decreasing the tan δ value. As hydrogels are viscoelastic materials, the storage modulus (G') represents their elastic behavior, while the loss modulus (G'') represents its viscous behavior. Thus, tan δ values below 1 represent a solid-like material, while over 1 a liquid-like. The viscoelasticity of the precursor gel can be characterized by rheology on oscillatory tests of amplitude and frequency sweep (Figure 2).[55]

As well as the shear-thinning behavior, the storage and loss modulus of the precursor gel can be modified not only by the composition of the material, but also by its molecular weight. Higher concentrations of hydrogel as well as higher molecular weight lead to smaller tan δ values.[50] Another alternative to improve the solid-like behavior of a precursor gel is by the addition of rheology modifiers that can be particles such as graphene oxide[58] and clays.[46]

3. Stimuli-Responsive Hydrogels

Hydrogels are used in 4D printing due to their swelling properties to create shape-morphing structures.[18] Smart hydrogels have been extensively employed because of their ability to respond to an external stimulus (temperature, pH, ionic strength and ionic concentration, electric field and light, etc.) by suffering a change in their swelling degree, as it will be further described. Since the number of smart-hydrogels is relatively limited, the capacity of non-responsive hydrogels to swell in aqueous media and either de-swell when dried or to change their swelling degree in another media, has also been explored, in that case the solvent absorption/desorption phenomena can be considered as the stimulus that triggers the change of shape. However, if the composition and structure of the hydrogel (smart or not) is isotropic, hydrogels expand isotropically and it only results in a linear expansion of the structure. In order to produce complex shape-transformations such as bending, folding, or twisting of the structures, it is necessary to create a swelling mismatch in the actuating part to generate internal stress.[11,63] In the literature, two kinds of use of hydrogel in shape-morphing structures can be distinguished: a) use of a single hydrogel chemical nature that exhibits different swelling degrees along the structure (anisotropy either due to anisotropic particles or due to different crosslinking degrees and densities); b) multimaterials hydrogel structures.

Shape-morphing also depends on the volume fraction of the materials as well as on the swelling variation upon application of the stimulus. Other relevant core aspects in the development of a shape-morphing structure produced by 4D printing is the actuation speed, the mechanical strength of the hydrogels, and the capacity to withstand several cycles of stimuli application without disintegrating and modifying the amplitude of the response.

Herein, hydrogels used in 4D printing are presented. First, smart hydrogels classified by stimulus are introduced. Then, non-stimuli responsive hydrogels and their use in multimaterials and composite structures are presented. The speed of response and relevant properties such as mechanical strength for the applications of the printed hydrogels are highlighted. The different hydrogels that have been printed and their properties are listed in **Table 1**. The advantages and limitations of each kind of stimulus are summarized in **Table 2**.

3.1. Smart Hydrogels: Classification by Stimulus

3.1.1. Temperature

As reported in Table 2, the most common stimulus used to bring about shape-changes in 4D printed hydrogels is heat. Poly(*N*-isopropylacrylamide) (PNIPAm) is by far the polymer that has been the most chosen to create thermo-sensitive printed structures.[5,26,37,43,44,50,64–68] In water, PNIPAm possesses a lower critical solution temperature (LCST) of 32 °C due to phase separation. Below its LCST, PNIPAm is hydrated. Nevertheless, above the LCST, its isopropyl side groups dehydrate partially

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Table 1. A review table for 4D printed hydrogels, the printing technique, the stimulus triggering the change of shape, and the demonstrated applications.

Stimulus	Material responsible for shape-morphing or functionality change	Material (Hydrogel: composition of the precursor material)	Printing technique and post-treatment steps	Proposed application(s)	Authors	Year	References
Temperature	Agarose	Agarose/PAAm: agarose + AAm + crosslinker + photoinitiator + laponite nanoclay	Extrusion		Guo et al.	2018	[49]
Temperature	PNIPAm	Alginate/PNIPAm: alginate + NIPAm + crosslinker + photoinitiator	Extrusion UV photopolymerization of the printed parts Immersion in $CaCl_2$ solution to crosslink alginate	Valve that opens/closes depending on the temperature of the water flowing through it	Bakarich et al.	2015	[44,66]
Temperature	PNIPAm	PNIPAM: NIPAm + crosslinker + photoinitiator + photoabsorber	Projection micro-stereolithography	Gripper Dumbbell-shaped structure	Han et al.	2018	[37]
Temperature	PNIPAm + NFC composites (anisotropic orientation of NFC)	PNIPAm/Nanofibrillated cellulose: NIPAm + NFC + crosslinker + photoinitiator + nanoclay	Extrusion UV photopolymerization	Flowers biomimetic	Gladman et al., Lewis	2016, 2017	[5, 84]
Temperature	PNIPAm	Bilayer structures: a) PNIPAm: NIPAm + crosslinker + photoinitiator + sodium alginate (rheological modifier) b) PAAm: AAm + crosslinker + photoinitiator + sodium alginate	Co-extrusion of the two precursor gels in a viscous solution UV photopolymerization of the printed bilayer		Uchida and Onoe	2019	[43]
Temperature	PNIPAm	Bilayer structures: a) PNIPAm: NIPAm + crosslinker + photoinitiator + laponite nanoclay (rheological modifier) b) PAAm: AAm + crosslinker + photoinitiator + laponite nanoclay	Co-extrusion of the two precursor gels UV photopolymerization of the printed bilayer	Tubular structures that mimic the buckled surface observed in cactus	Liu et al.	2019	[67, 69]
Temperature + Hydration	Melting of SA segments (temperature) DMAAm segments (hydration)	Bilayer structures: 2 grades of poly(*N*,*N*-dimethyl acrylamide-*co*-stearyl acrylate) varying the SA/DMAAm ratio: SA + DMAAm monomers + crosslinker + photoinitiator	Stereolithography	Gripper	Shiblee et al.	2019	[2]
Temperature	PNIPAm/pHEMA (Swelling mismatch between the two hydrogels)	Multimaterial structures: a) Polyether-based/PNIPAm: polyurethane pre-polymer + NIPAm + crosslinker + photoinitiator b) Polyether-based polyurethane/pHEMA: polyurethane pre-polymer + HEMA + crosslinker + photoinitiator	Extrusion (2 heads)		Naficy et al.	2017	[50]
Temperature	PNIPAm	Bilayer structures: a) PNIPAm: NIPAm+ crosslinker + photoinitiator + carbomer (rheological modifier) b) PAAm: AAm + crosslinker + photoinitiator + carbomer	Extrusion		Chen et al.	2019	[26]
Temperature	PMEOMA (Swelling mismatch and drying in air)	Copolymer of PEGDA+ HEMA+ SPMA + 30wt% of MEO_2MA + aliphatic urethane diacrylate + photoinitiator	Stereolithography	Thermal-responsive hydrogel gripper	Ji et al.	2019	[19]
Temperature + pH	F127DA (Temperature) + PAA (pH)	PAA/F127DA:Copolymer of AA and F127DA + photoinitiator	Stereolithography	Valve that responds to temperature and pH of the water flowing through it	Dutta and Cohn	2017	[35]
pH	PAA	Copolymer of PEGMA + 5 to 30 wt% of AA+ photoinitiator + photoabsorber + different dimethacrylate crosslinkers	Stereolithography	Scaffolds for tissue engineering	Garcia et al.	2018	[39]

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Table 1. Continued.

Stimulus	Material responsible for shape-morphing or functionality change	Material (Hydrogel: composition of the precursor material)	Printing technique and post-treatment steps	Proposed application(s)	Authors	Year	References
pH	P2VP	Filaments for FDM of P2VP + ABS (reinforcing material)	Fused deposition modeling Crosslinking of the printed part with DBB and quaternization with BE	Flow regulating device sensitive to pH	Nadgorny et al.	2016	[73]
Ionic concentration Swelling/deswelling	Alginate (Ca^{2+} concentration) Alginate and hyaluronic acid (Swelling/deswelling)	Alginate and hyaluronic acid modified with methacrylate groups, with or without cells, covalently crosslinked	Extrusion	Hollow self-folding tubes of small diameters (as low as 20 µm)	Kirillova et al.	2017	[47]
Ionic strength	PSPMA	Copolymer of HEA + HEMA + SPMA + polycaprolactone diacrylate (PCLDA) as crosslinker + photoinitiator	Visible light Specific technique developed		Huang et al.	2017	[28]
Ion concentration and ionic strength	PNIPAm	3 layers: a) (P(AA-*co*-AAm)) b) (P(AA-*co*-NIPAm)) c) P(AA-*co*-AAm))/P(AA-*co*-NIPAm)	Extrusion Crosslinking of PAA by Fe_3+ in $FeCl_3$ solution	Grips	Zheng et al.	2018	[79]
Electric field	PAA	PAA: AA + PEGDA as crosslinker + photoinitiator	Projection microstereolithography Immersion of the printed structure in electrolyte to ionize the carboxylic groups of PAA	Soft robotic actuations including gripping, transporting, and bidirectional locomotion	Han et al.	2018	[81]
Light temperature	SP (presence/absence of blue light) PNIPAm (Temperature)	PNIPAm matrix containing fibers functionalized with spirobenzopyran (SP) chromophores	Simulation		Kuksenok et al.	2016	[64]
Temperature Near Infrared light	PNIPAm (Temperature) RGO transfert the energy of the light into thermal energy provoking thermal-transition of PNIPAm (light)	Multimaterials structure: a) PNIPAm + reduced graphene oxide (RGO: photo-thermal agent) b) PAAm	Photolithographic polymerization to produce stripes Injection of NIPAm/RGO solution in the interspaces Thermal polymerization of PNIPAm		Wang et al.	2019	[51]
Magnetic field	Magnetic field (Fe_3O_4)	PAAm + carbomer (rheological modifier) + 10% w/v ferromagnetic Fe_3O_4 nanoparticles	Extrusion		Chen et al.	2019	[26]
Desolvation and swelling in acetone/deswelling by acetone evaporation in air	PEG—Desolvation and swelling/deswelling	PEG: PEGDA + photoinitiator + photoabsorber	Digit light processing	Complex shapes	Zhao et al.	2017	[27]
Hydration/dehydration Swelling mismatches between the two materials	PEG/PPG	Multimaterial structure: a) PEG: PEGDA + photoinitiator + photoabsorber b) PPG: PPGDA + EDDET thiol (to reduce the Tg and modulus of PPGDA) + photoinitiator + photoabsorber	Digit light processing		Zhao et al.	2018	[38]

Table 1. Continued.

Stimulus	Material responsible for shape-morphing or functionality change	Material (Hydrogel: composition of the precursor material)	Printing technique and post-treatment steps	Proposed application(s)	Authors	Year	References
Hydration/dehydration Swelling mismatches between the two materials	Carboxymethyl cellulose	Multimaterial structure: a) Carboxymethyl cellulose/HEC/Cellulosic fibers (50% volume fraction, width 14.2 ± 2.6 µm) + montmorillonite (rheological modifier) + citric acid (crosslinker). b) Carboxymethyl cellulose/HEC + citric acid	Extrusion Temperature (120 °C) to promote crosslinking with citric acid	Bioinspired by pinecone	Mulakkal et al.	2018	[42]
Hydration/dehydration Swelling mismatch due to anisotropic orientation of NFC	PDMAAm + NFC composites (Anisotropic orientation of NFC)	PDMAAm/Nanofibrillated cellulose: DMAAm + photoinitiator + nanoclay + nanofibrillated cellulose	Extrusion UV photopolymerization	Flowers biomimetic	Gladman et al.	2016	[5]
Hydration/dehydration	Patented polyacrylated composition	Polyacrylated monomer (patented composition): Vinyl caprolactam + polyethylene + epoxy diacrylate oligomer + photoinitiator	Inkjet UV photopolymerization layer-by-layer		Raviv et al.	2014	[7]
Hydration/dehydration	Hydrophilic UV curable precursor solution (Not detailed)	Hydrophilic UV curable precursor solution (not detailed)	Inkjet UV photopolymerization layer-by-layer		Tibbits et al.	2014	[133]

resulting in water expulsion and a consequent contraction of the hydrogel.[65] This volume transition from an expanded to a collapsed state is reversible. PNIPAm is a biocompatible hydrogel that is widely used in biomedical applications since its LCST is close to the body temperature. However, the PNIPAm LCST can be shifted by adding co-monomers during its synthesis.[37] This polymer is obtained by the free-radical polymerization of *N*-isopropylacrylamide (NIPAm) that can be either thermally[51] or light-induced.[5,37,43,50,66,68,69] PNIPAm networks are obtained by chemical crosslinking[26,37,50,66] commonly with *N,N'*-methylenebisacrylamide (MBAAm) or by physical crosslinking using nanoclay, for example.[5] It can be either printed by light-based techniques[37,68] or extrusion of a gel precursor containing the monomer and a gelification agent (nanoclays,[69] alginate,[43] carbomer,[26] etc.) followed by polymerization of the monomer in the printed part.[5,26,43,50,64,66,69]

Bakarich et al. added alginate in the NIPAm solution because of its gelation capacity in the presence of divalent cations[66] and because of superior mechanical properties of alginate/PNIPAm hydrogels when compared to pure PNIPAm, which is fragile. They investigated the influence of varying the NIPAm content on the rheological properties and gelation behavior of the precursor gel, and on the swelling behavior and mechanical properties of the polymerized and crosslinked hydrogel. By increasing the concentration of NIPAm from 10 to 20 w/v%, insignificant change in the swelling degree was observed below LCST. On the contrary, the swelling decreased with the increased NIPAm concentration above LCST due to the higher contraction capacity of the polymer. Cooling the alginate/PNIPAm hydrogels containing 10 to 20 w/v% of NIPAm from 60 to 20 °C implied in a linear expansion ranging from 41 to 49%, respectively. For all hydrogel compositions, the tensile strength and elastic modulus at 60 °C (low-swollen state) were higher than at 20 °C (high-swollen state). Besides, if the ionically crosslinked alginate network improved the mechanical properties of the hydrogels at 20 °C, it has been shown that it decreased the

Table 2. Advantages and limitations of 4D printed hydrogel-based structures for different stimuli.

Stimulus	Advantages	Limitations	References
Temperature	Ease of operation	Slow response	[5,26,35,37,43,49,64,66,69]
pH	Ease of preparation of the solutions	Need of pH solutions; slow response	[35,39, 73]
Ion concentration	Ease of preparation of the solutions	Need of ionic solutions	[28,47,79]
Electric field	Fast response	Need of electrolyte and electrodes	[81]
Light	Remotely controlled	Difficult to control the penetration of light intensity into depth	[64]
Magnetic field	Remotely controlled	Only achievable with particles	[26]
Absorption/desorption	Ease of operation	Slow response	[5–7,27,38,42]

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tensile strength at 60 °C. The authors printed a multimaterial valve in which the alginate/PNIPAm hydrogel was able to control the flow of water by contracting and blocking the flow when the temperature of the water was above the LCST.

Similarly, Naficy et al.[50] developed a precursor gel composed of NIPAm and polyether-based polyurethane (PU) which composition permitted to tune the printability, the swelling ratio and to get robust mechanical properties. Once printed, NIPAm was polymerized by UV-exposure, thus creating an interpenetrated network of PNIPAm/PU. Preliminary tests permitted to observe a phase separation between PNIPAm and PU provoked during UV-induced polymerization when using water as solvent at room temperature. Therefore, the authors chose ethanol as solvent. Such phase separation should be avoided since it results in poor mechanical properties. Surprisingly, the mass ratio of PU/NIPAm did not affect the swelling ratio of the hydrogels, but increasing the length of the polyether segment (number of ether units varied from 5 to 70) of PU leads to an increase in the swelling. Concerning temperature, at 60 °C, the resulting hydrogels exhibit a swelling ratio 380% lower when compared to the swelling ratio at 20 °C, leading to a 24–55% linear dimensional change. However, the LCST of PNIPAm was shifted to higher temperatures as the length of PU segment decreased. The mechanical characterization of the hydrogels in compression, tension and in loading-unloading cycles of compression were found to be similar to that of the PU network, and the tensile strength and elongation at break were significantly superior at 60 °C than at 20 °C (1150 ± 15 kPa and 275 ± 14% at 60 °C, and 397 ± 9 kPa and 68 ± 7% at 20 °C for a PU with ten ether units in the polyether segment).

Han et al.[37] deeply investigated the influence of precursor solution compositions (chemical crosslinker/NIPAm ratio and NIPAm concentration) on the swelling behavior of PNIPAm printed with Projection Microstereolithography (PμSL) below and above its LCST.[37] They used the positively charged ionic methacrylamidopropyltrimethyl-ammonium chloride (MAPTAC) co-monomer to shift the LCST to higher temperatures (in the range of 30–40 or 40–60 °C depending on the molar ratio of MAPTAC to NIPAm). They printed a dumbbell-shaped structure with a left half made of pure PNIPAm and the right half made of PNIPAm with 0.4 M of MAPTAC. As shown in **Figure 3**, both sides were similarly fully swollen at low temperature, whereas upon temperature increase, the left half begun to shrink earlier (35 °C) than the right side creating a structure that changes symmetry with temperature variation.

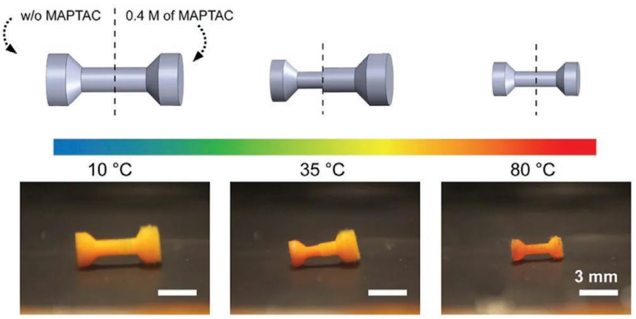

Figure 3. The dumbbell-shaped structure is made of two hydrogels compositions: the left half is pure PNIPAm and the right half is made of PNIPAm with 0.4 M of MAPTAC, an ionic monomer. When immersed in water at low temperature, the two parts are similarly fully swollen. When the water temperature increases, the left half shrink at 32 °C that corresponds to its LCST. A further increase of temperature provokes the shrinkage of the right half, and at 80 °C a symmetric structure is obtained again. Reproduced under the terms of a Creative Commons Attribution 4.0 International License.[37] Copyright 2018, Springer Nature.

Besides PNIPAm, other hydrogels that also possess a LCST have been explored, such as poly(2-(2-methoxyethoxy) ethyl methacrylate) (PMEOMA) or poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO). Ji et al.[19] produced a thermal-responsive gripper using DLP technique to copolymerize 2-(2-methoxyethoxy)ethyl methacrylate (MEO_2MA) and a non-responsive hydrogel (polyethylene glycol diacrylate (PEGDA) and 2-hydroxyethyl methacrylate (HEMA)). Hydrogel rectangular strips were printed layer-by-layer. Highly crosslinked grooves were printed on one side of the strips. By controlling the orientation of the grooves with respect to the length of the strips, perpendicularly or with a 45° inclination, bending or curling movement of the strips were obtained, respectively. The copolymer LCST in water was around 32 °C. Below and above the LCST, the hydrogel absorbed 80% and 20% of water, respectively. This change in swelling behavior permitted the curling of the branch of a gripper at a temperature below the LCST and the closing of the gripper. A ball of 0.15 g could be captured by the gripper in a water bath at room temperature (below LCST), which was then removed from this bath and placed into a bath with warm water (60 °C) to recover its original shape and to release the ball.[19]

PEO-PPO-PEO triblock copolymers are thermoresponsive polymers that are extensively used in drug delivery, wound healing, and tissue engineering due to their biocompatibility. These polymers are known by their commercial names Poloxamers or Pluronics. In aqueous solution, by increasing their concentration or the temperature of the solution, the unimers self-assemble into micelles, which form a hydrophilic corona of PEO blocks while the PPO blocks form the hydrophobic core. Upon a subsequent increase in concentration or temperature, the micelles organize into a liquid crystal structure, provoking the gelation of the solution.[70] This thermal behavior is reversible and the gelation temperature can be tuned by controlling the concentration of the solution. Due to the shear-thinning behavior of the gel and to the possibility of controlling the rheological properties, gels of PEO-PPO-PEO triblock copolymers have been widely used as extrusion gel, inclusively in bioprinting. Dutta et al. modified the chain end of Pluronic F127, $(EO)_{99}$-$(PO)_{65}$-$(EO)_{99}$ to get dimethacrylated unimers (F127DA).[35] The methacrylate groups allow to crosslink the micelles covalently or to react during the free-radical polymerization of another monomer. In that study, acrylic acid (AA) was copolymerized with F127DA by SLA. The printed parts exhibited an enhanced swelling at low temperature in comparison to temperatures above the gelation temperature of F127, and the authors showed the possibility to develop thermosensitive valves (**Figure 4**).

Agarose is another thermoresponsive hydrogel that thermoreversible sol-gel transition is used to produce shape changes.[49] Flexible agarose chains are dissolved in the sol state above 35 °C, whereas the chains self-assemble below this temperature

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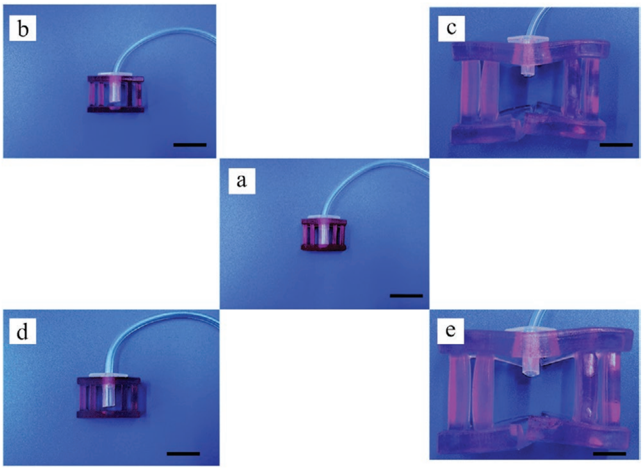

Figure 4. Printed valve structure of PAA/F127DA sensitive to pH due to the PAA polymer and to temperature due to F127DA, submitted to different conditions of pH and temperature (pH/temperature): a) dry; b) 2.0/37 °C; c) 7.4/37 °C; d) 2.0/6 °C; e) 7.4/6 °C (Bar: 2 cm). Reproduced with permission.[35] Copyright 2017, Royal Society of Chemistry.

and form nanofibers that aggregate through H-bonds into a tightly packed 3D network.[71] Guo et al.[49] prepared a precursor gel containing agarose, acrylamide (AAm), and laponite to produce printed pieces by inkjet printing at 95 °C (sol state of agarose). After printing, poly(acrylamide) (PAAm) polymerization and chemical crosslinking was carried out, resulting in a tough double network hydrogel in which the agarose nanofibers act as reinforcement at 35 °C, as shown in **Figure 5**a. By heating the hydrogel in the range of 55–85 °C, the nanofibers are disassembled into flexible chains inside the crosslinked PAAm matrix, thus softening the hydrogel, as shown by the decrease of the storage modulus E' in Figure 5d. Different pieces were printed and such phenomenon was explored by cooling down the structures to 35 °C, then heating up to 95 °C, imposing some deformation, and cooling it back again, maintaining the deformation. When heated again, the original shape was recovered and the damages created in the hydrogel network during deformation were restored, showing healing capacity due to the sol-gel transition of agarose (Figure 5b,c).

Using copolymers composed of blocks of swellable hydrogel and blocks of crystalline polymer is an interesting strategy to obtain a thermosensitive hydrogel. The crystalline parts act as physical crosslinkers, avoid the dissolution of the material and restrict the swelling of the hydrogel blocks. The higher the proportion of crystalline repetitive units in the copolymer, the lower is the swelling degree. Then, when the system is submitted to a temperature higher than the melting temperature of the crystalline blocks, these crosslinking points disappear and an increase in the hydrogel swelling is noticed.[2] As a consequence, the contrast in the swelling degrees below and above the melting temperature of the crystalline segments is accentuated when the content of crystalline blocks is high. This change in swelling is also accompanied by a decrease of the actuation force of the system, since the crystalline regions increase the mechanical stiffness and mechanical resistance. Recently and for the first time, Shiblee et al. explored such kind of material

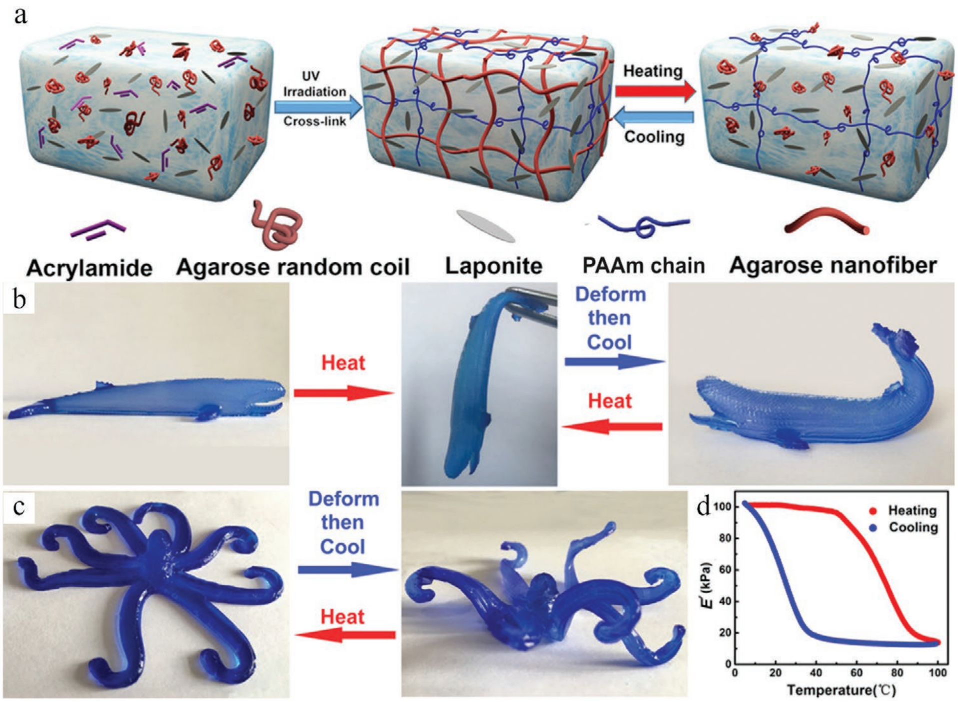

Figure 5. Thermo-responsive hydrogel of agarose, PAAm, and laponite: a) Scheme representing the polymerization and crosslinking of AAm by UV-light, followed by the reversible self-assembly of agarose to form nanofibers below 35 °C; b) a printed whale like hydrogel changes its shape, being softened and deformed at high temperature and then cooled down while maintaining the deformation; c) softening and hardening cycles of an octopus like hydrogel; d) evolution of storage modulus (E′) during heating and cooling cycles due to agarose thermosensitivity. Adapted with permission.[49] Copyright 2018, American Chemical Society.

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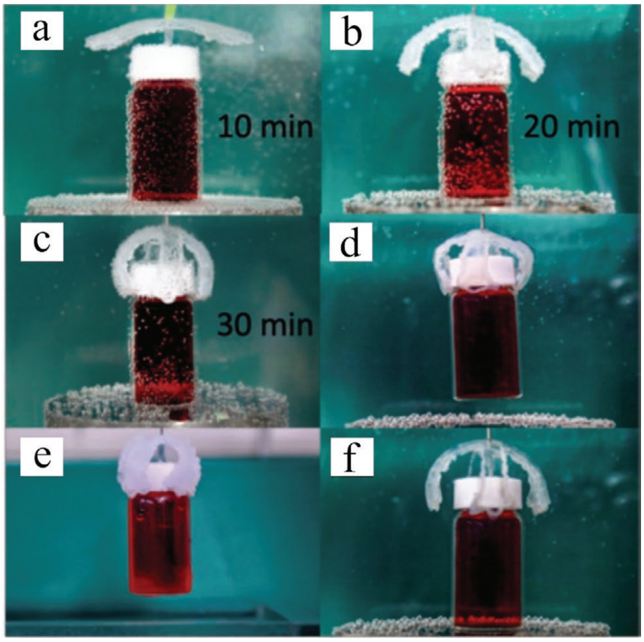

Figure 6. Gripper consisting of a bilayer structures containing two grades of copolymers of P(DMAAm-*co*-SA) with different SA contents, that thermo-sensitivity is due to the melting and recrystallization of the SA blocks: immersed in hot water (50 °C): a) after 10 min, b) after 30 min, c) in the gripped state, d) releasing the vial after 20 min immersed in cold water (30 °C), e) releasing the vial in air at room temperature, and f) releasing the vial in water at 70 °C due to the shape memory property of the layer with a higher SA content. Adapted with permission.[2] Copyright 2019, Wiley-VCH.

and printed a bilayer sheet of poly(*N,N*-dimethyl acrylamide-*co*-stearyl acrylate) (PDMAAm-*co*-SA) of two polymers containing different proportions of the crystalline monomer stearyl acrylate (SA).[2] The temperature increased the swelling degree, but also the deswelling kinetics in air due to faster water evaporation. The deformation of the bilayer system, and the reversibility and response time were shown to be dependent on the temperature, allowing the manufacture of a thermoresponsive gripper (**Figure 6**). In the bilayer structure, the layer that contains a higher proportion of SA permits to control the response time and recovery process along with change of temperature, whereas the other layer is responsible for the high swelling degree.

3.1.2. pH

pH-responsive hydrogels are highly studied as stimuli responsive polymers in 4D printing. The change of pH of the surrounding media triggers a structural or chemical change that alters the swelling. Polyelectrolyte hydrogels have acidic or basic pendant moieties on the polymer chains that can protonate or ionize with a variation of the pH of the surrounding medium, and are good candidates for 4D printing.

Poly(acrylic acid) (PAA) is a well-known pH-responsive polymer that is a weak acid with a pK_a around 4.3. When immersed in a medium which pH is below the pKa value, the carboxylic groups of PAA are protonated, whereas they ionize to form carboxylates above the pKa. The ionization creates mobile positive charges in the solution and fixed negative charges on the polymeric chains that causes electrostatic repulsion between the chains and a consequent increase in the swelling degree of the hydrogel network. PAA is easily polymerized by free-radical polymerization of AA and covalently or ionically crosslinked. It is used as superabsorbent and its low cost makes this hydrogel attractive. However, it suffers from low mechanical properties that limit its application in 4D printing. In their work, Dutta and Cohn[35] printed a system that has proved[72] superior tenacity, consisting of a copolymer of PAA crosslinked with micelles of F127DA. As already explained, F127DA is responsible for thermal-responsive properties while AA performs as the pH-sensitive monomer. By increasing the ratio between AA and F127DA, a more pronounced pH-sensitivity was noticed. A wide range of water uptakes was obtained by tuning the composition of the hydrogel and combining the responsiveness of the two components (water uptake up to ≈5000 wt%), permitting to create a valve sensitive to pH and temperature of the fluids, as shown in Figure 4.

In another work from Garcia et al.,[39] AA was copolymerized with poly(ethylene glycol) methacrylate (PEGMA) to create a pH-sensitive scaffold for tissue engineering with antimicrobial properties,[39] using SLA printing technique. Varying the amount of AA between 5 and 30 wt% in the precursor solution varied the swelling difference between basic and acidic pH, and all hydrogel chemical compositions changed their swelling back and forth upon environmental pH variation. However, the increase in AA content tended to reduce the compressive modulus from 26 to 15 MPa.[39]

In an original work, Nadgorny et al.[73] produced filaments for FDM (Fused Deposition Modeling) of poly(2-vinylpyridine) (P2VP) reinforced with acrylonitrile-butadiene-styrene (ABS) and printed these filaments using a simple low-cost commercial FDM printer.[73] P2VP undergoes a globule-to-coil transition upon protonation below pH of 4.0 leading to an increase in its swelling degree. Once printed, the pyridine groups were covalently crosslinked with 1,4-dibromobutane (DBB) to ensure sample integrity in aqueous media, and quaternized with 1-bromoethane (BE) to tune the charge on P2VP, thus increasing its swelling degree. Varying the crosslinking degree and the quaternization degree, different swelling kinetics and swelling degrees were obtained in solution of pH 2.0. The authors created a flow-regulating device by filling a glass capillary with such crosslinked and quaternized P2VP and showed a significant decrease of the flow rate when the pH of the flowing solution was changed from pH ≤ 3.0 to pH ≥ 7.0.

3.1.3. Ion Concentration and Ionic Strength

Ion concentration and ionic strength are important parameters that influence sweling degree in hydrogels. The ionic strength is a measure of concentration of all electrolytes dissociated into ions when dissolved in water. Ions are used in different manners to trigger changes in hydrogel swelling, depending on the chemical structure of the hydrogels. First, ionic interactions have been extensively applied to form physical crosslinking in charged hydrogels. Di- or tri-valent cations are used to create

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ionic crosslinking of anionic polymers, which most common example is alginate that can be crosslinked by divalent metal cations.[74] The swelling degree of these hydrogels is controlled by the crosslinking density, that is, the concentration of cations in the material.[75] This first strategy was used to tune the behavior of alginate and hyaluronic acid, two polysaccharides that are highly used in bioprinting due to their low cost, biocompatibility, shear-thinning behavior, and their capacity to serve as cell support and to promote cell differentiation in vitro. In order to make them photo-crosslinkable, Kirillova et al.[47] reacted them with methacrylic anhydride to form methacrylated alginate (AA-MA) and methacrylated hyaluronic acid (HA-MA). Modified-polymer gels were extruded to form thin rectangular films that were further exposed to UV-light and a crosslinking gradient along the film thickness was created. Once immersed in aqueous solution, the films self-bended to form tubes that diameters depended on the immersion medium among other parameters. Indeed, the swelling of both hydrogels decreased in the presence of monovalent ions that screened the charges present along the polysaccharides chains. Moreover, the swelling ratio of alginate could be even more reduced, about ninefold, in the presence of 0.1 м of Ca^{2+} due to ionic crosslinking of alginate. A reversible folding/unfolding movement of the tubes was obtained in response to the absence/presence of Ca^{2+}, respectively. In the presence of Ca^{2+} in the immersion solution, the hydrogel was stiff and swelled scarcely, resulting in the unfolding of the tubes. By immersing the unfolded tubes in a solution containing a chelating agent that binds to Ca^{2+}, the ionic crosslinking degree was reduced, thus the AA-MA hydrogel swelled and the tubes folded again.

The alteration in the ionic strength of the surrounding solution of polyelectrolyte hydrogels impacts their swelling behavior. When placed in an electrolyte, the groups of the polymer chain are ionized and counterions are formed in the hydrogel. When an osmotic pressure is developed between the hydrogel and the electrolyte solution, water and hydrated counterions diffuse into the hydrogel to equilibrate the concentrations of counterions, thus resulting in the swelling of the hydrogel.[76] Either polyelectrolyte homopolymers can be used as pH-responsive material, or a certain proportion of pH-sensitive monomers can be introduced in a copolymer to adjust its swelling behavior. For example, 2 wt% of the monomer 3-sulfopropyl methacrylate potassium salt (SPMA) was copolymerized with hydroxyethyl acrylate (HEA) and hydroxyethylmethacrylate (HEMA) by DLP.[28] Poly(3-sulfopropyl methacrylate) (PSPMA) being a strong polyelectrolyte,[77] it permitted to introduce ionic strength-sensitivity to the hydrogel. The change in the shape of the printed structure relied on its shrinkage when immersed in 0.1 м NaCl solution, which swelled back when in distilled water.

In Section 3.2.1, the use of the thermosensitivity of PNIPAm in 4D printing has been highlighted. Besides its thermoresponsiveness, PNIPAm also exhibits a phase transition at a critical concentration of NaCl aqueous solution, which depends on temperature. The swelling degree decreases reversibly with an increase in NaCl concentration in the surrounding media.[78] Zheng et al. used these properties and printed multilayered structures by a multiple-nozzles extrusion system.[79] They prepared three viscous gels: the first one was non-responsive and composed of poly(acrylic acid-*co*-acrylamide) (P(AA-*co*-AAm)); the second one was sensitive to ionic strength and composed of 90 v% of poly(acrylic acid-*co*-*N*-isopropyl acrylamide) (P(AA-*co*-NIPAm)) and 10 v% of P(AA-*co*-AAm); and a third gel was developed from an intermediate composition (50 v% of P(AA-*co*-AAm) and 50 v% of (P(AA-*co*-NIPAm)) to serve as an intermediate bonding gel. After printing, the structures were immersed into $FeCl_3$ solution to form robust ionic crosslinking arising from the formation of a coordination complex between the carboxyl group of the AA repetitive unit (COO^-) and Fe^{3+}. Different constructs were prepared by printing layers of non-responsive gel fibers above which the intermediate bonding gel fibers were added and finally the responsive gel was printed on the top. Due to the responsivity of the PNIPAm segments to ionic strength, the shrinkage of the responsive layer when immersed in a 4 м NaCl solution led to the shape morphing of the structures after 50 s, that were reversed quickly (90 s) by immersion in water. The quick actuation is explained by the low diameter of the fibers (500 µm) that results in a low diffusion distance of the ions, and the reversibility is attributed to the toughness of the hydrogels. By raising the NaCl concentration from 0.1 to 4 м, the shrinkage, the actuation speed and the elastic modulus increased (from 0.38 to 13.93 MPa for the responsive hydrogel). Depending on the angle between the printed lines of each layer, deformations into rolls, tubes and cylinder helices were programmed. Thanks to the output force generated by the constructs when immersed in saline solution, the authors fabricated a gripper able to grip and release a ball of 10-times the weight of the gripper.[79]

3.1.4. Electrical Field

Electroactive hydrogels respond to an external electrical field and their actuation is easy to control in a non-invasive way. The swelling mismatch in the structure is triggered by the application of the external electric field, and equipment that permit precise control of duration of electrical pulses and current magnitude are currently available.[80] Moreover, the advantage of such a system is that the initial electroactive hydrogel can have a homogeneous chemical composition and crosslinking degree, which simplifies the printing.

Two classes of electroactive hydrogels exist: electric conductive hydrogel (conduction arises from electron mobility—intrinsically conductive polymer can be used as a second network or use of a percolated network of conductive particles in the hydrogel) and ionic conductive hydrogels (conduction due to ions mobility). To date, only one example of the second class of hydrogel has been explored in 4D printing.[81] In ionic conductive hydrogels, a polymer that possesses ionic groups along the chains is placed in an electrolyte and these groups get ionized, forming counterions in the hydrogel. As already explained, water diffuses into the hydrogel to equalize the concentrations of counterions, so the hydrogel swells. By placing two electrodes in the electrolyte apart from the hydrogel device and applying an electric field between the electrodes, the cations of the solution are attracted to the cathode (and anions attracted by the anode), thus creating a concentration gradient of cations and anions in the electrolyte. This gradient results in different osmotic pressures on each side of the hydrogel product (side close to the

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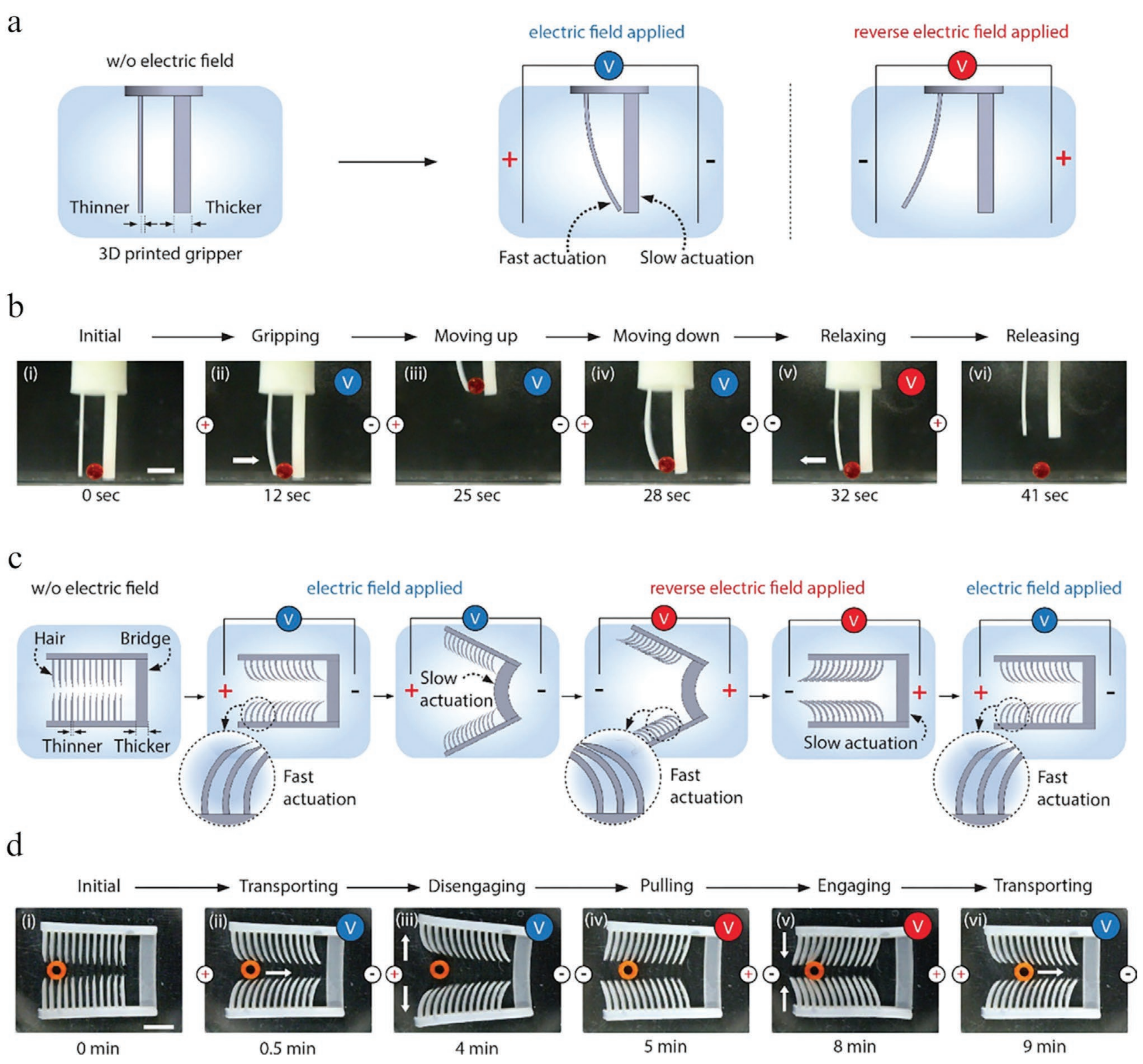

Figure 7. Soft robots created with PAA, an electroactive hydrogel, immersed in a polyelectrolyte and in-between two electrodes: a) Scheme of the shape-morphing of a gripper composed of two beams of different thicknesses; when an electric field is applied between the two electrodes, the thinner beam bends toward the cathode due to the different osmotic pressure created between the two faces of the beam; b) photographs of the grippers submitted to different electric fields; c) scheme of a transporter consisting of hairs and a bridge with different characteristic thicknesses; d) photographs of the transporter under action by applying electric fields in alternating directions. All scale bars indicate 5 mm. Adapted with permission.[81] Copyright 2018, American Chemical Society.

cathode and the one close to the anode). The osmotic pressure gets unbalanced on each side of the hydrogel, different swelling degrees are created, which leads to the bending of the hydrogel form toward the cathode or the anode.[80]

Han et al.[81] obtained such ionic conductive hydrogel of PAA covalently crosslinked by PEGDA by PμSL. The authors determined the optimal electrolyte concentration that favors the heterogeneous swelling of the hydrogel part. Moreover, the bending curvature of filament of hydrogel could be easily tuned by controlling the external electric field strength. The thinner the printed part, the larger bending curvatures and the faster the actuation. Thanks to the high resolution of PμSL, the authors printed structures with different regions with precisely controlled dimensions and actuation speeds as illustrated in **Figure 7**a,b. Small robots were fabricated and bidirectional locomotion of the objects demonstrated the high potential of such hydrogels in soft robotic (Figure 7c,d).

3.1.5. Light

Stimuli by pH, ionic strength, swelling/deswelling, and external field on electroactive ionic conductive hydrogels exhibit a strong limitation due to the limited actuation speed that is

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dependent on the diffusion of molecular species (ions or water) within the hydrogel structure. Moreover, all of the previously quoted stimuli as well as thermally sensitive hydrogels respond globally, so the movement of the structures should be programmed before printing. The use of light as stimulus permits a quick actuation and non-invasive stimulation, therefore specific regions of the sample can be irradiated to trigger specific and localized reconfigurations[51,64] at any moment. Light-sensitive particles, such as carbon nanotubes and graphene-based particles, can be dispersed into the hydrogel matrix.[82,83] Wang et al. used a composite of PNIPAm and reduced graphene oxide (RGO).[51] By irradiating this material with near infrared light, the RGO transformed the energy of the radiation into heat, thus provoking the thermal response of PNIPAm. A light intensity of 5 mW cm^{-2} enabled to raise the local temperature from 25 to 53 °C within 30 s. By inserting regions of this composite into a non-responsive matrix, a swelling mismatch is provoked generating stress and consequent deformation. By directing the light on a specific region of the strips, only a small portion of the strip was deformed. On the contrary, immersing the structure in water at 50 °C (above the LCST of PNIPAm) led to a global deformation of the structure. The transformation was reversible, but the return to the original shape took more time than the deformation step due to the chain relaxation that occurred during swelling. Using computational modeling, Kuksenok et al.[64] simulated the deformations induced by light irradiation of a fiber-filled hydrogel. In that case, the hydrogel itself did not respond to light, but the embedded fibers did. The fibers were functionalized with spirobenzopyran (SP) chromophores moieties that are hydrophilic in the absence of light and become hydrophobic under blue light. Different deformations were obtained by changing the radii of spirobenzopyran functionalization around the fibers, light intensity and positions of the post in the hydrogel matrix. The fibers also acted as reinforcement and their presence inside the hydrogel permitted the amplification of a small deformation to the matrix.[64]

3.1.6. Magnetic Field

Magnetic hydrogels are obtained by incorporating magnetic particles into the precursor gel or solution, forming a composite actuated by a programmed and external magnetic field. The media in which the particles are dispersed must be viscous to prevent particle agglomeration. Chen et al. printed an octopus, which tentacles were made of crosslinked PAAm with 10% w/v ferromagnetic Fe_3O_4 nanoparticles, and the head of the octopus was made of pure PAAm which is a non-responsive hydrogel.[26] The soft robot was actuated by a programmed magnetic field and was able to respond quickly to the stimulus by displacing itself.

3.2. Swelling/Deswelling Process of Non-Responsive Hydrogels

All the precedent examples involved smart hydrogels to produce shape-morphing objects, which limits the range of polymers that can be used. To obtain the movement of the structure without using smart hydrogels, it is necessary that the printed structure fulfills two criteria: a) it must have regions of different swelling degrees to generate a stress distribution during swelling or to exhibit different swelling degrees in different directions; b) it must be able to absorb and desorb the solvent(s) that produce(s) the swelling/deswelling process. The different swelling degrees in the structure can arise from the selection of two or more chemically distinct hydrogels that absorb different amounts of solvent (see Section 3.3), or it can be obtained from one hydrogel composition that possesses regions with different water uptakes (either due to dissimilar crosslinking degrees or with swelling restricted in one direction by the presence of anisotropic fillers). Herein, we describe the hydrogels used in 4D printing that belong to this second class.

3.2.1. Single Hydrogel Compositions with Regions of Distinct Crosslinking Degrees

Moving parts can be created using a non-responsive hydrogel such as PEGDA,[27] poly(hydroxyethyl methacrylate),[28] or copolymers,[19] in which the movement is permitted by the water absorption/deswelling process. The whole moving part can be composed of a single polymer. However, in order to create stress distribution in the structure, regions of different water uptake are printed. To do so, the simplest strategy consists in creating regions of different density, controlled by monomer conversion and crosslinking degrees, which is easy to control in light-based printing techniques (Section 2.1.2). If the printed part is planar, the gradient can be produced along the longitudinal direction of the printed part and/or along the perpendicular one.[19,27,28,37,38,47]

In flat 2D hydrogel sheets, the location of lines of higher crosslinking degree and their angle with the longitudinal direction of the sheet enable to produce bending or twisting movement upon immersion in water.[19] Deswelling occurs when the sample is removed from the swelling medium and exposed to air and, eventually, to temperature. The kinetic of water desorption is generally slow and depends on the hydrogel chemical structure, on the temperature at which the hydrogel is exposed,[19] on relative humidity and on the thickness of the parts. Due to the intrinsic hydrophilic characteristic of hydrogels, the total removal of water upon drying is almost impossible, so the total recovery of the shape upon deswelling state is not totally achievable[19] and should take into account during the design of the product.

In their work, Zhao et al.[27] printed a PEGDA-based network by stereolithography, and controlled the oligomers conversion and crosslinking degree in a 2D flat sheet. After printing, the structure was immersed in water to remove the unreacted oligomers, which provoked the contraction of the network in the regions where the oligomers were removed and a consequent folding of the structure. The flat sheet structure was recovered once immersed in acetone, due to the higher swelling of PEGDA in acetone than in water, allowing swelling of the least crosslinked regions. When removed from acetone, the acetone molecules volatilized, the structure deswelled, and the flat sheets folded to form the origami structure (**Figure 8**). For a 0.19 mm thick sheet, 30 s were enough to complete the unfolding movement in water, and 2 min led to acetone

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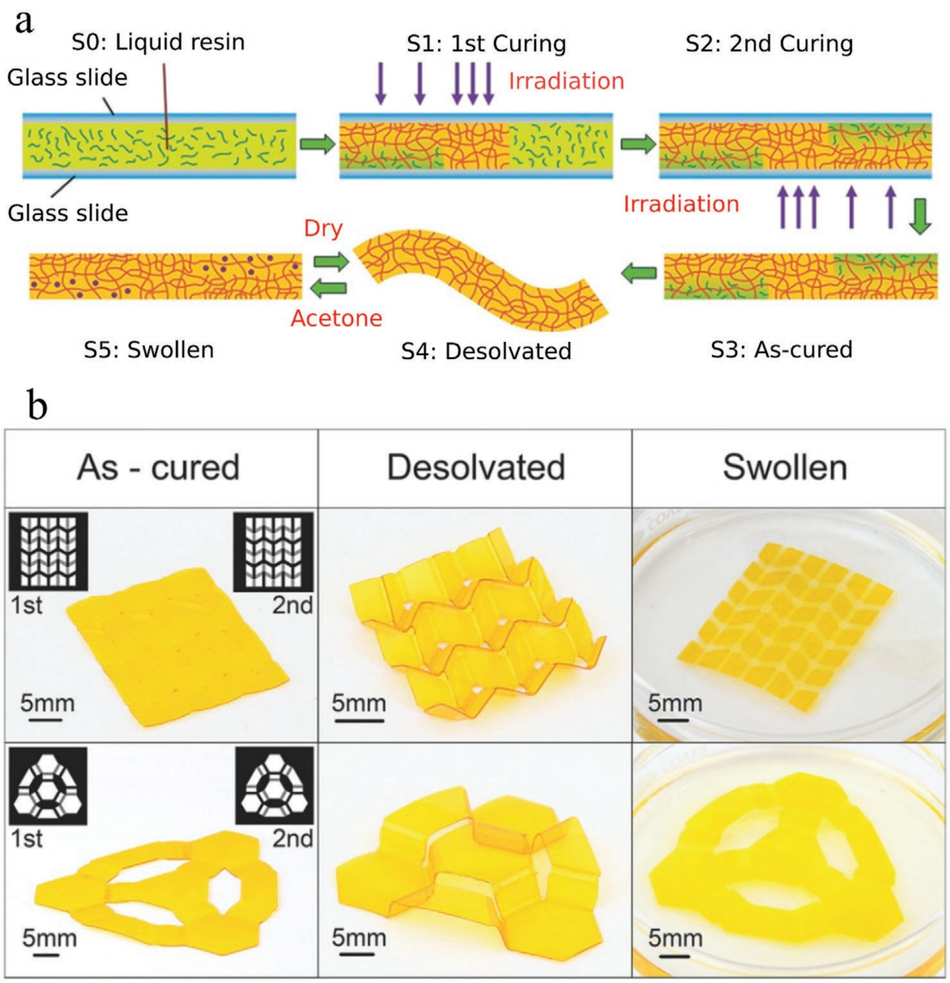

Figure 8. Flat sheets reversibly transform into origami by reversible acetone absorption and drying: a) Schematic figures of grayscale photoprinting perform on the two faces of the device, desolvation induced self-folding, and swelling induced shape recovery in acetone; b) the as-cured flat pattern, desolvated origami shape, and swollen flat shape of different 3D origami structures (first line: Miura origami, second line: kirigami lattice). Adapted with permission.[27] Copyright 2017, Wiley-VCH.

volatilization. Cycles of unfolding in acetone and folding by drying were repeatable.[27]

3.2.2. Use of Anisotropic Particles in Non-Responsive Hydrogels

One can create anisotropy in the printed structure by controlling the alignment of anisotropic particles like fibers or platelets with high aspect ratio. A smart way to align these particles using extrusion-based printing is to make use of the shear stress provoked when the ink flows through the nozzle. The particles are thus aligned in the longitudinal direction of the nozzle. Such shear-induced alignment can be controlled by printing parameters such as the nozzle diameter and printing speed. Higher shear is produced when the nozzle diameter is decreased and when the printing speed is increased. Another benefit of using particles in hydrogels is their capacity to reinforce the matrix.[5,42]

This stress-induced alignment mechanism has been used by Gladman et al.[5] to orientate nanofibrillated cellulose of high aspect ratio (±100) which was previously dispersed in a precursor gel of *N,N*-dimethylacrylamide (DMAAm) or NIPAm mixed with clay. This resulted in anisotropic stiffness (the values of the elastic moduli in the longitudinal and transverse directions were 40 and 20 kPa, respectively) and consequent anisotropic swelling (swelling strains of 10% and 40%, respectively) (**Figure 9**). First, the authors explored the relationship between the curvature of a bilayer structure made of the same composite and the orientation of the fibers within the two layers, elastic moduli, swelling ratios, ratio of layers thickness, and interfilament spacing. After developing a mathematical

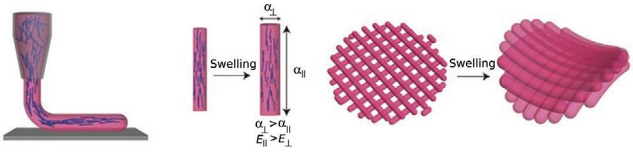

Figure 9. Shear-induced alignment of cellulose nanofibrils within the printed filament, resulting in anisotropic stiffness and swelling. Adapted with permission.[5] Colyright 2016, Springer Nature.

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model, they were able to combine different flat bilayer patterns to program various folding movements, and thus succeeded to mimic the complex morphology of the orchid *Dendrobium helix*. The method of 4D printing a hydrogel composite structure containing anisotropic particles have been patented by Lewis and Gladman, the same authors, in 2017.[84,85]

In the future, it can be expected that functional anisotropic particles, such as electric or magnetic particles, can be used in hydrogel matrices to remotely control their orientation by applying external stimuli in the printed structure, creating anisotropy.[86,87]

3.3. Hydrogels in Multimaterials Structures

In accordance with the definitions proposed by Ashby, Bréchet or Kromm[88–90] a multimaterial or an architectured material is the "association of one or several materials disposed according to a predefined architecture such that a representative volume element has at least one dimension that is very small compared with the dimensions of the entire structure."

Hydrogels are used in multimaterials structures that combine responsive materials and/or non-responsive ones that can be thermoplastic polymers or materials of other natures. The shape change in such structures depends on the relative positions of the materials, volume fraction of the material as well as the extent of swelling variation upon stimulus (when only one stimulus is applied) or of the various stimuli. It is not always necessary to select a stimuli-responsive hydrogel[6,7] since the swelling/deswelling of the hydrogel part can be used to produce the movement of the annex parts. In case of multimaterial structures, the interfacial bonding between the different materials is a critical aspect to be well engineered in order to avoid delamination. Moreover, the actuation force of the hydrogel should be adequate for promoting the dislocation of the annex parts, considering that the volume, material density, and geometrical constraints of these parts may hinder the expansion of the hydrogel.

One common multimaterial architecture used in 4D hydrogel printing is the bilayer that consists in printing two layers of hydrogels with different swellings.[38,43,50,79] The swelling or shrinking mismatch leads to the folding of the structure upon the side where the hydrogel of lower swelling is. The responsiveness of one or both of the hydrogel to specific stimuli can trigger such movement. Here again, a good adhesion between the two layers is necessary to avoid the delamination due to large differential dimensional change. As mentioned in Section 3.1.3, Zheng et al.[79] optimized the formulation of a hydrogel to create an interface layer composed of a mixture of the materials used in each layer. Both the swelling degree and the interfacial bonding strength between the distinct hydrogel were taken into account to select the optimal formulation.

4. Applications

4D printing supports the fabrication of complex and customized geometries with spatial control for diverse applications,[91,92] as reported in Table 1. Early development of the field has been more focused on exploring the development of printable materials that exhibit adequate response to stimuli, but has provided few concrete applications. Herein, we detail the different fields in which 4D printed hydrogels have been applied (in tissue engineering, sensors, actuators, and soft robotics). The design of origami is not treated here. The necessities in terms of materials properties for each application are also addressed in this section. This work also reports other potential applications in diverse areas (fashion design, food manufacturing, architecture, furniture design, etc.). An overview of the actual applications of 4D printed hydrogels is represented in **Figure 10**.

Figure 10. Overview of the actual and potential applications of 4D printed hydrogels with their individual requirements and respective stimuli for them to be triggered.

In fact, 4D printing field has been highlighted in 2019 in a full page of the 12th Annual Edition of the 2019 Tech Trends Report by Amy Webb, founder of The Future Today Institute—a collection of emerging science and technology trends that are expected to influence business, government, education, media, and society in the coming year.[93] Thus, many other applications may appear in the future.

4.1. Tissue Engineering and Therapeutic-Delivery Systems

Hydrogels are excellent materials for using as scaffolds in tissue engineering due to their similarities with extracellular matrix, like high hydrophilicity, water permeability, and softness. Extracellular matrix differs among biological tissues. Still, the basic function of providing support for tissue and ligands for cellular attachment is preserved.[94] The complex hierarchical composition of the tissues and their dynamic remodeling by sensing the environment (mechanical stimulus, pH, enzymes, etc.) are difficult to achieve with conventional fabrication techniques. The 4D printing of hydrogel-based constructs with desired properties

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and network structures would permit to precisely design microenvironments that resemble the native tissues.[95] It is well-known that cells not only recognize substrate composition, but also respond to evolution of surface topology and external mechanical stimuli with time.[96] Although 3D bioprinting brought significant improvement in the overall cell organization[97] by controlling the spatial depositing of the cells together with the materials, the fourth dimension triggered by physiologic stimulus should contribute to simulate dynamic environments for the cells.[98–100] Thanks to the fourth dimension, the controlled evolution of hydrogels surface properties along time may permit to modulate molecular and cellular adhesion,[101] whereas the repetitive mechanical force applied to cells along the shape-changing cycles may influence their differentiation.[102] An example that highlights the potential of 4D printing of hydrogels to create vascularized constructs has been recently published.[47] Self-folding hollow tubes were fabricated with two different modified natural polymers (AA-MA and HA-MA) that are known for supporting cell survival and differentiation. Modified alginate showed reversible folding-unfolding movement depending on the presence/absence of Ca^{2+}. These tubes are similar to the smallest blood vessels and have shown cellular viability.[47]

In the field of medicine, 4D printing must also find applications to create small-molecules delivery systems (such as drug, enzyme, DNA, etc.).[96,103] Encapsulation and release of therapeutic agents by folding/unfolding hydrogel macro-movement is the easiest mechanism for building such constructs, however a control of the constructs function and shape at the microscale should permit to tune the local concentration of released therapeutics to the treated tissues and to reach a more precise dosage.[98] If the therapeutic molecule is directly incorporated in the printed precursor material, the photostability of the molecule should be taken into account in case a light-based printing technique is used.[104] The change in shape and volume will also be employed for mini-invasive implantation of cell-laden constructs, artificial organs or therapeutic-delivery hydrogels that can be inserted in the body in their low-volume state and then deploy due to a specific stimulus present at the implantation site.

Among the materials that have been already successfully printed (Table 1), one can notice some biocompatible hydrogels that have potential for tissue engineering and drug delivery (PNIPAm, PAA, P(AA-*co*-NIPAm)), PEGDA, F127, alginate, etc.), however the range of materials available for such applications is broader, as mentioned in the review of Ashammakhi et al.[91] The hydrogel composition (polymers, crosslinkers, fillers, additives such as light absorbers) should be adequately selected considering the stimulus (physiologic or externally controlled stimulus) and cell viability. For example, hydration/dehydration is not a stimulus that should be envisaged for tissue engineering due to the necessity to maintain a hydrated environment for the cells, which implies the presence of a smart hydrogel in the 4D constructs. However, hydration/dehydration stimulus can be adequate for therapeutics release. In addition, the design of printed materials able to respond to more than one type of physiological stimuli will permit to create scaffolds more adapted to the complex microenvironments of the human body.[105]

The mechanical properties of the hydrogels should be similar to the one of living tissues that are replaced or reconstructed.[106,107] Engineering structures that mimic natural tissue is still emerging, but gaining complexity, gradient of composition and properties will be necessary for 4D printing to open the door for personalized functional artificial organs. The development of new printers able to rapidly grade and vary the ratios of different hydrogel compositions,[108] as well as new rapid prototyping approaches such as the variable property rapid prototyping,[109] will enable to fabricate functionally graded 4D hydrogel structures.[110]

In biomedical applications, the progressive biodegradation of the structure can be beneficial since the implanted material does not have to be removed surgically. The range of biodegradable smart hydrogels is relatively limited. Designing a new smart biodegradable hydrogel necessitates good knowledge in polymer chemistry since it implies synthesizing a new polymer backbone architectures that contains cleavable groups or chemically modifying the polymeric backbone of a smart hydrogel to insert cleavable crosslinking groups,[111] and then adapting the precursor material composition to the specific printing technology to be used (see Section 2). Moreover, the biocompatibility and efficiency should be tested in cell cultures and in animal models, that can be an expensive and time-consuming process.[91]

Tissue engineering application presents a particular challenge for material programmation and prediction of the number of response and reversion cycles, since a change in the shape-morphing amplitude, mechanical force applied on the cells, and surface modifications of the printed structure should be expected due to the impact of the neotissue development and to the possible biodegradation of the hydrogel matrix.[112]

4.2. Actuators

4D printed hydrogels actuators are an interesting class of materials within the emerging field of soft robotics. Contrary to the traditional silicone soft actuators, hydrogels are hydrophilic, biocompatible, they can exhibit self-healing capacity and are stimuli-responsive.[113] In order to achieve the multifunctionality of natural organisms, biomimetic soft robots promises to combine sensing and controlling upon passive mechanics and active movements. Most of the soft robots that have been fabricated by 4D printing react to ions concentration,[79] electric field,[81] magnetic field,[26] and more frequently to temperature,[2,19,37,66] converting energy obtained from the external stimuli to execute specific tasks, namely, activating grippers, walking robots, and artificial muscles.[114] These kinds of actuators have been developed so far. In a surgery or endoscopy, for instance, soft robots might reach remote areas of the human body. The device navigates through a natural and narrow orifice to then pierce in a target organ and then self-deploy or self-lock on site to execute a specific task. To biopsy a gastrointestinal tract tissue, for example, an external magnetic field might orientate the device toward the desired location[115,116] and transform it into a tweezer on-site.[51]

Hydrogel-based soft actuators must be resilient and mechanically stable;[113] they have to withstand several cycles of stimuli

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application without disintegrating, maintain the same shape-morphing amplitude and mechanical properties along time.[114] The output force should also be large enough to drive shape change. Moreover, in some applications, a quick actuation speed is required. Developing adequate hydrogel compositions that fulfill all these requirements is a challenging issue.[117] Hydrogel is a class of polymer that exhibits low mechanical properties in comparison with shape memory polymers, independently of the processing technique used to shape it. However, printed hydrogels typically exhibit even inferior mechanical properties (lower elastic modulus, reduced strain at break and toughness) than those prepared by casting, as shown by Bakarich et al. for alginate/PAAm double network hydrogels,[44,67,118] due to effects of light absorption that results in lower monomer conversion.

Good load-bearing properties can be achieved by developing Double Network hydrogels,[50,66,119] that fracture energy is in the range of 100–9000 J m^{-2} (compared to 10 J m^{-2} for a single hydrogel network). The efforts made for the development of flexible and tough double network hydrogels by combining the chemical nature of the networks[49,50,66] and crosslinking systems (physical and/or chemical)[79] will certainly benefit the field of 4D printing. Tough hydrogels allow the creation of thinner parts in the printed structure, being it an advantage since the swelling mechanism occurs by water diffusion in many cases (Table 2), which is relatively slow in hydrogels (water diffusivity in hydrogels are in the range of 10^{-10} to 10^{-9} m^2 s^{-1}).[38,79]

Hydrogel composites systems are also promising candidates for creating actuators. Nano or microparticles-reinforced hydrogels are also promising candidates for actuators.[120] In that case, the chemical nature of the particle, its surface chemistry, its size, its aspect ratio and amount allow tuning the interaction with the matrix as well as the mechanical and swelling characteristics of the composites hydrogel. These particles, and in particular ceramic and metallic particles, act as viscosifier and can impact light absorption and hinder the crosslinking reactions of hydrogels. The use of anisotropic fillers such as short fibers can serve to produce anisotropic stiffness and strength in the printed actuator. Hydrogels nanocomposites comprising nanoparticles sensitive to light or to magnetic fields would permit to create actuators with quick actuation speed. In case of extrusion printing, the agglomeration of such particles can clog and consequently decrease the resolution, or even hinder the extrusion process.

Besides, hydrogels with self-healing capacity will propel the use of this class of materials for soft actuators[121,122] provided that their self-healing mechanisms is spontaneous or can be provoked by the same external stimulus that is responsible for fourth dimension.[123]

4.3. Sensors as Smart Valves

Hydrogels might act as smart valves in both sensors and actuators for control and manipulation of fluids. Microfluidic devices use hydrogels as pumps and gates to regulate the flow of a liquid through stimuli. The mechanical toughness and actuation speed are also relevant for this application. Moreover, a good sealing between the actuating and non-actuating parts of the device, and the ability to withstand the fluid pressure are required.[113] A system of a combined thermally responsive covalent crosslinked network of PNIPAm and calcium alginate hydrogels were utilized for controlling water flow. The smart valve achieved a large strain up to 35 ± 3%, and stress up to 20.9 ± 0.6 kPa in a constrained contraction tests.[10,66] Another example combines PAA and F127DA that have the ability to respond to temperature and pH of the fluid.[35] This stimuli combination deals with water uptake controlling of the hydrogel, as shown in Figure 4.

4.4. Miscellaneous Applications: Current and Future Perspectives in Related Fields

4D additive manufacturing using hydrogels may find many potential future applications in areas as self-assembly materials (for building applications), self-disassembly materials (for security applications), and bioengineering (e.g., stents, living electrodes, and edible electronics).[123] Besides the previously quoted applications of 4D printing of hydrogels, the field may broaden to collide with the creative industries such as fashion design as well as other industries such as food manufacturing. Several applications will arise from the biologically inspired hydrogels-based printed structures based on biomimicry core concepts. Those novel applications may relate to researches on the design and production of materials, as well as device geometry and functionalities that mimic biological structures.[92] This section discusses some of the potential applications brought by interdisciplinary research in several contexts and industries.

In the food industry, sensory experiences for the palate and cost reduction in packaging/transportation have been strongly encouraged and are a playground for additive manufacturing. The concept of “flat packaging” enables companies to benefit from low shipping costs due to the compactness of the 2D segments while maintaining the desired function and appearance of the 3D end-products once submitted to the external stimulus. The Tangible Media Group–Media Lab–MIT developed a fully functional 2D pasta packaging that becomes 3D during cooking due to the contact with heated water.[124] In the 4D pasta process, a multimaterial structure made of edible materials was obtained, and the shape-morphing process is triggered by hydration during cooking. Whereas gelatin (protein), agar (soluble fiber) and starch (carbohydrate) swell when immersed in water, cellulose fibers do not, so these fibers can be used as anisotropic fillers and as shape constraints based on the principle explained in Section 3.2.2. The swelling behavior and melting temperature of gelatin is also dependent on its molecular weight, consequently, by tuning the cooking temperature, gelatin can transform from a solid state to a liquid state. Thus, this pasta is both sensitive to hydration and can be temperature sensitive. The dehydration of the pasta in the consumer's dish also leads to a progressive movement of the pasta structure, providing an interactive dining experience for the user. Even if this work refers to a transformation of 2D films into 3D shapes, the concept is similar to 4D printing[124] even if no repetitive cycles of change of shape are necessary in this application.

From reactive shape morphing clothing, which optimizes for weather conditions according to the environmental humidity via material programmability that benefits from reversibly self-folding origami,[125] to sweat response[126] lots has been thought of at the junction of the creative and the manufacturing industries. Yao et al. demonstrated via a prototype dressed by dancers that bacteria-powered clothing may respond to the body's needs. In this cloth, a thin elastomeric film was recovered by a layer of *Bacillus subtilis*, a bacteria sensitive to moisture that size reversibly changes with ambient relative humidity.[127] This fabric may be seen as living clothes that react in real time to heat and sweat mapping with tiny vents to curl open or flatten closed as exertion levels demanded. Hydrogels may substitute such living nanoactuators by considering smart hydrogels sensitive to enzymes[128] of biochemical agents. Other recent works sign future applications in this direction such as smart pH-responsive antimicrobial hydrogel scaffolds prepared by 4D printing[39] and surface tension-assisted additive manufacturing[129] that might impact both tissue and textile engineering. Another avenue for textile design is a 4D printing system for designing and fabricating morphing three-dimensional shapes out of simple linear elements[3] and combining them into more complex geometries later. Applications involving hydrogels might spread soon in sports clothing, with medical or cosmetic purposes, sensorial experiences or even purely aesthetic.

As architecture has been a field highly involved with additive manufacturing from conception to implementation, it comes across as promising future area of applications of hydrogels for developing shape-morphing solutions. The incorporation of such materials into built structure will serve as an interface between the synthetic matter and climate conditions, permitting to the architecture to respond to the light or humidity conditions along daytime.[68] So far heat-sensitive stretchable hydrogel skeletons developed by Khoo and Shin[68] have demonstrated implementation possibilities for the soft and evolving architecture. Three main directions have been identified by those authors for 4D printed hydrogels applications in the field of building design. The first one is to improve the performance of glazing and window, by placing a thermosensitive hydrogel such as PNIPAm within two glasses sheet. This thermally sensitive hydrogel would become opaque with heat (coming from temperature or incident light) in order to serve as thermotropic shading. The second application relates to new architectural skeletons for existing building components, with the hydrogel skeleton serving as flexible pattern on a rigid part, such as glass surface, and permitting to regulate temperature, therefore reducing energy consumption. Finally, the authors of that study proposed to use printed hydrogels as responsive architectural elements for building façades cover. In that case, the hydrogel is used to perform structural, sensing and actuation functions.[68] The cover can be made of many individual modules and can be applied to an existing façade, and act as an adaptive shading element that responds to environmental stimuli. Under low temperature, the module can contract and allow light transmission into the building, whereas when heated by the sunlight, the module can expand to obstruct the passage of light. Such structure would improve the environmental performance of buildings and new aesthetic possibilities may be envisaged. Although the Hydroceramic project developed at the Institute for Advanced Architecture of Catalonia was not mentioned as 4D printing technique in 2013–2014, this kind of panel could be fabricated via additive manufacturing. This multimaterial structure was composed of 3 different phases: hydrogel as the smart material, fabric as the water channel, and the ceramic as the supportive material, so that the proposed panel could be a passive evapotranspiration system able to lower the temperature of an interior space by 5 °C.[130] Such kind of project seems to be on the route to evolve as a sustainable additive manufacturing shape-changing solution according to environmental stimuli. Such application in architecture will be achievable with hydrogels resistant to weather conditions like photo-oxidation, presence of dust and acid rains, and should withstand several hydration/dehydration cycles maintaining the same shape-morphing amplitude to maintain the functionality of the built structures. Another application of interest is related to furniture. The classical application divulged by Skylar Tibbits and his lab at the MIT at its early years was that 4D printing might enable people to buy furniture, bring it home and watch it assemble itself.[12] Other mentioned possible applications were tiny apartments that could benefit from transformative furniture that could evolve along the daytime or year seasons according to relative humidity, temperature or natural light intensity, so that space use could be optimized. Synthetic hydrogels with mechanically robust and tunable properties also indicate opportunities for designers to digitally fabricate responsive structures and skins for interior design.[68] However, such an application has been largely unexplored in the literature.

Such different potential applications mentioned above suggest the 4D printing field is clearly influencing areas that might have been unimaginable some years ago. Although it is already given that hydrogel technology clears the way for four-dimensional printing applications in several fields, it still faces challenges. For example, single network hydrogel dehydration usually results in a brittle, porous material, which limits applications either within high temperature systems or interfaces susceptible of evaporating water molecules into the atmosphere.[131] It means that in contexts that the environmental condition changes brusquely or randomly due to several variables, subsequent loss of solvent in the hydrogels can result in an instability on the actuated shape.[132] In these cases, the hydrogel applicability might be limited, as in aerospace, despite the enthusiasm of a few research groups. However, some strategies cited in previous sections can be applied to increase the mechanical robustness of hydrogels (Double network hydrogels, hydrogel composites, self-healing hydrogels...), and the design of hydrogel-based structures for use in air conditions is feasible. In that case, the structure swelling is provoked by absorption of water molecules from air, that is, humidity, but the response time is expected to be longer than in immersion in water.[114]

In addition to the applications presented in this section, more and more researchers are inspired to think about novel application scenarios for hydrogel 4D printing. The low cost and accessibility of hydrogels might also encourage exploration of new design possibilities by implementing kinetic, adaptive and performative capabilities.[68] Another promising perspective relied on the development of multi-functional composite materials to incorporate several stimuli in order to achieve response mechanisms in challenging environments. It is expected

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that new developments of materials and technology better motivate users to think about the multi-dimensionalities of 4D printing,[3] and this will give continuous input to researchers to explore a myriad of other design spaces that interface with humans' lifestyles in several ways.

5. Conclusion and Perspectives

For some of the 4D printing pioneers, printing could be described as a "materials science chamber" where different materials, properties, and micro and macro architectures could be mixed and matched to produce material behaviors and capabilities which would not have been enabled via other manufacturing processes. The development of 4D printing has revealed more and more possibilities for the conception of smart printing using materials designed to forecast change processes. Hydrogels are taking a key role on this in accordance with their capability to optimize their formulation, to customize compositions and combination in composites and multimaterial structures. Even if smart hydrogels have been the materials of choice for the sensitivity to environmental stimulus, non-responsive hydrogels have attracted attention to expand the range of materials and also allow to obtain programmed and complex shape changes by swelling/deswelling by tuning their internal structure (crosslinking and density) or by combining them with other materials. The potential of 4D printing of hydrogels has already been demonstrated for tissue engineering, soft actuators and valve applications. However, to launch potential printed devices to the several fields of engineering and creative industries, a better technology integration of additive manufacturing, design, and smart materials is expected. In terms of materials properties, improvements are needed in adequacy for each application (biodegradation, improved toughness, speed response, actuation force, self-healing capacity, resistance to weather conditions). The innovation of double network hydrogels, supramolecular hydrogels, hydrogel composites such as nanoparticle-reinforced hydrogels, synthesis of new stimuli-responsive polymers, crosslinking chemistry and multimaterial combinations are toolboxes that should permit the expansion of this technology. As a result of the development of new applications, disruptive futures computer-aided design and graphics will embrace the shape alterations and hydrogels characteristics in a more realistically and real-time modeling approach.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

4D printing, hydrogels, multimaterials, shape-morphing, smart polymers, stimuli-responsive hydrogels

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