

Review

Design and Fabrication of Functional Hydrogels through Interfacial Engineering*

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Abstract Hydrogels have drawn considerable attention in the past two decades due to their excellent biocompatibility and multi-stimuli responsiveness. They have a wide range of applications in the fields related to tissue engineering, sensors and biomedicine. Their applications are strongly influenced by the surface properties of hydrogels and the interfacial interactions between hydrogels and other substrates. In particular, the surface wettability and adhesion of hydrogels decide their applications as drug carriers and wound dressing materials. Nevertheless, there is a lack of systematic discussion on the surface functionalization strategies of hydrogels. Therefore, this review aims at summarizing the strategies of functionalizing the surfaces of hydrogels and bonding hydrogels with other solid substrates. It also explores the challenges and future perspectives of interfacial engineering of hydrogels.

Keywords Hydrogels; Interfacial reaction; Surface functionalization; Wettability; Adhesion

INTRODUCTION

Hydrogels, composed of 3D crosslinked hydrophilic polymers and a large amount of free and bonded water molecules, have been widely used in areas ranging from tissue engineering, cellular immobilization to biological medicine due to their unique physical and chemical properties^[1–4]. During the past two decades, hydrogels have been extensively studied by researchers all over the world. A variety of hydrogels with diverse amazing properties have been developed, such as high mechanical strength hydrogels^[5–8], anisotropic hydrogels^[9–14], nonswellable hydrogels and various stimuli-responsive hydrogels^[15–22]. The design and fabrication of these hydrogels have mostly focused on the structures and compositions of their 3D networks. In contrast, the importance of the hydrogel surfaces has often been underestimated or ignored. Thus, systematic discussion and research on the surface and interfacial properties of hydrogels are necessary.

The surface properties possess the same research values compared with the bulk phases of materials. As for hydrogels, the surface properties impart unique performance of hydrogels, and some traditional properties can

* This work was financially supported by the National Natural Science Foundation of China (No. 21574004), Xiamen Southern Oceanographic Center (No. 14GQT61HJ31), the 111 project (No. B14009), the Fundamental Research Funds for the Central Universities, the National ‘Young Thousand Talents Program’ and the Academic Excellence Foundation of BUAA for PHD Students.

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Invited paper for special issue of “Hydrogel”

Received May 9, 2017; Revised June 15, 2017; Accepted June 16, 2017

doi: 10.1007/s10118-017-1995-5

also be realized through rational interfacial engineering. For instance, nonswellable hydrogel can be realized by covalently bonding elastomer on its surface^[23]; controlled drug release can be realized by surface modification of hydrogels with hydrophobic alkane or stimuli-responsive molecules^[24, 25]. Moreover, a number of special and desired properties of hydrogels have been developed based on interfacial engineering. Therefore, tuning the surface and interfacial properties of hydrogels plays an important role in broadening the practical applications of hydrogels.

To date, the key research fields related to surface properties of hydrogels include contact lens^[26–28], controlled drug release^[16, 20], cell adhesion and translocation^[29–34], and the combination of hydrogels with diverse substrates^[23, 35–38]. For contact lens, their surface wettability and protein adsorption are the key factors that influence the comfort and safety of contact lens; these factors can be regulated by surface grafting of the hydrogel substrates of contact lens. Controlled drug release and cell adhesion can also be realized by surface modification of hydrogels with functional molecules. Moreover, the bonding of hydrogels with diverse substrates can be realized by introducing of non-covalent interaction or covalent bonds between hydrogels and substrates. These examples show that the surface properties of hydrogels are critical to the practical applications of hydrogel materials.

So far, the research on the interfacial engineering of hydrogels is still in its infancy. There is a lack of systematic reports of the strategies functionalizing the surfaces of hydrogels and bonding hydrogels with solid substrates. This review therefore aims at bridging this gap by summarizing the strategies of surface functionalization of hydrogels. Starting from the functional hydrogel surfaces in biological systems, then three types of strategies are reviewed here: chemical modification, assembly of micro/nanoparticles and bonding hydrogel to solid substrates. The applications generated by surface functionalized hydrogels are also presented. Finally, this paper concludes with the current challenges and future perspectives in the field of interfacial engineering of hydrogels.

FUNCTIONAL HYDROGEL SURFACES IN BIOLOGICAL SYSTEMS

Hydrogels are familiar to us due to their widespread existence in the nature. For example, some of terrestrial organisms and most of marine organisms are covered by hydrogel materials on their surfaces. Undoubtedly, these natural hydrogels play a vital role in the life activities of organisms. As shown in Figs. 1(a)–1(c), carp, filefish and seaweed can keep their surfaces clean in oil-polluted water due to the existence of gel-like watery mucus on their surfaces. These biological surfaces show superoleophobicity and low oil-adhesion in the underwater environment^[39–44]. Additionally, hydrogels can act as adhesives in biological systems. As shown in Fig. 1(d), the tree frog toe pads show high adhesion upon smooth surface with the assistance of gel-like mucus on their surface^[45]. Moreover, the existence of hydrogels can also result in low adhesion surfaces. As shown in Fig. 1(e), the peristome of pitcher plants is fully wettable because its surface is covered by gel-like materials, which prevents insect foot attachment by the delayed drainage of the thin water film between the adhesive pad and the surface^[46–48].

Studies of these interesting natural phenomenon have shown that the complex surface structures are the key to realizing these excellent properties of hydrogels. Consequently, constructing structured surfaces by mimicking biological surfaces has become one of the most important subjects for researchers to fabricate functional hydrogel-based materials. For instance, inspired by the oil-repellent nature of fish's composite surface, Liu and co-workers used hydrogels to fabricate artificial underwater superoleophobic surface by replicating fish scales^[49]. As a result, the poly-acrylamide (PAM) hydrogel film with fish-scale structures showed underwater superoleophobicity. They examined the underwater wettability of oil droplet upon silicon substrates with different surface topographies, revealing and analyzing the relationship between surface topography and wetting behavior in the three-phase system (liquid/liquid/solid). It was found that the micro/nano-structures on the substrate could trap substantial water molecules in it, leading to underwater superoleophobicity. Therefore, they proposed a theory that a hierarchical surface structure is the key for underwater superoleophobicity. Based on

this, a series of artificial hydrogels with the hierarchical surface structure were developed. For example, Lin *et al.* developed a nanocomposite hydrogel for robust underwater superoleophobicity^[50]. In this work, a mold method was used to fabricate hydrogel with micro-/nanostructured surfaces. It was observed that the as prepared hydrogel with hierarchical surface structure showed underwater superoleophobicity and low oil-adhesion. In the same year, Chen *et al.* reported a thermal-responsive poly(*N*-isopropylacrylamide) (PNIPAM) hydrogel with tunable surface wettability and oil-adhesion at the water/solid interface^[51]. By designing and constructing ordered micro-structures on the surfaces of hydrogels, the wetting behavior of oil droplet in underwater environment could be tailored. Moreover, the surface wettability of PNIPAM-hydrogel switched from a superoleophobic and low adhesive state (below the LCST of PNIPAM) to an oleophobic and high adhesive state (above the LCST of PNIPAM) in response to the temperature change.

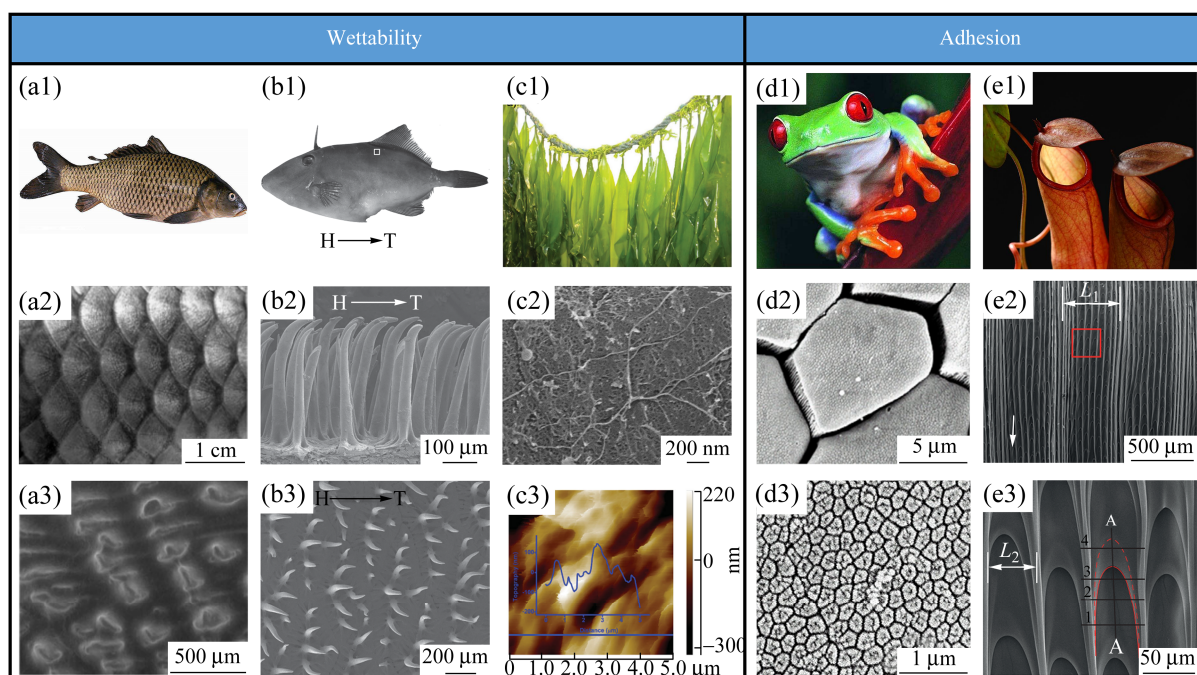


Fig. 1 Functional hydrogel surfaces in biological systems: (a1, a2) Photographs of carp and fish scales, (a3) SEM images of fish scales (Reprinted with permission from Ref. [49]; Copyright (2009) Wiley-VCH); (b1) Photograph of filefish *N. septentrionalis*, (b2, b3) SEM images of fish skin in side-view and top-view, respectively (Reprinted with permission from Ref. [42]; Copyright (2014) Wiley-VCH); (c1) Picture of seaweed *S. japonica*, (c2, c3) SEM and AFM images of *S. japonica* (top view) (Reprinted with permission from Ref. [41]; Copyright (2015) Wiley-VCH); (d1–d3) Photograph of tree frog and SEM images showing the morphology of tree frog toe pads (Reprinted with permission from Ref. [45]; Copyright (2009) Company of Biologists Ltd.); (e1) Photograph of *Nepenthes alata*, (e2, e3) SEM images showing the surface features of the peristome in the pitchers of *N. alata* (Reprinted with permission from Ref. [46]; Copyright (2016) Nature Publishing Group)

Other methods have also been employed to construct structured surfaces of hydrogels. Using the filtration method, Teng *et al.* developed a strong, underwater superoleophobic PNIPAM-clay nanocomposite hydrogel applicable as an oil/water separation film. The underwater superoleophobicity of the nanocomposite hydrogel was attributed to the rough surface structure with mountain-like protrusions^[52]. In addition, a superhydrophilic and underwater superoleophobic hydrogel-coated copper mesh was reported by Xue *et al.*, which consisted of rough nanostructured hydrogel coatings and microscale porous metal substrate. Due to the underwater superoleophobicity and low oil-adhesion of structured hydrogel coated mesh, it could selectively and effectively separate water from oil/water mixture^[53].

CHEMICAL MODIFICATION

Chemical modification is a well-developed and widely used strategy in the field of material chemistry. Herein, it refers to the surface modification strategies of hydrogels through chemical reaction. Chemical modification of hydrogels is usually utilized to tune the surface properties of hydrogels used as contact lens. The reason is that the conventional contact lens suffers from the dehydration and protein (native tear film) adsorption on the surfaces, thus reducing the overall comfort of the lens^[54, 55]. This problem can be solved to a certain extent by some physical methods; however, they always cause undesirable leakage of the incorporated hydrophilic polymers^[56–58], exposing silicone components to the surface^[59, 60]. In contrast, chemical modification is a more feasible means to fabricate powerful fouling-resistant materials, since the chemical stability of covalent bonds between the substrate and grafted polymer is sufficient for real applications.

For the chemical treatment methods, a few strategies have been employed in the modification of lens surfaces. Earlier in 2014, Xu *et al.* reported a one-step method to functionalize the surfaces of contact lens with zwitterionic polymer^[26]. Results showed that the zwitterionic polymers modified contact lenses had significant improvement of surface-wettability, superior properties of antibacterial adhesion and strong resistance to protein adsorption than pristine contact lens. Figure 2(a) shows the zwitterionic polymer used in this work, a diblock copolymer composed of 3-trimethoxysilyl-propyl-methacrylate (MPS) and 2-methacryloyloxyethyl phosphorylcholine (MPC). The surface modification was attributed to the existence of highly active silanol groups in MPS, which provided stable adhering layers with C–O–Si bonds by silylation reaction with the surface hydroxyl of contact lens. It is worth pointing out that PMPS-*b*-PMPC can be immobilized on most of the currently commercially available lenses by one-step modification while maintaining their excellent clinical performance and biocompatibility.

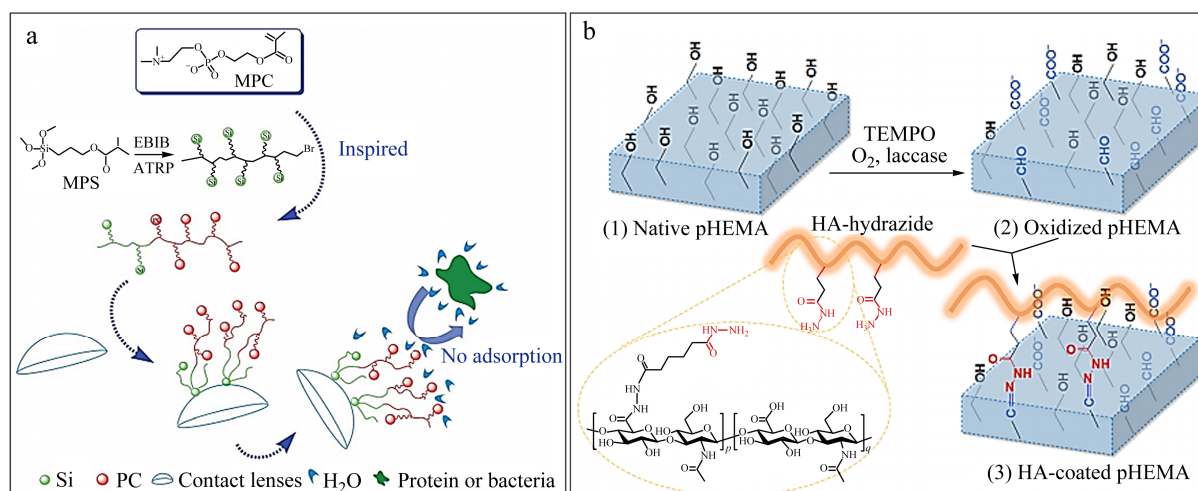


Fig. 2 Hydrophilic modification of hydrogel substrates: (a) Surface modification of contact lenses with PMPS-*b*-PMPC to obtain high resistance to protein adsorption and bacterial adhesion (Reprinted from Ref. [26] with permission from The Royal Society of Chemistry); (b) Preparation of hyaluronic acid coated pHEMA hydrogel (Reprinted with permission from Ref. [28]; Copyright (2016) American Chemical Society)

Additionally, Deng and co-workers reported a “click” chemistry approach to functionalize the surfaces of poly(2-hydroxyethyl methacrylate) (pHEMA)-based contact lenses with hyaluronic acid (HA). HA is a carbohydrate that contributes to the wettability of the native tear film^[28]. The strategy proposed in this work was a two-step preparation technique, as shown in Fig. 2(b), laccase/TEMPO-mediated oxidation of hydroxyl on pHEMA-based hydrogel, followed by covalent grafting of hydrazide-functionalized HA on its surface *via* simple immersion. The results showed that the HA-modified hydrogel was more hydrophilic, more water retentive, and

less protein binding than unmodified pHEMA, while the favorable transparency, refractive, and mechanical properties of native lens were well preserved. Recently, Xu and co-workers reported a grafting strategy on silicon hydrogels with natural amino acids for ophthalmological applications^[27]. The modification strategy of this work was described as follows. Glycidyl methacrylate (GMA) was firstly copolymerized into a hydrogel as functional monomer. It was found that the surface of as-prepared hydrogels was covered by the epoxy groups, then amino acids were grafted onto silicone hydrogels by epoxy ring opening reaction. Specifically, the epoxy groups on hydrogels were opened by $-NH_2$ groups of amino acids in alkaline solutions, forming $-NH-$ groups. The silicone hydrogels with the surface enrichment of hydrophilic amino acids showed protein fouling resistance upon specific protein.

Through rational chemical modification, not only the hydrogels with enhanced hydrophilicity were fabricated, but also the hydrogels with superhydrophobicity on their surface were achieved. Hydrophobic interfaces, such as cell membranes and certain nucleoporin hydrogels, are key prerequisites to diffusion control^[61–64]. It is supposed that ideally, hydrogels with hydrophobic surface layers resemble cells with membranes that separate subcellular matters from the extracellular matrix. Taking this into consideration, a few works have been published by our group.

The *N*-alkylation reaction has been extensively used to graft target groups on tertiary amines, which was introduced into our work to functionalize the surfaces of hydrogels^[24]. Anchor monomers with tertiary amino groups (dimethylaminopropylacrylamide) were first copolymerized into the hydrogel network. The surface of as-prepared hydrogel was covered by the dimethylamino group. Then, the surface modification was realized by immersing the as-prepared hydrogels into an oil phase, in which modifiers were dissolved. Because the water is immiscible with oil phase, organic solvent was unable to penetrate through the surfaces of hydrogels. Consequently, the quaternization reaction took place only at the hydrogel/oil interface. As a result, the as-prepared post-modified hydrogels showed stable superhydrophobicity on their surfaces (Fig. 3a), while the intrinsic superhydrophilicity and biocompatibility of hydrogel inner network were well preserved. The heterogeneous wettability across the surface and the inner network of hydrogel was successfully created; such wetting disparity showed significant influence on preventing immediate diffusion of substances between the hydrogel and the aqueous environment on different scales. Furthermore, a photo-responsive hydrogel was also reported by our group^[25]. By introducing a kind of photo-responsive molecule (1-(4-iodobutyl)-3,3-dimethylindoline-6-nitrobenzospiropyran) (IBSP) as modifiers, the surface wettability of the as-prepared hydrogel was reversibly switched in response to ultraviolet (UV) and visible (Vis) light irradiation (Fig. 3b). Moreover, due to the photo-responsive ring open and ring close mechanism of IBSP, the underwater oil wettability and underwater oil-adhesion upon this modified hydrogel were also reversibly switched by UV and Vis light illumination. By taking advantage of the photo-responsive property of IBSP-modified hydrogels, a photo-responsive controlled release system was developed.

It is worth noting that the above-mentioned method is a ubiquitous strategy to functionalize the surfaces of synthetic hydrogels. As shown in Fig. 3(c), a series of molecules can be used as modifiers, such as hexadecyl iodide, 1-iodohexadecane, 1-iododecane, 1-iodooctane, iodine octane, poly(4-bromomethyl styrene), and IBSP, *etc.*

Except for the above-mentioned strategies, Hu *et al.* also developed a surface modification method for hydrogels to realize the controlled drug release^[65]. In this work, pHEMA was used as hydrogel substrate. Initially, the surface modification of hydrogel was conducted by bromination reaction using 3-bromo-1-propyne (BP). Then, β -cyclodextrin (β -CD) was grafted onto hydrogel surface by thiol-yne click chemistry. The as-prepared β -CD modified hydrogel was more hydrophilic and showed good protein resistant property compared with the pristine hydrogel. Most importantly, the β -CD molecules grafted onto hydrogel surface benefited to aggregating drug molecules in hydrogels, thus influencing the drug release behaviors. Moreover, there were several advantages of thiol-yne photopolymerization utilized in this work, such as high efficiency, mild reaction condition and low toxicity.

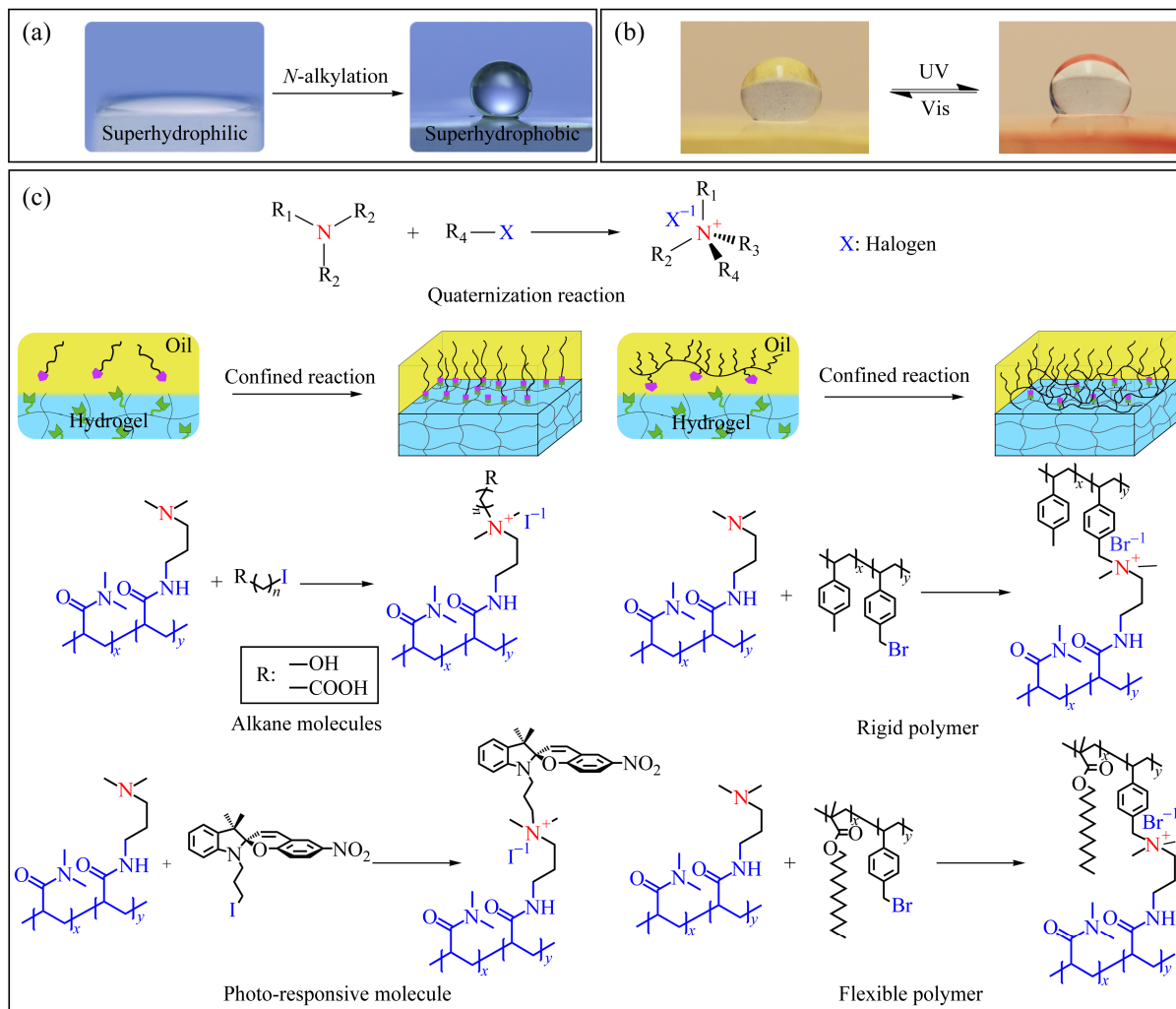


Fig. 3 Hydrophobic modification of hydrogels: (a) Photographs of a water drop (2 μL) deposited on hydrogel before (left) and after (right) the modification (Reprinted with permission from Ref. [24]; Copyright (2016) Wiley-VCH); (b) Photographs of a water drop (10 μL) sitting on IBSP-modified hydrogel (1 cm \times 1 cm \times 1 cm) upon visible and UV light irradiation (Reproduced from Ref. [25] with permission from The Royal Society of Chemistry); (c) The quaternization reaction at the oil/water interface as a ubiquitous strategy to functionalize the surfaces of synthetic hydrogels (A large variety of molecules can be used as modifiers, for instance, alkane molecules, stimuli-responsive molecule, and rigid and flexible polymer.)

ASSEMBLY OF MICRO/NANOPARTICLES

Unlike chemical grafting, the surface properties of hydrogels can also be regulated by physical combination of hydrogels with micro/nanoparticles. The strategies used to functionalize hydrogel surfaces with micro/nanoparticles are summarized as follows.

Wettability

Figure 4(a1) shows a hydrophobic gelatin methacryloyl (GelMA) hydrogel reported by Oliveira *et al.* This hydrogel was fabricated by the adhesion of hydrophobic microparticles onto the surfaces of hydrogels^[66]. The hydrophobic microparticles used in this work were prepared by chemical modification of the pristine diatomaceous earth (DE) with 1*H*,1*H*,2*H*,2*H*-perfluorodecyltriethoxysilane (PFDTs) (Fig. 4a2). Then hydrogels coated with a uniform layer of hydrophobic microparticles were produced by rolling the cross-linked hydrogels

over the PFDTS-DE microparticles. The as-prepared microparticles-coated GelMA hydrogel was hydrophobic (Figs. 4a3–4a5) floating on the surface of water. This floating hydrogel moved directly on the surface of water under the electrostatic force. For the surface wettability of hydrogel, there is still another more advanced hydrogel material with tunable surface wettability reported by Huang *et al.*^[67]. In this work, a hydrogel with tunable wettability (from superhydrophobic to superhydrophilic) was fabricated by coating its surface with silanized glass particles, known for superhydrophobic. Thus, in the contracted state, the surface of as-prepared hydrogel was superhydrophobic due to the layers of silanized particles. When the hydrogel expanded under the influence of a specific external stimulus, the surface became superhydrophilic (Figs. 4b1–4b4). Moreover, by using pH and temperature responsive hydrogel as substrates, hydrogels with tunable wettability in response to pH and temperature were also fabricated, respectively. Eventually, a system that responds to multiple stimuli including pH, temperature and stretch, was successfully constructed by using multiple stimuli-responsive hydrogels.

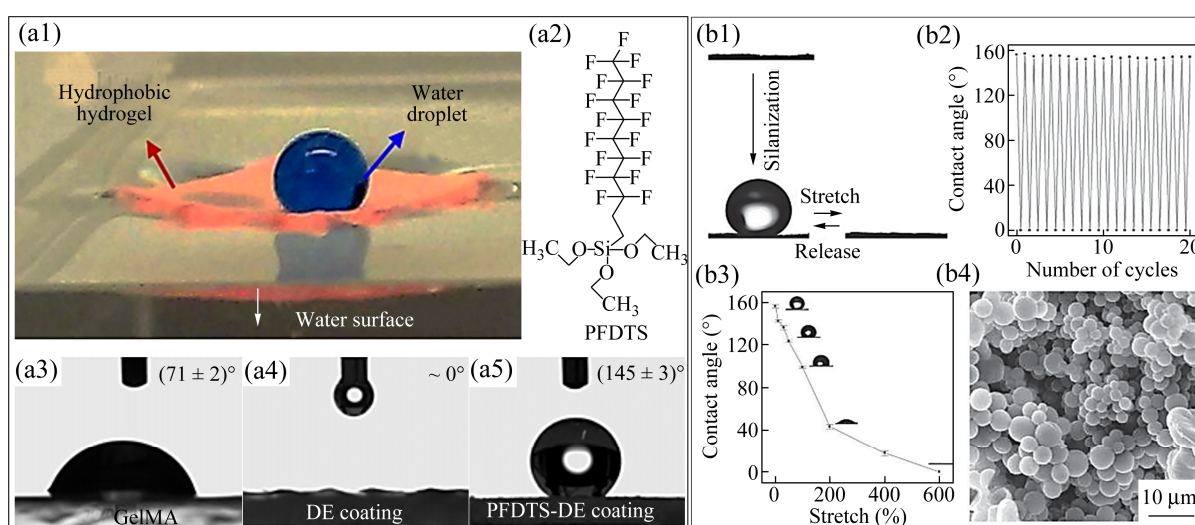


Fig. 4 Superhydrophobic hydrogels by nanoparticles modification: (a1) Photograph showing a water droplet (dyed in blue) on top of a hydrophobic GelMA hydrogel block (The GelMA structure was placed on a pool of water.), (a2) 1H,1H,2H,2H-perfluorodecyltriethoxysilane (PFDTS) used to modify diatomaceous earth (DE), (a3–a5) water contact angle measurement of cross-linked GelMA, GelMA coated with pristine DE microparticles, and GelMA coated with hydrophobic PFDTS-DE microparticles (Reproduced with permission from Ref. [66]; Copyright (2016) American Chemical Society); (b1) The water contact angle showing that the surface became superhydrophilic, when the material was stretched, (b2) the reversible switch from superhydrophobicity to superhydrophilicity (at least for 20 times), (b3) the water contact angle tuned by stretching the material to different extents, (b4) SEM image of the glass particles on the surface of the material (Reprinted with permission from Ref. [67]; Copyright (2015) Wiley-VCH)

Adhesion

The micro/nanoparticles can not only regulate the surface wettability of hydrogels, but also enhance the adhesion of hydrogels. Rose *et al.* proposed a method to physically enhance the adhesion between hydrogel and biological tissues by introducing inorganic nanoparticles as adhesives^[68]. Figures 5(a1) and 5(a2) show the concept of gluing swollen polymer networks together using particles. The nanoparticles used here had comparable diameters with the gel network mesh size. Network chains were adsorbed on nanoparticles and anchor particles to gel pieces. Particles acted as connectors between gel surfaces. Adsorbed chains also formed bridges between particles. By spreading a drop of silica solution on the gel surface, two gel pieces were glued together after being brought into contact for few seconds (Fig. 5a3). This work provided a simple way for assembling synthetic and biological hydrogels as well as biological tissues without substantially affecting the rigidity or permeability of the assembly.

In addition, polydopamine (PDA) has a similar structure to that of mussel-adhesive proteins, which show high adhesion with a wide range of substrates by forming covalent and/or non-covalent interactions with them^[69]. Due to its good biocompatibility, PDA was usually utilized as a coating layer to modify material surfaces, promoting cell adhesion and proliferation. Han *et al.* developed a PDA coated nanoparticles (PDA-NPs) as adhesive to functionalize the surfaces of hydrogel^[33]. The as-prepared PDA-NPs coated hydrogels not only showed enhanced cell adhesion, but also served as wound dressing materials, as shown in Fig. 5(b).

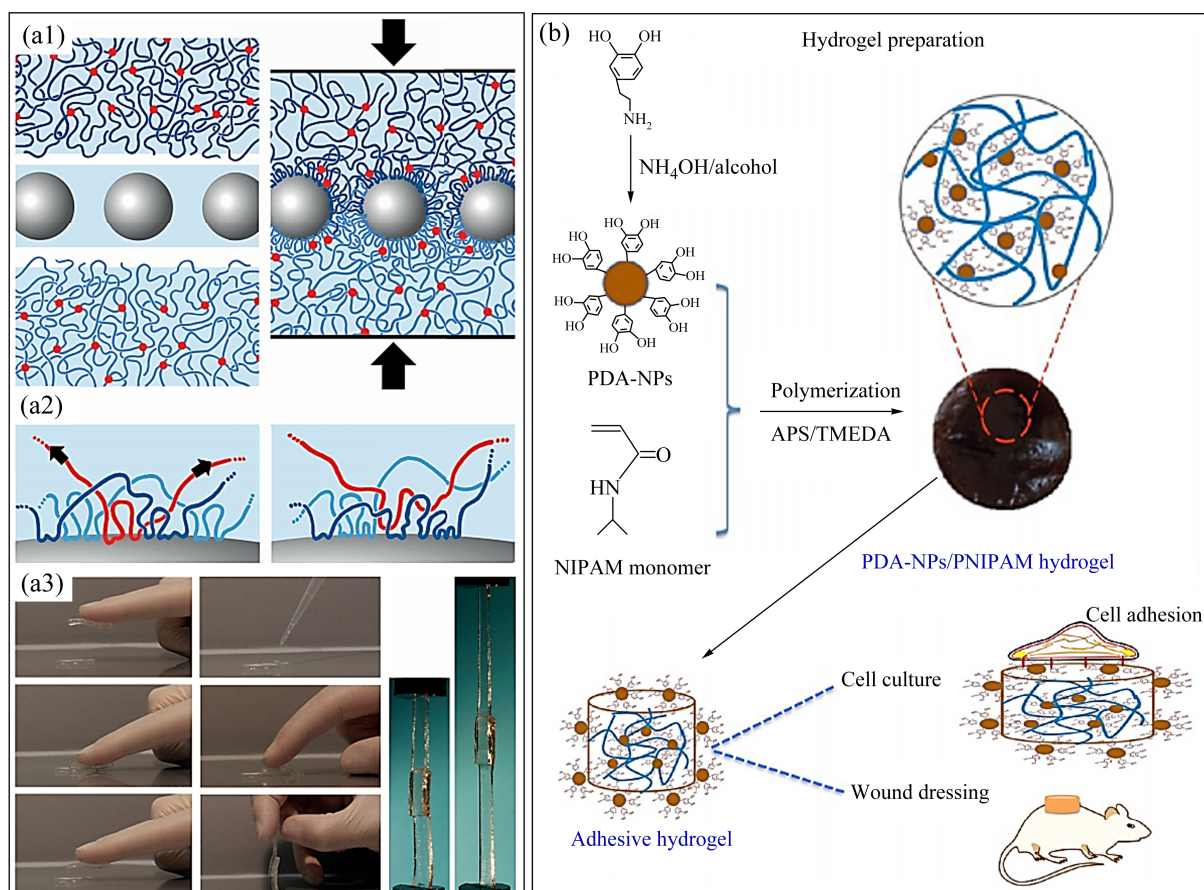


Fig. 5 Hydrogels with high adhesion by using nanoparticles as adhesives: (a1) Schematic illustration of the concept of gluing swollen polymer networks using particles, (a2) schematic illustration of the mechanism of energy dissipation under stress, (a3) pristine hydrogels not stick to themselves and two gel pieces glued together after spreading a drop of silica nanoparticle solution on the gel surface and being brought into contact for few seconds (Reprinted with permission from Ref. [68]; Copyright (2014) Nature Publishing Group); (b) Schematic of the PDA-NPs/PNIPAM hydrogel fabrication (PDA-NPs were prepared by oxidative self-polymerization, PDA-NPs/PNIPAM hydrogel was obtained by free radical polymerization. PDA-NPs coated on hydrogel surfaces to enhance cell/tissue adhesiveness of the hydrogels.) (Reprinted with permission from Ref. [33]; Copyright (2016) American Chemical Society)

BONDING HYDROGEL TO SOLID SUBSTRATES

The weak binding capacity of hydrogels upon various substrates is the key issue that restricts the development and applications of these materials in broader field. To solve this problem, more attention should be paid to the interfacial interaction between hydrogels and other substrates. So far, a few strategies were reported to combine hydrogels with other substrates, which could be divided into non-covalent interaction and covalent interaction.

Non-covalent Interaction

Similar to the above-mentioned work using PDA-NPs as interfacial adhesive, Lee *et al.* reported a polydopamine

coated thermal-responsive hydrogel for cell sheets engineering^[32]. It was found that the as-prepared PDA-coated hydrogel showed enhanced adhesiveness upon cell sheets compared with pristine hydrogel. Facile cell sheet harvest and translocation were realized through PDA-coated thermal-responsive hydrogel (Fig. 6a).

Except for using inorganic nanoparticles as adhesives^[68], Kato and co-workers found that a wrinkled adhesive interface effectively enhanced the adhesion between hydrogels^[70]. The wrinkle structure was formed by the elasticity mismatch between hydrogels and adhesive polyion complex layers when electrophoresis was carried out between cationic and anionic semi-IPNs (Figs. 6b1–6b3). The discovery of the wrinkle structure for adhesion at the interface contributes considerably to the development of a novel adhesion strategy of soft materials.

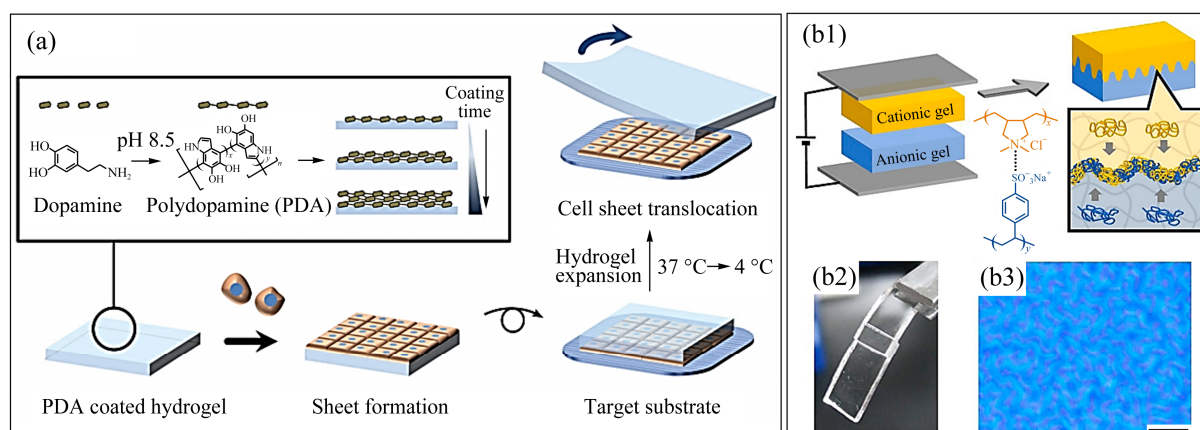


Fig. 6 Non-covalent bonding of hydrogels with substrates: (a) Schematic diagram of the protocol for cell sheet translocation onto a target surface using a temperature-induced shape-changing hydrogel with controlled cell adhesion by polydopamine (PDA) coating (Reprinted from Ref. [32] with permission from The Royal Society of Chemistry); (b1) Schematic illustration of wrinkle formation of adhered cationic and anionic gels by electrophoresis, (b2) macroscopic and (b3) phase-contrast microscopic observations of adhered gel interfaces (The gels were cut into 5 mm × 15 mm strips, with an adhesion area of 2 mm × 5 mm. The scale bar was 10 μm.) (Reprinted with permission from Ref. [70]; Copyright (2016) American Chemical Society)

Covalent Interaction

Unlike the physical adhesion between hydrogels and other substrates, covalent bonding of hydrogels onto substrates is generally irreversible. Tougher bonding of hydrogels upon substrates can be achieved through covalent bonds. For example, Zhang and co-authors reported a hydrogel coated polydimethylsiloxane (PDMS) with a durable hydrophilic and protein resistant surface^[71]. The fabrication of this stable antifouling hydrogel coating on the PDMS combined chemical modification (silanization reaction) and surface microstructure construction of PDMS substrate. The detailed strategy is illustrated in Fig. 7(a). At first, PDMS was oxidized by air plasma and H₂O/H₂O₂/HCl solution to generate superficial hydroxyl groups. Then 3-(trimethoxysilyl)-propyl methacrylate (TMSPPMA) was used as an adhesive to chemically bond the PDMS and the hydrogel coating together, which was introduced onto the PDMS surface by silanization reaction. Finally, the hydrogel coating was formed by curing the hydrogel precursor solution among the micropillars by photopolymerization under UV light.

Additionally, Yuk *et al.* developed a hydrogel-elastomer hybrid material with robust interface^[23]. The hybrids were formed by bonding tough hydrogels of interpenetrating polymer networks with elastomers. Fabrication was described in detail as follows. The hydrogel part of the hybrids was a physically crosslinked hydrogel, infiltrated with monomer/macromonomer solution of the other polymer networks. The surface of a cured elastomer with patterned microstructures was treated with photo-initiator benzophenone. The pre-shaped hydrogel and elastomer were assembled together followed by ultraviolet irradiation to chemically crosslink the other polymer network in the hydrogel. The as-prepared hybrids showed robust interface between hydrogel and

elastomer (Fig. 7b1). The photos of the hydrogel-elastomer interface during the peeling test also represented the robust interface between two substrates (Figs. 7b2 and 7b3). Later in the same year, a strategy that bonds the hydrogels to diverse non-porous surfaces was also reported by their group^[35]. It was a two-step method. The first step was to functionalize the target substrate with amino-silane (TMSPMA), and then the chemical anchoring of long-chain polymer network was achieved by crosslinking the hydrogel networks to functional silanes grafted surfaces of various solids (Fig. 7c1). The universality of this method was tested by diverse substrates including

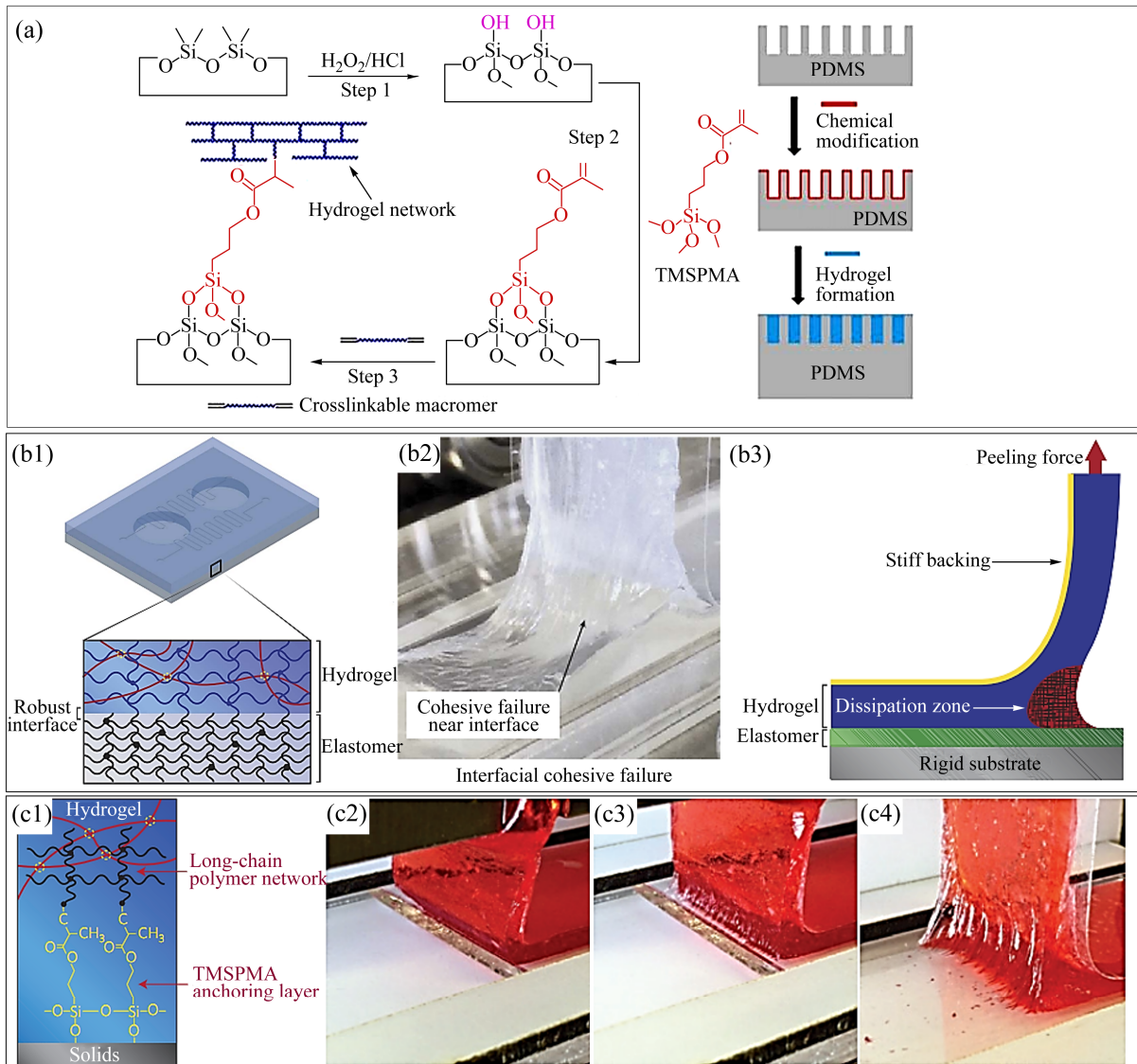


Fig. 7 Covalent bonding of hydrogels with solid substrates: (a) Schematic illustration of PDMS surface modification to form hydrogel coatings (Reprinted with permission from Ref. [71]; Copyright (2016) American Chemical Society); (b1) The resultant hydrogel-elastomer hybrid forming extremely robust interfaces due to the polymer network in the hydrogel covalently anchored on elastomer surface, (b2) photos of the hydrogel-elastomer interface during peeling test, (b3) schematic illustration of the 90°-peeling test (Reprinted with permission from Ref. [23]; Copyright (2016) Nature Publishing Group); (c1) The chemical anchoring of long-chain polymer networks by crosslinking the networks to functional silanes grafted on the surfaces of various solids, (c2–c4) photos of the peeling process of a tough hydrogel with its long-chain network chemically anchored on a glass substrate (Reprinted with permission from Ref. [35]; Copyright (2016) Nature Publishing Group)

glass, Si wafer, ceramic, titanium and aluminium. Compared with physical interactions, the chemical anchorage resulted in a higher intrinsic work of adhesion and significant energy dissipation of the bulk hydrogel during detachment. Figures 7(c2)–7(c4) show the photos of the peeling process of a tough hydrogel with its long-chain network chemically anchored on a glass substrate.

CONCLUSIONS AND OUTLOOK

In this review, the strategies functionalizing the surface of hydrogels are summarized. Quaternization reaction, silylation reaction, epoxy ring-opening reaction and click reaction are utilized to chemically grafting functional molecules onto the surface of hydrogels. In contrast, electrostatic interaction, van der Waals' force, self-assembly of inorganic micro/nanoparticles were adopted as physical methods to functionalize the surface of hydrogels. Based on these methods, hydrogels with lower protein adsorption, tunable wettability, high cell/tissue adhesiveness, and controllable drug release properties were developed. These surface modification strategies broaden the list of functional hydrogels and expand into diverse complicated biomedical and practical applications that may not be achievable for the classical homogeneous bulk hydrogel.

However, despite the fascinating progresses, there are still many opportunities and challenges in this promising field, including the preparation of hydrogels with enhanced biological adhesion, and the fabrication of hydrogels with mechanical robust barriers. Moreover, facile and efficient strategies to prepare large-area, long-term stable structured hydrogel surfaces should be developed. The durability of hydrogels in the extreme environment needs to be improved as well. Future advances in functional hydrogel materials will require thoughtful integration of rational interfacial engineering and 3D network design of hydrogels. Consequently, more attention should be paid to developing new interfacial engineering techniques to achieve more functional hydrogel materials and broaden their applications in areas related to marine antifouling, tissue engineering, sensors and biological medicine.

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