ACS MATERIALS LETTERS
www.acsmaterialsletters.org

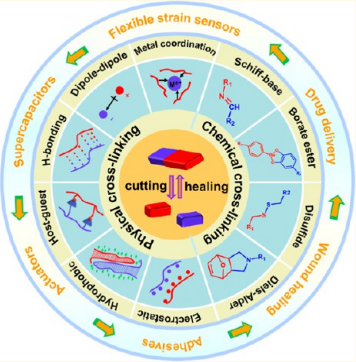
Self-Healing Hydrogels: From Synthesis to Multiple Applications

Hongyan Yin,[∇] Fangfei Liu,[*,∇] Tursun Abdiryim,[*] and Xiong Liu[*]

Cite This: *ACS Materials Lett.* 2023, 5, 1787−1830

Read Online

ABSTRACT: **Due to the good reliability and long-term stability, self-healing hydrogels have emerged as promising soft materials for tissue engineering, smart wearable sensors, bioelectronics, and energy storage devices. The self-healing mechanism depends on reversible chemical or physical cross-linking interactions. Self-healing hydrogels with fascinating features (including mechanical performances, biocompatibility, conductivity, antibacterial ability, responsiveness, etc.) are being designed and developed according to the practical application requirements. In this review, the recent progress on self-healing hydrogels in their synthesis strategies and multiple applications is summarized. Their synthesis strategies involve reversible chemical or physical cross-linking processes or a combination of the two. Their recent applications include flexible strain sensors, supercapacitors, actuators, adhesives, wound healing, drug delivery, tumor treatment, 3D printing, etc. Finally, the current challenges, future development, and opportunities for self-healing hydrogels are discussed.**



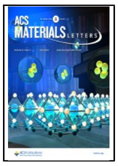
1. INTRODUCTION

Hydrogels are soft materials with a 3D network structure that is able to absorb large amounts of water. Hydrogels can maintain a certain shape in a water environment without structural damage, and their cross-linking densities and hydrophilicity would influence the water absorption capacity.[1−3] The maximum water content in hydrogels can reach up to 99%. The aggregation form of hydrogels is neither solid nor liquid but a special form between solid and liquid. Almost all hydrophilic polymers can be used to form hydrogels.[4−6] According to the different synthetic materials, they can be divided into natural polymer (including cellulose, chitosan, alginate, and gelatin) hydrogels[7−9] and chemically synthesized (including poly(vinyl alcohol), poly(acrylic acid), and poly(ethylene glycol)) hydrogels.[10−12] According to different cross-linking types, they are also sorted into physical cross-linking hydrogels,[13−16] chemical cross-linking hydrogels[17,18] and physical/chemical dual cross-linking hydrogels.[19−21] Due to their good biocompatibility, biodegradability, and flexibility, hydrogels are appropriate for applications in wound healing,[22−25] as drug carriers,[26,27] in tissue engineering,[28,29] as sensors,[30−32] actuators,[33−35] and wearable electronics,[36,37] in catalysis,[38] in solar water purification,[39−41] as supercapacitors,[42,43] etc.

Although hydrogels have shown promising prospects, traditional hydrogels are easily damaged during use.[44−47] The damage would have an impact on the integrity of hydrogels, leading to the reduction or even loss of functions and mechanical performance, thus limiting their practicability. In nature, organisms generally can repair their own damage after injury, which is referred to as self-healing performance. On the basis of this characteristic of organisms, people hope to develop self-healing polymeric materials, so as to prolong the service life. Urban et al. postulated that polymer networks are subjected to mechanical damage, resulting in the cleavage and/or sliding of polymer chains at the molecular level, which will subsequently form reactive groups that may or may not cause conformational variations in the wound site.[48] If partial polymer chain mobility and/or diffusion leads to contact between reactive groups, bonds would reform or the physical network would be restored. The self-healing process depends on physical or chemical events at the molecular level or a combination of them.[49,50] Physical self-healing processes generally include interchain diffusion, shape-memory effects, and phase separation, as well as the incorporation of superparamagnetic nanoparticles.[50] Chemical self-healing processes involve the introduction of dynamic covalent bonds.[50] In addition, physical and chemical events may be combined to construct self-healing polymeric materials.[50]

In recent years, self-healing performance has been introduced into polymer hydrogel networks to enhance the durability and

Received: March 29, 2023
Accepted: April 27, 2023
Published: May 26, 2023



https://doi.org/10.1021/acsmaterialslett.3c00320

service life. Self-healing hydrogels can be applied in adjuvant cancer therapy, drug carriers, biological tissue engineering, wound dressings, actuators, human sensors, robotics, 3D printing, contact lenses, etc.[51−55] The self-healing processes can be segmented into spontaneous and nonspontaneous processes. In some systems, the self-healing process can take place spontaneously. However, in other systems, the self-healing process requires external stimuli including temperature, pH, electricity, light, magnetism, pressure, gas, etc.[23,56−59] The self-healing mechanisms involve hydrogen bonds between various substrates, host−guest interactions, hydrophobic interactions, Schiff base bonds, disulfide bonds, etc. However, in practical applications of hydrogels, not only is self-healing performance required, but other abilities such as mechanical performance, rheological performance, conductivity, and adhesion ability also should be taken into account.[60,61] Therefore, a variety of synergistic approaches are used to fabricate self-healing hydrogels, so that some conflicting cases among properties can be eliminated.[62,63]

> However, in practical applications of hydrogels, not only is self-healing performance required, but other abilities such as mechanical performance, rheological performance, conductivity, and adhesion ability also should be taken into account.

As previously stated, self-healing hydrogels have shown promising application prospects due to their excellent properties. By combining a hydrophilic hydrogel matrix with conductive materials (including conductive polymers, conductive metal particles, carbon nanotubes, etc.), self-healing conductive hydrogels can be used in flexible sensors,[64,65] actuators,[66] supercapacitors,[33,67] soft robots,[68−70] batteries,[71,72] etc. Self-healing hydrogels prepared by integrating noncytotoxic and biocompatible natural polymer materials (chitosan, amino acids, sodium alginate, silk fibroin, etc.) into a hydrogel matrix can be used as drug delivery carriers.[73] The introduction of magnetic substances into the self-healing hydrogels is applied for biological engineering.[74] When dopamine and catechol compounds are applied to prepare hydrogels, the obtained hydrogels with self-healing and adhesive abilities can serve as wound dressings, adhesives, hemostatic agents, and so on.[44,75−79] Self-healing hydrogels can also act as controlled-release switches, smart valves, etc.[80,81] All in all, with the continuous development of synthesis technologies, self-healing hydrogels have broad application prospects in biomedicine,[82,83] energy storage devices,[84−86] and flexible electronics.[87]

So far, some previous reviews have highlighted the subject of self-healing hydrogels.[4,7,10,88−91] According to the literature search, self-healing hydrogels have been widely used in flexible strain sensors, supercapacitors, actuators, adhesives, wound healing, drug delivery, tumor therapy, 3D printing, and so on. As a result, it is critical to summarize recent advances in self-healing hydrogels. First, this review briefly describes their physical and chemical cross-linking mechanisms. Especially, we highlight the recent applications involving biomedical, energy-related, and electronic fields (Figure 1). In addition, the existing problems in this field and future research directions are also discussed.

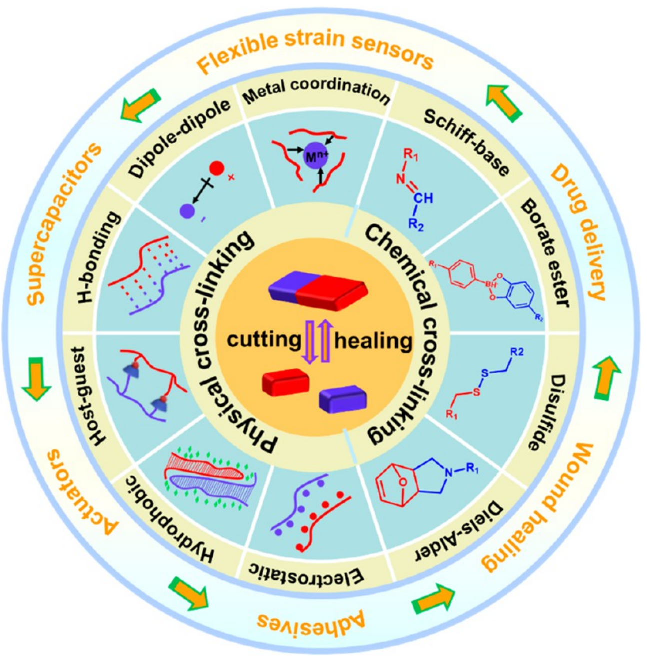


Figure 1. Synthesis and applications of self-healing hydrogels.

2. SYNTHESIS OF SELF-HEALING HYDROGELS

In the past few years, self-healing hydrogels have been widely researched due to their long service life, good durability, and ability to repair their own damage. The self-healing ability is achieved from dynamic covalent bonds, noncovalent bonds, or a combination of both. For self-healing hydrogels, their damaged structures are restored to generate a new cross-linked network, and the mechanical and rheological performances of self-repaired hydrogels also may be recovered fully or partially. Physical cross-linking, such as hydrogen bonding,[60,92,93] host−guest,[63,94] metal coordination,[95] hydrophobic,[96] electrostatic,[97] and dipole−dipole interactions,[98,99] can be applied to prepare self-healing hydrogels. Furthermore, reversible chemical cross-links, including Schiff base bonds,[100] borate bonds,[101,102] disulfide bonds,[103] hydrazone bonds,[104] and Diels−Alder cycloaddition reaction,[105] are also suitable for the construction of self-healing hydrogels. The self-healing performance obtained through physical cross-linking is generally autonomous, but the mechanical properties of such hydrogels are poor. A nonautonomous self-healing mechanism is generated from reversible chemical cross-linking, and the obtained hydrogels have excellent mechanical properties, while the self-healing properties require external stimuli, such as temperature,[106] light,[107−109] pH,[110] salt,[111] or magnetism.[112] Therefore, the preparation process of self-healing hydrogels is often carried out through a combination of multiple dynamic interactions.[83,113−116] Some representative synthetic strategies for self-healing hydrogels are listed in Table 1.

2.1. Physical Cross-Linking.

Physically cross-linked self-healing hydrogels are composed of noncovalent bonds to form a network structure. Physical cross-linking usually includes hydrogen bonding, host−guest, metal coordination, hydrophobic, and electrostatic interactions. The number and strength of physical cross-linking interactions decide the self-healing ability of physically cross-linked hydrogels.

Hydrogen bonding cross-linking is the most common synthetic strategy for self-healing hydrogels,[128,129] because hydrogen bonding is present in many natural compounds

Table 1. Synthesis Strategies of Self-Healing Hydrogels

cross-linking types	self-healing mechanism	materials	self-healing ability	features	applications	ref
physical cross-linking	hydrogen bond	PVA/PAA/tannic acid	57.9%	simple and easy to obtain, autonomic self-healing ability, but poor mechanical properties	[a]	117
	hydrophobic interaction	HAPAM/CNCs@CNTs	7 days		human−machine interface	118
	metal coordination	PPy/G-Zn-tpy	1 min		electrical circuit	119
	host−guest interaction	Alg-βCD/PAAm-Ad	[a]		cell encapsulation	120
chemical cross-linking	Schiff base	AHA-Cys	40 min	high mechanical properties, respond to external stimuli, but long healing time	drug delivery, bioprinting, smart robots and tissue regeneration	121
	hydrazone bond	[TPE-P(DMA-*stat*-DAA)]-DTDPH	24 h		topical drug delivery	122
	D−A interaction	D-2000/TAA/BMI	>80%		flexible strain sensors	105
	borate ester bond	borax-PVA	83% (5 times)		monitoring human movement	115
	disulfide bond	thiol-disulfide	1 h		hydrogel coatings	123
multiple cross-linking	hydrogen bond and borate ester bond	MXene/PVA	0.15 s	formation of energy dissipation mechanism to enhance mechanical properties and self-healing properties simultaneously, but complex preparation process	wearable capacitive electronic skin	124
	host−guest interaction and hydrazone bond	HA/γ-PGA	1 h		cell culture scaffolds	125
	hydrogen bonding, hydrophobic interactions and ionic coordination	AM/AA/stearyl methacrylate	86%		human motion detection	126
	host−guest interaction and borate ester bond	B-CD/Fc-PVA/borax	95%		wearable strain sensors	127

[a] Not described.

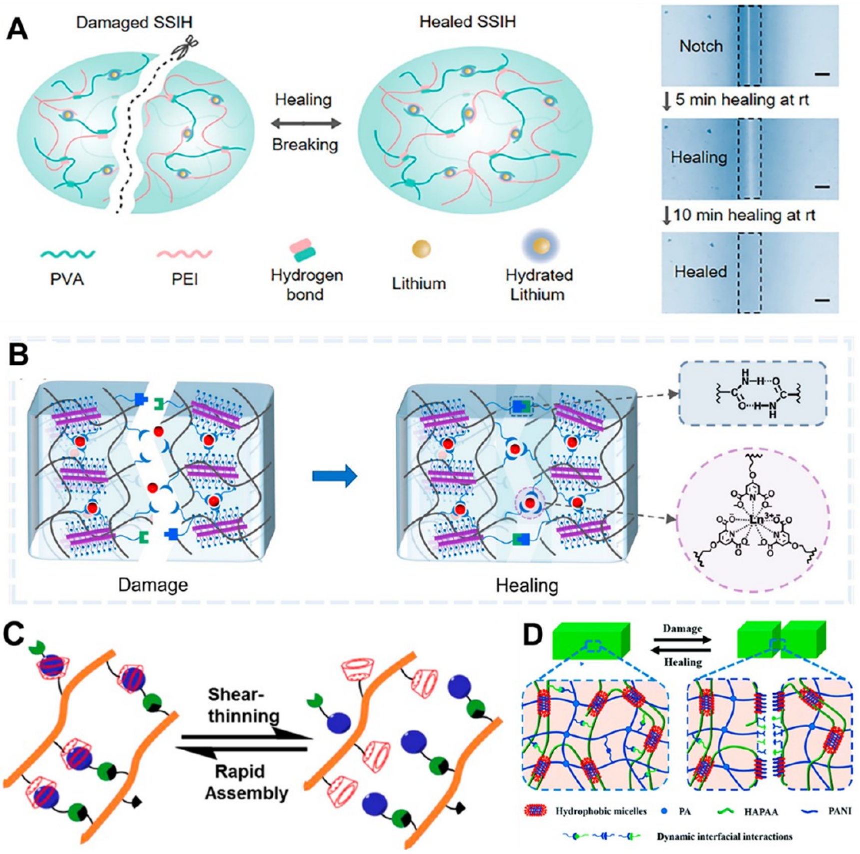


Figure 2. Schematic diagrams of self-healing hydrogels: (A) Obtained from hydrogen bonding. Reproduced with permission from ref 131. Copyright 2022 Wiley-VCH GmbH. (B) Obtained from metal coordination. Reproduced with permission from ref 132. Copyright 2022 American Chemical Society. (C) Obtained from host−guest interaction. Reproduced with permission from ref 133. Copyright 2022 Elsevier. (D) Obtained from hydrophobic interaction. Reproduced with permission from ref 134. Copyright 2021 Royal Society of Chemistry.

(proteins, amino acids, polysaccharides, etc.) and synthetic compounds (alcohols, phenols, ammonia, etc.). Hydrogen bonding is generally generated from hydrogen atoms and more electronegative atoms based on electrostatic interactions (bond energy: 42 kJ mol^{-1}). Hydrogen bonds are stronger than intermolecular forces, but much weaker than covalent and ionic bonds. The formation and breaking of hydrogen bonds are quite rapid, usually within picoseconds. For example, conductive self-healing hydrogels composed of PGA and PEDOT:PSS had favorable self-healing properties on account of the introduction of PEDOT:PSS and a strong hydrogen bond interaction.[130] The LED indicator light can be turned on again after the severed hydrogel had healed for 10 s. The self-healing rates of elongation and breaking strength reached 90% and 65%, respectively, after 24 h. The hydrogel samples can self-repair in a relatively short time (2 s) while retaining their mechanical performance. In another work, a superstretching, rapidly self-healing hydrogel was produced by forming a polymer framework consisting of hydrogen bonding and electrostatic interactions between poly(vinyl alcohol) and polyethylenimine and then embedding Li^+ into the framework.[131] The self-healing ability was improved via adding dynamic hydrogen bonds. At room temperature, the hydrogel incision grew to from one piece after 5 min (healing efficiency: 69.46%) and completely disappeared after 10 min (healing efficiency: 84.31%) and could reach 5586% deformation (Figure 2A).

The host−guest interaction, which is derived from van der Waals forces and hydrophobic and π−π stacking interactions between macromonomers with different structures but matching size, is also applied to construct self-healing hydrogels. The macrocyclic hosts mainly include crown ether derivatives, cyclodextrin derivatives, and calixarene derivatives.[135−137] The guest molecules mainly involve aromatic molecules, amines, and amino acids.[138] For example, hydrogels with outstanding self-healing, injectability, and pH-responsiveness were prepared using β-cyclodextrin and 1-adamantane as the substrates and then adding hydrazine adipate, *N*-hydroxysuccinimide, and other raw materials (Figure 2C).[133] The hydrogel could quickly recover within 10 min under stimulation (self-healing efficiency up to 97.5%). The hydrogel system also has slow water degradation and pH responsiveness, as well as the ability to accurately release drugs and achieve antitumor efficacy. In addition, sliding polymer systems from host−guest interactions between cyclodextrin and PEG are also used to synthesize self-healing hydrogels.[139−142] The slide-ring hydrogels were formed from slidable cross-links between PEG and hydroxypropyl-α-cyclodextrin rings, which could generate strain-induced crystallization to rapidly self-reinforce their toughness.[143] The host−guest interaction between PEG- and dopamine-grafted hyaluronic acid and α-cyclodextrin is able to build polyrotaxanes for constructing self-healing hydrogels, which showed good injectability, self-healing performance, and shear-thinning ability.[144] The hydrogel can be applied to load donepezil drug, which realized sustained drug delivery. PEG-grafted chitosan and α-cyclodextrin were also combined to fabricate dynamic hydrogels with shear-thinning properties.[145] Furthermore,

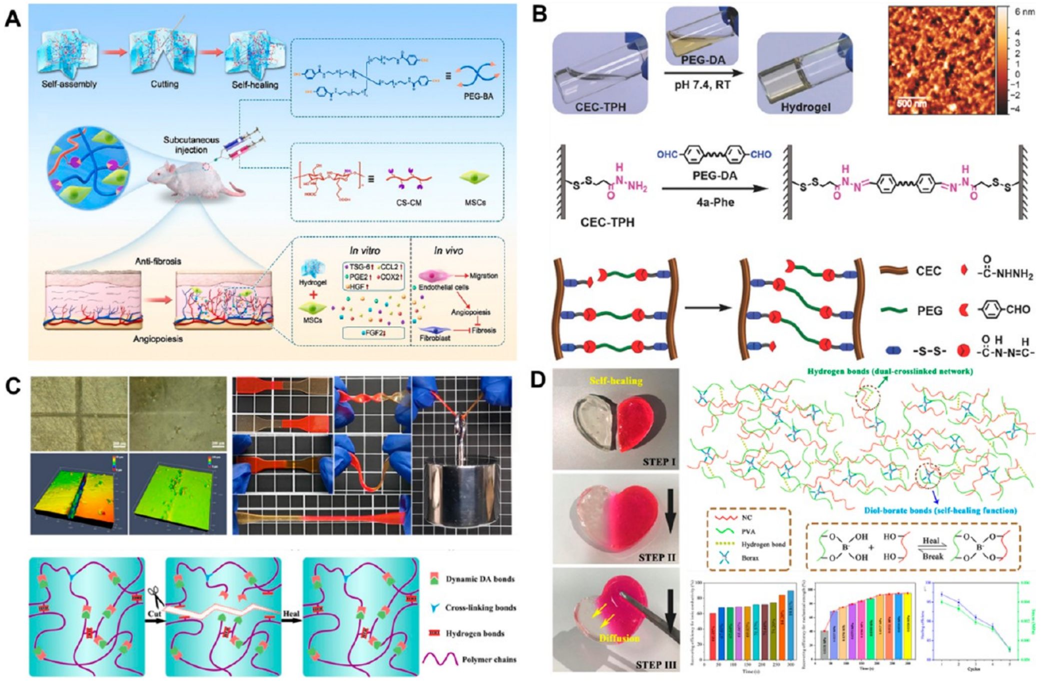


Figure 3. Schematic diagrams of self-healing hydrogels: (A) Obtained from Schiff base bonds. Reproduced under the terms of a Creative Commons CC-BY 4.0 License from ref 153. Copyright 2022 The Authors. (B) Obtained from acylhydrazone bonds. Reproduced with permission from ref 155. Copyright 2017 John Wiley and Sons. (C) Obtained from Diels−Alder bonds. Reproduced with permission from ref 105. Copyright 2022 Elsevier. (D) Obtained from borate ester bonds. Reproduced with permission from ref 115. Copyright 2022 Elsevier.

Schiff-base bonds are introduced into slide-ring polymer systems to prepare polyrotaxane-based self-healing hydrogels. Hydroxypropylated polyrotaxane-bearing aldehydes were cross-linked with glycol chitosan via Schiff-base reaction to form polyrotaxane-based self-healing hydrogels with high mechanical toughness.[146] The slide-ring effect endowed the hydrogels with excellent softness and stretchability, and Schiff-base cross-linking was responsible for self-healing ability, which could facilitate cell proliferation.

Metal coordination is also a common strategy to synthesize self-healing hydrogels.[147−149] Metal coordination is the interaction between transition metal atoms or ions and molecules (NH_3, H_2O) or ions (Cl^-, CN^-, NO_2^-, etc.) containing lone pair electrons. For example, peptide F9 and 4′-pyridyl-alanine could form a redox antibacterial self-healing hydrogel in the presence of Cu(II) ions.[95] Cu(II) had good redox properties and the coordination of Cu(II) with 4′-pyridyl-alanine produced a good self-healing property. A reduction process could be performed with the help of ascorbate, leading to the decrease of the self-healing property. In another example, a luminescent hydrogel with superior mechanical strength and self-healing performance was designed from acrylamide, lanthanide metals, and amino clays (Figure 2B).[132] The self-healing property was derived from the dynamic coordination and hydrogen bonding of lanthanide metals.

In addition, hydrophobic interactions (the tendency of nonpolar substances to aggregate and exclude water molecules in aqueous solutions) and electrostatic interactions (intermolecular forces between polar molecules) are also widely used to design self-healing hydrogels.[80] As an example, double-network hydrogels were prepared by incorporating the conductive polymer polyaniline into the hydrogel matrix of poly(acrylic acid) (Figure 2D).[134] Hydrogels were cross-linked by hydrophobic micelles of CTMAB. The micelles can be re-cross-linked after rupture (30 min) due to hydrogen bonding and electrostatic interactions, resulting in excellent tensile and self-healing ability. In another example, a self-healing hydrogel was synthesized via mixing chitosan, ethylene glycol chitosan, carboxymethyl chitosan, and sodium alginate with silver-containing Preyssler-type phosphotungstate (AgP_5W_{30}) solution.[97] Experimental results showed that amino groups were important for gelation because of strong electrostatic interactions. In addition, the strong electrostatic effect also imparted self-healing ability to the hydrogel. This broken hydrogel was restored to its integrity after being placed together for 1 min. The hydrogel structure was destroyed by applying high strain and recovered by removing the high strain. After three cycles, the self-healing properties were still retained.

2.2. Chemical Cross-Linking. Reversibly chemically cross-linked self-healing hydrogels are mostly formed from Schiff base, acylhydrazone, disulfide, and borate ester bonds, as well as Diels−Alder cycloaddition reactions. Compared with physically cross-linked hydrogels, self-healing hydrogels obtained by reversible chemical cross-linking generally have higher mechanical properties but require longer repair time.

Schiff base bonds are imino or alkane imino structures obtained by the condensation between active carbonyl and amino compounds. Dynamic Schiff base bonds can well ensure the self-healing ability of hydrogels and are widely used in the synthesis of hydrogels.[103,150−152] For example, injectable self-healing hydrogels from reversible Schiff base bonds between benzaldehyde and amino groups, loaded with mesenchymal stem cells, had been designed for the treatment of systemic sclerosis (Figure 3A).[153] The self-healing property of hydrogel allowed it to be injected without being damaged, and the healed hydrogel had sufficient mechanical strength. In another example, hydrogels were cross-linked through Schiff base bonds between methylacrylyl gelatin and oxidized glucose, resulting in high self-

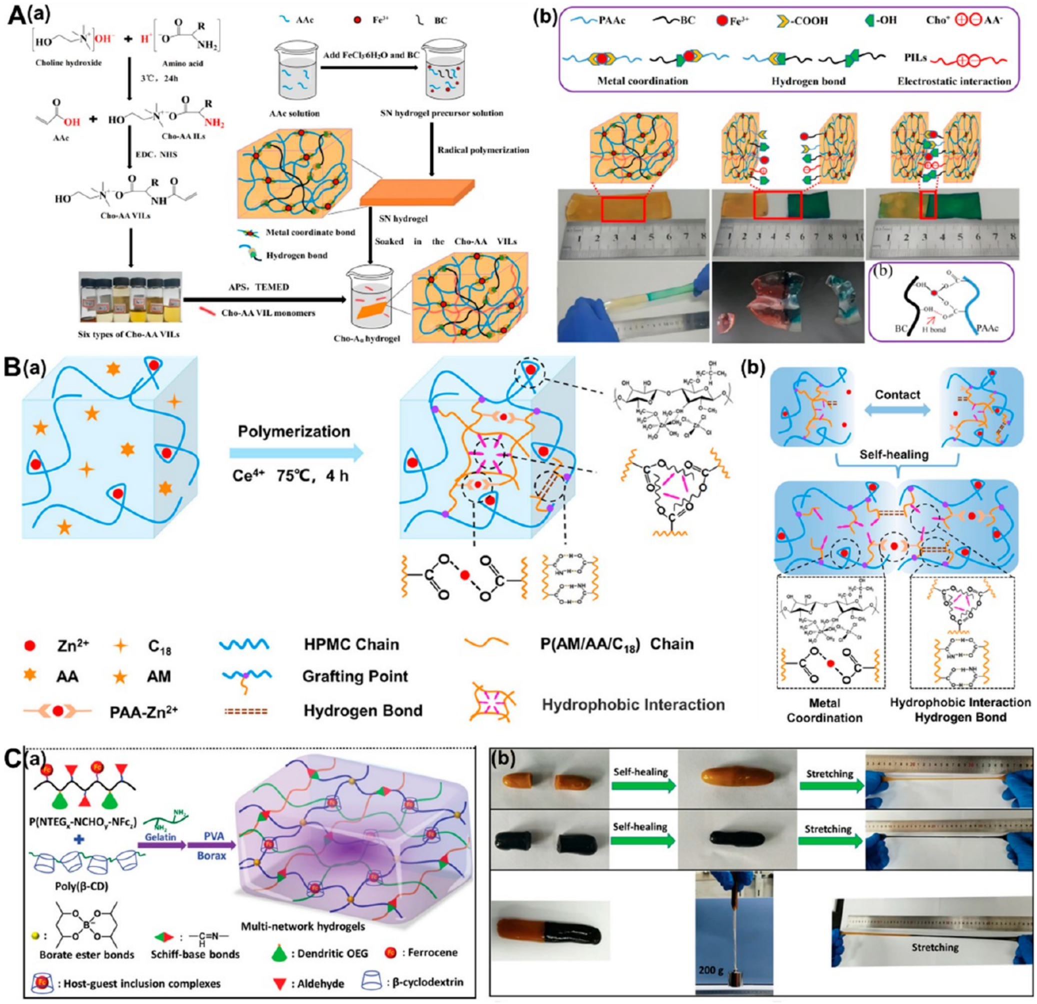


Figure 4. Schematic diagrams of self-healing hydrogels obtained from multiple cross-linking. (A) Self-healing hydrogels obtained from electrostatic interactions, metal coordinate bonds, and H-bonds. Reproduced with permission from ref 160. Copyright 2022 Elsevier. (B) Self-healing hydrogels obtained from metal coordination and H-bonds. Reproduced with permission from ref 126. Copyright 2022 American Chemical Society. (C) Self-healing hydrogels obtained from host–guest interaction, Schiff base, and borate ester bonds. Reproduced with permission from ref 161. Copyright 2021 John Wiley and Sons.

healing and injectable ability.[154] The hydrogel could load osteogenic peptides and angiogenic peptides through the Schiff base bonds. Peptide-loaded hydrogels were injectable and self-healing and could be used for minimally invasive vascular and bone regeneration.

Acylhydrazone bonds, obtained from the condensation between hydrazine and carbonyl (aldehydes or ketones), are also used to construct self-healing hydrogels. The acylhydrazone bonds are similar to the Schiff base bonds, but they have higher reactivity and better stability in water.[90] By introducing acylhydrazone bonds, self-healing hydrogels were prepared from dihydrazide-functionalized carboxyethyl cellulose and dibenzaldehyde-functionalized poly(ethylene glycol) using 4-amino-DL-phenylalanine (4a-Phe) as a catalyst (Figure 3B).[155] The exchange of acylhydrazone bonds would be accelerated with the help of 4a-Phe, which promoted the self-healing ability. The hydrogels exhibited dynamic and reversible features. The hydrogels could heal themselves after 6 h without external stimuli. Due to the good biocompatibility and reversible acylhydrazone bonds, the hydrogels were used as 3D culture scaffolds for L929 cells to maintain high viability and proliferative ability. An injectable self-healing hydrogel was designed through acylhydrazone bonds between aldehyde-modified hyaluronic acid and hydrazide-modified hyaluronic acid.[156] The dynamic characteristics of acylhydrazone bonds allowed for flowability of the hydrogel, which maintained the injectability and could be used for 3D printing to form stable structures.

Diels–Alder cycloaddition reactions represent a series of highly selective cycloaddition reactions between dienes and dienophiles. Diels–Alder reaction is a typical dynamic reversible interaction, which does not involve side reactions and byproducts, so it has become an important method to synthesize dynamically cross-linked hydrogels. Researchers successfully assembled a flexible self-healing hydrogel sensor by spraying silver nanowires and two-dimensional MXene onto an elastic matrix consisting of poly(propylene glycol) bis(2-aminopropyl ether), tris(2-aminoethyl) amine, furfuryl amine, and bismaleimide based on dynamic Diels–Alder reaction (Figure 3C).[105] The self-healing property of the hydrogel was provided by Diels–Alder reaction and hydrogen bonding. A crack in the cleaved hydrogel gradually disappeared after self-healing for 1 h at 130 °C (observed by laser scanning confocal microscopy).

The healed samples can withstand bending, torsion, tension, and loading after 6 h.

Furthermore, self-healing hydrogels are also able to be synthesized with borate ester bonds and disulfide bonds.[157−159] For instance, a rigid nanocellulose network and a PVA network were used as the hydrogel framework while borax served as the cross-linking agent to prepare self-healing hydrogels (Figure 3D).[115] The interface of two hydrogels would disappear after contact for 5 min without external force. The ionic conductive and mechanical performances of the healed hydrogels could recover 89.81% and 93%, respectively. After five repetitions, the healing efficiency still maintained 83%. The diol−borate bonds could be formed from the −OH groups of nanocellulose and poly(vinyl alcohol) and $B(OH)_4^-$, which could improve the self-healing ability. In another example, a disulfide hydrogel system with rapid self-healing properties was prepared based on a poly(ethylene glycol) grafted poly(ethyl methacrylate) derivative.[123] The hydrogel had the ability to rapidly repair microcracks (25 mm) without any stimulation conditions. The thicker the coating, the shorter the self-healing time (only 10 min for one sample). Simultaneously, the self-healing ability was not only affected by the coating thickness but also by the cross-linking degree. The self-healing behavior could be controlled by temperature (48 h complete healing at 20 °C; 2 h complete healing at 35 °C). Meanwhile, the self-healing behavior was also controlled by humidity (2 h for complete healing with a humidity of 80% RH). Therefore, high temperature and humidity could improve the self-healing process. This was all due to the disulfide exchange reaction on the scratch contact surface, resulting in chemical bonding and ultimately damage healing.

2.3. Multiple Cross-Linking.

A hydrogel with a single chemical or physical cross-linking strategy has many limitations generally. Covalently cross-linked hydrogels are rigid and tough, but the energy dissipation mechanism in the system is lacking. The resulting hydrogels are hardly able to provide high stretch and elasticity and show slow self-healing rates. Furthermore, the mechanical properties of physically cross-linked hydrogels are often unsatisfactory. At present, the synergy of multiple reversible dynamic bonds has become a trend to prepare various self-healing hydrogels.[127] For instance, by combining metal coordination (between the −COOH of acrylic acid and Fe^{3+} and the −OH of bacterial cellulose and Fe^{3+}) and hydrogen bonding (between the −COOH of acrylic acid and the −OH of bacterial cellulose), ionic conductive hydrogels with good self-healing ability and fatigue resistance were fabricated (Figure 4A).[160] On the one hand, the metal coordination between the −COOH of acrylic acid and Fe^{3+} provided self-healing capability for hydrogel. On the other hand, the metal coordination bond increased the cross-linking sites, thus enhancing the tensile strength. Simultaneously, the stretchability of the hydrogel could be reduced by limiting the deformation of the cross-linking network. Bacterial cellulose, as a rigid material, increased the mechanical property. Hydrogen bonding provided self-healing properties and improved ductility.

In another study, a self-healing hydrogel was prepared from gelatin, dialdehyde TEMPO-oxidized nanofibrillated cellulose (DATNFC), and Fe^{3+}, showing high mechanical strength.[131] In the hydrogel system, the dynamic Schiff base, metal coordination, and hydrogen bonds among the −COOH, −OH, and −CHO groups of DATNFC, the −OH and $-NH_2$ groups of gelatin, as well as Fe^{3+}, conferred the self-healing ability. Fe^{3+} enhanced the mechanical strength. The self-healing response time of hydrogels was 100 ms, and the gauge factor (GF) value of the self-healing hydrogels (5.49%: 2.455; 30.00%: 2.477) was higher than that of the original hydrogels (5.49%: 2.242; 30.00%: 1.819). The hydrogels also had better tensile properties and antifatigue properties due to enhanced energy dissipation via multiple cross-linking. In addition, hydrogels were prepared by dissolving hydroxypropyl methylcellulose in $ZnCl_2$ solution using acrylamide, acrylic acid, and stearic methacrylate as substrates and cerium ammonium nitrate as initiator, showing super tensile properties (3280%), excellent frost resistance (−32 °C), high electrical conductivity (2.0 S m^{-1}), outstanding self-healing performance (86%) and fatigue resistance (Figure 4B).[126] The self-healing mechanism came from the metal coordination and hydrogen bonds. The hydrogel can be used to manufacture smart wearable devices with excellent strain sensitivity, antifreeze properties, and low-temperature adhesion performance.

Dynamic hydrogels also could be formed from host−guest interactions, Schiff base bonds, and borate ester bonds. A self-healing hydrogel consisting of poly(vinyl alcohol), gelatin, and poly(β-cyclodextrin) showed excellent tensile and self-healing properties and biocompatibility (Figure 4C).[161] The hydrogel was able to heal within 5 min after being cleaved and had a self-healing rate of 95.6%. Multiple dynamic interactions could give hydrogels good remodeling properties, which are very beneficial for making flexible sensors with specific shapes. The coordination between the −COOH groups of gelatin and the metals endowed the hydrogel with adhesive properties. Adding carbon nanotubes into the hydrogel could increase electrical conductivity and mechanical properties. At this point, the conductivity was 1.67 S m^{-1}. The hydrogel could be reshaped to simulate the properties of human skin to write and draw on a mobile phone screen. The hydrogel could be designed as a strain sensor to observe human movements. The design strategies for multidynamic hydrogels have greatly expanded the applications of hydrogels, which makes them widely interesting to researchers.

2.4. A Summary of Synthesis Strategies.

All kinds of self-healing hydrogels are designed and structured via physical cross-linking and reversible chemical cross-linking, as well as a combination of both. Subsequent to damage, mechanical and rheological properties can be repaired completely or partly. For different cross-linking strategies, self-healing hydrogels show some specific features in some specific circumstances.

Dynamic physical cross-linking is less stable as well as more sensitive to changes in external factors (pH and so on). Physically cross-linked self-healing hydrogels heal faster and have higher healing efficiency but low toughness and poor mechanical properties. Hydrogen bonds are frequently used to prepare self-healing hydrogels, and their damage and reestablishment occur rapidly,[162,163] which is usually applied for short time drug delivery.[164] Nevertheless, hydrogen bonds are usually used in conjunction with other bonding mechanisms due to their weak force.[165,166] Hydrophobic interactions are more powerful than hydrogen bonding interactions. Their primary advantage is that they are simpler to control, because the number and shape of hydrophobic parts can be varied.[167,168] Metal coordination interactions, in particular, are a more stable force. As a result, self-healing hydrogels with metal coordination have higher mechanical properties than other self-healing hydrogels prepared by physical cross-linking.[169,170] Host−guest interactions involve electrostatic interactions and van der Waals forces, which can be applied to form supramolecular self-healing

Table 2. Important Performances of Self-Healing Conductive Hydrogel-Based Strain Sensors in Recent Literature

polymer materials	self-healing mechanism	self-healing rate	mechanical behavior	GF	response time	strain detection range	ref
DCMC/chitosan/PAA/Al^{3+}	metal coordination, Schiff base bonds, hydrogen bonds	>90%	strain: 800%	15.56	[a]	[a]	30
Gel/NaCl/Gly/H_2O	hydrophobic interaction, ionic interaction, hydrogen bonds	91%	fracture strain: 300%; tensile stress: 0.38 MPa	2.48	30 ms	0−200%	31
PVA/SA/TA/borax	borate ester bonds, hydrogen bonds	93.56%	stretchability: 780%	15.98	[a]	[a]	32
MXene/CS/DMAEA-Q	electrostatic interactions, hydrogen bonds	[a]	strain: >5000%	>0.9 (50−400%)	[a]	5−400%	64
MXene/LA-Ag NPs	hydrogen bonds, coordination bonds, electrostatic interactions	93% (72 h)	strain: 304.44 kPa	9.17	[a]	>175%	87
CMC/DA	hydrogen bonds, noncovalent interactions from PDA	98.37% (3 h)	stretchability: 700%	4.741	[a]	[a]	109
PAC/SiO_2-g-PAAm	hydrogen bonds	96.5	stretchability: 1600%	5.86		50−500%	129
(Cho-AA PILs)/Fe^{3+}/PAA	metal coordination, hydrogen bonds	87.1%	[a]	2.65	100 ms	0−200%	160
gel/DATNFC/Fe^{3+}	Schiff base bonds, hydrogen bonds, coordination bonds	[a]	compressive stress: 1310 kPa	2.24 (6% strain)	200 ms	[a]	131
β-CD/Fc/PVA/borax	borate ester bonds, host−guest interaction	95%	stretchability: 436%; fracture strength: 41.0 kPa	5.9	[a]	[a]	127
SA/PVA/Gly	hydrogen bonds, borate ester bonds	92%	elongation at break: 1500%; tensile toughness: 3.6 MJ m^{-3}	3.33	[a]	0−1500%	132
PVA/PDDA//CNCs/PA/	hydrogen bonds	85.0% (4 h)	stress: 1.0 MPa	[a]	310.0 ms	0.0−600.0%	194
PAA/CNF-Gly	borate bond	[a]	stretch: ∼980%	3.496		10−700%	195
BCW/TA/PAA/Fe^{3+}/Gly/H_2O	hydrogen bonds, coordination interaction	91%	stress: 203 kPa; elongation at break: 1950%	5.2	[a]	1200−1900%	196
starch/PVA/borax	hydrogen bonds, borate ester bond	94.3%	fracture strain: 688%	1.02	≤180 ms	110−200%	197
TNPs/Ad/β-CD/PPy/AAm	host−guest interactions	[a]	stretchability: 1860%; stress: 180 kPa	0.41 (0−300%); 1.15 (300−1800%)	[a]	0−1800%	137
PVA/borax/SF/TA	borate ester bond	[a]	strain: >1000%	1.66	[a]	>650%	198
PU/PANI	D−A covalent bonds, hydrogen bonds, ionic interactions,	[a]	elongation at break: 500%	2.89	[a]	[a]	199
LMs/PAA/GO	supramolecular interactions	[a]	[a]	9.86	[a]	>400%	148
poly(thioctic acid)/PANI/sulfonate	hydrogen bonds, ionic bonds,	almost complete self-healing (12 h)	elongation at break: 4000%	2.18		0−400%	200

[a] Not described.

hydrogels. By selecting suitable host and guest molecules, self-healing hydrogels that interact with host and guest are designed for sensing and drug delivery.[171−173]

Dynamic chemical cross-linking is more stable and robust than physical cross-linking. Schiff base bonds can also be used to prepare hydrogels with self-healing. Schiff base bonds can form under benign conditions and are divided into two types: aliphatic and aromatic. The stability of an aromatic Schiff base is greater than that of an aliphatic Schiff base. Schiff base bonds would cleave in an enzymatic or acidic environment. They are frequently used in medication carriers because of their biocompatibility and degradability. However, this type of hydrogel is usually unstable and particularly prone to hydrolysis.[174−176] Hydrazone bonds are similar to Schiff base bonds, but hydrazone bonds are more stable in water-containing systems than Schiff base bonds. The meso-polymerization effect during hydrolysis slows down the hydrolysis and transamination of acylhydrazone bonds.[177] Hydrazone bonds are sensitive to temperature and pH, and a gel−sol transition can be produced by altering the pH of the surroundings. The most important feature of hydrazone bonds is that they can form spontaneously under physiological conditions, but their generation rate is slow.[178] Under physiological conditions, hydrogels based on hydrazone bonds can achieve rapid self-healing, and they are commonly used as injectable hydrogel carriers in living organisms.[179−181] The durability of borate ester bonding usually relies on temperature and pH, and borate ester bonding has been frequently exploited in the preparation of rapidly self-healing hydrogels.[182,183] Compared to Schiff base, hydrazone, and borate ester bonds, the biomedical uses of the Diels−Alder reaction are restricted. This is due to the special conditions for generation and cleavage of the Diels−Alder bond, such as high temperature (typically 100 °C) and longer time.[184] The reaction does, however, have simple conditions, no byproducts, and good thermal reversibility. As a result, if the temperature for Diels−Alder bond cleavage and generation can be reduced, it may be useful in the biomedical field.[185,186] The disulfide bond is another dynamic chemical cross-link, but it has attracted less interest for the fabrication of self-healing hydrogels as due to the high design requirements (temperature, reaction environment, redox processes, etc.) its application areas are limited.[187,188]

In general, whether physically or chemically cross-linked self-healing hydrogels, their self-healing process is accomplished with dissociation and reorganization of the system's components. The difference is that physical cross-linking leads to a fast but unstable self-healing process, whereas chemical cross-linking

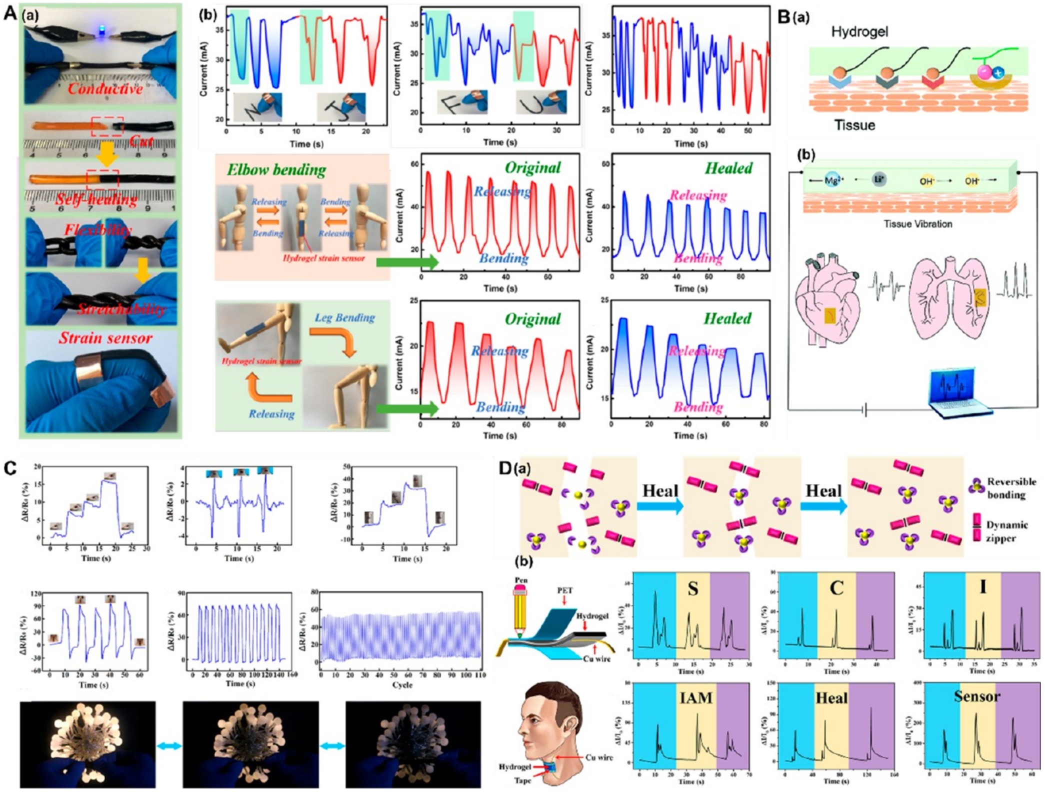


Figure 5. (A) Self-healing conductive hydrogels consisting of oxidized cellulose nanofibers, graphene, and poly(acrylic acid) for flexible electronic sensors. Reproduced with permission from ref 201. Copyright 2020 Elsevier. (B) A novel tissue adhesion conductive hydrogel sensor based on amphoteric ions and dopamine-modified clay nanosheets. Reproduced with permission from ref 150. Copyright 2020 Royal Society of Chemistry. (C) A hydrogel strain sensor prepared using AAm and GMA-Ad as monomers and TNPs as physical cross-linking agents. Reproduced with permission from ref 137. Copyright 2021 Elsevier. (D) Muscle-inspired dual sensing self-healing hydrogels. Reproduced with permission from ref 202. Copyright 2019 American Chemical Society.

results in a slow but stable self-healing process. Generally, a single physical or chemical cross-linking strategy does not satisfy the multiple requirements of self-healing hydrogels (including toughness, mechanical strength, self-healing ability, etc.). The perfect integration self-healing ability with mechanical strength is a difficulty in the creation of self-healing hydrogels. This is typically accomplished by merging a rigid network with a brittle network or by adding cross-linked sites to the hydrogel network, and reversible dynamic cross-linking can serve as a sacrificial bond to resist energy dissipation. Mechanical flaws produced by a single cross-linking network can be corrected by designing multiple cross-linking networks. In order to create self-healing hydrogels with mechanical durability and greatly expand their application range, it is important to combine several dynamic cross-linking interactions.[189−193]

3. APPLICATIONS OF SELF-HEALING HYDROGELS

Owing to their specific rheological properties and biomimetic features, hydrogels have gradually become a kind of intelligent materials with multiple functions. In particular, self-healing hydrogels can repair their own damage after injury, possessing unique advantages to prolong their service life and durability. As mentioned above, self-healing hydrogels could be smoothly prepared through reversible chemical or physical cross-links or the combination of both. Access to easy synthesis of self-healing hydrogels allows for full investigation of their properties and various applications. The representative uses for self-healing hydrogels are emphasized in the sections that follow. These applications involve flexible strain sensors, supercapacitors, actuators, adhesives, wound healing, drug delivery, cancer therapy, etc.

3.1. Flexible Strain Sensors. Conductive hydrogels have attracted considerable attention in the realm of flexible strain sensors, because they can transform subtle external variations (forces and deformation) into measurable electric signals (such as resistance, current, etc.). Conductive hydrogels can be endowed with some remarkable properties (including flexibility, stretchability, adhesiveness, biocompatibility, freezing tolerance, and self-healing performance) to suit the particular demands of flexible strain sensors. Inspired by skin and muscle, self-healing conductive hydrogels hold excellent promise for wearable equipment and implantable biological tissues, as well as artificial electrical skins. Importantly, the introduction of self-healing properties into wearable hydrogel strain sensors allows for the repair of microcracks, fractures, as well as other analogous structural damage, which improves the sensitivity of strain sensors. The ability for self-healing also has the potential to boost the service life of wearable strain sensors, increasing their reusability, durability, and reliability. In this section, the uses of self-healing conductive hydrogels in flexible strain sensors are introduced. Table 2 shows the important performances of self-healing conductive hydrogel-based strain sensors in recent literatures.

Conductive hydrogels that are exceptionally stretchy, tough, and self-healing are commonly used in the fabrication of flexible strain sensors. Self-healing conductive composite hydrogels composed of graphene, poly(acrylic acid), and TEMPO-

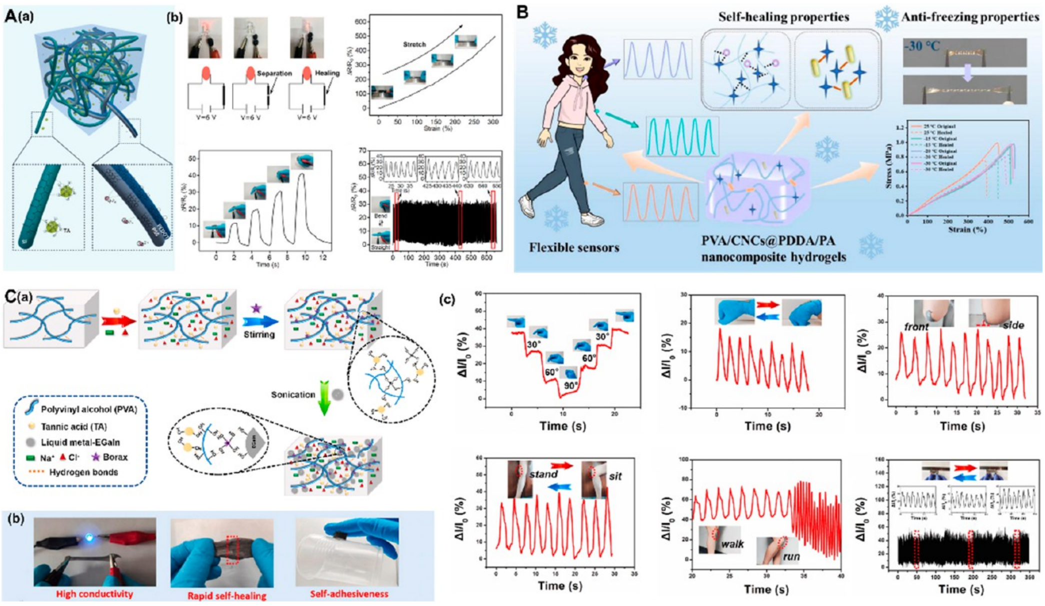


Figure 6. (A) A conductive hydrogel adhesive prepared via supramolecular interaction between tannic acid and silk fibroin. Reproduced with permission from ref 203. Copyright 2020 John Wiley and Sons. (B) Schematic diagram of a hydrogel system obtained from poly(diallyldimethylammonium chloride), cellulose nanocrystals, phytic acid, water/glycerol, and poly(vinyl alcohol). Reproduced with permission from ref 194. Copyright 2022 Elsevier. (C) Conductive hydrogels fabricated from liquid metals for wearable sensors and biomimetic skin. Reproduced with permission from ref 204. Copyright 2021 Elsevier.

oxidized cellulose nanofibers (TOCNFs) were designed as flexible strain sensors (Figure 5A).[201] The composite hydrogels with tough mechanical strength were prepared via physical and chemical double-cross-linking. TOCNFs enhanced the dispersion of graphene in the composite hydrogels and increased the mechanical properties, viscoelasticity and electrical conductivity of composite hydrogels. The obtained composite hydrogel showed high compression stress (2.54 MPa) and storage modulus (32.8 kPa) and excellent tensile properties (0.32 MPa, 850%) and conductivity (2.5 S·m^{-1}). In addition, the hydrogel exhibited outstanding self-recovery ability in 12 h (healing efficiency: 96.7%) because of the reversible coordination cross-links. The self-healing hydrogel can be utilized as a strain sensor (GF: 5.8) to monitor human motions.

Self-healing hydrogels also should have good stable performance and responsiveness, so it can recognize not only knuckle movements but also complex spatial movements. Pei et al. demonstrated hydrogel sensors based on polyzwitterionic polymers and dopamine-modified clay nanosheets (Figure 5B).[150] The hydrogels were prepared by one-pot free radical polymerization of [2-(methacryloyloxy)ethyl]dimethyl-(3-sulfopropyl) ammonium hydroxide (SBMA) in the presence of dopamine-modified clay and *N*,*N*′-methylene bis(acrylamide) with a molar ratio to SBMA of 3×10^{-4}. Microfibers were formed in the hydrogels via polydopamine (PDA) generation to enhance the stretchability and toughness. The excellent mechanical properties could be explained via ionic interactions. Meanwhile, hydrogels exhibited superior self-healing (including mechanical and electrical properties) because of physical adsorption of clay nanosheets by polymer chains and dipole−dipole bonds of zwitterionic chains. The electrical property's fast self-healing ability improved the dependability of the sensor. Furthermore, the zwitterionic polymer chains as a network assisted ion transport, and the zwitterionic groups helped to improve conductivity and increase sensitivity. The combined action of PDA and SBMA allowed hydrogels to adhere tightly to organs. Due to strong adhesion and excellent biocompatibility, conductive hydrogel sensors can be directly attached to the organs or tissues to monitor human activities (such as swallowing, knuckle and knee flexion) through wired transmission and wireless transmission communication. These findings highlighted hydrogels' significant potential for in vivo implanted tissues and wearable devices.

By the design of the specific cross-linker, a highly tough and stretchable hydrogel strain sensor with good self-healing property was constructed (Figure 5C).[137] The self-healing hydrogel was fabricated through the one-pot free-radical polymerization of AAm and GMA-1-amantadine hydrochloride monomers using *β*-cyclodextrin topological nanoparticles (TNPs) as a physical cross-linker. The TNP-cross-linked hydrogels showed outstanding mechanical performance (stress: 180 kPa, elongation: 1860%) and self-healing ability because of the host−guest interactions between *β*-cyclodextrin and 1-adamantanamine, as well as polymer chain entanglement. Furthermore, the introduction of salt/polypyrrole was able to increase the sensitivity of the strain sensor. The obtained strain sensor exhibited good electrical conductivity (initial resistivity: 6.4−7.8 Ω m), sensing range (0−1800%), and fatigue tolerance (withstanding over 100 cycles of stretching and recovery at 400% strain). The strain sensor can monitor human activity for multiple applications. This topological physical cross-linker will broaden the evolution of stretchable self-healing and tough hydrogel strain sensors.

To mimic the microstructure and versatility of human muscles, polyaniline nanofibers were contained in a poly(acrylic acid) hydrogel to build a temperature-sensitive hydrogel strain sensor with self-healing and antifreezing abilities (Figure 5D).[202] Fe^{3+} ions could bind with the −COOH of poly(acrylic acid) to form reversible tridentate coordination to realize self-healing. The $-NH_2$ in PANI NFs can form hydrogen bonds with nearby chains to produce strong "dynamic zippers", which could quickly heal after fracture. After 6 h, the hydrogel's self-healing

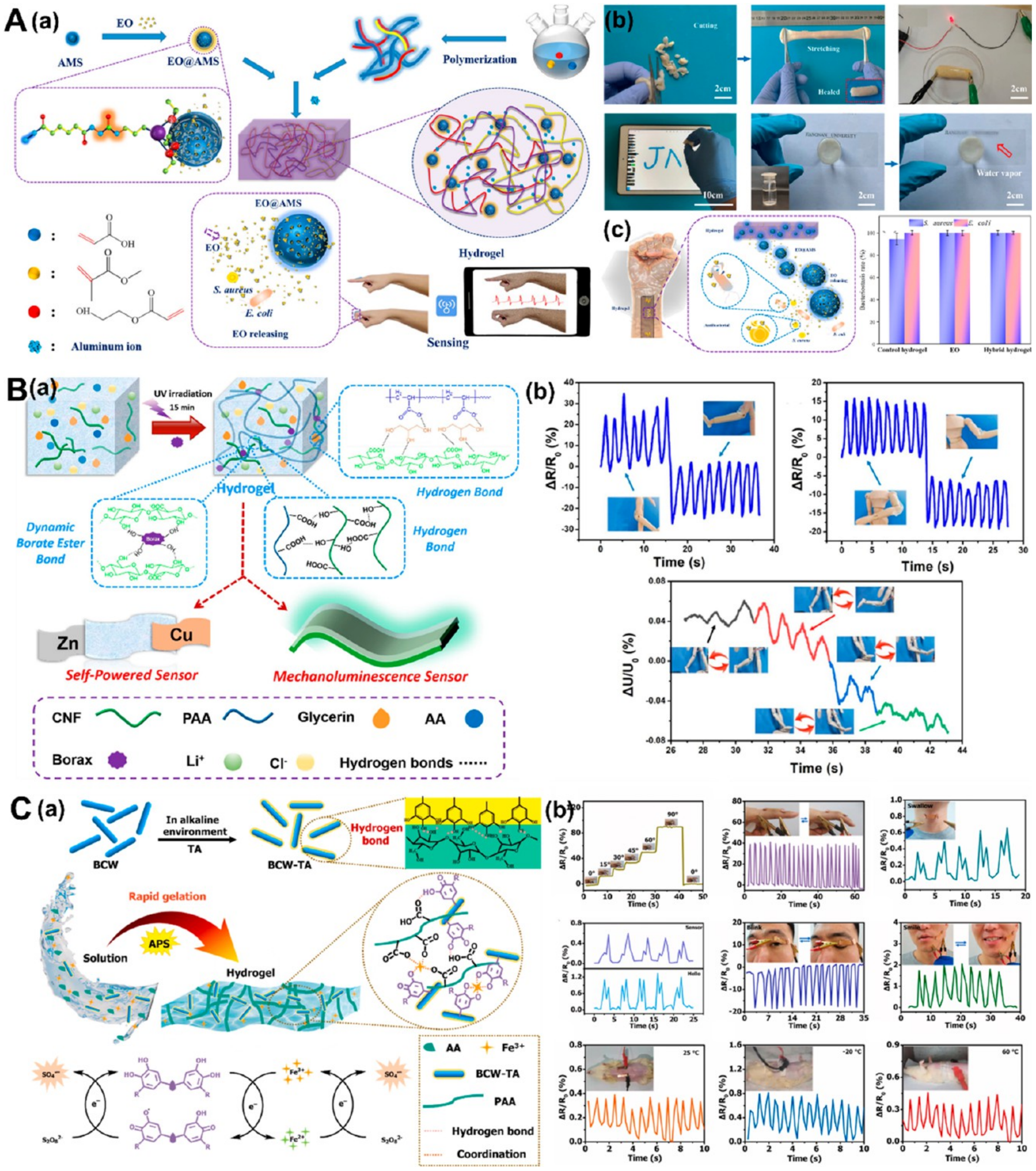


Figure 7. Application of self-healing hydrogels in flexible strain sensors. (A) **Schematic diagram of a flexible sensor assembled from a hydrogel obtained by combining mesoporous silica loaded with lemon essential oil and aluminum ions. Reproduced with permission from ref 154. Copyright 2022 American Chemical Society.** (B) **Preparation of tannic acid–Fe^{3+} activated fast polymerization ion-conductive hydrogel. Reproduced with permission from ref 195. Copyright 2022 Elsevier.** (C) **Schematic diagram of the hydrogel sensor obtained through mixing poly(acrylic acid), cellulose nanofibers, and glycerol. Reproduced with permission from ref 196. Copyright 2022 Elsevier.**

effectiveness was 90.8%. Meanwhile, the −OH of glycerol formed hydrogen bonds with PANI to enhance stretchability (1500%). The electrostatic interaction between PAA and PANI improved the mechanical properties (maximum stretch: 991%; maximum stress: 35.68 kPa). Glycerol enhanced frost resistance due to ice crystallization inhibition, so the self-healing hydrogels can work at −26 °C with nearly 800% stretchability and high self-healing. The self-healing hydrogel had a highly linear thermal response (TCR = $-0.0164\ ^\circ C^{-1}$), low detection limit (5% strain), and sensitive electrical responses (GF: 18.28). The hydrogel-based sensor has good mechanical and thermal sensitivity, was used as a "heat indicator" to measure human forehead temperature, and could serve as sensitive touch recognition keyboards.

Biocompatible, conductive, self-healing hydrogel adhesives can be used to develop flexible strain sensors. A kind of conductive hydrogel adhesive was prepared through the supramolecular interactions (especially H-bonding) between tannic acid and silk fibroin, followed by doping with PEDOT and PSS (Figure 6A).[203] The hydrogel adhesives showed exceptional stretchability up to 32000% and good adhesive strength (69.4 ± 5.3 kPa). In addition, the hydrogel adhesives had repetitive adhesion behaviors and underwater adhesion ability. Tannic acid and silk fibroin formed hydrogen bonds, which gave the hydrogel adhesive good self-healing performance. In vitro tests confirmed that hydrogel adhesives have good biocompatibility and antibacterial properties. Conductive hydrogel adhesives could be obtained by doping with conductive polymers. The resulting conductive hydrogel adhesives had a conductivity of $(3.17 \pm 0.32) \times 10^{-2}$ S m^{-1}. Furthermore, the healed hydrogel adhesives had a similar conductivity ($(3.07 \pm 0.29) \times 10^{-2}$ S m^{-1}) to the original one. Subsequently, a flexible strain sensor was constructed using the conductive hydrogel adhesives. The good reliability of this

Table 3. Important Properties of Self-Healing Hydrogel-Based Supercapacitors in Recent Literature

polymer materials	self-healing mechanism	self-healing efficiency	mechanical behavior	conductivity	specific capacitance	ref
PVA/PA/Fe^{3+}	coordination bonds, hydrogen bonds	72%	tensile stress: 0.618 MPa; tensile strain: 924%	21 mS cm^{-1}	1526 mF cm^{-2} (0.5 mA cm^{-2})	205
PVA/PPy/KCl	hydrogen bonds	[a]	[a]	[a]	244.81 mF cm^{-2} (0.47 mA cm^{-2})	206
Fe_3O_4/Au/MEP	Au−SR bonds	86.3	stretchability: 2250%, elongation at break: 1200%		1264 mF cm^{-2}	207
azo-PAM/α-CDP/LiCl	host−guest interaction	90% (5 self-healing cycles)	stretch: 50%	43.25 mS cm^{-1}	2.2 mF cm^{-2} (0.2 mA cm^{-2})	208
PVA/Gly/H_2SO_4	hydrogen bonds	[a]	elongation at break: 242%, tensile strength:0.55 MPa		476 mF cm^{-2} (at 0.2 mA cm^{-2})	209
Fe^{3+}/AMPSZn/AAZn	ionic bonds	[a]	[a]	6.6×10^{-4} S cm^{-1}	145.6 F g^{-1} (65.52 W h kg^{-1})	210
PANI/PVA/CPBA/Ca^{2+}	borate ester bonds, ionic bonds	49.8% (4 h, 70 °C)	elongation at break: 633%, tensile strength: 2.21 MPa	136 S m^{-1}	78.5 F g^{-1}	211
PEI/PVA/Bn/LiCl	[a]	strain self-healing efficiency: 94.3% (2 min)	elongation at break: 1223%, tensile strength: 34.6 kPa	21.49 mS cm^{-1}	16.7 mF cm^{-2}	212
PAA/EG/APS	hydrogen bonding, ester bonds	[a]	strain: 861.8% (under stress of 225 kPa)	16.7 mS cm^{-1}	67.1 F g^{-1} (1 A g^{-1})	213
PVA/agar/$EMIMBF_4$/Li_2SO_4	hydrogen bonds	>80% (5 self-healing cycles)	tensile stress: 1012.3 kPa, strain: 418.6%	43.6 mS cm^{-1}	28 F g^{-1} (1 A g^{-1})	214

[a] Not described.

hydrogel sensor was proven by the repeated finger bending test (around 400 times). As a result, the conductive hydrogel adhesives have potential for the construction of healable bioelectronics with good deformability. In another example, nanocomposite hydrogels with self-healing ability were successfully prepared by grafting functional poly(diallyldimethylammonium chloride) onto cellulose nanocrystals, followed by cross-linking with poly(vinyl alcohol) (Figure 6B).[194] Water/glycerol was used as the solvent system, and phytic acid was used as a cross-linking agent. Due to hydrogen bond interactions, hydrogels demonstrated good self-healing performance (85.0%). The addition of phytic acid increased the freezing resistance. Furthermore, the hydrogel exhibited high sensitivity (GF = 0.9) and rapid response (310.0 ms), broad strain monitoring range (0−600%), and excellent reproducibility. The hydrogel sensor also can monitor human motion signals at −30 °C for 24 h.

Liquid metals are a kind of suitable conductive filler for preparing hydrogel strain sensors with self-healing ability. Liquid metals can enhance electrical conductivity and mechanical properties of hydrogels. Eutectic gallium indium (EGaIn) has been extensively studied. EGaIn was introduced into a PVA/tannic acid hydrogel system to obtain self-healing, antifreezing, and adhesive wearable sensors for biomimetic skin (Figure 6C).[204] The resulting hydrogels showed good self-adhesive performance owing to the hydrogen bonds between tannic acid and PVA and the borate ester bonds between borax and −OH of PVA and tannic acid. The assembled hydrogel flexible sensor had good strain sensitivity (GF: 2.59) and electrical conductivity (3.63 S m^{-1}), because EGaIn was equally scattered in the PVA hydrogel network system. The hydrogel flexible sensor also exhibited excellent temperature sensitivity (as low as −10 °C), toughness (1.9 MJ m^{-3}), tensile strength (1.13 MPa), and compressive strength (4.59 MPa). In addition, the sensor was capable of stably recording and distinguishing vocal, swallowing, and signature actions.

In some other studies, researchers have been devoted to designing and developing multifunctional self-healing hydrogels for strain sensors. A self-healing and antibacterial strain sensor was prepared by introducing mesoporous silica loaded with lemon essential oil and aluminum ions into a polyacrylate hydrogel (Figure 7A).[154] The hydrogen bonding and ionic bonding endowed the hydrogels with high self-healing efficiency (97.6%). The good ionic conductivity allowed the hydrogel to have good sensing properties for human health monitoring.

A multifunctional composite hydrogel with good mechanical, self-healing and antifreezing properties was also synthesized by mixing sodium alginate, PVA, and glycerol.[132] The produced hydrogels had good self-healing properties (healing efficiency: 92%) and tensile performance (1500%) and sensitivity (GF: 3.33). Frost-resistant hydrogels with high tensile properties (980%), good adhesiveness (25.4 kPa), and good self-healing performance can also be fabricated from poly(acrylic acid), cellulose nanofibers, and glycerol (Figure 7B).[195] The hydrogel could be constructed into an emergency power supply as well as a strain sensor to distinguish bending direction of human actions. To rapidly prepare multifunctional self-healing hydrogels, a dual self-catalytic strategy based on the TA−Fe^{3+} system was used to initiate the polymerization process (Figure 7C).[196] A TA-functionalized bacterial cellulose nanowhisker was selected to activate the polymerization of acrylic acid and *N*,*N*′-methylene bis(acrylamide) with the help of $FeCl_3$ and ammonium persulfate in a glycerol/water system. The hydrogels could be obtained rapidly within 4 s. The hydrogel had good self-healing ability (91%), high stretchability of 1950%, and freezing resistance (retaining 95% stretchability at −20 °C). In particular, the sensor had a sensitivity of 5.2 and a stable sensing performance from −20 to 60 °C.

3.2. Supercapacitors. Flexible supercapacitors have been considered as novel energy storage devices due to their advantages such as lightweight, rapid charge/discharge rate, small size, portability, high power density, suitable flexibility, as well as long service life. With the development of flexible materials, in the realm of flexible supercapacitors, hydrogel electrolytes have garnered much attention. On the one hand, the 3D network structure of hydrogels can provide a large surface area and good ion/electron transmission. On the other hand, conductive hydrogels can provide high electrochemical activity, good specific capacitance, structural flexibility, and electrolyte permeability. Furthermore, the self-healing ability might

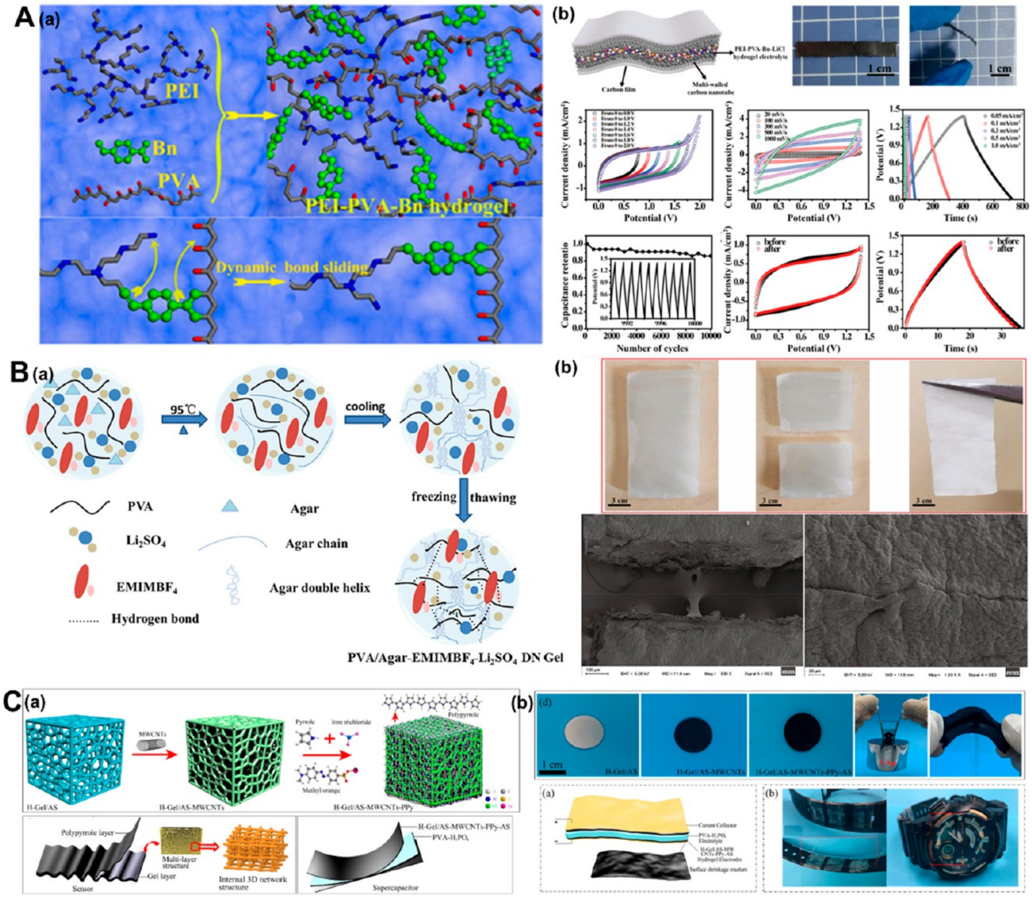


Figure 8. (A) Preparation strategy of slidable polymer network hydrogel electrolyte. Reproduced with permission from ref 212. Copyright 2020 American Chemical Society. (B) PVA/agar dual network hydrogel electrolyte prepared by a simple physical cross-linking and freeze/thaw method. Reproduced with permission from ref 214. Copyright 2021 Elsevier. (C) Gel-based polypyrrole hydrogel assembly of flexible sensors and supercapacitors. Reproduced with permission from ref 215. Copyright 2021 American Chemical Society.

increase the durability and reliability of flexible supercapacitors. Self-healing flexible supercapacitors are able to work under extreme distortion and recover their original performance after damage. The self-healing performance gives the flexible supercapacitors not only better energy storage, but also better cycling stability. Nevertheless, it is a challenge to realize mechanical stretchability and self-healing performance in flexible supercapacitors. Self-healing conductive hydrogels hold huge promise in designing and developing self-healing flexible supercapacitors because of tunable structures, excellent conductivity, and flexibility. This section discusses the use of self-healing conductive hydrogels for flexible supercapacitors. Table 3 outlines some representative examples of self-healing hydrogels used as supercapacitors and their key properties.

Hydrogel-based supercapacitors are currently widely used to construct wearable as well as portable electronic devices. Yet, mechanical damage due to frequent stretching, bending, and squeezing limits what actually functions. Self-healing ability may withstand mechanical damage. Meanwhile, flexible electrochemical energy storage devices must be high-capacity and highly flexible. An innovative design idea of hydrogel electrolyte and assembly method for an integrated hydrogel supercapacitor was presented for self-healing flexible supercapacitors (Figure 8A).[212] Specifically, the self-healing hydrogels were constructed with slidable polymer networks based on cross-linking reactions of PEI, PVA, and 4-formylphenylboronic acid (Bn). The prepared hydrogel was capable of incorporating various electrolytes (LiCl, NaCl, etc.) because PEI was able to dissolve many electrolytes. Furthermore, PEI increased ionic conductivity by promoting ion pair ionization. The slidable polymer network hydrogel with electrolytes showed good tensile properties (elongation at break: 1223%, strength: 34.6 kPa), superior self-healing ability (rate of 94.3% within 2 min), and high ionic conductivity (21.49 mS cm^{-1}). An electric double layer supercapacitor was constructed using multiwalled carbon nanotubes as electrodes and hydrogels as electrolytes. The flexible supercapacitors showed a working potential window within 1.4 V, excellent specific capacitance (16.7 mF cm^{-2}), outstanding cycling stability (reaching 10,000 cycles), as well as good deformability, etc.

In order to conquer the shortcomings of traditional electrolytes under adverse climate change, a new type of flexible double-network hydrogel supercapacitor with good mechanical flexibility, self-healing ability, and temperature range was designed (Figure 8B).[214] Hydrogel electrolytes were prepared by a simple physical cross-linking and freeze/thaw strategy. The first network of the double-network hydrogel electrolyte was established via the cross-linking of agar chains, and the second network was generated from PVA hydrogel due to ice crystal formation. In addition, Li_2SO_4 was added to increase the conductivity and 1-ethyl-3-methylimidazolium tetrafluoroborate ($EMIMBF_4$) was used to enhance the working temperature range. The double network allowed the hydrogel electrolyte to restore its structure during deformation or fracture, thereby

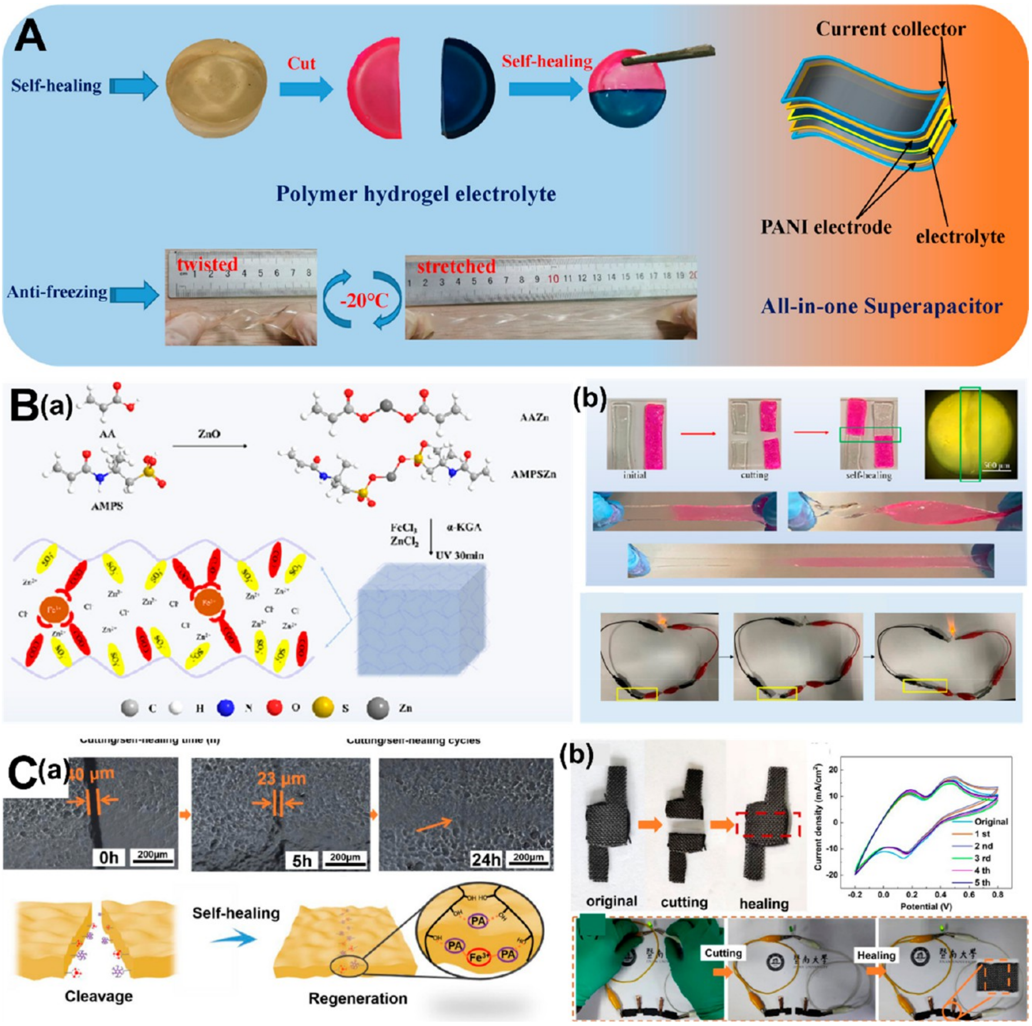


Figure 9. **(A) Integrated self-healing and freeze-resistant supercapacitor using poly(vinyl alcohol), glycerin, and sulfuric acid by freeze−thaw cycle method. Reproduced with permission from ref 209. Copyright 2022 Elsevier. (B) Self-healing zinc-ion composite capacitors based on 2-acrylamide-2-methyl-1-propanesulfonic acid and zinc acrylate. Reproduced with permission from ref 210. Copyright 2022 Elsevier. (C) Schematic diagram of a hydrogel with redox activity made on the basis of poly(vinyl alcohol) and phytic acid as self-healing electrolyte to prepare a supercapacitor. Reproduced with permission from ref 205. Copyright 2022 Elsevier.**

improving strength and fatigue resistance. Thus, the flexible supercapacitors based on PVA/agar−EMIMBF$_4$−Li$_2$SO$_4$ hydrogel electrolyte demonstrated superior capacity in a wide operating temperature range (−30 to 80 °C) and excellent self-healing ability (up to 80%, after 5 cycles). The introduction of ionic liquids could improve the operating temperature range of the hydrogel electrolyte. A supercapacitor assembled with a hydrogel and activated carbon had excellent specific capacitance (28 F g^{-1}) in 0.3 A g^{-1} and Coulombic efficiency of more than 85%. The supercapacitors have significant conductivity (43.6 mS cm^{-1}) and long charge and discharge times.

The fabrication process of double-network hydrogel electrodes is tedious, and it remains a challenge to produce at large scale stretchable, self-healing, inexpensive supercapacitors. Gelatin-based polypyrrole hydrogels with good strength, stretchability, and conductivity were manufactured by a plain soaking−heating−template coating−stripping strategy (Figure 8C).[215] Multiwalled carbon nanotubes (MWCNTs) have been utilized to enhance the electrochemical performance of hydrogel electrodes. When the hydrogel was soaked in (NH$_4$)$_2$SO$_4$ solution, folds were formed on its surface to enhance the capacitance and mechanical properties. A flexible supercapacitor with excellent performance was produced from the hydrogel electrode. The specific capacity was 112.5 F g^{-1} (0.5 A g^{-1}). After 5000 cycles, the capacitance maintenance was 98.1%. In another study, Zhu and his colleagues fabricated a self-healing and freeze-resistant hydrogel electrolyte using PVA, glycerol, and sulfuric acid based on the freeze−thaw cycle method (Figure 9A).[209] The hydrogel electrolyte used aniline as the electrode to obtain an integrated supercapacitor. The hydrogen bonding between glycerol and PVA provided good self-healing capability (specific capacitance retention of 48.5% after 10 cutting/healing cycles). The addition of glycerol endowed the hydrogel electrolyte with freeze-resistance (capacitance retention of 56.3% at −20 °C). At 0.2 mA cm^{-2}, the specific capacitance of the proposed supercapacitor was 476 mF cm^{-2}, the power density was 100 μW cm^{-2}, and the energy density was 33 μWh cm^{-2}.

A novel form of energy storage system is zinc ion hybrid capacitors. However, the low density and poor durability limit its application. A fabrication strategy for a high electrochemical capacity and self-healing zinc ion composite capacitor was proposed based on the formation of Fe^{3+} cross-linked anionic copolymers of zinc 2-acrylamido-2-methyl-1-propanesulfonate

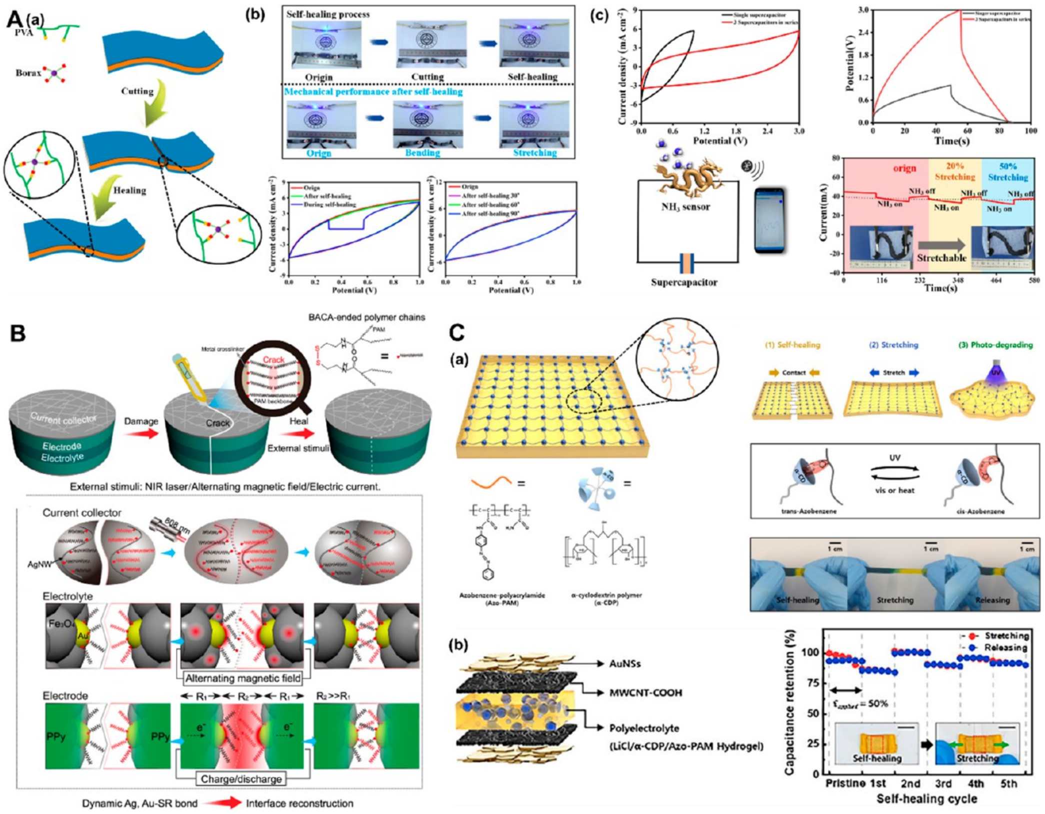


Figure 10. (A) Mechanism of hydrogel-based self-healing supercapacitors obtained from polypyrrole and borax cross-linked poly(vinyl alcohol)/KCl. Reproduced with permission from ref 206. Copyright 2021 John Wiley and Sons. (B) Schematic diagram of hydrogel and assembly of repairable supercapacitor device. Reproduced under terms of a Creative Commons CC-BY 4.0 License from ref 207. Copyright 2021 Springer Nature. (C) Self-healing and photodegradable hydrogel prepared from azobenzene acrylamide and α-cyclodextrin and the schematic diagram of supercapacitor prepared from the hydrogel. Reproduced with permission from ref 208. Copyright 2021 Elsevier.

and zinc acrylate in the presence of $ZnCl_2$ (Figure 9B).[210] The composite capacitor had a rate density of 1.01 kW kg^{-1} and energy density of 205.3 Wh kg^{-1}. The ionic interaction between $-COO^-$ and Fe^{3+} afforded self-healing abilities, and the capacitor recovered a certain capacitance even after complete severance. The zinc ion hybrid capacitor can operate normally while being bent at low temperatures (−18 °C). A redox-active self-healing hydrogel electrolyte based on PVA, phytic acid, and Fe^{3+} was used to fabricate flexible supercapacitors (Figure 9C).[205] The reversible cross-linking between Fe^{3+} and phytic acid not only improved the self-healing property (72%) but also improved the mechanical properties (924% tensile strain). Moreover, the introduction of Fe^{3+} further improved the electrochemical activity. The resulting hydrogel-based supercapacitor had an excellent energy density of 0.25 mWh cm^{-2} (0.212 mW cm^{-2}) and an ultrahigh capacitance of 1526 mF cm^{-2} (0.5 mA cm^{-2}) with excellent cycling stability. Most importantly, the electrochemical properties of the severed hydrogel can also be recovered after healing, which greatly improved the stability, durability, and safety of the supercapacitor. The above series of examples demonstrate the unique advantages of self-healing ability in enhancing the safety and stability of energy storage devices.

A self-healing, flexible integrated supercapacitor formed from a PVA hydrogel was prepared for a self-powered smart sensor (Figure 10A).[206] The hydrogel was fabricated by cross-linking PVA/KCl with polypyrrole and borax. After two cut hydrogels were placed together and heated at 85 °C for 20 s, an LED became bright again by connecting the hydrogel in the circuit and LED brightness did not change even after multiple deformations (stretching or bending). Upon assembling the hydrogels into a supercapacitor, the supercapacitor's specific capacitance was 244.81 mF cm^{-2}, and it could be recycled 2000 times. Connecting the supercapacitor to an ammonia sensor, the supercapacitor could be fully charged by a commercial solar cell and then could power the ammonia sensor. In another example, a hydrogel-based supercapacitor with triple responsive self-healing performance under light, electrical, and magnetic stimuli was designed using Au-loaded magnetic Fe_3O_4 and polyacrylamide hydrogels (MFPs) as the electrolyte, PPy-based MFPs as the electrodes, and Ag nanowire films as the current collectors (Figure 10B).[207] The MFP hydrogel had high tensile property of 2250%. The strain healing efficiency of the hydrogel was 86.3%. Notably, the capacitance of the supercapacitor could recover more than 90% in 10 light, electrical, and magnetic healing cycles. The area capacitance of the device was up to 1264 mF cm^{-2}. In addition, photodegradable hydrogel supercapacitors with fast self-healing ability at room temperature were designed through the host−guest interaction of azobenzene-based polyacrylamide and α-cyclodextrin polymer, and gold nanosheet-functionalized MWCNTs and LiCl have been added to the hydrogel to increase the conductivity and mechanical performance (Figure 10C).[208] The supercapacitor had a wide range of dynamic deformations and damage, good tensile properties (maximum strain at break: 1066% and maximum tensile strength: 70 kPa), good self-healing (over 90% within 4 h), and excellent elasticity (up to 500 times repeatedly). The original capacitor had a maximum power of 0.85 mW cm^{-2} and the energy density was 0.24 μWh cm^{-2}. These works clearly showed that supercapacitors prepared from self-healing conductive hydrogels could be used as energy storage devices, skin-attachable electronic devices, etc.

3.3. Actuators. In nature, plants or animals can respond to external stimuli, leading to the variation of geometric shape. Inspired by the specific behaviors of plants or animals, various soft actuators have been developed, which can change shapes or motions depending on external factors such as temperature, pH, chemicals, solvents, salts, etc. Hydrogels have gained much interest and presented promising uses in soft actuators because of their high percentage of water, 3D structures, flexibility, biocompatibility, as well as volume expansion/contraction behaviors under external stimuli. Hydrogel actuators are mostly used for target grasping, transport, and controlled release through some kind of periodic stimulation. Due to the stimulus responsiveness and softness of hydrogels, hydrogel actuators can achieve reversible shape transformation behaviors, including bending, twisting, and other complex three-dimensional transformations. Nevertheless, hydrogel actuators would be subjected to damage or cracks during use, which will be not beneficial to their performance and service life cycle. Therefore, researchers usually focus on a hydrogel's self-healing performance when designing hydrogel actuators. The self-healing property allows hydrogels to operate with better fatigue resistance to achieve better cycling and service life. Meanwhile, the self-healing property can better assist the shape memory behaviors to accomplish the target object grasping, walking, swimming, etc. In this section, we will highlight recent developments in self-healing hydrogel actuators, and the related performance is outlined in Table 4.

Inspired by the structure of jellyfish fluorescent protein and fine-sizing control of transmembrane proteins in biofilms, an integrated biologically fluorescent protein molecule was designed and synthesized to construct fluorescent, electrically responsive, super tough, and self-healing hydrogel actuators (Figure 11A).[217] The self-assembly of amphiphilic 2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS), sodium dodecyl sulfate, and hydrophobic 4-(6-(3-(6-methyl-4-oxo-1,4-dihydropyrimidin-2-yl)ureido)hexylcarbamoyloxy)-butyl acrylate (UPyHCBA) could form micelles. Acrylamide was added to the micellar solution to generate self-healing hydrogels via micellar polymerization. The sulfonic acid group of AMPS enhanced fluorescence emission. In addition, sodium dodecyl sulfate—sodium chloride—AMPS micelles dissolved UPyHCBA monomers in relatively small space and formed dense electron rich clusters, which also promoted the fluorescence emission of hydrogels. The hierarchical structure of the polyelectrolyte—surfactant micelle (ESM) hydrogel not only enhanced the fluorescence emission but also formed a sustained structure with superior toughness (fracture stress: 238 kPa; elongation at break: 1518%; toughness: 1678 kJ m^{-3}). The dynamic dissociation and reorganization of the physical cross-links provided self-healing ability to the hydrogel. The hydrogel could convert electrical energy into mechanical energy. When the hydrogel was placed in an electric field of 30 V, the hydrogel immediately bent toward the cathode (maximum bending angle: 90°, 5 min). When the hydrogel was placed in an electric field of −30 V, the hydrogel bent in the opposite direction. It only took 10 min for the sample to recover to its initial position.

A new supramolecular polymer dual network strategy was proposed to prepare self-healing, self-adhesive, frost-resistant, highly tensile, and conductive hydrogels for the construction of

Table 4. Important Properties of Self-Healing Hydrogel-Based Actuators in Recent Literature

polymer materials	self-healing mechanism	self-healing efficiency	mechanical behavior	other properties	response performance	ref
PNIPAM/PAA/Fe^{3+}	hydrogen bonds; Fe^{3+}-mediated ionic interactions	[a]	tensile strength: 250 kPa; elongation at break: 1300%	ultrafast thermoresponsiveness (9 s)	thermoresponsive	34
HNTs@PDA/PAAm	[a]	76%	tensile strength (original hydrogel): 0.133 MPa	63 s for recovering 720% shape change	light responsive	216
UPy/PAMPS/SDS	quadruple hydrogen bonds, hydrophobic association and encapsulation	[a]	fracture stress: 238 kPa; elongation at break: 1518%	high transmittance (91%)	electroresponsive	217
PVA/borax/P(ATU-*co*-AM))	borate bonds, hydrogen bonds	over 90% (10 min)	tensile strength of 3.6 MPa	highly efficient shape memory effect (recovered within 260 s)	pH-driven, Ca^{2+}-driven shape memory behavior	218
HSAH/PHEAA/DESs	HSAH supramolecular network	60%	stretchability: more than 4000%; toughness up to 800 J m^{-2}	temperature range −40 °C to 60 °C	[a]	219
MXene/PAA/PAM	hydrogen interactions	[a]	[a]	[a]	photothermally induced actuator	220

[a] Not described.

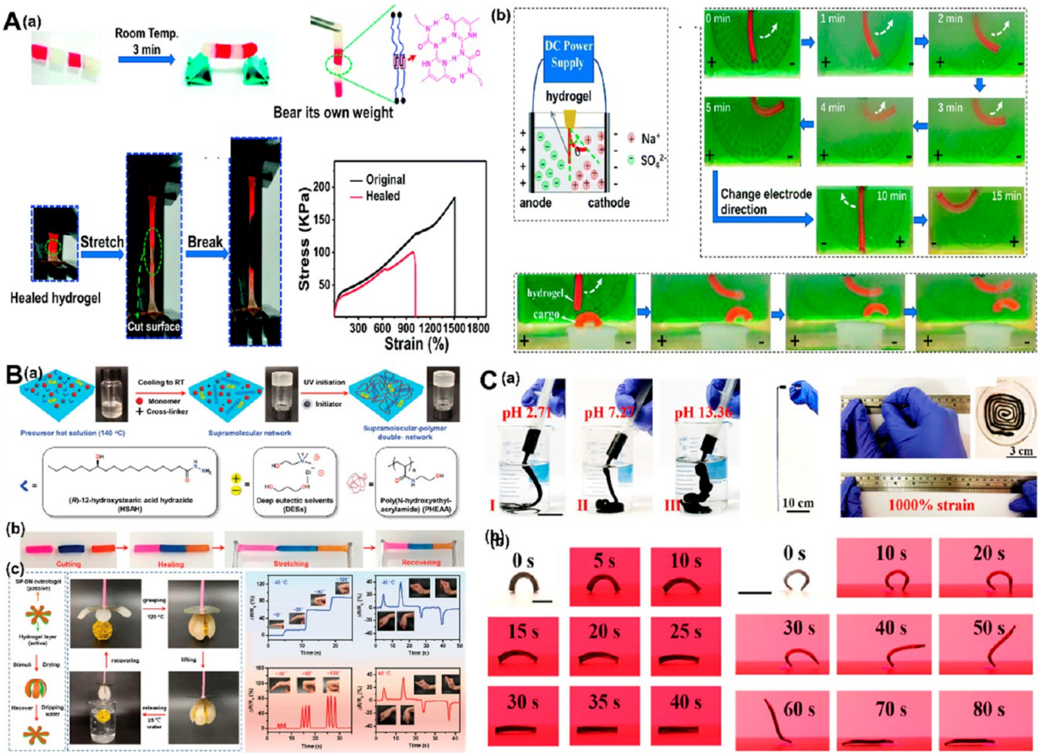


Figure 11. Self-healing hydrogel actuators. (A) Two-response self-healing hydrogel actuators prepared from AMPS and UPyHCBA. Reproduced with permission from ref 217. Copyright 2021 Royal Society of Chemistry. (B) SP-DN eutectic gel actuator with excellent bidirectional detection capability (two perpendicular directions) and detection of irregular surfaces (complex muscle movements). Reproduced with permission from ref 219. Copyright 2022 Royal Society of Chemistry. (C) Self-healing and near-infrared responsive actuators based on MXene hydrogels. Reproduced with permission from ref 220. Copyright 2021 American Chemical Society.

soft actuators (Figure 11B).[219] Briefly, a supramolecular double-network polymer (SP-DN) was fabricated in the one-pot using (*R*)-12-hydroxystearic acid hydrazide (HAH), *n*-hydroxyethyl acrylamide (HEAA) monomer, deep eutectic solvent, and MBA. The elongation of SP-DN eutectogels was over 4000%, and the strain was more than 5000% under biaxial tension. SP-DN eutectogels not only had excellent mechanical strength (0.26 MPa) but also had higher toughness (maximum fracture strain 4400%) and self-repair ability. Meanwhile, SP-DN eutectogels had a wide temperature range (−40 °C to 60 °C) and superior compression recovery elasticity. A temperature-triggered actuator could be assembled using the SP-DN hydrogels. The actuator crimped at high temperatures due to the severe volume contraction of the hydrogel; thus the target was held by the actuator. The gripper could grip balls with a diameter of 25 mm and weight of 1.5 g and was able to easily lift molecular models (30 and 50 g).

A self-healing MXene-based hydrogel was also designed for soft actuators (Figure 11C).[220] To obtain the hydrogel, MXene was used as a cross-linking agent to induce rapid gelation (74 s) of various monomers. MXene was used not only as a conductive nanomaterial but also as a multifunctional cross-linker. MXene could obviously enhance the stretchable performance (over 1000%) of hydrogels via dynamic interactions (hydrogen bonds and chelation interactions). The dynamic interactions also endowed the hydrogels with great self-healing capability (92.19%, 6 h), and hydrogels demonstrated long-term self-healing capability even after 15 days. A double-deck hydrogel actuator was assembled using a poly(acrylic acid)−MXene hydrogel as the positive layer and a poly(acrylamide)−MXene hydrogel as the passive layer. Due to the photothermal capability of MXene and the thermal response properties of the hydrogel, the resulting actuator showed a near-infrared response with a shape transition behavior. After a period of NIR irradiation, the height and curvature of the actuator was altered due to the uneven photothermal capacity between the positive and negative layers. Upon fixing a section of the actuator and placing the actuator in a 2D network, the actuator could be flipped 180° and recovered under NIR irradiation. The MXene-based hydrogel reveals a novel method for preparing self-healing and near-infrared responsive actuators.

In another example, a novel semi-interpenetrating network hydrogel with self-healing ability was cross-linked by dynamic borate ester and hydrogen bonds between PVA chains.[218] Hydrogels exhibited excellent tensile performance (up to 3.6 MPa), self-healing efficiency (up to 90%), and dual-actuated shape memory behavior. The copolymer poly(1-allyl-2-thiourea-*co*-acrylamide) was incorporated into the PVA/borax network to form a semi-interpenetrating network, which enhanced the Ca^{2+}-driven shape memory behavior of the hydrogel. The "S-Ca-S" cross-linking formed by the sulfur atom of the thiourea group binding to Ca^{2+} provided the Ca^{2+}-driven shape memory behavior to the hydrogel. The hydrogel actuators could mimic the bending behavior of the *Mimosa* plant. The hydrogel shrank and became opaque after immersion in Ca^{2+} solution, while it could restore transparency over at least 5 cycles after immersion in deionized water. A four-arm grasper was manufactured through a double-layer hydrogel. The grasper precisely controlled and moved plastic bags by utilizing the expansion and shrinkage characteristics of the hydrogels.

A composite hydrogel actuator with good NIR-triggered shape memory and outstanding self-healing ability was designed from polyacrylamide–gelatin.[216] The composite hydrogel was composed of halloysite nanotubes, polydopamine, and polyacrylamide–gelatin. The composite hydrogel had outstanding self-healing, mechanical properties, and NIR-triggered shape memory capability. The modified nanotubes could cross-link polyacrylamide to improve the mechanical properties (tensile strength: 0.133 MPa). The dense cross-linking formed by gelatin and acrylamide endowed the hydrogel with strong elastic properties and accelerated recovery after curling. The maximum healing efficiency of the composite hydrogel was 76% in the NIR region, and the NIR-triggered shape recovery process was quite rapid (63 s). Recovery of the twisted hydrogel took place within only 220 s under NIR light irradiation. The hydrogels with + shapes were immersed in water at 80 °C for 10 s, resulting in the shape of flower petals. After being placed in ice water for 30 s and then irradiated with NIR light for 20 s, the hydrogel actuator could be returned to its original shape. Besides, the hydrogel actuator with NIR-responsive self-healing ability can accomplish target grasping and trapping via the shape actuation function of the hydrogel, which greatly broadens the application range of self-healing hydrogels.

3.4. Adhesives. At present, hydrogel adhesives are commonly utilized in biomedical fields including wound healing and tissue glues. Hydrogel adhesives can adhere to tissues to effectively seal bleeding wounds without causing new damage and prevent leakage of fluids or gas. Generally, hydrogel adhesives should have good biocompatibility and biodegradability. Depending on practical needs, a strong self-healing capability is also crucial for hydrogel adhesives. Self-healing hydrogel adhesives have the potential to repair themselves to prolong their service life and durability, which allows them to overcome the drawbacks induced by damage or cracks. Hydrogel adhesives are environmentally responsive (pH, temperature, etc.) and the hydrogel's self-healing ability enables it to adapt to environmental changes. The self-healing property also enhances the synergistic effect of the components of the hydrogel system. Hydrogel adhesives with self-healing properties can be reusable medical devices. This section reviews the application progress of self-healing hydrogels in adhesives. As shown in Table 5, self-healing hydrogels used as adhesives have different self-healing mechanisms and adhesion mechanisms (including hydrogen bonds, hydrophobic associations, electrostatic interactions, coordination interaction, Schiff-base bonds, etc.) due to the diverse compositions.

A novel initiator-free photo-cross-linked hydrogel adhesive was designed with inspiration from plants.[225] In this method, the hydrogel was obtained by simply combining the coumarin derivative Pho-CA and acrylamide monomer in water under irradiation with UV light. The process of hydrogel formation was very similar to the growth process of plants in nature. The hydrogel demonstrated excellent self-healing, tensile (1600%), and fluorescence properties and possessed reversible adhesion to a variety of substrates (glass, paper, leaves, rubber). The hydrogel's reversible adhesion property was adjusted by varying its water content: the adhesion would be lost under wet conditions, while the adhesion would recover in the dried state. Based on the special properties of coumarin, this hydrogel did not require the addition of cross-linkers and initiators. Furthermore, the hydrogel could be used for efficient antibacterial activity and data encryption–decryption. A customizable two-layer structure was used to design a multifunctional hydrogel adhesive with self-healing, sticking, and inherent antibacterial capabilities.[221] The first hydrogel

Table 5. Important Properties of Self-Healing Hydrogel-Based Adhesives in Recent Literature

polymer materials	self-healing mechanism	self-healing efficiency	adhesion mechanism	adhesion performance	ref
LS/PVP	hydrogen bonds, hydrophobic interactions	strength recovery of 95%; strain at break recovery of 83%; toughness recovery of 80%	hydrogen bonds, hydrophobic associations, electrostatic interactions	pigskin: 58.1 kPa; wood: 66.6 kPa; steel: 47.0 kPa	14
CHI/ACHI/PA	imine linkage	it took only 30 min to fuse two different colored hydrogels into a single unit	electrostatic interactions, hydrogen bonds	*a*	221
AAm/κ-carrageenan/Fe^{3+}	coordination interaction	stress healing efficiency of 80%	coordination interaction	average adhesion energy: 1450 J m^{-2}	222
N-[3-(4-hydroxyphenyl) propanamido]chitosan/(DF-PF)	*a*	>95%	Schiff base bonds, hydrophobic interaction	artificial skin: binding strength of 7 ± 0.6 N cm^{-2} (~70 ± 6 kPa)	223
gel/CS/borax	Schiff base bonds, hydrogen bonds	when two cut hydrogels were joined together, they could fuse together in less than 20 min without the intervention of external conditions	Schiff base bonds, hydrogen bonds	maximum bond strength: 30.64 ± 0.9 kPa	224

[a] Not described.

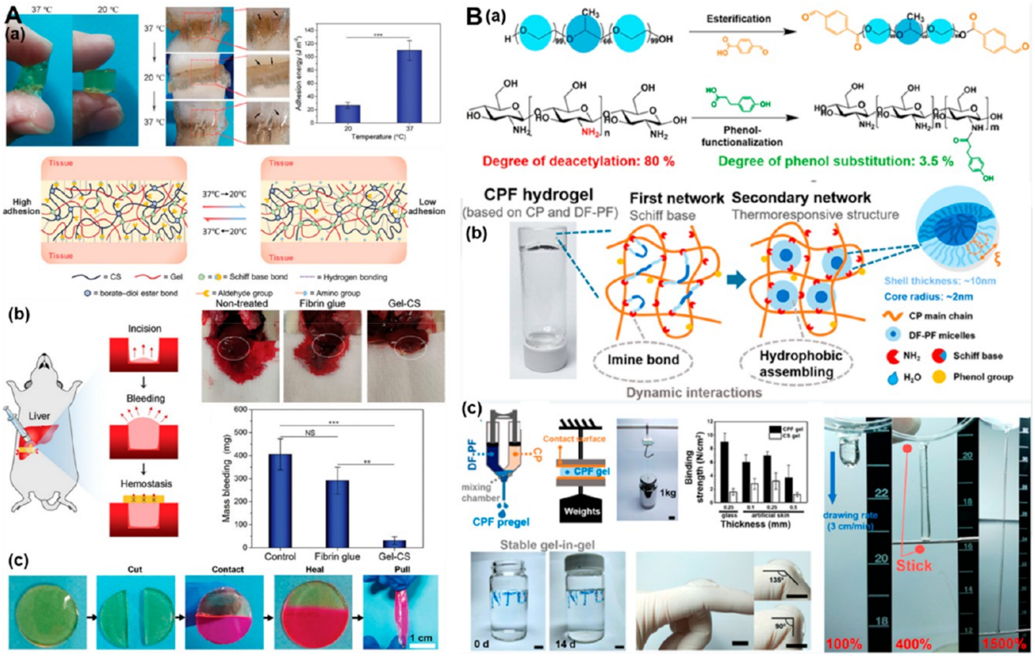


Figure 12. (A) Injectable hydrogel adhesive based on chitosan and gelatin. Reproduced with permission from ref 224. Copyright 2021 Wiley-VCH GmbH. (B) A self-healing hydrogel that rapidly adhered to artificial skin in 30 s. Reproduced with permission from ref 223. Copyright 2021 American Chemical Society.

layer, which exhibited outstanding self-healing and self-adhesive capabilities, was created via the dynamic chemical cross-linking of the aldehyde group of aldehyde-chitosan with the amino group of chitosan. The second layer of hydrogel was obtained by adding phytic acid to the first layer. It took only 30 min to heal two different colored hydrogels into a single unit. Electrostatic interactions and hydrogen bonding supplied the hydrogel with adhesion capabilities. The hydrogel could adhere well to the skin when the finger was bent from 0° to 90°. The hydrogel exhibited good biocompatibility and killed *Staphylococcus aureus* and *Escherichia coli*. Therefore, the hydrogel could be used as a trauma dressing to adhere to the tissue and could effectively inhibit bacteria.

A novel polyampholytic terpolymer (PAT) hydrogel was designed to enhance skin adhesion.[226] The PAT hydrogel was obtained by the polymerization of the neutral monomer *N*,*N*-dimethylacrylamide (DMAAm) (or 2-hydroxyethyl methacrylate (HEMA)), the cationic monomer 3-(methacrylamide)-propyltrimethylammonium chloride (MPTC), and the anionic monomer sodium *p*-styrenesulfonate (NaSS). The skin adhesion and self-healing ability of PAT hydrogels were enhanced due to the incorporation of DMAAm. Optimizing the feed concentration window of neutral monomer (0.3−0.5M) enhanced the epidermal adhesion of the PAT hydrogel (17.0−19.7 N) and realized high toughness (251−379 mJ m^{-3}), self-healing ability, and Young's modulus (21−29 kPa). According to this research, decreasing the strength and density of the ion-pair connections within the optimum window boosted the hydrogel's adherence to the skin.

To realize minimally invasive surgery in the medical field, hydrogel adhesives need to display not only good self-healing property but also injectability and self-adhesion. Based on the above, an injectable natural biopolymer-based hydrogel adhesive with good self-healing ability was designed by mixing chitosan, gelatin, and borax (Figure 12A).[224] The adhesive demonstrated strong adhesion on the tissue surface and was completely released from the adhered tissue to a solid state as required. Tissue adhesion of hydrogels was provided by dynamic Schiff bases and hydrogen bonding. When two cut hydrogels were joined together, they could assemble in less than 20 min without the intervention of external conditions. The hydrogels also exhibited good adhesion to pigskin, rubber, and glass materials, as well as underwater adhesion. The hydrogels had an adhesion energy with the pigskin of up to approximately 120 J m^{-2} at 37 °C. The adhesion energy was 20 J m^{-2} when hydrogels were cooled to 20 °C. The experimental results showed that the hydrogel's adherence was thermally reversible and could be altered between high and low adhesion states. Meanwhile, the experiments also demonstrated that the hydrogel was biocompatible and degradable. Based on the various outstanding properties of the hydrogel as mentioned above, the hydrogel adhesive is an ideal surgical sealant and hemostatic agent in laparoscopic surgery.

Inspired by biological phenolic chemistry, a self-healing hydrogel adhesive was quickly constituted via the Schiff-base bonding between phenolic chitosan and bifunctional aldehyde-based Pluronic-F127 cross-linking agent (Figure 12B).[223] The obtained hydrogel was temperature-responsive due to the secondary micellar structure formed from the bifunctional cross-linking agent. Experiments had shown that the hydrogel could adhere to artificial skin (up to 7 kPa) and bond quickly (within 30 s). The cohesion of phenolic and layered structures in the system provided the adhesion to the hydrogel. In addition, the hydrogel reversibly enhanced its rigidity owing to the structure of the micellar linkage. The hydrogels could be used to culture stem cells, proving the good biocompatibility. The hydrogel also had biodegradability and self-healing ability (self-healing efficiency over 95%). This presented strategy demonstrates the application prospects of multifunctional hydrogels for use in adhesives.

3.5. Wound Healing. Many people experience skin injuries caused by accidents or surgical operations every year. In general, the injured skin is unable to rapidly repair itself. In severe cases, skin wounds can result in disability or death. Wound dressings are essential to wound healing and can restore the skin function. Wound healing has several stages including wound cleansing, hemostasis, bacterial suppression, and wound regeneration. The ideal wound dressings must possess biocompatibility, good adhesion properties, superior antimicrobial properties, and good self-healing properties to ensure safety and anti-infection with no peeling and no breakage. However, conventional wound dressings do not inhibit bacteria well or do not adhere well to the wound, resulting in poor protection and greatly prolonging the healing time. Most importantly, most conventional dressings are not suitable for sport wounds. Hydrogels are considered as ideal wound dressings because of their unique properties and functionalities. Hydrogels with self-healing properties have demonstrated unique advantages. Self-healing properties are essential to ensure the adhesion, fracture resistance, and deformability of the hydrogels for wound dressings. Injectable self-healing hydrogels are able to adapt to irregular wound shapes and maintain a good microenvironment inside the wound. The self-healing properties make the dressings less prone to peeling and fracture when the hydrogels are damaged by external forces. On the one hand, the self-healing hydrogels protect the wounds without hindering oxygen and water transfer due to the natural porous structures of the hydrogels. Furthermore, the self-healing ability enables the hydrogel dressings to adequately protect the wounds when the hydrogels are stretched, bent, or folded. In this section, we focus on self-healing hydrogels in wound healing applications. Table 6 includes selected works on the application of self-healing hydrogels in wound healing.

Hyaluronic acid has exhibited crucial physiological features in organisms, which can be used to prepare hydrogel dressings. Hyaluronic acid not only canpromote wound healing but also is the best moisturizing substance with exceptional water retention in nature. Meanwhile, hyaluronic acid is biocompatible and biodegradable. Hyaluronic acid has shown unique advantages in the preparation of self-healing hydrogel dressings. A wound healing self-healing hydrogel was prepared using dynamic acyl hydrazone bonds between aldehyde-modified sodium hyaluronate and cellulose nanocrystals and hydrazine-modified sodium hyaluronate (Figure 13A).[230] The hydrogels had high self-healing ability (stress/strain self-healing efficiency: 100%, 4 h) due to the existence of dynamic hydrazone bonds, disulfide bonds, and hydrogen bonds. The introduction of aldehyde-modified cellulose nanocrystals in the hydrogel increased its elasticity and strength (G'= 800 Pa). The hydrogel provided a perfect moisturizing environment and promoted wound healing after injection into the wound site. The wound healing rate of the platelet-rich plasma-loaded hydrogel was 95.28 ± 0.56% (15 days). The platelet-rich plasma-loaded hydrogel promoted skin wound healing though accelerating angiogenesis and granulation tissue development. A Schiff base network hydrogel dressing with photothermal antibacterial properties, self-healing properties, and antioxidant properties was prepared from hyaluronic acid modified with dihydrazide, poly(ethylene glycol-*co*-glycerol sebacate) functionalized benzaldehyde, and cuttlefish melanin nanoparticles (Figure 13B).[231] The hydrogel dressing may adapt to repetitive movements caused by human wounds. The hydrogel has exceptional self-healing characteristics thanks to the hydrogen bonds and dynamic Schiff base bonds. The hydrogel's self-healing effectiveness was as high as 102% (37 °C, 2 h). The catechol moiety imparted high adhesion

Table 6. Important Properties of Self-Healing Hydrogels in Wound Healing in Recent Literature

polymer materials	self-healing mechanism	self-healing performance	wound healing assessment	antibacterial performance evaluation	ref
β-CD/PEI/PVA	hydrogen bonds	elongation up to 150% (after healing)	effectively promote healing 7 days before trauma	wound inflammatory cells were significantly reduced on day 7 with excellent antibacterial performance against Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*	12
PDA NPs/GC/OHA-Dop/GG/borax,	Schiff base bonds, hydrogen bonds, borate ester bonds	[a]	newly formed dermis is tightly bound to the epidermis (after 14 days)	killing rates of *Escherichia coli* and *Staphylococcus aureus* by hydrogel were 98.20% and 73.13%, respectively, after 10 min of NIR irradiation	19
GelMA/AA/$CuCl_2$	coordination bonds, hydrogen bonds	[a]	wound healed completely on day 21	survival rates of *Staphylococcus aureus* and *Escherichia coli* were 7.5% and 0.0%, respectively (after 9 h)	51
TA/DPPH/PEG/CA/DA	ionic bonds, hydrogen bonds	cut hydrogels were fused together within 3 min	wound healed completely on the 21st day	[a]	76
HPCS/PNIPAM/β-CD/AD	host−guest interactions	large damage above 5 mm could be completely self-healed	average healing rate 99.5% (14 days)	antibacterial activity against *Staphylococcus aureus*	63
QCS/TA	ionic bonds, hydrogen bonds	92% (tensile property)	average healing rate 92.8% (14 days)	killing rate of hydrogel against *Staphylococcus aureus* and *Escherichia coli* was more than 99% (2 h)	227
GO-BPEI/CMCS/PEG-CHO	amide bonds	[a]	wound closed completely in 14 days	hydrogels exhibited 120% relative cell viability (3 days of continuous NIR irradiation)	228
HPC/4-carboxyphenyl boronic acid/lignin	borate ester bonds, hydrogen bonds	it only takes 10 min for two hydrogels to heal into a complete hydrogel	wound healed completely on the 15th day	killing rate of hydrogel against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* was 100% (2 h)	229

[a] Not described.

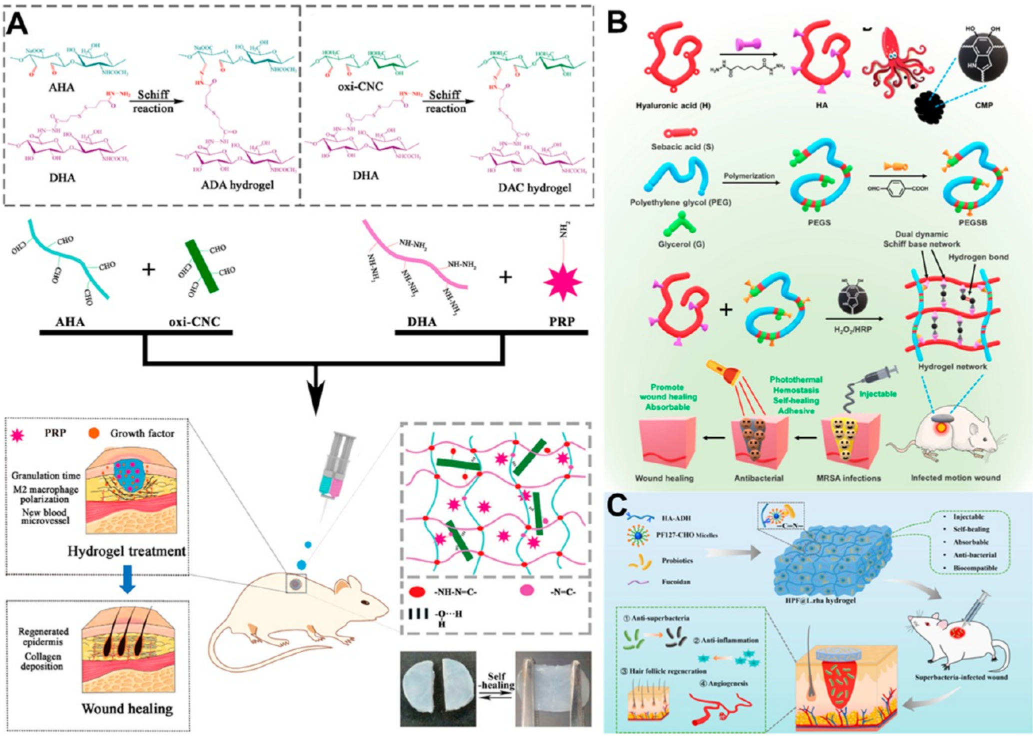


Figure 13. (A) Self-healing hydrogel wound dressing. Reproduced with permission from ref 230. Copyright 2022 Elsevier. (B) Antibacterial, self-healing, and antioxidant property hydrogels. Reproduced with permission from ref 231. Copyright 2022 Elsevier. (C) Hydrogel wound dressing with good antibacterial and self-healing properties. Reproduced with permission from ref 103. Copyright 2022 American Chemical Society.

strength (up to 13 kPa) to the hydrogel. The tensile properties of the hydrogels exceeded 200%. The lethality of the hydrogels against both Gram-negative and Gram-positive bacteria was more than 90% under NIR irradiation. After NIR irradiation of the hydrogel dressing, the wound healed completely at 14 days. The experiment confirmed that the hydrogel dressing could stop bleeding, inhibit infection, and promote wound healing.

The Schiff base reaction of adipic dihydrazide-modified hyaluronic acid, Pluronic F127-CHO, and sulfated polysaccharide fucoidan was utilized to design a self-healing hydrogel dressing for wound healing (Figure 13C).[103] The Schiff base bonding endowed it with superior self-healing capability. In vitro antibacterial experiments demonstrated that the hydrogel dressing processed good antibacterial performance. The wound healing rate using the hydrogel dressing loaded with probiotics was 96.7 ± 2.8% (14 days). Hydrogel dressings exhibited rapid wound healing ability owing to the antibacterial action of probiotics and the good moisturizing wound condition created by the hydrogel.

Other natural polymers (including chitosan and gelatin) are commonly utilized to prepare hydrogel-based wound dressings with self-healing ability, because they have unique biological activities and the potential to stop bleeding, improve wound healing, and accelerate skin regeneration. By using the Schiff base reaction to combine poly(dextran-*g*-4-formylbenzoic acid) and carboxymethyl chitosan, a self-healing hydrogel was created. Next, to improve the hydrogel's mechanical behavior, antimicrobial peptide-grafted polyacrylonitrile (PAN) nanofibers were added (Figure 14A).[232] The cationic portions of antimicrobial peptides could eliminate bacteria, as well as activate platelets and coagulation. The mechanical properties of the hydrogels were increased via introducing nanofibers. Studies confirmed that hydrogels were degradable under physiological conditions. The hydrogel dressing had the ability to significantly speed up the healing of chronic wounds and promote tissue ingrowth. To accelerate the wound healing, a self-healing carboxymethyl chitosan (CMCS)−Fe/Al^{3+} hydrogel was designed (Figure 14B).[233] The hydrogel was produced by the coordination cross-links between carboxymethyl chitosan and Fe^{3+}/Al^{3+}. The produced hydrogels demonstrated self-healing, injectability, and multiresponsiveness. The hydrogel has been given self-healing and thermal responsiveness by the coordination bonds. The $-NH_2$ group on CMCS could interact with the dianion of SO_4^{2-}, causing the phase separation of the hydrogel and reducing its adhesion. A novel physicochemical double cross-linked hydrogel with self-healing ability was also designed for healing dynamic burn wounds, which was obtained by Schiff base bonds between catechol-modified oxidized hyaluronic acid (OD) and aminated gelatin (AG), as well as the chelation of OD and Fe^{3+} (Figure 14C).[234] Compared to single cross-linking, the double cross-linked hydrogels exhibited excellent mechanical properties (G': 535 kPa) and adhesion strength (19.3 kPa) and good shape adaptation (97.1 ± 1.3%). During wound healing, the double cross-linked hydrogels showed biodegradability, antibacterial activity (killing-efficiency: 100%), and hemostatic ability. Treated wounds had shorter healing time (burn wound healing: 15 days) and more intact skin structure compared to that with conventional dressings. Polysaccharide-based hydrogels with self-healing properties composed of carboxymethyl chitosan, sodium alginate, and tannic acid were also demonstrated to have good inhibition of inflammation and to promote wound healing in animal injury experiments (Figure 14D).[235]

In another study, self-healing hydrogels were used to repair wounds of diabetic skin ulcers. The hydrogels composed of silk

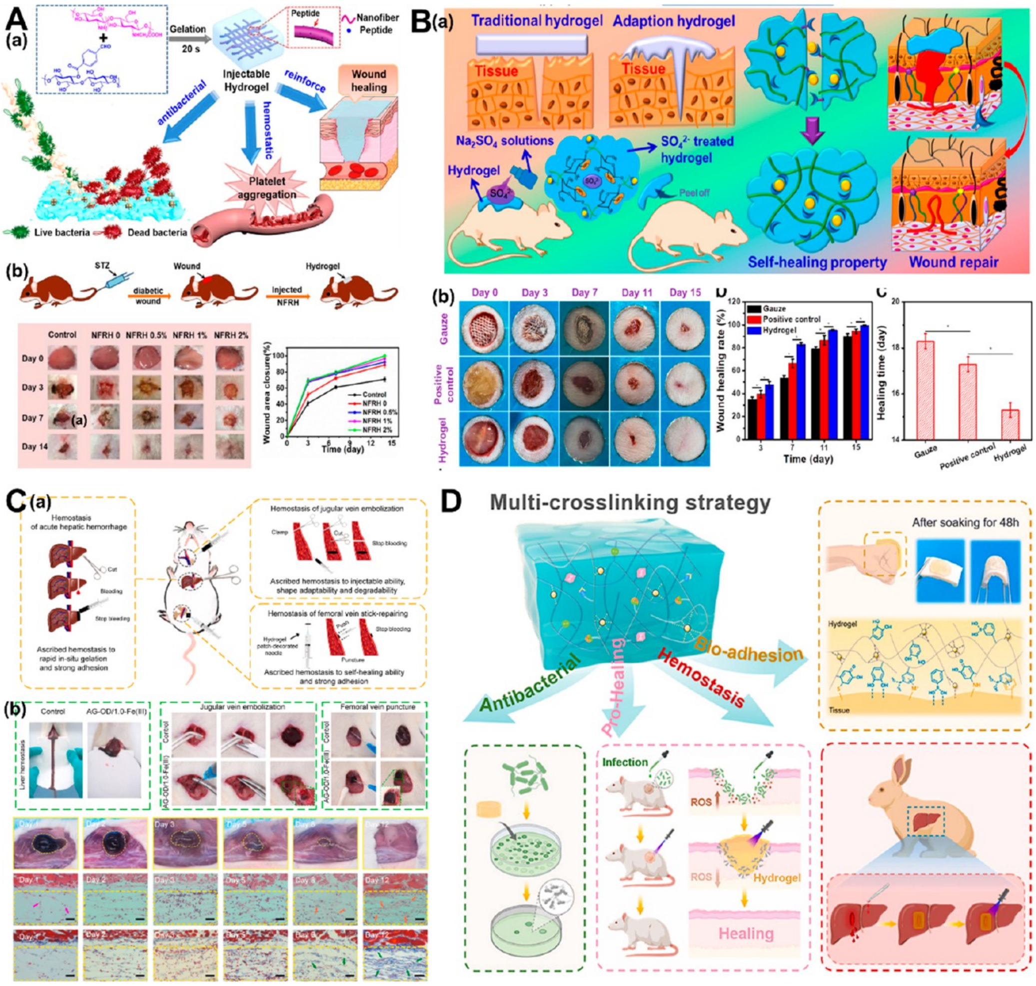


Figure 14. (A) Diagram of the hydrogel dressing preparation using nanofibers reinforced by peptide modifications. Reproduced with permission from ref 232. Copyright 2021 Elsevier. (B) Diagram of wound dressing preparation of injectable carboxymethyl chitosan hydrogel. Reproduced with permission from ref 233. Copyright 2021 American Chemical Society. (C) Design strategies for physicochemical double cross-linked hydrogels for dynamic burn wounds. Reproduced with permission from ref 234. Copyright 2021 Elsevier. (D) Schematic diagram of a multifunctional hydrogel that can be used for hemostasis and wound healing. Reproduced with permission from ref 235. Copyright 2022 Elsevier.

fibroin, chitosan, and platelet-rich plasma (PRP) provided a new therapeutic approach for clinically nonhealing diabetic wounds (Figure 15A).[236] Briefly, PRP promoted the proliferation of cells in vitro. Silk fibroin, a natural fibrin, was resistant to enzymatic hydrolysis and prolonged the bioactivity of hydrogels. Chitosan ensured sustainable release of bioactive components in hydrogels. Like an ideal dressing for treating diabetic wounds, the hydrogel overcame the shortcoming of the rapid degradation of conventional hydrogels. The hydrogel had biocompatibility, biodegradability, suitable mechanical properties, and excellent self-healing properties and could promote angiogenesis and diabetic wound healing.

Hydrogel dressings with self-healing performance are also applied for postoperative repair and clinical studies in vivo. A self-healing ionic conductive hydrogel (POG) made up of biocompatible PAA, sodium alginate, and gelatin, was reported for the treatment of myocardial infarction (Figure 15B).[237] The addition of aldehyde-based PAA into the hydrogel system increased the quantity of Schiff base bonds, ionic coordination, and hydrogen bonds. The internal nanochannels of PAA endowed the hydrogel with superuniform conductivity. POG hydrogels had tunable mechanical ability (compressive strain: >85%; tensile strain: >500%), excellent ionic conductivity ($(35.36 \pm 7.72) \times 10^{-3}$ S cm^{-1}), moderate elasticity (37.04 ± 2.75 kPa) and rapid self-healing properties. Meanwhile, The mechanical and ionic conductivity of POG hydrogels were simply adjusted to meet the needs of cardiac tissue. Cardiomyocytes cultured in POG hydrogels showed more pronounced orientation and elongated sarcomeres compared to cardiomyocytes embedded in PPy or CNT hydrogels. The findings demonstrate that hydrogels can be used to repair damaged heart muscle.

Furthermore, an injectable self-healing supramolecular hydrogel was designed for gastric perforation healing (Figure 15C).[238] The ABA triblock copolymer with a hydrophilic poly(ethylene glycol) block, a temperature-responsive poly(*N*-isopropylacrylamide) block, and a pH-sensitive acrylyl-6-aminopropionic acid block was designed to adapt to the gastric environment and was applied to prepare an injectable self-healing supramolecular hydrogel. Owing to the special effect of the block, the copolymer solution was well adapted to the gastric environment. Hydrogels showed self-healing ability through the synergy of hydrogen bonds and hydrophobic interactions under an acidic environment. The hydrogels also had excellent anti-biofouling proper-

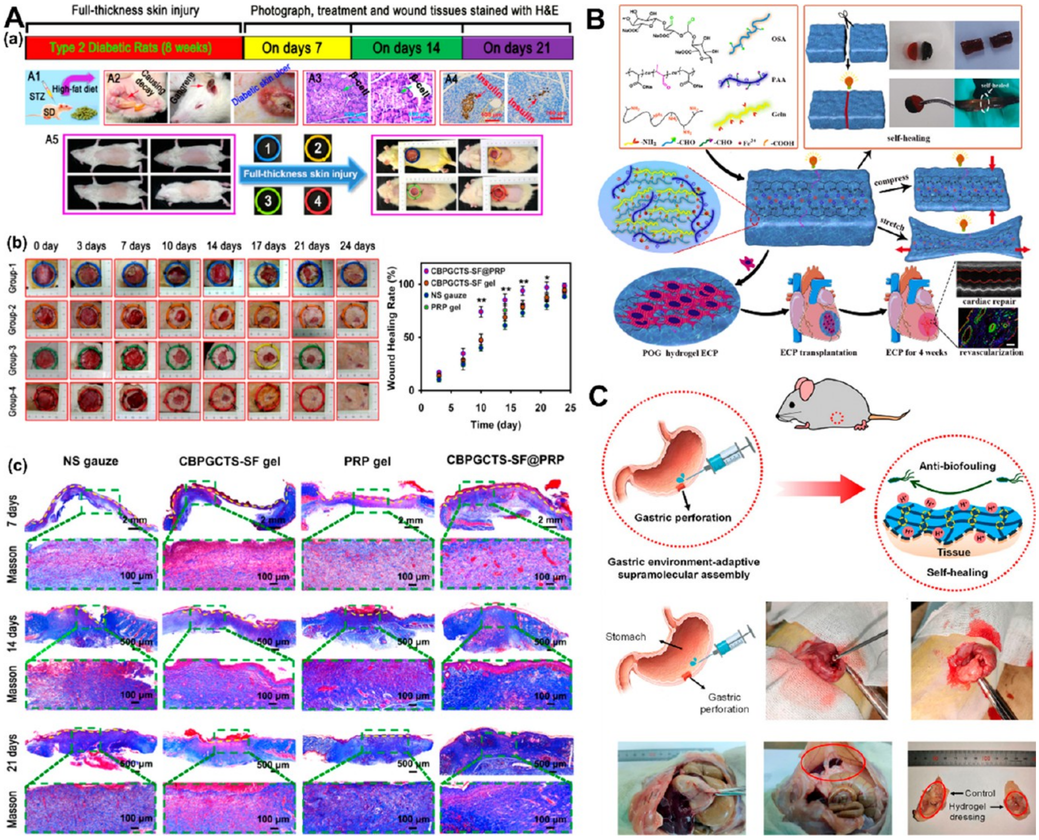


Figure 15. Self-healing hydrogels were used in wound healing. (A) Preparation of PRP-loaded hydrogels for promoting angiogenesis in wound healing. Reproduced with permission from ref 236. Copyright 2020 American Chemical Society. (B) POG self-healing hydrogel was used to restore myocardial infarction. Reproduced with permission from ref 237. Copyright 2021 Elsevier. (C) Preparation of injectable self-healing hydrogel for gastric perforation healing. Reproduced with permission from ref 238. Copyright 2021 American Chemical Society.

ties. An in vivo rat model demonstrated that the supramolecular hydrogel could simplify the surgical process, reduce postoperative adhesion, and suppress inflammatory response in the gastric perforation therapy. The self-healing supramolecular hydrogels are expected to be used in more clinical studies.

3.6. Drug Delivery and Cancer Therapy. Self-healing hydrogels with excellent biocompatibility, nontoxicity, degradability, and long-term operability can be exploited as perfect cancer treatment carriers. Due to their hydrophilic properties and 3D cross-linked network structures, hydrogels can provide a bionic 3D microenvironment, which allows hydrogel carriers to be well integrated in living organisms. Hydrogels can serve as drug carriers to realize local drug delivery. This approach is similar to targeted cancer therapy, which can improve the efficiency of drug use. Hydrogel carriers allow the drugs to produce even better results at high concentrations. Based on the stimulatory reactivity of the hydrogels, controlled release and degradation rates of drugs are generally achieved by altering the physical and chemical cross-link structures of the hydrogels. The self-healing properties of hydrogels allow for effective encapsulation of drugs and the recovery of structures and properties during controlled drug release. Importantly, the self-healing properties also accomplish a long service life and cycle time of the hydrogel carriers. After the completion of drug release, hydrogels can degrade in vivo because of their biocompatibility and degradability. Hydrogels as drug delivery carriers do not cause side effects to the organisms. Thus, injectable self-healing hydrogels are an ideal vehicle for implantable drug delivery in cancer therapy. In this section, some typical examples of self-healing hydrogels used in drug delivery and cancer therapy are discussed in detail. Table 7 shows a variety of self-healing hydrogels in drug delivery and cancer therapy.

Intelligent hydrogels have been extensively researched as a potential medication delivery medium. Hydrogels typically achieve regulated medication release when stimulated. pH is often used as an intrinsic stimulus to allow controlled drug release from hydrogels. Injectable and self-healing hydrogels, obtained by using chitosan and hydroxysuccinate sugars, could be used to achieve effective drug release.[239] The self-healing hydrogel had good biocompatibility (cell viability: 97.30%, cell proliferation 98.84% at 7 days), antimicrobial properties (90%), mechanical stability (compressive stress: 173 kPa at 60% strain), adhesion (adhesion strength: 2763 kPa), and thermal stability. The hydrogel had excellent self-healing properties (99.89%). Most importantly, the self-healing hydrogel exhibited a pH-controlled drug release behavior, demonstrated with 5-fluorouracil as a model drug. In pH 2.0−7.4, the hydrogel released 90% to 60% 5-fluorouracil. The hydrogel could be used in drug delivery systems due to the pH-responsive −COOH in hydroxysuccinate sugars.

Besides, pH and redox dual-responsive injectable self-healing hydrogels were designed via 3,3′-dithio(propionic acid dihydrazide)-modified hyaluronic acid and aldehyde-modified hyaluronic acid.[221] The hydrogel had wonderful self-healing ability and shape recovery owing to the presence of acylhydrazone bonds. The hydrogel fragments were fused into a tightly connected hydrogel block for 2 h at room temperature.

Table 7. Important Properties of Self-Healing Hydrogels in Drug Delivery and Cancer Therapy in Recent Literature

polymer materials	self-healing mechanism	self-healing efficiency	mechanism of drug delivery dependence	key performance	ref
OSG/CHI	Schiff base bonds	99.89%	pH	compressive stress (at 60% strain): 173 kPa; adhesive strength: 2763 kPa; antibacterial efficiency: 90%	239
AAlg/Acs/ADH/$FeCl_2$	Schiff base bonds and ionic interactions	78.3 ± 6% (compressive tests)	time	more than 85% of the cells survived (within 72 h) with a compressive breaking strength of ≈48 kPa	240
HA-CHO/GC	Schiff base bonds and coordination bonds	self-healing hydrogels can support their own weight without breaking	hydrogel process and dissolution	hydrogel was released continuously for 6 days and completely released on the seventh day	241
N,O-CMCS/MAGG	Schiff base bonds	hydrogel was completely devoid of seams in light microscope images taken 4 h after self-healing	pH	Dox-loaded hydrogel had a significant killing effect on MCF-7 cells (72%)	242
CECT-ADH/PEG-DA	acyl hydrazone bonds	95%	solid content	no inflammatory cells were found in the tissue surrounding the hydrogel injection, 32 days after injection	243
TA/F127	Schiff base bonds	[a]	pH	continuous linear release pattern was observed within 6 days	244
OA/nSi/DNA nucleotides	imine bonds	[a]	[a]	viscosity up to 3257 Pa	245
MPC/FBEMA	Schiff base bonds	[a]	pH	storage modulus up to 2211 Pa	246
curcumin/PVA/PBA	boronic ester bonds	hydrogel fragments became one piece after 1 h	H_2O_2, HCl, fructose, mannitol	[a]	247
HA-TPH/HA-CHO	disulfide bonds and acylhydrazone bonds	[a]	redox and pH	[a]	221
CEC-ADH/AD-CHO/CEC-CD	host−guest interactions	97.5%	pH	pH-responsive; cell survival higher than 95% (after 3−7 days)	133
PEG/CMCS/HAP/GO	Schiff base bonds	it only took 10 min for the cut hydrogel to stick together	NIR	storage modulus: 2850 Pa; photothermal conversion and photostability	248
DF-PEG/CS-*g*-PNIPAAm/{Mo_{154}}	Schiff base bonds and electrostatic interactions	pores on the hydrogel closed completely in just 4 min at room temperature	pH/NIR	pH-sensitive and NIR-responsive; photothermal stability	249
PULL-CHO/CS-*g*-PEG/MNPs	Schiff base bonds	hydrogel network collapsed under large strain (200%), and the storage modulus and loss modulus healed to their original values immediately after removing the strain	magnetothermal	storage modulus 1020 Pa; viability of cells cultured with hydrogel was higher than 90%	250
TiO_2/TPU/PAAm	hydrogen bonds	after healing, the elastic modulus of the hydrogel reached 70% of the initial value within 300 s	[a]	elongation at break: 2283%; adhesive strength: 9.46 kPa; inhibition rates of hydrogel against *Escherichia coli* and *Staphylococcus aureus* were 96.3% and 103.6%, respectively	251
P(NIPAM-*stat*-AH/pectin-CHO)	acylhydrazone bonds	it only took 24 h for two hydrogels to make one hydrogel	thermal	sustained release rate of the hydrogel was 54.1% in buffer pH = 7.4; hydrogel was reduced within 28 days of injection	252

[a] Not described.

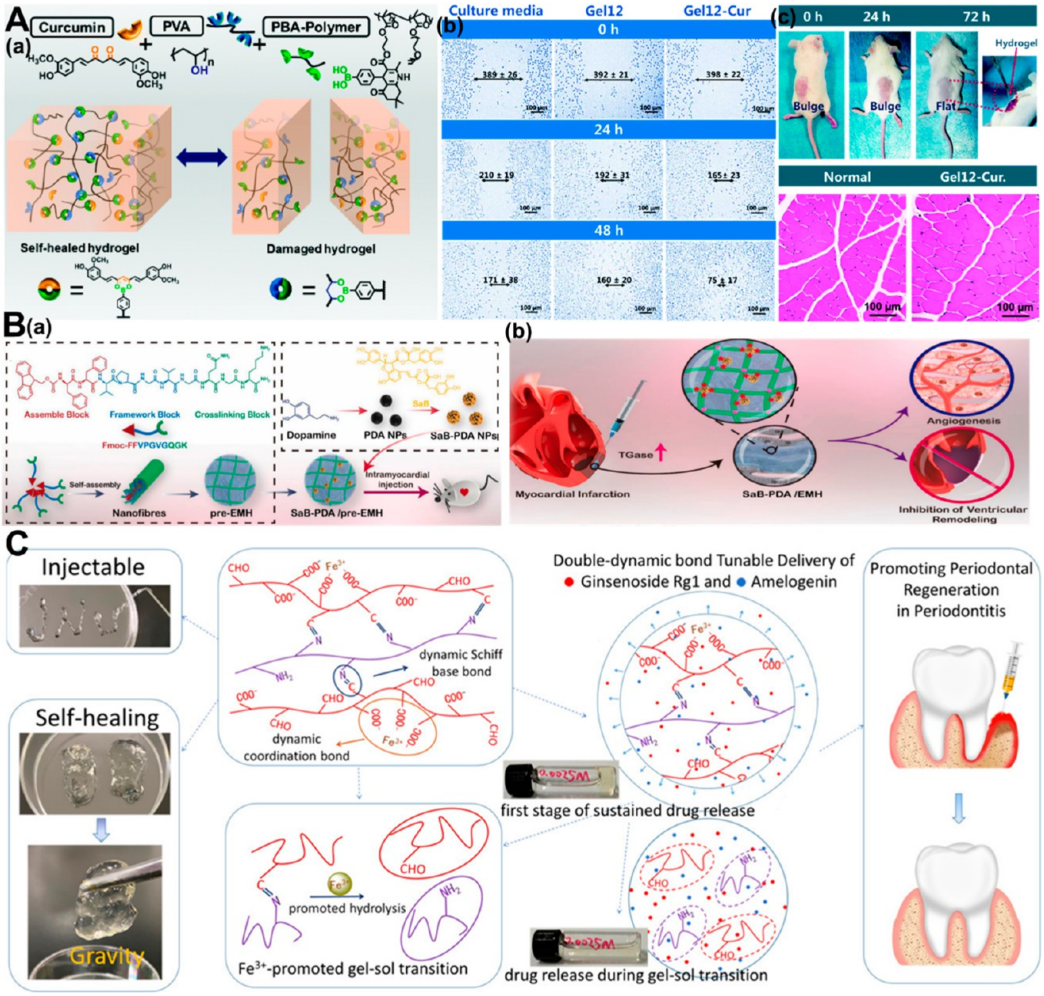


Figure 16. (A) Multiresponsive self-healing hydrogel synthesized from phenylboronic acid and poly(vinyl alcohol). Reproduced with permission from ref 247. Copyright 2021 Royal Society of Chemistry. (B) Self-healing injectable peptide hydrogel as a carrier of salvianolic acid B. Reproduced with permission from ref 253. Copyright 2021 Elsevier. (C) Schematic of the self-healing injectable hydrogel prepared by hyaluronic acid and glycol-chitosan to promote periodontal regeneration. Reproduced with permission from ref 241. Copyright 2021 American Chemical Society.

The hydrogel also exhibited a reversible sol–gel transition behavior under redox conditions owing to the dynamic changes between disulfide bonds and sulfhydryl functional groups. The hydrogel would swell when pH exceeded 7.4 and shrink when pH was less than 7.4. The mechanical capacity of the hydrogel was significantly improved at pH = 2 (the storage modulus: 35.3 kPa). The mechanical loss of the hydrogel increased with increasing pH. Controlling the pH values could result in the hydrogel's volume contraction and reversible transformation. Biocompatibility experiments confirmed that the cell survival rate of all injectable hydrogels exceeded 85%. Under acidic and reducing conditions, the hydrogel served as a matrix to control the release of bioactive proteins and promote the proliferation of chondrocytes.

Glucose oxidase, acetylcholine esterase, and urease were integrated into a polyacrylamide hydrogel to create a pH-responsive, biocatalytically controlled DNA hydrogel for drug delivery.[253] The stiffness of the hydrogel would recover 89% of the initial value in a self-healing experiment. Glucose oxidase and insulin were added into the DNA-based hydrogels. Glucose-induced pH changes could control the release of insulin from the hydrogels at glucose concentrations of 200–400 mg mL^{-1}. Insulin was released within 30 min, and glucose concentrations became saturated in the process. The release of insulin could be cycled by treating the hydrogel with glucose and urea. Thus, the hydrogel could mimic the function of the pancreas. In another DNA-based self-healing hydrogel study, the hydrogel was cross-linked though the aldehyde group of alginate and the amino group of nucleotides to form a reversible imine bond.[245] The self-healing hydrogel may be utilized as a carrier for injectable drugs such as simvastatin. Nucleotides formed physical cross-links with silicon nanosheets through electrostatic interactions. The reason for the good self-healing properties of hydrogels was the reversible dynamic cross-linking. The addition of silicon nanosheets made the hydrogel injectable (shear modulus:10–1000 Pa), enhanced the mechanical ability, and promoted the long-term release of simvastatin. The study confirmed that the sustained release mechanism of the drug was mainly driven by the hydrophobic interaction of the drug with the nitrogenous base pairs on the DNA chain. The contact experiments of the hydrogel with human adipose stem cells confirmed the biocompatibility and nontoxicity of the hydrogel (85% cell viability after 24–72 h). The hydrogel slightly changed the drug release half-life at pH = 4.5 from 4.9 days to 4.77 days. The simvastatin could maintain osteogenesis by releasing from the nanocomposite hydrogel. In addition, the simvastatin released

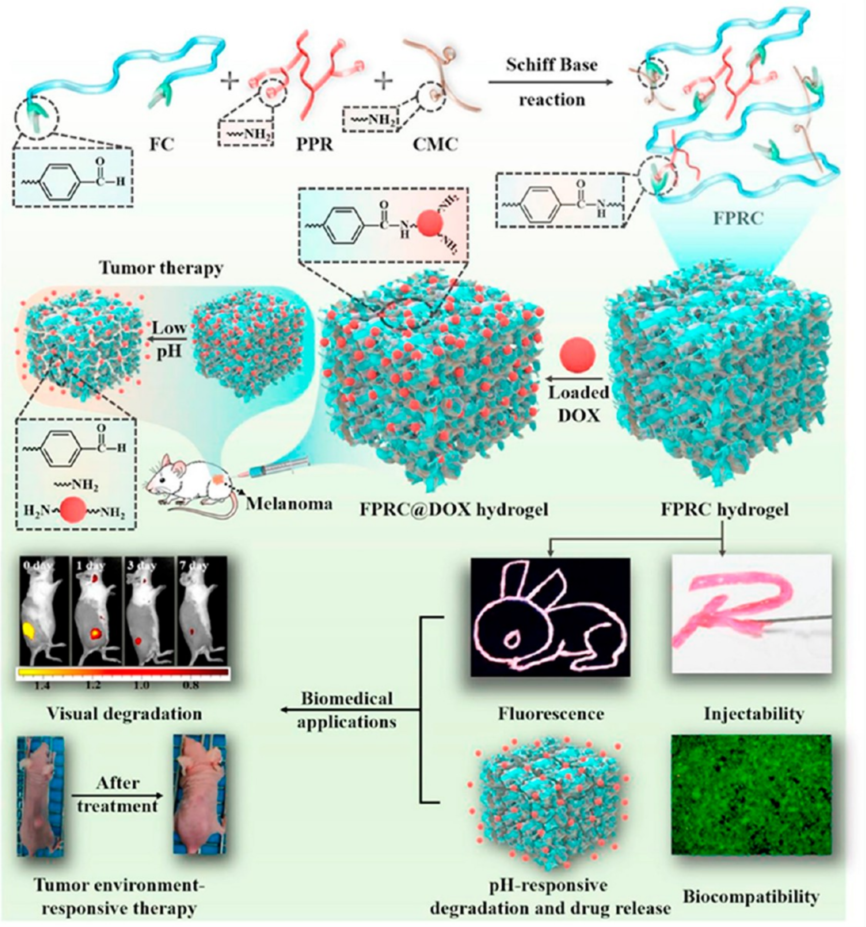


Figure 17. Synthesis mechanism of FPRC@DOX hydrogel and application in local melanoma treatment. Reproduced with permission from ref 254. Copyright 2020 Elsevier.

from the hydrogel had the ability to improve the migration of stem cells in vitro.

A multiresponse self-healing hydrogel was prepared from phenylboric acid, curcumin, and PVA to control the release of curcumin (Figure 16A).[247] Dynamic borate ester bonds endowed the curcumin-loaded hydrogels with self-healing and fluidity. Borate ester bonds hydrolyze under acidic conditions; thus the addition of HCl/NaOH into hydrogels could make it quickly decompose and regenerate. In addition, the hydrogels were responsive to hydrogen peroxide, fructose, mannitol, and water (response sensitivity: hydrogen > peroxide > HCl > fructose > mannitol > water). Cell culture experiments demonstrated that the hydrogels were biocompatible (96% survival after 48 h). In vitro wound tests showed that artificial wounds healed rapidly under hydrogel coverage. This was because the hydrogel as a wound dressing can continuously release curcumin, which could be degraded by different sugars, and the drug's controlled release could promote wound healing.

Drug-encapsulated self-healing hydrogels have the ability to promote blood supply and restrain extracellular matrix degradation in the therapy of myocardial infarction. A self-healing injectable peptide hydrogel was fabricated via the self-assembly of a peptide (Fmoc-FFVPGVGQGK) with the addition of salvianolic acid B (SaB)-loaded polydopamine nanoparticles (SaB-PDA), which could be used for the treatment of myocardial infarction (Figure 16B).[253] The inclusion of transglutaminase significantly enhanced the hydrogel's mechanical strength (up to 24.8 times). SaB-PDA enhanced the effectiveness of self-healing and slowed the release of SaB. SaB could be continually released about 17% in 96 h. The hydrogel's strong capacity for self-healing may enable it to remain in the beating ventricular wall longer. The in vitro and in vivo studies demonstrated that the hydrogels had excellent biocompatibility. Last but not least, rats with heart failure could recover with the help of the hydrogel after 4 weeks. Pathological sections showed that the hydrogel was very beneficial for ventricular remodeling and angiogenesis. The above conclusions indicated that the self-healing injectable peptide hydrogel was a promising solution treatment for myocardial infarction. Injectable and self-healing hydrogels obtained from hyaluronic acid and glycolic chitosan can promote periodontal regeneration in periodontitis (Figure 16C).[241] The self-healing hydrogel could withstand its own weight without damage owing to the Schiff base and the coordination network at the contact interface. After 7 days, the hydrogel containing 0.01 M $FeCl_3$ released about 90% of ginsenoside RG1 and amelogenin. The hydrogel (0.0025 M $FeCl_3$) continued to release the drug for over 6 days. The sustained release time of the drug can be controlled through changing the molecular structure of the hydrogel. The release of drugs in the hydrogel can be accomplished through the gel−sol transition process. The drug release increased with the hydrogel's gradual degradation, reaching complete drug release after full degradation. The diffusion process and hydrogel dissolution process affected the

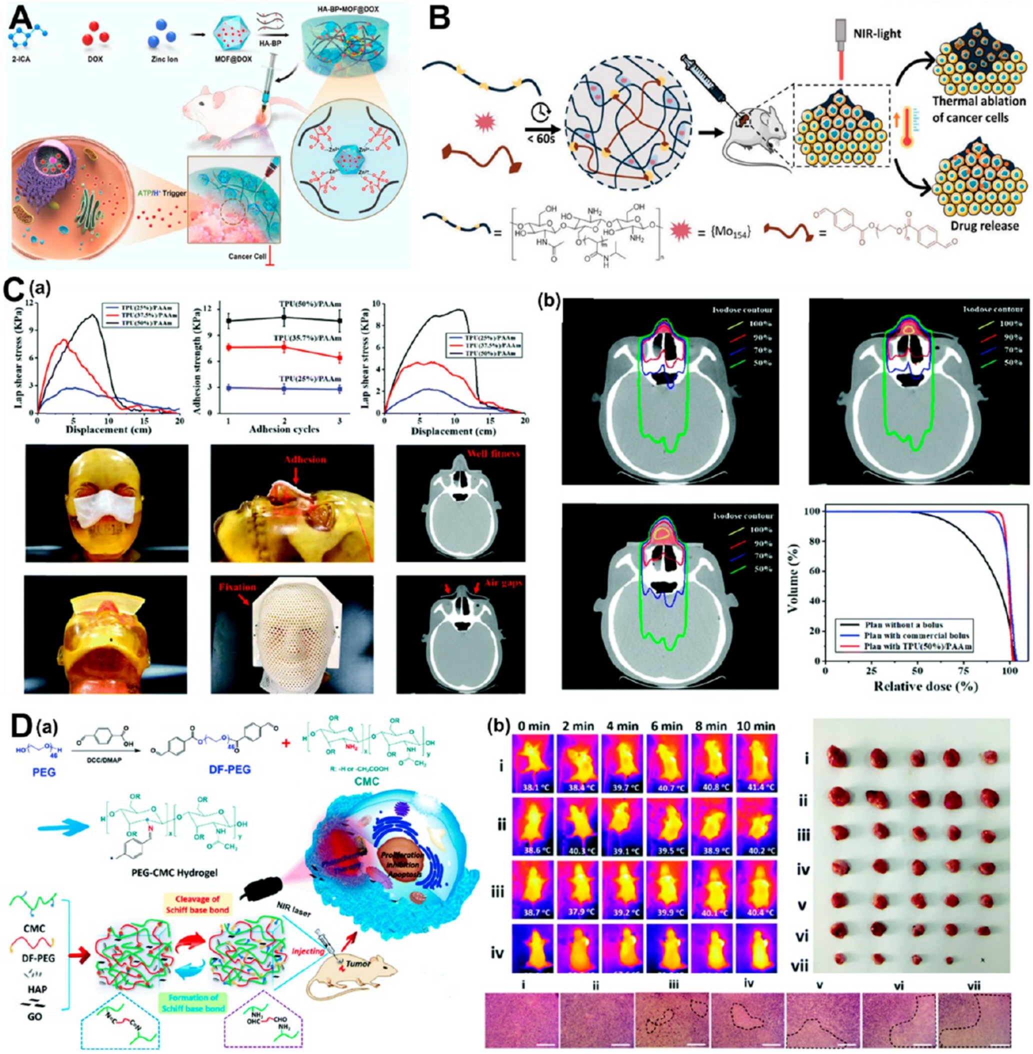


Figure 18. (A) Protocol design of hydrogels for injectable local drug delivery systems in cancer treatment. Reproduced with permission from ref 255. Copyright 2022 Elsevier. (B) Schematic application of injectable self-healing hydrogels in cancer therapy. Reproduced under terms of a Creative Commons CC-BY License from ref 249. Copyright 2021 John Wiley and Sons. (C) Schematic illustration of the design of PAAm hydrogels for radiotherapy of cancer. Reproduced with permission from ref 256. Copyright 2020 Royal Society of Chemistry. (D) Schematic design of self-healing nanocomposite hydrogel and its effect on tumor cells. Reproduced with permission from ref 248. Copyright 2021 Royal Society of Chemistry.

drug release performance of hydrogels. Ginsenoside RG1 had an anti-inflammatory effect to achieve a local noninflammatory microenvironment, while amelogenin played a role in promoting periodontal regeneration in periodontitis.

Cancer is generally characterized by late detection and high mortality. In the treatment of cancer, radiation therapy is an effective way to control local recurrence of cancer. But radiotherapy can cause some damage to the surrounding healthy tissues, resulting in dermatitis in mild cases and skin necrosis in severe cases. Currently, biodegradable hydrogels with good antimicrobial properties, biocompatibility, and drug release function have been prepared and applied to radiation therapy for cancer. Commercial pills do not fit well into tissues, which will affect the drug release function of the pills, while self-healing hydrogels can solve the drawbacks of commercial pills. Self-healing injectable hydrogels allow for precise, continuous, and controllable drug delivery, thus greatly improving the durability and efficacy and inhibiting tumor growth. Researchers have conducted some studies on self-healing hydrogels loaded with antitumor drugs. Biodegradable self-healing hydrogels can improve the efficiency of drug therapy. A biodegradable self-healing citrate hydrogel scaffold (FPRC) was designed for local melanoma treatment (Figure 17).[254] F127-CHO as a primary network provided a certain temperature sensitivity and offered aldehyde groups for hydrogel formation. Polycitrate−polyamine−rhodamine B polymer (PPR), as a promising fluorescent indicator (at 365 nm excitation), could be used to detect the degradation of hydrogels in vivo and provided amino groups. Carboxymethyl chitosan enhanced the biocompatibility and structural stability of hydrogels. The hydrogel exhibited a sol-to-gel process between 25 and 37 °C. The cross-linking of the aldehyde group and the amino group to form Schiff base bonds provided self-healing properties (1 h). Doxorubicin (DOX) was loaded into the self-healing hydrogel to effectively kill cancer cells. In comparison to free DOX, the FPRC@DOX hydrogel may continuously release DOX to have a much better A375 cell killing ability (3 days). Compared with FPRC hydrogels, FPRC@DOX hydrogels also had obvious killing ability against A375 cell. When FPRC@DOX hydrogel was injected into mice with melanoma cells, the hydrogel showed excellent tumor

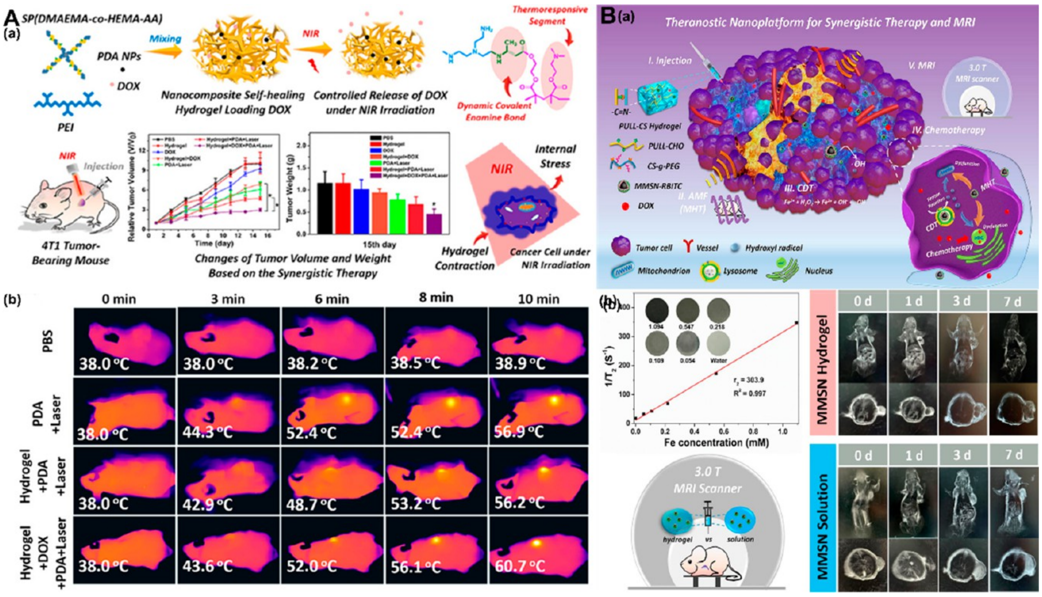


Figure 19. (A) Self-healing hydrogels containing polydopamine nanoparticles for photothermal therapy of tumors. Reproduced with permission from ref 257. Copyright 2020 American Chemical Society. (B) Nanocomposite hydrogel with good anticancer properties against 4T1 tumor cells. Reproduced with permission from ref 250. Copyright 2020 Elsevier.

treatment effect (14 days). Immunohistochemical examination further confirmed that the hydrogel could inhibit tumor cell growth with low side effects.

A self-healing injectable hydrogel was fabricated from bisphosphonate-modified hyaluronic acid (HA-BP) and MOF and was used to load DOX for tumor therapy (Figure 18A).[255] Bisphosphonate (BP)−Zn^{2+} interaction conferred self-healing properties on the hydrogel. Two hydrogel sections could be quickly fused together after slicing. The DOX-loaded hydrogel had sustained drug release and anticancer effects. Antitumor experiments in mice showed a significant reduction in tumor volume to 33 ± 9 mm^3 after injection for 15 days. Meanwhile, the hydrogel had a long-term inhibitory effect on tumor growth (showing anticancer activity in vivo within one month after a single injection) owing to the continuous release of DOX. The hydrogel had a strong inhibitory effect on colorectal tumors. A self-healing hydrogel with NIR- and pH-responsive behaviors was also reported for the encapsulation of DOX for tumor therapy, which consisted of benzaldehyde functionalized poly(ethylene glycol), poly(isopropylacrylamide) functionalized chitosan, and $\{Mo_{154}\}$ (Figure 18B).[249] The dynamic imine bonds and electrostatic interactions conferred rapid self-healing properties on the hydrogels. Drug release from hydrogels containing DOX was pH-responsive. Faster and more complete drug release occurred at pH = 5.5 or pH = 6.2. The drug release of hydrogel could reach 91% when pH was 6.2 (4 h). In short, the acidic environment facilitated drug release. Meanwhile, the self-healing hydrogel also had photothermal conversion ability and exhibited NIR-responsive drug release behavior. This self-healing hydrogel utilized the dual responsive effect to exert great therapeutic effect in cancer treatment and ablate a melanoma tumor in vivo.

A self-healing polyurethane (TPU)/polyacrylamide (PAAm) hydrogel containing TiO_2 nanoparticles was developed for the radiation therapy of cancer (Figure 18C).[256] The hydrogel had excellent mechanical properties (elongation at break of 2283% at 90 kPa tensile stress), adhesive properties (10.74 kPa), and self-healing properties (healing for 2 h at room temperature). The experiments proved that strong hydrogen bonds could build up the healing efficiency of hydrogels. TiO_2 nanoparticles were photocatalytically active and had antibacterial capabilities. After adding 2,2-bis(hydroxymethyl)propionic acid to modify TiO_2, TiO_2 nanoparticles were evenly dispersed in the hydrogel system, which increased the antibacterial properties. *Escherichia coli* and *Staphylococcus aureus* were susceptible to the hydrogel's antibacterial properties by 96.3% and 103.6%, respectively. Preclinical feasibility assessment showed that the hydrogel provided 100% planning target volume coverage at 90% dose, while the same level of commercial bolus only provided 98.5% planning target volume coverage, indicating a better fit between the hydrogel and the skin tissue. In addition, the hydrogel had good adhesion and could be well attached to the medical head model. The hydrogel could be used in the radiotherapy of cancer, and was effective in the radiotherapy of superficial tumors.

An innovative injectable biodegradable self-healing hydrogel composed of pectic aldehyde and *N*-isopropylacrylamide was used as an antineoplastic drug delivery carrier.[251] Due to the thermal response of *N*-isopropylacrylamide, the hydrogel showed NIR/temperature dual responsive behavior. The hydrogel demonstrated good self-healing capability (24 h for healing process) because of the presence of dynamic acylhydrazone linkages. The self-repair ability of the hydrogel could maintain stability during drug reloading and enhance the therapeutic performance. By adjusting the amount of pectic aldehyde in the hydrogel, the mechanical properties may be controlled. When the ratio of pectic aldehyde to *N*-isopropylacrylamide was 2:1, the hydrogel had excellent mechanical properties and flexibility. The hydrogel had good drug release performance at a lower pH (88% drug release in pH 5.4 within 72 h). Furthermore, the hydrogel was injectable, so it could be used to load anticancer medications, detect tumors, continuously release drugs, as well as reduce drug diffusion. The treatment effect was significantly improved, and local antitumor therapy can be achieved.

Table 8. Important Properties of Self-Healing Hydrogels for 3D Printing in Recent Literature

polymer materials	self-healing mechanism	self-healing efficiency	main performance	ref
P(HEMA-*co*-AAc)	hydrogen bonds	hydrogel scratches were recovered after only 1 min	tensile strength up to 41.3 MPa, fracture strain up to 4336%, modulus up to 352 MPa, toughness up to 56.23 MJ m^{-3}	258
TA/$CaCl_2$/rGO/SF	hydrogen bonds	95% (1 min)	adhesion strength on skin up to 18.6 kPa; adhesion strength on muscle 3.7−5.5 kPa, and lowest adhesion strength on heart 4.0−5.0 kPa; stretching property: 20500% to 24000%; Young's modulus: 21.7 MPa	259
AA/NVP/CMC/$ZnCl_2$	hydrogen bonds, coordination bonds	81% (stress), 91% (strain)	tensile toughness: 3.38 MJ m^{-3}; resistance response sensitivity: 1.16; strain response range: 1000%	260
DF-PEG/Chi-Ph	imine bonds, $\pi-\pi$ stacking interaction,	hydrogel fragments were formed in the mold within 10 min and the properties of the bulk hydrogel were fully restored after 6 h	hydrogel was photo-cross-linked within 60 s; cell viability: 90%	261
AHA/CMC/GEL/PEG-SG	Schiff base bonds	obvious fusion occurred at the contact interface of the hydrogel block after 10 min	gelation time was less than 1 h; elastic modulus: ∼100 Pa	262
PVA/AAc/PEGDA/TPO	hydrogen bonds	average tensile strength recovered 72% after 12 h of healing	elastic shear modulus <0.1 MPa	263
CHI/HA	electrostatic interactions	rupture strain of the healing hydrogel changed from 92% to 74%	uniformity coefficient of 3D bioprinting was close to 1 at a moderate speed of 300 mm/min or 600 mm/min	264
β-CD-AOI_2/A-TEG-Ad/GelMA	host−guest interactions	80%	compression modulus: 0.63 MPa; gelation time: 10 s at 25 °C; reached a stable modulus in 30 s; elastic modulus up to 40.68 kPa	265
CNTs/Ca^{2+}/PAA/SA	chelation	86.6 (storage modulus)	conductivity: 22.5 S/cm; relative viability of the cells: 97.8% (at 72 h); degradation rate in water: 22% (7 days); maximum sensitivity: 3.33 kPa^{-1}; gauge factor: 6.29	266

For hydrogel systems, temperature is considered a well-controlled stimulation for drug release in cancer therapy. A temperature-responsive nanocomposite hydrogel with self-healing ability was prepared from the modified poly(ethylene glycol) and carboxymethyl chitosan using graphene oxide as a photothermal agent and nano-hydroxyapatite as a tumor suppressor (Figure 18D).[248] It only took 10 min for the hydrogel fragments to stick together. After illumination with a NIR laser (808 nm) for 10 min, the hydrogel's temperature rose with the concentration of graphene oxide. The photothermal conversion process of the hydrogel was reversible and had certain stability. The inhibition of 4T1 cell activity by the hydrogel could be achieved by controlling the temperature of the hydrogel. The temperature of hydrogel was controlled by adjusting the NIR irradiation time. The therapeutic effects of the hydrogels were long-lasting and did not harm the surrounding healthy biological tissue. By using photothermal therapy, the hydrogel could effectively stop tumor cells from proliferating.

In another study, thermoresponsive self-healing hydrogels were prepared by forming dynamic covalent enamine bonds between amino groups in PEI and acetoacetate groups in four-arm star poly(2-(dimethylamino)ethyl methacrylate-*co*-2-hydroxyethyl methacrylate) and using PDA as the photothermal agent, which were used for photothermal therapy of tumors (Figure 19A).[257] The hydrogel realized the hydrophilic–hydrophobic transition and contraction via adjusting the temperature to achieve controlled drug release. The hydrogel had prominent self-healing ability (the gel strength recovered to 90% after three cycles). The hydrogel's shear thinning qualities made it possible to inject it into the designated area. The photothermal properties were proven by observing the microscopic morphological changes and volume shrinkage of hydrogels. The temperature change of the hydrogel was diffused in all directions with the irradiation point as the center, and the hydrogel showed high photothermal conversion efficiency. The nanocomposite hydrogel had biocompatibility (cell activity remained above 90% after 24 or 48 h). The hydrogel can be used for photothermal therapy of tumors. The experiment of intratumor injection in mice demonstrated that drug was equally dispersed within the tumor and had a long retention time in the tumor site.

Under physiological conditions, self-healing magnetothermal hydrogels, as drug carriers, had excellent drug encapsulation rates and minor damage to human healthy tissues. A magnetothermal self-healing hydrogel was formed from benzaldehyde functionalized pullulan (PULL-CHO) and poly(ethylene glycol) (PEG)-modified chitosan (CS-*g*-PEG) for cancer therapy (Figure 19B).[250] The cross-linking of the amino group of CS-*g*-PEG and aldehyde group of PULL-CHO resulted in the strong self-healing ability. Mesoporous silica nanospheres containing $Mn_{0.6}Zn_{0.4}Fe_2O_4$ nanoparticle cores (MMSN-RBITC) were prepared and labeled with rhodamine B isothiocyanate (RBITC) and could be loaded into the hydrogel system. The resulting hydrogel could be used for magnetothermal chemotherapy of cancer. After uptake of MMSN-RBITC, cell apoptosis was further induced by chemical kinetics based on the catalytic production of hydroxyl radical. In vitro experiments proved that the nanocomposite hydrogel had good anticancer properties against 4T1 tumor cells. The synthesized hydrogel had clear mesoporous morphology and responded to the tumor microenvironment. The nanocomposite hydrogel was a promising drug delivery system with good magnetothermal effect and controlled drug release behavior. The work provides a feasible scheme for accurate diagnosis and treatment of cancer.

4. 3D PRINTING OF SELF-HEALING HYDROGELS

The 3D printing technique can construct objects layer by layer, which allows for rapid prototyping to form various complex structures. Different from traditional printing technology, the 3D printing technique is rich in printing materials such as metal, ceramic, plastic, and so on. Hydrogels are widely utilized for the 3D printing process because of their unique properties including flexibility, stretchability, deformability, and biocompatibility, as well as easy designability. By 3D printing, hydrogels can be made into specific shapes, which can be applied in biomimetic tissues and electronic devices. In practice, 3D printing technology requires hydrogels to have better shear stress and rheological properties and enough time to complete structural integrity. All these factors are related to the gelation mechanism of hydrogels. Self-healing hydrogels with reversible cross-linking possess shear thinning properties. Artificial biomimetic devices in long-term contact with human tissue would need to repair themselves because biological tissues have inherent self-healing ability. Self-healing hydrogels have shown considerable promise in 3D printing. The self-healing ability enables hydrogels to self-repair after being damaged, which undoubtedly makes hydrogels show great advantages in 3D printed materials. The self-healing performance not only increases the toughness and recoverability of hydrogels but also gives hydrogels good rheological properties and stable cross-linking when being printed and extruded. Hydrogels with self-healing performance exhibit unique advantages in 3D printing: self-healing ability allows the desired target to form a homogeneous monolithic 3D structure, thus circumventing the limitation of premature gelation of hybrid materials. The following section mainly introduces the use of self-healing hydrogels in the realm of 3D printing. Self-healing hydrogels can be utilized in biomedical and flexible electronic fields with the help of 3D printing technique as shown in Table 8.

3D-printed self-healing hydrogels have great possibilities in advanced biomedical fields. A 3D-printed and self-healing hyaluronic acid/chitosan hydrogel was designed for controlled drug release.[264] Hyaluronic acid has the characteristics of biodegradability, nontoxicity, and biocompatibility, and chitosan is a natural polysaccharide with antibacterial activity and adhesion. The degradation rate of the hydrogel was about 80% at 37 °C in pH 5.0. The reversible electrostatic interaction between chitosan and hyaluronic acid endowed the hydrogel with the self-healing property. The cured hydrogel's fracture strain dropped from 92% to 74%. The Young's modulus of the hydrogel after healing was higher than the initial value. An in vitro cytotoxicity assay showed that the cell viability in the presence of the hydrogel was 84.2%. The hydrogel could also be utilized to administer anti-inflammatory drugs (diclofenac) and antibiotics (rifampicin). In addition, the hydrogel could be used for 3D printing because of its shear-thinning performance. At medium speeds (300 mm/min or 600 mm/min), the uniformity coefficient of the bioink solution was approximately 1, exhibiting the accuracy accomplished by 3D bioprinting.

An infiltration-induced suspension bioprinting (IISBP) technique was reported for a 3D-printed self-healing hydrogel scaffold.[269] The hyaluronic acid suspension system was mainly prepared from sodium hyaluronate dissolved in PBS buffer. The hyaluronic acid support liquid had a shielding effect on cytotoxic ultraviolet rays and could be restored after repeated cuts. The

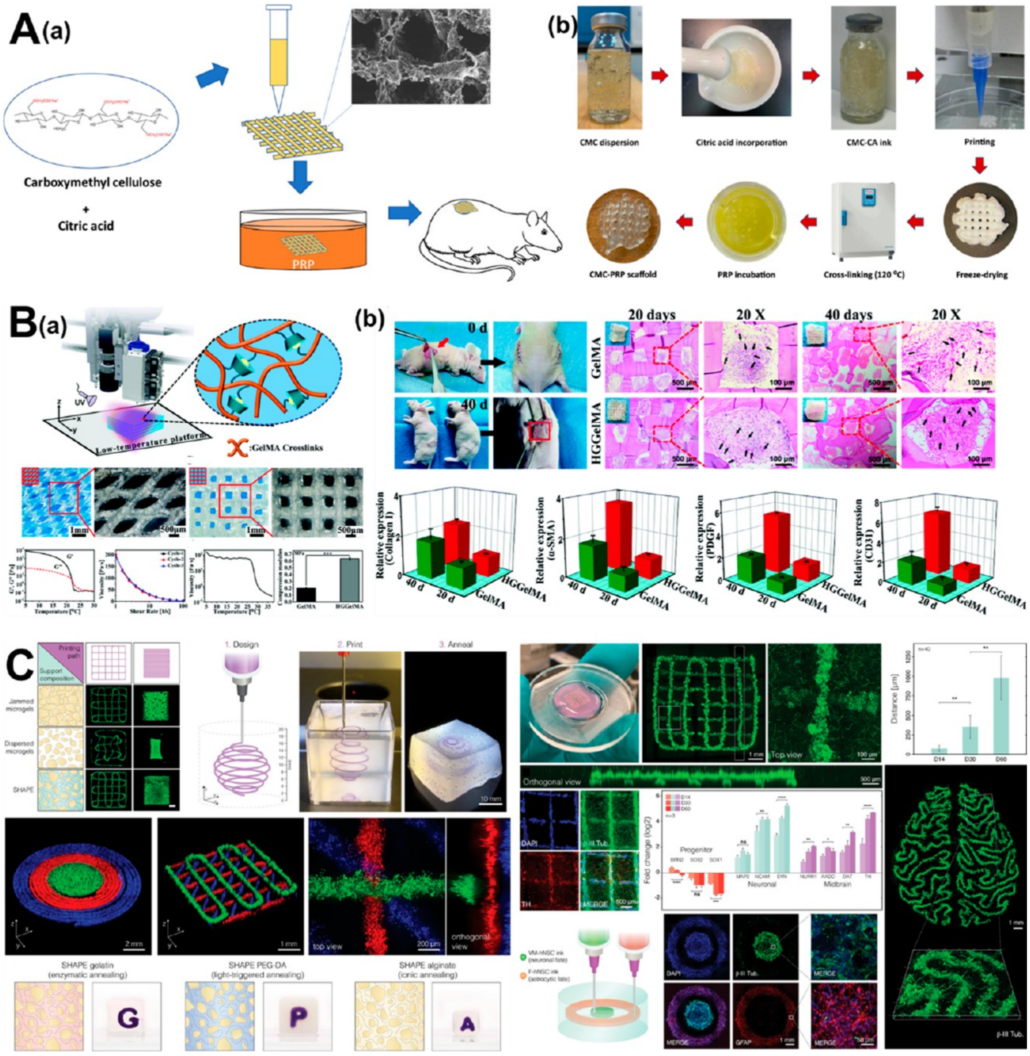


Figure 20. (A) 3D printing scaffold obtained from carboxymethylcellulose. Reproduced with permission from ref 267. Copyright 2022 Elsevier. (B) A novel 3D printing self-healing hydrogel composed of three-armed host−host supramolecular compounds copolymerized with gelatin methacryloyl. Reproduced with permission from ref 265. Copyright 2019 Royal Society of Chemistry. (C) A self-healing annealable particle−extracellular matrix composite prepared from alginate particles and extracellular matrix by thermal cross-linking. Reproduced under terms of a Creative Commons CC-BY License from ref 268. Copyright 2022 John Wiley and Sons.

bioink was prepared by grafting the methylacrylyl group onto the gelatin molecular chain. The adjustment range of IISBP printing ink on the structural resolution of 3D printing scaffold was 37.5% to 169.2%. The mechanical properties of the printing support may be adjusted by osmotic reaction of the hyaluronic acid support groove. By designing the spatial distribution of the concentration of hyaluronic acid suspension, nonuniform 3D printing scaffolds with gradient or multilayer structures were obtained. At the end of printing, the cell viability was above 95%. Over time, the cell survival rate was maintained at about 90%. The technology could meet the requirements of 3D cell culture. The cell adhesion in the printed scaffolds reached the maximum during cell culture on the third day. This technique used the existing bioinks to print a variety of cell-loaded scaffolds that could be applied to promote angiogenesis in vitro.

In another example, a 3D-printed self-healing hydrogel scaffold was fabricated using carboxymethyl cellulose (CMC) for diabetic wound repair (Figure 20A).[267] The elastic modulus of the hydrogel decreased after applying 100% strain to the hydrogel. When the strain was restored to 0.5%, the elastic modulus also returned to the initial value. This indicated that the CMC hydrogel had sufficient self-healing property. The hydrogel could be used as a scaffold for wound healing after 3D printing. CMC scaffolds loaded with platelet-rich plasma (PRP) could release growth factors to promote angiogenesis and cell migration. Therefore, CMC-PRP stents could be used to treat diabetic wounds. The protein release from the CMC-PRP scaffold was $232 \pm 41\ \mu g\ mg^{-1}$ (72 h). On day 7, the protein was completely released due to complete dissolution of the scaffold. The release of vascular endothelial growth factor (VEGF) reached the maximum value at 24 min (18.6 ± 4.8 pg mg^{-1}). Transforming growth factor-β_1 (TGF-β_1) release was 821.1 ± 405.2 pg mg^{-1}. Studies had shown that CMC can also induce cell migration. After treating scratched cells with CMC and CMC-PRP, and the scratches healed almost completely by 24 h.

A 3D-printable self-healing supramolecular hydrogel (HGGelMA) was fabricated by copolymerization of a novel three-armed host−guest supramolecular compound (HGSM) and gelatin methyl propylene, showing good cell compatibility and histocompatibility (Figure 20B).[265] Covalent cross-linking could sustain the overall shape of the hydrogel, while the reversible host−guest interaction between β-cyclodextrin and

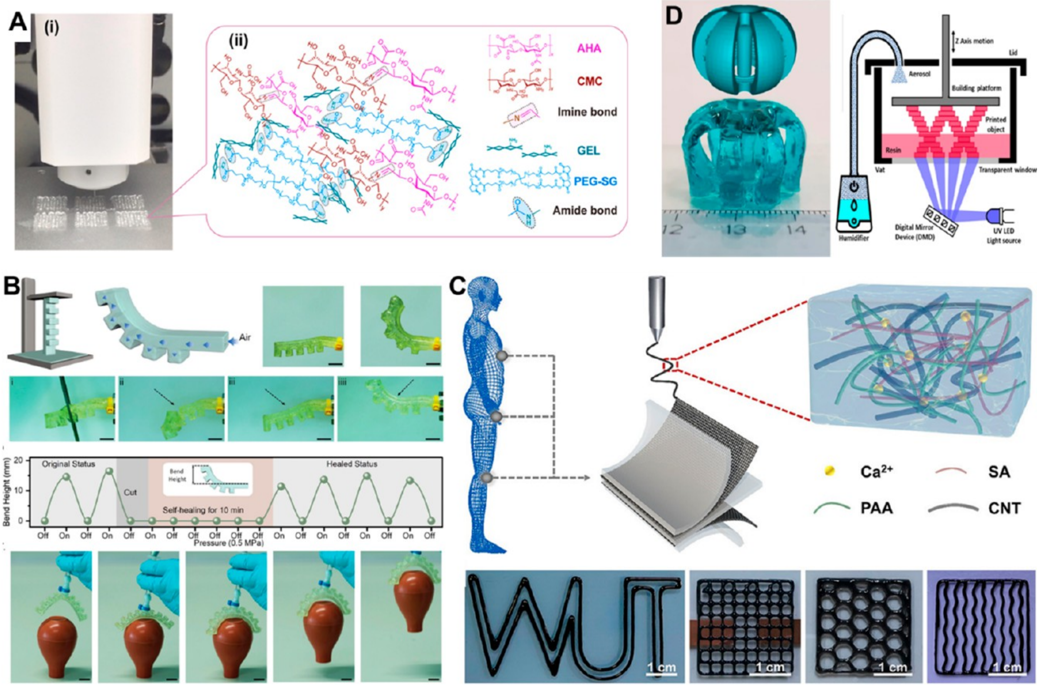


Figure 21. (A) Printable microstructures of AHA/CMC hydrogels and TSHSP hydrogels and cell proliferation patterns in hydrogel samples. Reproduced under terms of a Creative Commons CC-BY-NC-ND 4.0 License from ref 262. Copyright 2021 The Authors. (B) The 3D printing hydrogel with good self-healing performance, injectable ability and pH response. Reproduced with permission under a Creative Commons CC-BY-NC License from ref 258. Copyright 2021 John Wiley and Sons. (C) Self-healing and 3D printable hydrogels obtained by combining carbon nanotubes with calcium ion chelates of poly(acrylic acid) and sodium alginate. Reproduced with permission from ref 266. Copyright 2021 American Chemical Society. (D) 3D printable self-healing hydrogel prepared from poly(vinyl alcohol) and acrylic acid. Reproduced with permission under a Creative Commons CC-BY 4.0 License from ref 263. Copyright 2021 Springer Nature.

adamantane could enhance the mechanical properties and give the hydrogel good self-healing performance. The HGGelMA hydrogel had the same compression modulus as natural soft tissue: 0.3−0.5 MPa. HGSM also could be applied to reinforce the mechanical strength of other natural polymer hydrogels (including hyaluronic acid and its derivatives). The HGGelMA hydrogel also had the ability to rapidly heal because the host−guest interaction was reversible. The self-healing rate of HGGelMA hydrogel improved to 80% as HGSM concentration increased. Besides, HGGelMA hydrogel had good 3D-printability. The 3D-printable HGGelMA hydrogel scaffold showed a refined and uniform porous structure, had good biocompatibility, cell compatibility and cell proliferation ability, and provided a good microenvironment for cell encapsulation, adhesion, and proliferation.

3D bioprinted self-healing hydrogels also allow cells to be programmed to assemble into complex 3D geometric shapes that can be used to study human diseases and screen the toxicity and effectiveness of drugs. A self-healing annealable particle-extracellular matrix (SHAPE) composite was proposed by thermally cross-linking alginate microgels with the extracellular matrix for accurate patterning of neuronal constructs (Figure 20C).[268] The SHAPE support material was filled with a viscous polymer solution composed of collagen, laminin, hyaluronic acid, and fibrin. The yield stress of the support material was about 10 Pa (4 °C), which met the requirements for ink-embedded printing. Human neural stem cells could be embedded in the SHAPE support materials by 3D printing. The material could program human stem cell patterns and generate subtype-specific neurons (for at least 2 months). The proposed printing method might design 3D printing structures arbitrarily by adjusting the pattern design and ink concentration. This method could create organ models to simulate 3D oxygen gradients.

A time-share structurally supported (TSHSP) self-healing hydrogel bioink was designed for development of tissue-like constructs by fast dynamic cross-linking of aldehyde-modified hyaluronic acid (AHA)/*N*-carboxymethyl chitosan (CMCS) and slow stable cross-linking of gelatin (Gel)/four-arm poly(ethylene glycol) succinylglutarate (PEG-SG) (Figure 21A).[262] The hydrogel was printed in a short time. The fast cross-linking of AHA/CMC ensured immediate printability after preparation. The slow-phase cross-linking of Gel/PEG-SG achieved structural stability at the time of printing. The robust Gel/PEG-SG network played a predominant role in the yield strain of TSHSP hydrogels, which conferred hydrogels with outstanding self-healing properties. Furthermore, the TSHSP hydrogel with high permeability provided a reliable basis for material exchange (nutrients and oxygen), ensuring considerable cellular activity, proliferation, and cell-to-cell interconnection of hydrogels. Hyaluronic acid and proteins played a crucial part in tissue reconstruction and repair. The amino reaction of PEG functionalized with succinimide active esters and proteins made the hydrogels more likely to bind to recipient tissues. Chitosan has natural antimicrobial properties because cations interfer with bacterial metabolism. The gelation system was proven to be effective in many aspects of biomanufacturing.

Moreover, 3D bioprinted self-healing hydrogels have the ability to simulate human tissues or organs by integrating specific biomaterials for various clinical simulation studies. Self-healing hydrogel support materials, made from hyaluronic acid and adamantane (Ad) or *β*-cyclodextrin (CD), could be used to print high cell-density tissue models.[270] The hydrogel support material could be reassembled after vacuum release because of the self-healing property based on host−guest interaction. The supporting hydrogel accurately located up to 10% of the sphere diameter. The printing time of each ball was about 40 s and the total distance was 12 mm. The cell viability in the printed spheres was as high as 90%−95% (24 h). Eight 3D bioprinted spheres could fuse into a ring of microscopic tissue after 4 days. The 3D bioprinting self-healing hydrogels could also be used to design models of local cardiac fibrosis. Experimental results proved that the models were endowed with some key parameters of cell cycle in healthy heart and injured heart, which could replicate the pathological scar features of myocardial infarction for therapeutic study.

3D printed self-healing hydrogels are also applied for the fabrication of soft robotics and flexible electronics. A 3D printed hydrogel with superior self-healing, injectability, and pH-responsive behavior was prepared from poly(hydroxyethyl methacrylate-*co*-acrylic acid), which could be used in wearable electronics, flexible actuators, and robots (Figure 21B).[258] The self-healing hydrogel had high tensile properties (tensile strength: 0.22−41.3 kPa; fracture strain: 12%−4336%), excellent self-healing ability (1 min), and long-term stability performance (one month). Hydrogen bonding allowed the hydrogel to self-heal quickly. The hydrogel system could be made into self-healing pneumatic actuators using 3D printing technology. The flexible actuators were able to repeatedly support steel scissors equivalent to 5.4 times their own weight. The 3D printing actuators were cut into two pieces, which could recover the ability to bend by applying pressure after healing for 10 min.

A bioinspired 3D-printed self-healing hydrogel with multi-conductivity was designed for wearable strain sensors (Figure 21C).[266] The 3D-printed self-healing hydrogel was designed by combining carbon nanotubes with calcium ion chelates of poly(acrylic acid) and sodium alginate. The hydrogel was printable owing to its appropriate viscosity and shear-thinning property. This hydrogel was self-supporting and did not require additional curing agents or ultraviolet light during the printing process. Furthermore, the hydrogel had excellent plasticity and tensile properties, and was easily stretched into long strips. The hydrogel's self-healing rate was approximately 86.6%. The hydrogel was printed on stretchable insulating tape and hooked up to the electrode to prepare a skin-like and highly sensitive strain sensors. The strain gauge coefficient is 6.29 (resistance mode) and 1.25 kPa^{-1}(capacitance mode). The skin-like strain sensor could make a stable response to external stimuli (respiration, knee flexion, and finger flexion) and was able to recognize a variety of stimulus signals. This hydrogel for 3D printing that is bioinspired, self-healing, and electronically conductive has a promising future in the development of skin-like strain sensors.

A 3D-printed self-healing hydrogel was fabricated by extrusion-based additive manufacturing (digital light processing) for potential applications in implantable sensors and soft robotics (Figure 21D).[263] This method solved the inherent incompatibility between reduction-type photopolymerization and self-healing ability. The water-based light-curing formula was adopted to generate a physical and chemical semi-interpenetrating network. In the hydrogel, PVA chains were uniformly distributed in a cross-linked acrylic matrix. This semi-interpenetrating network allowed the hydrogel to repair damage by reversible physical cross-linking. Besides, hydrogen bonds in the system also increased the self-healing ability. The self-healing process occurred quickly without any external triggers at room temperature. The high-resolution digital light processing printing method was achieved at the weight ratio of PVA/acrylic acid of 0.8. The sample was able to withstand bending deformation immediately after contact of two cut halves without applying tensile stress and recovered 72% of the premier tensile strength after healing for 12 h. The hydrogel could be applied to prepare 3D-printed structures (body-centered cubic lattice and axisymmetric structures). The complex 3D printable hydrogel could be prepared by low-cost commercial printers and commercial materials to precisely control the printing compositions. The prepared hydrogels have applications ranging from biomedicine to flexible electronics.

Additionally, the light-cured 3D printing technology was reported to manufacture a self-healing hydrogel-based flexible sensor.[260] Polyacrylate-*n*-vinyl-2-pyrrolidone and carboxymethyl cellulose were used as the double network, and the liquid−solid separation of hydrogels was realized by means of coordination bonding as well as hydrogen bonding. The viscosity of the hydrogel ink was less than 1.3 Pa s, which conformed to the requirements of light-curing 3D printing technology. The hydrogel showed the high toughness of 3.38 MJ m^{-3} and excellent self-healing performance. The strain response range of the assembled flexible sensor was close to 1000%, and the resistance response sensitivity was 1.16. A hydrogel manipulator was also designed and assembled, and showed excellent sensing performance. As a result, the 3D-printed and designable self-healing hydrogels provide a novel idea to prepare wearable flexible sensors.

5. CONCLUSIONS AND PERSPECTIVES

Hydrogels with self-healing properties have shown superior promise in many applications due to the good reliability, durability, and long-term stability. One of the clearest representative features of this class of hydrogels is the dynamic reversible behaviors, in which they have the ability to recover their structural and functional integrity. Our review overviews the recent progress on self-healing hydrogels in terms of their synthesis strategies and multiple applications. Generally, these hydrogels are designed from reversible chemical or physical cross-linking interactions or a combination of both. By carefully designing the cross-linking types and polymer network compositions, self-healing hydrogels possessing specific functions and properties are capable of being readily fabricated. Self-healing hydrogels also can be endowed with various fascinating properties (including good mechanical performances, biocompatibility, stretchability, conductivity, adhesion, antibacterial ability, responsiveness, etc.), which promotes their use in a variety of sectors, including flexible strain sensors, supercapacitors, actuators, adhesives, wound healing, drug delivery, cancer therapy, etc. Although encouraging progress has been made in the synthesis strategies and functional optimization for self-healing hydrogels, the research is still far away from practical applications. For self-healing hydrogels, challenges and opportunities coexist in the process of rapid development.

5.1. Synthesis Strategies. At present, there is much research on the cross-linking mechanisms of self-healing hydrogels. Physical cross-linking and reversible chemical cross-linking are extensively used in synthesizing various self-healing hydrogels. Additionally, a combination of physical and reversible chemical cross-linking is also preferred for the design of self-healing hydrogels. For self-healing hydrogels, all or part of their mechanical and rheological properties can be restored after damage. However, self-healing properties are usually opposed to other mechanical properties (elasticity, strength, flexibility, etc.). When designing hydrogels, researchers should optimize the self-healing properties without reducing elasticity and flexibility. Second, dominant cross-linking modes and sacrificial bonds in various self-healing mechanisms should be studied. It is well-known that hydrogel systems have a variety of physical and chemical cross-links. Obviously, the self-healing cross-linking mechanism of hydrogels is usually not single one. However, there is no accurate study on the dominant role of self-healing mechanisms in current studies, either from the micro- or macroscale perspective. It is also necessary to consider the effects of coordination and antagonism of different self-healing mechanisms. These are significant obstacles in the design of self-healing hydrogels. Meanwhile, more scientific quantitative calculation and evaluation of self-healing performance are needed. Without a reasonable model to evaluate and simulate the self-healing performance, reasonable optimization and improvement cannot be carried out in specialized purposes. According to published literature, a hydrogel's self-healing property is mostly evaluated by visual observation of hydrogels and by detecting the recovery percentage of mechanical properties or the recovery of electrical conductivity of cut self-healing hydrogels. There does not appear to be a standard calculation method for the self-healing properties. Therefore, it is very necessary to study a scientific and rational quantitative calculation and evaluation of self-healing properties. Moreover, some self-healing systems require certain external conditions (such as optical, electrical, magnetic, pH, temperature, etc.) to trigger healing, which limits the application of self-healing hydrogels.

> The combination of multiple dynamic cross-linking interactions is a significant direction for the synthesis of self-healing hydrogels with mechanical toughness, which will tremendously extend their application range.

5.2. Self-Healing Hydrogels for Flexible Electronics. Conductive hydrogels with high self-healing performance are particularly suitable for the advancement of soft electronics. By the introduction of conductive fillers (such as PPy, PEDOT, PANI, graphene, CNTs, MXene, etc.) or free ions (such as KCl, NaCl, LiCl, ionic liquids, etc.), self-healing hydrogels can be endowed with good electrical or ionic conductivity. When conductivity is introduced into self-healing hydrogels, hydrogel-based flexible strain sensors can transform subtle external variations (forces and deformation) into detectable electrical signals (such as resistance, current, capacitance, etc.). Self-healing conductive hydrogels have extensive promise in wearable equipment and implantable biological tissues, as well as artificial electronic skins. The self-healing property allows for the repair of microcracks, fractures, and other analogous structural damage, which will improve the reusability, durability, and reliability. Besides, self-healing hydrogel electrolytes have attracted interest in the realm of flexible supercapacitors. Self-healing flexible supercapacitors show good ability to work under extreme distortion and recover their original performance after damage, which expands their application range. The self-healing performance gives the flexible supercapacitors better cycling stability. To satisfy the practical application requirements for flexible electronics, self-healing conductive hydrogels are generally combined with multifunctionalities, including anti-freezing, antidrying, self-adhesive, and flexible features. Nevertheless, it is difficult to optimize the multifunctionalities.

5.3. Self-Healing Hydrogels for Biomedical Applications. Self-healing hydrogels also have been highlighted in biomedical applications, for instance adhesives, wound healing, drug delivery, tumor treatment, etc. Self-healing hydrogels may be able to imitate the chemical, electrical, and biological processes of living tissues. Hydrogel adhesives with self-healing ability can be attached to tissues to effectively seal bleeding wounds without causing new damage and prevent leakage of fluids or gas. Self-healing hydrogel dressings have demonstrated unique advantages, such as adapting to irregular wound shapes and being less prone to peeling and fracture under forces. In addition, self-healing injectable hydrogels allow for precise, continuous, and controllable drug delivery, thus greatly improving the durability and efficacy and inhibiting tumor growth. Although self-healing hydrogels are promising biomaterials, more in vitro and in vivo tests should be performed for clinical applications. For example, the self-healing behaviors in living organisms need to be demonstrated. It is necessary to carefully understand the long-term stability, biocompatibility, and degradability of these hydrogels in the living body. It is also significant to systematically investigate possible interactions between self-healing hydrogels and organisms. Additional clinical trials are needed to increase the regulatory properties of self-healing hydrogels for higher safety in humans.

5.4. 3D Printing Technique for Self-Healing Hydrogels. The 3D printing technique can be applied for self-healing hydrogels, to make them into specific shapes for biomimetic tissues and electronic devices. Self-healing hydrogels with reversible cross-linking have shear thinning properties that are required for 3D printing. Self-healing hydrogels show a unique advantage for 3D printing: self-healing ability allows the desired target to form a homogeneous monolithic 3D structure, thus circumventing the limitations of premature gelation. With the help of 3D printing, self-healing hydrogels can form various complex and detailed structures to satisfy the miniaturization and personalization demands.

5.5. Challenges and Future Perspectives. In summary, self-healing hydrogels have shown a bright future in many fields. The actual application requirements will drive further study and evolution for a variety of high-performance self-healing hydrogels. Future self-healing hydrogel research should take into account the following.

(1) Mechanically robust hydrogels with self-healing performance. For self-healing hydrogels, self-healing qualities are usually opposed to other mechanical properties. In general, with the enhancement of the mechanical performance of hydrogels, their self-healing capacity would weaken and their healing time would be delayed. So, it is difficult to develop mechanically robust hydrogels with rapid self-healing capability. The possible strategies are to introduce multiple dynamic cross-linking into double network or nanocomposite hydrogel systems to increase self-healing ability without compromising the mechanical performance.

(2) Multifunctional hydrogels with self-healing performance. Conductive hydrogels have shown huge promise in

flexible electronics. Self-healing ability can enhance the reliability, durability, and long-term stability of hydrogel-based flexible electronics. In addition to self-healing ability, other features including antifreezing, antidrying, self-adhesive, and antiswelling properties are also vital for hydrogel-based flexible electronics. However, it is hard to combine self-healing ability with other performance features. For example, to realize underwater sensing performance, conductive hydrogels need to be endowed with antiswelling ability against water-absorbing expansion by increasing the cross-link density. Nevertheless, high cross-link density is disadvantageous for self-healing ability. Besides, hydrogel-based flexible electronics should adapt to extreme conditions (high temperature or extreme cold) in practical applications. Ethylene glycol is introduced into hydrogel electrolytes to simultaneously adjust the freeze resistance and self-healing performance via inhibiting the water molecules from freezing and dynamically regulating the molecular interaction between polymer chains and water, and the hydrogel could work properly and have self-healing ability at −20 °C.[268] Nevertheless, the incorporation of organic solvents usually reduces the conductivity of self-healing hydrogels. More work should be done to balance the conductivity and self-healing capability in hydrogel-based flexible electronics.

(3) Injectable or implantable hydrogels with self-healing ability. Self-healing, injectable or implantable hydrogels are appropriate for bioelectronics and biomedicine. Many of the self-healing systems currently studied require certain external stimuli (light, electricity, magnetism, pH, temperature, etc.). However, in living organisms, pH is the most common triggering mechanism. Light, electricity, magnetism, and temperature can cause damage to the organisms. This limits the application of self-healing hydrogels in injectable or implantable uses. In addition, to fulfill the demands of injectable and implantable applications, more in vitro and in vivo tests need be required. The long-term stability, biodegradability, and cytotoxicity of self-healing hydrogels in living organisms need be carefully evaluated. Biocompatible and biodegradable biopolymers (such as chitosan, protein, collagen, etc.) are appealing materials for the manufacture of self-healing hydrogels. 3D printing technology also provides a possibility for self-healing hydrogels to generate tiny, shape-specific devices for injectable and implantable applications. Self-healing hydrogels are anticipated to have enormous promise as injectable or implantable materials in the near future.

In further advances, challenges and tasks are inescapable, while enormous opportunities and impressive innovations will keep emerging. It is believed that this review will give a comprehensive understanding of the creation of self-healing hydrogels and boost this flourishing field forward.

AUTHOR INFORMATION

Corresponding Authors

Fangfei Liu − *State Key Laboratory of Chemistry and Utilization of Carbon Based Energy Resources, College of Chemistry, Xinjiang University, Urumqi 830017 Xinjiang, PR China*; Email: liufangfei1214@163.com

Tursun Abdiryim − *State Key Laboratory of Chemistry and Utilization of Carbon Based Energy Resources, College of Chemistry, Xinjiang University, Urumqi 830017 Xinjiang, PR China*; orcid.org/0000-0003-3828-7986; Email: tursunabdir@sina.com.cn

Xiong Liu − *State Key Laboratory of Chemistry and Utilization of Carbon Based Energy Resources, College of Chemistry, Xinjiang University, Urumqi 830017 Xinjiang, PR China*; orcid.org/0000-0002-7113-2313; Email: liuxiong.1991@qq.com

Author

Hongyan Yin − *State Key Laboratory of Chemistry and Utilization of Carbon Based Energy Resources, College of Chemistry, Xinjiang University, Urumqi 830017 Xinjiang, PR China*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acsmaterialslett.3c00320

Author Contributions

$^{\nabla}$Hongyan Yin and Fangfei Liu contributed equally to this work. CRediT: **Hongyan Yin** conceptualization, Writing − original draft; **Fangfei Liu**: Conceptualization, Writing − review & editing, Supervision; **Tursun Abdiryim** Conceptualization, Writing − review & editing, Supervision; **Xiong Liu**: Conceptualization, Methodology, Formal analysis, Validation, Investigation, Writing − original draft, Writing − review & editing, Supervision.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was financially supported by the Xinjiang Tianchi Doctoral Project (No. TCBS202120), Xinjiang Tianchi Yingcai Project (No. 51052300523), and National Natural Science Foundation of China (No. 52163020). The helpful discussion with Dr. Jinwei Zhang (College of Biomass Science and Engineering, Sichuan University) is gratefully acknowledged.

ABBREVIATIONS

AAc	acrylic acid
AAZn	zinc acrylate
ACHI	aldehyde−chitosan
AD	adamantyl
ADH	adipic acid dihydrazide
Alg-βCD	β-cyclodextrin-grafted alginate
PAAm-Ad	adamantane-grafted polyacrylamide
A-TEG-Ad	acryloylated tetra(ethylene glycol)-modified adamantane
BCW	bacterial cellulose nanowhisker
Bn	4-formylphenylboronic acid
CEC-ADH	carboxyethyl cellulose-grafted adipic dihydrazide
CECT-ADH	adipic dihydrazide-grafted carboxyethyl chitin
Chi-Ph	phenol-functionalized chitosan
CMC	carboxymethyl cellulose
CNC	cellulose nanocrystal
CNT	carbon nanotube
CS	chondroitin sulfate
CS-*g*-PNIPAAm	thermoresponsive derivative from chitosan

DA	dopamine
DCMC	dialdehyde carboxymethyl cellulose
DF-PF	difunctional Pluronic-F127 cross-linker
DF-PEG	dibenzaldehyde-terminated telechelic poly(ethylene glycol)
DTDPH	dithiodipropionic acid dihydrazide
EG	ethylene glycol
Fc	ferrocene
FBEMA	4-formylbenzoate ethyl methacrylate
GelMA	gelatin methacrylate
Gly	glycerol
GO	graphene oxide
HA-CHO	aldehyde-modified hyaluronic acid
HAPAM	hydrophobically associating polyacrylamide
HNT@PDA	halloysite nanotube@polydopamine
HPCS	hydroxypropyl chitosan
LA-Ag NP	lignin amine−silver nanoparticle
LM	liquid metal
MFP	magnetic Fe_3O_4 and polyacrylamide
MPC	2-methacryloyloxyethyl phosphorylcholine
N,O-CMCS	*N*,*O*-carboxymethyl chitosan
$nTiO_2$	nano-titanium dioxide
OA	oxidized alginate
OSG	oxidized succinoglycan
PAA	poly(acrylic acid)
PAAm-Ad	adamantane-grafted polyacrylamide
PAMPS	poly(2-acrylamido-2-methyl-1-propanesulfonic acid)
PBA	phenylboronic acid
PDDA	poly(diallyldimethylammonium chloride
PEG-CHO	aldehyde terminated poly(ethylene glycol)
PEG-DA	dibenzaldehyde-terminated poly(ethylene glycol)
PEI	polyethylenimine
P(HEMA-*co*-AAc)	poly(hydroxyethyl methacrylate-*co*-acrylic acid)
P(NIPAM-*stat*-AH)	poly(*N*-isopropylacrylamide-*stat*-acylhydrazide)
PU	polyurethane
PVA	poly(vinyl alcohol)
QCS	quaternary ammonium chitosan
SA	sodium alginate
SDBS	sodium dodecylbenzenesulfonate
SiO_2-g-PAAm	SiO_2-*g*-polyacrylamide
TAA	tris(2-aminoethyl) amine
TPO	diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide
TPE	tetraphenylethylene
Tpy	2,2′:6′,2″-terpyridine
α-CDP	*α*-cyclodextrin polymer
β-CD-AOI_2	isocyanatoethyl acrylate-modified *β*-cyclodextrin
AAlg	aldehyde−alginate
ACS	acrylic acid−chitosan
Ad	1-amantadine hydrochloride
AD-CHO	ethyl-1-adamantane 4-formylbenzoate
AHA	aldehyde hyaluronic acid
AMPSZn	2-acrylamido-2-methylpropanesulfonate zinc
APS	ammonium persulfate
Azo-PAM	Azobenzeno-polyacrylamide
BMI	bismaleimide
CA	citric acid
CEC-CD	carboxyethyl cellulose-grafted chitosan
CHI	chitosan
Cho-AA PIL	choline−amino acid polyionic liquid
CMCS	carboxymethyl chitosan
CNF-Gly	cellulose nanofibril−glycerol
CPBA	4-carboxyphenylboronic acid
CS-*g*-PEG	poly(ethylene glycol) (PEG)-modified chitosan
Cys	cystamine dihydrochloride
DATNFC	(2,2,6,6-tetra-methylpiperidine-1-oxyl)-oxidized nanofibrillated cellulose
DMAEA	*N*,*N*-dimethylamino ethyl acrylate
DF-PEG	dibenzaldehyde functionalized poly(ethylene glycol)
DPPH	2,2-diphenyl-1-picrylhydrazyl
D-2000	poly(propylene glycol) bis(2-aminopropyl ether)
$EMIMBF_4$	1-ethyl-3-methylimidazolium tetrafluoroborate
F127	Pluronic F127
GC	glycol chitosan
Gel	gelatin
GG	guar gum
GO-BPEI	branched polyethylenimine grafted with graphene oxide
HAP	hydroxyapatite
HA-TPH	3,3′-dithiobis(propanoic dihydrazide) modified hyaluronic acid
HPC	hydroxypropyl cellulose
HSAH	(*R*)-12-hydroxystearic acid hydrazide
LS	Iignosulfonate
MAGG	multialdehyde guar gum
MNP	$Mn_{0.6}Zn_{0.4}Fe_2O_4$
N-CMC	*N*-carboxymethyl chitosan
nSi	silicate-based nanoparticles
NVP	poly(acrylic acid) (AA)−*N*-vinyl-2-pyrrolidone
OHA-dop	oxidized hyaluronic acid
PA	phytic acid
PAAm	polyacrylamide
PANI	polyaniline
P(ATU-*co*-AM)	poly(1-allyl-2-thiourea-*co*-acrylamide)
PDA NP	polydopamine nanoparticle
pectin-CHO	pectin aldehyde
PEGDA	poly(ethylene glycol) diacrylate
PEG-SG	4-arm poly(ethylene glycol) succinimidyl glutarate
PHEAA	poly(*N*-hydroxyethylacrylamide)
PNIPAM	poly(*N*-isopropylacrylamide)
PPy	polypyrrole
PULL-CHO	benzaldehyde-functionalized pullulan
PVP	polyvinylpyrrolidone
rGO	reduced graphene oxide
SDS	sodium dodecyl sulfate

SF	silk fibroin
TA	tannic acid
TNP	topological nanoparticle
TPU	polyurethane
TPE-P(DMA-*stat*-DAA)	TPE−poly(*N*,*N*-dimethylacrylamide-*stat*-diacetone acrylamide)
UPy	2-ureido-4-[1*H*]-pyrimidone
β-CD	*β*-cyclodextrin
γ-PGA	poly(*γ*-glutamic acid)
PEDOT	poly(3,4-ethylenedioxythiophene)
PSS	poly(styrene sulfonate)
CTMAB	cetyltrimethylammonium bromide
AAm	acrylamide
NF	nanofiber

REFERENCES

(1) Liu, X.; Inda, M. E.; Lai, Y.; Lu, T. K.; Zhao, X. Engineered Living Hydrogels. *Adv. Mater.* **2022**, *34*, 2201326.

(2) Fu, F.; Wang, J.; Zeng, H.; Yu, J. Functional Conductive Hydrogels for Bioelectronics. *ACS Mater. Lett.* **2020**, *2*, 1287−1301.

(3) Li, F.; Tang, J.; Geng, J.; Luo, D.; Yang, D. Polymeric DNA hydrogel: Design, synthesis and applications. *Prog. Polym. Sci.* **2019**, *98*, 101163.

(4) Tang, S.; Richardson, B. M.; Anseth, K. S. Dynamic covalent hydrogels as biomaterials to mimic the viscoelasticity of soft tissues. *Prog. Mater. Sci.* **2021**, *120*, 100738.

(5) Mredha, M. T. I.; Jeon, I. Biomimetic anisotropic hydrogels: Advanced fabrication strategies, extraordinary functionalities, and broad applications. *Prog. Mater. Sci.* **2022**, *124*, 100870.

(6) Zhang, C.; Wu, B.; Zhou, Y.; Zhou, F.; Liu, W.; Wang, Z. Mussel-inspired hydrogels: from design principles to promising applications. *Chem. Soc. Rev.* **2020**, *49*, 3605−3637.

(7) Zhang, K.; Feng, Q.; Fang, Z.; Gu, L.; Bian, L. Structurally Dynamic Hydrogels for Biomedical Applications: Pursuing a Fine Balance between Macroscopic Stability and Microscopic Dynamics. *Chem. Rev.* **2021**, *121*, 11149−11193.

(8) Zhang, Y. S.; Khademhosseini, A. Advances in engineering hydrogels. *Science* **2017**, *356*, eaaf3627.

(9) Liu, F.; Jamal, R.; Abdiryim, T.; Liu, X. Polydopamine-based polysaccharide materials for water treatment. *Cellulose* **2022**, *29*, 8025−8064.

(10) Bertsch, P.; Diba, M.; Mooney, D. J.; Leeuwenburgh, S. C. G. Self-Healing Injectable Hydrogels for Tissue Regeneration. *Chem. Rev.* **2023**, *123*, 834−873.

(11) Liu, X.; Lin, W.; Astruc, D.; Gu, H. Syntheses and applications of dendronized polymers. *Prog. Polym. Sci.* **2019**, *96*, 43−105.

(12) Liu, D.; Qiu, J.; Xu, R.; Liu, J.; Feng, J.; Ouyang, L.; Qian, S.; Qiao, Y.; Liu, X. *β*-CD/PEI/PVA composite hydrogels with superior self-healing ability and antibacterial activity for wound healing. *Compos. Part B Eng.* **2022**, *238*, 109921.

(13) Peng, X.; Wang, W.; Yang, W.; Chen, J.; Peng, Q.; Wang, T.; Yang, D.; Wang, J.; Zhang, H.; Zeng, H. Stretchable, compressible, and conductive hydrogel for sensitive wearable soft sensors. *J. Colloid Interface Sci.* **2022**, *618*, 111−120.

(14) Cao, J.; Zhao, Y.; Jin, S.; Li, J.; Wu, P.; Luo, Z. Flexible Lignin-based hydrogels with Self-healing and adhesive ability driven by noncovalent interactions. *Chem. Eng. J.* **2022**, *429*, 132252.

(15) Chen, C.; Wang, Y.; Zhang, H.; Zhang, H.; Dong, W.; Sun, W.; Zhao, Y. Responsive and self-healing structural color supramolecular hydrogel patch for diabetic wound treatment. *Bioact. Mater.* **2022**, *15*, 194−202.

(16) Su, G.; Zhang, Y.; Zhang, X.; Feng, J.; Cao, J.; Zhang, X.; Zhou, T. Soft yet Tough: a Mechanically and Functionally Tissue-like Organohydrogel for Sensitive Soft Electronics. *Chem. Mater.* **2022**, *34*, 1392−1402.

(17) Tang, L.; Wang, L.; Yang, X.; Feng, Y.; Li, Y.; Feng, W. Poly(N-isopropylacrylamide)-based smart hydrogels: Design, properties and applications. *Prog. Mater. Sci.* **2021**, *115*, 100702.

(18) Su, J.; Zhang, L.; Wan, C.; Deng, Z.; Wei, S.; Yong, K. T.; Wu, Y. Dual-network self-healing hydrogels composed of graphene oxide@ nanocellulose and poly(AAm-co-AAc). *Carbohydr. Polym.* **2022**, *296*, 119905.

(19) Guo, H.; Huang, S.; Xu, A.; Xue, W. Injectable Adhesive Self-Healing Multiple-Dynamic-Bond Crosslinked Hydrogel with Photothermal Antibacterial Activity for Infected Wound Healing. *Chem. Mater.* **2022**, *34*, 2655−2671.

(20) Zhang, Y.; Yuan, B.; Zhang, Y.; Cao, Q.; Yang, C.; Li, Y.; Zhou, J. Biomimetic lignin/poly(ionic liquids) composite hydrogel dressing with excellent mechanical strength, self-healing properties, and reusability. *Chem. Eng. J.* **2020**, *400*, 125984.

(21) Wang, Y.; Jia, Y.; Ren, H.; Lao, C.; Peng, W.; Feng, B.; Wang, J. A mechanical, electrical dual autonomous self-healing multifunctional composite hydrogel. *Mater. Today Bio.* **2021**, *12*, 100138.

(22) Ding, X.; Li, G.; Zhang, P.; Jin, E.; Xiao, C.; Chen, X. Injectable Self-Healing Hydrogel Wound Dressing with Cysteine-Specific On-Demand Dissolution Property Based on Tandem Dynamic Covalent Bonds. *Adv. Funct. Mater.* **2021**, *31*, 2011230.

(23) Maleki, A.; He, J.; Bochani, S.; Nosrati, V.; Shahbazi, M. A.; Guo, B. Multifunctional Photoactive Hydrogels for Wound Healing Acceleration. *ACS Nano* **2021**, *15*, 18895−18930.

(24) Zhang, H.; Sun, X.; Wang, J.; Zhang, Y.; Dong, M.; Bu, T.; Li, L.; Liu, Y.; Wang, L. Multifunctional Injectable Hydrogel Dressings for Effectively Accelerating Wound Healing: Enhancing Biomineralization Strategy. *Adv. Funct. Mater.* **2021**, *31*, 2100093.

(25) Zhou, L.; Pi, W.; Cheng, S.; Gu, Z.; Zhang, K.; Min, T.; Zhang, W.; Du, H.; Zhang, P.; Wen, Y. Multifunctional DNA Hydrogels with Hydrocolloid-Cotton Structure for Regeneration of Diabetic Infectious Wounds. *Adv. Funct. Mater.* **2021**, *31*, 2106167.

(26) Yang, Y.; Xu, L.; Wang, J.; Meng, Q.; Zhong, S.; Gao, Y.; Cui, X. Recent advances in polysaccharide-based self-healing hydrogels for biomedical applications. *Carbohydr. Polym.* **2022**, *283*, 119161.

(27) Li, D. Q.; Wang, S. Y.; Meng, Y. J.; Guo, Z. W.; Cheng, M. M.; Li, J. Fabrication of self-healing pectin/chitosan hybrid hydrogel via Diels-Alder reactions for drug delivery with high swelling property, pH-responsiveness, and cytocompatibility. *Carbohydr. Polym.* **2021**, *268*, 118244.

(28) Jiang, X.; Feng, T.; An, B.; Ren, S.; Meng, J.; Li, K.; Liu, S.; Wu, H.; Zhang, H.; Zhong, C. A Bi-Layer Hydrogel Cardiac Patch Made of Recombinant Functional Proteins. *Adv. Mater.* **2022**, *34*, 2201411.

(29) El-Husseiny, H. M.; Mady, E. A.; Hamabe, L.; Abugomaa, A.; Shimada, K.; Yoshida, T.; Tanaka, T.; Yokoi, A.; Elbadawy, M.; Tanaka, R. Smart/stimuli-responsive hydrogels: Cutting-edge platforms for tissue engineering and other biomedical applications. *Mater. Today Bio.* **2022**, *13*, 100186.

(30) Ling, Q.; Liu, W.; Liu, J.; Zhao, L.; Ren, Z.; Gu, H. Highly Sensitive and Robust Polysaccharide-Based Composite Hydrogel Sensor Integrated with Underwater Repeatable Self-Adhesion and Rapid Self-Healing for Human Motion Detection. *ACS Appl. Mater. Interfaces* **2022**, *14*, 24741−24754.

(31) Wu, M.; Wang, X.; Xia, Y.; Zhu, Y.; Zhu, S.; Jia, C.; Guo, W.; Li, Q.; Yan, Z. Stretchable freezing-tolerant triboelectric nanogenerator and strain sensor based on transparent, long-term stable, and highly conductive gelatin-based organohydrogel. *Nano Energy* **2022**, *95*, 106967.

(32) Zhao, L.; Ren, Z.; Liu, X.; Ling, Q.; Li, Z.; Gu, H. A Multifunctional, Self-Healing, Self-Adhesive, and Conductive Sodium Alginate/Poly(vinyl alcohol) Composite Hydrogel as a Flexible Strain Sensor. *ACS Appl. Mater. Interfaces* **2021**, *13*, 11344−11355.

(33) Zhang, Z.; Gao, Y.; Gao, Y.; Jia, F.; Gao, G. A self-adhesive, self-healing zwitterionic hydrogel electrolyte for high-voltage zinc-ion hybrid supercapacitors. *Chem. Eng. J.* **2023**, *452*, 139014.

(34) Li, Y.; Liu, L.; Xu, H.; Cheng, Z.; Yan, J.; Xie, X. M. Biomimetic Gradient Hydrogel Actuators with Ultrafast Thermo-Responsiveness

and High Strength. *ACS Appl. Mater. Interfaces* **2022**, *14*, 32541−32550.

(35) Leray, N.; Talantikite, M.; Villares, A.; Cathala, B. Xyloglucan-cellulose nanocrystal-chitosan double network hydrogels for soft actuators. *Carbohydr. Polym.* **2022**, *293*, 119753.

(36) Chen, K.; Hu, Y.; Wang, F.; Liu, M.; Liu, P.; Li, C.; Yu, Y.; Xiao, X.; Feng, Q. Ultra-stretchable, adhesive, and self-healing MXene/polyampholytes hydrogel as flexible and wearable epidermal sensors. *Colloids Surf. A Physicochem. Eng. Aspects* **2022**, *645*, 128897.

(37) Yu, X.; Zhang, H.; Wang, Y.; Fan, X.; Li, Z.; Zhang, X.; Liu, T. Highly Stretchable, Ultra-Soft, and Fast Self-Healable Conductive Hydrogels Based on Polyaniline Nanoparticles for Sensitive Flexible Sensors. *Adv. Funct. Mater.* **2022**, *32*, 2204366.

(38) Wang, L.; Xu, H.; Gao, J.; Yao, J.; Zhang, Q. Recent progress in metal-organic frameworks-based hydrogels and aerogels and their applications. *Coord. Chem. Rev.* **2019**, *398*, 213016.

(39) Lei, C.; Guan, W.; Guo, Y.; Shi, W.; Wang, Y.; Johnston, K. P.; Yu, G. Polyzwitterionic Hydrogels for Highly Efficient High Salinity Solar Desalination. *Angew. Chem., Int. Ed.* **2022**, *61*, 202208487.

(40) Guo, Y.; Bae, J.; Fang, Z.; Li, P.; Zhao, F.; Yu, G. Hydrogels and Hydrogel-Derived Materials for Energy and Water Sustainability. *Chem. Rev.* **2020**, *120*, 7642−7707.

(41) Zhou, X.; Guo, Y.; Zhao, F.; Yu, G. Hydrogels as an Emerging Material Platform for Solar Water Purification. *Acc. Chem. Res.* **2019**, *52*, 3244−3253.

(42) Zhao, Y.; Liang, Q.; Mugo, S. M.; An, L.; Zhang, Q.; Lu, Y. Self-Healing and Shape-Editable Wearable Supercapacitors Based on Highly Stretchable Hydrogel Electrolytes. *Adv. Sci.* **2022**, *9*, 2201039.

(43) Liu, Y.; Abdiryim, T.; Jamal, R.; Liu, X.; Fan, N.; Niyaz, M.; Zhang, Y. High-performance Quasi−Solid−State hybrid supercapacitor for Self−powered strain sensor based on poly (3, 4−propylenedioxythiophene)/NiS_2@Hollow carbon sphere composite and sulfonated cellulose hydrogel electrolyte. *Appl. Surf. Sci.* **2023**, *608*, 154989.

(44) Yang, Y.; Shi, K.; Yu, K.; Xing, F.; Lai, H.; Zhou, Y.; Xiao, P. Degradable Hydrogel Adhesives with Enhanced Tissue Adhesion, Superior Self-Healing, Cytocompatibility, and Antibacterial Property. *Adv. Healthcare Mater.* **2022**, *11*, 2101504.

(45) Mohamadhoseini, M.; Mohamadnia, Z. Supramolecular self-healing materials via host-guest strategy between cyclodextrin and specific types of guest molecules. *Coord. Chem. Rev.* **2021**, *432*, 213711.

(46) Muir, V. G.; Burdick, J. A. Chemically Modified Biopolymers for the Formation of Biomedical Hydrogels. *Chem. Rev.* **2021**, *121*, 10908−10949.

(47) Zhang, Y. Z.; El-Demellawi, J. K.; Jiang, Q.; Ge, G.; Liang, H.; Lee, K.; Dong, X.; Alshareef, H. N. MXene hydrogels: fundamentals and applications. *Chem. Soc. Rev.* **2020**, *49*, 7229−7251.

(48) Yang, Y.; Urban, M. W. Self-healing polymeric materials. *Chem. Soc. Rev.* **2013**, *42*, 7446−7467.

(49) Yang, Y.; Ding, X.; Urban, M. W. Chemical and physical aspects of self-healing materials. *Prog. Polym. Sci.* **2015**, *49*−*50*, 34−59.

(50) Wang, S.; Urban, M. W. Self-healing polymers. *Nat. Rev. Mater.* **2020**, *5*, 562−583.

(51) Chen, J.; He, J.; Yang, Y.; Qiao, L.; Hu, J.; Zhang, J.; Guo, B. Antibacterial adhesive self-healing hydrogels to promote diabetic wound healing. *Acta Biomater.* **2022**, *146*, 119−130.

(52) Iftime, M. M.; Rosca, I.; Sandu, A. I.; Marin, L. Chitosan crosslinking with a vanillin isomer toward self-healing hydrogels with antifungal activity. *Int. J. Biol. Macromol.* **2022**, *205*, 574−586.

(53) Yuan, L.; Li, Z.; Li, X.; Qiu, S.; Lei, J.; Li, D.; Mu, C.; Ge, L. Functionalization of an Injectable Self-Healing pH-Responsive Hydrogel by Incorporating a Curcumin/Polymerized β-Cyclodextrin Inclusion Complex for Selective Toxicity to Osteosarcoma. *ACS Appl. Polym. Mater.* **2022**, *4*, 1243−1254.

(54) Wang, S.; Chi, J.; Jiang, Z.; Hu, H.; Yang, C.; Liu, W.; Han, B. A self-healing and injectable hydrogel based on water-soluble chitosan and hyaluronic acid for vitreous substitute. *Carbohydr. Polym.* **2021**, *256*, 117519.

(55) Cao, J.; He, G.; Ning, X.; Wang, C.; Fan, L.; Yin, Y.; Cai, W. Hydroxypropyl chitosan-based dual self-healing hydrogel for adsorption of chromium ions. *Int. J. Biol. Macromol.* **2021**, *174*, 89−100.

(56) Jing, H.; Feng, J.; Shi, J.; He, L.; Guo, P.; Guan, S.; Fu, H.; Ao, Y. Ultra-stretchable, self-recovering, self-healing cationic guar gum/poly(stearyl methacrylate-co-acrylic acid) hydrogels. *Carbohydr. Polym.* **2021**, *256*, 117563.

(57) Cheng, Q.; Ding, S.; Zheng, Y.; Wu, M.; Peng, Y. Y.; Diaz-Dussan, D.; Shi, Z.; Liu, Y.; Zeng, H.; Cui, Z.; Narain, R. Dual Cross-Linked Hydrogels with Injectable, Self-Healing, and Antibacterial Properties Based on the Chemical and Physical Cross-Linking. *Biomacromolecules* **2021**, *22*, 1685−1694.

(58) Liu, Q.; Ji, N.; Xiong, L.; Sun, Q. Rapid gelling, self-healing, and fluorescence-responsive chitosan hydrogels formed by dynamic covalent crosslinking. *Carbohydr. Polym.* **2020**, *246*, 116586.

(59) Samadian, H.; Maleki, H.; Allahyari, Z.; Jaymand, M. Natural polymers-based light-induced hydrogels: Promising biomaterials for biomedical applications. *Coord. Chem. Rev.* **2020**, *420*, 213432.

(60) Hardman, D.; George Thuruthel, T.; Iida, F. Self-healing ionic gelatin/glycerol hydrogels for strain sensing applications. *NPG Asia Materials.* **2022**, *14*, 11.

(61) Deng, Z.; Wang, H.; Ma, P. X.; Guo, B. Self-healing conductive hydrogels: preparation, properties and applications. *Nanoscale* **2020**, *12*, 1224−1246.

(62) Ren, P.; Li, J.; Zhao, L.; Wang, A.; Wang, M.; Li, J.; Jian, H.; Li, X.; Yan, X.; Bai, S. Dipeptide Self-assembled Hydrogels with Shear-Thinning and Instantaneous Self-healing Properties Determined by Peptide Sequences. *ACS Appl. Mater. Interfaces* **2020**, *12*, 21433−21440.

(63) Zhu, D. Y.; Chen, Z. P.; Hong, Z. P.; Zhang, L.; Liang, X.; Li, Y.; Duan, X.; Luo, H.; Peng, J.; Guo, J. Injectable thermo-sensitive and wide-crack self-healing hydrogel loaded with antibacterial anti-inflammatory dipotassium glycyrrhizate for full-thickness skin wound repair. *Acta Biomater.* **2022**, *143*, 203−215.

(64) He, Y.; Deng, Z.; Wang, Y. J.; Zhao, Y.; Chen, L. Polysaccharide/Ti_3C_2Tx MXene adhesive hydrogels with self-healing ability for multifunctional and sensitive sensors. *Carbohydr. Polym.* **2022**, *291*, 119572.

(65) Wei, J.; Wan, F.; Zhang, P.; Zeng, Z.; Ping, H.; Xie, J.; Zou, Z.; Wang, W.; Xie, H.; Shen, Z.; Lei, L.; Fu, Z. Bioprocess-inspired synthesis of printable, self-healing mineral hydrogels for rapidly responsive, wearable ionic skin. *Chem. Eng. J.* **2021**, *424*, 130549.

(66) Diehl, F.; Hageneder, S.; Fossati, S.; Auer, S. K.; Dostalek, J.; Jonas, U. Plasmonic nanomaterials with responsive polymer hydrogels for sensing and actuation. *Chem. Soc. Rev.* **2022**, *51*, 3926−3963.

(67) Peng, K.; Zhang, J.; Yang, J.; Lin, L.; Gan, Q.; Yang, Z.; Chen, Y.; Feng, C. Green Conductive Hydrogel Electrolyte with Self-Healing Ability and Temperature Adaptability for Flexible Supercapacitors. *ACS Appl. Mater. Interfaces* **2022**, *14*, 39404−39419.

(68) Jiao, Y.; Lu, Y.; Lu, K.; Yue, Y.; Xu, X.; Xiao, H.; Li, J.; Han, J. Highly stretchable and self-healing cellulose nanofiber-mediated conductive hydrogel towards strain sensing application. *J. Colloid Interface Sci.* **2021**, *597*, 171−181.

(69) Zhao, W.; Zhang, D.; Yang, Y.; Du, C.; Zhang, B. A fast self-healing multifunctional polyvinyl alcohol nano-organic composite hydrogel as a building block for highly sensitive strain/pressure sensors. *J. Mater. Chem. A* **2021**, *9*, 22082−22094.

(70) Wang, T.; Fan, X.; Koh, J. J.; He, C.; Yeow, C. H. Self-Healing Approach toward Catalytic Soft Robots. *ACS Appl. Mater. Interfaces* **2022**, *14*, 40590−40598.

(71) Hu, S.; Wang, L.; Huang, T.; Yu, A. A conductive self-healing hydrogel binder for high-performance silicon anodes in lithium-ion batteries. *J. Power Sources* **2020**, *449*, 227472.

(72) Zhao, S.; Xia, D.; Li, M.; Cheng, D.; Wang, K.; Meng, Y. S.; Chen, Z.; Bae, J. Self-Healing and Anti-CO(2) Hydrogels for Flexible Solid-State Zinc-Air Batteries. *ACS Appl. Mater. Interfaces* **2021**, *13*, 12033−12041.

(73) Huang, K.; Xu, H.; Chen, C.; Shi, F.; Wang, F.; Li, J.; Hu, S. A novel dual crosslinked polysaccharide hydrogel with self-healing and stretchable properties. *Polym. Chem.* **2021**, *12*, 6134−6144.

(74) Zhao, W.; Zhou, M.; Lv, L.; Fu, H. Self-healing, conductive and magnetic ZnF2O4/MCNT/PPy ternary composite hydrogels. *J. Alloys Compd.* **2021**, *886*, 161083.

(75) Zhang, B.; He, J.; Shi, M.; Liang, Y.; Guo, B. Injectable self-healing supramolecular hydrogels with conductivity and photo-thermal antibacterial activity to enhance complete skin regeneration. *Chem. Eng. J.* **2020**, *400*, 125994.

(76) Wu, K.; Fu, M.; Zhao, Y.; Gerhard, E.; Li, Y.; Yang, J.; Guo, J. Anti-oxidant anti-inflammatory and antibacterial tannin-crosslinked citrate-based mussel-inspired bioadhesives facilitate scarless wound healing. *Bioact. Mater.* **2023**, *20*, 93−110.

(77) Huang, W.; Cheng, S.; Wang, X.; Zhang, Y.; Chen, L.; Zhang, L. Noncompressible Hemostasis and Bone Regeneration Induced by an Absorbable Bioadhesive Self-Healing Hydrogel. *Adv. Funct. Mater.* **2021**, *31*, 2009189.

(78) D'Souza, A.; Yoon, J. H.; Beaman, H.; Gosavi, P.; Lengyel-Zhand, Z.; Sternisha, A.; Centola, G.; Marshall, L. R.; Wehrman, M. D.; Schultz, K. M.; Monroe, M. B.; Makhlynets, O. V. Nine-Residue Peptide Self-Assembles in the Presence of Silver to Produce a Self-Healing, Cytocompatible, Antimicrobial Hydrogel. *ACS Appl. Mater. Interfaces* **2020**, *12*, 17091−17099.

(79) Yeo, Y. H.; Park, W. H. Dual-crosslinked, self-healing and thermo-responsive methylcellulose/chitosan oligomer copolymer hydrogels. *Carbohydr. Polym.* **2021**, *258*, 117705.

(80) Kim, J. W.; Kim, S.; Jeong, Y. R.; Kim, J.; Kim, D. S.; Keum, K.; Lee, H.; Ha, J. S. Self-healing strain-responsive electrochromic display based on a multiple crosslinked network hydrogel. *Chem. Eng. J.* **2022**, *430*, 132685.

(81) Deng, M.; Zhang, M.; Huang, R.; Li, H.; Lv, W.; Lin, X.; Huang, R.; Wang, Y. Diabetes immunity-modulated multifunctional hydrogel with cascade enzyme catalytic activity for bacterial wound treatment. *Biomaterials* **2022**, *289*, 121790.

(82) Correa, S.; Grosskopf, A. K.; Lopez Hernandez, H.; Chan, D.; Yu, A. C.; Stapleton, L. M.; Appel, E. A. Translational Applications of Hydrogels. *Chem. Rev.* **2021**, *121*, 11385−11457.

(83) Shang, X.; Wang, Q.; Li, J.; Zhang, G.; Zhang, J.; Liu, P.; Wang, L. Double-network hydrogels with superior self-healing properties using starch reinforcing strategy. *Carbohydr. Polym.* **2021**, *257*, 117626.

(84) Panda, S.; Deshmukh, K.; Khadheer Pasha, S. K.; Theerthagiri, J.; Manickam, S.; Choi, M. Y. MXene based emerging materials for supercapacitor applications: Recent advances, challenges, and future perspectives. *Coord. Chem. Rev.* **2022**, *462*, 214518.

(85) Li, L.; Wu, P.; Yu, F.; Ma, J. Double network hydrogels for energy/environmental applications: challenges and opportunities. *J. Mater. Chem. A* **2022**, *10*, 9215−9247.

(86) Xu, T.; Liu, K.; Sheng, N.; Zhang, M.; Liu, W.; Liu, H.; Dai, L.; Zhang, X.; Si, C.; Du, H.; Zhang, K. Biopolymer-based hydrogel electrolytes for advanced energy storage/conversion devices: Properties, applications, and perspectives. *Energy Stor. Mater.* **2022**, *48*, 244−262.

(87) Jiang, L.; He, S.; Liu, A.; Zhang, J.; Liu, J.; He, S.; Shao, W. Preparation and characterization of self-healable and wearable hydrogels with ultrasensitive sensing performances. *Compos. Part B Eng.* **2022**, *239*, 109982.

(88) Talebian, S.; Mehrali, M.; Taebnia, N.; Pennisi, C. P.; Kadumudi, F. B.; Foroughi, J.; Hasany, M.; Nikkhah, M.; Akbari, M.; Orive, G.; Dolatshahi-Pirouz, A. Self-Healing Hydrogels: The Next Paradigm Shift in Tissue Engineering? *Adv. Sci.* **2019**, *6*, 1801664.

(89) Wang, W.; Zhang, Y.; Liu, W. Bioinspired fabrication of high strength hydrogels from non-covalent interactions. *Prog. Polym. Sci.* **2017**, *71*, 1−25.

(90) Taylor, D. L.; In Het Panhuis, M. Self-Healing Hydrogels. *Adv. Mater.* **2016**, *28*, 9060−9093.

(91) Khatib, M.; Zohar, O.; Haick, H. Self-Healing Soft Sensors: From Material Design to Implementation. *Adv. Mater.* **2021**, *33*, 2004190.

(92) Qin, Y.; Mo, J.; Liu, Y.; Zhang, S.; Wang, J.; Fu, Q.; Wang, S.; Nie, S. Stretchable Triboelectric Self-Powered Sweat Sensor Fabricated from Self-Healing Nanocellulose Hydrogels. *Adv. Funct. Mater.* **2022**, *32*, 2201846.

(93) Yang, M.; Cheng, Y.; Yue, Y.; Chen, Y.; Gao, H.; Li, L.; Cai, B.; Liu, W.; Wang, Z.; Guo, H.; Liu, N.; Gao, Y. High-Performance Flexible Pressure Sensor with a Self-Healing Function for Tactile Feedback. *Adv. Sci.* **2022**, *9*, 2200507.

(94) Wang, C.; Zhang, J.; Chen, H.; Wang, Z.; Huang, C.; Tan, Y. Supramolecular topology controlled self-healing conformal hydrogels for stable human−machine interfaces. *J. Mater. Chem. C* **2022**, *10*, 8077−8088.

(95) D'Souza, A.; Marshall, L. R.; Yoon, J.; Kulesha, A.; Edirisinghe, D. I. U.; Chandrasekaran, S.; Rathee, P.; Prabhakar, R.; Makhlynets, O. V. Peptide hydrogel with self-healing and redox-responsive properties. *Nano Converg.* **2022**, *9*, 18.

(96) Sarmah, D.; Karak, N. Physically cross-linked starch/hydrophobically-associated poly(acrylamide) self-healing mechanically strong hydrogel. *Carbohydr. Polym.* **2022**, *289*, 119428.

(97) Fan, B.; Cui, N.; Xu, Z.; Chen, K.; Yin, P.; Yue, K.; Tang, W. Thermoresponsive and Self-Healing Hydrogel Based on Chitosan Derivatives and Polyoxometalate as an Antibacterial Coating. *Biomacromolecules* **2022**, *23*, 972−982.

(98) Chen, K.; Liu, M.; Wang, F.; Hu, Y.; Liu, P.; Li, C.; Du, Q.; Yu, Y.; Xiao, X.; Feng, Q. Highly Transparent, Self-Healing, and Self-Adhesive Double Network Hydrogel for Wearable Sensors. *Front. Bioeng. Biotechnol.* **2022**, *10*, 846401.

(99) Liu, J.; Zhang, L.; Wang, N.; Zhao, H.; Li, C. Nanofiber-reinforced transparent, tough, and self-healing substrate for an electronic skin with damage detection and program-controlled autonomic repair. *Nano Energy* **2022**, *96*, 107108.

(100) Liu, Y.; Lin, S. H.; Chuang, W. T.; Dai, N. T.; Hsu, S. H. Biomimetic Strain-Stiffening in Chitosan Self-Healing Hydrogels. *ACS Appl. Mater. Interfaces* **2022**, *14*, 16032−16046.

(101) Zhang, B.; Li, S.; Wang, Y.; Wu, Y.; Zhang, H. Halloysite nanotube-based self-healing fluorescence hydrogels in fabricating 3D cube containing UV-sensitive QR code information. *J. Colloid Interface Sci.* **2022**, *617*, 353−362.

(102) Wang, H.; Xie, X. Q.; Peng, Y.; Li, J.; Liu, C. S. Self-healing mechanism and bioelectrochemical interface properties of core-shell guanosine-borate hydrogels. *J. Colloid Interface Sci.* **2021**, *590*, 103−113.

(103) Mei, L.; Zhang, D.; Shao, H.; Hao, Y.; Zhang, T.; Zheng, W.; Ji, Y.; Ling, P.; Lu, Y.; Zhou, Q. Injectable and Self-Healing Probiotics-Loaded Hydrogel for Promoting Superbacteria-Infected Wound Healing. *ACS Appl. Mater. Interfaces* **2022**, *14*, 20538−20550.

(104) Wang, Y.; Chen, Y.; Zheng, J.; Liu, L.; Zhang, Q. Three-Dimensional Printing Self-Healing Dynamic/Photocrosslinking Gelatin-Hyaluronic Acid Double-Network Hydrogel for Tissue Engineering. *ACS Omega* **2022**, *7*, 12076−12088.

(105) Zhang, L.; Zhang, X.; zhang, H.; Xu, L.; Wang, D.; Lu, X.; Zhang, A. Semi-embedded robust MXene/AgNW sensor with self-healing, high sensitivity and a wide range for motion detection. *Chem. Eng. J.* **2022**, *434*, 134751.

(106) Zhou, S.; Wu, B.; Zhou, Q.; Jian, Y.; Le, X.; Lu, H.; Zhang, D.; Zhang, J.; Zhang, Z.; Chen, T. Ionic Strength and Thermal Dual-Responsive Bilayer Hollow Spherical Hydrogel Actuator. *Macromol. Rapid Commun.* **2020**, *41*, 1900543.

(107) Wu, K.; Wu, X.; Zhang, Y.; Chen, S.; Qiao, Z.; Wei, D.; Sun, J.; Fan, H. Semiconvertible Hyaluronic Hydrogel Enabled Red-Light-Responsive Reversible Mechanics, Adhesion, and Self-Healing. *Biomacromolecules* **2022**, *23*, 1030−1040.

(108) Jiang, X.; Yan, N.; Wang, M.; Feng, M.; Guan, Q.; Xu, L. Magnetic nanostructure and biomolecule synergistically promoted Suaeda-inspired self-healing hydrogel composite for seawater evaporation. *Sci. Total Environ.* **2022**, *830*, 154545.

(109) Li, Y.; Li, L.; Zhang, Z.; Cheng, J.; Fei, Y.; Lu, L. An all-natural strategy for versatile interpenetrating network hydrogels with self-

healing, super-adhesion and high sensitivity. *Chem. Eng. J.* **2021**, *420*, 129736.

(110) Jian, Y.; Wu, B.; Le, X.; Liang, Y.; Zhang, Y.; Zhang, D.; Zhang, L.; Lu, W.; Zhang, J.; Chen, T. Antifreezing and Stretchable Organohydrogels as Soft Actuators. *Research* **2019**, *2019*, 2384347.

(111) Wu, S.; Hua, M.; Alsaid, Y.; Du, Y.; Ma, Y.; Zhao, Y.; Lo, C. Y.; Wang, C.; Wu, D.; Yao, B.; Strzalka, J.; Zhou, H.; Zhu, X.; He, X. Poly(vinyl alcohol) Hydrogels with Broad-Range Tunable Mechanical Properties via the Hofmeister Effect. *Adv. Mater.* **2021**, *33*, 2007829.

(112) Dong, Y.; Wang, S.; Ke, Y.; Ding, L.; Zeng, X.; Magdassi, S.; Long, Y. 4D Printed Hydrogels: Fabrication, Materials, and Applications. *Adv. Mater. Technol.* **2020**, *5*, 2000034.

(113) Wu, S.; Zhang, Z.; Xu, R.; Wei, S.; Xiong, F.; Cui, W.; Li, B.; Xue, Y.; Xuan, H.; Yuan, H. A spray-filming, tissue-adhesive, and bioactive polysaccharide self-healing hydrogel for skin regeneration. *Mater. Des.* **2022**, *217*, 110669.

(114) Ma, Y.; Liu, K.; Lao, L.; Li, X.; Zhang, Z.; Lu, S.; Li, Y.; Li, Z. A stretchable, self-healing, okra polysaccharide-based hydrogel for fast-response and ultra-sensitive strain sensors. *Int. J. Biol. Macromol.* **2022**, *205*, 491−499.

(115) Zhang, L.; Wan, C.; Su, J.; Zhang, C.; Wei, S.; Tian, W.; Liu, X.; Cheng, W.; Li, X.; Li, X.; Guo, X.; Yong, K.-T.; Wu, Y. A dual-crosslinked self-healing and antibacterial nanocellulose hydrogel for monitoring of human motions. *Mater. Des.* **2022**, *215*, 110464.

(116) Heidarian, P.; Gharaie, S.; Yousefi, H.; Paulino, M.; Kaynak, A.; Varley, R.; Kouzani, A. Z. A 3D printable dynamic nanocellulose/nanochitin self-healing hydrogel and soft strain sensor. *Carbohydr. Polym.* **2022**, *291*, 119545.

(117) Fan, H. L.; Wang, J. H.; Jin, Z. X. Tough, Swelling-Resistant, Self-Healing, and Adhesive Dual-Cross-Linked Hydrogels Based on Polymer-Tannic Acid Multiple Hydrogen Bonds. *Macromolecules* **2018**, *51*, 1696−1705.

(118) Su, G.; Cao, J.; Zhang, X.; Zhang, Y.; Yin, S.; Jia, L.; Guo, Q.; Zhang, X.; Zhang, J.; Zhou, T. Human-tissue-inspired anti-fatigue-fracture hydrogel for a sensitive wide-range human−machine interface. *J. Mater. Chem. A* **2020**, *8*, 2074−2082.

(119) Shi, Y.; Wang, M.; Ma, C.; Wang, Y.; Li, X.; Yu, G. A Conductive Self-Healing Hybrid Gel Enabled by Metal-Ligand Supramolecule and Nanostructured Conductive Polymer. *Nano Lett.* **2015**, *15*, 6276−81.

(120) Ren, P.; Wei, D.; Ge, X.; Wang, F.; Liang, M.; Dai, J.; Xu, L.; Zhang, T. Injectable supramolecular hydrogels based on host−guest interactions with cell encapsulation capabilities. *Colloids Surf. A Physicochem. Eng. Aspects* **2021**, *628*, 127338.

(121) Li, S.; Pei, M.; Wan, T.; Yang, H.; Gu, S.; Tao, Y.; Liu, X.; Zhou, Y.; Xu, W.; Xiao, P. Self-healing hyaluronic acid hydrogels based on dynamic Schiff base linkages as biomaterials. *Carbohydr. Polym.* **2020**, *250*, 116922.

(122) Shen, J. F.; Wang, X. M.; An, H.; Chang, L. M.; Wang, Y.; Li, W. J.; Qin, J. L. Cross-linking induced thermoresponsive hydrogel with light emitting and self-healing property. *J. Polym. Sci. A Polym. Chem.* **2019**, *57*, 869−877.

(123) Wang, L.; Cao, Q.; Wang, X.; Wu, D. Visible light triggered controlled formation of rapidly self-healing hydrogels based on thiol−disulfide exchange. *Soft Matter* **2022**, *18*, 3004−3012.

(124) Chae, A.; Murali, G.; Lee, S. Y.; Gwak, J.; Kim, S. J.; Jeong, Y. J.; Kang, H.; Park, S.; Lee, A. S.; Koh, D. Y.; In, I.; Park, S. J. Highly Oxidation-Resistant and Self-Healable MXene-Based Hydrogels for Wearable Strain Sensor. *Adv. Funct. Mater.* **2023**, 2213382.

(125) Ma, X.; Yang, R.; Wang, P.; Liu, S.; Xu, H.; Ye, Z.; Chi, B. Bioinspired dual dynamic network hydrogels promote cartilage regeneration through regulating BMSC chondrogenic differentiation. *Mater. Today Chem.* **2022**, *23*, 100648.

(126) Zhao, X.; Wang, H.; Luo, J.; Ren, G.; Wang, J.; Chen, Y.; Jia, P. Ultrastretchable, Adhesive, Anti-freezing, Conductive, and Self-Healing Hydrogel for Wearable Devices. *ACS Appl. Polym. Mater.* **2022**, *4*, 1784−1793.

(127) Liu, X.; Ren, Z.; Liu, F.; Zhao, L.; Ling, Q.; Gu, H. Multifunctional Self-Healing Dual Network Hydrogels Constructed via Host-Guest Interaction and Dynamic Covalent Bond as Wearable Strain Sensors for Monitoring Human and Organ Motions. *ACS Appl. Mater. Interfaces* **2021**, *13*, 14612−14622.

(128) Zhao, D.; Feng, M.; Zhang, L.; He, B.; Chen, X.; Sun, J. Facile synthesis of self-healing and layered sodium alginate/polyacrylamide hydrogel promoted by dynamic hydrogen bond. *Carbohydr. Polym.* **2021**, *256*, 117580.

(129) Yu, X.; Zheng, Y.; Zhang, H.; Wang, Y.; Fan, X.; Liu, T. Fast-Recoverable, Self-Healable, and Adhesive Nanocomposite Hydrogel Consisting of Hybrid Nanoparticles for Ultrasensitive Strain and Pressure Sensing. *Chem. Mater.* **2021**, *33*, 6146−6157.

(130) Zhang, C.; Wang, M.; Jiang, C.; Zhu, P.; Sun, B.; Gao, Q.; Gao, C.; Liu, R. Highly adhesive and self-healing γ-PGA/PEDOT:PSS conductive hydrogels enabled by multiple hydrogen bonding for wearable electronics. *Nano Energy* **2022**, *95*, 106991.

(131) Wang, C.; Liu, Y.; Qu, X.; Shi, B.; Zheng, Q.; Lin, X.; Chao, S.; Wang, C.; Zhou, J.; Sun, Y.; Mao, G.; Li, Z. Ultra-Stretchable and Fast Self-Healing Ionic Hydrogel in Cryogenic Environments for Artificial Nerve Fiber. *Adv. Mater.* **2022**, *34*, e2105416.

(132) Li, B.; Li, Z.; Li, H. Ultrastretchable Luminescent Nanocomposite Hydrogel with Self-Healing Behavior. *ACS Appl. Polym. Mater.* **2022**, *4*, 2329−2336.

(133) Jiang, X.; Zeng, F.; Yang, X.; Jian, C.; Zhang, L.; Yu, A.; Lu, A. Injectable self-healing cellulose hydrogel based on host-guest interactions and acylhydrazone bonds for sustained cancer therapy. *Acta Biomater.* **2022**, *141*, 102−113.

(134) Su, G.; Yin, S.; Guo, Y.; Zhao, F.; Guo, Q.; Zhang, X.; Zhou, T.; Yu, G. Balancing the mechanical, electronic, and self-healing properties in conductive self-healing hydrogel for wearable sensor applications. *Mater. Horiz.* **2021**, *8*, 1795−1804.

(135) Fang, G.; Yang, X.; Chen, S.; Wang, Q.; Zhang, A.; Tang, B. Cyclodextrin-based host−guest supramolecular hydrogels for local drug delivery. *Coord. Chem. Rev.* **2022**, *454*, 214352.

(136) Xiong, H.; Li, Y.; Ye, H.; Huang, G.; Zhou, D.; Huang, Y. Self-healing supramolecular hydrogels through host-guest interaction between cyclodextrin and carborane. *J. Mater. Chem. B* **2020**, *8*, 10309−10313.

(137) Chen, J.; Xu, X.; Liu, M.; Li, Y.; Yu, D.; Lu, Y.; Xiong, M.; Wyman, I.; Xu, X.; Wu, X. Topological cyclodextrin nanoparticles as crosslinkers for self-healing tough hydrogels as strain sensors. *Carbohydr. Polym.* **2021**, *264*, 117978.

(138) Liu, X.; Zhao, L.; Liu, F.; Astruc, D.; Gu, H. Supramolecular redox-responsive ferrocene hydrogels and microgels. *Coord. Chem. Rev.* **2020**, *419*, 213406.

(139) Araki, J.; Ito, K. Recent advances in the preparation of cyclodextrin-based polyrotaxanes and their applications to soft materials. *Soft Matter* **2007**, *3*, 1456−1473.

(140) Jiang, L.; Liu, C.; Mayumi, K.; Kato, K.; Yokoyama, H.; Ito, K. Highly Stretchable and Instantly Recoverable Slide-Ring Gels Consisting of Enzymatically Synthesized Polyrotaxane with Low Host Coverage. *Chem. Mater.* **2018**, *30*, 5013−5019.

(141) Takata, T. Switchable polymer materials controlled by rotaxane macromolecular switches. *ACS Cent. Sci.* **2020**, *6*, 129−143.

(142) Kureha, T.; Aoki, D.; Hiroshige, S.; Iijima, K.; Aoki, D.; Takata, T.; Suzuki, D. Decoupled thermo- and ph-responsive hydrogel microspheres cross-linked by rotaxane networks. *Angew. Chem., Int. Ed.* **2017**, *56*, 15393−15396.

(143) Liu, C.; Morimoto, N.; Jiang, L.; Kawahara, S.; Noritomi, T.; Yokoyama, H.; Mayumi, K.; Ito, K. Tough hydrogels with rapid self-reinforcement. *Science* **2021**, *372*, 1078−1081.

(144) Hwang, C.; Song, Y.; Kim, H.-J.; Lee, K.-J.; Lee, J.; Kim, D.-D.; Cho, H.-J. Polypseudorotaxane and polydopamine linkage-based hyaluronic acid hydrogel network with a single syringe injection for sustained drug delivery. *Carbohydr. Polym.* **2021**, *266*, 118104.

(145) Vandera, K.-K. A.; Pague, C.; Omar, J.; González-Gaitano, G.; Ways, T. M. M.; Khutoryanskiy, V. V.; Dreiss, C. A. Formation of Supramolecular Gels from Host−Guest Interactions between PEGylated Chitosan and α-Cyclodextrin. *Macromol. Mater. Eng.* **2023**, 2200646.

(146) Cho, I. S.; Ooya, T. Cell-encapsulating hydrogel puzzle: polyrotaxane-based self-healing hydrogels. *Chem.—Eur. J.* **2020**, *26*, 913−920.

(147) Charlet, A.; Lutz-Bueno, V.; Mezzenga, R.; Amstad, E. Shape retaining self-healing metal-coordinated hydrogels. *Nanoscale* **2021**, *13*, 4073−4084.

(148) Zhang, Z.; Tang, L.; Chen, C.; Yu, H.; Bai, H.; Wang, L.; Qin, M.; Feng, Y.; Feng, W. Liquid metal-created macroporous composite hydrogels with self-healing ability and multiple sensations as artificial flexible sensors. *J. Mater. Chem. A* **2021**, *9*, 875−883.

(149) Li, X.-X.; Wang, M.; Dai, J.; Liu, H.; Qin, H. Assembled caseins as crosslinkers for tough, adhesive and self-healing hydrogels towards flexible sensors. *J. Mater. Chem. A* **2022**, *10*, 14300−14309.

(150) Pei, X.; Zhang, H.; Zhou, Y.; Zhou, L.; Fu, J. Stretchable, self-healing and tissue-adhesive zwitterionic hydrogels as strain sensors for wireless monitoring of organ motions. *Mater. Horiz.* **2020**, *7*, 1872−1882.

(151) Xu, J.; Tai, C.-H.; Chen, T.-Y.; Hsu, S.-h. An anti-inflammatory electroconductive hydrogel with self-healing property for the treatment of Parkinson's disease. *Chem. Eng. J.* **2022**, *446*, 137180.

(152) Juan, L. T.; Lin, S. H.; Wong, C. W.; Jeng, U. S.; Huang, C. F.; Hsu, S. H. Functionalized Cellulose Nanofibers as Crosslinkers to Produce Chitosan Self-Healing Hydrogel and Shape Memory Cryogel. *ACS Appl. Mater. Interfaces* **2022**, *14*, 36353−36365.

(153) Nie, M.; Kong, B.; Chen, G.; Xie, Y.; Zhao, Y.; Sun, L. MSCs-laden injectable self-healing hydrogel for systemic sclerosis treatment. *Bioact. Mater.* **2022**, *17*, 369−378.

(154) Liu, H.; Ni, Y.; Hu, J.; Jin, Y.; Gu, P.; Qiu, H.; Chen, K. Self-Healing and Antibacterial Essential Oil-Loaded Mesoporous Silica/Polyacrylate Hybrid Hydrogel for High-Performance Wearable Body-Strain Sensing. *ACS Appl. Mater. Interfaces* **2022**, *14*, 21509−21520.

(155) Yang, X.; Liu, G.; Peng, L.; Guo, J.; Tao, L.; Yuan, J.; Chang, C.; Wei, Y.; Zhang, L. Highly Efficient Self-Healable and Dual Responsive Cellulose-Based Hydrogels for Controlled Release and 3D Cell Culture. *Adv. Funct. Mater.* **2017**, *27*, 1703174.

(156) Muir, V. G.; Qazi, T. H.; Weintraub, S.; Torres Maldonado, B. O.; Arratia, P. E.; Burdick, J. A. Sticking Together: Injectable Granular Hydrogels with Increased Functionality via Dynamic Covalent Inter-Particle Crosslinking. *Small* **2022**, *18*, 2201115.

(157) Zhang, X.; Waymouth, R. M. 1,2-Dithiolane-Derived Dynamic, Covalent Materials: Cooperative Self-Assembly and Reversible Cross-Linking. *J. Am. Chem. Soc.* **2017**, *139*, 3822−3833.

(158) Shahi, S.; Roghani-Mamaqani, H.; Talebi, S.; Mardani, H. Chemical stimuli-induced reversible bond cleavage in covalently crosslinked hydrogels. *Coord. Chem. Rev.* **2022**, *455*, 214368.

(159) Zhang, Y.; Ding, Z.; Liu, Y.; Zhang, Y.; Jiang, S. White-light-emitting hydrogels with self-healing properties and adjustable emission colors. *J. Colloid Interface Sci.* **2021**, *582*, 825−833.

(160) He, X.; Dong, J.; Zhang, X.; Bai, X.; Zhang, C.; Wei, D. Self-Healing, Anti-Fatigue, antimicrobial ionic conductive hydrogels based on Choline-Amino acid polyionic liquids for Multi-Functional sensors. *Chem. Eng. J.* **2022**, *435*, 135168.

(161) Liu, F.; Liu, X.; Gu, H. Multi-Network Poly(β-cyclodextrin)/PVA/Gelatin/Carbon Nanotubes Composite Hydrogels Constructed by Multiple Dynamic Crosslinking as Flexible Electronic Devices. *Macromol. Mater. Eng.* **2022**, *307*, 2100724.

(162) Rabideau, B. D.; Ismail, A. E. Mechanisms of hydrogen bond formation between ionic liquids and cellulose and the influence of water content. *Phys. Chem. Chem. Phys.* **2015**, *17*, 5767−5775.

(163) Gaffney, K. J.; Piletic, I. R.; Fayer, M. D. Hydrogen bond breaking and reformation in alcohol oligomers following vibrational relaxation of a non-hydrogen-bond donating hydroxyl stretch. *J. phys. chem. A* **2002**, *106* (41), 9428−9435.

(164) Steinel, T.; Asbury, J. B.; Zheng, J.; Fayer, M. D. Watching hydrogen bonds break: a transient absorption study of water. *J. Phys. Chem. A* **2004**, *108* (50), 10957−10964.

(165) Zhang, Z.; Li, T.; Chen, B.; Wang, S.; Guo, Z. Self-healing supramolecular hydrogel of poly(vinyl alcohol)/chitosan carbon dots. *J. Mater. Sci.* **2017**, *52* (17), 10614−10623.

(166) Ye, X.; Li, X.; Shen, Y.; Chang, G.; Yang, J.; Gu, Z. Self-healing ph-sensitive cytosine- and guanosine-modified hyaluronic acid hydrogels via hydrogen bonding. *Polymer* **2017**, *108*, 348−360.

(167) Jacob, R. S.; Ghosh, D.; Singh, P. K.; Basu, S. K.; Jha, N. N.; Das, S.; Sukul, P. K.; Patil, S.; Sathaye, S.; Kumar, A.; Chowdhury, A.; Malik, S.; Sen, S.; Maji, S. K. Self healing hydrogels composed of amyloid nano fibrils for cell culture and stem cell differentiation. *Biomaterials* **2015**, *54*, 97.

(168) Abbas, M.; Xing, R.; Zhang, N.; Zou, Q.; Yan, X. Antitumor photodynamic therapy based on dipeptide fibrous hydrogels with incorporation of photosensitive drugs. *ACS Biomater. Sci. Eng.* **2018**, *4* (6), 2046−2052.

(169) Li, Y.; Yan, J.; Liu, Y.; Xie, X.-M. Super Tough and Intelligent Multibond Network Physical Hydrogels Facilitated by Ti_3C_2Tx MXene Nanosheets. *ACS Nano* **2022**, *16* (1), 1567−1577.

(170) Azevedo, S.; Costa, A. M. S.; Andersen, A.; Choi, I. S.; Birkedal, H.; Mano, J. F. Bioinspired Ultratough Hydrogel with Fast Recovery, Self-Healing, Injectability and Cytocompatibility. *Adv. Mater.* **2017**, *29*, 1700759.

(171) Miyamae, K.; Nakahata, M.; Takashima, Y.; Harada, P. Self-healing, expansion−contraction, and shape-memory properties of a preorganized supramolecular hydrogel through host−guest interactions. *Angew. Chem., Int. Ed.* **2015**, *54*, 8984.

(172) Loebel, C. C.; Rodell, B.; Chen, M. H.; Burdick, J. A. Shear-thinning and self-healing hydrogels as injectable therapeutics and for 3D-printing. *Nat. Protocol.* **2017**, *12*, 1521−1541.

(173) Nakahata, M.; Takashima, Y.; Yamaguchi, H.; Harada, A. Redox-responsive self-healing materials formed from host− guest polymers. *Nat. Commun.* **2011**, *2*, 511.

(174) Qu, J.; Zhao, X.; Ma, P. X.; Guo, B. pH-responsive self-healing injectable hydrogel based on N-carboxyethyl chitosan for hepatocellular carcinoma therapy. *Acta Biomater.* **2017**, *58*, 168−180.

(175) Tseng, T. C.; Tao, L.; Hsieh, F. Y.; Wei, Y.; Chiu, I. M.; Hsu, S. h. An injectable, selfhealing hydrogel to repair the central nervous system. *Adv. Mater.* **2015**, *27* (23), 3518−3524.

(176) Ding, F. Y.; Wu, S. P.; Wang, S. S.; Xiong, Y.; Li, Y.; Li, B.; Deng, H. B.; Du, Y. M.; Xiao, L.; Shi, X. W. A dynamic and self-crosslinked polysaccharide hydrogel with autonomous self-healing ability. *Soft Matter* **2015**, *11*, 3971.

(177) Tu, Y.; Chen, N.; Li, C.; Liu, H.; Zhu, R.; Chen, S.; Xiao, Q.; Liu, J.; Ramakrishna, S.; He, L. Advances in injectable self-healing biomedical hydrogels. *Acta Biomater.* **2019**, *90*, 1−20.

(178) Nguyen, R.; Huc, I. Optimizing the reversibility of hydrazone formation for dynamic combinatorial chemistry. *Chem. Commun.* **2003**, *8*, 942−943.

(179) Wei, Z.; Yang, J. H.; Liu, Z. Q.; Xu, F.; Zhou, J. X.; Zrinyi, M.; Osada, Y.; Chen, Y. M. Novel Biocompatible Polysaccharide-Based Self-Healing Hydrogel. *Adv. Funct. Mater.* **2015**, *25*, 1352.

(180) Deng, G.; Tang, C.; Li, F.; Jiang, H.; Chen, Y. Covalent cross-linked polymer gels with reversible sol gel transition self-healing properties. *Macromolecules* **2010**, *43* (3), 1191−1194.

(181) Mckinnon, D. D.; Domaille, D. W.; Cha, J. N.; Anseth, K. S. Biophysically defined and cytocompatible covalently adaptable networks as viscoelastic 3d cell culture systems. *Adv. Mater.* **2014**, *26* (6), 865−872.

(182) Yesilyurt, V.; Webber, M. J.; Appel, E. A.; Godwin, C.; Langer, R.; Anderson, D. G. Injectable self-healing glucose-responsive hydrogels with ph-regulated mechanical properties. *Adv. Mater.* **2016**, *28* (1), 86−91.

(183) Gaballa, H.; Shang, J.; Meier, S.; Theato, P. The glucose-responsive behavior of a block copolymer featuring boronic acid and glycine. *J. Polym. Sci. A Polym. Chem.* **2019**, *57*, 422−431.

(184) Kavitha, A. A.; Singha, N. K. Click Chemistry" in Tailor-Made Polymethacrylates Bearing Reactive Furfuryl Functionality: A New Class of Self-Healing Polymeric Material. *ACS Appl. Mater. Interfaces* **2009**, *1* (7), 1427−1436.

(185) Kirchhof, S.; Brandl, F. P.; Hammer, N.; Goepferich, A. M. Investigation of the diels−alder reaction as a cross-linking mechanism

for degradable poly(ethylene glycol) based hydrogels. *J. Mater. Chem. B* **2013**, *1* (37), 4855−4864.

(186) Lü, S.; Bai, X.; Liu, H.; Ning, P.; Wang, Z.; Gao, C.; Ni, B.; Liu, M. An injectable and self-healing hydrogel with covalent cross-linking in vivo for cranial bone repair. *J. Mater. Chem. B* **2017**, *5* (20), 3739−3748.

(187) Lei, Z. Q.; Xiang, H. P.; Yuan, Y. J.; Rong, M. Z.; Zhang, M. Q. Room-temperature self-healable and remoldable cross-linked polymer based on the dynamic exchange of disulfide bonds. *Chem. Mater.* **2014**, *26* (6), 2038−2046.

(188) Østergaard, H.; Tachibana, C.; Winther, J. R. Monitoring disulfide bond formation in the eukaryotic cytosol. *J. Cell Biol.* **2004**, *166* (3), 337−345.

(189) Li, J.; Wang, J. X.; Li, H. X.; Song, N.; Wang, D.; Tang, B. Z. Supramolecular materials based on AIE luminogens (AIEgens): construction and applications. *Chem. Soc. Rev.* **2020**, *49*, 1144−1172.

(190) Ji, X. F.; Li, Z.; Hu, Y. B.; Xie, H. L.; Wu, W. J.; Song, F. Y.; Liu, H. X.; Wang, J. G.; Jiang, M. J.; Lam, J. W. Y.; Tang, B. Z. Bioinspired hydrogels with muscle-like structure for AIEgen-guided selective self-healing. *CCS Chem.* **2021**, *3*, 1146−1156.

(191) Guaresti, O.; Crocker, L.; Palomares, T.; Alonso-Varona, A.; Eceiza, A.; Fruk, L.; Gabilondo, N. Light-driven assembly of biocompatible fluorescent chitosan hydrogels with self-healing ability. *J. Mater. Chem. B* **2020**, *8*, 9804−9811.

(192) Xie, S. W.; Ren, B. P.; Gong, G.; Zhang, D.; Chen, Y.; Xu, L. J.; Zhang, C. F.; Xu, J. X.; Zheng, J. Lanthanide-doped upconversion nanoparticle-cross-linked double-network hydrogels with strong bulk/interfacial toughness and tunable full-color fluorescence for bioimaging and biosensing. *ACS Appl. Nano Mater.* **2020**, *3*, 2774−2786.

(193) Zhang, Y. D. Y.; Ding, Z. Y.; Liu, Y.; Zhang, Y. P.; Jiang, S. M. Whitelight-emitting hydrogels with self-healing properties and adjustable emission colors. *J. Colloid Interface Sci.* **2021**, *582*, 825−833.

(194) Nie, Y.; Yue, D.; Xiao, W.; Wang, W.; Chen, H.; Bai, L.; Yang, L.; Yang, H.; Wei, D. Anti-freezing and self-healing nanocomposite hydrogels based on poly(vinyl alcohol) for highly sensitive and durable flexible sensors. *Chem. Eng. J.* **2022**, *436*, 135243.

(195) Zhou, Z.; Liu, K.; Ban, Z.; Yuan, W. Highly adhesive, self-healing, anti-freezing and anti-drying organohydrogel with self-power and mechanoluminescence for multifunctional flexible sensor. *Compos. Part A Appl. Sci. Manuf.* **2022**, *154*, 106806.

(196) Wang, J.; Dai, T.; Wu, H.; Ye, M.; Yuan, G.; Jia, H. Tannic acid-Fe^{3+} activated rapid polymerization of ionic conductive hydrogels with high mechanical properties, self-healing, and self-adhesion for flexible wearable sensors. *Compos. Sci. Technol.* **2022**, *221*, 109345.

(197) Wang, Y.; Garcia, C. R.; Ding, Z.; Gabrilska, R.; Rumbaugh, K. P.; Wu, J.; Liu, Q.; Li, W. Adhesive, Self-Healing, and Antibacterial Chitosan Hydrogels with Tunable Two-Layer Structures. *ACS Sustain. Chem. Eng* **2020**, *8*, 18006−18014.

(198) Zheng, H.; Lin, N.; He, Y.; Zuo, B. Self-Healing, Self-Adhesive Silk Fibroin Conductive Hydrogel as a Flexible Strain Sensor. *ACS Appl. Mater. Interfaces* **2021**, *13*, 40013−40031.

(199) Fang, Y.; Xu, J.; Gao, F.; Du, X.; Du, Z.; Cheng, X.; Wang, H. Self-healable and recyclable polyurethane-polyaniline hydrogel toward flexible strain sensor. *Compos. Part B Eng.* **2021**, *219*, 108965.

(200) Hou, K. X.; Zhao, S. P.; Wang, D. P.; Zhao, P. C.; Li, C. H.; Zuo, J. L. A Puncture-Resistant and Self-Healing Conductive Gel for Multifunctional Electronic Skin. *Adv. Funct. Mater.* **2021**, *31*, 2107006.

(201) Zheng, C.; Lu, K.; Lu, Y.; Zhu, S.; Yue, Y.; Xu, X.; Mei, C.; Xiao, H.; Wu, Q.; Han, J. A stretchable, self-healing conductive hydrogels based on nanocellulose supported graphene towards wearable monitoring of human motion. *Carbohydr. Polym.* **2020**, *250*, 116905.

(202) Ge, G.; Lu, Y.; Qu, X.; Zhao, W.; Ren, Y.; Wang, W.; Wang, Q.; Huang, W.; Dong, X. Muscle-Inspired Self-Healing Hydrogels for Strain and Temperature Sensor. *ACS Nano* **2020**, *14*, 218−228.

(203) Luo, J.; Yang, J.; Zheng, X.; Ke, X.; Chen, Y.; Tan, H.; Li, J. A Highly Stretchable, Real-Time Self-Healable Hydrogel Adhesive Matrix for Tissue Patches and Flexible Electronics. *Adv. Healthcare Mater.* **2020**, *9*, 1901423.

(204) Zhou, Z.; Qian, C.; Yuan, W. Self-healing, anti-freezing, adhesive and remoldable hydrogel sensor with ion-liquid metal dual conductivity for biomimetic skin. *Compos. Sci. Technol.* **2021**, *203*, 108608.

(205) Lin, J.-h.; Du, X.-s. Self-healable and redox active hydrogel obtained via incorporation of ferric ion for supercapacitor applications. *Chem. Eng. J.* **2022**, *446*, 137244.

(206) Ma, H.; Lv, F.; Shen, L.; Yang, K.; Jiang, Y.; Ma, J.; Geng, X.; Sun, T.; Pan, Y.; Xie, Z.; Xue, M.; Zhu, N. Self-Healing All-in-One Energy Storage for Flexible Self-Powering Ammonia Smartsensors. *Energy Environ. Mater.* **2022**, *5*, 986−995.

(207) Qin, H.; Liu, P.; Chen, C.; Cong, H. P.; Yu, S. H. A multi-responsive healable supercapacitor. *Nat. Commun.* **2021**, *12*, 4297.

(208) Kim, J.; Kim, J. W.; Kim, S.; Keum, K.; Park, J.; Jeong, Y. R.; Jin, S. W.; Ha, J. S. Stretchable, self-healable, and photodegradable supercapacitor based on a polyelectrolyte crosslinked via dynamic host-guest interaction. *Chem. Eng. J.* **2021**, *422*, 130121.

(209) Zhu, K.-h.; Han, X.-d.; Ye, S.-f.; Cui, P.-x.; Dou, L.-y.; Ma, W.-b.; Heng, S.; Tao, X.-y.; Wei, X.-y Flexible all-in-one supercapacitors enabled by self-healing and anti-freezing polymer hydrogel electrolyte. *J. Energy Storage* **2022**, *53*, 105096.

(210) Ji, G.; Hu, R.; Wang, Y.; Zheng, J. High energy density, flexible, low temperature resistant and self-healing Zn-ion hybrid capacitors based on hydrogel electrolyte. *J. Energy Storage* **2022**, *46*, 103858.

(211) Zou, Y.; Chen, C.; Sun, Y.; Gan, S.; Dong, L.; Zhao, J.; Rong, J. Flexible, all-hydrogel supercapacitor with self-healing ability. *Chem. Eng. J.* **2021**, *418*, 128616.

(212) Liu, J.; Huang, J.; Cai, Q.; Yang, Y.; Luo, W.; Zeng, B.; Xu, Y.; Yuan, C.; Dai, L. Design of Slidable Polymer Networks: A Rational Strategy to Stretchable, Rapid Self-Healing Hydrogel Electrolytes for Flexible Supercapacitors. *ACS Appl. Mater. Interfaces* **2020**, *12*, 20479−20489.

(213) Zhao, J.; Gong, J.; Wang, G.; Zhu, K.; Ye, K.; Yan, J.; Cao, D. A self-healing hydrogel electrolyte for flexible solid-state supercapacitors. *Chem. Eng. J.* **2020**, *401*, 125456.

(214) Peng, H.; Gao, X.; Sun, K.; Xie, X.; Ma, G.; Zhou, X.; Lei, Z. Physically cross-linked dual-network hydrogel electrolyte with high self-healing behavior and mechanical strength for wide-temperature tolerant flexible supercapacitor. *Chem. Eng. J.* **2021**, *422*, 130353.

(215) Liu, C.; Wang, X.; Zhang, H. J.; You, X.; Yue, O. Self-Healable, High-Strength Hydrogel Electrode for Flexible Sensors and Supercapacitors. *ACS Appl. Mater. Interfaces* **2021**, *13*, 36240−36252.

(216) Cao, X.; Liu, H.; Yang, X.; Tian, J.; Luo, B.; Liu, M. Halloysite nanotubes@polydopamine reinforced polyacrylamide-gelatin hydrogels with NIR light triggered shape memory and self-healing capability. *Compos. Sci. Technol.* **2020**, *191*, 108071.

(217) Liu, T.; Wang, F.; Wu, Q.; Chen, T.; Sun, P. Fluorescent, electrically responsive and ultratough self-healing hydrogels via bioinspired all-in-one hierarchical micelles. *Mater. Horiz.* **2021**, *8*, 3096−3104.

(218) Xue, S.; Wu, Y.; Liu, G.; Guo, M.; Liu, Y.; Zhang, T.; Wang, Z. Hierarchically reversible crosslinking polymeric hydrogels with highly efficient self-healing, robust mechanical properties, and double-driven shape memory behavior. *J. Mater. Chem. A* **2021**, *9*, 5730−5739.

(219) Liang, Y.; Wang, K.; Li, J.; Zhang, Y.; Liu, J.; Zhang, K.; Cui, Y.; Wang, M.; Liu, C. S. Low-molecular-weight supramolecular adhesives based on non-covalent self-assembly of a small molecular gelator. *Mater. Horiz.* **2022**, *9*, 1700−1707.

(220) Ge, G.; Zhang, Y. Z.; Zhang, W.; Yuan, W.; El-Demellawi, J. K.; Zhang, P.; Di Fabrizio, E.; Dong, X.; Alshareef, H. N. Ti_3C_2Tx MXene-Activated Fast Gelation of Stretchable and Self-Healing Hydrogels: A Molecular Approach. *ACS Nano* **2021**, *15*, 2698−2706.

(221) Xu, Y.; Lu, G.; Chen, M.; Wang, P.; Li, Z.; Han, X.; Liang, J.; Sun, Y.; Fan, Y.; Zhang, X. Redox and pH dual-responsive injectable hyaluronan hydrogels with shape-recovery and self-healing properties for protein and cell delivery. *Carbohydr. Polym.* **2020**, *250*, 116979.

(222) Miao, Y.; Xu, M.; Zhang, L. Electrochemistry-Induced Improvements of Mechanical Strength, Self-Healing, and Interfacial Adhesion of Hydrogels. *Adv. Mater.* **2021**, *33*, 2102308.

(223) Lin, S.-H.; Papadakis, C. M.; Kang, J.-J.; Lin, J.-M.; Hsu, S.-h. Injectable Phenolic-Chitosan Self-Healing Hydrogel with Hierarchical Micelle Architectures and Fast Adhesiveness. *Chem. Mater.* **2021**, *33* (11), 3945−3958.

(224) Zhou, L.; Dai, C.; Fan, L.; Jiang, Y.; Liu, C.; Zhou, Z.; Guan, P.; Tian, Y.; Xing, J.; Li, X.; et al. Injectable Self-Healing Natural Biopolymer-Based Hydrogel Adhesive with Thermoresponsive Reversible Adhesion for Minimally Invasive Surgery. *Adv. Funct. Mater.* **2021**, *31* (14), 2007457.

(225) Wang, N.; Yu, K. K.; Li, K.; Li, M. J.; Wei, X.; Yu, X. Q. Plant-Inspired Multifunctional Fluorescent Hydrogel: A Highly Stretchable and Recoverable Self-Healing Platform with Water-Controlled Adhesiveness for Highly Effective Antibacterial Application and Data Encryption-Decryption. *ACS Appl. Mater. Interfaces* **2020**, *12*, 57686−57694.

(226) Lee, J. H.; Lee, D. S.; Jung, Y. C.; Oh, J. W.; Na, Y. H. Development of a Tough, Self-Healing Polyampholyte Terpolymer Hydrogel Patch with Enhanced Skin Adhesion via Tuning the Density and Strength of Ion-Pair Associations. *ACS Appl. Mater. Interfaces* **2021**, *13*, 8889−8900.

(227) Guo, S.; Ren, Y.; Chang, R.; He, Y.; Zhang, D.; Guan, F.; Yao, M. Injectable Self-Healing Adhesive Chitosan Hydrogel with Antioxidative, Antibacterial, and Hemostatic Activities for Rapid Hemostasis and Skin Wound Healing. *ACS Appl. Mater. Interfaces* **2022**, *14*, 34455−34469.

(228) Zhang, X.; Tan, B.; Wu, Y.; Zhang, M.; Xie, X.; Liao, J. An injectable, self-healing carboxymethylated chitosan hydrogel with mild photothermal stimulation for wound healing. *Carbohydr. Polym.* **2022**, *293*, 119722.

(229) Deng, P.; Chen, F.; Zhang, H.; Chen, Y.; Zhou, J. Conductive, Self-Healing, Adhesive, and Antibacterial Hydrogels Based on Lignin/Cellulose for Rapid MRSA-Infected Wound Repairing. *ACS Appl. Mater. Interfaces* **2021**, *13*, 52333−52345.

(230) Li, S.; Dong, Q.; Peng, X.; Chen, Y.; Yang, H.; Xu, W.; Zhao, Y.; Xiao, P.; Zhou, Y. Self-Healing Hyaluronic Acid Nanocomposite Hydrogels with Platelet-Rich Plasma Impregnated for Skin Regeneration. *ACS Nano* **2022**, *16* (7), 11346−11359.

(231) Li, M.; Liang, Y.; Liang, Y.; Pan, G.; Guo, B. Injectable stretchable self-healing dual dynamic network hydrogel as adhesive anti-oxidant wound dressing for photothermal clearance of bacteria and promoting wound healing of MRSA infected motion wounds. *Chem. Eng. J.* **2022**, *427*, 132039.

(232) Qiu, W.; Han, H.; Li, M.; Li, N.; Wang, Q.; Qin, X.; Wang, X.; Yu, J.; Zhou, Y.; Li, Y.; Li, F.; Wu, D. Nanofibers reinforced injectable hydrogel with self-healing, antibacterial, and hemostatic properties for chronic wound healing. *J. Colloid Interface Sci.* **2021**, *596*, 312−323.

(233) Cao, J.; Wu, P.; Cheng, Q.; He, C.; Chen, Y.; Zhou, J. Ultrafast Fabrication of Self-Healing and Injectable Carboxymethyl Chitosan Hydrogel Dressing for Wound Healing. *ACS Appl. Mater. Interfaces* **2021**, *13*, 24095−24105.

(234) Yuan, Y.; Shen, S.; Fan, D. A physicochemical double cross-linked multifunctional hydrogel for dynamic burn wound healing: shape adaptability, injectable self-healing property and enhanced adhesion. *Biomaterials* **2021**, *276*, 120838.

(235) Zou, C. Y.; Lei, X. X.; Hu, J. J.; Jiang, Y. L.; Li, Q. J.; Song, Y. T.; Zhang, Q. Y.; Li-Ling, J.; Xie, H. Q. Multi-crosslinking hydrogels with robust bio-adhesion and pro-coagulant activity for first-aid hemostasis and infected wound healing. *Bioact. Mater.* **2022**, *16*, 388−402.

(236) Qian, Z.; Wang, H.; Bai, Y.; Wang, Y.; Tao, L.; Wei, Y.; Fan, Y.; Guo, X.; Liu, H. Improving Chronic Diabetic Wound Healing through an Injectable and Self-Healing Hydrogel with Platelet-Rich Plasma Release. *ACS Appl. Mater. Interfaces* **2020**, *12*, 55659−55674.

(237) Song, X.; Wang, X.; Zhang, J.; Shen, S.; Yin, W.; Ye, G.; Wang, L.; Hou, H.; Qiu, X. A tunable self-healing ionic hydrogel with microscopic homogeneous conductivity as a cardiac patch for myocardial infarction repair. *Biomaterials* **2021**, *273*, 120811.

(238) Wang, W.; Zeng, Z.; Xiang, L.; Liu, C.; Diaz-Dussan, D.; Du, Z.; Asha, A. B.; Yang, W.; Peng, Y. Y.; Pan, M.; Narain, R.; Liu, J.; Zeng, H. Injectable Self-Healing Hydrogel via Biological Environment-Adaptive Supramolecular Assembly for Gastric Perforation Healing. *ACS Nano* **2021**, *15*, 9913−9923.

(239) Kim, Y.; Hu, Y.; Jeong, J. P.; Jung, S. Injectable, self-healable and adhesive hydrogels using oxidized Succinoglycan/chitosan for pH-responsive drug delivery. *Carbohydr. Polym.* **2022**, *284*, 119195.

(240) Mondal, P.; Chatterjee, K. Injectable and self-healing double network polysaccharide hydrogel as a minimally-invasive delivery platform. *Carbohydr. Polym.* **2022**, *291*, 119585.

(241) Guo, H.; Huang, S.; Yang, X.; Wu, J.; Kirk, T. B.; Xu, J.; Xu, A.; Xue, W. Injectable and Self-Healing Hydrogels with Double-Dynamic Bond Tunable Mechanical, Gel-Sol Transition and Drug Delivery Properties for Promoting Periodontium Regeneration in Periodontitis. *ACS Appl. Mater. Interfaces* **2021**, *13*, 61638−61652.

(242) Pandit, A. H.; Nisar, S.; Imtiyaz, K.; Nadeem, M.; Mazumdar, N.; Rizvi, M. M. A.; Ahmad, S. Injectable, Self-Healing, and Biocompatible N,O-Carboxymethyl Chitosan/Multialdehyde Guar Gum Hydrogels for Sustained Anticancer Drug Delivery. *Biomacromolecules* **2021**, *22*, 3731−3745.

(243) Yang, X.; Yang, H.; Jiang, X.; Yang, B.; Zhu, K.; Lai, N. C.; Huang, C.; Chang, C.; Bian, L.; Zhang, L. Injectable chitin hydrogels with self-healing property and biodegradability as stem cell carriers. *Carbohydr. Polym.* **2021**, *256*, 117574.

(244) Li, P.; Sui, Y.; Dai, X.; Fang, Q.; Sima, H.; Zhang, C. Dynamic Tannic Acid Hydrogel with Self-Healing and pH Sensitivity for Controlled Release. *Macromol. Biosci.* **2021**, *21*, e2100055.

(245) Basu, S.; Pacelli, S.; Paul, A. Self-healing DNA-based injectable hydrogels with reversible covalent linkages for controlled drug delivery. *Acta Biomater.* **2020**, *105*, 159−169.

(246) Wu, M.; Chen, J.; Huang, W.; Yan, B.; Peng, Q.; Liu, J.; Chen, L.; Zeng, H. Injectable and Self-Healing Nanocomposite Hydrogels with Ultrasensitive pH-Responsiveness and Tunable Mechanical Properties: Implications for Controlled Drug Delivery. *Biomacromolecules* **2020**, *21*, 2409−2420.

(247) Pan, R.; Liu, G.; Zeng, Y.; He, X.; Ma, Z.; Wei, Y.; Chen, S.; Yang, L.; Tao, L. A multi-responsive self-healing hydrogel for controlled release of curcumin. *Polym. Chem.* **2021**, *12*, 2457−2463.

(248) Qi, Y.; Qian, Z.; Yuan, W.; Li, Z. Injectable and self-healing nanocomposite hydrogel loading needle-like nano-hydroxyapatite and graphene oxide for synergistic tumour proliferation inhibition and photothermal therapy. *J. Mater. Chem. B* **2021**, *9*, 9734−9743.

(249) Guedes, G.; Wang, S.; Fontana, F.; Figueiredo, P.; Linden, J.; Correia, A.; Pinto, R. J. B.; Hietala, S.; Sousa, F. L.; Santos, H. A. Dual-Crosslinked Dynamic Hydrogel Incorporating {Mo154} with pH and NIR Responsiveness for Chemo-Photothermal Therapy. *Adv. Mater.* **2021**, *33*, e2007761.

(250) Wang, C.; Zhao, N.; Huang, Y.; He, R.; Xu, S.; Yuan, W. Coordination of injectable self-healing hydrogel with Mn-Zn ferrite@mesoporous silica nanospheres for tumor MR imaging and efficient synergistic magnetothermal-chemo-chemodynamic therapy. *Chem. Eng. J.* **2020**, *401*, 126100.

(251) Hou, Y.; Song, Y.; Sun, X.; Jiang, Y.; He, M.; Li, Y.; Chen, X.; Zhang, L. Multifunctional composite hydrogel bolus with combined self-healing, antibacterial and adhesive functions for radiotherapy. *J. Mater. Chem. B* **2020**, *8*, 2627−2635.

(252) An, H.; Yang, Y.; Zhou, Z.; Bo, Y.; Wang, Y.; He, Y.; Wang, D.; Qin, J. Pectin-based injectable and biodegradable self-healing hydrogels for enhanced synergistic anticancer therapy. *Acta Biomater.* **2021**, *131*, 149−161.

(253) Chen, R.; Zhu, C.; Xu, L.; Gu, Y.; Ren, S.; Bai, H.; Zhou, Q.; Liu, X.; Lu, S.; Bi, X.; Li, W.; Jia, X.; Chen, Z. An injectable peptide hydrogel with excellent self-healing ability to continuously release salvianolic acid B for myocardial infarction. *Biomaterials* **2021**, *274*, 120855.

(254) Wang, M.; Chen, M.; Niu, W.; Winston, D. D.; Cheng, W.; Lei, B. Injectable biodegradation-visual self-healing citrate hydrogel with high tissue penetration for microenvironment-responsive degradation and local tumor therapy. *Biomaterials* **2020**, *261*, 120301.

(255) Zeng, Y.; Zhang, C.; Du, D.; Li, Y.; Sun, L.; Han, Y.; He, X.; Dai, J.; Shi, L. Metal-organic framework-based hydrogel with structurally

dynamic properties as a stimuli-responsive localized drug delivery system for cancer therapy. *Acta Biomater* **2022**, *145*, 43−51.

(256) Hou, Y.; Song; Sun, X.; Jiang, Y.; He, M.; Li, Y.; Chen, X.; Zhang, L. Multifunctional composite hydrogel bolus with combined self-healing, antibacterial and adhesive functions for radiotherapy. *J. Mater. Chem. B* **2020**, *8*, 2627−2635.

(257) Wang, C.; Zhao, N.; Yuan, W. NIR/Thermoresponsive Injectable Self-Healing Hydrogels Containing Polydopamine Nanoparticles for Efficient Synergistic Cancer Thermochemotherapy. *ACS Appl. Mater. Interfaces* **2020**, *12*, 9118−9131.

(258) Wang, Z.; Cui, H.; Liu, M.; Grage, S. L.; Hoffmann, M.; Sedghamiz, E.; Wenzel, W.; Levkin, P. A. Tough, Transparent, 3D-Printable, and Self-Healing Poly(ethylene glycol)-Gel (PEGgel). *Adv. Mater.* **2022**, *34*, e2107791.

(259) Kadumudi, F. B.; Hasany, M.; Pierchala, M. K.; Jahanshahi, M.; Taebnia, N.; Mehrali, M.; Mitu, C. F.; Shahbazi, M. A.; Zsurzsan, T. G.; Knott, A.; Andresen, T. L.; Dolatshahi-Pirouz, A. The Manufacture of Unbreakable Bionics via Multifunctional and Self-Healing Silk-Graphene Hydrogels. *Adv. Mater.* **2021**, *33*, e2100047.

(260) Wu, Y.; Zeng, Y.; Chen, Y.; Li, C.; Qiu, R.; Liu, W. Photocurable 3D Printing of High Toughness and Self-Healing Hydrogels for Customized Wearable Flexible Sensors. *Adv. Funct. Mater.* **2021**, *31*, 2107202.

(261) Liu, Y.; Wong, C. W.; Chang, S. W.; Hsu, S. H. An injectable, self-healing phenol-functionalized chitosan hydrogel with fast gelling property and visible light-crosslinking capability for 3D printing. *Acta Biomater.* **2021**, *122*, 211−219.

(262) Chen, H.; Fei, F.; Li, X.; Nie, Z.; Zhou, D.; Liu, L.; Zhang, J.; Zhang, H.; Fei, Z.; Xu, T. A structure-supporting, self-healing, and high permeating hydrogel bioink for establishment of diverse homogeneous tissue-like constructs. *Bioact. Mater.* **2021**, *6*, 3580−3595.

(263) Caprioli, M.; Roppolo, I.; Chiappone, A.; Larush, L.; Pirri, C. F.; Magdassi, S. 3D-printed self-healing hydrogels via Digital Light Processing. *Nat. Commun.* **2021**, *12*, 2462.

(264) Maiz-Fernandez, S.; Barroso, N.; Perez-Alvarez, L.; Silvan, U.; Vilas-Vilela, J. L.; Lanceros-Mendez, S. 3D printable self-healing hyaluronic acid/chitosan polycomplex hydrogels with drug release capability. *Int. J. Biol. Macromol.* **2021**, *188*, 820−832.

(265) Wang, Z.; An, G.; Zhu, Y.; Liu, X.; Chen, Y.; Wu, H.; Wang, Y.; Shi, X.; Mao, C. 3D-printable self-healing and mechanically reinforced hydrogels with host-guest non-covalent interactions integrated into covalently linked networks. *Mater. Horiz.* **2019**, *6*, 733−742.

(266) Wei, J.; Xie, J.; Zhang, P.; Zou, Z.; Ping, H.; Wang, W.; Xie, H.; Shen, J. Z.; Lei, L.; Fu, Z. Bioinspired 3D Printable, Self-Healable, and Stretchable Hydrogels with Multiple Conductivities for Skin-like Wearable Strain Sensors. *ACS Appl. Mater. Interfaces* **2021**, *13*, 2952−2960.

(267) Diaz-Gomez, L.; Gonzalez-Prada, I.; Millan, R.; Da Silva-Candal, A.; Bugallo-Casal, A.; Campos, F.; Concheiro, A.; Alvarez-Lorenzo, C. 3D printed carboxymethyl cellulose scaffolds for autologous growth factors delivery in wound healing. *Carbohydr. Polym.* **2022**, *278*, 118924.

(268) Kajtez, J.; Wesseler, M. F.; Birtele, M.; Khorasgani, F. R.; Rylander Ottosson, D.; Heiskanen, A.; Kamperman, T.; Leijten, J.; Martinez-Serrano, A.; Larsen, N. B.; Angelini, T. E.; Parmar, M.; Lind, J. U.; Emneus, J. Embedded 3D Printing in Self-Healing Annealable Composites for Precise Patterning of Functionally Mature Human Neural Constructs. *Adv. Sci.* **2022**, *9*, e2201392.

(269) Wang, C.; Honiball, J. R.; Lin, J.; Xia, X.; Lau, D. S. A.; Chen, B.; Deng, L.; Lu, W. W. Infiltration from Suspension Systems Enables Effective Modulation of 3D Scaffold Properties in Suspension Bioprinting. *ACS Appl. Mater. Interfaces* **2022**, *14*, 27575−27588.

(270) Daly, A. C.; Davidson, M. D.; Burdick, J. A. 3D bioprinting of high cell-density heterogeneous tissue models through spheroid fusion within self-healing hydrogels. *Nat. Commun.* **2021**, *12*, 753.