

Review

Skin-like hydrogel devices for wearable sensing, soft robotics and beyond

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SUMMARY

Skin-like electronics are developing rapidly to realize a variety of applications such as wearable sensing and soft robotics. Hydrogels, as soft biomaterials, have been studied intensively for skin-like electronic utilities due to their unique features such as softness, wetness, biocompatibility and ionic sensing capability. These features could potentially blur the gap between soft biological systems and hard artificial machines. However, the development of skin-like hydrogel devices is still in its infancy and faces challenges including limited functionality, low ambient stability, poor surface adhesion, and relatively high power consumption (as ionic sensors). This review aims to summarize current development of skin-inspired hydrogel devices to address these challenges. We first conduct an overview of hydrogels and existing strategies to increase their toughness and conductivity. Next, we describe current approaches to leverage hydrogel devices with advanced merits including anti-dehydration, anti-freezing, and adhesion. Thereafter, we highlight state-of-the-art skin-like hydrogel devices for applications including wearable electronics, soft robotics, and energy harvesting. Finally, we conclude and outline the future trends.

INTRODUCTION

The skin is the largest organ of human body and serves as the first physical, thermal, and hygroscopic barrier between the external environment and the body's internal components. Importantly, the skin contains the largest amount of sensing receptors to perceive various environmental stimuli that humans encounter, such as pressure, strain, humidity, temperature, and pain (Figure 1A). To date, tremendous skin-inspired flexible and stretchable devices have been developed based on our understanding of the human skin's sensing functions (Benight et al., 2013; Cheng et al., 2019; Kim et al., 2011a, 2011b, 2016a; Lei and Wu, 2018; Liang et al., 2013; Lipomi et al., 2011; Oh et al., 2016; Pelrine et al., 2000; Sekitani et al., 2008, 2009; Sun et al., 2006, 2014; Ying et al., 2020a, 2020c, 2021b, 2021c; Yu et al., 2020d; Zang et al., 2013). These advances have revolutionized wearable electronics and other related fields. Current skin-like wearable devices have already been used for personal health monitoring [e.g., detection of glucose, uric acid, lactose, heart rate, blood pressure, ion levels, stress level, strain, tactile, temperature, humidity (Trung and Lee, 2016; Xu et al., 2020; Yu et al., 2020b)], for communication between humans and devices [e.g., human-machine interfaces (Wang et al., 2018a)], and for wearable robotic assistance [e.g., exosuits and artificial prosthetics (Mengüç et al., 2014; Zhao et al., 2016)]. On the other hand, next-generation soft robotics requires a variety of stretchable sensors to be 'worn' on soft-bodied robots for sensing and perception during interaction with their surroundings, where the sensing capability of skin-like electronics will be highly useful to improve the soft robot designs (Shih et al., 2020). Because of the inherent material match and functional complementarity between the skin-like devices and soft robots, there have been significant efforts to develop skin-like stretchable and wearable sensors for integration with soft robotic systems. Biological (Justus et al., 2019), optical (Larson et al., 2016; Zhao et al., 2016), strain (Kim et al., 2020c), and tactile (Booth et al., 2018; Thuruethel et al., 2019) sensing capabilities have been embedded into soft robots to enable them to interact with their users and the environment more intelligently.

Among various materials for constructing skin-like devices, stretchable and tough ionic hydrogel is one of the most suitable candidates. Hydrogel mimics multiple properties and functions of biological systems, such as their superior softness and hydration, excellent material biocompatibility, and unique ionic sensing functions (Bao et al., 2020; Lee et al., 2018a; Sheng et al., 2019; Yang and Suo, 2018). In addition, their tunable mechanical properties with on-demand design of toughness, stretchability, and elasticity can

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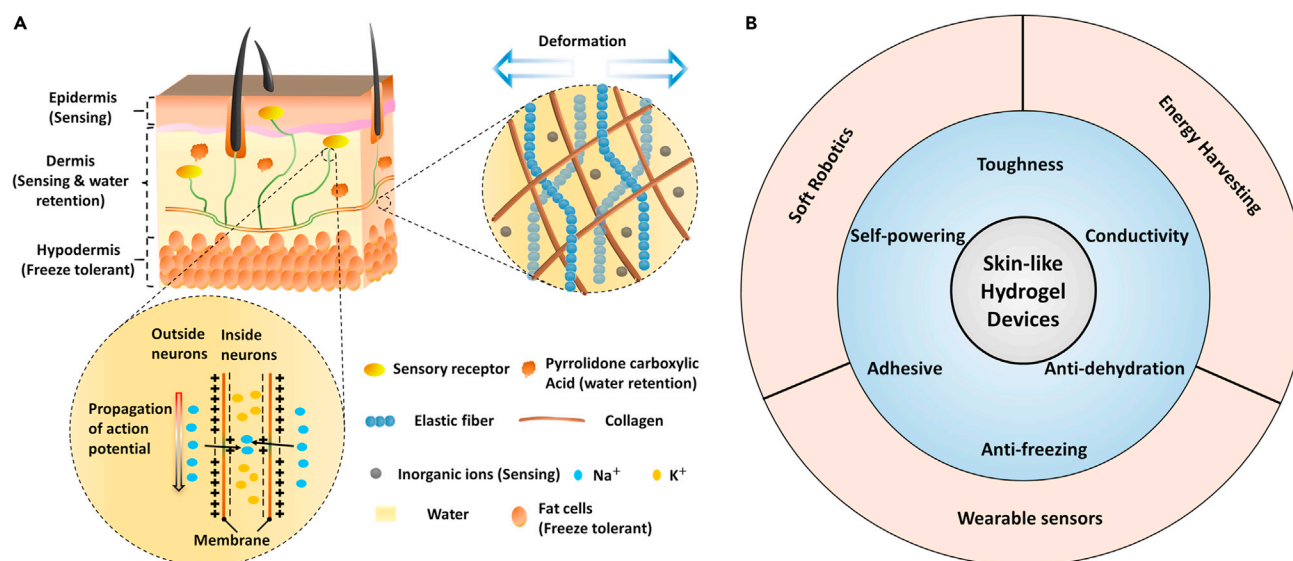


Figure 1. Skin-like hydrogel devices

(A) Schematic of the human skin that resists physical deformation due to the elastin fiber and collagen in the dermis layer, maintains the body temperature due to the fat cells in the hypodermis layer, holds water due to the hygroscopic substance (i.e., pyrrolidone carboxylic acid), and transports ionic signal directionally within sensory neurons.

(B) Main features of hydrogels (e.g., toughness, ionic conductivity, anti-dehydration, anti-freezing, adhesive, and self-powering) desired for practical use as wearable sensors, soft robotics and energy harvesting devices.

accommodate the diverse mechanical properties of substrates the hydrogel devices will be mounted on (e.g., cloth, skin, soft robot body, and tissue). Thus, hydrogels could potentially reduce the mechanical, electrical, and/or biological mismatches between soft-robotic/human bodies and traditional electrical counterparts (Yuk et al., 2019a). So far, a variety of hydrogel-based, skin-like devices have been developed for applications including wearable sensing, soft robotic sensing, and energy harvesting (Figure 1B). These devices are capable of transducing touch, pressure, deformation, humidity, and temperature inputs into changes of electrical signals (e.g., capacitance, resistance, open circuit voltage [OCV], and short circuit current [SCC]), thus mimicking the sensing functions of the natural skin.

The development of hydrogel devices, however, is still in the early stage and facing many challenges. For example, most existing hydrogel devices have limited functionality to sense only one stimulus. As a sensing component, they usually require external power supplies. In addition, hydrogel devices are not stable during open-air operations, and cannot maintain mechanical deformability and electrical conductivity in cold environments. Moreover, conventional hydrogels usually have poor adhesive capability and cannot ensure firm adherence to substrates of different materials (e.g., human skins, fabric clothes, and elastomers), limiting the fidelity of signals acquisition during wearable and soft robotic sensing under various conditions (e.g., dry and wet surfaces, sweaty skin, subzero temperature, and dynamic deformation and movement). Therefore, in this review we primarily aim to summarize the current strategies that address these challenges for those real-world applications.

There have been several reviews on hydrogel materials and their device applications, which focus their toughening mechanism (Chen et al., 2015; Gong, 2010; Peak et al., 2013; Zhao, 2014), enhanced environment adaptability (Zhou et al., 2019), adhesive mechanism (Peak et al., 2013; Yang et al., 2020), bio-electronics (Yuk et al., 2019a), ionotronics (Yang and Suo, 2018), and soft machines (Liu et al., 2020d). This review will put an emphasis on the state-of-the-art skin-like ionic hydrogel devices with specific features for emerging application areas such as wearable electronics, soft robotics, and energy harvesting. We start with a brief introduction to the fundamentals of hydrogel and strategies to increase its toughness and conductivity. Thereafter, we review recent advances of ionically conductive hydrogel devices with advanced merits such as anti-dehydration, anti-freezing, and adhesion. Then, we summarize state-of-the-art applications of skin-like hydrogel devices for wearable electronics, soft robotics, and some other important applications such as energy harvesting. Finally, we conclude with a perspective discussion on

the remaining challenges and opportunities, and also propose a number of future directions in the field. We hope this review will bring new insights on how to design new types of hydrogel devices for seamless merging of humans, wearables, and robots.

OVERVIEW OF HYDROGEL-BASED MATERIALS

Hydrogel is defined as a class of three-dimensional (3D) hydrophilic polymer networks infiltrated with high water content. Natural hydrogels exist in most soft tissues of animals and plants. With hundreds of millions of years of evolution, soft tissues have achieved many key features to enable sophisticated functions in nature due to their water-containing and elaborate structures (Fan and Gong, 2020). For example, there are a variety of soft tissues in our human bodies made of natural hydrogels containing 60–90 wt% water, ranging from tendons, muscles, cartilages, and skin (tough and strong) to mucosa, extracellular matrix, axon, and brain (brittle and weak) (Fan and Gong, 2020; McGurk, 2013; Liu et al., 2020d; Zhao, 2014). On the other hand, inspired by nature, people have been exploring the artificial counterparts of natural hydrogels to mimic both their structures and functions since the birth of synthetic hydrogels in 1960 (Fan and Gong, 2020; Wichterle and Lim, 1960).

Currently, synthetic hydrogels (here simply termed as hydrogels) possess tunable chemical, mechanical, and electrical properties and behave uniquely like both solids and fluids (Zhang and Khademhosseini, 2017). Thus, hydrogels have been widely explored for various applications including drug delivery (Drury and Mooney, 2003), ophthalmology (Dong et al., 2006; Kopeček, 2009), wound dressing (Drury and Mooney, 2003; Hakkarainen et al., 2016), and tissue engineering (Drury and Mooney, 2003; Lee and Mooney, 2001; Peppas and Merrill, 1977). In addition, hydrogels can respond (mainly in the form of volume swelling and shrinking) under different stimuli [e.g., light (Takashima et al., 2012), temperature (Yoshida et al., 1995), pH (Shastri et al., 2015), and ionic strength (He et al., 2012)], which has been utilized for sensing and actuation (Calvert, 2008, 2009; Gong, 2006; Osada and Gong, 1998; Peppas et al., 2006). However, conventional hydrogels (e.g., single-network [SN] hydrogels) are usually soft, weak, and brittle, and have limited stretchability (<100%), low elastic moduli (~10 kPa), and small fracture energy (0.1–10 J/m²) (Chen et al., 2015; Gong, 2010; Zhang and Khademhosseini, 2017). They are prone to permanent breakage, hindering their potential applications requiring high mechanical toughness or stretchability (e.g., artificial load-bearing bio-tissues, wearable electronics, and soft robotics). Therefore, novel hydrogels with enhanced mechanical properties need to be designed. In addition, most pristine synthetic hydrogels have relatively low electrical conductivity because of the low-concentration mobile ions in its water contents. Therefore, empowering hydrogels with superior conductivity is essential for applications such as wearable and soft robotic sensing. In this section, we briefly introduce fundamentals to toughen hydrogel. Then, we introduce several general strategies for designing ionically conductive hydrogels.

Tough hydrogel and its double-network format

Over the last two decades, significant efforts have been made to improve the mechanical strength and fracture toughness of conventional hydrogels, broadening their biomedical applications. The fracture toughness is defined as the energy per unit area required to make a notched crack propagate (Gong, 2014). Typical hydrogel toughening strategies include: topological hydrogels with slide-ring cross-linking points (Fleury et al., 2007; Ito, 2007, 2010; Okumura and Ito, 2001; Peppas and Merrill, 1976), hydrogels cross-linked with nanocomposite or macromolecular microsphere composites (Aouada et al., 2011; Gao et al., 2014; Haraguchi, 2007; Haraguchi and Li, 2005, 2006; Haraguchi and Takehisa, 2002; Haraguchi et al., 2002; Huang et al., 2007; Liu et al., 2012; Miyazaki et al., 2007; Wang et al., 2010), double-network (DN) hydrogels (Berger et al., 2004; Gong et al., 2003; Sun et al., 2012; Ying et al., 2020a), tetra-arm polyethylene glycol (PEG) hydrogels (Sakai et al., 2008, 2010), hydrogels cross-linked by strong cooperative hydrogen bonding (Song et al., 2013), hydrogels enhanced with physical interactions (Bai et al., 2011; Li et al., 2012; Tuncaboylu et al., 2012; Zhang et al., 2015b), hydrogels with hybrid chemical and physical cross-linkers (Berger et al., 2004; Henderson et al., 2010; Kersey et al., 2007; Kong et al., 2003; Sun et al., 2012, 2013), and hydrogels with crystalline or transformable domains (Brown et al., 2009; Peppas and Merrill, 1977; Stauffer and Peppas, 1992). Readers can refer to recent review articles that have summarized the progress of tough hydrogels, including their preparation, mechanical properties, toughening mechanisms, and applications (Chen et al., 2015; Gong, 2010; Nonoyama and Gong, 2015; Peak et al., 2013; Wang et al., 2020c; Zhang and Khademhosseini, 2017; Zhao, 2014). In this section, we focus on one specific tough hydrogel—DN hydrogel, because of its high popularity and unique properties. For instance, the DN hydrogel

Table 1. Mechanical properties of existing DN hydrogels

Water content	~90%
Tensile fracture strain	1000–2000%
Elastic modulus	0.1–10 MPa
Fracture toughness	100–16,000 J/m ²
Failure compressive nominal stress	20–60 MPa
Compressive fracture stain	90%–95%

has achieved one of the highest mechanical performance (e.g., fracture toughness) so far (Haque et al., 2012).

DN hydrogel has received tremendous attention since it was first developed by Gong et al. in 2003 with a fracture toughness of over 1000 J/m² (Gong et al., 2003), in which monomers are subsequently polymerized into two networks in the presence of cross-linkers via a two-step synthesis method. Later on, Sun et al. (2012) further enhanced the fracture toughness of DN hydrogel by at least one order of magnitude. The synthesis details about this remarkable work will be highlighted in the following paragraph. By the classical definition, DN hydrogel consists of two polymer networks with strong asymmetric structures and contrasting properties such as network density, rigidity, molecular weight, cross-linking density, and so on (Gong et al., 2003; Haque et al., 2012; Nonoyama and Gong, 2015). In general, material selection of the two networks can be from the same or different polymer systems (Haque et al., 2012; Nonoyama and Gong, 2015). In terms of structure, DN hydrogel is a type of gel that has a very specific structure of two interpenetrating polymer networks (IPN). The first network is densely cross-linked and is stiff, rigid yet brittle, and the second network is sparsely cross-linked and is soft, stretchable and ductile. The molar concentration of the second network is usually tens of times that of the first network (Ahmed et al., 2014; Gong et al., 2003; Haque et al., 2012; Matsuda et al., 2019; Nonoyama and Gong, 2015).

In principle, any hydrogel possessing IPN structures can be regarded as a DN hydrogel; however, the DN hydrogels with the contrasting network structures and properties make them quite different from the conventional IPN system (Haque et al., 2012). Compared with SN hydrogels, the DN hydrogels are much tougher due to a synergistic effect of their binary structures rather than a linear combination of two SN components (Philippova et al., 1998). Currently, the widely accepted explanation of this high mechanical fracture toughness is that the first network serves as sacrificial bonds by breaking into small clusters during deformation, which can efficiently disperse the stress around the crack tip into the surrounding damage zone, while the long polymer chains of the second network effectively store a large amount of elastic energy from the mechanical load before the fracture takes place (Haque et al., 2012). In other words, the strong mechanical toughness is largely attributed to the effective de-concentration of locally applied stress and dissipation of the crack energy through combinations of two networks with different structures and densities (Gong et al., 2003). In addition, strong network entanglement and chain interaction could contribute to the enhanced toughness of DN hydrogel as well (Chen et al., 2015). The toughness can be tuned through adjusting the synthesis parameters including the molar ratio between the first and second networks, their cross-linking densities (Gong et al., 2003), and the lengths of the polymer chains (Li et al., 2014). DN hydrogels show excellent mechanical properties, which have been summarized into Table 1 (Chen et al., 2015; Gong, 2010; Nonoyama and Gong, 2015; Philippova et al., 1998; Zhang and Khademhosseini, 2017). For example, containing high water content (~90 wt%), DN hydrogels provides 0.1–10 MPa in elastic modulus, 1000%–2000% in tensile fracture strain, 20–60 MPa in failure compressive fracture stress, 90%–95% in compressive fracture stain, and 100–16,000 J/m² in fracture energy. These parameters are comparable to those of rubbers and soft load-bearing bio-tissues (Gong, 2010; Philippova et al., 1998).

DN hydrogels can be mainly categorized into two types based on their network structures: chemically-chemically cross-linked networks and physically-chemically cross-linked networks. DN hydrogels such as poly(2-acrylamido-2-methylpropanesulfonic acid)-poly(acrylamide) (PAMPS-PAAm) (Gong et al., 2003), poly(ethylene glycol)-poly(acrylic acid) (PEG-PAA) (Myung et al., 2007), and most hydrogels synthesized by the molecular stent methods (Nakajima et al., 2012, 2013) belong to the chemically-chemically cross-linked category. Chemical cross-links that are commonly used in hydrogels include permanent covalent cross-links (e.g., carbon-carbon bonds, carbon-nitrogen bonds, carbon-oxygen bonds, carbon-sulfide bonds, and silicon-oxygen bonds) and dynamical covalent cross-links (e.g., imine bond, boronated ester bond, disulfide bond, hydrazone

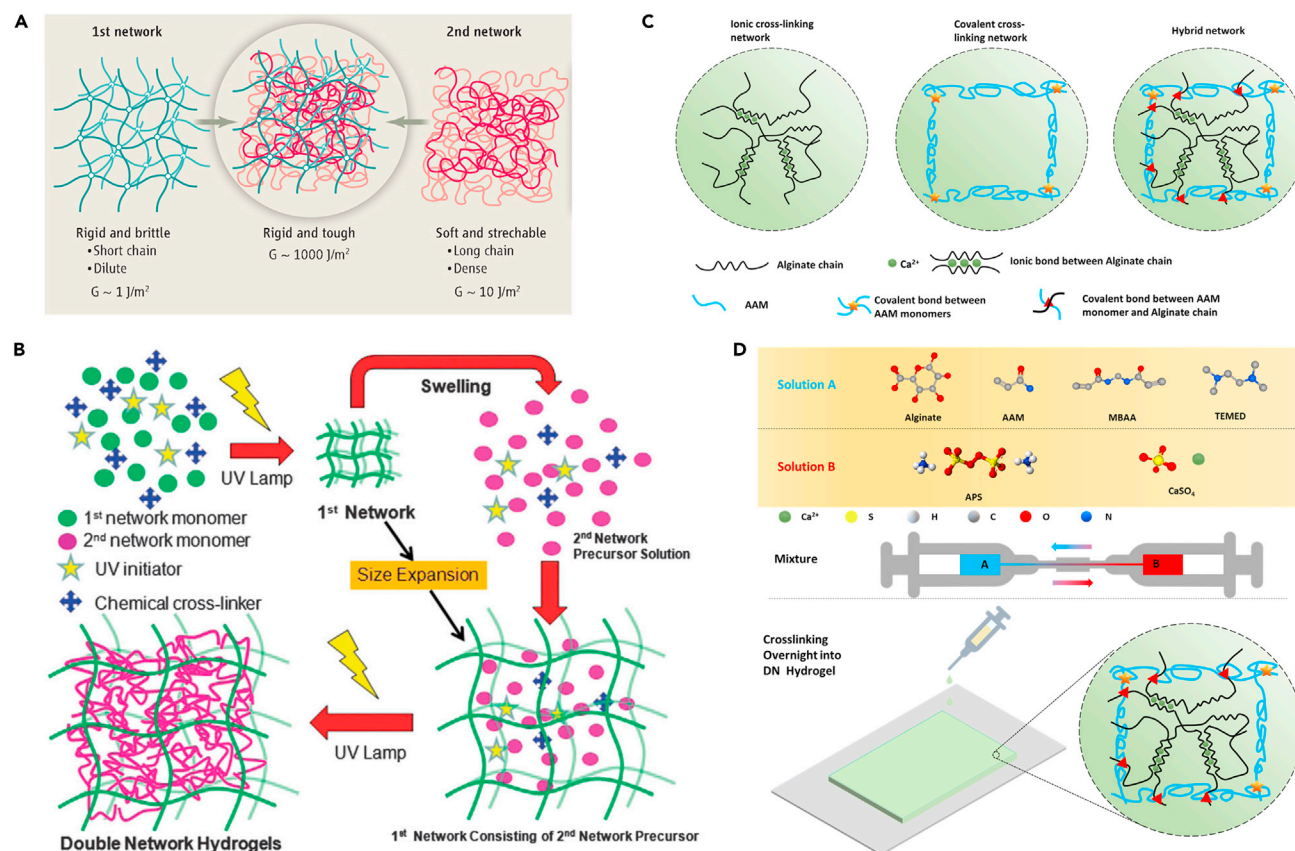


Figure 2. Two typical DN hydrogel structures and their synthesis strategies

(A) By combining two different hydrogel networks, tough DN hydrogels can be created. Reprinted and adapted with permission from Ref. (Gong, 2014), 2014 American Association for the Advancement of Science.

(B). Classical two-step polymerization method to prepare chemically–chemically cross-linked DN hydrogels. Reprinted and adapted with permission from Ref. (Chen et al., 2015), Royal Society of Chemistry.

(C) The composition of a typical physically–chemically cross-linked alginate–PAAm hydrogel.

(D) Preparation of the physically–chemically cross-linked alginate–PAAm DN hydrogel.

bond, oxime bond, and reversible diels-alder reaction) (Zhao et al., 2021a). For example, the PAMPS–PAAm DN hydrogel was formed by covalently cross-linking strong polyelectrolytes (i.e., PAMPS) as the first network and subsequently covalently cross-linking the second-network monomers (AAM) diffused from the precursor solution into the first-network gel (Figures 2A and 2B) (Gong et al., 2003).

While the recently developed DN hydrogels such as carrageenan–epoxy–amines (Stevens et al., 2013), polysaccharides–epoxy–amines (Stevens et al., 2013), agarose–PAAm (Chen et al., 2013; Ying et al., 2020a), and alginate–PAAm (Sun et al., 2012) belong to the physically–chemically cross-linked category, in which the first network is usually physically cross-linked while the second network is chemically cross-linked. The physically cross-links that are commonly used in hydrogels including strong physical cross-links (e.g., crystalline domain, glassy nodule, and helical association) and weak physical cross-links (e.g., hydrogen bond, electrostatic interactions, coordination complex, host–guest interaction, hydrophobic association, and π – π interaction) (Zhao et al., 2021a). For example, the alginate–PAAm DN hydrogel is formed by ionically cross-linking alginate chains as the first network and covalently cross-linking the second-network monomers (AAM) into PAAm (Figures 2C and 2D). During polymerization, there are also hybrid cross-links between the first network and the second network, which is the origin of network entanglement and chain interaction mentioned before.

Since the chemically–chemically cross-linked DN hydrogels have been studied for almost ten years earlier than the physically–chemically cross-linked ones, our understanding of the former’s mechanism is much

more in depth. However, increasing attention has recently been paid to the physically–chemically cross-linked hydrogels because of the less toxic cross-linking agents they involve. In addition, the irreversible failure of covalent bonds in the first network of chemically–chemically cross-linked DN hydrogels could be a limitation for the material’s self-healing property (Gong, 2010). In contrast, excellent self-healing properties can be realized on physically–chemically DN hydrogels (Chen et al., 2015; Gong, 2010).

Currently, there are several methods to prepare DN hydrogels, including classical two-step polymerization (Gong et al., 2003), one-pot methods (Chen et al., 2013; Sun et al., 2012), molecular stent methods (Nakajima et al., 2012, 2013), and their combination with other technologies such as 3D printing (Bakarich et al., 2014; Muroi et al., 2013). Here, we will mainly discuss the difference between the two-step and one-pot methods.

The classical two-step method is very popular because of its mature and robust protocol and easy of operation (Gong et al., 2003). Taking the free-radical synthesis of PAMPS-PAAm DN hydrogel as an example (Figure 2B). In the first step, strong polyelectrolyte (PAMPS) is free-radically polymerized to form a covalently cross-linked, rigid and brittle first network, which thereafter immerses and swells in a precursor solution containing neutral second-network monomers (AAm), initiators, and cross-linkers for certain period of time (e.g., 24 h) to reach equilibrium. In the second step, AAm is polymerized to form a loosely cross-linked yet stretchable second network (PAAm) inside the first brittle network (Gong et al., 2003). The finally synthesized DN hydrogel fall into the chemically–chemically cross-linked category. The two-step method can also be adapted to synthesize physically–chemically cross-linked DN hydrogels [e.g., agarose-PAAm hydrogel (Ying et al., 2020a)], which could construct the DN tough hydrogel with reversible bindings in the first network.

On the other hand, Sun et al. (2012) developed a simple one-pot method to synthesize a new type of hybrid physically–chemically cross-linked alginate-PAAm DN hydrogels (Figure 2D). Briefly, sodium alginate, CaSO_4 , AAm, N,N'-methylenebis(acrylamide) (MBAA), tetramethyl-ethylenediamine (TEMED), and ammonium persulfate (APS) were mixed and cured in a sealed chamber overnight, during which ionic cross-linking took place to form the first alginate network while free radical polymerization of AAm and covalent cross-linking occurred to form the second PAAm network (Figure 2D).

Overall, for both methods the mechanical properties of the hydrogel can be readily tuned by simply adjusting the concentrations of monomers, initiators, and cross-linkers (Chen et al., 2013; Gong et al., 2003; Sun et al., 2012). The one-spot method is more advantageous in terms of constructing the DN hydrogels with complex shapes, reducing synthesis time, and saving the monomer solution of the second network (Chen et al., 2015). However, the two-step method shows better stability due to its low swelling ratio in an aqueous environment (Ying et al., 2020a) as well as the suitability for the synthesis of both physically–chemically and chemically–chemically cross-linked DN hydrogels (Gong et al., 2003; Ying et al., 2020a).

Conductive hydrogels and its ionic type

The main composition of the human body is hydrogel. Neuron signals are transmitted in the hydrogel-like human body through the transmembrane movement of sodium, potassium, calcium, and chloride ions through ion channels on neuron cells (Figure 1A) (Lee et al., 2018a; Ying et al., 2020a). While significant efforts have been made to engineer flexible electrical components to interface the human body with artificial devices, technical challenges still exist due to the mismatches of the mechanical properties and charge carriers (electrons versus ions) of the flexible electronics and the human tissue (Lee et al., 2018a; Ying et al., 2020a).

Hydrogels are a class of promising biocompatible media to bridge the human-machine gap since they possess tunable mechanical properties with on-demand design of toughness, stretchability, and elasticity to accommodate the diverse mechanical properties of the human tissues (Liu et al., 2020d; Zhu et al., 2020). Pristine hydrogels are generally considered as electrical insulators due to the low-concentration mobile charge carriers in its water contents (Liu et al., 2020d; Yuk et al., 2019a). Currently, there are several strategies to empower hydrogels with good conductivity (Amoli et al., 2019; Lee et al., 2018a; Peng et al., 2020; Rong et al., 2018a; Liu et al., 2020d; Wang et al., 2020c; Yang and Suo, 2018; Yuk et al., 2019a), including nanocomposite-based conductive hydrogels (e.g., CNT, graphene, and metal nanomaterials serving as conductive fillers), conducting-polymer-based conductive hydrogels, electrolyte/polyelectrolyte-based conductive hydrogels, and other types (e.g., ionic-liquid-based conductive gels). Except nanomaterial-

based conductive hydrogels, most conductive hydrogels use ions to transmit signals within the conductor, which better mimics the ion transports in tissues and has the potential to offer an unconventional yet improved interface between human body and electronics. In this section, we mainly introduce the ionically conductive hydrogels: (1) electrolyte/polyelectrolyte-based conductive hydrogels; (2) conducting-polymer-based conductive hydrogels; and (3) other novel ionically conductive gels.

Electrolyte/polyelectrolyte-based conductive hydrogels

Electrolyte-based conductive hydrogels. Aqueous solutions with salts (electrolytes) have been utilized for many applications including the daily use of alkaline batteries and ionically stimulating electrodes (Zhao et al., 2018a). However, solution-based electrolyte devices have issues such as potential liquid leakage, limiting their biomedical applications (e.g., medical wearables). Electrolytes-based conductive hydrogels are promising alternatives due to their both solid- and fluid-like behaviors. The porous structure of the polymeric skeleton makes conductive hydrogels behave like solids, but the presence of polar solvent (H_2O) enables its liquid-like ionically conductive performance. Ionic current occurs under electric fields due to the conduction of ions. When the applied potential is above the voltage threshold of water electrolysis (i.e., 1.23 V), the ionic current is mainly faradaic; in contrast, the ionic current is mainly capacitive (transient) once the applied potential is below 1.23V. Currently, salts such as NaCl, LiCl, and KCl have been incorporated into hydrogel matrices (e.g., the PAAm hydrogel) to achieve ionic conductive hydrogels. By adjusting the salt concentrations, conductive hydrogels can achieve a conductivity on the order of magnitude of 10 S/m, which can be regarded as comparable charge conductors (Lee et al., 2018a). Those conductive hydrogels have been demonstrated to serve as artificial muscle (Keplinger et al., 2013), artificial skin (Kim et al., 2016a; Sun et al., 2014), artificial axon (Yang et al., 2015b) and energy harvester (Pu et al., 2017). Among different salts, LiCl is the most frequently used one for incorporation into hydrogels (Keplinger et al., 2013; Kim et al., 2016a; Pu et al., 2017; Sun et al., 2014; Yang and Suo, 2018) due to its excellent conductivity, and hygroscopic and anti-freezing properties. Those features are important for the practical applications of wearable and soft robotic sensing.

Polyelectrolyte-based conductive hydrogels. Polyelectrolyte has been incorporated into hydrogels for constructing conductive hydrogels as well (Lee et al., 2018a). Polyelectrolyte is a type of polymer with dissociating electrolyte groups in their repeated units. Depending on the electricity of mobile counterions fixed to the polymeric backbone chains, polyelectrolytes can be categorized into polycations and polyanions. They can dissociate in aqueous solutions similar to ordinary electrolytes while their solutions are usually viscous. Typical natural polyelectrolytes include polypeptides, glycosaminoglycans, and DNAs and typical synthetic polyelectrolytes include PAMPS, poly (diallyldimethylammonium chloride) (PDAC), poly (sodium styrene sulfonate) (PSS), and polyacrylic acid (PAA). Different from ionic conduction within regular electrolyte-based hydrogels, polyelectrolytes-based conductive hydrogels possess selective ionic conduction. Their charged functional groups on polymeric backbone chains only allow for the free transportation of oppositely charged ions. This feature has been explored to construct ion-selective membranes for applications such as seawater desalination (Lee et al., 2018a), hydrogel ionic diodes (Cayre et al., 2007; Lee et al., 2019; Ying et al., 2020a), and energy harvesting (Ying et al., 2020a; Zhou et al., 2017).

In summary, as a relatively facile and straightforward strategy to enable hydrogels with ionic conductivity, electrolyte-based conductive hydrogels have been mainly applied in non-invasive scenarios such as epidermal sensing (Sun et al., 2014; Ying et al., 2020a). These conductive hydrogels face challenges for implantable applications due to their poor biocompatibility. The salt concentration in those conductive hydrogels is usually more than 1 M, much higher than the electrolyte concentration in body fluids (0.15 M–0.3 M), leading to the ions diffusing from conductive hydrogels to human bodies. The ionic diffusion from hydrogels to the extracellular fluid usually induces disorders of water and salt metabolism as well as the conductivity instability of conductive hydrogels (Liu et al., 2020d; Yuk et al., 2019a).

Conducting-polymer-based hydrogels

The conductivity of conventional conductive hydrogels is usually limited, typically 6–9 orders of magnitude lower than that of metals (Keplinger et al., 2013); this could further hinder their biomedical applications (e.g., hydrogel bioelectronics for implantable neural signal recording and nerve/deep brain stimulation). In contrast, the recent advances of conducting-polymer-based hydrogel offers much higher conductivity, promising for the emerging field of hydrogel bioelectronics (as it provides increased signal-to-noise ratio and enhanced stimulation capability) (Mawad et al., 2016; Rivnay et al., 2017; Yuk et al., 2019a). Conducting

polymers, such as Polypyrrole (PPy) (Shi et al., 2015), polyaniline (PAni) (Mawad et al., 2016; Pan et al., 2012; Stejskal et al., 1998), and poly(3,4-ethylenedioxythiophene) doped with polystyrene sulfonate (PEDOT:PSS) (Lee et al., 2016; Liu et al., 2020b; Lu et al., 2019; Yao et al., 2017; Yuk et al., 2020; Zhang et al., 2020b), are synthetic polymers conducting electrons through π -conjugated structures. Conducting polymers swell in wet environments and become electrically conductive hydrogels with tissue-like mechanical properties and watery contents. Recently, conducting polymers have gained increasing attention for developing hydrogel bioelectronics due to their advantages such as tunable mechanical and electrical properties, biocompatibility, flexibility, electrochemical stability, and processability for chemical modification (Liu et al., 2020d; Zhao et al., 2017). In addition, the co-presence of ionic and electronic conduction within conducting-polymer-based hydrogels can lower the interfacial impedance for bioelectronic applications (Liu et al., 2019b; Lu et al., 2019). Conducting-polymer-based hydrogels can be prepared by two strategies: 1) forming interpenetrating polymer networks (IPNs) between conducting polymers and non-conducting hydrogel networks (Liu et al., 2019b) and 2) forming pure conducting polymer hydrogels (Lu et al., 2019).

Here, we compare the difference of their fabrication methods using PEDOT:PSS hydrogel as an example because of their excellent biocompatibility and exceptional electrochemical stability as a bioelectronic material (Berggren and Richter-Dahlfors, 2007; Zhang et al., 2020b). The commercially available PEDOT:PSS usually possesses poor solubility in water (a universal solvent for bioelectronic materials) (Zhang et al., 2015a). Therefore, chemical solvents such as glycerol (Liu et al., 2020b), dimethyl sulfoxide (DMSO) (Zhang et al., 2015a), ethylene glycol (EG) (Lee et al., 2016), acids (Yao et al., 2017), and ionic liquid (Liu et al., 2019b) are usually adopted as secondary dopants to increase their solubility and conductivity by reinforcing the intermolecular interactions (Lee et al., 2016; Liu et al., 2019b, 2020b; Yao et al., 2017; Zhang et al., 2015a).

IPNs, for example, were formed between PEDOT:PSS and non-conducting hydrogel networks (i.e., PAAm) during PEDOT:PSS-PAAm hydrogel synthesis in the EG aqueous solution, possessing a 200% stretchability (Lee et al., 2016). On the other hand, a mechanically tunable and conductive IPN hydrogel was formed by the ionic-liquid-induced gelation of loosely cross-linked PEDOT:PSS hydrogel and a subsequently interpenetrated polymerization of a soft and stretchable network [i.e., polyacrylic acid (PAAc)] (Figures 3A and 3B) (Feig et al., 2018). The as-made gels possess ultra-soft and tunable moduli over three biologically relevant orders of magnitude (8–374 kPa) without compromising their conductivity (>10 S/m) or stretchability (>100%), which is promising to compliantly interface with a wider range of bio-tissues from the brain (0.5–1 kPa) to the skin and certain regions of the heart (100–500 kPa) (Feig et al., 2018).

Most existing IPN-based hydrogels, however, involve PEDOT:PSS blended with other compositions such as non-conductive polymers, sacrificing their electrical conductivity and/or electrochemical performance since the non-conductive hydrogel network acts as an electrical insulator (e.g., their electrical conductivity is typically below 100 S/m in deionized water) (Lu et al., 2019; Liu et al., 2020d). A recent work achieved the highest electrical conductivity (880 S/m) through forming a pure PEDOT:PSS hydrogel with over 95% water (Yao et al., 2017). However, this pure conductive hydrogel requires concentrated sulfuric acid for fabrication and the extraordinary conductivity is tested in an acidic solution (pH = 1), unsuitable for most implementable applications (Yao et al., 2017). Recently, Lu et al. designed pure PEDOT:PSS hydrogels with the addition of volatile DMSO into aqueous PEDOT:PSS solution, followed by controlled dry-annealing and rehydration steps. The resultant hydrogels yield a set of properties highly desirable for bioelectronic applications, including high electrical conductivity (~2000 S/m in PBS, ~4000 S/m in deionized water), good stretchability (>35% strain), low Young's modulus (~2 MPa), superior mechanical, electrical and electrochemical stability, and tunable isotropic/anisotropic swelling in wet physiological environments (Figures 3C and 3D) (Lu et al., 2019). While most pure PEDOT:PSS hydrogels were fabricated at elevated temperatures, they are unsuitable for *in-situ* synthesis and are difficult to seamlessly conform to irregular biological tissue surfaces. Recently, Zhang et al. designed a room-temperature-formed PEDOT:PSS (RT-PEDOT:PSS) conductive hydrogel that is injectable, soft, and healable (Zhang et al., 2020b). Spontaneous gelation occurred at room temperature by simply mixing PEDOT:PSS suspension with 4-dodecylbenzenesulfonic acid (DBSA), a widely used secondary dopant (surfactant), without any additional treatments (Figure 3E) (Zhang et al., 2020b). Organic electrochemical transistors (OECTs) with injected RT-PEDOT:PSS hydrogel fibers were demonstrated. This technology, along with other demonstrated applications such as soft and elastic microelectronics for localized low-voltage neuromodulation (Liu et al., 2019b) and morphing electronics for neuromodulation in growing tissue (Liu et al., 2020b) (Figure 3F), will further push PEDOT:PSS hydrogels toward practical biomedical applications.

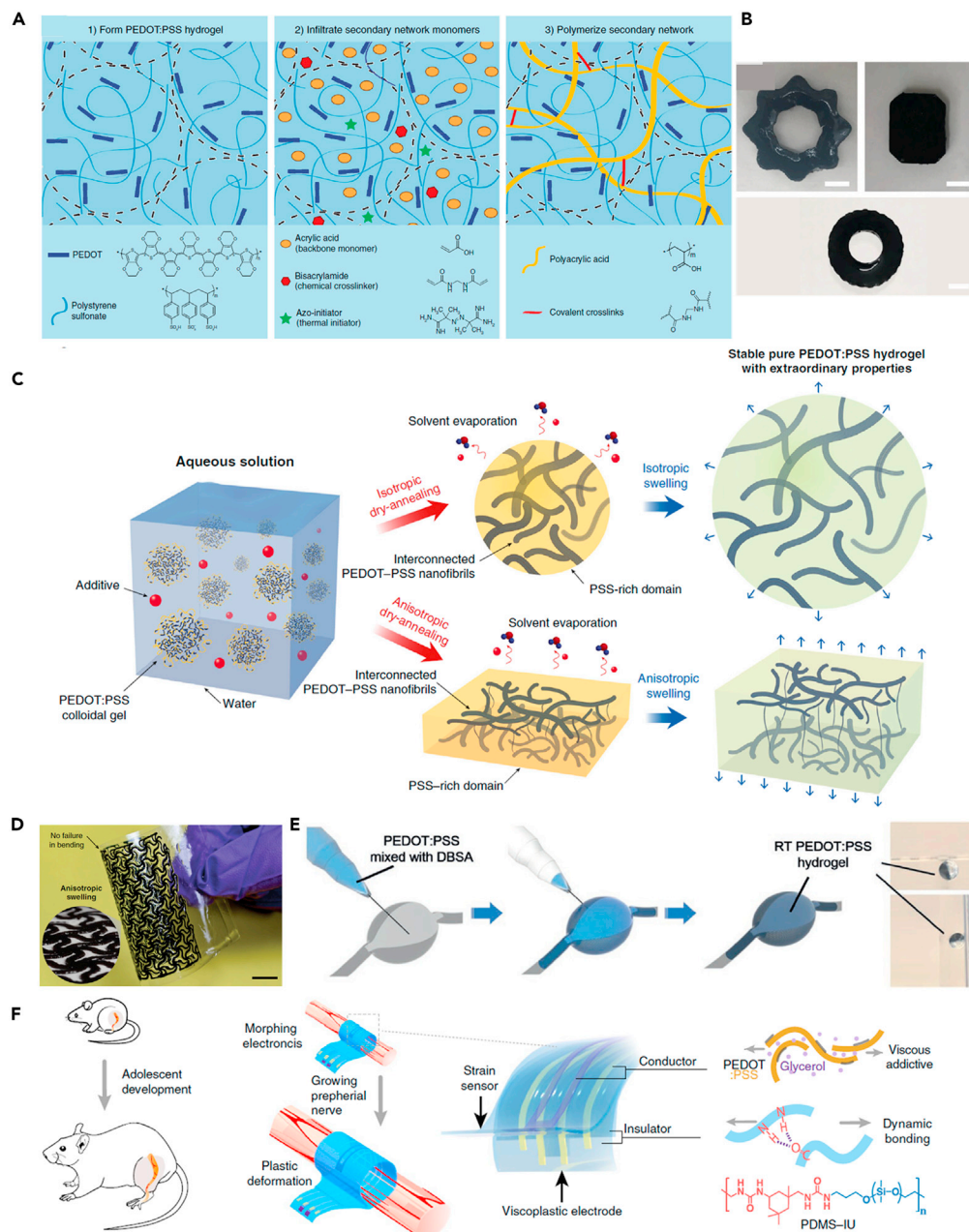


Figure 3. Conducting-polymer-based hydrogels

(A) Process for fabricating conductive PEDOT:PSS-based IPN hydrogels.

(B) PEDOT:PSS/acrylic acid mixture casted into different silicone soap molds. Reprinted and adapted with permission from Ref. (Feig et al., 2018).

(C) Dry-annealing and swelling processes of pure PEDOT:PSS with DMSO as the additive.

(D) Robust laminate of pure PEDOT:PSS hydrogel pattern. Reprinted and adapted with permission from Ref. (Lu et al., 2019).

(E) Schematic of injectable RT-PEDOT:PSS hydrogels. Reprinted and adapted with permission from Ref. (Zhang et al., 2020b).

(F) Schematics of morphing electronics enable neuromodulation in growing tissue. Reprinted and adapted with permission from Ref. (Liu et al., 2020b).

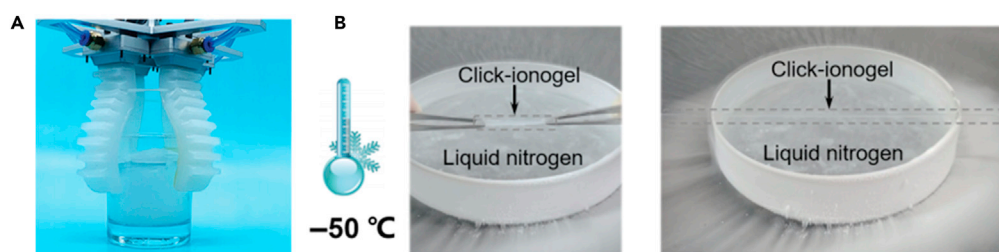


Figure 4. Miscellaneous novel conductive gels

(A) Photographs of a zwitterionic PIL-based soft gripper holding a cup of ice water. Reprinted and adapted with permission from Ref. (Liu et al., 2020c), Royal Society of Chemistry.

(B) Photographs of a click-ionogel stretched above liquid nitrogen (at about -50°C). Reprinted and adapted with permission from Ref. (Ren et al., 2019), 2019 American Association for the Advancement of Science.

With the rapid development of conducting-polymer-based hydrogels, there are still some persisting challenges worth further exploration in order to realize their practical biomedical applications. More detailed mechanisms and examples of conducting-polymer-based hydrogels can be found in previous reviews (Green and Abidian, 2015; Peng et al., 2020; Rong et al., 2018a; Yuk et al., 2019a).

Miscellaneous novel conductive gels

Currently, several novel ionically conductive gels have been explored as well, providing great potential for diverse applications. Among them, polymeric ionic liquids (PILs) and ionogels made from ionic liquids (ILs) are getting increasing attention due to their both polymeric and ionically conductive features. PILs and ionogels are usually nonvolatile, never drying out in both ambient and extremely hot environments, and not frozen at low temperature. Therefore, PILs and ionogels are good complementary materials of ionic conductive hydrogels for biomedical applications.

Polymeric Ionic Liquids (PILs). Before the introduction of PILs, ILs will be described first here. ILs are defined as molten organic salts that are composed of organic cations and organic/inorganic anions with melting temperature below 100°C . ILs have many interesting physicochemical properties such as ionic conductivity (10^{-2} – 1 S/m), negligible vapor pressure, thermal stability, non-flammability, wide electrochemical stability window ($\sim 5.7\text{ V}$), wide tolerant temperature range (up to 200 – 300°C), and tunable physical/chemical properties (due to numerous combinations of the cations and anions) (Cao et al., 2019; Le Bideau et al., 2011; Sun et al., 2017; Zhang et al., 2020c). ILs have been widely applied in areas such as synthetic chemistry, catalysis, energy storage, and recently sensors and actuators (Buzzeo et al., 2004; Calvert, 2008; Le Bideau et al., 2011; MacFarlane et al., 2014; Plechkova and Seddon, 2008; Watanabe et al., 2017; Zhang et al., 2020c). However, the liquid feature of ILs could induce certain complexity such as leakage, difficulty of handling, non-portability, and almost impossibility of miniaturization (Bisri et al., 2017; Ye et al., 2013; Zhang et al., 2020c).

The most straightforward strategy for PIL synthesis is the polymerization of ILs into PILs (or called ionic polymers or novel polyelectrolytes). PILs can be prepared by either chemical cross-linking of IL monomers (Steed, 2011) or physical assembly of block polymers (Miranda et al., 2013). PILs retain unique properties of ILs along with the intrinsic polymeric feature without leakage issue. Similar to conventional polyelectrolytes, PILs can be categorized into polycations that bear cations, polyanions that bear anions, and unique polyzwitterions that bear both anions and cations in the polymeric backbone. Contrary to conventional polyelectrolytes that are water soluble, most PILs are only soluble in polar organic solvents since the typical counter-anions of PILs [e.g., tetrafluoroborate (BF_4^-), hexafluorophosphate (PF_6^-), bis(trifluoromethanesulfonyl)amide (TFSI^-), bis(-fluorosulfonyl)imide (FSI^-), trifluoroacetic (CF_3CO_2^-), and dicyanamide (DCA^-)] are hydrophobic while the counter-anions (e.g., Cl^- , Br^- and I^-) of conventional cationic polyelectrolytes are hydrophilic; on the other hand, conventional anionic polyelectrolytes consist of metallic counter-cations (e.g., Li^+ , Na^+ and K^+), while typical counter-cations of PILs [1-Butyl-3-methylimidazolium (BMIM^+), 1-Ethyl-3-methylimidazolium (EMIM^+) and 1-methyl-3-octylimidazolium (OMIM^+)] are organic. Interestingly, polyzwitterions, as a unique type of PILs, are water soluble and consist of zwitterionic moieties as monomers. Polyzwitterions have recently been explored for many applications. For example, a soft PIL-based anti-freezing ionic skin for a soft robotic gripper has been developed based on one type of zwitterionic PIL. This zwitterionic PIL gel exhibited a

stretchability of 900%, self-healing property, anti-freezing capability, and high ionic conductivity (1.1 S/m) at low temperature (-20°C) (Figure 4A) (Liu et al., 2020c).

Ionogels. Another strategy is to introduce ILs into physically or chemically cross-linked networks of polymer matrices to form ionogels (or ionoelastomers). Ionogels keep most properties of ILs without the leakage and exhibit an elastomeric feature. Therefore, ionogels have been applied to construct lithium-ion batteries (Wu et al., 2017), fuel cells (Zhang et al., 2019), solar cells (Le Bideau et al., 2011), electrochemical sensors (Khodagholy et al., 2012), wearable sensors (Yiming et al., 2021a), actuators (Chen et al., 2014), ionic diodes (Lee et al., 2018a), and energy harvesters (Yiming et al., 2021b). For example, one IL-based ionogel was prepared by the thiol-ene click chemistry (Ren et al., 2019), in which solution A [poly(ethylene glycol) diacrylate (PEGDA), pentaerythritol tetraacrylate (PETA; cross-linker for covalent network), and anionic benzene tetracarboxylic acid (BTCA; cross-linker for the ionic bond network) dissolved in methanol] was mixed with solution B [mixture containing PIL-BF₄, triethylamine (TEA; a catalyst for the thiol-ene click reaction), and 1,2-ethanedithiol (ED) dissolved in methanol] at room temperature to form the gel; then the IL [i.e., 1-propyl-3-methylimidazolium fluoborate (IL-BF₄)] was introduced into the prepared gel at 80°C under vacuum for 24 h. This ionogel exhibits excellent mechanical properties, high resilience after 10,000 fatigue cycles, high ionic conductivity, high transparency, and good nonflammability over a wide temperature range (-75° to 340°C). A click-ionogel-based triboelectric nanogenerator was demonstrated with excellent mechanical, freeze-thaw, and heat stability (Figure 4B) (Ren et al., 2019).

Overall, both PILs and ionogels have shown great potential for flexible electronics such as flexible sensors, energy storage devices, and electronic skins. However, the complexity of their synthesis methods and relatively high costs may limit their broad applications. In addition, most of the previously reported biomedical applications using PILs and ionogels are non-invasive; their *in-vivo* biocompatibility should be further examined if the target application is *in vivo*. The relatively low conductivity of ionogel and PILs, compared to the conducting-polymer-based hydrogels, may hinder their applications for wearable bioelectronics such as implantable neural signal recording, nerve stimulation, and deep brain stimulation.

The combination of conductivity and toughness

Tough and conductive hydrogels made from double networks are very attractive for developing flexible electronics, soft actuators and sensors, and soft robots. Recently, several attempts have been made to construct hydrogels that are both ionically conductive and mechanically tough. The simplest material design strategy is to incorporate electrolytes or polyelectrolytes into an existing neutral tough hydrogel matrix. For example, NaCl has been introduced into a poly(vinyl alcohol)/poly(acrylic amide) (PVA/PAAM) DN hydrogel to prepare PVA/PAAM/NaCl conductive tough hydrogel via a one-pot method (Chen et al., 2020a). Two oppositely charged polyelectrolytes can be incorporated into an agarose/PAAM DN tough hydrogel to create an ionic diode (Ying et al., 2020a).

While the incorporation of monovalent ions could impair the mechanical performance of some non-neutral tough hydrogels such as the most popular alginate/PAAM tough hydrogel (Li et al., 2014; Yang et al., 2013), the addition of neutral hygroscopic chemicals (e.g., glycerol) could suppress this negative influence and maintain both the conductivity and toughness (Ying et al., 2021a). This is due to noncovalent interactions between the hydrogel polymer chains and the neutral hygroscopic chemicals (Han et al., 2018). The reduced competition of the monovalent ions for binding sites on the alginate chains could protect the ionic cross-links (Ying et al., 2021a).

In addition, inspired by IPN formation of DN hydrogel synthesis, conductive monomers could be polymerized into a first/second-network hydrogel matrix to form IPN hydrogels with both conductivity and mechanical toughness (Dai et al., 2010; Li et al., 2016; Wang et al., 2018b; Zhu et al., 2018a).

MATERIAL DESIGNS FOR NEW PROPERTIES AND FUNCTIONALITIES

Natural living systems possess complex tissue and organ structures composed of active hydrogels to survive in complicated and diverse environments. For example, properties such as freeze tolerance, dehydration resistance, self-healing, and biodegradability are commonly found in certain mammals, fishes, frogs, insects, and bacteria. In addition, certain animals (e.g., mussels) can form adhesion in wet environments.

Inspired by nature, conductive-hydrogel-based biomimetic materials have been intensively studied to develop stretchable electronics for various applications such as wearable physical/biosensing, human-machine interaction and soft robotics. Many hydrogel devices reveal advanced merits such as anti-freezing, anti-dehydration, self-healing, biodegradability, and adhesive capability (Wang and Urban, 2020; Yang and Suo, 2018; Yuk et al., 2019a; Zhang and Khademhosseini, 2017). Those advanced properties further highlight conductive hydrogels as a multifunctional material for practical applications. In this section, we highlight several key issues of hydrogel devices and the recent advances to empower hydrogels with enhanced merits including anti-freezing, anti-dehydration, and adhesive capabilities.

Anti-dehydration and anti-freezing capabilities

The water content inside hydrogel and the state of the water molecules will seriously affect the properties of hydrogels. There are three different states of water in a hydrogel, namely free water (fast exchange), intermediate water (slow exchange), and unfrozen bound water. Regular hydrogels easily lose water in the open air and inevitably freeze at subzero temperatures due to the abundant existence of free water, losing their mechanical stretchability and electrical conductivity and severely hindering their practical applications for wearable sensing and robotics.

In order to enhance the long-term ambient stability and anti-freezing capability of hydrogels, it is necessary to convert the free water into the other two states as much as possible. Inspired by nature, hygroscopic substances (e.g., salts, organic solvents and combinations thereof) have been added into regular hydrogels to sustain its ambient stability; in addition, an epithelium-like elastomer layer can be coated on hydrogel to reduce the evaporation rate as well. On the other hand, most hygroscopic substances are cryoprotective. Therefore, in this section, we will discuss different strategies to enhance the anti-dehydration and anti-freezing capabilities of hydrogels; moreover, some novel nonvolatile gels will be briefly presented in the end.

Salts-incorporated hydrogels

Pure salts in high concentration (>1 M), such as sodium chloride (NaCl), lithium chloride (LiCl), potassium acetate (KAc), magnesium chloride ($MgCl_2$), calcium chloride ($CaCl_2$), and their combinations have been incorporated into both regular and tough hydrogels (Bai et al., 2014; Morelle et al., 2018) to enhance their water retention capacity as well as their freezing tolerance. For example, LiCl is more hydrable compared with other salt species, and PAAm hydrogel containing high content of LiCl (12 M) can retain over 70% of its initial water even in extremely dry environment (RH = 10%) for 5 days. This high water retention capacity and low water evaporation of LiCl-incorporated PAAm hydrogel is due to the stronger bond strength between dissolved cation/anion and the water molecule pairs (Bai et al., 2014; Morelle et al., 2018). The freezing point of this LiCl-PAAm was accordingly reduced to -80°C and their conductivity is relatively high in such a low temperature. However, most monovalent ions (e.g., Li^+ , Na^+ and Cl^-) could impair the mechanical performance of some tough hydrogels with ionic cross-linking (e.g., alginate/PAAm hydrogel) (Yang et al., 2013). In order to protect their toughness, multivalent-ionic salts such as $CaCl_2$ were incorporated into the regular alginate/PAAm tough hydrogel to increase its anti-freezing capability (Morelle et al., 2018). Without reporting its ambient stability, the freezing point of this hydrogel (with 30 wt% $CaCl_2$) can be as low as -57°C . Although the toughness of this hydrogel reduces to 2000 J/m^2 from the original 9000 J/m^2 due to its reduced stretchability ($\lambda = 4.5$), it can still be stretched more than four times their initial length and have a fracture toughness of 5000 J/m^2 at -57°C (Morelle et al., 2018).

Organic-solvent-incorporated hydrogel

Alternatively, organic solvents such as glycerol (Chen et al., 2018; Han et al., 2018; Ju et al., 2020; Liu et al., 2019a; Qin et al., 2019; Yang et al., 2019), EG (Chen et al., 2019; Liao et al., 2019; Rong et al., 2017, 2018b), DMSO (Nian et al., 2019), sorbitol (Chen et al., 2018), and the combination thereof (Chen et al., 2018) have been incorporated into both regular and tough hydrogels to enhance the water retention capacity and decrease the freeze point of water-based devices for applications such as batteries (Nian et al., 2019), flexible solid-state supercapacitors (Rong et al., 2018b), flexible wearable devices (Chen et al., 2019; Liao et al., 2019; Yang et al., 2019) operating under extreme environments. In addition, the anti-freezing and anti-dehydration capabilities of hydrogels as well as their mechanical and electrical properties can be altered by adjusting the concentrations of organic contents. For example, we found that the incorporation of glycerol with an optimal concentration of 66.5 wt% into alginate/PAAm tough hydrogel can maintain 75% of its original mass even after 30 days in an extremely dry environment (RH = 15%) and the freezing point can

reach down to -97°C . these results are due to the glycerol's strong water-retaining capability and its effective freeze-inhibiting effect by altering the water state in hydrogels. In addition, different from the salts-incorporated strategy, the elastic modulus and mechanical toughness of glycerol-incorporated hydrogels were found to be enhanced due to the noncovalent interactions (hydrogen bonds) between the hydroxyl groups on glycerol chains and carboxyl/amino groups on alginate/PAAm chains (Ying et al., 2021a).

Currently, there are mainly two strategies (the one-pot synthesis and the two-step solvent exchange method) to add organic solvents into hydrogels. For example, during one-pot synthesis, binary solvent-water systems can be mixed into polymer (Rong et al., 2017) or monomer (Han et al., 2018) solutions before network cross-linking; while during two-step solvent exchange, the as-fabricated hydrogel can be soaked into the binary solvent-water system for a while (e.g., 3 h) to reach the equilibrium state (Chen et al., 2018). The one-pot synthesis is usually regarded as a more reagent-saving and environment-friendly method while the two-step solvent exchange method can avoid the complicated synthesis optimization steps because the binary solvent was introduced after polymerization and cross-linking of hydrogels (e.g., ionic cross-linking of alginate network, polymerization of AAm and covalent cross-linking of PAAm network for alginate/PAAm tough hydrogel) (Chen et al., 2018). In addition, the two-step solvent exchange method can be conveniently expanded to fabricate tough hydrogels with various cryoprotective solutions to realize different anti-freezing, conductivity and mechanical parameters as desired (Ying et al., 2021a).

Hydrogels incorporated with both organic solvents and salts

Some pure nontoxic salts (e.g., NaCl and KCl) have limited water retention capacity and limited freeze-inhibiting capability, although they have been commonly used to construct hydrogel-based devices. For example, hydrogels laden with 5.4 M NaCl remain only 35% of the original mass after 15 days at RH=15% due to the evaporation of water and loss its high transparency because of the salt precipitation once RH is below 63%; in addition, its freezing point is -22°C (Ying et al., 2021a). While most organic-solvents-incorporated hydrogels can achieve both good ambient stability and anti-freezing capability, these hydrogels (or called organohydrogels) suffer from low conductivity and are thus unsuitable for wearable and robotic applications. Recently, more studies focus on the incorporation of salts (Chen et al., 2019; Qin et al., 2019; Rong et al., 2018b; Song et al., 2020; Xie et al., 2018; Yang et al., 2019), conductive polymers (Rong et al., 2017) or conductive fillers (Han et al., 2018; Liao et al., 2019) together with organic solvents into hydrogels to increase their conductivity, ambient stability, and anti-freezing capacity. As one of the most popular methods, incorporating monovalent salts and binary solvents into hydrogels is facile through solvent exchange (Ying et al., 2021a). Surprisingly, it was found that the common nontoxic monovalent ions (e.g., Na^{+} and Cl^{-}) at high concentration did not impair the mechanical performance of tough hydrogels with ionic cross-links (e.g., alginate/PAAm tough hydrogel) (Ying et al., 2021a). This mechanical robustness is probably due to the incorporation of the binary solvent system. Solvents like glycerol introduce noncovalent interactions within the hydrogel polymer chains (Han et al., 2018), and increase the polymer network density due to a slight hydrogel shrinkage ($\sim 10\%$ in length) during solvent exchange (Chen et al., 2018). In addition, the incorporation of glycerol reduces the competition between sodium ions and calcium ions for the binding sites on the alginate chains, protecting the ionic cross-links (Ying et al., 2021a).

As introduced previously, conductive polymers (e.g., PEDOT:PSS) have already been added into the hydrogel matrix for bioelectronic applications (Yuk et al., 2019a). In order to increase the solubility of PEDOT:PSS and its conductivity, chemical solvents such as glycerol, sorbitol, DMSO, and EG are usually adopted as secondary dopants (Lee et al., 2016; Liu et al., 2019b, 2020b; Zhang et al., 2015a). Although their ambient stability and anti-freezing capability were not studied because of their implantable bioelectronic applications, those conductive hydrogels usually consist of good electrical and mechanical performance (Lee et al., 2016; Rong et al., 2017) as well as superior ambient stability and anti-freezing capability (Rong et al., 2017).

In addition, inspired by the robust lamination of elastomer-like epidermis and hydrogel-like dermis within mammalian skins, water can be retained for at least 2 days through encapsulating the hydrogel with a layer of elastomer (Yuk et al., 2016a). Although coating with an elastomer can only slow down but cannot eliminate long-term dehydration completely due to their relatively high permeability of water (Yang and Suo, 2018), this hydrophobic coating strategy can be combined with the salt addition (Le Floch et al., 2017) and even salt-solvent addition (Xie et al., 2018) to further prevent the fluctuation of water content in the hydrogel as well as maintain its anti-freezing ability and conductivity. Moreover, hydrophobic coating can

prevent naked hydrogels from many potential issues such as swelling, ions leakage in the aqueous environment, and instability in the acid environment and at high temperature, which can extend their potential application scenarios (Liu et al., 2018a). Hydrophobic coating can also broaden the selection scope of hygroscopic/cryoprotective chemicals, which do not need to be limited to those nontoxic chemicals (Lee et al., 2018b).

Novel nonvolatile gel

As we mentioned before, conductive gels such as PILs (Liu et al., 2020c; Miranda et al., 2013; Steed, 2011) and ionogels (Armand et al., 2009; Cao et al., 2019; Fukushima et al., 2005; Kim et al., 2020a; Le Bideau et al., 2011; Lee et al., 2010; Ren et al., 2019; Wang et al., 2003; Zhang et al., 2020c; Zhao et al., 2007) originating from ILs are usually nonvolatile, never dry out in both ambient and extremely hot environments, and never freeze at low temperature. To our best knowledge, the best anti-freezing capability of these nonvolatile gels can reach at least -75°C (Ren et al., 2019) and no weight changes are observed in ambient conditions (Kim et al., 2020a), under high vacuum (6×10^{-4} Pa) or high humidity (RH = 99%) (Cao et al., 2019). Further improvement is needed to improve the material's stretchability, enhance the conductivity, reduce the cost, and develop new device fabrication methods.

Hydrogel adhesives

Hydrogel as a biocompatible material has gained a lot of attention for wearable sensors (Kim et al., 2016a; Parida et al., 2017; Pu et al., 2017; Sun et al., 2014; Ying et al., 2020a), implantable bioelectronics (Liu et al., 2019b, 2020b; Wang et al., 2019a; Yuk et al., 2020) and soft robotics (Cheng et al., 2019; Larson et al., 2016; Shih et al., 2020). However, hydrogel devices typically have poor surface adhesion and cannot adhere strongly to surfaces of different materials; the insecure adhesion of the hydrogel device causes fidelity issues of sensing signal acquisition and brings motion-induced signal artifacts during operations. The past several years have witnessed the rapid progress of hydrogel adhesive development, which will be briefly reviewed in this section.

Hydrogel-solid materials bonding

Solid materials including metal, glass, ceramics, silicone and plastic are commonly used in robotics (Keplinger et al., 2013), biomedical devices (Dong et al., 2006; Peppas et al., 2006), and soft electronics (Yuk et al., 2020). Strong hydrogel bonding to diverse solid surfaces has remained a challenge due to the nature of hydrogels that contain significant amounts of water. In 2016, Yuk et al. (Yuk et al., 2016b) invented a new adhesion strategy, in which the precursors of long-chain polymer networks of tough hydrogels (e.g., PAAm-alginate, PAAm-hyaluronan, PAAm-chitosan, PEGDA-alginate, PEGDA-hyaluronan) were cast on the non-porous 3-(Trimethoxysilyl)propyl methacrylate (TMSPMA)-silanized solid surfaces including glass, silicon, ceramics, titanium and aluminum. During the curing of tough hydrogels, methacrylate groups on the functionalized surface covalently grafted PAAm or PEGDA networks (Figures 5A and 5B). Compared with other physical interactions and non-tough hydrogel chemical bonding, this design provides an interfacial toughness value over $1,000 \text{ J/m}^2$ due to simultaneous chemical anchorage and significant energy dissipation of bulk tough hydrogel during detachment (Yuk et al., 2016b). This interfacial toughness is comparable with the toughest bonding found between a tendon and a bone in humans (800 J/m^2) (Moretti et al., 2005).

Hydrogel-soft materials bonding

Soft elastomers such as PDMS, Ecoflex, VHB are commonly used for soft robotics and soft electronics (Cheng et al., 2019; Zhang and Khademhosseini, 2017). The delamination issues occurred, due to no hydrogel-elastomer bonding, in previous studies involving devices such as soft actuator (Keplinger et al., 2013), soft energy harvester (Parida et al., 2017), and wearable sensor (Kim et al., 2016a; Sun et al., 2014). Strongly bonding hydrogels to elastomers could empower soft robots with novel functions such as multimodal sensing capability. Yet, the hydrogel-elastomer assembly is another challenge due to their significant contrast of surface. In addition, the adhesion should be able to withstand large deformations (over 100% stretchability) for soft robotic applications, in which the connection between the hydrogel and the elastomer must be strong (Yang et al., 2020). The previous strategy of strongly bonding hydrogels to rigid solids is generally inapplicable for forming hydrogel-elastomer hybrids with robust interfaces. The possible bonding failure is due to the fact that oxygen permeable elastomers could inhibit the free radical polymerization of the hydrogel polymers (Dendukuri et al., 2008; Van Amerongen, 1946) and hydrophobic recovery of saline-functionalized elastomer surfaces could significantly lower the effectiveness of hydrogel bonding

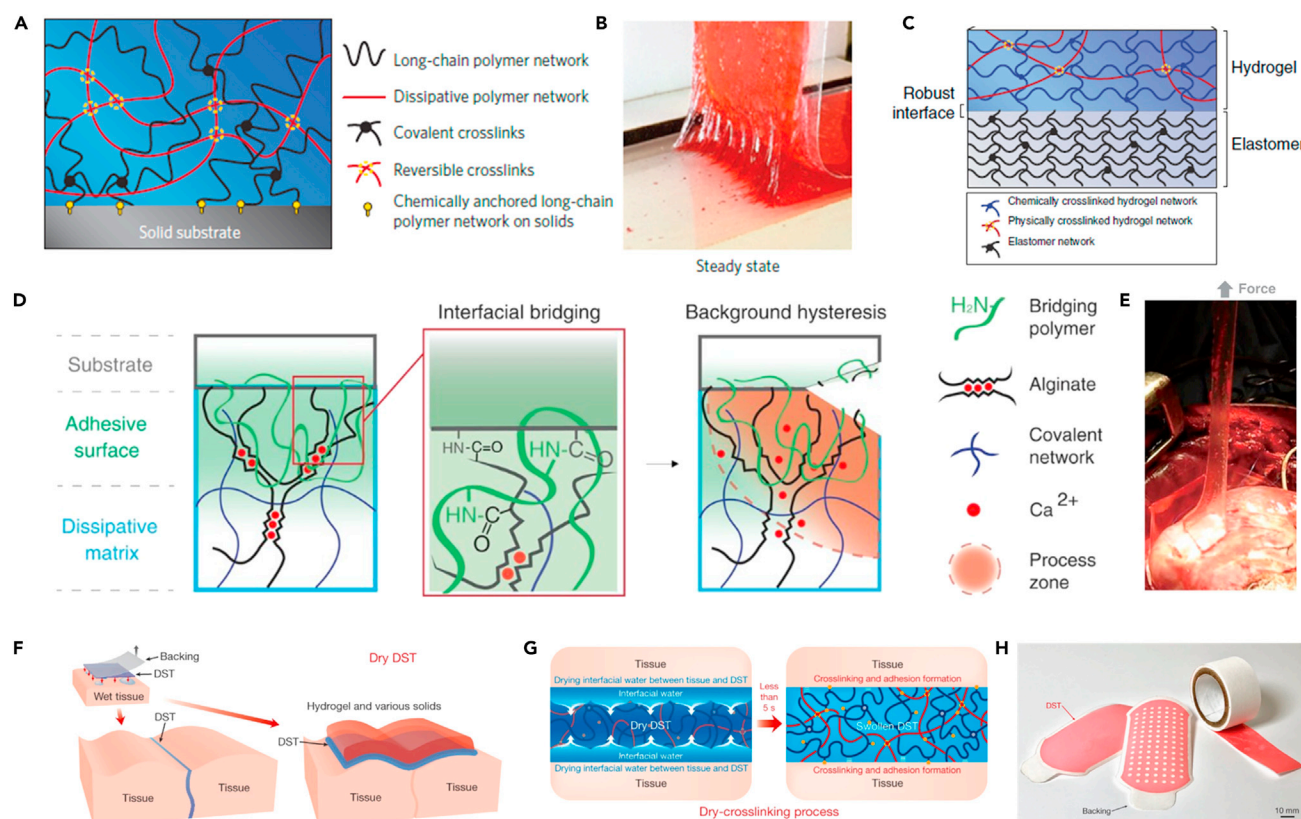


Figure 5. Hydrogel adhesives

(A) The tough bonding between hydrogel and solid surfaces.
 (B) Photograph of the peeling process of a tough hydrogel with its long-chain network chemically anchored on a glass substrate. Reprinted and adapted with permission from Ref. (Yuk et al., 2016b), Nature publish group.
 (C) The tough bonding between hydrogel and soft materials. Reprinted and adapted with permission from Ref. (Yuk et al., 2016a), Nature Publish Group.
 (D) Design of hydrogel tough adhesives.
 (E) *In-vivo* test on a beating porcine heart with blood exposure. (D and E) Reprinted and adapted with permission from Ref. (Li et al., 2017a), American Association for the Advancement of Science.
 (F) Tissue adhesive takes the form of a dry DST.
 (G) The dry cross-linking mechanism for the DST integrates the drying of interfacial water by hydration and swelling of the dry DST, temporary cross-linking, and covalent cross-linking.
 (H) The DST can take on various shapes owing to its high flexibility in fabrication. (F–H) Reprinted and adapted with permission from Ref. (Yuk et al., 2019b), Nature Publish Group.

on elastomers (Fritz and Owen, 1995; Zhou et al., 2010). Yuk et al. (Yuk et al., 2016a) described a method in which the precursors of tough hydrogels (e.g., PAAm-alginate, PAAm-hyaluronan, PAAm-chitosan, PEGDA-alginate, and PEGDA-hyaluronan) with physically cross-linked first network were gently mounted on the freshly benzophenone-treated elastomer surfaces (e.g., PDMS, Ecoflex, polyurethane, latex, and VHB). During photo-curing of the second network of the tough hydrogel, PAAm or PEGDA networks were covalently grafted to the methacrylate groups on the active elastomer surfaces (Figure 5C). This method achieved an elastomer-hydrogel hybrid with an adhesion energy over 1000 J/m² and 700% stretchability. This strategy has been utilized to coat a thin layer of hydrogel skin on a wide range of common polymers with arbitrary geometries and shapes, including medical tubing, foley catheters, and cardiac pacemaker leads with low friction and anti-fouling property (Yu et al., 2019). Soft and stretchable nanogenerators fabricated by this robust hydrogel-elastomer interfacial bonding method have been demonstrated recently with enhanced mechanical reliability and ambient stability (Lee et al., 2018b; Liu et al., 2018b).

However, the above strategy is not suitable to construct soft devices with microstructures patterned on cured elastomers (or hydrogels) due to the infiltration of pre-gel solutions (or pre-elastomer resins) into the surface microstructures. In addition, the elastomer cannot be bonded on a preformed hydrogel of

arbitrary shape. Recently, Suo et al. designed a strategy to coat and print various hydrogels and elastomers of arbitrary shapes and with strong adhesion, in which silanes can be incorporated as coupling agents into the precursors of both the hydrogel and elastomer to form strong bonding independent of the sequence of network formation (Liu et al., 2018a). This hydrophobic coating can enhance the hydrogel stability even at high temperatures (Liu et al., 2018a). Later on, an ionic hydrogel skin sensor was adhered to a soft gripper through this strategy for soft robotic sensing (Cheng et al., 2019).

Hydrogel-tissue bonding

Hydrogel as a biocompatible material has recently been applied for biomedical applications including wearable electronics, implantable electronics, and wound healing. However, bonding between hydrogel and tissue is usually poor due to the complex environment of biological tissues (bloody, wet, and dynamic, etc.), limiting their further applications. Existing commercially available tissue adhesives such as cyanoacrylate adhesives (Super Glue), albumin-based adhesives (BioGlue), fibrin glue (TISSEEL, Baxter), polyethylene glycol-based adhesives (COSEAL, Baxter and DURASEAL, and Confluent Surgical) (Li et al., 2017a; Sierra, 1993; Vakalopoulos et al., 2015; Wallace et al., 2001) are either cytotoxic, brittle, or non-wet-adherable (Li et al., 2017a; Vakalopoulos et al., 2015). In addition, none of the above-mentioned chemical modifications are suitable for tissue adhesion due to the toxic chemicals involved and long adhesion time during multiple steps of reaction. In 2017, Li et al., described a method to empower tough hydrogel surfaces (e.g., alginate/PAAm) with a strong adhesive by employing a bridging polymer that bears positively charged primary amine groups to achieve strong tissue-hydrogel adhesion (Li et al., 2017a). Such a bridging polymer can be absorbed to the tissue surface through both electrostatic attraction and covalent bonding. For covalent bonding, amide bond ($-\text{COO}-\text{NH}-$) can be formed in the presence of two common coupling reagents [1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC) and N-hydroxysulfosuccinimide (NHS)] between: (1) primary amine groups on bridging polymers and carboxylic acid groups on both the tough hydrogel matrix and to-be-adhered tissue substrates (e.g., skin) and (2) carboxylic acid groups on the tough hydrogel matrix (mainly the alginate network) and primary amine groups on the to-be-adhered tissue substrates. In addition, the bridging polymer can penetrate into the permeable tissue surfaces to form physical entanglements and chemical anchors (Figures 5D and 5E). Suitable bridging polymers include chitosan, polyallylamine, and polyethylenimine. During peeling, strong adhesion energy of more than $1,000 \text{ J/m}^2$ was achieved due to the electrostatic interactions, covalent bonds, and physical interpenetration between the tissue and hydrogel, and energy dissipation of the tough hydrogel matrix (Li et al., 2017a). Such an adhesion strategy was further applied on a PNIPAM-alginate DN hydrogel to realize a mechanically active adhesive dressing to accelerate wound closure (Blacklow et al., 2019). However, this method takes certain period of time (more than 30 min), which is undesirable during surgery. More recently, Yuk et al. reported an alternative tissue adhesive in the form of a dry double-sided tape (DST) made from a combination of a biopolymer (gelatin or chitosan) and cross-linked poly(acrylic acid) (PAAc) grafted with N-hydroxysuccinimide ester (Figures 5F–5H) (Yuk et al., 2019b). By removing interfacial water from the tissue surface, the dry DST becomes wet and can form a fast temporary cross-linking to the wet tissue surface within 5s. The NHS ester groups grafted on the PAAc also couple covalently with the primary amine groups on various tissues within a few minutes to provide tough and long-term stable adhesion (Yuk et al., 2019b).

In summary, in this section we mainly introduced several strategies to realize tough and strong adhesion between hydrogel and various substrates including metal, plastics, glass, ceramics, PDMS, Ecoflex, VHB, and tissues. Readers can refer to other review articles for more details (Lee et al., 2018a; Li et al., 2021; Ma et al., 2021; Nam and Mooney, 2021; Pei et al., 2021; Yang and Suo, 2018). While most existing hydrogel adhesives are permanent, novel adhesives designed with on-demand detachability and other functions (e.g., ambient stability, anti-freeze, anti-swell, conductivity, reversibility, and degradability) are needed in many practical applications including wearables, implantables, and robots. For example, we reported an ambient stability and anti-freezing conductive tough hydrogel with diverse adhesions for wearable sensing and soft robotics (Ying et al., 2021a). Yang et al. reported a PH-triggered, on-demand detachable adhesive (Yang et al., 2018). Chen et al. reported a saline solution (glutathione and sodium bicarbonate)-triggered benign detachable tissue adhesive (Chen et al., 2020c). Kim et al. reported a low-voltage (1 V) reversible electroadhesion based on an ionoelastomer diode (Kim et al., 2020b).

APPLICATIONS OF SKIN-LIKE HYDROGEL DEVICES

Skin-like hydrogel devices show tremendous potential to reduce the mechanical, electrical, and/or biological mismatch between humans and robots/machines, blurring the boundary between soft-robotic/human

bodies and engineering electrical/electronic devices. In a human–robot interaction loop, wearable hydrogel skins/sensors can empower the robot with human-like sensation to sense the mechanical, thermal and other biochemical stimuli from the environment. Also, hydrogel-based or hydrogel-integrated soft robots can interact with humans and the environment more effectively with low safety concerns. This section will summarize the recent progress of hydrogel-based wearable sensors and soft robots. In addition, compliant hydrogel-based energy harvesters for wearable and soft robotic applications will be discussed as an emerging topic.

Hydrogel-based sensors

Sensory receptors in our human skin can perceive various environmental stimuli including pressure, strain, deformation, humidity, temperature, and pain. So far, many skin-inspired flexible and stretchable wearable electronics have been demonstrated. Among them, skin-like hydrogel devices, especially wearable sensors, have attracted notable attention due to their softness, skin-like ionic sensing nature, biocompatibility, and tunable mechanical properties. Herein we will discuss the details of these hydrogel wearable devices including wearable biophysical and biochemical sensors and briefly highlight the current challenges.

Hydrogel-based biophysical sensors

Hydrogel wearables have been designed to measure various biophysical stimuli such as strain, stress and temperature, mimicking the sensation of human skins. Currently, hydrogel-based wearable biophysical sensors mainly monitor the external stimuli by providing electrical signals including resistance, capacitance, and some self-generated signals such as open-circuit voltage and short-circuit current.

Hydrogel-based biomechanical sensors. Hydrogel-based sensors have been developed to monitor the cardiovascular conditions (e.g., blood pressure and heart/pulse rate) and body movements (e.g., skin strain caused by movement) indicating a person's health conditions. In this regard, hydrogel-based pressure and strain sensors will be discussed below.

Hydrogel-based pressure sensors with skin-like sensation have been demonstrated in recent years, with measurement ranges from the low-pressure regime (<10 kPa; generated by gentle touch, intraocular pressure, and intracranial pressure) to the medium-pressure regime (10–100 kPa; generated by the heart beating, blood pressure wave, respiration, and object hand manipulation, and blood pressure) and to the high-pressure regime (>100 kPa; generated by body weight and other types of input) (Bai et al., 2020; Pan et al., 2014; Pu et al., 2017; Sun et al., 2014; Trung and Lee, 2016; Zhu et al., 2018b). The sensing mechanisms of hydrogel pressure sensors have been based primarily on pressure-induced changes in capacitance (Bai et al., 2020; Sun et al., 2014; Xie et al., 2018; Zhu et al., 2018b), triboelectricity (Lee et al., 2018b; Liu et al., 2018b; Pu et al., 2017), and piezoresistivity (Ko et al., 2018; Pan et al., 2014; Tai et al., 2015).

Capacitance-based ionic hydrogel pressure sensors. Capacitors are usually constructed by sandwiching a dielectric layer between two conductors. The capacitance C is given by the equation $C = \epsilon_0 \epsilon_r (A/d)$, where ϵ_0 is the vacuum permittivity, ϵ_r is the relative permittivity of the dielectric material, A is the overlapping area of the two conductor plates, and d is the thickness of the dielectric layer in between. For capacitive pressure sensors, the parameters of the dielectric layer (ϵ_r , A , and d) can be sensitive to pressure input. The change of thickness d is commonly used for the detection of applied pressure to the sensor. Various elastomers including PDMS, Ecoflex, and VHB with low modulus values are usually used as the dielectric layer on soft and stretchable capacitive pressure sensors. Upon being deformed to λ times its original thickness, both the width and the thickness of the dielectric changed by a factor $1/\sqrt{\lambda}$ due to hydrogel's incompressibility. As a result, the ratio of the capacitance of the deformed sensor (C) to that of the undeformed sensor (C_0) is shown in Equation 1.

$$\frac{C}{C_0} = \frac{\epsilon_0 \epsilon_r \left(\frac{1}{2} \cdot \frac{1}{2} \cdot w \right)}{\epsilon_0 \epsilon_r \left(\frac{l \cdot w}{d} \right)} = \lambda^{-2} \quad (\text{Equation 1})$$

Accordingly, the gauge factor (GF) of the capacitance-based ionic hydrogel pressure sensors is $GF = \frac{C-C_0}{(1-\lambda)C_0} = (1+\lambda)/\lambda^2$, where $\lambda = 1-\epsilon$, here ϵ is the pressure-induced strain.

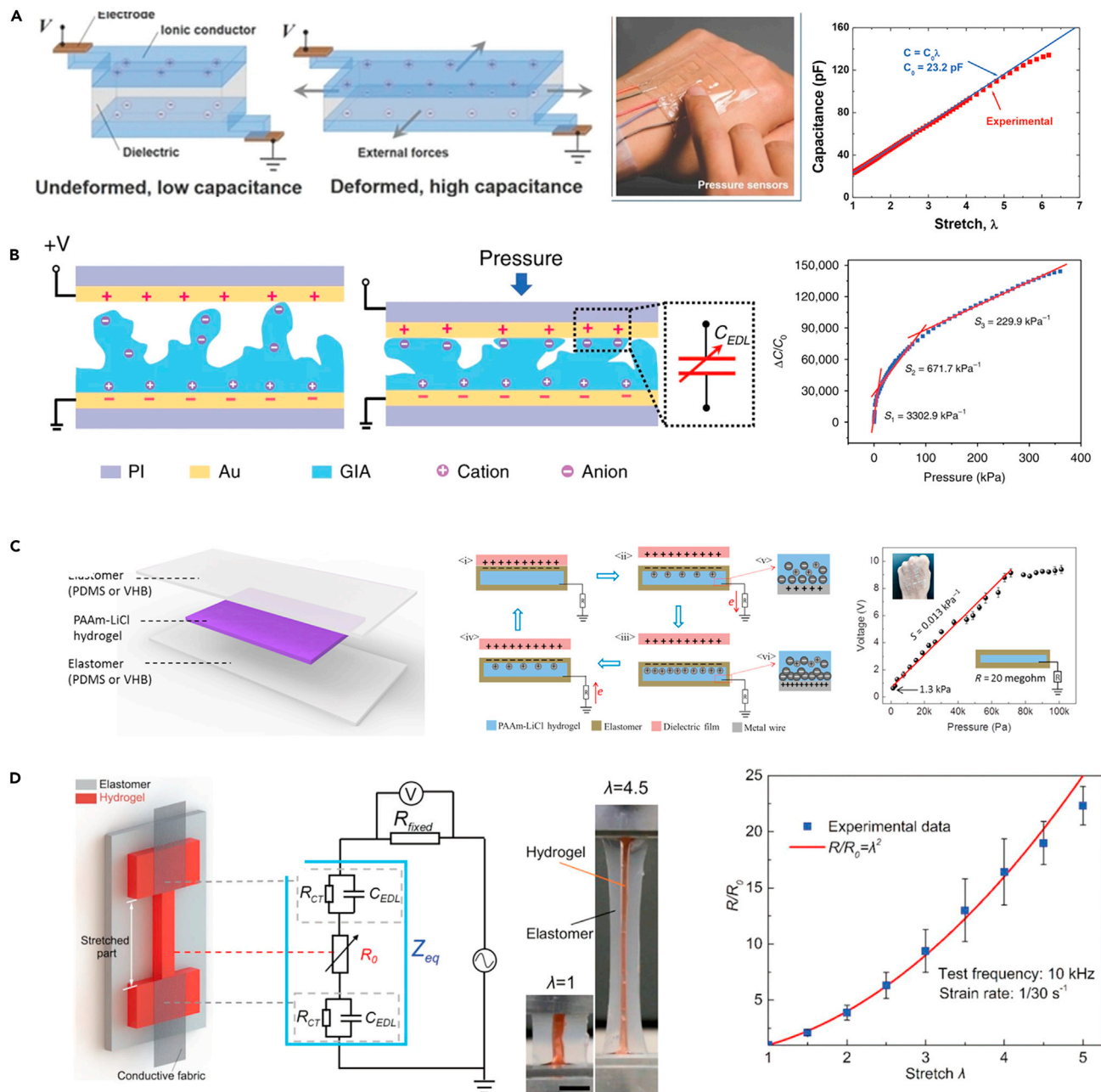


Figure 6. Hydrogel-based biomechanical sensors

(A) Capacitance-based ionic hydrogel pressure sensors. Reprinted and adapted with permission from Ref (Sun et al., 2014).

(B) Graded intrafillable architecture-based ionic hydrogel pressure sensor. Reprinted and adapted with permission from Ref. (Bai et al., 2020).

(C) Triboelectric nanogenerator-based ionic hydrogel pressure sensor. Reprinted and adapted with permission from Ref. (Pu et al., 2017).

(D) Resistance-based ionic hydrogel strain sensor. Reprinted and adapted with permission from Ref. (Cheng et al., 2019).

Sun et al. (2014) developed a transparent, stretchable hydrogel-based wearable pressure sensor by sandwiching an elastomer layer between two PAAM hydrogel layers (containing NaCl) with two metallic electrodes (Figure 6A). The whole sensor was encapsulated by two additional layers of VHB for electrical insulation and water retention. The equivalent series capacitance is dominated by the hydrogel-elastomer-hydrogel capacitance other than the capacitance of the electrical double layer (EDL) in the hydrogel-metal interface because the latter one is much larger. The thickness of the elastomer is decreased as well as its area increased if there is any pressure applied, leading to the increase of capacitance. This hydrogel-based

pressure sensor showed high resolution in the range of 1 kPa, which is sensitive enough to detect a gentle touch of a finger (<10 kPa) (Sun et al., 2014). Later, a hydrogel-based sensor array was developed and can sense multiple gentle finger touches even in bending and stretch statuses (Sarwar et al., 2017). In addition, based on the capacitive sensing mechanism, a PAAm hydrogel containing lithium chloride with metallic electrodes at both ends was designed into a soft, stretchable and transparent touchpad for human-machine interaction with negligible delay ($\sim 10^{-3}$ s) (Kim et al., 2016a).

Current hydrogel-based capacitive pressure sensors usually suffer from low response rate, low sensitivity and limited or saturated response under high pressures (>100 kPa), while applications such as robotic manipulation and pressure monitoring (in human body) demand both high sensitivity and high-pressure resolution at pressures over 100 kPa. Bai et al. developed a hydrogel-based capacitive pressure sensor with ultra-broad pressure sensing range with high sensitivity as well as fast response (Bai et al., 2020). By engineering graded intrafillable microstructures on the ionic hydrogel, a mechanically dynamic EDL was formed between hydrogels and the metal. This flexible capacitive pressure sensor exhibits an unprecedentedly high sensitivity ($S_{\min} > 220 \text{ kPa}^{-1}$) over a broad pressure range (0.08 Pa–360 kPa), an ultrahigh pressure resolution (18 Pa or 0.0056%) over the full pressure range, and a fast response time (<20 ms at 1 kHz for the loading of 5 kPa) (Figure 6B) (Bai et al., 2020).

Triboelectricity-based ionic hydrogel pressure sensors. Most above-mentioned flexible/stretchable capacitance-based pressure sensors require a continuous power supply. Differently, the recently developed triboelectric nanogenerator (TENG) could use its self-generated current and voltage signals to monitor the applied pressure without external power. For the first time, Pu et al. reported a soft skin-like triboelectric nanogenerator (STENG) that enables both biomechanical energy harvesting and tactile sensing by hybridizing elastomer and ionic hydrogel as the electrification layer and the electrode, respectively (Pu et al., 2017). An STENG-based artificial electronic skin with 3×3 sensor arrays was fabricated, which is pressure sensitive. The skin can be used for wearable touch/pressure perception based on the self-generated OCV, with a comparable sensitivity of 0.013 kPa^{-1} and a resolution of 1.3 kPa (Figure 6C) (Pu et al., 2017). This work provides new opportunities of multifunctional power sources for potential applications in soft/wearable electronics.

The strain signal on the human body can be measured for healthcare applications such as diagnosis, rehabilitation assistance and activity monitoring. Hydrogel-based strain sensors have been demonstrated in recent years, with capabilities ranging from the detection of small (e.g., breath, wrist pulse, vibration of the vocal cords, heartbeat) to large body deformations (e.g., the body joint movements) (Zhang et al., 2020a). The sensing mechanisms of ionic hydrogel strain sensors have been based primarily on changes in resistance (Cheng et al., 2019; Fan et al., 2019; Liu et al., 2020b; Manandhar et al., 2012; Tian et al., 2017) and capacitance (Dai et al., 2019; Lei and Wu, 2018; Sun et al., 2014), which will be introduced below. Their performance such as stretchability, sensitivity (gauge factor), hysteresis, and linearity will be presented.

Resistance-based ionic hydrogel strain sensors. The resistance (R) of a material is given by the equation $R = \rho \cdot l / A$, where ρ is the resistivity, l the length, and A the cross-sectional area of the material. Note that the deformation of an ionic hydrogel only changes the configuration of its polymer network and water molecules with negligible effect on its ionic conductivity (Cheng et al., 2019). Upon deformation to λ times its original length, the cross-sectional area of ionic hydrogel is reduced by the same factor of λ due to incompressibility of hydrogel materials. As a result, the ratio of the resistance of the stretched hydrogel (R) to that of the unstretched hydrogel (R_0) is $R/R_0 = \lambda^2$ (Cheng et al., 2019). Accordingly, the GF of the resistance-based ionic hydrogel strain sensors is shown in Equation 2:

$$GF = \frac{R - R_0}{(\lambda - 1)R_0} = \lambda + 1 \quad (\text{Equation 2})$$

GF increased with the applied strain, which makes stretchable ionic hydrogels ideal as large-strain sensors. For example, an ionic PAAm hydrogel was adhered to an elastomeric soft robot for motion sensing (Figure 6D) (Cheng et al., 2019). GF of the hydrogel-based strain sensor increases from 2 to 6 within a large strain range (0–400%). Additionally, Tian et al. developed a strategy for 3D printing of transparent and conductive hydrogel. With sub-millimeter printing resolution, resistance-based LiCl/PAAm hydrogel strain sensors were printed for human-machine interaction and soft robotics applications (Tian et al., 2017). This

3D printing technology may enhance the GF of resistive hydrogel strain sensors by accurately printing wavy shape hydrogels to better monitor small strains such as vocal vibration.

Capacitance-based ionic hydrogel strain sensors. Capacitance-based ionic hydrogel sensor is another common type of device for strain monitoring. The mechanism of capacitance-based strain sensing has been introduced in the section of [Capacitance-based ionic hydrogel pressure sensors](#). Similarly, the parameters of the dielectric layer (length l , width w and thickness d) can be sensitive to the applied strain. Upon uniaxially stretching to λ times its original length, both the width and the thickness of the dielectric layer reduce by a factor $\sqrt{\lambda}$ due to incompressibility of hydrogels. As a result, the ratio of the capacitance of the stretched strain sensor (C) to that of the unstretched (C_0) is shown in [Equation 3](#):

$$\frac{C}{C_0} = \frac{\frac{\epsilon_0 \epsilon_r (1+\lambda) \cdot l \cdot (1-\sqrt{\lambda}) \cdot w}{(1-\sqrt{\lambda}) \cdot d}}{\epsilon_0 \epsilon_r \left(\frac{l \cdot w}{d} \right)} = \lambda \quad (\text{Equation 3})$$

Accordingly, the GF of the capacitance-based ionic hydrogel strain sensor is $GF = \frac{C-C_0}{(\lambda-1)C_0} = 1$. The capacitance of capacitance-based ionic hydrogel strain sensors increases linearly with the applied strain. Therefore, the capacitance-based ionic hydrogel strain sensors have a better linearity than the resistance-based ones. In addition, the capacitance-based strain sensor has less hysteresis and is usually temperature independent ([Lei and Wu, 2018](#)). However, this linear response range is limited to a certain strain level because of the reduced permittivity of the dielectric layer at large strains ([Tröls et al., 2013](#)). For example, the ionic skin developed by Sun et al. can monitor the strain change with maximum stretchability around 500% ([Sun et al., 2014](#)). At large stretches near rupture, the measured capacitance was slightly lower than that of the theoretical prediction ([Sun et al., 2014](#)). Therefore, capacitance-based ionic hydrogel strain sensors have certain limitation in large strain sensing applications.

The above-mentioned stretchable capacitance- or resistance-based pressure sensors usually require an external power supply; in contrast, several recently developed hydrogel-based soft ionic diodes could realize self-powered strain sensing without requiring a power supply ([Hou et al., 2017](#); [Kim et al., 2020a](#); [Ying et al., 2020a](#)). For example, a hydrogel-based ionic diode with a stretchability of 400% was constructed using a bilayer of double-network hydrogels with positively and negatively charged polyelectrolytes (PSS and PDAC) in its two separate layers ([Ying et al., 2020a](#)). By forming a depletion layer (or call ionic double layer) in the interface of the two hydrogel layers, the built-in potential can change in response to the deformation (pressure, compressive strain, and stretching strain) of the bilayer and the deformation-induced re-diffusion of mobile ions within the depletion layer. Larger deformation results in a larger change of the built-in potential ([Hou et al., 2017](#); [Kim et al., 2020a](#); [Ying et al., 2020a](#)).

Hydrogel-based temperature sensors. Temperature sensation is another critical functionality of human skin and plays a significant role in human perception. Several types of hydrogels are able to respond to the change of temperature, including the commonly used thermoresponsive poly(N-isopropylacrylamide) (PNIPAM) hydrogels and other cross-linkable polymers such as N,N-dimethylacrylamide (DMAAm) and 2-(dimethyl maleimide)-N-ethyl-acrylamide (DMIAAm) ([Banerjee et al., 2018](#)). For example, the polymeric structure of PNIPAM switches between hydrophilic and hydrophobic states at its lower critical solution temperature (LCST, 30–35°C) ([Schild, 1992](#)), leading to changes in the volume and shape of the polymeric hydrogel ([Yoshida et al., 1995](#)). This feature has been utilized for the design of adaptive microlenses ([Dong et al., 2006](#)) and smart windows ([Li et al., 2019](#)).

Traditional thermoresponsive hydrogels, however, are generally electrically non-conductive, while conductive hydrogels are promising for more accurate and quantitative sensing applications. In addition, traditional thermoresponsive hydrogels usually do not consist of good mechanical performance due to their single-network structure. Therefore, Shi et al. recently introduced the conductive polymer hydrogels (PANI or PPy) into PNIPAM hydrogels through *in-situ* formation of continuous network of conductive polymer hydrogels ([Figure 7A](#)) ([Shi et al., 2015](#)). This unique interpenetrating binary network structure empowers the hybrid hydrogels with high electrical conductivity (0.84 ± 0.02 S/m), high thermoresponsive sensitivity (significant volume change as well as corresponding resistance change within 10 s) and enhanced mechanical properties. The significant and rapid electrical signal (e.g., resistance) change of these hybrid hydrogels in a cooling-heating cycle (between 25 and 50°C) may find bioelectronic applications as wearable temperature sensors ([Shi et al., 2015](#)).

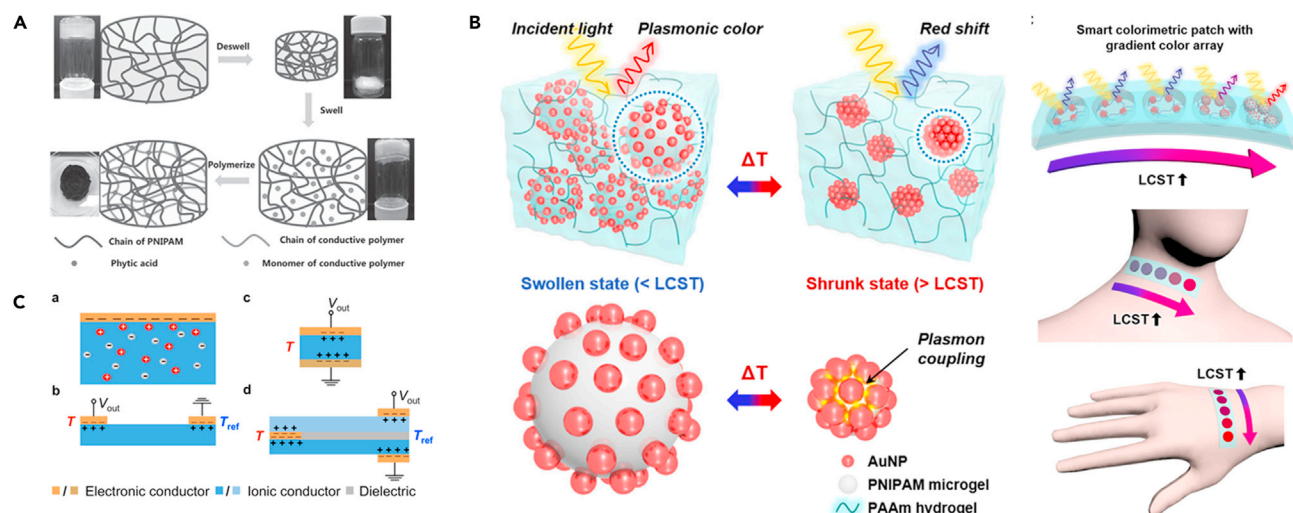


Figure 7. Hydrogel-based temperature sensor

(A) Schematic illustration of synthesis process of a hybrid hydrogel composed of PNIPAM and conductive polymers. Reprinted and adapted with permission from Ref. (Shi et al., 2015).

(B). Schematic illustration of the plasmonic microgels in the PAAm hydrogel under swollen and shrunk states and schemes of a sensor array patch attached to human skin at different positions (neck and hand). Reprinted and adapted with permission from Ref. (Choe et al., 2018).

(C) Three principles of stretchable elastomeric thermocouple. Reprinted and adapted with permission from Ref. (Wang, 2019).

Alternatively, gold nanoparticles were decorated on PNIPAM to form raspberry-shaped plasmonic microgels that were thereafter embedded in stretchable PAAm hydrogels to construct a smart colorimetric thermometer patch (Figure 7B) (Choe et al., 2018). This as-fabricated hydrogel film achieved a fast (1 s) and efficient thermoresponsive color change with a temperature-sensing resolution of 0.2°C. This thermoresponsive colorimetric patch allowed high-sensitivity and repeatable temperature monitoring without any external power source over the temperature range of 29–40°C. By encapsulating the hydrogel film with polydimethylsiloxane (PDMS), it can be stretched by up to 90% without showing a color change (Choe et al., 2018). This robust, temperature-sensitive, yet stretch-insensitive colorimetric temperature sensing patch can be potentially applied to wearable and robotic sensing.

On the other hand, an ionic hydrogel conductor (NaCl-PAAm gel) was demonstrated as a novel soft, transparent, and stretchable temperature sensor (Wang, 2019). The voltage across the EDL at the electrode-hydrogel interface is sensitive to temperature. Therefore, based on three unique designs of electrode-hydrogel junctions (Figure 7C), this hydrogel sensor can use the self-generated voltage difference to monitor the change in temperature. This temperature sensor shows much higher sensitivity and a faster thermal response than the traditional thermocouples. In addition, the generated voltage is only sensitive to temperature but insensitive to stretch (Wang, 2019). The mechanically stretchable yet stretch-insensitive temperature sensing ability makes this hydrogel thermocouple highly useful for conformal temperature monitoring in healthcare and soft robotics applications.

The measuring range of the above-mentioned hydrogel-based sensors typically ranges from room temperature to 50°C because common hydrogels are intrinsically volatile at high temperatures and freezable at sub-zero temperatures. In order to broaden their temperature sensing range to the extremely hot or cold environment, strategies such as adding glycerol, EG and CaCl₂ (Li et al., 2020) or using nonvolatile PILs (Liu et al., 2020c) can be adopted.

Hydrogel-based biochemical sensors

Wearable biochemical sensors hold great potential for healthcare analytics due to their good portability, low cost, non-invasiveness, and ease of operation. Existing biochemical sensors have already been demonstrated for personal health monitoring and fitness monitoring by detecting various analytes including glucose, uric acid, lactate, ions level, stress level, humidity, and PH (Bariya et al., 2018; Heikenfeld et al., 2019; Kim et al., 2019; Zhao et al., 2021b). Hydrogels have been widely used as a sensing material for

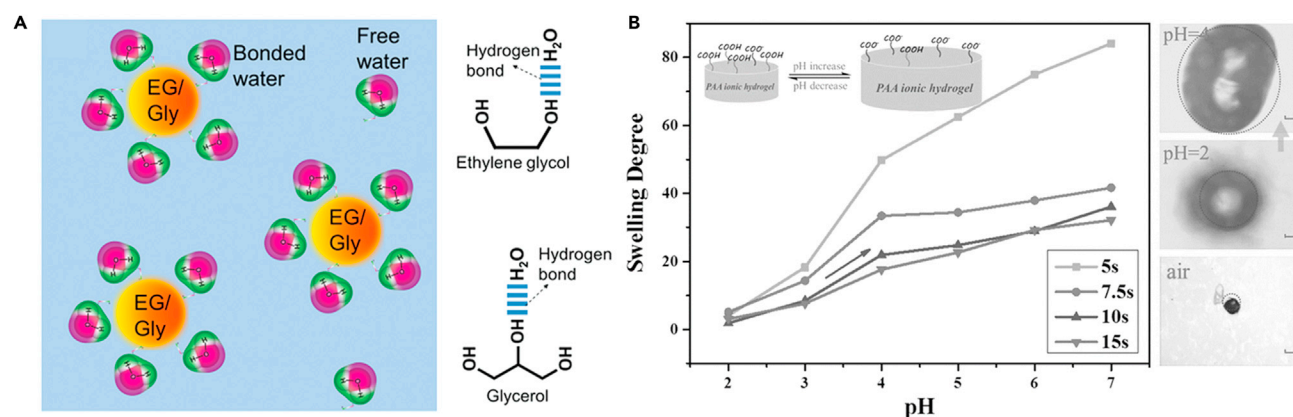


Figure 8. Hydrogel-based biochemical sensor

(A) Schematics of organohydrogel-based humid sensors based on the mechanism of hygroscopic EG/glycerol molecules capable of adsorbing water molecules (via forming hydrogen bonds), which improves both the water-holding and humidity sensing capabilities of the organohydrogel. Reprinted and adapted with permission from Ref. (Wu et al., 2019a).

(B) Poly(acrylic acid) ionic hydrogel for pH sensing Reprinted and adapted with permission from Ref. (Yin et al., 2016).

wearable biochemical monitoring and point-of-care detection (Banerjee et al., 2018; Culver et al., 2018; Tavakoli and Tang, 2017; Liu et al., 2020d).

Hydrogel-based humidity sensors. Humidity level is an important parameter of human physiology. Although humidity is not a biochemical signal, we discuss hydrogel-based humidity sensors in this section as it is usually measured simultaneously with other biochemical parameters for physiological monitoring. The moisture level of our skin can provide valuable physiological and metabolic information. On the other hand, moisture monitoring of a wound site would also provide information about its healing status (Derakhshandeh et al., 2018; Gianino et al., 2018). Hydrogel is promising for the development of epidermal wearable and stretchable humidity sensors. In order to achieve a wide measurement range of hydrogel humidity sensors, hygroscopic materials such as EG and glycerol are usually incorporated into the hydrogel matrix to enhance its ambient stability. For example, a ionic hydrogel-based, ambient-stable and stretchable artificial skin with humidity sensing capability was developed recently (Ying et al., 2020a). By incorporating EG, the hydrated double network can absorb, or release water based on the ambient humidity and will not dry out and can still be highly stretchable even in the extremely dry environment. Due to humidity-included geometric and ion concentration changes, this diode-like stretchable hydrogel sensor can monitor the humidity change (13%–85%) by four electrical signals: resistance, capacitance, SCC and OCV (Ying et al., 2020a). Wu et al. reported EG/glycerol modified carrageenan/PAAm organohydrogels for humidity sensing (Figure 8A) (Wu et al., 2019a). Due to the facile formation of strong hydrogen bonds between H₂O molecules and hydrophilic groups in the binary solvent and DN polymer chains, this stretchable (1225% strain), self-healing and transparent ion-conductive hydrogel displayed high humidity sensitivity (within a wide range of 4–90%), good stability, high linearity, and fast response (0.27 s) and recovery rate (0.3 s) for human respiration monitoring (Wu et al., 2019a). The family of hygroscopic-chemical-incorporated ionic hydrogels as new humidity responsive materials is promising for wearable applications.

Hydrogel-based glucose sensors. Metabolic molecules such as glucose, lactate acid, and uric acid are important indicators of human health conditions. Therefore, the continuous monitoring of these indicators is important for personal healthcare, diagnostics, and physiological monitoring. Currently, many epidermal wearable biosensors have been developed to non-invasively monitor the glucose level in sweat (Gao et al., 2016), tears (Elsherif et al., 2018; Kim et al., 2017), saliva (Kim et al., 2015a; Tseng et al., 2018), and interstitial fluid (ISF) (Chen et al., 2017b; Kim et al., 2019). Among them, hydrogels have been utilized for the development of wearable glucose sensors (Elsherif et al., 2018; Zhang et al., 2020d). The mechanisms of hydrogel based glucose sensors are mainly based on electrochemical sensing (Guascito et al., 2011; Ren et al., 2006; Su et al., 2013; Vaddiraju et al., 2009; Wu and Yin, 2013; Zhai et al., 2013), optical sensing (Mesch et al., 2015; Suri et al., 2003; Vilozny et al., 2011; Zhang et al., 2013, 2014; Kim et al., 2016b; Wu et al., 2019b; Ying et al., 2020b), sensing based on geometric change (Cambre and Sumerlin, 2011; Hisamitsu et al., 1997; Kataoka et al., 1998; Kitano et al., 1991a, 1991b), and electrical sensing (Kajisa and Sakata, 2017; Shang et al., 2016).

Some mechanisms such as geometric changes have been utilized to design the glucose-responsive wearable insulin patch for regulation of blood glucose (Lee et al., 2017; Wang et al., 2020a; Yu et al., 2020a). Despite its popularity for glucose biosensing, hydrogels are mainly used as binding matrices for enzyme (e.g., glucose oxidase)-based electrochemical detection. The integration of ionic hydrogel for wearable glucose sensing is still largely missing. In the future, the shape and structure change of ionic conductive hydrogels (e.g., doped with boronic acid) in response to the various glucose levels as well as their corresponding change of electrical and optical parameters can be leveraged for design of novel wearable hydrogel-based glucose sensors (Elsherif et al., 2018; Shang et al., 2016).

Hydrogel-based pH sensors. The pH level is an important biochemical parameter of our body's physiological environment. Variations in pH can be either the cause or effect of a disease or a biological dysfunction (e.g., cancer, wound infection, or skin disorder) (Ghoneim et al., 2019). Therefore, the measurement of this essential parameter is important for personal healthcare. Today, conductive polymers such as polyaniline (PANI) have been widely used for pH sensing because of their high conductivity, stability, ion-exchanging ability and biocompatibility (Abu-Thabit et al., 2016; Ghoneim et al., 2019; Zhao et al., 2018b). Hydrogel can also be used for pH sensing based on the change of its geometric/optical/electrical/mechanical parameters induced by pH change (Naficy et al., 2014; Richter et al., 2008; Shastri et al., 2015; Tavakoli and Tang, 2017; Trinh et al., 2006; Yin et al., 2016; Zhang et al., 2004; Zhao et al., 2018b). Poly(acrylic acid) (PAA), an ionic hydrogel with a high density of carboxylic acids, superior biocompatibility, high water absorptivity, and good thin-film formability, has attracted remarkable interests for pH sensor design (Figure 8B) (Yin et al., 2016). Currently, PAA and its copolymerization with other hydrogels have been used for pH sensing (Gu et al., 2009; Richter et al., 2004; Ruan et al., 2003; Trinh et al., 2006; Yin et al., 2016). For instance, the poly(vinyl alcohol)-poly(acrylic acid) (PVA-PAA) hydrogel swells due to pH value change, leading to mechanical deformation of the attached metal plate and a corresponding change of capacitive or resistive signals (Trinh et al., 2006). Richter et al. showed that the swelling of a PVA-PAA-coated quartz crystal microbalance pH sensor had a short response time of 500 ms, a shrinking time of 800 ms, and sensitivity of 13.2 kHz/pH, in the pH range of 3–10 (Richter et al., 2004). In addition, the PVA-PAA hydrogel is highly stretchable (Wang et al., 2017), which could be useful for wearable and stretchable pH sensors.

Summary

In this section, various skin-inspired hydrogel-based wearable sensors have been reviewed. Biophysical stimuli sensing (e.g., pressure, strain, and temperature) as well as biochemical stimuli sensing (e.g., humidity, glucose, and pH) were summarized along with their sensing mechanisms and performance (e.g., sensitivity, linearity, range, hysteresis, resolution, and response time). In addition, current ionic hydrogels as electrode or coating have also been applied for measurement of electrophysiological signals such as electrocardiogram (ECG) and electroencephalogram (EEG) (Liu et al., 2020a; Wang et al., 2019a; Yuk et al., 2020). Human skin can perceive multiple environmental stimuli simultaneously with negligible mutual interference. This feature has inspired the development of many multifunctional wearable sensors for detecting strain, pressure, temperature, humidity, glucose, and ions (Gao et al., 2016; Harada et al., 2014; Ho et al., 2016; Nassar et al., 2016; Segev-Bar et al., 2017; Tien et al., 2014), including some ionic-hydrogel-based designs (Lei and Wu, 2018; Lei et al., 2017; Ying et al., 2020a). Ionic hydrogel can simultaneously respond to multiple stimuli such as pH, ions, strain, pressure, temperature, humidity (Liu et al., 2020d), which will bring undesired coupling between different sensing modalities. For signal decoupling, there have been several strategies developed. For example, the previously mentioned stretchable and wearable colorimetric patches can decouple temperature from strain using simple color signals (Choe et al., 2018). Also, different electrical signals have different degrees of correlation with those external stimuli. Our previous study of the hydrogel-based ionic diode showed that the resistance and SCCD signals show more obvious changing trends with the RH change than the capacitance and OCV signals in the full RH range; the OCV outputs showed little correlation with the RH change, the SCCD mode is more suitable for humidity sensing (Figure 9A) (Ying et al., 2020a). In addition, to better decouple the sensing of multiple stimuli, multiple sensing modules (each for a different stimulus) can be integrated on the same device substrate through microfabrication or 3-D printing. Recently, Lei and Wu developed a type of biomimetic ionotronics to imitate natural skins using supramolecular polyelectrolyte hydrogels with multiple sensory capabilities (Figure 9B) (Lei and Wu, 2018). A sandwich configuration of a VHB dielectric layer between two conductive ionic hydrogel layers are connected with three metal electrodes, in which a parallel-plate capacitive sensor and an ionic resistive sensor were formed. The parallel-plate capacitance is insensitive to temperature and increases linearly with tensile strain, while the resistive sensor signal is both temperature- and strain-sensitive. Consequently, with

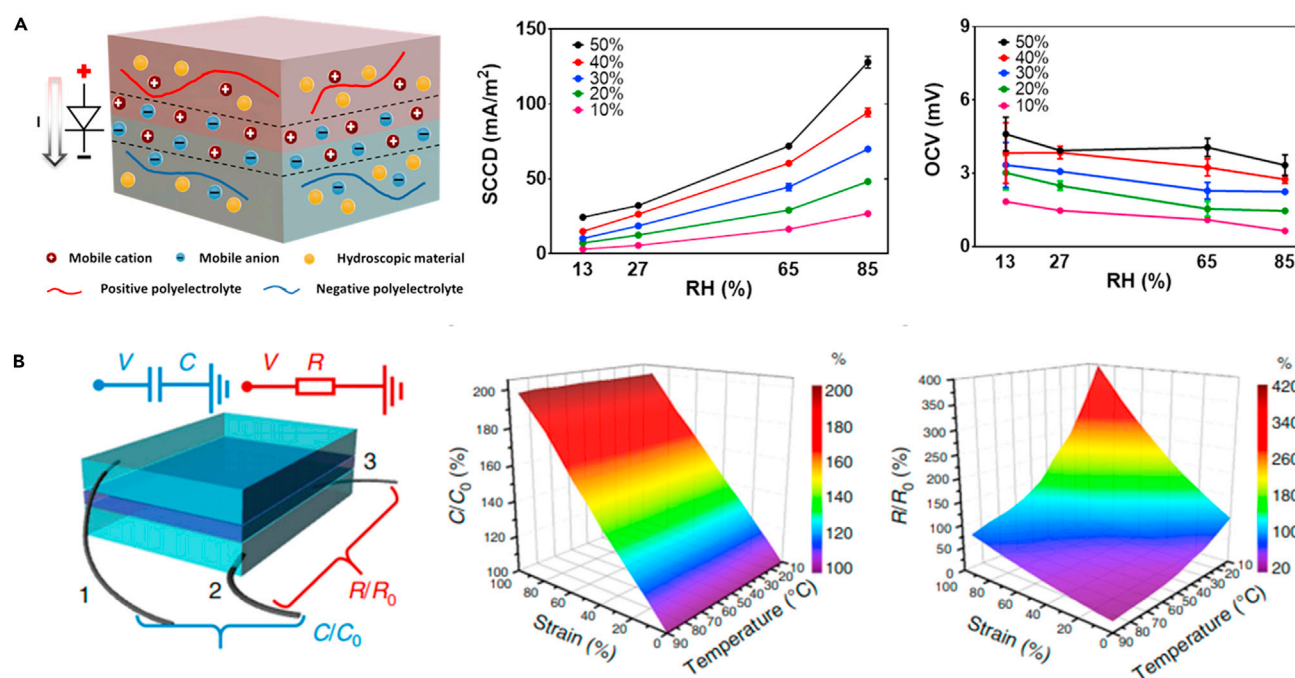


Figure 9. Hydrogel based multimodal sensation

(A) Strain and humidity sensing by an ionic diode-based artificial skin. Reprinted and adapted with permission from Ref. (Ying et al., 2020a).

(B) Strain and temperature sensing of a three-layer biomimetic skin. Reprinted and adapted with permission from Ref. (Lei and Wu, 2018).

both strain and temperature stimuli the capacitive sensor can distinguish the strain stimuli and meanwhile the temperature variation can be derived from the resistive signal change (Lei and Wu, 2018).

Ionic hydrogels for soft robotics

Soft robots are a type of bioinspired robots mimicking soft-bodied biological systems, which can deform and actuate continuously. As a complement to the rigid-bodied robots used extensively in manufacturing, soft robots have been developed to bridge the gap between the hard machines and soft humans due to their unprecedented adaptability to unstructured environments (Rus and Tolley, 2015). Constructed from intrinsically soft and/or stretchable materials, soft robots hold great potential for many application scenarios, including human-machine interaction, safely manipulation, navigation in space-restricted, rough and/or harsh environments with good resilience, and human rehabilitation and assistance (Chen et al., 2020b; Rus and Tolley, 2015; Shih et al., 2020). Currently, soft materials such as silicone rubbers, elastomers (Ecoflex and PDMS) VHB, paper and their combinations have been used for the design and fabrication of soft robots (Chen and Pei, 2017; Chen et al., 2020b; Gu et al., 2018; Larson et al., 2016; Li et al., 2017b; Shepherd et al., 2011).

Hydrogels have also been used soft robot designs (Banerjee et al., 2018; Liu et al., 2020d; Yang and Suo, 2018). Through modification of hydrogels with other functional groups/additives/nanofillers, hydrogel-based soft robots can response (e.g., change shapes and/or structures) to external stimuli such as heat (Kim et al., 2015b), light (Qian et al., 2019; Zhao et al., 2019), pH (Beebe et al., 2000; Duan et al., 2017), humidity (Gladman et al., 2016), electrical fields (Morales et al., 2014; Yang et al., 2015a), ions (Palleau et al., 2013), magnetic signals (Huang et al., 2016), biomolecules (Shastri et al., 2015), pneumatic (Baumgartner et al., 2020) and hydraulic pressures (Yuk et al., 2017). Readers can refer to several previous review papers for more details (Ding et al., 2020; Erol et al., 2019; Liu et al., 2020d). In addition, ionic conductive hydrogels can respond to stimuli including electrical fields and mechanical deformation, and have been integrated into traditional soft robots as sensing skins or into soft dielectric actuators as soft electrodes.

Ionic hydrogel-based robotic skins

Stretchable skin-like devices capable of physical and chemical sensation are valuable for human-like robots and smart rehabilitative devices. Due to its merits such as high optical transparency, electrical

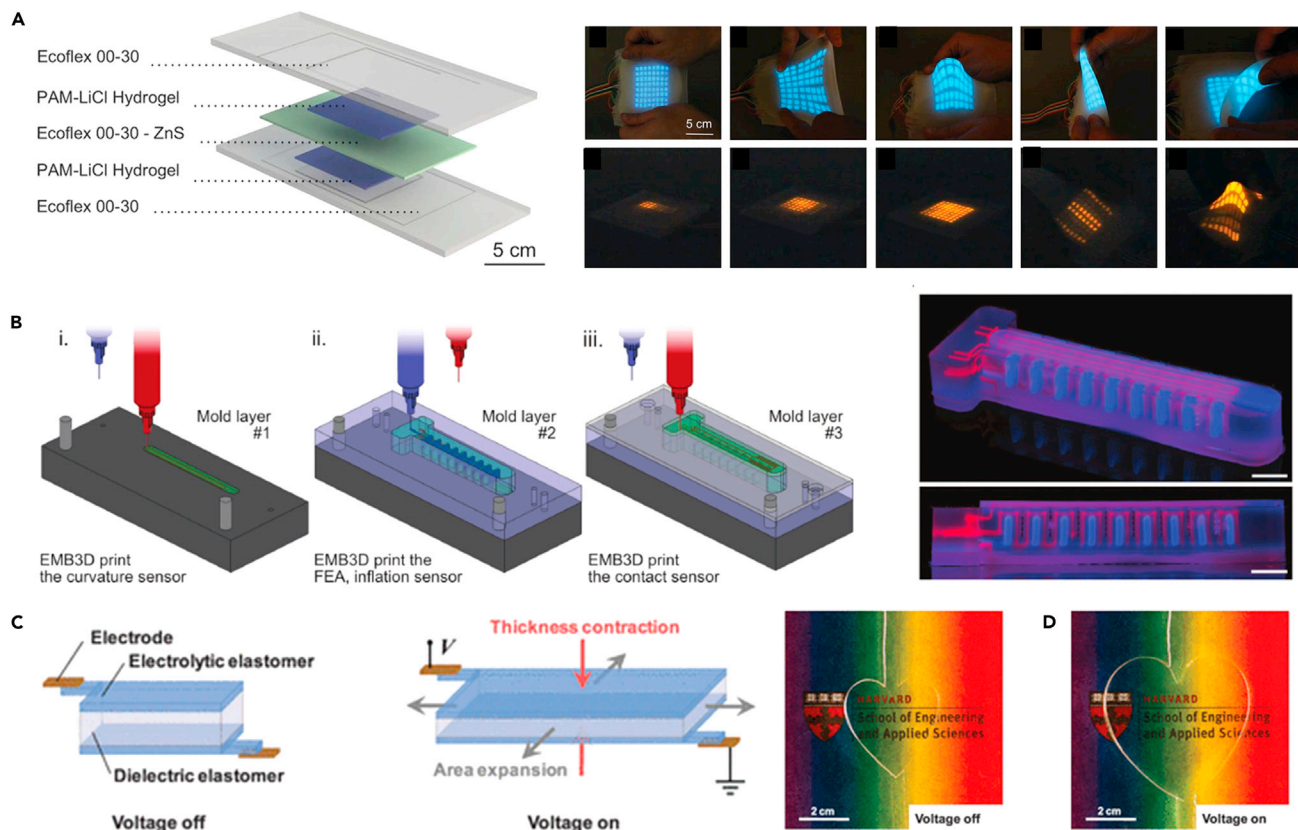


Figure 10. Ionic hydrogels for soft robotics

(A) Highly stretchable electroluminescent skin for optical signaling and tactile sensing. Reprinted and adapted with permission from Ref. (Larson et al., 2016).

(B) Soft somatosensitive actuator innervated with multiple soft sensors (curvature sensor, the inflation sensor and the contact sensor). Reprinted and adapted with permission from Ref. (Truby et al., 2018).

(C) Ionic hydrogel-based stretchable electrodes for dielectric elastomer actuators. Reprinted and adapted with permission from Ref. (Kepplinger et al., 2013).

conductivity and mechanical stretchability, ionic hydrogel is a good material candidate for fabricating robotic skins.

Inspired by octopuses that have a stretchable skin and color-tuning organs to control both body posture and color for visual communication and disguise, Larson et al. presented a hyperplastic light emitting capacitor (HLEC) skin (Larson et al., 2016). The skin was formed by sandwiching a dielectric Ecoflex layer, doped with electroluminescent ZnS phosphors, between two ionic hydrogel (LiCl-PAAm) electrodes, and then encapsulating the sandwich structure between two layers of Ecoflex thin-film (Figure 10 A). This HLEC skin can change its illuminance and capacitance simultaneously under deformation (up to 480% strain). Arrays of individually controllable pixels in thin rubber sheets were fabricated using replica molding and serve as stretchable displays with good spatial resolution. After integrating into a soft robot, the HLEC skin allows the robot to sense their actuation state and external mechanical inputs and to communicate through coloration (Larson et al., 2016). Organic liquid crystal-based electroluminescent devices have also been developed based on transparent ionic hydrogel (Yang et al., 2016, 2017).

While the previous designs were mainly for empowering soft robots with single-mode sensing, the next-generation soft robots may require skin-like multimodal somatosensory feedback for enhanced robotic intelligence. Truby et al. recently used embedded 3D printing technology to print conductive ionogel soft sensors into a soft robotic finger (Truby et al., 2018). By embedding multiple sensor networks, this soft robotic finger consists of haptic, proprioceptive, and thermoreceptive sensing capabilities (Figure 10B). This approach is promising for constructing soft robots, wearable and haptic devices requiring multimodal sensation for closed-loop and machine learning-based control (Truby et al., 2018). IL-based ionogel sensors can endow

soft robots with sensing capability at subzero temperature (Liu et al., 2020c). Furthermore, enabled by the strong adhesion of ionic hydrogel to an elastomeric soft robotic body, the robot can sense large deformation (Cheng et al., 2019).

Ionic hydrogel-based stretchable electrodes for soft actuators

Electrically powered muscle-mimicking actuators [e.g., dielectric elastomer actuator (DEA)] offer high actuation strain (>100%), high energy efficiency (80%), and unique self-sensing capability (Acome et al., 2018), and have enabled a wide range of applications. In a DEA structure, stretchable conductors are needed to realize the electromechanical transduction. Currently, many stretchable conductors exist, including carbon grease, serpentine-shaped metallic wires, carbon nanotubes, graphene sheets, silver nanowires, liquid metals, and saline solutions. However, these conductors are limited by their low optical transparency, low stretchability, or liquid-like property.

Ionic hydrogels are transparent, solid, highly stretchable, and conductive, and hold great potential for DEA electrode fabrication. For example, Keplinger et al. built a transparent, high-speed, large-strain soft actuator realized by sandwiching a layer of dielectric elastomer between two layers of highly stretchable and transparent ionic hydrogel (NaCl-PAAm). Due to the short response time (~10 ms) of free ions in the hydrogel matrix in response to external electric fields (Liu et al., 2020d) and the large capacitance within the hydrogel-electrode EDL, this assembled hydrogel-elastomer-hydrogel DEA can operate at frequencies over 10 kHz and voltages over 10 kV. When a high voltage (e.g., 10 kV) is applied between the hydrogel ionic conductors, the main voltage drop is across the dielectric elastomer on the order of ~10 kV, leading to a large amount of ions of different charge polarities collecting on the two surfaces of the dielectric elastomer. The electrical attraction between the oppositely charged ions can reduce the thickness and increase the area of the dielectric elastomer, leading to the electromechanical actuation (Keplinger et al., 2013). In addition, the electromechanical actuation is achieved without electrochemical reaction between the metal electrodes and the hydrogel due to a small voltage drop (<1V) across the interface EDL (Figure 10C).

Similarly, an ionic conductive hydrogel (LiCl-PAAm) served as an electrode sandwiched between two dielectric elastomers to fabricate the fins of a soft fish (Li et al., 2017b). When a voltage was applied between the encapsulated hydrogel conductor and the surrounding tap water, opposite charges accumulated on both sides of the dielectric elastomer, inducing a Maxwell stress that deformed the soft fin to a lower-curvature structure. This design enabled the fish body and fins flapped between the actuated and the rest states, leading to the exceptionally fast propulsion motions of the soft fish with a swimming speed of 6.4 cm/s (i.e., 0.69 body length per second) (Li et al., 2017b).

Hydrogel-based energy harvesting

The rapid growth of wearable electronics and soft robotics partially relies on power sources that are mechanically flexible, stretchable and even biocompatible. So far, flexible energy storage devices [e.g., supercapacitors (Hu et al., 2009; Pushparaj et al., 2007; Scrosati, 2007) and batteries (Hu et al., 2009, 2010)] have been developed to reduce the constraint on our human body and the soft robotic body. On the other hand, energy harvesting devices such as solar cells and nanogenerators have been made into flexible formats in the past decade (Peet et al., 2007; Wang et al., 2012; Xu et al., 2010; Yoon et al., 2010). In particular, recently-developed triboelectric nanogenerators (TENGs), which convert mechanical energy into electricity based on the coupling effect of contact electrification and electrostatic induction, have gained great attention due to their advantages such as high voltage output, simple structure, environmental friendliness, and low costs (Bae et al., 2014; Chun et al., 2016; Wang et al., 2015a, 2015b). Several stretchable TENGs have been reported based on the conductive materials (Chen et al., 2017a; Lai et al., 2016; Yi et al., 2015, 2016) including carbon nanotubes (Wang et al., 2016), graphene (Kim et al., 2014), silver nanowires (Hwang et al., 2015) and, more recently, ionic hydrogels (Pu et al., 2017).

Ionic-hydrogel-based TENGs have enabled applications in soft robotics and wearable devices. For example, Wang et al. reported the first soft skin-like TENG (STENG) for both biomechanical energy harvesting and tactile sensing. The device involves elastomer and ionic hydrogel as the electrification layer and electrodes, respectively (Figure 6C). With high stretchability (1160%) and transparency (96.2%), this STENG achieved an instantaneous peak power density of 35 mW/m² (Pu et al., 2017). Wang et al. further enhanced the bonding between the ionic conductive hydrogel and the electrification elastomer through interface

modification with benzophenone (BP) upon UV irradiation. With better mechanical reliability, the device achieved a significantly reduced dehydration rate compared with the unmodified STENG, enabling its potential application in harsh environments (Liu et al., 2018b). In addition, other important features such as self-healing and anti-contamination were further realized on hydrogel-based TENG to open up new opportunities in human-machine interaction, health monitoring, wearable and implantable electronics, and soft robotics (Lee et al., 2018b; Parida et al., 2017).

Several novel materials such as PILs and ionogels were also utilized as the conductive gels for TENG. The as-fabricated devices consist of practically useful features such as ambient stability and anti-freezing capability, and can realize mechanical energy harvesting over a wide temperature range due to the intrinsically nonvolatile performance of ILs (Liu et al., 2020c; Ren et al., 2019; Sun et al., 2019). Those stretchable TENGs could broaden their soft robotic and wearable applications under harsh environments.

TENG has been demonstrated for harvesting various mechanical energies with effective frequency typically at >10 Hz (Ying et al., 2020a). However, their performance in the low frequency range (e.g., less than 1 Hz of human motions) decay dramatically (Zhou et al., 2017). Alternatively, a recently developed hydrogel ionic diode has been proved to harvest low frequency mechanical energy with a high output current of $13.5 \mu\text{A}/\text{cm}^2$. Further stacking five units with parallel structure, the hydrogel diode device can generate an output current of $64.3 \mu\text{A}/\text{cm}^2$ and power density of $0.48 \mu\text{W}/\text{cm}^2$ (Zhou et al., 2017). While the previous hydrogel-based ionic diodes are usually not stretchable (Cayre et al., 2007; Zhou et al., 2017), and sometimes not transparent (Hou et al., 2017; Zhou et al., 2017), our recent development of a hydrogel-based artificial ionic skin (AISkin) made from an ionic diode structure, which possesses high toughness, stretchability, ambient stability and transparency. The AISkin consists of a bilayer double-network hydrogel with hygroscopic substances and positively and negatively charged polyelectrolytes (PSS and PDAC) in its two separate layers. Due to its excellent mechanical performance (stretchability: 400%; fracture toughness: $1826 \text{ J}/\text{m}^2$), the AISkin can reach an energy output per stimulus at $3,200 \mu\text{J}/\text{m}^2$ and generate a peak output current of $128 \mu\text{A}/\text{cm}^2$ at the low frequency (0.02–0.5 Hz) (Ying et al., 2020a). Two layers of liquid-free PILs with oppositely charged mobile ionic species can also form a diode-like junction, yielding an ionic double layer. Similarly, the deformable ionic diode junction enabled the transduction of mechanical movements into electrical signals for sensing and energy harvesting while showing good ambient stability (Kim et al., 2020a).

CONCLUDING REMARKS AND FUTURE PERSPECTIVES

Hydrogels represent an important class of materials possessing broadly tunable physical and chemical properties. Efforts devoted to engineering hydrogel devices with skin-like properties and functionalities have expanded their applications in different areas such as wearable sensing, soft sensors and actuators, and stretchable electronics. Over the past decade, substantial progress has been made to develop hydrogel materials with high mechanical toughness, stretchability, and/or conductivity. In addition, the development of nature-inspired hydrogel devices with enhanced merits (e.g., anti-dehydration, anti-freezing and bio-adhesion) has flourished recently. This review summarized the recent hydrogel materials development and device application in wearable sensing, soft robotics, and energy harvesting. Despite the exciting advances, there are several challenges to be further addressed.

Multimodal sensation

Currently, skin-inspired ionic hydrogel sensors are mainly designed to have single or dual operation modality (Liu, 2020). However, the human skin possesses a multimodal sensation capability. Therefore, new designs of hydrogel materials and structures are worth exploring to realize new types of multimodal sensors. For example, in biological systems, Na^+ or K^+ ion channels can efficiently discriminate Na^+ or K^+ from other alkali cations and even from each other, while traditional ionic hydrogel sensors have never been able to sense those differences. Existing stretchable hydrogel sensors were focused on measuring biophysical signals; the realization of multimodal (biophysical and biochemical) sensing capabilities would extend the functionalities of wearables and robots. Sensing of touch, pressure, deformation, temperature and humidity and even detecting the presence of chemical and biological markers in the environment would be useful for a wide range of applications (Li and Mooney, 2016; Mostafalu et al., 2018; Trombino and Cassano, 2020; Wang et al., 2018a).

New fabrication strategies

Currently, skin-inspired hydrogel devices are usually fabricated directly from bulk hydrogel and the patterning and integration mainly rely on manual assembly. Miniaturization and scalable fabrication of hydrogel devices will enrich the functionality of a single device and reduce the device-to-device variation. Most proof-of-concept ionic hydrogel devices featured millimeter thickness (Yang and Suo, 2018). Fabrication of thinner hydrogel films with good breathability, durability, stretchability, and biocompatibility improve the user's comfort and reduce/avoid irritation over long-term use. For example, 3D printing of hydrogel has allowed the fabrication of strain sensors (Tian et al., 2017) and the patterning of highly conductive and soft hydrogel microstructure with high resolution ($\sim 30\ \mu\text{m}$) for bioelectronic neural recording (Yuk et al., 2020). 3D printing is also promising to highly integrate multimodal sensation into a single soft robot (Truby et al., 2018). In addition, existing microfabrication techniques such as soft lithography could be possible for constructing micrometer-sized hydrogel arrays for building a large number of sensing modules with different modality.

Improved Intelligence based on hydrogel ionic computing and big data

The ultimate goal of ionotronics is to develop an integrated intelligent system, which consists of ionic sensing, ionic wiring, ionic memory/computing, and ionic decision/actuation components. Today, stretchable hydrogel ionic sensing, wiring, and actuation have been demonstrated (Yang and Suo, 2018) while stretchable hydrogel ionic computing has rarely been reported to realize seamless signal transduction from input to output ends within a closed loop. The gap of stretchable hydrogel memory/computing may be filled in the near future considering the recently developed stretchable ionic diodes (Kim et al., 2020a; Lee et al., 2019; Wang et al., 2019b; Ying et al., 2020a). Stretchable hydrogel ionic diode, as the counterpart of semiconductive electronic diode, could be a basic component to construct stretchable transistors and more integrated ionotronic systems. On the other hand, massive datasets would be collected during long-term wearing of highly integrated hydrogel sensors for personalized healthcare. Artificial intelligence can be integrated to enhance the data processing and analysis for personalized health monitoring and disease prediction/prognosis. Full automation is another opportunity for soft robotics equipped with multimodal hydrogel sensors. Advanced, big data-driven control methods could facilitate closed-loop controlled operations of soft robots, through real-time processing of feedback signals from highly integrated and distributed soft hydrogel sensors (Liu et al., 2020d; Wang et al., 2020b).

Stretchable power-storage devices

The development of stretchable energy supply systems is another challenge to achieve more stable and longer lasting ionic hydrogel systems for wearables and soft robotics. The trend to integrate multiple hydrogel sensor arrays into wearable/robotic platforms will increase the power consumption during continuous monitoring as well as large existing actuation power consumption. Even though the development of self-powered devices [e.g., integration of stretchable solar cells (El-Atab et al., 2019), stretchable TENG-based sensing and energy harvesting (Pu et al., 2017), stretchable ionic diode-based sensing and energy harvesting (Kim et al., 2020a; Ying et al., 2020a) and biofuel-powered e-skin (Yu et al., 2020c)] suggests promising solutions to solve this issue, their power generation efficiency remains problematic. Therefore, the development of wearable and stretchable power-storage devices with large capacities is important for future wearable and soft robot designs.

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AUTHOR CONTRIBUTIONS

B.Y. and X.L. conceived the theme and designed the manuscript structure. B.Y. wrote the manuscript. X.L. supervised this work and edited the manuscript.

DECLARATION OF INTERESTS

The authors declare no conflict of interest.

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