

# Stimuli-responsive polymer gels

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Stimuli-responsive polymer gels have received considerable attention due to their singular mechanical properties, which make them materials of choice for niche applications. Polymer gels comprising either physical or chemical cross-links can undergo controlled and reversible shape changes in response to an applied field. The stimulus or external field applied may include thermal, electrical, magnetic, pH, UV/visible light, ionic or metallic interactions or combinations thereof. The shape change can manifest itself in two-dimensional actuation, bending motion, or three-dimensional actuation, volume change. This reversible contraction and expansion of polymer gels as well as their mechanical properties are similar to that of biological muscles. This review will describe and critique some of the recent advances in the field of stimuli-responsive polymer gels including the design of new classes of polymeric gels, controlled actuation in response to external stimuli, and ability to tailor material properties for different applications.

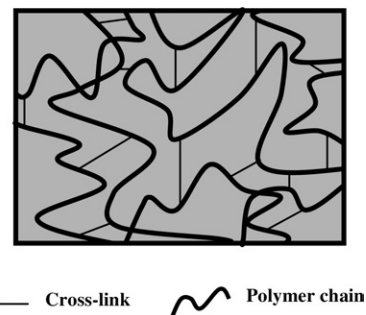
## 1. Introduction to gels

Pierre-Gilles de Gennes during his Nobel lecture in 1991 recognized the place of gels among the broad category of “soft matter”.<sup>1</sup> Focusing on the phenomenological characteristics, polymer gels are three-dimensional networks swollen by a large amount of solvent. Solid-like gels are characterized by: i) the absence of an equilibrium modulus; ii) the presence of a storage modulus,  $G'(\omega)$ , that exhibits a pronounced plateau extending to times at least of the order of seconds; and iii) the presence of a loss modulus,  $G''(\omega)$ , that is considerably smaller than the storage modulus in the plateau region.<sup>2</sup> The presence of liquid-like behavior on molecular length scales combined with solid-like macroscopic properties makes them very unique systems.<sup>3</sup>

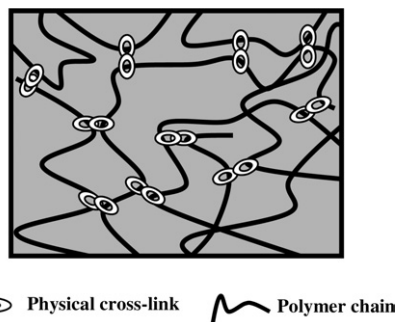
Polymer gels are classified as chemical- and physical gels, depending on the nature of cross-links (Fig. 1 and Fig. 2, respectively). In chemical gels, a three-dimensional network is achieved through permanent covalent bonds usually achieved by cross-linking as shown in Fig. 1, while physical gels are formed by the growth of physically connected aggregates, as shown in Fig. 2.<sup>4,5</sup> In a physical gel, depending on the nature of each gelling system, the junctions may be hydrogen bonds, crystalline regions, ionic clusters, or phase-separated microdomains.<sup>4,6</sup>

## 2. Responsive materials or actuators

There has been enormous interest in polymer gels that undergo a reversible and controlled two- or three-dimensional shape change in response to an applied field.<sup>7–10</sup> A cartoon representation of stimuli-responsive gels that undergo several reversible shape changes is shown in Fig. 3. For example, if a certain type of stimulus is used to change the primary shape to the



**Fig. 1** Schematic representation of chemical gels generated by chemical cross-linking.



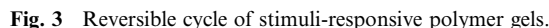
**Fig. 2** Formation of physical gels *via* non-covalent bonding of polymer chains.

secondary shape, one could envisage the use of a different stimulus to change the secondary shape of the polymer gel to the tertiary state.

These stimuli-responsive gels will be the focus of this review article.<sup>8–10</sup> The response of polymers gels to external stimuli is controlled by parameters such as shape or dimensional change (strain) of the material, the force (stress) that it is capable of exerting, the speed of the response, shape recovery, and

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|        | Polymer  | Type of stimulus                           |
|--------|--|--|
| BIS    | Bisacrylamide                                    |  |
| PAA    | Poly(acrylic acid)                               | pH   |
| PAAEM  | Poly(acetoacetoxyethyl methacrylate)             |  |
| PAm    | Poly(acrylamides)                                |  |
| PBA    | Poly(butyl acrylate)                             |  |
| PDEA   | Poly[2-(diethylamino)ethyl methacrylate]         | pH   |
| PDMS   | Poly(dimethylsiloxane)                           | <sup>a</sup> E-field, <sup>b</sup> T-field |
| PDPA   | Poly[2-(diisopropylamino)ethyl methacrylate]     | pH   |
| PEO    | Poly(ethylene oxide)                             | T-field                                    |
| PGMA   | Poly(glycerol monomethacrylate)                  |  |
| PHEMA  | Poly(hexyl ethyl methacrylate)                   |  |
| PHFBMA | Poly(hexafluorobutylmethacrylamide)              | T-field                                    |
| PLG    | Poly(glutamic acid)                              | pH   |
| PLLA   | Poly(L-lactides)                                 |  |
| PMMA   | Poly(methyl) methacrylate                        |  |
| PMPC   | Poly[2-(methacryloyloxy)ethyl phosphorylcholine] | E-field, T-field                           |
| PNaA   | Poly(sodium acrylate)                            | pH   |
| PNaVBA | Poly(sodium-4-vinylbenzoate)                     | pH   |
| PNCL   | Poly( <i>N</i> -vinylcaprolactone)               | T-field, pH                                |
| PNIPAM | Poly( <i>N</i> -isopropylacrylamide)             | T-field                                    |
| PPO    | Poly(propylene oxide)                            | T-field                                    |
| PSMA   | Poly(stearyl methacrylate)                       |  |
| PVIm   | Poly( <i>N</i> -vinylimidazole)                  | pH   |

<sup>a</sup> Electrical field. <sup>b</sup> Thermal field.

### 2.1. Thermally responsive polymers

Thermoresponsive homo-, random, block, and dendritic polymer gels discussed in this review include: i) physical and chemical hydrogels; ii) physical and chemical organogels; and iii) liquid-crystalline polymers, LCPs.

Physical hydrogels of PNIPAM and PEO show a lower critical solution temperature (LCST) around 32 °C, which is exploited in producing temperature-responsive materials. Graft copolymers, PNIPAM brushes attached to the PHEMA main chain, in water have been used as models to study thermal actuation that occur at the nanometre scale.<sup>37</sup> A sharp change of hydrodynamic radius of the polymer brushes through a small temperature variation can be driven by LCST transition of PNIPAM brushes. This change in hydrodynamic radius has been attributed to a transition from cylindrical brushes to spherically collapsed forms.<sup>37</sup> PEO grafted with phosphatidyl choline along with a co-surfactant self-assemble at room temperature in water to form one-dimensional non-birefringent LC (physical) gel. This gel reversibly transitions into a two-dimensional birefringent fluid with decrease in temperature to about 16 °C.<sup>38</sup> This is a singular approach to scaffolds of thermo-responsive lipid mesophases. As a step forward, Pelah and co-workers incorporated highly deformable red blood cells between PNIPAM gel and cover glass, and/or patterned PNIPAM gel.<sup>39</sup> When the temperature is higher than LCST of PNIPAM, the polymer gel shrinks, which causes the deformation of embedded cells. The deformation of cells can be transformed into biochemical responses, which play critical roles in cell development, migration, and morphology.<sup>39</sup>

Chemical hydrogels of PNCL, PNaA-*co*-PAA, PNIPAM-*co*-PBA, PHFIPMA-*co*-PMMA, PHFBMA-*co*-PMMA, and PNIPAM-*co*-PDEA with divinyl or bisacrylamide cross-links show better mechanical strength and tunability of properties in comparison to the corresponding physical hydrogels.<sup>40–42</sup> For example, aqueous solutions of NIPAM and *N*-ethylacrylamide (NEAm) were polymerized by free-radical methods and cross-linked within channels of a microfluidic device. The volume change of these chemical gels associated with thermal stimuli can be reversibly actuated using heating units built into this microfluidic device. This gel can open and close the valves of the microfluidic device with reversible volume change. This method has a number of advantages, such as the tunability of LCST between 32–75 °C, fast actuation, and ability of the gel to withstand high pressures.<sup>43</sup> Chemical hydrogels consisting of an active layer comprising thermo-sensitive cross-linked PNIPAM–PAM and a passive layer of glutaraldehyde cross-linked PVA–PVME exhibit optical transition over a wide temperature range. Temperature change causes a volume change in PNIPAM, while temperature results in a change in cloud point of PVA. These layered chemical hydrogels show both change in volume and optical properties in response to temperature.<sup>44</sup>

A disadvantage of PNIPAM chemical hydrogels is that the bisarylamide cross-links are not biocompatible or biodegradable.<sup>45</sup> Some researchers have developed biodegradable hydrogels composed of PNIPAM, PLLA, and dextran.<sup>46,47</sup> A new class of polyphosphazene bearing dipeptide ethyl esters and ethylene oxide units that show sol-gel transitions in aqueous solutions has been developed.<sup>48</sup> The properties of these thermosensitive polymers are dependent on composition of the copolymers, length of the ethylene oxide block, the type of peptide, and pH. These physical gels develop cross-links due to reaction

between peptide esters, and also undergo hydrolytic degradation under physiological conditions. These polymers can be used as biodegradable thermo-responsive gels in drug-delivery applications, injectable gels in artificial pancreas, and promotion of nerve regeneration.<sup>48–50</sup>

Thermo-responsive block copolymers with tunable incorporation of hydrophobic, PPO, and hydrophilic, PEO, units include PEO-*b*-PPO-*b*-PEO<sup>51</sup> and PPO-*b*-PEO-*b*-PPO.<sup>52</sup> The copolymers PEO-*b*-PPO-*b*-PEO and PPO-*b*-PEO-*b*-PPO form hydrogels at a specific temperature and concentration *via* either a jammed micelle<sup>51</sup> or micellar bridges mechanism,<sup>52</sup> respectively. Other star copolymers including PNIPAM-PMPC-PNIPAM form free-standing physical hydrogels at 37 °C.<sup>53</sup> Double hydrophilic block copolymers, PNIPAM-*b*-PVIIm, form micelles in methanol–water mixtures that act as self-catalyzing nanoreactors, wherein the esterolysis catalytic activity can be tailored by the choice of solvent and temperature.<sup>54</sup> Similarly, triblock copolymers, PSMA-*b*-PNIPAM-*b*-PSMA with carboxylic acid end-groups, form core–shell aggregates in different organic solvents. These self-assembled structures show thermo- and pH-responsive properties through LCST of NIPAM and carboxylic end-groups, respectively.<sup>55</sup>

Liquid-crystalline polymers combine the properties of a physically or a chemically cross-linked network (elastomer) and liquid-crystalline motifs or mesogens within the same system.<sup>20</sup> These mesogens include: i) nematic phases are formed by rod-like or disc-like units that have long-range orientational order; ii) cholesteric phases are formed by chiral nematic mesogens; iii) smectic mesophases are formed when rod-like molecules arrange in layers; iv) columnar mesophases are formed by disc-like molecules that arrange in a column. Due to the coupling between the lightly cross-linked elastic network and the orientation of the mesogens, liquid-crystalline elastomers (LCE) show anisotropic mechanical response, optical anisotropy, and structure-dependent deformation by external field.<sup>2,19–20</sup> Block copolymer examples include terphenyl units at the end block, which acts as a physical cross-linker and the central main chain liquid-crystalline block showing spontaneous elongation along the nematic director responding to the thermal stimulus. The melt-spun fiber showed a 500 % change in dimension caused by the order–disorder transition of liquid crystals with a permanent length recovery at a temperature above nematic–isotropic transition temperature.<sup>56</sup>

Cross-linked silicones and polyurethanes are used in shape-memory materials. Ultra-sensitive thermal bimorphs using different thermal expansion coefficients of silicones and polystyrenes have been reported recently. Atomic force microscopy (AFM) silicone tips were used as substrates and PS layer was attached to only one side with plasma-enhanced chemical vapor deposition polymerization. The observed temperature resolution of bimaterial micro-cantilevers was close to 0.2 mK with thermal sensitivity of 2 nm mK<sup>−1</sup>.<sup>57</sup> Fabrication of micro-devices that allows high-precision optical alignment is possible using thermal actuation of silicones. Silicones has been cured inside the cavity of an aluminium block. The heating of the block causes the thermal expansion of rubber in the direction along the alignment axis. The block was coupled with optical instrumentation to demonstrate the precise positioning of ball lens between two single-mode optical fibers. The observed precision of positioning

obtained from the silicone rubber device was better than 200 nm over a range of 20 μm.<sup>58</sup> In another example, shape-memory polyurethanes that are activated by lasers has been proposed as micro-actuators in endovascular thrombectomy. The shape-memory polymer was photothermally actuated using 810 nm laser light to move the thrombotic vascular occlusion through a catheter.<sup>59</sup>

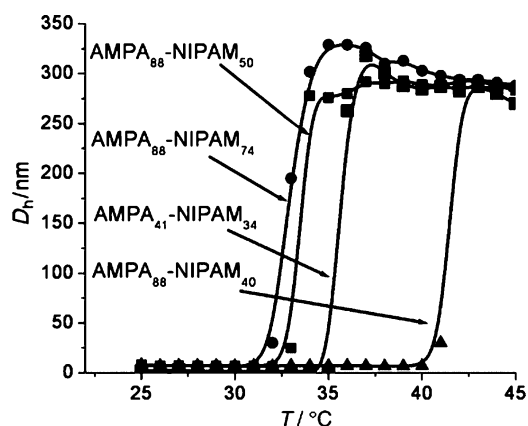
## 2.2 pH-responsive materials

Polymers bearing ionic groups in the main or the side chain are counter-balanced with the oppositely charged ions that can diffuse in and out of the polymer chains.<sup>31</sup> Physical cross-linking in these polymers occurs due to aggregation of ionic units at the nanometre scale, and provides a viscoelastic response. Ionic interactions in polymers impact mechanical properties and increases compatibility between different polymers in blends. Examples include ionic polymers, polyelectrolytes, conjugated polymers doped with ions, and uncharged polymers that are gelled using ionic molecules such as ionic liquids and solvent-bearing ionic groups. These polymers show a reversible change in shape and/or volume when subjected to external fields including electrical, thermal, and pH.<sup>30,31,36,37,60</sup> The change in shape of polyelectrolyte gels in response to external stimuli is similar to the biological motions related to muscle and ciliary movement at the molecular level, resulting in biomimetic materials.<sup>29,61,62</sup>

The pH-responsive gels can be used in microfluidic systems. The device would comprise a set of connectors, valves, pumps and along with the gel as the actuating material.<sup>63</sup> As the pH varies, the gel networks change from the neutral to negatively charged and thus undergoes a volume transition from the collapsed to the expanded state due to osmotic pressure. The flow control valve made of PAA and PHEMA was manufactured by a combination of photopolymerization, lithography and microfluidics, which give faster responses and are capable of autonomous control.<sup>61</sup>

A novel pH- and ionic strength-responsive hydrogel has been synthesized by cross-linking PLG and PEO. The swelling of this hydrogel varied with pH and increased at higher ionization of the PLG, which result from not only the electrostatic effects (ion–ion repulsion and internal ion osmotic pressure), but also the secondary structural attributes associated with the polypeptide backbone. By modifying the hydrophobicity of polypeptide and the degree of ionization, the overall extent of pH-responsive swelling can be controlled. Rapid swelling and de-swelling behavior was observed when the PLG-*co*-PEO hydrogel was transferred between high- and low-pH buffer solutions. A drug-release study of the hydrogel by using lysozyme as a model protein showed fast de-swelling of the hydrogel to be an effective means to facilitate lysozyme release.<sup>64</sup>

The cell cytoplasm and extracellular cellular matrix (ECM) are composite aqueous solution of multiple solutes, proteins, and electrolytes intersected by the multifaceted three-dimensional structure of negatively charged polyelectrolytes such as actin filaments/microtubule and aggrecan/hyaluronic acid. Protein mobility within this complex environment is therefore suspected to deviate notably from mobility in dilute solutions due to a complicated sum of the intrinsic viscosity of the liquid cell



**Fig. 4** Variation of hydrodynamic diameter with temperature for a 0.5 % (w/w) aqueous solution of the diblock copolymers (heating rate =  $0.1\text{ }^{\circ}\text{C min}^{-1}$ ); At room temperature, the block copolymers exist as unimers in aqueous solution and self-assemble into vesicles when the solution temperature is increased due to phase separation of PNIPAM (reprinted with permission from ref. 69).

medium, nonspecific binding of probe molecule to macromolecules, and the mechanical barriers as imposed by the network. Therefore, studies on protein diffusion in polyelectrolyte gel will be crucial to the understanding of the biochemical kinetics of the cell.<sup>61,62</sup>

These are two different polymer architectures that actuate with change in pH, namely, polyelectrolyte brushes<sup>63–66</sup> and polyelectrolyte block copolymers.<sup>67–70</sup> Fig. 4 shows the dramatic change of hydrodynamic radii of poly(AMPA-*b*-NIPAM) in aqueous solution due to the phase transition of poly(NIPAM) blocks. The transition temperature could be modulated by changing the length of each block. At low pH values, the vesicle was largest (310 nm at pH 3), and increasing pH value of the solution decreased the size of the particles (*e.g.*, 220 nm at pH 10.8). In both cases the macro-dimensional change can be summed up as contributions from the nanometre scale. Triblock copolymers bearing acrylic acid in the central block in one system and amino groups in the central block in another system, polyacids and polybases were coated on top of each other to form a bipolymeric strip and saturated with THF to make miscible end blocks. This bimorph shows a pH response that result in motion that bends on the layers preferentially; the nanometre thick films show a response time in seconds. This displacement can be manipulated to be either linear or a curling fashion, and this effect will function at smaller length scales as well as macroscopic scales.<sup>63,70</sup> Triblock copolymers PDEA-*b*-PMPC-*b*-PDEA, PDPA-*b*-PMPC-*b*-PDPA, with pH-responsive PDEA or PDPA,<sup>71</sup> respectively, in the end blocks will form physical hydrogels at  $37\text{ }^{\circ}\text{C}$ .<sup>72</sup> At pH of 8 or less, these amino groups are protonated and the block copolymer remains in solution, while under alkaline pH conditions, the PDEA and PDPA are sufficiently hydrophobic to form physical hydrogels. These polymers will also respond to change in pH. Other triblocks include PNaVBA-*b*-PEO-*b*-PNaVBA that will show a reversible volume change with pH above 4 and remains in solution below 4,<sup>73</sup> while triblock PDEMA-*b*-PGMA-*b*-PDEMA remains in methanol–water and isopropanol–water solution and forms physical gels under neutral or alkaline conditions.<sup>73</sup> Triblock and three-arm

star diblock copolymers were synthesized with atom transfer radical polymerization (ATRP) initiated by bifunctional and trifunctional initiators, respectively, with the central block, PGMA and the outer pH-responsive PDEA or PDPA blocks. The hydrogel formed from these block copolymers show pH response; the free-standing gel formation is observed at neutral or higher pH, but dissolved in acidic solution.<sup>73</sup> Armes and co-workers utilized the emulsion polymerization of 2-(diethylamino)ethyl methacrylate with a bifunctional oligo(propylene oxide)-based diacrylate cross-linker and a PEO-based macromonomer as the stabilizer to make the cross-linked stabilized latexes of approximately 250 nm in diameter, which show reversible swelling properties in water by adjusting the pH. At low pH, swollen microgels caused by protonation of the tertiary amine units are formed, while compact latex particles due to the deswelling occurring when pH is greater than 7. Platinum nanoparticles with well-defined structures can be efficiently impregnated into these microgels by incorporating precursor Pt compounds followed by metal reduction. This nanocomposite can be used as recoverable colloidal catalyst supports.<sup>74</sup>

### 2.3 UV- and visible light-sensitive materials

Light-sensitive hydrogels includes UV-sensitive and visible light-sensitive hydrogels. Upon exposure to UV or visible light, polymer gels undergo reversible photomechanical changes. UV-sensitive hydrogels bearing leuco derivatives or triphenylmethane units will swell in the presence of a UV field and will contract when the field is removed; however this volume transition is discontinuous. Visible light-sensitive hydrogels were prepared using copper chlorophyll bound to NIPAM, which shrinks in response to visible light and contracts when the light source is removed.<sup>45</sup> This can be used in photoresponsive artificial muscles, switches, and memory devices.<sup>45</sup> A problem noted is that the response time is slow and chlorophyll can get leached out of the polymer matrix.

Other photoactuators include cross-linked PMMA- and PAM-bearing dyes and LC elastomers bearing photochromic mesogens.<sup>29,75–77</sup> These polymer gels are composed of: i) elements that exert two- and three-dimensional action at the sub-micron level; ii) these elements interact in a cohesive manner resulting in macroscopic movement, however, the photomechanical response of these systems need to be improved.<sup>29,75–77</sup> Other aspects that need improvement include: i) coupling the movement of the aligned mesogens with the movement of the polymer network for three-dimensional motion for soft actuator; ii) fatigue resistance; iii) biocompatibility.<sup>29,75–77</sup>

### 2.4 Electromechanical actuation

Electroactive polymers (EAP) convert electrical energy into mechanical energy.<sup>25</sup> EAPs can actuate either electronically (driven by electric field)<sup>78</sup> or ionically (mobility or diffusion of ions).<sup>25,79</sup> Commonly used electronic EAPs include elastomers and dielectrics.<sup>24,26,78,80</sup> Ionic EAPs include conducting polymers, polyelectrolyte gels, and ionic polymer metal composites.<sup>25,81,82</sup> Electronic EAPs show rapid response, large strain, good dc activation, and high mechanical energy density but require high operating voltages (100–1000 V). Ionic EAPs operate at



low voltages (1–3 V) but require a protective layer for operation in air, and show low electromechanical coupling efficiency, and slow response. This topic has been discussed in a recent review article by Spontak and co-workers.<sup>80</sup> Electromechanical actuators have projected use in delivery of precise doses of very small quantities of drugs through implants,<sup>15,19</sup> mechanical grippers, sensors, and IPMC operated artificial eye developed by Earmex.<sup>83–85</sup>

## 2.5 Magneto-responsive materials

Polymer fluids composed of magnetic nanoparticles are becoming increasingly important for applications in catalysis, separation sciences, and biosciences.<sup>86,87</sup> Schmidt and co-workers have developed a new strategy to grow PHEMA from surfaces of magnetite nanoparticles to prepare core-shell thermoresponsive gels.<sup>86</sup> These gels form stable dispersions in a solvent above the upper critical solution temperature, while particles precipitate below the UCST. These materials can be used for magnetic separation kits and for catalytic systems.<sup>86</sup> Colloidal microgels of PNVC-co-PAAEM-co-PVIm with BIS cross-linker were prepared by radical polymerization. These polymers incorporate thermosensitive PVCL units (LCST of 28 °C) and pH-sensitive PVIm.<sup>88</sup> Below the LCST, the polymer exists as a swollen chemical gel in water, and above the LCST the gel shrinks to exclude water. Fig. 5 shows the volume phase-transition temperature ( $T_{tr}$ ) of poly(vinylcarproolactam-co-acetoacetoxyethyl methacrylate-co-vinylimidazole). The transition temperature can be tailored by PVIm and PAAEM weight fractions in the copolymer. At pH of 4 or less, the complete protonation of PVIm occurs resulting in extreme swelling and also shifts the LCST towards higher temperature. These protonated microgels were used to template magnetic nanoparticles, which decreases the swelling further and shifts the volume phase-transition temperature to higher values. These hybrid materials respond reversibly to temperature, pH, and magnetic fields which can be used for specific targeting of cancer cells and controlled drug release.<sup>88</sup>

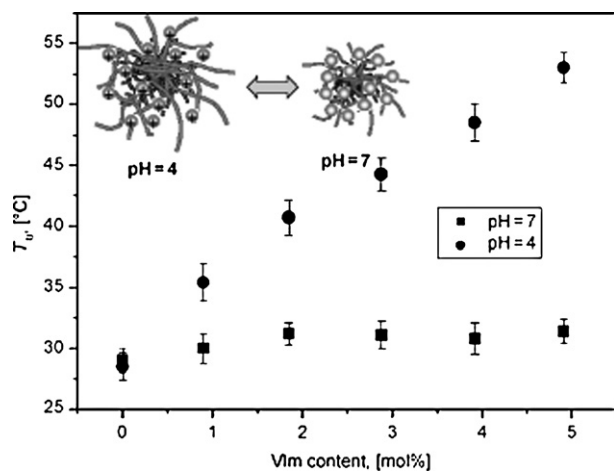
Polymers bearing liquid crystals (LCs) or comprising magnetic particles respond to external magnetic fields by shape

change.<sup>37,89–91</sup> Magnetostrictive polymer gels are a sub-class of soft materials containing magnetizable components, which have been embedded in the gel during the cross-linking process.<sup>37,89–91</sup> These magnetic particles can be aligned resulting in materials with anisotropic mechanical and magnetic properties with fast response.<sup>89,91</sup> Farshad and Le Roux have performed a number of compression tests on the cylindrical shaped specimen of polymer gel. Higher values of compression modulus or stresses of the samples in the presence of the magnetic field compared with ones in the absence of magnetic field were observed. The magnetic induction of the gel increased due to the presence of the magnetic particles resulting in stiffening and strengthening effect on the magnetostrictive gels affording a new class of actuators.<sup>37,87,92,93</sup>

## 2.6 Other stimuli-responsive materials

Tabata and co-workers have studied self-oscillating gels which exhibits ciliary actuation.<sup>94</sup> In this study, poly(NIPAM-co-Ru(bpy)<sub>3</sub>) is immersed in an aqueous solution at constant temperature of 20 °C. A chemical wave is generated by the periodic redox changes of Ru(bpy)<sub>3</sub> due to the Belousov–Zhabotinsky (BZ) reaction, which manifests itself in the lighter color of the oxidized state. This redox reaction alters the hydrophobic and the hydrophilic properties of the polymer chains and results in swelling and deswelling of the gel. Thereby a stable chemical wave, which has a specific frequency and velocity, is produced. This chemical wave can be visualized because it corresponds to the motion of the light-colored oxidized part of the gel. The realization of this circular motion actuator made from self-oscillating polymer gel is similar to the propagation of the electrical signal in heart.<sup>94</sup> Yoshida and co-workers studied the effect of concentration of various substrates (malonic acid, sodium bromate and nitric acid) on redox changes of Ru(bpy)<sub>3</sub> (BZ reaction) in polymer gels.<sup>95</sup> A decrease in the initial concentration of NaBrO<sub>3</sub> has a strong effect on the period; that is, an increase in the period both in the gel and the solution system. Unlike solutions, a decrease in the concentration of malonic acid in gels causes a change in the waveform of the oscillating profiles of redox changes measured as mole fraction of the oxidized catalyst (Ru<sup>3+</sup>). Responsive properties of chiral polymers bearing bpy and other heterocyclic ligands act as recognition sites for transition metal ions. These gels are promising candidates to model mechanism for metallo-gelation and as sensors.<sup>96,97</sup>

Crossed helical structures are common in invertebrates, such as worms, providing skin or cuticle reinforcement with various geometrical arrangements.<sup>98,99</sup> These structures are capable of containing and protecting the inner part of the body and allow motion, which takes place by effect of the increase in body internal pressure. Worm motion can be mimicked using a gel included in a cylindrical braided structure. Gel swelling consequent to hydration forces the braided structure to pass from the minimum to the maximum angle, hence generating useful work. These gel systems, capable of changing shape and/or volume as a result of chemical or electrical stimuli, can be used to drive the shape changes in a similar fashion and the designs can be tailored to give a range of responses.<sup>99</sup>



**Fig. 5** Volume phase-transition temperature ( $T_{tr}$ ) of VCL-AAEM-PVIm microgels as a function of PVIm content. The degree of swelling is controlled by PVIm content in a microgel (reprinted with permission from ref. 88).

In some hybrid metallo-polymer gels there are two levels of cross-linking present: i) permanent cross-linking, which creates a stiff permanent scaffold in organic solvents; and ii) reversible metal-ligand cross-linking, which results in tough gels. These materials can be programmed to fail under stress by varying the extent of each type of cross-linking. These stress-induced reactions within the polymer can be used to initiate chemistries that can heal the damage resulting in self-healing materials.<sup>100</sup>

Kang and Bae synthesized a new glucose-sensitive hydrogel which is based on sulfonamide chemistry with covalently conjugated glucose oxidase and catalase. The pH-induced full swelling transition of the gel occurred in the pH range 6.5 ~ 7.5. In a glucose concentration range of 0–300 mg dl<sup>-1</sup> in an isotonic phosphate buffered saline solution (pH 7.4), the pH inside the gel varied from 7.4 to 7.2. At the same glucose concentration range, the gel showed reversible glucose dependent swelling without hysteresis from 12 to 8 (water (g)/polymer (g)).<sup>101</sup>

A new conjugation technique to prepare polymerizable peptides that may be useful for biological sensing and other applications have been introduced. An  $\alpha$ -chymotrypsin-responsive peptide has been used as a model to determine the optimal conditions for the preparation and dissolution of poly(acrylamide) hydrogels with proteases. Methacrylamide groups were selectively coupled to cysteine residues in the presence of amines and alcohols by utilizing a disulfide-exchange reaction in aqueous, acidic buffer. The tetrapeptide sequence was used as a cross-linker to create poly(acrylamide) hydrogels that dissolves when subjected to either a flowing or stationary solution of  $\alpha$ -chymotrypsin. The described conjugation technique might also find utility in materials that will chemically release peptide reagents in response to a stimulus (reduction of disulfide bonds) or the preparation of other biologically relevant biopolymer hybrids (*i.e.*, DNA, sugars, lipids). The presented technique may furthermore be developed to more complex protease-peptide recognition systems with applications toward biowearables detection.<sup>102</sup>

### 3. Current and future directions of the field

Concurrent developments in design of new responsive polymers along with structure-property evaluation, fabrication of materials, and modeling of materials are vital for the applications of polymer gels. Firstly, bio-responsive hydrogels and elastomers that show a response to enzymes, proteins, and other combinations of stimuli are important for biotechnological applications of shape-memory including modulated drug-release studies, biosensors, diagnostics, tissue regeneration/wound healing, cell-encapsulation membranes and hybrid organ development.<sup>103–107</sup> Major considerations for the usage of these materials include biocompatibility, bio-degradability, mechanical strength, response time under physiological conditions, and good correlation between *in vitro* and *in vivo* studies.<sup>14,106,108,109</sup> Secondly, stimuli-responsive polymer gels are good candidates for the design of microfluidic channels to fabricate elements for separation, catalysis, sensing, surface modifications, and dosing micro-volumes of liquids.<sup>110–114</sup> Lastly, an exciting and important direction for stimuli-responsive materials is the design of new polymer gels that produce nanoscale fractal patterns for renewable energy applications.<sup>18,115,116</sup>

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