ACS APPLIED MATERIALS & INTERFACES

Research Article

Versatile Surface Modification of Hydrogels by Surface-Initiated, Cu0-Mediated Controlled Radical Polymerization

Kaihuan Zhang, Wenqing Yan, Rok Simic, Edmondo M. Benetti, and Nicholas D. Spencer*

Cite This: ACS Appl. Mater. Interfaces 2020, 12, 6761−6767

Read Online

| ACCESS | Metrics & More | Article Recommendations | SI Supporting Information |

ABSTRACT: Surface-initiated controlled radical polymerization mediated by a Cu0 plate (SI-Cu0 CRP) emerges as a versatile and efficient method for the functionalization of the exposed surfaces of hydrogels with a wide variety of polymer brushes. When a Cu0 plate is placed in contact with initiator-bearing hydrogel surfaces in the presence of ligand and monomer and under ambient conditions, it rapidly consumes dissolved oxygen from the reaction mixture, further acting as a source of catalyst and leading to the rapid growth of hydrogel-bound polymer chains. Three types of functional surfaces have been prepared as examples of the wide range of potential materials that can be synthesized in this way, including a hydrogel with a protective, hydrophobic surface, a lubricious hydrogel, as well as a hydrogel with thermally switchable frictional properties.

KEYWORDS: *hydrogels, lubricious surfaces, surface-initiated polymerization, surface modification, polymer brushes*
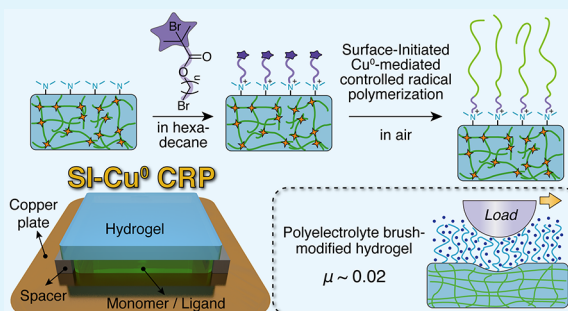
INTRODUCTION

Hydrogels are composed of a cross-linked polymer network and a large amount of water and are widely used in materials science in applications that include soft electronics, drug-delivery systems, tissue-engineering supports, sensors, and actuators.[1−3] Despite the widespread use of hydrogel-based materials, and recent developments in the fabrication of hydrogels with improved mechanical properties,[4,5] enhanced biocompatibility,[6,7] and self-healing properties,[8] only a few studies have been reported focusing on the modification and functionalization of their exposed surfaces. Surface-modification strategies involving alkylation reactions at the hydrogel/oil interface have been recently reported, yielding superhydrophobic layers on hydrogel surfaces.[9] Moreover, the introduction of reactive double bonds or anchoring groups at the exposed surface of elastomers has enabled the formation of hydrogel "skins" with tunable tribological and wetting properties.[10−12] Despite these initial attempts, a simple and versatile route for the surface-confined modification of hydrogels with a variety of functionalities, as well as the controlled grafting of polymer assemblies presenting different chemistries and properties still represent significant challenges. The development of an efficient method to generate polymer-brush-based layers on hydrogels, selectively on their exposed surfaces, could widen the applicability and enrich the properties of such materials.[13,14] Technologically relevant interfacial properties, such as lubrication and biopassivity, could be precisely adjusted on hydrogel-based biomaterials; thus, reducing unspecific protein contamination within

physiological environments and improving the integration of cell-seeded hydrogel scaffolds in the surrounding medium. Moreover, diffusion of biomolecules or smaller species from the environment through the hydrogel matrix could be controlled by confined functionalization with polymer-brush-based coatings that display stimuli-responsive properties.

Controlled radical polymerization methods, including atom-transfer radical polymerization (ATRP) and reversible addition fragmentation chain-transfer polymerization (RAFT), have been recently applied for the fabrication and modification of the inner structure of polymer networks.[15,16] For instance, structurally tailored and engineered macromolecular (STEM) gels have been introduced by Cuthbert et al.[17−19] The STEM networks were prepared by incorporating ATRP inimers, i.e., compounds that act as both initiators and monomers, yielding polymer networks that could be locally modified at a later stage, via the grafting of compositionally different polymers within the gel structure. Following a different approach, Chen et al. have exploited photoinduced RAFT to insert monomers into "parent" gels, thus generating complex networks and introducing a "living additive manufacturing" strategy to fabricate polymeric materials with variable bulk properties.[20] Although the composition and properties of polymer networks

could be finely adjusted and, in some cases,[18] spatially controlled, by means of these methods, the modifications were not purely confined to the materials' surfaces, and thus did not enable the modulation of interfacial properties independently from those of the bulk.

In the search for an efficient and versatile method to selectively modify the exposed surface of hydrogels with polymer films featuring tunable chemistry and interfacial properties, we turned our attention to surface-initiated controlled radical polymerization mediated by copper plates (SI-Cu^0 CRP), which was recently reported as a successful grafting process to grow compositionally diverse polymer brushes from a variety of supports, under ambient conditions.[21−28] During SI-Cu^0 CRP, a copper plate facing an ATRP-initiator-bearing support acts as a source of catalyst, which in the presence of ligand diffuses to the initiating surface to trigger the rapid growth of polymer brushes. Due to the highly confined nature of this process, SI-Cu^0 CRP is highly tolerant to oxygen, which is rapidly consumed by the oxidation of the Cu^0 surface.[21,26] Furthermore, it requires very small volumes of reaction mixtures, which are sandwiched between the opposing surfaces.

Here, we demonstrate that when functional hydrogels are used as initiating supports, SI-Cu^0 CRP under ambient conditions enables the rapid growth of a variety of polymer brushes, which are specifically located at the surface of the hydrogel. This leads to spatially structured hydrogel−polymer brush interfaces with tunable lubrication properties and responsive behavior.

■ EXPERIMENTAL SECTION

Materials. 2-Hydroxyethyl methacrylate (HEMA), 1-vinyl-2-pyrrolidinone (NVP), 2-(dimethylamino)ethyl methacrylate (DMAE-MA), ethylene glycol dimethacrylate, poly(ethylene glycol) methyl ether acrylate (OEGA, average M_n 480), N-isopropylacrylamide (NIPAM), 2-(methacryloyloxy)ethyltrimethylammonium chloride (METAC, 75 wt % in H$_2$O), 3-sulfopropyl methacrylate potassium salt (SPMA), 2-methacryloyloxyethyl phosphorylcholine (MPC), fluorescein O-methacrylate, N,N,N′,N′,N″-pentamethyldiethylenetriamine (PMDETA), 2,2′-bipyridine, 2-bromo-2-methylpropionic acid, 4-(dimethylamino)pyridine (DMAP), 2-bromoethanol, 11-bromo-1-undecanol, hexadecane, LiBr, NaHCO$_3$, and MgSO$_4$ were purchased from Sigma-Aldrich (MO). Dodecyl methacrylate (C12MA, a mixture of C12−C16 methacrylic acid alkylester) was purchased from Merck (Hohenbrunn, Germany). 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) was obtained from Fluorochem Ltd. (Hadfield, U.K.). 2,4,6-Trimethylbenzoyl chloride was purchased from TCI Chemicals (Tokyo, Japan). Dimethyl phenylphosphonite and 6-bromo-1-hexanol were purchased from abcr GmbH (Karlsruhe, Germany). Alcian Blue 8GS was purchased from Fluka AG (Buchs, Switzerland). 2-Butanol was purchased from Roth AG (Gerlafingen, Switzerland). N-isopropylacrylamide was purified by crystallizing it from a 60:40 (v/v) toluene/hexane mixture prior to use, while other monomers were used without any purification. Copper plates (99.9%) were obtained from Conrad Electronic AG (Wollerau, Switzerland).

Synthesis of Lithium Phenyl-2,4,6-Trimethylbenzoylphosphinate (LAP). 2,4,6-Trimethylbenzoyl chloride (4.9 mL, 0.029 mol) was added slowly to an equimolar amount of dimethyl phenylphosphonite (5.0 g) under continuously stirring. The mixture was reacted for 20 h at room temperature and then excess lithium bromide (10.2 g) in 2-butanone (150 mL) was added. The reaction was then heated to 50 °C and a white precipitate was formed after 20 min. The mixture was cooled to room temperature, allowed to stand for 4 h, and then filtered. The filtrate was washed and filtered three times with 2-butanone to remove unreacted lithium bromide, and excess solvent was removed under vacuum. The product, lithium phenyl-2,4,6-

trimethylbenzoylphosphinate was recovered as white flakes (8.0 g, 93%).

Synthesis of 2-Bromoethyl α-Bromoisobutyrate (C2-Br Modifier). 2-Bromoethyl α-bromoisobutyrate was synthesized by an esterification reaction between 2-bromoethanol and 2-bromoisobutyric acid. In a typical procedure, 13.6 g of 2-bromoethanol (1 equiv), 20.0 g of 2-bromoisobutyric acid (1.1 equiv), 31.3 g of EDC hydrochloride (1.5 equiv), and 0.68 g of DMAP (0.05 equiv) were dissolved in 200 mL of dichloromethane in a 500 mL round-bottom flask equipped with a stirring bar in an ice bath. The solution was purged with N$_2$ for 20 min and allowed to warm up to room temperature. After 24 h, the solution was washed with 250 mL of 1 M HCl solution, saturated NaHCO$_3$ solution, and brine, three times each. The organic phase was collected and dried over anhydrous MgSO$_4$. The solvent was removed under vacuum to yield a light yellow liquid product (yield 83%).

Synthesis of 6-Bromohexyl α-Bromoisobutyrate (C6-Br Modifier). 2-Bromohexyl α-bromoisobutyrate was synthesized by an esterification reaction between 6-bromo-1-hexanol and 2-bromoisobutyric acid. In a typical procedure, 10.0 g of 6-bromo-1-hexanol (1 equiv), 10.0 g of 2-bromoisobutyric acid (1.1 equiv), 15.6 g of EDC hydrochloride (1.5 equiv), and 0.33 g of DMAP (0.05 equiv) were dissolved in 150 mL of dichloromethane in a 250 mL round-bottom flask equipped with a stirring bar in an ice bath. The solution was purged with N$_2$ for 20 min and allowed to warm up to room temperature. After 24 h, the solution was washed with 250 mL of 1 M HCl solution, saturated NaHCO$_3$ solution, and brine, three times each. The organic phase was collected and dried over anhydrous MgSO$_4$. The solvent was removed under vacuum to yield a light yellow liquid product (yield 82%).

Synthesis of 11-Bromoundecanyl α-Bromoisobutyrate (C11-Br Modifier). 2-Bromohexyl α-bromoisobutyrate was synthesized by an esterification reaction between 11-bromo-1-undecanol and 2-bromoisobutyric acid. In a typical procedure, 40.0 g of 11-bromo-1-undecanol (1 equiv), 29.2 g of 2-bromoisobutyric acid (1.1 equiv), 45.3 g of EDC hydrochloride (1.5 equiv), and 0.95 g of DMAP (0.05 equiv) were dissolved in 300 mL of dichloromethane in a 500 mL round-bottom flask equipped with a stirring bar in an ice bath. The solution was purged with N$_2$ for 20 min and allowed to warm up to room temperature. After 24 h, the solution was washed with 350 mL of 1 M HCl solution, saturated NaHCO$_3$ solution, and brine, three times each. The organic phase was collected and dried over anhydrous MgSO$_4$. The solvent was removed under vacuum to yield a light yellow liquid product (yield 85%).

Preparation of Initiator-Modified p(HEMA−NVP−DMAEMA) Hydrogel. p(HEMA−NVP−DMAEMA) hydrogel was first prepared by copolymerizing HEMA (20 wt %), NVP (10 wt %), DMAEMA (20 wt %), and ethylene glycol dimethacrylate (0.1 wt %) with LAP (0.15 wt %) as initiator in H$_2$O under 365 nm UV for 40 min. The as-prepared hydrogels were thoroughly washed with Milli-Q water and the residual water on hydrogel surface was removed under a N$_2$ flow. Subsequently, the hydrogel was immersed in a hexadecane solution with bromoalkyl α-bromoisobutyrate modifier (1 wt %) for 12 h.

Cu^0-Mediated Controlled Radical Polymerization on Hydrogel Surface. A copper plate (10 × 10 cm^2) was washed with 4 M HCl for 5 min. The initiator-modified hydrogel substrate was sandwiched with the copper plate leaving a gap of ∼0.5 mm with the aid of two Si wafer shims. A polymerization mixture including monomer (2 M) and PMDETA or 2,2′-bipyridine (50 mM) was injected into the gap by using a pipette and the reaction was left under ambient conditions for 15 min. For the SI-Cu^0 CRP of OEGA, NIPAM, METAC, SPMA, and MPC, water or methanol−water mixture (1:1 v/v) were used as solvents. For the SI-Cu^0 CRP of C12MA and the copolymerization of OEGA and fluorescein O-methacrylate, DMF was used as a solvent.

Instruments and Characterization. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance III 300 MHz spectrometer. Fourier-transform infrared (FTIR) spectra were obtained by a Bruker ALPHA spectrometer equipped with a single-reflection diamond attenuated total reflection (ATR)
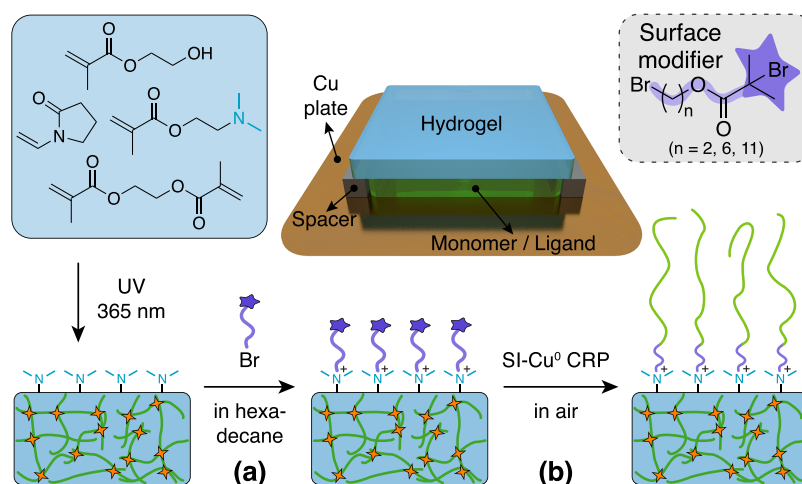
Figure 1. Preparation of polymer-brush-grafted hydrogel surfaces via interfacial modification and subsequent grafting polymerization. (a) Initiator-modified p(HEMA−NVP−DMAEMA) hydrogel substrates were first prepared by a confined reaction with a surface modifier at the interface between the aqueous hydrogel matrix and an oil (hexadecane) phase. (b) Surface functionality can be varied by grafting different polymer layers to the hydrogel via SI-Cu^0 CRP in air.

accessory. Fluorescence images were captured using an Axio Imager M1m microscope (Zeiss, Germany). Scanning electron microscopy (SEM) images were taken with a LEO Gemini 1530 instrument (Carl Zeiss GmbH, Oberkochen, Germany). Friction tests were performed on a standard pin-on-disc tribometer (CSM Instruments, Peseux, Switzerland). The stroke length was set to 10 mm and sliding speeds were varied from 0.1 to 10 mm s^{-1}. The normal load was set to 0.6 N, which corresponds to a contact pressure of about 20 kPa. The coefficient of friction (μ) was defined as the friction force divided by the normal load and was determined for each cycle from the middle 20% of the stroke length.

RESULTS AND DISCUSSION

As illustrated in Figure 1, a surface modifier, bromoalkyl α-bromoisobutyrate was selectively immobilized on the surface of a dimethylamino group-containing hydrogel through an interfacial quaternization reaction. The pendant α-bromoisobutyrate group served as a typical ATRP initiating group for the subsequent radical polymerization. Surface-initiated radical polymerization was then used to graft various polymer brushes onto the hydrogel surface in the air by using a copper plate as the catalyst source without the need for additional Cu$^{I/II}$ salts.[21,22]

The hydrogels used as substrates for the subsequent interfacial growth of polymer brushes by SI-Cu^0 CRP were synthesized by UV polymerization of 2-hydroxyethyl methacrylate (HEMA), N-vinyl-2-pyrrolidone (NVP), and 2-(dimethylamino)ethyl methacrylate (DMAEMA) in the presence of ethylene glycol dimethacrylate as the cross-linker and lithium phenyl-2,4,6-trimethylbenzoylphosphinate (LAP) as the UV initiator (Figure 1). p(HEMA−NVP)-based hydrogels have been frequently employed in the formulation of soft contact lenses, and possess good mechanical properties and relatively low water content of ∼60%, which implies a relatively high surface concentration of polymer chains. The introduction of DMAEMA as a comonomer during hydrogel synthesis provided reactive dimethylamino groups for the immobilization of bromoalkyl α-bromoisobutyrate species through an interfacial quaternization reaction, leading to the formation of an ATRP-initiator layer (Figure 1a).[9,29]

Three surface modifiers with different alkyl chain lengths between the primary bromine function and the α-bromoiso-

butyrate group were synthesized, including 2-bromoethyl α-bromoisobutyrate (C2-Br), 6-bromohexyl α-bromoisobutyrate (C6-Br), and 11-bromoundecanyl α-bromoisobutyrate (C11-Br) (see Figures S1−S3 in the Supporting Information). Since the reaction between the hydrophobic surface modifiers and the dimethylamino groups at the hydrogel surface was carried out in hexadecane, which is immiscible with the aqueous phase incorporated within the network, the formation of the ATRP initiator layers remained confined to the hexadecane/hydrogel interface. Dichloromethane as the oil phase has also shown to be an effective solvent for the quaternization reaction at the hydrogel surface, but displays imperfect immiscibility with water and therefore penetrates the hydrogel for up to micrometers from the outer surface.[9] Thus, in this case, subsequent grafting of a hydrophilic polymer brush may give rise to a thick swollen layer just under the hydrogel surface due to the high osmotic pressure. To retain the bulk mechanical properties, hexadecane is preferably employed to provide more surface-confined modification of the hydrogel.

As illustrated in Figure 1, an activated copper plate was covered with the modified hydrogel, using Si wafer shims as spacers to generate a gap of ∼0.5 mm (see Experimental Section). The gap between the metallic plate and the hydrogel was filled with polymerization mixtures including different monomers, solvents, and ligands. We note here that the spacing distance was optimized according to a reference experiment with a tilted copper plate (Figure S4), which is also consistent with the previously reported procedures by Jordan et al.[21] The grafting polymerizations were conducted in air under ambient conditions and without degassing the polymerization mixtures. The oxygen dissolved in the reaction medium was rapidly consumed by the oxidation of the Cu^0 surface, generating a Cu$_x$O oxide layer (crucial to the SI-Cu^0 CRP process) that serves as source of Cu^I and Cu^{II} species, which in the presence of N,N,N′,N′,N″-pentamethyldiethylenetriamine (PMDETA) ligand diffuse to the initiator-bearing interface triggering the growth of polymer grafts.[21,26]

SI-Cu^0 CRP of a mixture of oligo(ethylene glycol) acrylate (OEGA) with trace amounts of fluorescein O-methacrylate in dimethylformamide (DMF) enabled the fabrication of brushes that could later be visualized on the hydrogel surface by
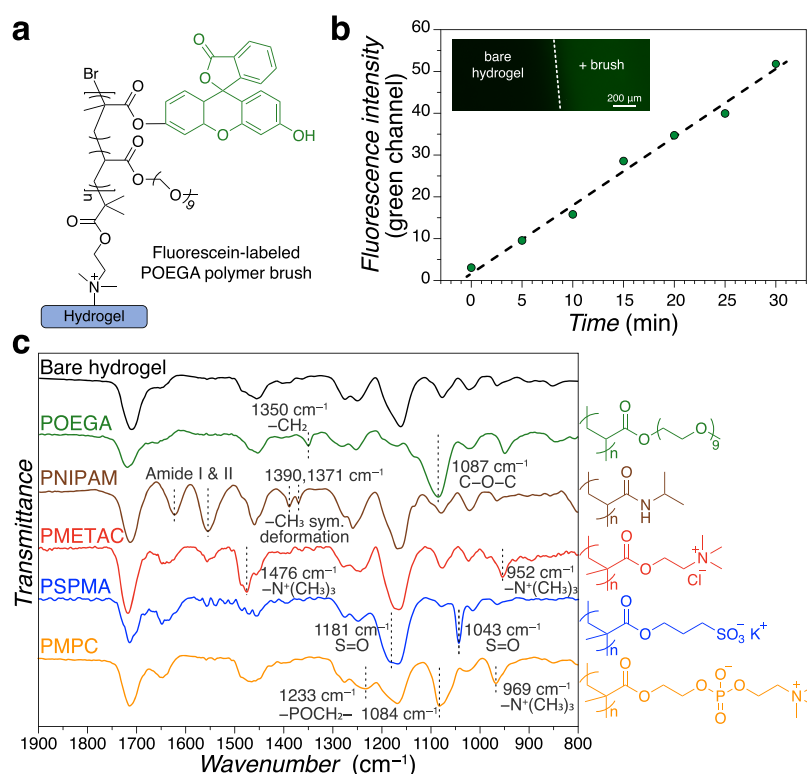
Figure 2. (a) A fluorescent, FITC-labeled POEGA polymer brush grafted onto a hydrogel surface. (b) Fluorescence intensity of an FITC-labeled polymer brush synthesized for different polymerization times. (c) ATR-FTIR spectra of bare hydrogel and various polymer brushes grafted on the hydrogel surface, including POEGA, PNIPAM, PMETAC, PSPMA, and PMPC.
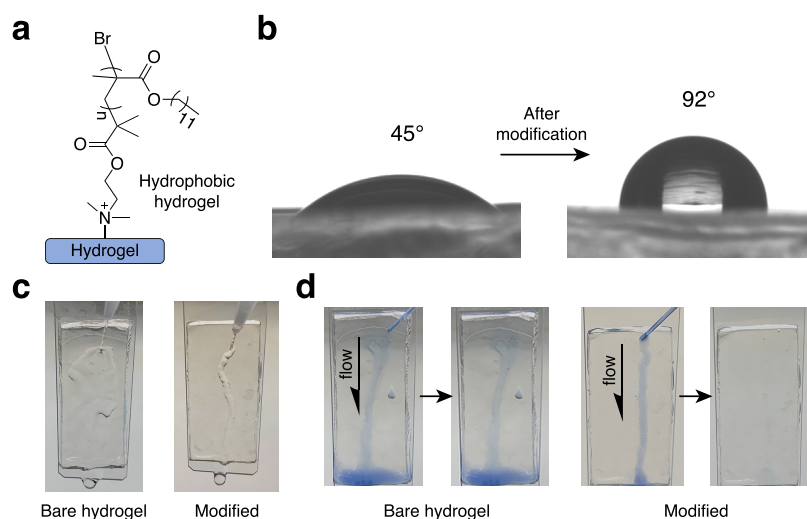
Figure 3. (a) Hydrophobic alkyl methacrylate polymer brush grafted on a hydrogel surface. (b) Water contact angles for the bare hydrogel and grafted polymer brush after SI-Cu^0 CRP. (c) Flow behavior of an impinging water jet on the surface of the bare hydrogel and hydrophobic polymer brush-modified hydrogel. (d) Images of bare hydrogel and modified hydrogel under a flow of an Alcian blue-containing aqueous solution, showing the barrier properties of the grafted hydrophobic polymer layer.

fluorescence microscopy (Figure 2a,b). The recorded linear increment in fluorescence intensity with increasing polymerization time suggested a progressive growth of POEGA brushes from the modified hydrogel surface and confirmed the controlled character of SI-Cu^0 CRP.[26]

A variety of hydrophilic and ionic monomers could be polymerized from ATRP initiator-modified hydrogels by SI-Cu^0 CRP, and using water or methanol–water mixtures as solvents for the polymerization process.[21,22] As shown in

Figure 2c, attenuated total reflection Fourier transform infrared (ATR-FTIR) spectroscopy confirmed the successful growth of relatively thick and compositionally diverse polymer brushes from the hydrogel surface following just 15 min of polymerization, including poly(N-isopropylacrylamide) (PNIPAM), poly(2-methacrylolyloxyethyl-trimethylammonium chloride) (PMETAC), poly(3-sulfopropyl methacrylate potassium salt) (PSPMA), and poly(2-methacryloyloxyethyl phosphorylcholine) (PMPC).

SI-Cu^0 CRP allowed the surface properties of hydrogels to be tuned, even to a large extent, for example by polymerizing a long-alkyl-side-chain methacrylate, yielding hydrophobic brush layers (Figure 3a). Specifically, poly(dodecyl methacrylate) (PC12MA) brushes could be successfully grown in DMF using 2,2′-bipyridine as a ligand (Figure S5). After 1 h of polymerization, the static water contact angle on the hydrogel surface increased from 45 to 92° (Figure 3b), indicating the successful formation of a uniform PC12MA brush coating.

Tuning of hydrogel wettability through SI-Cu^0 CRP was further demonstrated by allowing a water jet to impinge on the hydrogel surface before and after modification with PC12MA brushes. As displayed in Figure 3c, the liquid jet was distorted and the water spread out when the jet reached the hydrophilic hydrogel surface before modification. In contrast, due to the hydrophobic character of the PC12MA brush, the impinging jet could not wet the modified hydrogel. The presence of a PC12MA brush additionally influenced the diffusion of small molecules from the solution through the functionalized hydrogel. As shown in Figure 3d, an Alcian blue solution could not penetrate through the hydrogel interface when the PC12MA brush was present at the interface, while the same dye could easily and quickly diffuse into the pristine matrix.

Loosely cross-linked or sparse network structures reduce the friction on hydrogel surfaces, as reported in our recent studies.[30,31] The growth of polyelectrolyte brushes by SI-Cu^0 CRP enabled the formation of highly swollen and lubricious polymer layers on p(HEMA−NVP−DMAEMA) hydrogels. SEM images of the freeze-dried hydrogel sample confirmed the different morphologies at the surface layer and in the bulk hydrogel (Figure S6). Tribological tests were performed by using a pin-on-disc device to evaluate the lubricity of PMPC-, PSPMA-, and PMETAC-modified hydrogels. An 18 mm diameter glass hemisphere was employed as a counter surface sliding against the differently modified hydrogel surface immersed in ultra-pure water in reciprocating mode with a stroke length of 10 mm (Figure 4a).

Representative friction loops recorded by pin-on-disc at a sliding velocity of 0.1 mm s^{-1} on bare and PMPC brush-modified hydrogels are shown in the Supporting Information (Figure S7). The oscillating signals ("stick-slip") appearing at lower sliding velocities indicate significant adhesion between the glass probe and the bare hydrogel surface during the sliding test. However, following the growth of a PMPC brush by SI-Cu^0 CRP, a stable coefficient of friction (μ) below 0.01 was recorded along the entire stroke length (Figure S7). The reduction in friction observed for polymer-brush-functionalized hydrogels was presumably due to a combination of their pronounced hydration, which provides a significant amount of fluid lubricant at the interface, and the osmotic pressure exerted by the brushes on the compressing probe, which confer to them a unique load-bearing capacity (Figure 4b).[31−33]

The sliding velocity plays an important role in determining the μ due to poro- and/or viscoelastic dissipation effects resulting from the deformation of the hydrogel surfaces. Within a range of sliding velocities included between 0.1 and 10 mm s^{-1}, PMPC, PSPMA, and PMETAC brush-bearing hydrogels all showed a significantly lower μ with respect to that recorded on the bare, unmodified hydrogel (Figure 4c). In particular, all the different brush interfaces were characterized by μ values ranging from 0.01 to 0.04. The higher, speed-dependent friction on bare hydrogel could be due to the shearing of a thin water layer between the glass surface and the almost
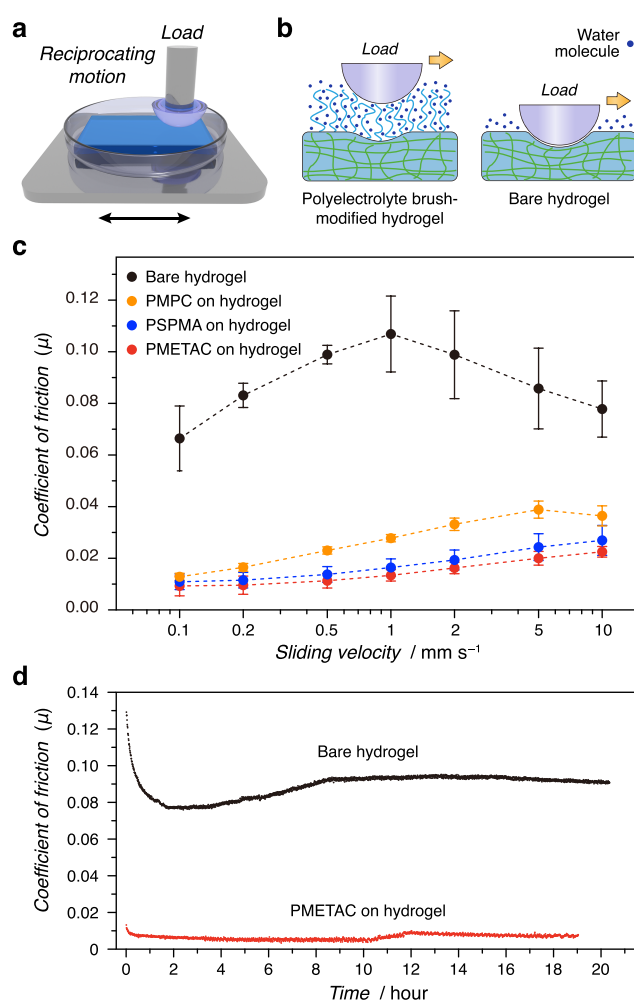

Figure 4. (a) Schematic of the tribological measurements performed in a linear reciprocating mode. (b) Schematic of the glass probe sliding against modified hydrogel and bare hydrogel. (c) Coefficients of friction for various polymer brush-grafted hydrogel surfaces (PMPC, PSPMA, PMETAC brushes on hydrogel, and bare p(HEMA−NVP−DMAEMA) hydrogel) at different sliding velocities under a constant load of 0.6 N. (d) Long-term sliding measurement of the bare hydrogel and PMETAC-modified hydrogel under a constant load of 0.6 N and sliding velocity of 1 mm s^{-1}.

impermeable cross-linked hydrogel surface. On the other hand, the lubricious surface of the polyelectrolyte polymer brush-modified hydrogels could enable an increased penetration depth of the shearing fluid and thus reduced and less speed-dependent friction.[31]

To investigate the long-term tribological performance of the polymer brush-modified hydrogels, the bare hydrogel and the PMETAC brush-bearing hydrogel were both slid against a glass hemisphere for 20 h. No visible wear was observed on the surface of either the bare hydrogel or the PMETAC brush-bearing hydrogel. As shown in Figure 4d, the μ of the bare hydrogel started at 0.13 and dropped to a value of about 0.08 in the 1st hour, presumably due to slight wear of the hydrogel surface. The bare hydrogel exhibited a μ value exceeding 0.09 for a majority of the 20 h measurement period. However, the μ of the PMETAC brush-bearing hydrogel showed a pronounced low value of around 0.01 over the entire measurement, indicating stable lubrication performance and no indication of a transition to the bare-gel value.

Stimuli-responsive polymer brushes have found myriad applications in fabricating adaptive or responsive smart materials by controlling surface wettability and morphology or harnessing stimulus-induced structural changes for mechanical actuation and sensing.[34,35] When p(HEMA−NVP−DMAEMA) hydrogel surfaces were functionalized by PNIPAM brushes, hydrogels exhibiting thermally switchable frictional properties were obtained. As PNIPAM brushes undergo a conformational change from swollen to collapsed grafts across the lower critical solution temperature (LCST) of the polymer in water, a simultaneous increment in friction is typically observed.[36−38] The tribological properties of PNIPAM brush-modified hydrogels were measured by pin-on-disc while varying the temperature of the aqueous medium between 20 and 40 °C. As reported in Figure 5, the average
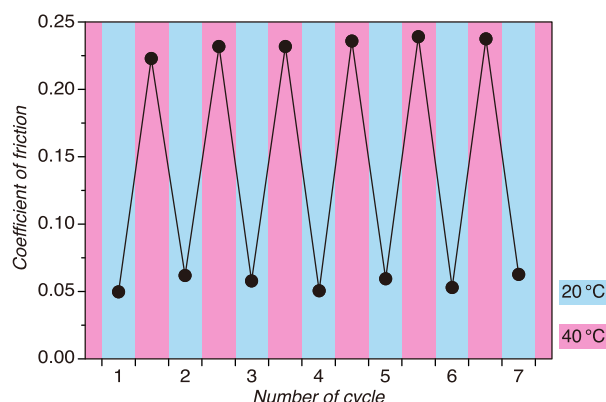
Figure 5. Coefficient of friction for PNIPAM-modified hydrogel surface measured under switching temperatures from 20 to 40 °C. The coefficient of friction is typically four times higher at 40 °C than that at 20 °C.

values of μ varied between 0.05 at 20 °C, and 0.23 at 40 °C. In addition, repeated temperature increments above PNIPAM LCST were mirrored by full recovery of brush lubricity when the temperature was subsequently decreased, confirming the reversibility in the interfacial properties of the brush-bearing hydrogels.

CONCLUSIONS

In conclusion, we have demonstrated that SI-Cu^0 CRP represents a highly versatile technique for the customized functionalization of hydrogels with chemically diverse polymer brushes under ambient conditions. The surface-confined grafting of various polymer brushes onto the hydrogel surface can be used to tailor the physicochemical properties of the system, e.g., hydrophobicity, lubricity, or thermal responsiveness. Controlled grafting of hydrophobic PC12MA-based brushes was shown to impart barrier properties toward the diffusion of small molecules from the surrounding medium through the hydrogel structure. Furthermore, grafting of polyelectrolyte brushes generated hydrogels with enhanced lubricity, nearly matching the nanotribological behavior typically observed within the articular joints of mammals. Finally, the growth of thermoresponsive brushes enabled the design of hydrogel surfaces with switchable interfacial properties. While the design principle may be extended for the development of coatings for other types of elastomeric and complex materials, the current functionalization strategy may already have practical applications in areas related to the modification and design of interfaces, such as bioactive scaffolds, artificial cartilage, and composite hydrogels.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsami.9b21399.

Synthesis route; ^{1}H and ^{13}C NMR spectra of bromoalkyl α-bromoisobutyrates; ATR-FTIR spectra; representative friction loop (PDF)

AUTHOR INFORMATION

Corresponding Author

Nicholas D. Spencer − *Laboratory for Surface Science and Technology, Department of Materials, ETH Zurich, Zurich 8093, Switzerland;* ● orcid.org/0000-0002-7873-7905; Email: nspencer@ethz.ch

Authors

Kaihuan Zhang − *Laboratory for Surface Science and Technology, Department of Materials, ETH Zurich, Zurich 8093, Switzerland;* ● orcid.org/0000-0002-7353-4180

Wenqing Yan − *Laboratory for Surface Science and Technology, Department of Materials, ETH Zurich, Zurich 8093, Switzerland*

Rok Simic − *Laboratory for Surface Science and Technology, Department of Materials, ETH Zurich, Zurich 8093, Switzerland;* ● orcid.org/0000-0002-5258-6192

Edmondo M. Benetti − *Laboratory for Surface Science and Technology, Department of Materials, ETH Zurich, Zurich 8093, Switzerland; Biointerfaces, Swiss Federal Laboratories for Materials Science and Technology (Empa), St. Gallen 9014, Switzerland;* ● orcid.org/0000-0002-5657-5714

Complete contact information is available at:
https://pubs.acs.org/10.1021/acsami.9b21399

Notes

The authors declare no competing financial interest.

REFERENCES

(1) Ionov, L. Hydrogel-Based Actuators: Possibilities and Limitations. *Mater. Today* **2014**, *17*, 494−503.

(2) Li, J.; Mooney, D. J. Designing Hydrogels for Controlled Drug Delivery. *Nat. Rev. Mater.* **2016**, *1*, No. 16071.

(3) Zhang, Y. S.; Khademhosseini, A. Advances in Engineering Hydrogels. *Science* **2017**, *356*, No. eaaf3627.

(4) Sun, J.-Y.; Zhao, X.; Illeperuma, W. R. K.; Chaudhuri, O.; Oh, K. H.; Mooney, D. J.; Vlassak, J. J.; Suo, Z. Highly Stretchable and Tough Hydrogels. *Nature* **2012**, *489*, 133−136.

(5) Gong, J. P.; Katsuyama, Y.; Kurokawa, T.; Osada, Y. Double-Network Hydrogels with Extremely High Mechanical Strength. *Adv. Mater.* **2003**, *15*, 1155−1158.

(6) Caló, E.; Khutoryanskiy, V. V. Biomedical Applications of Hydrogels: A Review of Patents and Commercial Products. *Eur. Polym. J.* **2015**, *65*, 252−267.

(7) Buwalda, S. J.; Vermonden, T.; Hennink, W. E. Hydrogels for Therapeutic Delivery: Current Developments and Future Directions. *Biomacromolecules* **2017**, *18*, 316−330.

(8) Taylor, D. L.; in het Panhuis, M. Self-Healing Hydrogels. *Adv. Mater.* **2016**, *28*, 9060−9093.

(9) Yao, X.; Chen, L.; Ju, J.; Li, C.; Tian, Y.; Jiang, L.; Liu, M. Superhydrophobic Diffusion Barriers for Hydrogels Via Confined Interfacial Modification. *Adv. Mater.* **2016**, *28*, 7383−7389.

(10) Zhao, T.; Wang, G.; Hao, D.; Chen, L.; Liu, K.; Liu, M. Macroscopic Layered Organogel−Hydrogel Hybrids with Controllable Wetting and Swelling Performance. *Adv. Funct. Mater.* **2018**, *28*, No. 1800793.

(11) Yuk, H.; Zhang, T.; Parada, G. A.; Liu, X.; Zhao, X. Skin Inspired Hydrogel-Elastomer Hybrids with Robust Interfaces and Functional Microstructures. *Nat. Commun.* **2016**, *7*, No. 12028.

(12) Yu, Y.; Yuk, H.; Parada, G. A.; Wu, Y.; Liu, X.; Nabzdyk, C. S.; Youcef-Toumi, K.; Zang, J.; Zhao, X. Multifunctional "Hydrogel Skins" on Diverse Polymers with Arbitrary Shapes. *Adv. Mater.* **2019**, *31*, No. 1807101.

(13) Zoppe, J. O.; Ataman, N. C.; Mocny, P.; Wang, J.; Moraes, J.; Klok, H.-A. Surface-Initiated Controlled Radical Polymerization: Stateof-the-Art, Opportunities, and Challenges in Surface and Interface Engineering with Polymer Brushes. *Chem. Rev.* **2017**, *117*, 1105−1318.

(14) Du, T.; Li, B.; Wang, X.; Yu, B.; Pei, X.; Huck, W. T. S.; Zhou, F. Bio-Inspired Renewable Surface-Initiated Polymerization from Permanently Embedded Initiators. *Angew. Chem., Int. Ed.* **2016**, *55*, 4260−4264.

(15) Braunecker, W. A.; Matyjaszewski, K. Controlled/Living Radical Polymerization: Features, Developments, and Perspectives. *Prog. Polym. Sci.* **2007**, *32*, 93−146.

(16) Matyjaszewski, K.; Tsarevsky, N. V. Macromolecular Engineering by Atom Transfer Radical Polymerization. *J. Am. Chem. Soc.* **2014**, *136*, 6513−6533.

(17) Cuthbert, J.; Beziau, A.; Gottlieb, E.; Fu, L.; Yuan, R.; Balazs, A. C.; Kowalewski, T.; Matyjaszewski, K. Transformable Materials: Structurally Tailored and Engineered Macromolecular (STEM) Gels by Controlled Radical Polymerization. *Macromolecules* **2018**, *51*, 3808−3817.

(18) Cuthbert, J.; Zhang, T.; Biswas, S.; Olszewski, M.; Shanmugam, S.; Fu, T.; Gottlieb, E.; Kowalewski, T.; Balazs, A. C.; Matyjaszewski, K. Structurally Tailored and Engineered Macromolecular (STEM) Gels as Soft Elastomers and Hard/Soft Interfaces. *Macromolecules* **2018**, *51*, 9184−9191.

(19) Cuthbert, J.; Martinez, M.R.; Sun, M.; Flum, J.; Li, L.; Olszewski, M.; Wang, Z.; Kowalewski, T.; Matyjaszewski, K. Non-Tacky Fluorinated and Elastomeric STEM Networks. *Macromol. Rapid Commun.* **2019**, *40*, No. 1800876.

(20) Chen, M.; Gu, Y.; Singh, A.; Zhong, M.; Jordan, A. M.; Biswas, S.; Korley, L. T. J.; Balazs, A. C.; Johnson, J. A. Living Additive Manufacturing: Transformation of Parent Gels into Diversely Functionalized Daughter Gels Made Possible by Visible Light Photoredox Catalysis. *ACS Cent. Sci.* **2017**, *3*, 124−134.

(21) Zhang, T.; Du, Y.; Muller, F.; Amin, I.; Jordan, R. Surface Initiated Cu(0) Mediated Controlled Radical Polymerization (SICuCRP) Using a Copper Plate. *Polym. Chem.* **2015**, *6*, 2726−2733.

(22) Zhang, T.; Du, Y.; Kalbacova, J.; Schubel, R.; Rodriguez, R. D.; Chen, T.; Zahn, D. R. T.; Jordan, R. Wafer-scale Synthesis of Defined Polymer Brushes under Ambient Conditions. *Polym. Chem.* **2015**, *6*, 8176−8183.

(23) Che, Y.; Zhang, T.; Du, Y.; Amin, I.; Marschelke, C.; Jordan, R. "On Water" Surface-initiated Polymerization of Hydrophobic Monomers. *Angew. Chem., Int. Ed.* **2018**, *57*, 16380−16384.

(24) Dehghani, E. S.; Du, Y.; Zhang, T.; Ramakrishna, S. N.; Spencer, N. D.; Jordan, R.; Benetti, E. M. Fabrication and Interfacial Properties of Polymer Brush Gradients by Surface-Initiated Cu(0)-Mediated Controlled Radical Polymerization. *Macromolecules* **2017**, *50*, 2436−2446.

(25) Zhang, T.; Benetti, E. M.; Jordan, R. Surface-Initiated Cu(0)-Mediated CRP for the Rapid and Controlled Synthesis of Quasi-3D Structured Polymer Brushes. *ACS Macro Lett.* **2019**, *8*, 145−153.

(26) Yan, W.; Fantin, M.; Spencer, N. D.; Matyjaszewski, K.; Benetti, E. M. Translating Surface-Initiated Atom Transfer Radical Polymerization into Technology: The Mechanism of Cu⁰-Mediated SI-ATRP under Environmental Conditions. *ACS Macro Lett.* **2019**, *8*, 865−870.

(27) Yan, W.; Fantin, M.; Ramakrishna, S.; Spencer, N. D.; Matyjaszewski, K.; Benetti, E. M. Growing Polymer Brushes from a Variety of Substrates under Ambient Conditions by Cu⁰-Mediated Surface-Initiated ATRP. *ACS Appl. Mater. Interfaces* **2019**, *11*, 27470−27477.

(28) Fantin, M.; Ramakrishna, S. N.; Yan, J.; Yan, W.; Divandari, M.; Spencer, N. D.; Matyjaszewski, K.; Benetti, E. M. The Role of Cu⁰ in Surface-Initiated Atom Transfer Radical Polymerization: Tuning Catalyst Dissolution for Tailoring Polymer Interfaces. *Macromolecules* **2018**, *51*, 6825−6835.

(29) Li, S.; Omi, M.; Cartieri, F.; Konkolewicz, D.; Mao, G.; Gao, H.; Averick, S. E.; Mishina, Y.; Matyjaszewski, K. Cationic Hyperbranched Polymers with Biocompatible Shells for siRNA Delivery. *Biomacromolecules* **2018**, *19*, 3754−3765.

(30) Zhang, K.; Simic, R.; Yan, W.; Spencer, N. D. Creating an Interface: Rendering a Double-Network Hydrogel Lubricious via Spontaneous Delamination. *ACS Appl. Mater. Interfaces* **2019**, *11*, 25427−25435.

(31) Meier, Y. A.; Zhang, K.; Spencer, N. D.; Simic, R. Linking Friction and Surface Properties of Hydrogels Molded Against Materials of Different Surface Energies. *Langmuir* **2019**, *35*, 15805−15812.

(32) Gong, J. P. Friction and Lubrication of Hydrogels-Its Richness and Complexity. *Soft Matter* **2006**, *2*, 544−552.

(33) Chen, M.; Briscoe, W. H.; Armes, S. P.; Klein, J. Lubrication at Physiological Pressures by Polyzwitterionic Brushes. *Science* **2009**, *323*, 1698−1701.

(34) Chen, T.; Ferris, R.; Zhang, J.; Ducker, R.; Zauscher, S. Stimulus-Responsive Polymer Brushes on Surfaces: Transduction Mechanisms and Applications. *Prog. Polym. Sci.* **2010**, *35*, 94−112.

(35) Stuart, M. A. C.; Huck, W. T. S.; Genzer, J.; Müller, M.; Ober, C.; Stamm, M.; Sukhorukov, G. B.; Szleifer, I.; Tsukruk, V. V.; Urban, M.; Winnik, F.; Zauscher, S.; Luzinov, I.; Minko, S. Emerging Applications of Stimuli-Responsive Polymer Materials. *Nat. Mater.* **2010**, *9*, 101−113.

(36) Roy, D.; Brooks, W. L. A.; Sumerlin, B. S. New Directions in Thermoresponsive Polymers. *Chem. Soc. Rev.* **2013**, *42*, 7214−7243.

(37) Sui, X.; Chen, Q.; Hempenius, M. A.; Vancso, G. J. Probing the Collapse Dynamics of Poly(N-isopropylacrylamide) Brushes by AFM: Effects of Co-nonsolvency and Grafting Densities. *Small* **2011**, *7*, 1440−1447.

(38) Ramakrishna, S. N.; Cirelli, M.; Kooij, E. S.; Gunnewiek, M. K.; Benetti, E. M. Amplified Responsiveness of Multilayered Polymer Grafts: Synergy between Brushes and Hydrogels. *Macromolecules* **2015**, *48*, 7106−7116.