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Hydrogels with Self-Healing Attribute

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Abstract

Given increasing environmental issues and energy crisis, mimicking nature to confer materials with self-healing attribute to prolong their lifespan is highly imperative. As representative of soft matter with extensive applications, hydrogels have gained significant attention. In this chapter, a survey of the current strategies for synthesizing self-healing hydrogels based on inorganic-based, polymer and nanocomposite hydrogels is covered and highlighted. Several examples for non-autonomic and autonomic self-healing hydrogels, according to the trigger exerted, are presented. General mechanisms accounting for self-healing hydrogels are listed. Some typical instances to outline the emerging applications of self-healing hydrogels are also provided. Finally, a perspective on the current trends and challenges is briefly summarized.

Keywords: self-healing, hydrogel, hydrogen bond, interactions, application

1. Introduction

After billions of years of evolution, living organisms in nature possess special functions, such as super-hydrophobicity, self-healing, self-cleaning and anti-reflection [1]. Among these, self-healing, the ability of a system or material to repair itself and regenerate function upon the infliction of damage, gained numerous academic curiosity, for this fascinating property would extend the working lifespan and broaden their applications of creatures. Inspired by this, scientists have been trying their best to design and impart intriguing self-healing properties to desired materials with low production costs and improved safety. As representative of soft matter with widespread applications, hydrogels with a self-healing attribute have been developed rapidly as “smart” materials [2].

2. Self-healing process

Self-healing hydrogels can be divided into two different categories according to the required additional external energy or trigger exerted on the hydrogels during the self-healing process: non-autonomic and autonomic.

2.1. Non-autonomic self-healing process

Non-autonomic self-healing hydrogels require a modest external trigger, such as heat or light. Trigger-responsive hydrogels adapting to the surrounding environment and responding to external stimuli are emerging as 'smart hydrogels'. Ultrasound is used in sonophoresis to disrupt skin transiently for needle-free transdermal drug delivery, and damage caused by sonophoresis can be self-healed by skin after the removal of ultrasound stimulus. Similarly, Ca^{2+} cross-linked alginate smart hydrogels were fabricated and ultrasonicated to accelerate drug release, but the Ca^{2+} in physiological fluids would allow crosslinks to self-heal upon removal of the stimulus [3].

Graphene-poly(N,N-dimethylacrylamide) (PDMAA) hydrogel exhibits a thermally triggered (heated at 37°C in air for 12 h), analogous to the healing of wounds in human tissues (37°C), and near-infrared laser-triggered (near-infrared laser irradiation treatment for 2 h), similar to a minimal invasive surgery procedure, self-healing behaviour [4].

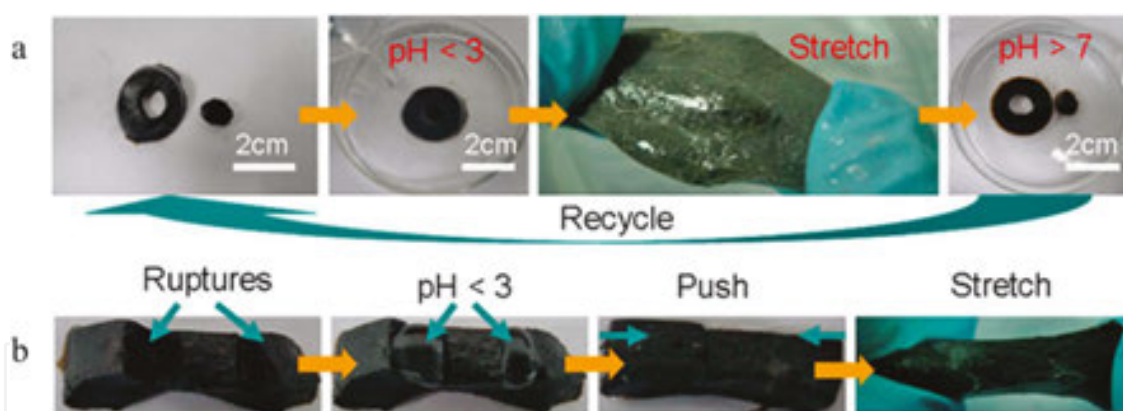


Figure 1. (a) Self-healing and recycling properties of GO/PAACA hydrogel; (b) self-healing process of the GO/PAACA hydrogel with two manual ruptures. The hydrogel was healed just by dripping two drops of acid solution into the ruptures and pushing the fresh surface into contact [5].

Besides ultrasound, heat and light, hydrogels can also self-heal through another important stimulation pH. After immersing in acid solution ($\text{pH} < 3$) completely for several seconds, the separated parts of punched GO/poly(acryloyl-6-aminocaproic acid) (PAACA) hydrogel were recombined together, the healed hydrogel separated again when being reintroduced into the high-pH solution (**Figure 1a**) [5]. It was a reversible process, demonstrating fast self-healing capability and reversibility of healing-separation-rehealing process to the pH stimulus. Dropping two drops of acid solution instead of immersing into acid solution can heal the ruptures too (**Figure 1b**).

2.2. Autonomic self-healing process

Compared with non-autonomic self-healing hydrogels, hydrogels with autonomic self-healing capacity do not require any additional external trigger, the damage itself is the stimulus for the healing. Below we highlight some recent examples of autonomic self-healing hydrogels.

The multiple ionic interactions between Fe^{3+} ions and carboxyl groups of poly(acrylic acid) (PAA) produced a non-covalent network of polymer chains [6]. Inter-chain bonding between PAA and ferric ions across the interface autonomously self-heals the damage and rejoins the two halves of the hydrogel. Rheology measurement is used to quantitatively assess the extent of damage or self-healing of the PAA hydrogel. The gel-like character ($G' > G''$) was recovered instantaneously, and G' and G'' were recovered to the initial values immediately. This disruption and recovery of the PAA hydrogel properties under different oscillatory shears can be repeated several times.

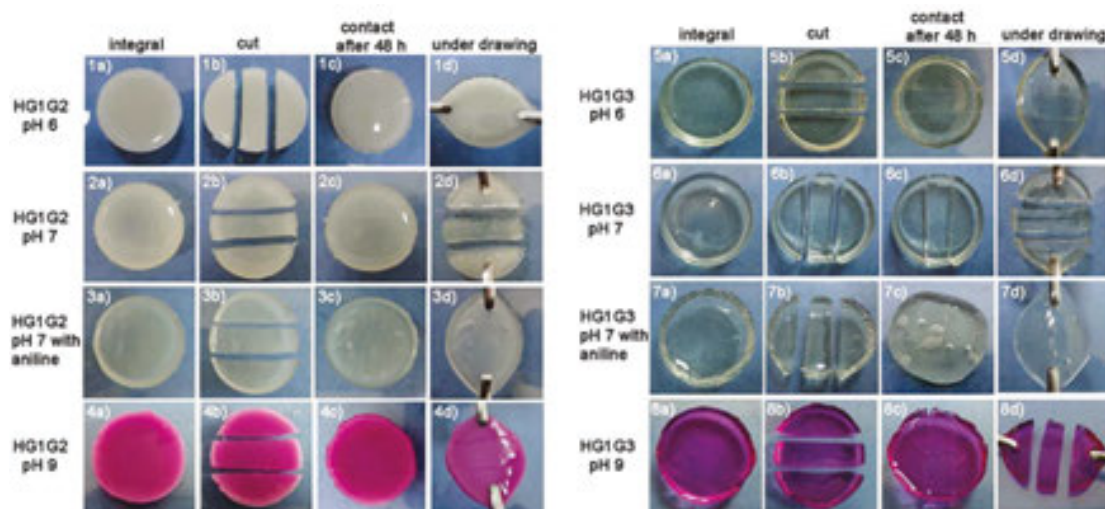


Figure 2. Self-healing properties of HG1G2 (10 wt%) and HG1G3(10 wt%) [7].

HG1G2 (prepared from aldehyde-terminated 3-armed PEO (G1) and dithiodipropionic acid dihydrazide (G2)) and HG1G3 (prepared from G1 and hexanedioic acid dihydrazide (G3)) hydrogels can automatically self-heal under both acidic (pH 3 and 6) and basic (pH 9) conditions through dynamic covalent bonds of acylhydrazone or disulphide (**Figure 2**). However, the hydrogels are not self-healable at pH 7 because both bonds are kinetically locked, whereas catalytic aniline added can accelerate the acylhydrazone exchange reaction and facilitate the hydrogels self-healing at pH 7. All of the self-healing processes are autonomic at room temperature in air [7].

3. Classification of self-healing hydrogels

The past decade has witnessed the rapid development of self-healing hydrogels. According to the materials utilized, self-healing hydrogels can be clarified into inorganic-based, polymer

and nanocomposite hydrogels. The important aspects of and trends in self-healing hydrogels are discussed in the following section.

3.1. Self-healing inorganic-based hydrogels

Generally speaking, hydrogels consist of cross-linked networks of hydrophilic polymers swollen with an aqueous solution. Herein, inorganic-based hydrogels, with or without organic macromolecules or metal ion as the crosslinkers, are those whose main building blocks are inorganic [8]. It is different from classical nanocomposite hydrogels with polymer as main building blocks, and nanofillers usually provide physical cross-linking sites [9]. With one- or two-dimensional (2D) basic building blocks, inorganic-based hydrogels have attracted great attention because the fascinating properties of inorganics may bring additional functions to the macroscopic hydrogels [10–12].

Numerous intriguing properties of novel inorganic graphene have prompted scientists to translate its 2D sheets into complex three-dimensional (3D) macrostructures. Shi's group had synthesized the first graphene hydrogel via facile one-step hydrothermal reduction of a highly concentrated graphene oxide (GO) aqueous dispersion in 2010 [13]. Strong hydrophilicity and electrostatic repulsion effect result in random and uniform dispersing of separated GO sheets in GO aqueous dispersion before reduction. After hydrothermal reduction, the oxygenated functionalities, located on the basal planes and at the edges of GO, decreased significantly, whereas π -conjugation restored largely. Combined with hydrophobic effect, π - π stacking interaction promoted flexible rGO sheets to partially overlap and interlock with each other for self-assembling into hydrogel. Hydrothermal reduction strategy is one of the most direct and non-chemical methods to produce graphene hydrogels without introducing any other chemicals or further purification treatment. In addition to hydrothermal reduction, ultrasonication is another additive-free approach for preparing graphene hydrogels [14].



Figure 3. Preparation schematic of graphene-based hydrogel with cross-linking structure [4].

Besides, GO sheets can readily self-assemble into hydrogels in water with the assistance of various promoters, including multivalent metal ions (e.g. Ca^{2+} , Mg^{2+} , Fe^{3+}) and polymer [15].

After the monomer solution free-radical polymerized in the graphene hydrogel network, graphene-based hydrogel can be obtained (**Figure 3**). Graphene-PDMAA hydrogels prepared through this method demonstrate thermally triggered and near-infrared laser-triggered self-healing capacity. The electrical conductivity and compressive strength of the

graphene-PDMAA hydrogels recover 60% and 82% approximately of the initial value through the thermally triggered self-healing process [4].

In another typical example, β -cyclodextrin (β -CD) functional graphene-PDMAA hydrogel with self-healing property can control drug linear release at the beginning of 7 h [16], making the double network graphene-based hydrogel potential candidate for anticancer drug carrier. However, single network β -CD functional graphene hydrogels can't self-heal. Therefore, the hydrogen bonding interaction between PDMAA and graphene attributed to self-healing capability of double network graphene-based hydrogels.

Clay, another typical inorganic widely spread on earth, distributes inhomogeneous charge on its disk-like structure. With this special structure and distributed ion, 'house-of-cards' structured hydrogel generates [17].

Figure 4. Schematic description of the formation mechanism for D-clay hydrogels [21].

Hydrogels with swollen clay as the basic building block and a small proportion of telechelic dendritic macromolecules as the crosslinker are fabricated readily by mixing the components in water at room temperature. Multiple adhesive termini in the telechelic dendritic macromolecules provide strong noncovalent interactions with clay in these hydrogels. Together with high mechanical strength, such supramolecular hydrogels are also featured by their rapid and complete self-healing behaviour [18]. Though the hydrogel can be fabricated facilely, key component telechelic dendritic macromolecules, physical crosslinker of the hydrogel, cannot be synthesized and obtained easily.

Catechol groups in 3,4-dihydroxy-L-phenylalanine (DOPA), a natural amino acid abundantly present in mussel adhesive proteins, are capable of forming metal-ligand complexes with various surfaces [19]. The reformation of catechol- Fe^{3+} complex after breaking can self-heal the damage [20]. Similar to catechol-ferric ion complexes in mussel-adhesive proteins fibres, clay-based hydrogels with polydopamine (PDOPA)-modified clay (D-clay) as the main building block and ferric ion (Fe^{3+}) as the physical crosslinker are constructed [21]. The coordination bonds between the PDOPA coating on clay nanosheets and Fe^{3+} drive the formation and self-heal the damage of the clay-based hydrogels (**Figure 4**).

3.2. Self-healing polymer hydrogels

Compared with inorganic-based hydrogels, polymer hydrogels are more biocompatible for they resemble biological systems in many ways. On the basis of this, self-healing polymer hydrogels gain much more attention. Li et al. [22] developed a kind of degradable and biocompatible poly(L-glutamic acid) (PLGA)-based self-healing hydrogels via host-guest interaction (**Figure 5a–h**). The self-healing ability of the hydrogels was confirmed by the macroscopic self-healing tests qualitatively (**Figure 5i**) and rheological measurements quantitatively. A 15% w/v PLGA30250 hydrogel in phosphate-buffered saline (PBS) at 37°C can totally degrade in 72 days. Cytotoxicity investigation had shown that the hydrogels could provide a suitable environment for cell growth. Taken together, the self-healing hydrogels could potentially be applied in biomedical fields.

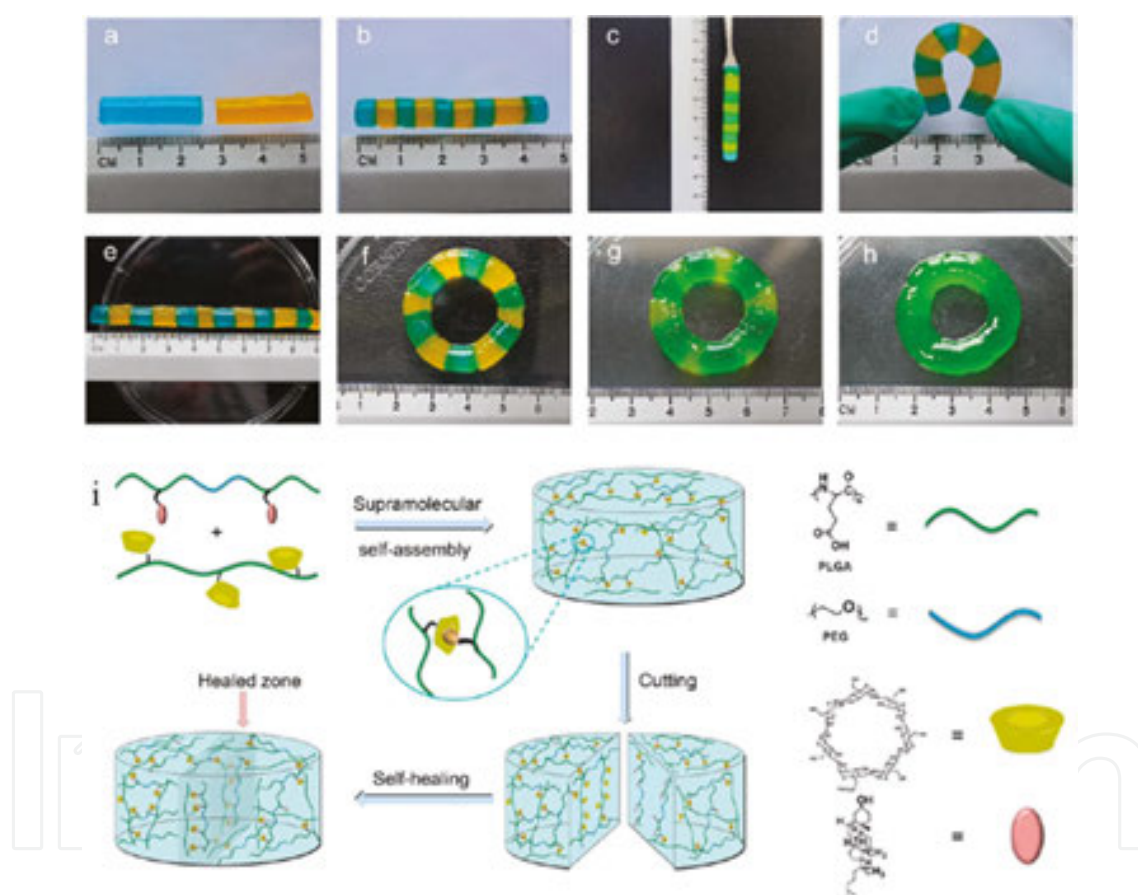


Figure 5. Flexibility of self-healing hydrogels: (a) two rod-like hydrogels stained with erioglaurine disodium salt (EDS) and tartrazine (TAR), respectively; (b and e) colour alternating hydrogel columns; (c) the self-healed hydrogel column held vertically by forceps; (d and f) the healed hydrogel rod bent to a semicircle or a circle. The evolution process of the colorant diffusion: Photo images of colour alternating hydrogel column stored for 1 (f), 12 (g) and 36 h (h). Preparation and self-healing process of supramolecular hydrogels (i) [22].

As a typical biocompatibility and nontoxicity macromolecule with crystalline nature, poly(vinyl alcohol) (PVA) has long been used to fabricate hydrogels via freezing/thawing methods [23, 24]. After self-healing for 12 h at room temperature without any external stimulus,

PVA hydrogel can withstand bending without failure at the interface (**Figure 6**). Tensile tests confirmed that the fracture stress after 48 h healing is ~ 200 kPa, and the healing efficiency is $\sim 72\%$ [24].

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Figure 6. Self-healing behaviour of PVA hydrogel: (a) two pieces of original hydrogel with and without rhodamine B for coloration; (b) two halves of the original hydrogels cut from the middle; (c) self-healed hydrogel upon bringing the two separate halves in contact for 12 h in air at room temperature without any external stimulus; (d) bending of the self-healed hydrogel; (e) stretching of the self-healed hydrogel to about 100% extension [24].

Self-healing attributes to the hydrogen bonding between PAA chains. However, hydrogen bonding is commonly a weak noncovalent bond. In order to solve the issue, diaminotriazine-diaminotriazine (DAT-DAT) hydrogen bonding is formed, and both the tensile and compressive strength can be significantly enhanced; after heating at 90°C for 3 h, healing efficiency (HE) is able to reach 84% and the strength of the mended hydrogel was up to 1 MPa, quite amazing in self-healing hydrogels [25]. Though mechanically robust, lack of effective energy dissipating made these hydrogels brittle. What's more, they don't have the antibacterial property, thus limiting their implantation application [26].

Polyimide (PI) is an important high-performance plastic, and there are many hydrogen bonding, π - π stacking interactions between the chains of its traditional precursor poly(amic acid) (PAA). These non-covalent interactions may confer PAA special attributes, such as self-healing, as macroscopic material. To verify our hypothesis, we aim to synthesize a PAA hydrogel. However, as is known to all, PAA is hydrophobic. In order to overcome this limitation, triethylamine (TEA) was utilized to react with the carboxyl of PAA, and a hydrophilic polyelectrolyte poly(amic acid) ammonium salt (PAS) was obtained (**Figure 7a**) [27]. The as-prepared PAS hydrogel is temperature responsive and robust. In addition, multiple intermolecular interactions, including hydrogen bonds, π - π stacking and polyanion-polycation interactions, served as a combined driving force for the self-healing of hydrogel networks (**Figure 7b,c**). On the basis of this pioneering work, PI aerogels with multifunction were fabricated [28]. Our strategy could open a pathway and possibility for the fabrication of other self-healing functional hydrogels through transformation of hydrophobic polymers to hydrophilic.

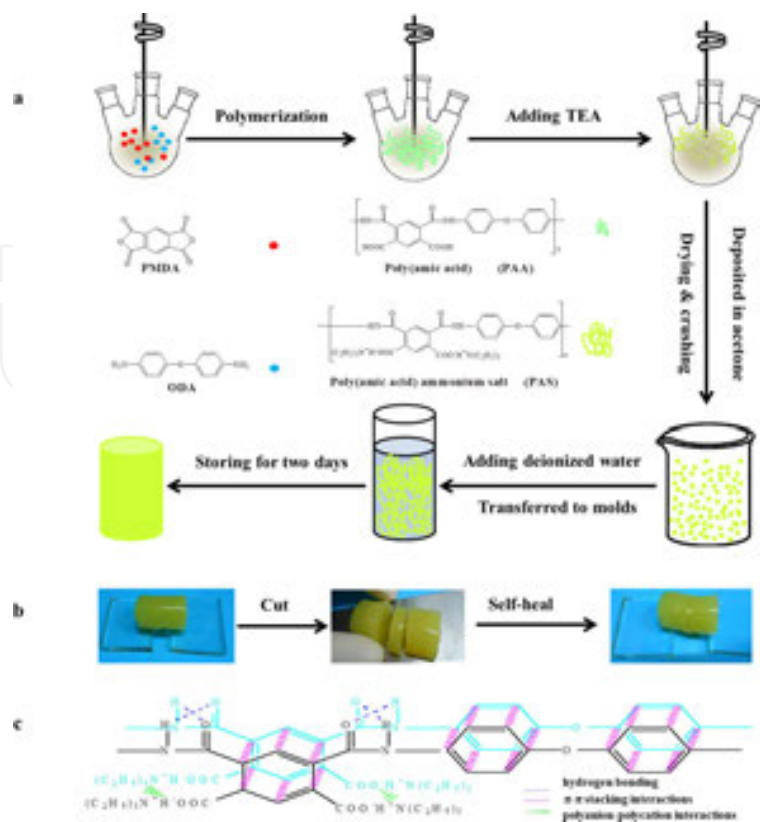


Figure 7. (a) Schematic diagram for the synthesis of PAS hydrogel; (b) self-healing process of PAS hydrogel; (c) possible interactions between PAS chains of PAS hydrogels [27].

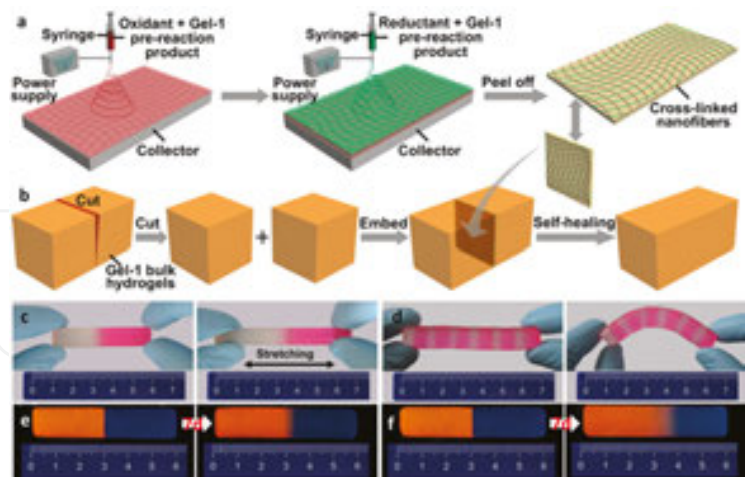


Figure 8. (a) Fabrication of gel-1 healing layer formed of nanofibre networks; (b) enhanced self-healing procedure upon embedding a healing layer into the damage area of gel-1 bulk hydrogels; a sample constructed by juxtaposing a healing layer between two hydrogel blocks exhibits extraordinary mechanical toughness: (c) before and after stretching; (d) a hydrogel column constructed from the connection of 12 hydrogel blocks alternating with six healing layers can be held horizontally and bended by hands; fluorescent images of hydrogels constructed by connecting together two hydrogel blocks (e) without and (f) with 0.05 wt% rhodamine B, respectively, stored for 7 days [29].

Substances	Healing conditions	Healing efficiency	Self-healing mechanisms	Ref.
PVA	RT, 48 h	~72%	Hydrogen bonds	[24]
PNAGA	90 °C, 3 h	84%	Hydrogen bonds	[25]
A6ACA	pH ≤3, <2 s	Hydrogen bonds	[30]	
PAMPSA	water, 72 h	~100%	Hydrogen bonds	[31]
PU	RT, 10 min	>60%	Quadruple hydrogen bonds	[32]
DNODN, BNOBN	RT, instantly	57%	Multiple intermolecular interactions	[33]
PAS	RT, instantly	Multiple intermolecular interactions	[27]	
P(AM-co-DMAPS)		~100%	Multiple intermolecular interactions	[34]
Poly(L-glutamic acid)	60 s		Host-guest interaction	[22]
pAA-6βCD/pAA-Fc	GSH aq, 24 h	84%	Host-guest interaction	[35]
PAAm	Press, few seconds	~100%	Hydrophobic interactions	[36]
Agar/HPAAm	RT, 24 h	40%	Hydrophobic interactions	[37]
PNIPAAm	24°C, 30 min	~100%	Hydrophobic interactions	[38]
PAAm	35°C, 3 min	98%	Hydrophobic interactions	[39]
Ferrocene-modified chitosan	RT, 4 h	~100%	Hydrophobic interaction	[40]
Dex-I-PEG	37°C, 12 h	98.7%	Diels-Alder reaction	[41]
GOX/CAT	RT, 5 h	100 %	Imine bonds	[42]
CSMA/SC	Moisture, RT, 2 h	Imine bonds	[43]	
Chitosan-PEG	RT, 2 h		Imine bonds	[44]
cPEG/BDBA	Rapidly		Boronate-catechol	[45]
Poly(acrylic acid)	RT, ~6 h	~88%	Fe ³⁺ -carboxylic	[6]
HG1G2	RT, 48 h		Acylhydrazone(acid) disulphide (base)	[7]

Table 1. Examples of various self-healing polymer hydrogels and their self-healing properties.

Noticeably, Fang et al. reported a new strategy to prepare robust, repeatable self-healing hydrogels assisted by a healing layer composed of electrospun nanofibre containing redox agents (**Figure 8a,b**) [29]. Self-healed hydrogels embedded with the electrospun nanofibre exhibit extraordinary mechanical toughness (**Figure 8c, d**). With the same composition of fibre layer as the bulk hydrogels, electrospun nanofibre with redox agents as healing layer can accelerate the molecular diffusion (**Figure 8e,f**), resulting in half of the healing time compared with the one without healing layer, and the healing efficiency is about 80%. This work provides promising avenues to endow electrospun cross-linked nanofibre networks with more potential applications.

Limited by the length of the chapter, other fascinating works cannot be introduced. To make up for this, herein, examples of various self-healing polymer hydrogels and their self-healing properties are summarized in **Table 1** [6, 7, 22, 24, 25, 27, 30–45].

3.3. Self-healing nanocomposite hydrogels

In general, nanocomposite hydrogels refer to cross-linked polymer networks swollen with water in the presence of nanoparticles or nanostructures [9]. The combination of self-healing hydrogels with nanostructures can lead to nanocomposite hydrogels with unique properties. Nanocomposite hydrogels with Fe_3O_4 nanoparticles make them magnetic hydrogels [46], and graphene nanosheets will afford the nanocomposite hydrogels high conductive, mechanical, absorption properties [47, 48] and shortened self-recovery time [49].

Figure 9. Self-healing nature of graphene-based hydrogel: left, schematic diagram of graphene-DNA hydrogel; and right, demonstration of self-healing properties [55].

One of the most frequently used nanoplatelets (NPs) in nanocomposite hydrogels over the past few years is clay nanoplatelets. Kazutoshi Haraguchi et al. [50], Haraguchi and Li [51] and Haraguchi [52] had conducted many pioneering works on clay-containing nanocomposite hydrogels through in situ free-radical polymerization. In 2011, his group reported two kinds of nanocomposite hydrogels, PDMAA-nanocomposite (D-NC) and PNIPA-nanocomposite (N-NC) [53]. Mechanical damage in NC hydrogels healed autonomously after 48 h at 37°C. While in contrast to the D-NC hydrogels, the N-NC hydrogels hardly self-heal at high temperature (50 or 80°C) after mechanical damage, which can be attributed to the coil-globule transition of PNIPAAm chains above lower-critical-solution temperature (LCST) (32°C). Using the same method, recently, Gao et al. [54] reported polyacrylamide/montmorillonite nanocomposite hydrogels (MnA hydrogels) with unprecedented stretchability and toughness, i.e.

high fracture elongation up to 11800% and fracture toughness up to $10.1 \text{ MJ}\cdot\text{m}^{-3}$. The MnA hydrogels demonstrated interesting self-healing properties. After self-healing directly at room temperature, the self-healed hydrogels became weak and easily disrupted at the interface. While drying the preliminarily jointed hydrogels to water content of about 10 wt% and reswollen at room temperature to its original water content, the fracture strains of self-healed hydrogels were very close to the as-prepared hydrogels. During the drying-reswelling procedure, the preliminary contact of the cut segments facilitated the diffusion of polymers across the interface. Subsequent drying is the driving force for diffused polymers to closely contact the clay platelets and vital to establish strong PAAm/MMT adhesion.

In addition to nanoclay, other nanosheets, such as GO, have also been used to develop self-healing nanocomposite hydrogels. Until now, there are mainly two approaches to introduce GO into the nanocomposite hydrogels: self-assembly and in situ polymerization.

Shi's group provided a new insight for the self-assembly graphene oxide and DNA into a composite hydrogel with high mechanical strength, stability and absorption capacity. This hydrogel was also self-healable after heating at 90°C for 3 min (**Figure 9**) [55]. After heating treatment, the blocks adhered to each other and the resulting self-healed hydrogel was strong enough to bridge two posts horizontally or allow vertical handle.

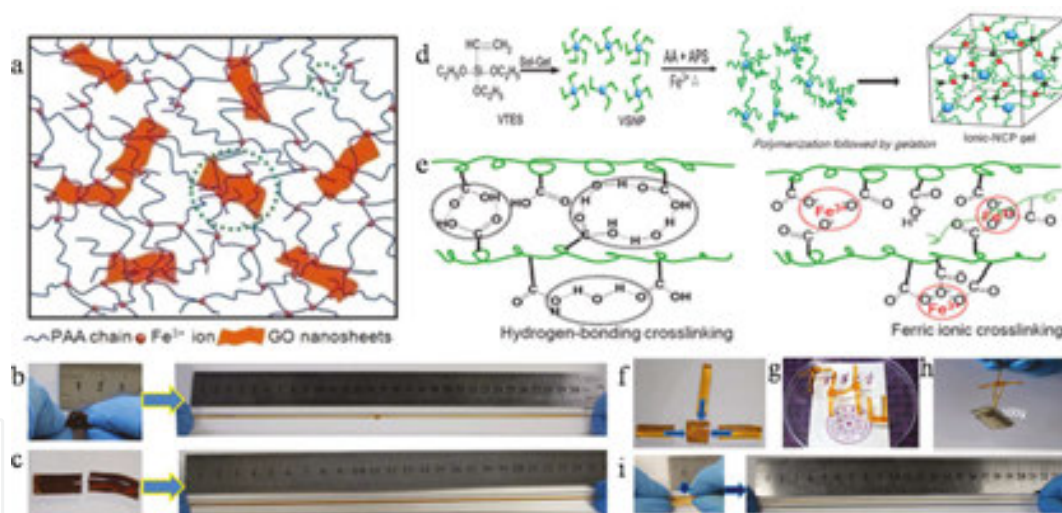


Figure 10. a) A scheme of the three-dimensional network structure of GO-PAA nanocomposite hydrogels facilitated by Fe^{3+} ions with dual cross-linking effects (the smaller green dotted circle represents the first cross-linking points that are Fe^{3+} ions creating ionic cross-linking among PAA chains, and the larger green dotted circle represents the second cross-linking points that are GO nanosheets linking PAA chains through coordination); the GO-PAA nanocomposite hydrogels can be (b) stretched over 30 times from a knotted state and (c) stretched over 20 times after being healed (45°C , 48 h) from a cut-off state [57]; (d) preparation of ionic-NCP gels; (e) illustration of the physical crosslinks formed by hydrogen bonding and Fe^{3+} ionic interactions; self-healing properties of ionic-NCP gels; (f) images of severed cylinder samples of different sizes that were connected and healed as indicated; (g) free-standing healed samples after incubation at 50°C for 48 h; and (h) the healed hydrogel suspending a 100 g weight; (i) stretching of the healed ionic-NCP gel to more than 18 times of its initial length [58].

GO/PAACA nanocomposite hydrogels with double network had been prepared through in situ polymerization. Ca^{2+} acted as crosslinkers through coordination interactions with both

oxygen-containing groups of GO nanosheets and polar groups of PAACA side chains, thus inducing the formation of the 3D cross-linked network. Meanwhile, Ca^{2+} content was an important factor to influence the mechanical properties of the fracture stress of the hydrogels. The as-prepared hydrogels are pH triggered and self-healable [5].

Zhong et al. [56–58] proposed a ‘single network, dual (or hierarchical) cross-linking’ strategy to prepare various tough and highly stretchable nanocomposite hydrogels. For example, nanocomposite hydrogels based on GO prepared by in situ free radical polymerization achieved remarkable synergistic effect (**Figure 10a**): (i) the reinforced-GO nanosheets provide excellent mechanical strength and the cross-linking site between GO nanosheet and PAA chain which triggered by Fe^{3+} ions; (ii) the matrix-PAA chains provide excellent flexibility; (iii) the linker- Fe^{3+} ions provide dynamic and recoverable cross-linking [57]. GO/PAA nanocomposite hydrogels demonstrated superior stretchability and exceptional self-healing properties (**Figure 10b,c**). When stretched, the ionic interaction among PAA chains can dynamically break and recombine to dissipate energy and homogenize the gel network simultaneously. Coordinated with PAA chains, GO nanosheets can maintain the configuration of the hydrogels and act as stress transfer centres transferring the stress to the polymer matrix. The healed GO-PAA nanocomposite hydrogels treated at 45°C for 48 h have the best mechanical properties, with a tensile strength of 777 kPa, elongation at break of 2980%, and the healed nanocomposite hydrogels have a tensile strength of ~ 495 kPa and elongation at break of $\sim 2470\%$. The self-healing stemmed from dynamic ionic interactions.

Besides two-dimensional nanosheets, 0-dimensional nanoparticles are also frequently introduced into hydrogels to endow hydrogel multifunction. Silica nanoparticles were hybridized with vinyl to graft an acrylic acid monomer on the surface for the growth of poly(acrylic) acid (PAA) [58]. Network structure of the obtained ionic cross-linked VSNP/PAA nanocomposite physical hydrogels (Ionic-NCP gels) consisted of ferric ion-mediated reversible physical cross-linking, intra- and inter-polymer chain hydrogen bonding, physical entanglement of the polymer chains and multivalent covalent cross-linking through the vinyl hybrid silica nanoparticles (VSNPs) (**Figure 10 d,e**). The prepared Ionic-NCP gels have excellent mechanical properties, with the tensile strength being approximately 860 kPa. In contrast, the hydrogel without ferric ions is much weaker, with a tensile strength less than 50 kPa at fracture, illustrating the importance of ionic cross-linking. In addition, these Ionic-NCP gels exhibit excellent self-healing properties, and the healed hydrogel could be stretched to approximately 15 times its initial length and possessed prominent tensile strength (**Figure 10f–i**).

Different from VSNPs who served as multivalent covalent cross-linking points, poly(2-dimethylaminoethyl methacrylate) (PDMAEMA) brush-modified silica nanoparticles (SiO_2 @PDMAEMA) acted as multifunctional noncovalent crosslinkers in a poly(acrylic acid) (PAA) network structure, dissipating energy, whereas the electrostatic interactions between cationic PDMAEMA and anionic PAA render the hydrogel self-healing properties [59]. Grafting of high-density PDMAEMA brushes onto the surface of SiO_2 nanoparticles contributed to the efficient self-healing property significantly. Self-healing efficiency of the healed SiO_2 @PDMAEMA/PAA hydrogel is nearly 100%, whereas that of the SiO_2 /PAA is only about

50% after 12 h, indicating that the physical adsorption between bare SiO₂ nanoparticles and PAA chains is relatively weak.

From the abovementioned examples, we can see that modification is necessary and vital to nanoparticles. Fe₃O₄ nanoparticles with carboxyl modification could be dispersed well in chitosan solution to form a stable ferrofluid due to the interaction between NH₂ on chitosan and carboxyl groups. External magnetic field exerted could help the as-prepared magnetic hydrogel to stay at the target position and bring hydrogel pieces together to ensure the self-healing process [46].

Moreover, there were other remarkable reports on the self-healing nanocomposite hydrogels: Liu et al. [60] reported self-healed graphene oxide composite hydrogels with very high tensile strengths (up to 0.35 MPa) and extremely high elongations (up to 4900%). Peng et al. [47] presented nanocomposite hydrogels with excellent electrical self-healing properties (completely healed after 20 s) and ultra-high water-absorption ability (up to 350 times). Du et al. [61] reported that multifunctional PPA/carbon nanotube (CNT) hydrogels could respond to a variety of environmental stimuli and exhibit autonomous self-healing properties in both wet and dried states, pointed out that hierarchical hydrogen bond manipulation is a general but powerful strategy to design and synthesize a host of multifunctional materials for versatile applications.

4. Self-healing mechanisms of hydrogels

As previously mentioned, research on self-healing hydrogels is fruitful. In general, self-healing mechanisms of these hydrogels can be illustrated physically and chemically. From the physical viewpoint, during self-repairing, flow of molecular segments across the interface allows the hydrogel networks to be broken at the interface to be rebuilt. As is known, this mechanism is the so-called molecule diffusion. To visualize the molecule diffusion mechanism, digital monitoring [6, 7, 42, 46, 62], scanning electron microscopy (SEM) and ultraviolet (UV) excitation are ideal methods and characterization techniques [29, 63]. Chemically, re-bonding of cleaved non-covalent interactions and dynamic covalent bonds after mechanical damage is particularly critical [2]. As depicted in **Figure 11**, non-covalent interactions between molecules or polymer chains include hydrogen bonds, hydrophobic interactions, crystallization, host-guest interactions, polymer-nanocomposite interactions and multiple intermolecular interactions. Dynamic covalent bonds include cyclohexenes (reversible Diels-Alder cycloaddition), sulphur-sulphur bonds (disulphide), boron-oxygen bonds (phenylboronate ester), carbon-nitrogen bonds (imine, acylhydrazone) and carbon-carbon/carbon-sulphur bonds (reversible radical reaction). Compared to dynamic covalent bonds, non-covalent interactions show a higher dynamic behaviour. Molecule diffusion physically and re-bonding of cleaved bonds chemically combine with each other to facilitate the self-healing of hydrogels.

Factors which accelerate polymer diffusion lead to the acceleration of self-healing [53]. In order to look into the underlying mechanism, the impact of many parameters on the self-healing

efficiency, including separation time [24], self-healing time [31, 53], temperature [30, 53], chain length [30, 64] and nanomaterial content [49, 60], should be deeply investigated. With long separation time, polymer chains at the interface could rearrange to minimize the surface energy. Thus the number of free groups on each surface decreases over time, which reduces the number of cleaved bonds that can be reformed across the interface when the two surfaces are brought together [24]. The longer self-healing time, the deeper polymer chains diffuse across the interface, and hence stronger interactions are formed. Temperature strongly affects the diffusion rate of the polymer chains. Short chains facilitate fast molecular diffusion but cannot diffuse deeper, while long chains confer high strength recovery at the interface to hydrogels [60]. Introducing nanomaterials, such as clay or GO, may prevent the polymer chains from diffusing deeper and shorten self-recovery time of the hydrogel, and chain length between nanosheets becomes smaller, with the increase of nanomaterial content [49, 53, 60]. What's more, self-healing properties of hydrogels can be tuned by parameters such as ratio of strong and weak hydrogen bonds [61] and number of freezing/thawing cycles [24].

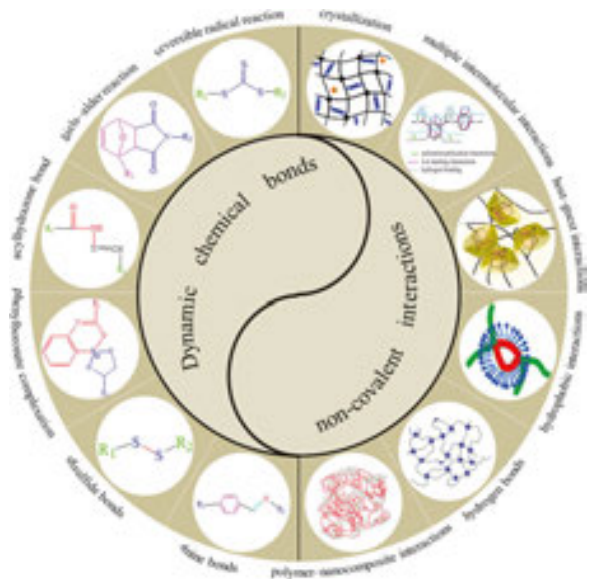


Figure 11. Various dynamic covalent bonds (left) and non-covalent interactions (right) used for self-healing of hydrogels.

Self-healing mechanisms of hydrogels are complicated, and serious effort should be made. Only if many impact parameters, including but not being limited to the abovementioned ones, on self-healing hydrogels are investigated deeply and systematically, we can design and utilize hydrogels well to a wide range of areas.

5. Potential applications of self-healing hydrogels

Hydrogels with self-healing attribute have aroused increasing interest for this fascinating property and would extend the working lifespan of materials. Consequently, they have been

widely explored for applications in the fields of biomedicine (scaffolds for tissue engineering, drug/cell carriers and tissue adhesives) and industry (coatings, sealants, sensors, superoleophobic and antibiofouling interfacial materials, enhanced oil recovery(EOR) and remote actuation) (**Figure 12**). Actually, all the superior contributions cannot be included in this chapter because of space constraint. Herein, some typical instances to outline the potential applications of self-healing hydrogels are summarized.

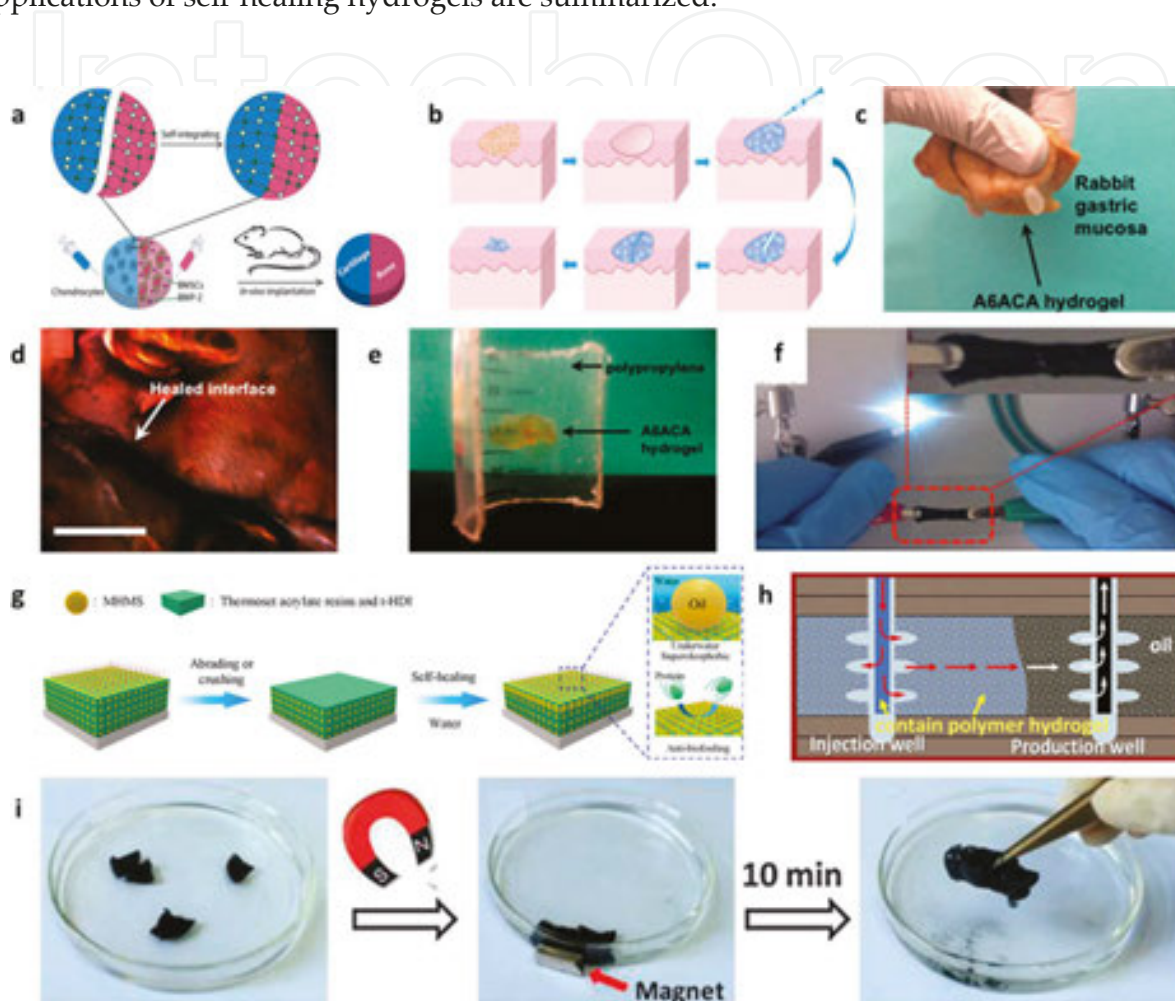


Figure 12. Applications in the fields of biomedicine (a, scaffolds for tissue engineering [67]; b, drug/cell carriers [43] and c, tissue adhesives [30]) and industry (d, coatings [30]; e, sealants [30]; f, sensors [47]; g, superoleophobic and anti-biofouling interfacial materials [74]; h, enhanced oil recovery (EOR) [34] and i, remote actuation [46]).

The above mentioned studies illustrate that hydrogels with self-healing attribute confer a possible solution to a wide range of biomedicine and industrial applications in the near future.

5.1. Biomedicine applications

5.1.1. Scaffolds for tissue engineering

Injectable hydrogels are particularly appealing because they provide homogeneous cell distribution within the desired tissue and are emerging as promising materials for tissue

engineering scaffolds [65, 66]. For instance, self-healing hydrogels encapsulating chondrocytes and bone marrow stem cells (BMSCs)/bone morphogenetic protein 2 (BMP-2) were merged together and then implanted subcutaneously in a nude mouse to form the cartilage-bone tissue complex (**Figure 12a**) [67]. The complex was successfully regenerated with cartilage occupying a larger volume ($\sim 70\%$) than bone ($\sim 30\%$), displaying capability of the self-integrating hydrogel as scaffold for growth of both bone and cartilage tissues.

5.1.2. Drug/cell carriers

After injection, the broken hydrogel fragments, encapsulated with pharmaceutical drugs/cells, could merge together at the target site, avoiding the risk of catheter clogging by premature polymerization [30, 68, 69]. Cells were encapsulated inside the chondroitin sulphate multiple aldehyde/N-succinyl-chitosan (CSMA/SC) injectable and self-healing hydrogel and retained their proliferative capacity in the hydrogel microenvironment (**Figure 12b**), demonstrating that the hydrogel can be used as a vehicle for the delivery of therapeutic cells [43].

5.1.3. Tissue adhesives

Acryloyl-6-aminocaproic acid (A6ACA) hydrogels adhere well to the gastric mucosa, and the adhesion is strong enough to support the weight of the hydrogel, and the hydrogels could potentially be used as tissue adhesives for stomach perforations (**Figure 12c**) [30].

5.2. Industrial applications

5.2.1. Coatings/sealants

When casting or coating onto substrates, self-healing hydrogels can be used as coatings and ultimately improve the performance and lifetime of implantable biomaterials [6, 70]. The rapid self-healing A6ACA hydrogels had been explored as coatings and could self-heal the imparted crack within seconds when exposed to (or sprayed with) low-pH buffers (**Figure 12d**) [30]. With another important application, A6ACA hydrogels are capable of sticking to various plastics, such as polypropylene and polystyrene, as sealants (**Figure 12e**) [30]. As a proof of concept, the hole of a polypropylene container could be sealed instantly after being coated with A6ACA hydrogel, and leakage of HCl acid in the container was prevented.

5.2.2. Sensors

As mentioned above, self-healing hydrogels with nanostructures could afford new properties to the original hydrogels. For example, with high electrical healing efficiency, self-healed rGO/superabsorbent polymer (SAP) hydrogels can light up light-emitting diode (LED) again (**Figure 12f**) and will find more practical applications in sensor systems [47].

5.2.3. Superoleophobic and antibiofouling interfacial materials

Marine biofouling and oil leakage accidents limit the application of marine vessels and plague people for thousands of years. To significantly improve the safety and prolong the lifetime of

marine vessels, self-healing underwater superoleophobic and antibiofouling interfacial materials through the self-assembly of hydrophilic polymeric chain-modified hierarchical microgel, miniature hydrogels with a size ranging from tens of nanometres to several micron [71–73], spheres had been prepared [74]. Once the surface is mechanically damaged, the surface materials can recover oil- and biofouling-resistant properties in water (**Figure 12g**), similar to the skins of some marine organisms such as sharks or whales and will serve in the underwater environment for a long time.

5.2.4. Enhanced oil recovery (EOR)

As is known, the development of enhanced oil recovery (EOR) techniques is vital to deal with the increasing energy crisis. An injection of polymer hydrogel would increase the viscosity of the injection fluid, which could efficiently prevent from bypassing the oil and enhance oil recovery (**Figure 12h**) [34]. Hydrogels with self-healing ability could repair the damage induced by injecting and transporting and maintain their functionalities for a longer period of time.

5.2.5. Remote actuation

The use of magnetic fields can allow remote actuation of self-healing nanocomposite hydrogels. Under an external magnetic field, ruptured sections of magnetic self-healing hydrogels can be facilely directed and automatically combined together, illustrating self-healing and remote actuation (**Figure 12i**) [46].

6. Conclusions

To summarize, mimicking nature to confer hydrogels with self-healing attribute has been a topic of growing interest over the past decade, and remarkable progress has been made. As depicted, brand new methods, such as dual-network, ‘single network, dual (or hierarchical) cross-linking’ strategy and DAT-DAT hydrogen bonding, are reported to endow self-healing of hydrogels with high strength. Hierarchical hydrogen bonds are constructed and flexibly modulated to tailor the properties of resultant hydrogels. Mussel serves as an important source of inspiration to design and fabricate catechol-containing hydrogels with self-healing properties. Nanostructures such as clay, graphene and Fe_3O_4 were introduced to confer appealing properties and functionality to hydrogel systems.

However, there is still significant room for improvement of self-healing hydrogels to meet industrial and application requirements: (i) first and foremost, when designing self-healing hydrogels, particular attention should be paid to cost, processability, toxicity, biocompatibility, mechanical properties and multi-functionalities; (ii) novel fabrication strategy should be developed; (iii) theoretical research on self-healing mechanism at the nanoscale and assessment systems for quantitatively evaluating self-healing performance should be improved; (iv) more potential applications of self-healing hydrogels should be explored.

To confront the aforementioned challenges and boom the self-healing of hydrogel field, researchers from material, chemistry, physics, biology and engineering should be cooperative multidisciplinary. Given the prolonging lifespan and efficient utilizations of resources and energy, novel multifunctional and commercial applications of self-healing hydrogels are awaited in the near future.

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