

Advanced Surfaces by Anchoring Thin Hydrogel Layers of Functional Polymers

Seidi Farzad, Zhao Wei-Feng, Xiao Hui-Ning, Jin Yong-Can, Saeb Mohammad Reza, Zhao Chang-Sheng

Cite this article as:

Seidi Farzad, Zhao Wei-Feng, Xiao Hui-Ning, Jin Yong-Can, Saeb Mohammad Reza, Zhao Chang-Sheng. Advanced Surfaces by Anchoring Thin Hydrogel Layers of Functional Polymers[J]. *Chinese J. Polym. Sci.*, 2021, 39(1): 14-34. doi: 10.1007/s10118-020-2474-y

View online: <https://doi.org/10.1007/s10118-020-2474-y>

Articles you may be interested in

[Suppression of Cell Adhesion on Polyacrylonitrile-Based Membranes by the Anchoring of Phospholipid Moieties](#)

Chinese J. Polym. Sci. 2006, 24(1): 103

[SELF ASSEMBLY OF ABC TRIBLOCK COPOLYMER THIN FILMS ON A BRUSH-COATED SUBSTRATE](#)

Chinese J. Polym. Sci. 2009, 27(4): 583

[SURFACE FUNCTIONALIZATION OF POLYSTYRENE TO BIND WITH FMRF PEPTIDES FOR NOVEL BIOCOMPATIBILITY](#)

Chinese J. Polym. Sci. 2010, 28(6): 895 <https://doi.org/10.1007/s10118-010-9168-9>

[纳米TiO₂粒子静电吸附引发剂及其原位锚固丙烯酸丁酯聚合](#)

ELECTROSTATIC ABSORPTION OF AZO INITIATOR ONTO TiO₂ PARTICLES AND *in situ* ANCHORING POLYMERIZATION OF BUTYL ACRYLATE FROM MODIFIED TiO₂

高分子学报. 2009(5): 445 <https://doi.org/10.3724/SP.J.1105.2009.00445>

[后官能化工艺制备侧链离子结构的部分氟化阴离子交换膜](#)

Preparation of Partly Fluorinated Anion Exchange Membranes with Side Chain Ionic Groups *via* a Post-functionalization Process

高分子学报. 2017(12): 1974 <https://doi.org/10.11777/j.issn1000-3304.2017.17059>

[有机薄膜光伏电池印刷制备与原位形貌检测](#)

Printing and *in situ* Morphology Detection of Organic Thin Film Photovoltaic Devices

高分子学报. 2019, 50(4): 352 <https://doi.org/10.11777/j.issn1000-3304.2019.19010>

Advanced Surfaces by Anchoring Thin Hydrogel Layers of Functional Polymers

Farzad Seidi^{a*}, Wei-Feng Zhao^b, Hui-Ning Xiao^{c*}, Yong-Can Jin^a, Mohammad Reza Saeb^d, and Chang-Sheng Zhao^{b*}

^a Provincial Key Lab of Pulp & Paper Sci and Tech, and Joint International Research Lab of Lignocellulosic Functional Materials, Nanjing Forestry University, Nanjing 210037, China

^b College of Polymer Science and Engineering, State Key Laboratory of Polymer Materials Engineering, Sichuan University, Chengdu 610065, China

^c Department of Chemical Engineering, University of New Brunswick, Fredericton, NB, E3B 5A3 Canada

^d Department of Resin and Additives, Institute for Color Science and Technology, 16765-654, Tehran, Iran

Abstract Surface design and engineering is a critical tool to improve the interaction of materials with their surroundings. Immobilization of soft hydrogels is one of the attractive strategies to achieve surface modification. The goal of this review is to provide a comprehensive overview of the different strategies used for surface tethering of hydrogel layers via crosslinking immobilization of pre-fabricated functional polymers. In this strategy, crosslinkable polymers are first prepared via various polymerization techniques or post-functionalization of polymers. Afterwards, the crosslinkable polymers are attached or tethered on the surfaces of substrates using a variety of approaches including photo-crosslinking, click reactions, reversible linkages, etc. For each case, the principles of hydrogel tethering have been explained in detail with representative examples. Moreover, the potential applications of the as-modified substrates in specific cases have also been addressed and overviewed.

Keywords Surface-anchoring; Polymerization; Thin hydrogel film; Immobilization; Post-functionalization

Citation: Seidi, F.; Zhao, W. F.; Xiao, H. N.; Jin, Y. C.; Saeb, M. R.; Zhao, C. S. Advanced surfaces by anchoring thin hydrogel layers of functional polymers. *Chinese J. Polym. Sci.* 2021, 39, 14–34.

INTRODUCTION

Performance of the materials is highly dependent on the surface characteristics because the surface has direct contact with the media. Virgin surfaces do not have satisfactory properties for many applications and faced undesired issues including fouling,^[1] corrosion,^[2] friction,^[3] and fogging.^[4] Therefore, the engineering of surfaces has been used extensively to improve their properties. Hydrogels as the most well-known soft materials are very promising for modification of the surfaces of various substrates. The soft structure of hydrogels in aqueous medium makes them excellent candidates in biomedical applications.^[5–8] One of the straightforward methods for immobilization of thin hydrogel layers on the surface of substrates is the fabrication of functional hydrophilic polymers and subsequent crosslinkings on the surfaces.

In this strategy, it is essential to synthesize functional and crosslinkable polymers using various polymerization techniques. Alternatively, commercially available (bio)polymers are modified first, followed by the crosslinking for their teth-

ering on substrate surfaces. The as-fabricated polymers must contain some crosslinkable groups such as benzophenone-moieties for photo-crosslinking, carbene/nitrene-precursors for photo/thermal crosslinking, thiol and/or ene-groups for thiol-ene click crosslinking, trialkoxysilane-units for siloxane-based crosslinking, catechol-units for bioinspired crosslinking and so on. Presented in the current review are the key features and main influencing factors in each strategy above in terms of the type of reaction. The effects of thin polymer hydrogel layers on the performance of surfaces are discussed in detail. Moreover, the potential applications of as-modified substrates are also described briefly added to provide an insight into the practical importance of the advanced surfaces anchored with the thin layers of polymer hydrogels.

PHOTO-CROSSLINKING USING BENZOPHENONE (BPH) UNITS

Moieties based on benzophenone (BPh) units are the most well-known photosensitizers widely used for surface photografting of pre-fabricated polymers. In this strategy, BPh units are covalently conjugated to the polymer backbones, substrate surfaces or both. By coating the surface with polymer solutions and exposing to UV-irradiation, radicals are generated by BPh units via H-abstraction from the substrate surface and

* Corresponding authors, E-mail: f_seidi@njfu.edu.cn (F.S.)

E-mail: hxiao@unb.ca (H.N.X.)

E-mail: zhaochsh70@scu.edu.cn (C.S.Z.)

Received June 3, 2020; Accepted June 24, 2020; Published online August 21, 2020

from the polymer chains. Radical-radical coupling creates C—C crosslinking points among polymer chains and also between the polymer chains with substrate surface. Since the surfaces of inorganic substrates (Au, Si, stainless steel,...) do not contain C—H groups, therefore, it is necessary that such surfaces are pre-modified either with BPh units or with other organic molecules bearing C—H bonds to enable them to participate in covalent attachment reactions.

The crosslinking density and the interface bonding strength are controlled by tuning the content of BPh units in polymer chains. Higher content of BPh units increases hydrogel toughness and creates more robust interfacial bonding between the hydrogel layer and surface of the substrate. However, high crosslinking density reduces the swelling and flexibility of tethered hydrogel layers. Moreover, the high content of BPh, due to its hydrophobic structure, not only further reduces the swelling but also increases the biofouling, thus negatively influencing the potential biomedical applications of hybrid materials. Another key factor that affects the thickness of the hydrogel layer is the condition of casting the polymer solution on the substrate surface. Polymer concentration is one of the most important factors in manipulating the thickness of hydrogel layers. Also, coating performance is affected by the hydrophilicity of surfaces. For instance, the coating of the aqueous solutions of photocrosslinkable polymers on hydrophilic surfaces tends to produce thicker layers than on hydrophobic ones. Therefore, pre-hydrophilization of surface with self-assembled monolayers (SAMs) of hydrophilic small molecules can enhance the attachment between the surface and hydrogel layer.

In one report, BPh moieties were inserted both in the polymer structure and on the substrate surface to increase attachment opportunities (Fig. 1).^[9] A series of water-soluble P(DMAAm-co-MaBPh) copolymers (DMAAm = *N,N*-dimethylacrylamide, MaBPh = 4-methacryloyloxybenzophenone) containing 0 mol%–14 mol% MaBPh were used for immobilization of hydrogels with dry thickness 100 nm on the surface of BPh-functionalized LaSFN9 prism by UV-irradiation. Since in this strategy, BPh is present both in polymer and on the substrate surface, therefore many crosslinking points can be created between polymer chains, thus leading to the thicker layers,

compared with the case in which the BPh is available only on the substrate surface.

Similarly, copolymers of *N*-alkylacrylamide monomers with 2 mol% MaBPh were used for attachment of thin hydrogels on the surface of BPh-modified glass slide or Si wafer (Fig. 1).^[10] The *N*-alkylacrylamide monomers were including *N*-methylacrylamide (MAAm), *N*-ethylacrylamide (EAAM), DMAAm, *N*-propylacrylamide (PAAm), *N,N*-diethylacrylamide (DEAAM), and *N*-butylacrylamide (BAAm). The dry thickness of the inserted layers was in the range of 200–400 nm and increased by swelling in water. The ratio of wet/dry thickness was higher for monomers with shorter alkyl chains so that for hydrogels made of MAAm and EAAM it was 5 and for DMAAM it decreased to 3.5 whereas hydrogels with longer alkyl chains showed slight swelling. Later, the swelling ratio of these surface anchored hydrogels in the presence of moist air as a function of humidity percent was determined using optical waveguide spectroscopy.^[11] By increasing the humidity, the swelling was increased. The dry film thickness of P(DMAAm-co-MaBPh) hydrogels was adjusted in the range of 49–716 nm by adapting the spin-coating conditions. The thickness was increased to reach 65–974 nm by increasing the humidity to 92%. The response of the hydrogels to the moisture and the ratio of the wet/dry thickness were almost independent of the thickness. The water swelling behavior of the hydrogels was highly affected by the MaBPh content. Higher content of MaBPh decreased the hydrophilicity of the hydrogel and increased the crosslinking density, which in turn lowered the swelling. The dry thickness for hydrogels with 1 mol%, 2.5 mol%, and 10 mol% of MaBPh was 649, 716, and 475 nm which increased, respectively, to 882, 952, and 561 nm at 92% of humidity. These types of hydrogel materials act like a surface lubricant and the lubrication mechanism was explained in detail by Li *et al.*^[12]

Steinbach *et al.* used poly(ethyl ethylene phosphate)s (PEEP) as new types of degradable hydrophilic polymers^[13] for hydrogel formation on the surface of BPh-modified Si wafers (Fig. 2).^[14] First, copolymerizations of cyclic phosphates including 2-pentyloxy-2-oxo-1,3,2-dioxaphospholane (PEP), 2-(2-ethylbutoxy)-2-oxo-1,3,2-dioxaphospholane (EBP), 2-(2-(furan-2-ylmethoxy)ethoxy)-2-oxo-1,3,2-dioxaphospho-

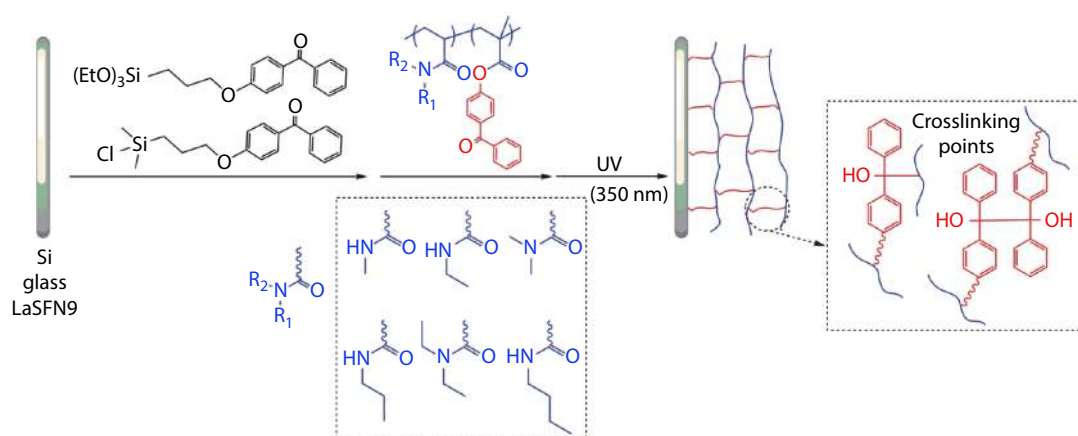


Fig. 1 Immobilization of polyacrylamide-based hydrogel layers on the surface of the solid substrate via the introduction of benzophenone photosensitizers on the surface of substrate and on the backbone of hydrogel precursor.^[9–12]

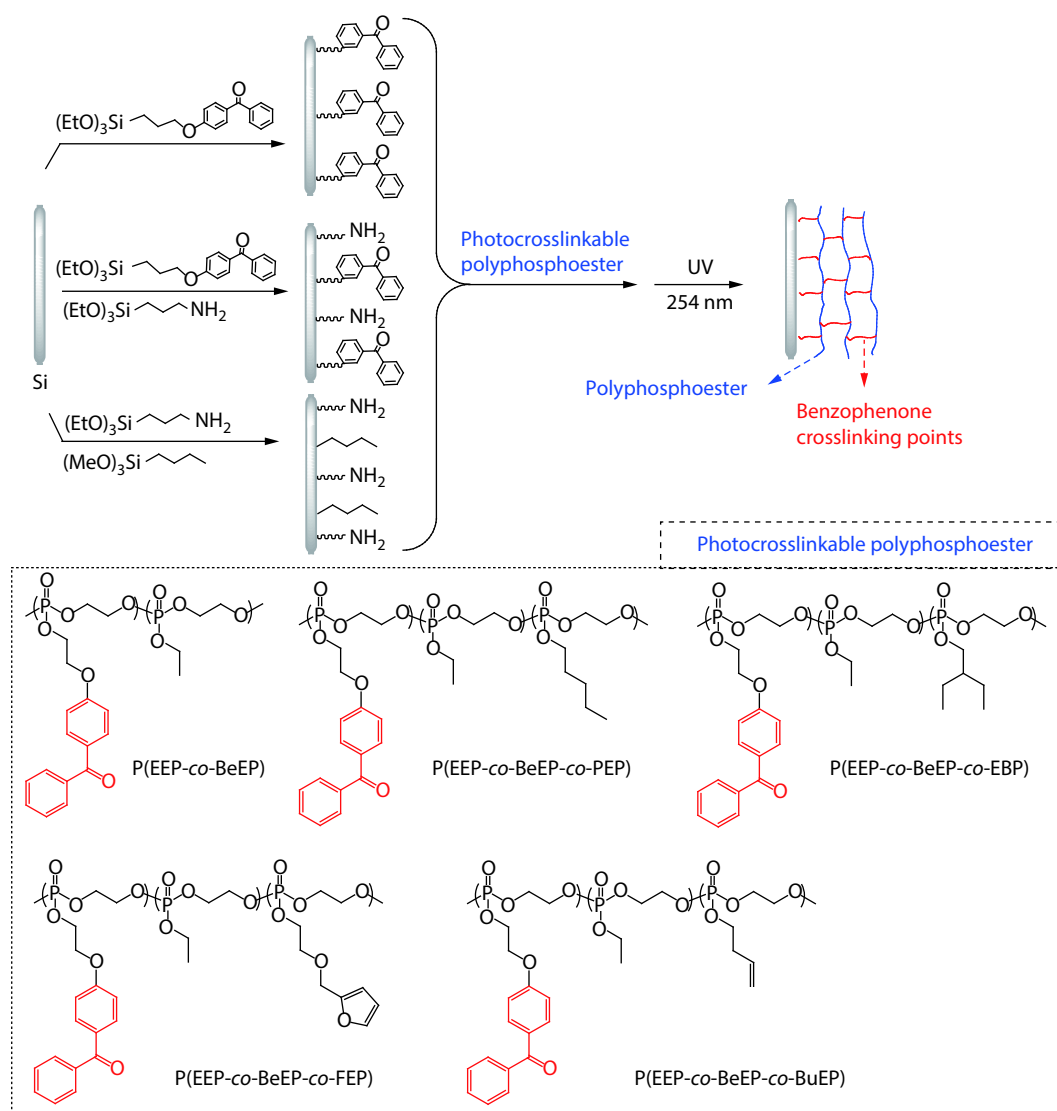


Fig. 2 Covalent attachment of polyphosphoester-based hydrogels on the surface of Si wafer.^[14]

lane (FuEP), 2-(2-(benzophenone-4-oxy)ethoxy)-2-oxo-1,3,2-dioxaphospholane (BeEP), and 2-(but-3-en-1-yloxy)-2-oxo-1,3,2-dioxaphospholane (BuEP) by ring-opening polymerization were performed to prepare P(EEP-co-BeEP), P(EEP-co-BeEP-co-PEP), P(EEP-co-BeEP-co-EBP), P(EEP-co-BeEP-co-FuEP), and P(EEP-co-BeEP-co-BuEP) copolymers. In all copolymers, the content of EEP was high (85 mol%–95 mol%) to maintain the hydrophilicity of the polymers. Surface of Si wafer was functionalized with pure 3-ethoxybenzophenone silane (3EBP), mixed 3EBP/3-aminopropyltriethoxysilane (APTES), or mixed APTES/trimethoxypropylsilane (PTMS) to immobilize amine, alkyl and BPh groups on the substrate surface. Crosslinking and photo-immobilization of the obtained polyphosphoesters was highly affected by several factors: (i) Treatment of Si wafer with pure 3EBP increased the surface hydrophobicity which caused the dewetting of hydrophilic polyphosphoesters. Therefore, surfaces modified with a 1/1 ratio of mixed 3EBP/APTES had higher hydrophilicity and facilitated the coating with hydrophilic polymers. (ii) No attach-

ment was obtained from P(EEP-co-BeEP-co-EBP) and P(EEP-co-BeEP) copolymers whereas P(EEP-co-BeEP-co-PEP), and P(EEP-co-BeEP-co-FuEP) generated hydrogel layers with the thicknesses of 78 and 164 nm, respectively. (iii) For covalent attachment of the polyphosphoester, the presence of BPh on the Si surface was not necessary and polyphosphoester could attach to the APTES/PTMS-modified Si surface. Indeed, the incorporated BPh units in the polymer chain structures were enough to exhibit a dual function of crosslinking and surface attachment. The thickness of the hydrogel layer was affected by the ratio of APTES/PTMS. Silicon surfaces with higher amino content were more hydrophilic, therefore immobilization of hydrophilic polyphosphoesters was easier and thicker layers were generated. By using Si surfaces modified with 1:1 molar ratio of APTES/PTMS, the thicknesses of P(EEP-co-BeEP-co-PEP), P(EEP-co-BeEP-co-FuEP) and P(EEP-co-BeEP-co-BuEP) layers were 104, 199, and 263 nm, respectively. Moreover, the static contact angle and roughness (RMS) of the surfaces were 21°–26° and 0.40–0.68 nm, respectively, which reveal very

smooth surfaces with high hydrophilicity.

Mixtures of a random terpolymer of P(DMAAm-co-MaBPh-co-SSNa) with biomolecules (DNA, oligonucleotides, and proteins) were used for one-step surface modification of various substrates including polystyrene (PS), cyclic olefin polymer (COP-01), polycarbonate (PC), Nexterion glass slides, polymethylmethacrylate (PMMA) and polypropylene (PP) via UV-irradiation (Fig. 3a).^[15] The immobilized hydrogel layer containing biopolymers could act as a microarray for the analytical detection of proteins and other biopolymers. Similarly, solution mixtures of photocrosslinkable copolymers, including P(DMAAm-co-MaBPh), P(DMAAm-co-MaBPh-co-GMA), and P(DMAAm-co-MaBPh-co-VPA) and a protein antibody (anti-BSA), were cast on the surface of PMMA substrates (Fig. 3b) and upon UV-irradiation turned into hydrogels to make a microarray structure for protein detection experiments.^[16] The density of the present antibodies on the substrate surface was controlled by adjusting the antibody:polymer feed ratio. In this way, antibody-containing hydrogel layers with a thickness of 15–55 nm were fabricated on the surface of the PMMA substrate. Due to the antifouling characteristic of the PDMAAm, non-specific protein adsorption was strongly prevented. On the other hand, protein adsorption is possible only for specific antibody-antigen interaction which results in very high signal-to-background ratios. Furthermore, the response can be tuned via adjusting the feed concentrations of P(DMAAm-co-MaBPh) photopolymer and antibody during the formation of the hydrogel layer.

Buller *et al.* used the copolymers of 2-(4-benzoylphenoxy)-ethyl methacrylate (BPEM) with oligo(ethylene glycol) methyl ether methacrylate (OEGMEMA) and di(ethylene glycol)methyl ether methacrylate (MEO₂MA) for thin film formation on the surface of APTES-modified Si wafer upon UV-irradiation (Fig. 3c).^[17] Copolymers without MEO₂MA did not show the lower critical solution temperature (LCST) whereas the ones prepared with MEO₂MA:OEGMEMA molar ratios in the range of 100:0 to 67:33 showed the cloud points of 22–57 °C. These water-soluble thermosensitive copolymers contained 0.1 mol%–1.3 mol% BPEM as a photo-crosslinker segment. The effect of BPEM content per each polymer chain was studied in detail based on the gel content and efficiency of the film formation. By changing the copolymerization condition, copolymers with M_n 49–292 kg/mol bearing 0.3–3.4 units of BPEM per each polymer chain were produced. The efficiency of the network formation was studied by comparing film thickness before and after UV-irradiation. In copolymers with BPEM unit ≤ 1 per each polymer chain, a poor crosslinking efficiency was reported. Under the best conditions, every BPEM unit can create one covalent bond with another chain, therefore, the minimum amount of the required benzophenone moieties to crosslink all polymer chains together is 1.^[18] Therefore, the thicknesses of the P(OEGMEMA-co-BPEM) bearing 0.1 and 1.0 BPEM units per each polymer chain were decreased to 32% and 85% of the initial spin-coated thickness after UV-irradiation. Additionally, in samples that BPEM units per each polymer chain were lower than 1, the efficiency of crosslinking was improved by increasing the molecular weight (MW) of the polymers. Indeed, without changing the

total content of BPEM only by increasing the polymer MW, it was possible to incorporate at least one PBEM in each polymer chain. The wet/dry thickness ratio of immobilized P(OEGMEMA-co-BPEM) films decreased from 20 to 4.5 by increasing the BPEM content from 0.1 mol% to 1 mol% due to the higher crosslinking. Additionally, for the thermosensitive P(OEGMEMA-co-MEO₂MA-co-BPEM) hydrogels, the wet thickness was a function of temperature so that for the one with cloud point 35 °C the wet thickness decreased from 200 nm at 20 °C to 75 nm at 65 °C. Similarly, a pH- and thermosensitive hydrogel layer was immobilized on the 3-(trimethoxysilyl)propyl acrylate (TMSPA)-functionalized glass surface using a terpolymer composed of benzophenone acrylamide (BPAm): NIPAm:AA under UV-irradiation (Fig. 3d).^[19] Due to the thermo-sensitivity of the hydrogel, the wet/dry swelling ratio was decreased from 2.5 at 23 °C to 1.1 at 50 °C. Also, a higher energy dose upon irradiation created denser structures so that the swelling ratio was decreased from 2.5 to 1.8 by increasing the energy dose from 2.5 J/cm² to 50 J/cm². Moreover, after the surface casting of the terpolymer, a two-step UV-irradiation process was applied to obtain hydrogel patterns with different crosslinking zones: (i) UV irradiation of the casted terpolymer film in the presence of photomasks, (ii) removing the photomasks and continuing the UV-irradiation. The areas covered with photomask had been exposed to UV less than the uncovered areas. Therefore, patterns with two different crosslinking zones and different swelling behaviours were prepared.

Photocrosslinkable P(HPA-co-BPAm) copolymers were prepared by reversible addition-fragmentation chain transfer polymerization (RAFT) of BPAm with *N*-(2-hydroxypropyl)acrylamide (HPA).^[20] By increasing the BPAm content, the hydrophilicity was decreased so that the copolymer containing 10 mol% BPAm was not water-soluble. The casting of an ethanolic solution of P(HPA-co-BPAm) on the surface of APTES-modified Si wafer and UV irradiation induced hydrogel formation (Fig. 3e). Monitoring of the UV spectrum of the hydrogel during the irradiation process showed that after 4 s, the intensity of the peak related to the benzophenone is decreased significantly indicating a short time is enough for hydrogel formation. Moreover, the thickness of the coated layer before and after UV-irradiation remained almost constant, which revealed high gel content of the process. The immobilized layer was highly stable and its dry thickness remained constant after incubation in phosphate buffer saline (PBS) for 24 h. Interestingly, regardless of the BPAm content the contact angle of all hydrogels was 46° whereas the wet/dry swelling ratio was 6.4, 2.0 and 1.7 for hydrogels containing 1 mol%, 5 mol% and 10 mol% of BPAm. No fetal bovine serum adsorption was detected on the surface of hydrogels, which reveal the ultra-low fouling characteristics.

CROSSLINKING VIA CARBENE GENERATION

Carbene is another type of active groups that have been used for surface tethering of hydrogels. Carbenes are generated by (1) α -elimination of HX or X₂ from an organic halide, or (2) α -elimination of N₂ from diazo-compounds upon $h\nu$ or heat treatment.^[22] Practically, the carbene formation from diazo-

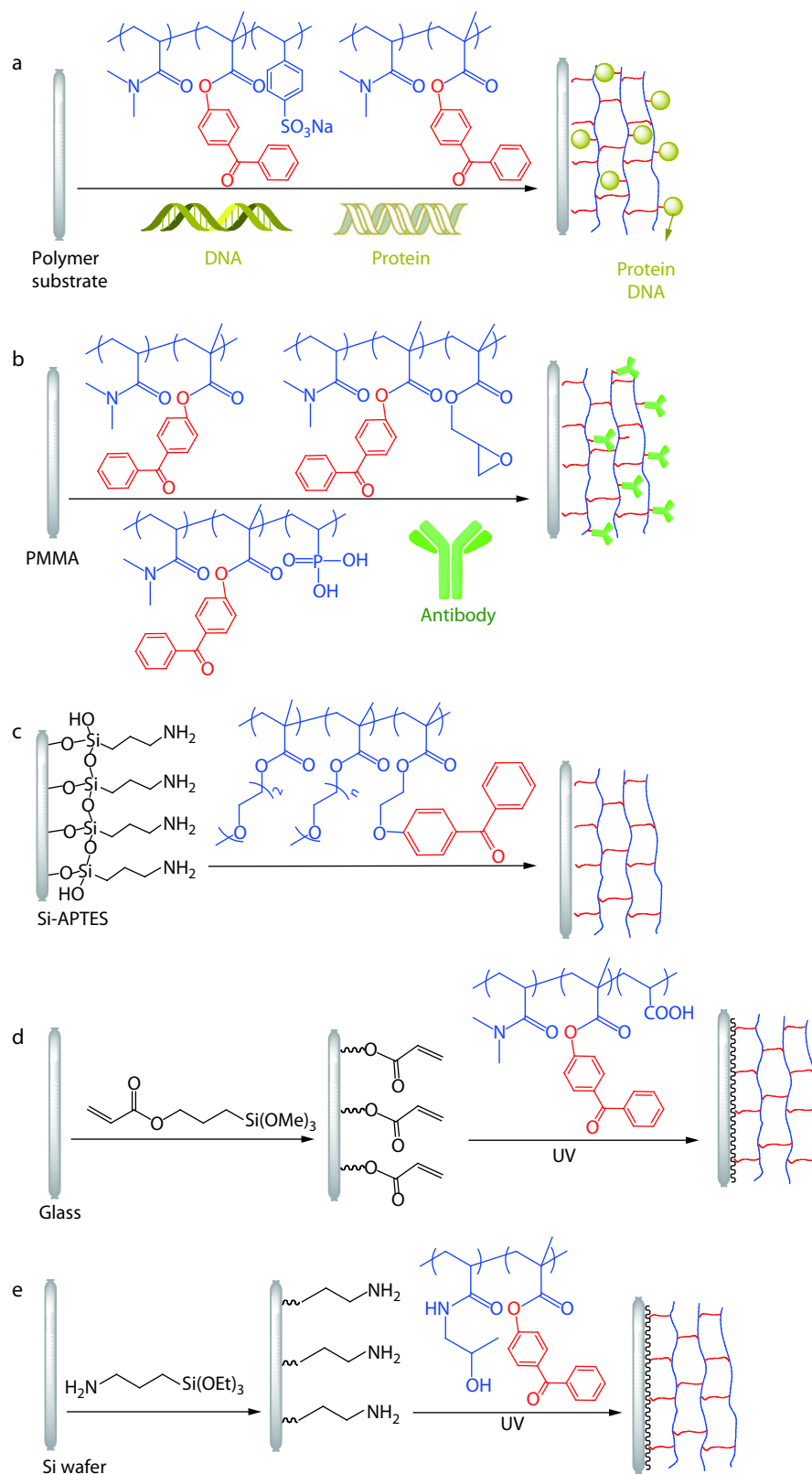


Fig. 3 Benzophenone-mediated attachment of (a) DNA/protein-containing polyacrylamide hydrogel on the surface of polymeric substrates,^[15,21] (b) antibody-containing polyacrylamide hydrogel on the surface of PMMA,^[16] and (c) thermosensitive hydrogels on the surface of Si wafer^[17] substrates, (d) P(NIPAm-co-AA-co-BPAm) hydrogels on the glass surface,^[19] and (e) P(HPA-co-BPAm) hydrogels on the glass/SiO₂ surfaces.^[20]

compounds is safe and has been only such a type used for the surface tethering of hydrogel films. Conjugated diazo compounds produce carbenes in milder conditions such as lower temperatures or higher UV wavelengths. Since carbenes are very reactive and unstable intermediates, instantly after generation involve in several reactions including insertion into single bonds (including C—H, N—H, O—H), addition to double bonds (such as C=C to create cyclopropane ring), and also rearrangement reactions. In the formation of hydrogel layers, C—H insertion reaction by carbenes is the most important one since C—H is the most available linkage in polymers. Like the BPh-strategy, surfaces without C—H bonds are required to be first modified with SAMs of small molecules containing C—H linkages to enable the surface for C—H insertion reactions.

In one report in 2013, carbene-crosslinked hydrogel layers were attached on the Si surface in a multistep process.^[23] Surface of Si wafer was first modified by a chlorosilane derivative of *N*-Boc (*tert*-butoxycarbonyl) protected tyrosine methyl ester (Fig. 4a). In parallel, hydrophilic copolymers of AA, DMAAm, NIPAm, and SSNa with methacrylate derivative of *N*-Boc protected tyrosine methyl ester (Fig. 4) containing 1 mol%–5 mol% of tyrosine were produced. The MW of copolymers was in the range of 1.0×10^5 – 3.0×10^5 g/mol indicating the presence of 10–50 tyrosine units per each polymer chain. This amount of crosslinking points is more than enough to create stable hydrogels. Diazotization of *N*-Boc protected tyrosine methyl ester units on the Si surface and in the backbone of copolymers was performed *via* the hydrolytic removal

of Boc groups and deprotecting primary amino groups with isoamyl nitrite. Casting of copolymers on the surface of modified Si wafer and heating at 80–180 °C (or irradiation at 250 or 365 nm) generated surface-attached hydrogels. Heating or irradiation produced carbene *via* the elimination of N₂ from diazo-groups on the Si surface and polymer structures. The generated carbenes can insert into C—H, O—H, and N—H linkages *via* direct and indirect mechanisms (Fig. 5a).^[24] In the indirect mechanism, carbene first undergoes the Wolff rearrangement to produce the ketene derivative which subsequently reacts with available nucleophiles in the surrounding medium such as hydroxyl and amino groups. On the other hand, direct insertion can occur especially with C—H linkages.

By studying the effect of temperature on the crosslinking behavior using a copolymer of NIPAm and tyrosine-based monomer it was observed that at 100 °C, very low gel content was obtained meaning that carbene formation was failed at this temperature. However, at $T > 120$ °C in 10 min gel content reached 100%. On the other hand, hydrogel formation and crosslinking *via* irradiation showed carbene generation can occur only at 250 nm but not at 365 nm. The thickness of the hydrogel layer could be controlled up to 100 nm *via* adjusting the spin-coating conditions. Similarly, the surface of Si wafer was modified by silanization with methyl 2-(4-(3-(chlorodimethylsilyl)propoxy)phenyl)acetate (PhAc-DMS) and then was tethered by a hydrogel layer of PDMAAm-based hydrophilic copolymers bearing diazo ester groups (poly-

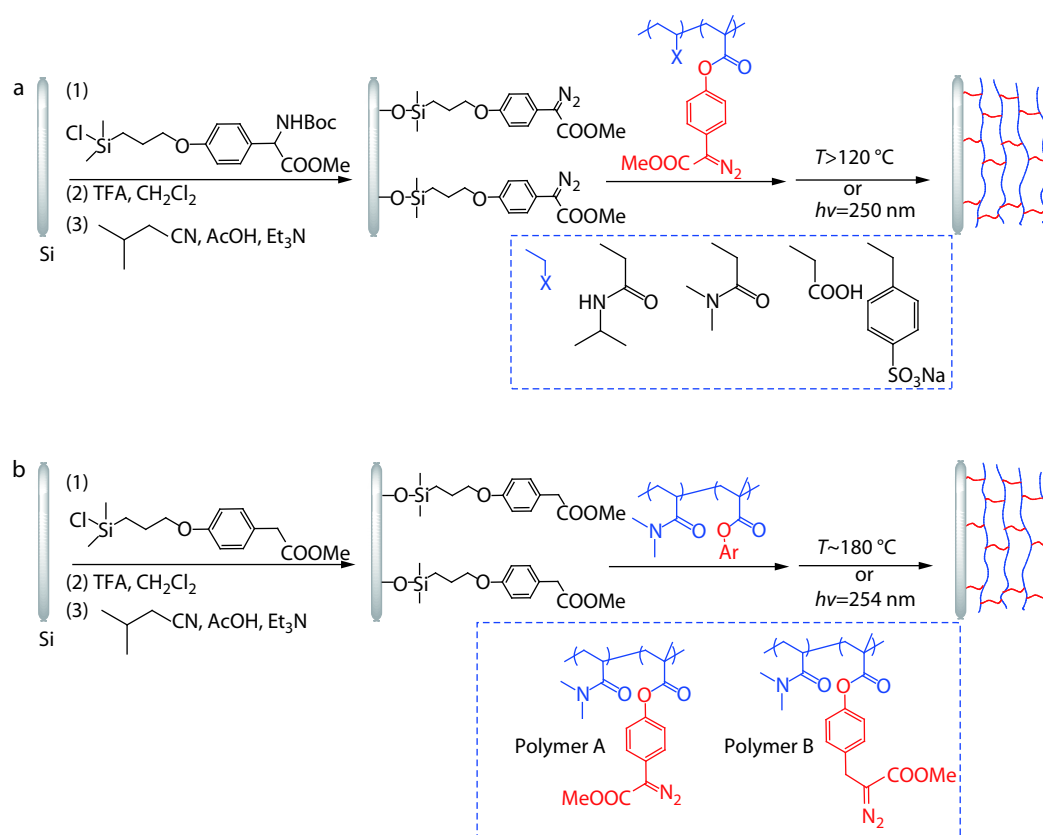


Fig. 4 General method for immobilization of hydrogel layers on the Si wafer surface by carbene formation (a),^[23] and (b).^[25]

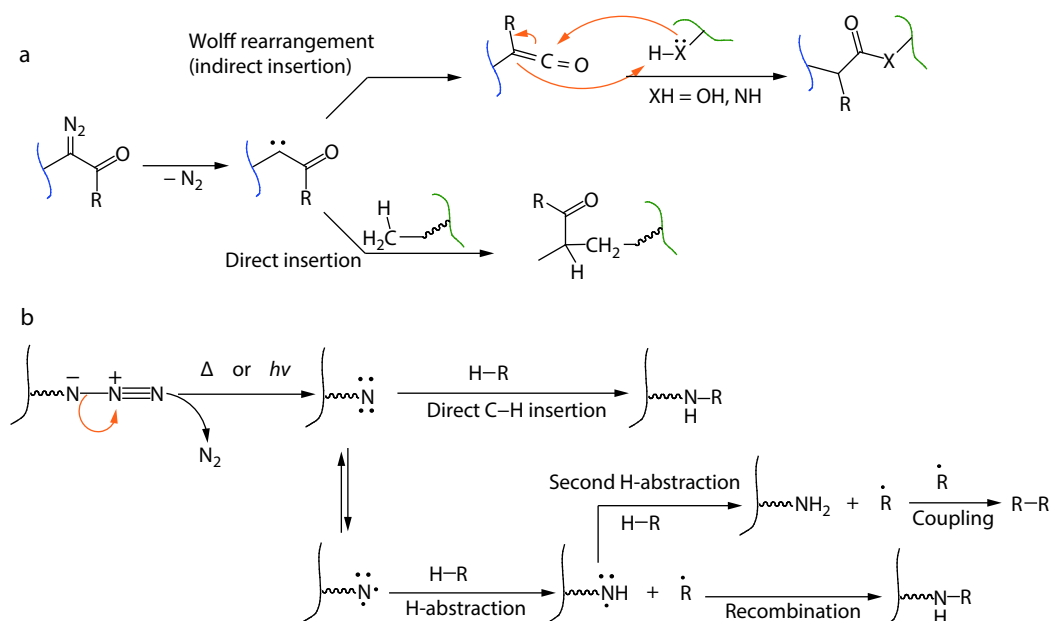


Fig. 5 (a) Mechanisms of direct and indirect carbene insertion into C—H, N—H, and O—H bonds,^[24] (b) thermolysis or photolysis of azides for nitrene generation and subsequent possible reactions of nitrene for the formation of new covalent bonds.^[26,27]

mers A and B in Fig. 4b).^[25] Casting of polymers on the surface of modified Si wafer and subsequent heat or UV-treatment induced covalent surface attachment of the polymers via carbene generation. The generated carbene groups undergo C—H insertion from neighbouring polymer chains or from surface inserted PhAc groups. Without Si functionalization with PhAc-DMS units, no polymer attachment was observed. By irradiation at 254 nm, after 10 min complete crosslinking and attachment of the inserted layers were obtained. However, irradiation at 360 nm needed longer gelation time and the behavior of crosslinkable copolymers was completely different. In this wavelength, polymer A (Fig. 4b) required 2 h for complete disappearance of diazo bond in the FTIR spectrum whereas no change in the intensity of the diazo peak was observed for polymer B (Fig. 4b). It shows that diazo group in polymer A which is conjugated directly with phenyl ring is more reactive toward UV-treatment. Despite photo-treatment, in thermal treatment the behaviours of copolymers were similar. Heating at 180 °C induced attachment of the polymers onto the Si surface in 30 min whereas at lower temperature yield of gelation decreased drastically. At 120 °C, after 2 h gel content remained below 30%–40%.

CROSSLINKING VIA NITRENE GENERATION

Nitrenes as another type of alternative reactive intermediate have been used extensively for surface tethering of polymers. Generally, nitrenes can be produced as reactive intermediates from photolysis or thermolysis of isocyanates and azides via elimination of CO or N_2 byproducts.^[28,29] However, since isocyanate is very reactive toward moisture and other nucleophiles, practically nitrene generation from azides is the most well-known method in polymer chemistry. For covalently tethering polymers to the surfaces, there are many reports

related to the nitrene generation from sulphonyl azides^[30,31] and perfluorophenyl azides (PFPA),^[32–36] however, only a few of these reports are related to the tethering of hydrophilic layers. It has been shown that sulphonyl azides^[26,27] and PFPA^[37,38] undergo degradation upon heating to produce nitrenes. The overall procedures for nitrene formation from azides and subsequent reactions are depicted in Fig. 5(b). Same as BPh and carbene, each nitrene in the ideal condition can create only one crosslinking point; therefore, polymers are required to have at least one nitrene precursor per each polymer chain to create a stable hydrogel. However, it is also possible to graft an ultra-thin layer of polymers bearing no nitrene precursors on the surfaces pre-modified with a SAM of nitrene precursors. In this case, there are only covalent attachment points between the surface with polymer chains without crosslinking between polymer chains. Therefore, the thickness of the tethered layer is strongly controlled by polymer chain length or MW. Higher MWs produce thicker layers. Also, the immobilization of nitrene precursors on the surface increases the adhesion of hydrogel layer to the surface through the generation of more interfacial covalent bonds. Moreover, multilayer hydrogels can be produced by repeating the tethering process with various types of polymers bearing nitrene precursors.^[30] Thickness, hydrophilicity, and functionalities of each layer can be tuned individually. In this strategy, due to the strong characteristic band of azide groups at 2100–2200 cm^{-1} in FTIR spectrum, the reaction can be monitored by following the disappearance of azide band.

Schuh *et al.* immobilized hydrogel layers composed of PDMAAm, PMAA, PAA, and PSSNa containing sulphonyl azide moieties on the surface of octadecyltrichlorosilane (OTS)-modified Si wafer (Fig. 6a).^[39] To generate nitrene on the backbone of polymers, 4-styrenesulphonyl azide (SSAz), as nitrene precursor, was radically copolymerized with DMAAm, MAA, AA, and SSNa. By heating the casted layers of polymers

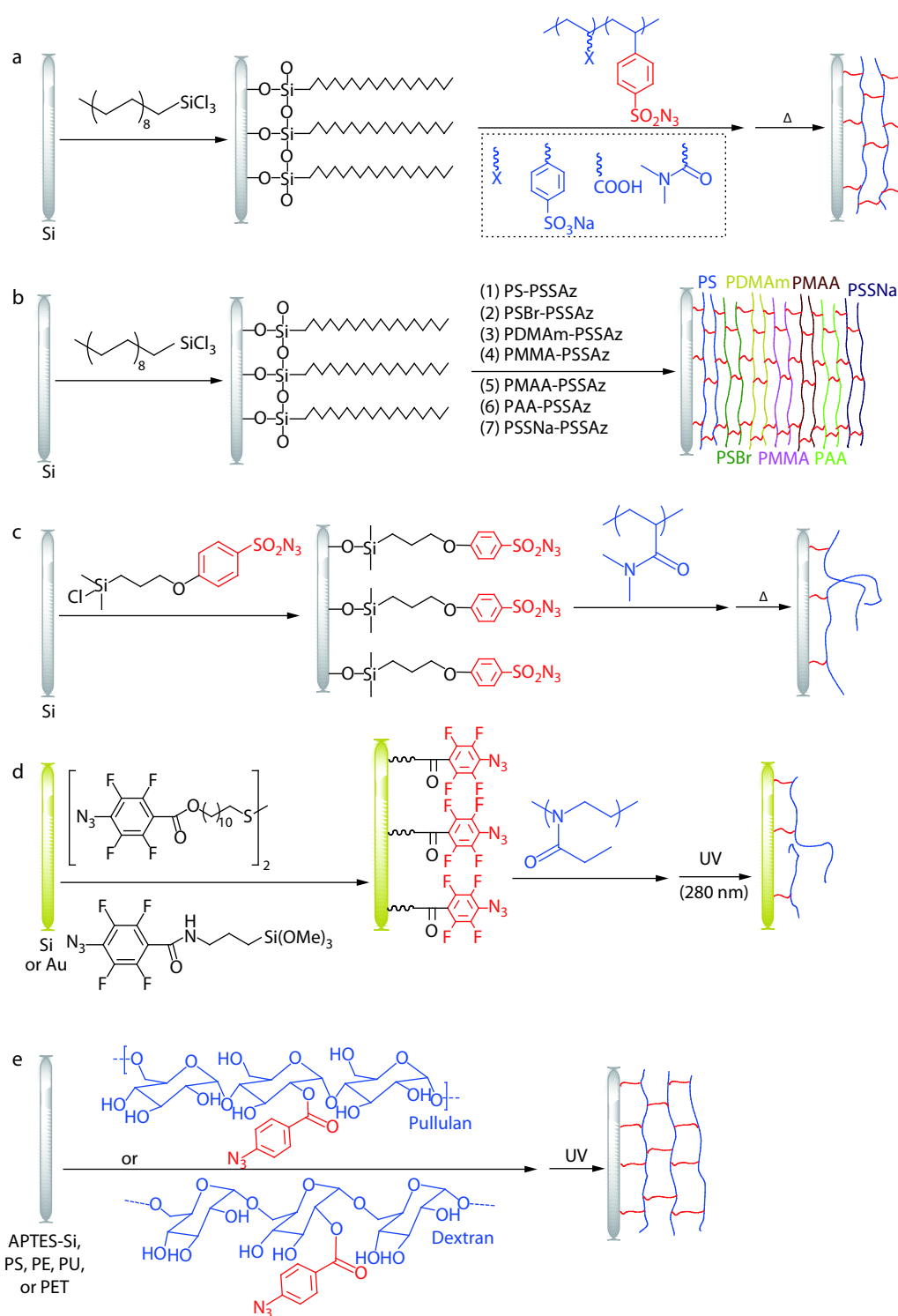


Fig. 6 (a) Immobilization of hydrogel layer on the surface of OTS-Si substrate using hydrophilic polymers containing sulfonamide moieties.^[39] (b) Layer-by-layer immobilization of hydrophilic and hydrophobic crosslinkable sulfonamide-containing polymers on the surface of OTS-Si wafer.^[30] Surface modification of substrates with (c) sulfonamide^[31] and (d) perfluorophenyl azide (PFPA)^[36,40] groups for tethering of monolayer films of hydrophilic polymers. (e) Tethering of pullulan,^[41] dextran^[42,43] based-hydrogels on the surface of Si wafer and polymeric membranes.

on the surface of OTS-Si at 140–170 °C, azide decomposition and nitrene production were completed in 1 h, and hydrogel layers with gel content of 95%–100% were produced via

C–H inserting methods. Immobilization of polymeric networks from copolymers containing the sulfonyl azide groups on the surface of OTS-modified Si wafer was later ex-

tended for controlled surface attachment of multilayers with various compositions.^[30] Indeed, after crosslinking and attachment of the first layer, the process repeated for inserting another network layer with another batch of crosslinkable polymer. The thickness of each layer was controlled by changing the polymer concentration for spin-coating. There was no limitation for the number of deposited crosslinked layers, their thickness, and their compositions. By sequential deposition and crosslinking of hydrophobic and hydrophilic polymers it was possible to generate AB-multilayer networks of hydrophilic-hydrophilic, hydrophobic-hydrophobic, and hydrophobic-hydrophilic with desired thickness. By this way, a seven-layer network composed of PS, poly(4-bromostyrene) (PSBr), PDMAAm, PMMA, PMAA, PAA, and PSSNa (each polymer contained 2 mol%–5 mol% SSAz) was immobilized on the surface of Si wafer *via* sequential tethering of each layer (Fig. 6b).

In another alternative way, the sulphonyl azide groups were immobilized directly on the Si surface and used for attachment to the polymers *via* thermal treatment (Fig. 6c).^[31] 4-(3-Chlorodimethylsilyl)propyloxybenzenesulphonyl azide derivative as a nitrene precursor was immobilized on the surface of Si wafer. The casting of the modified Si with PDMAAm and heating to higher than 120 °C tethered a monolayer film on the Si surface. The attached layer was highly stable so that after extensive Soxhlet extraction with ethanol it remained stable. By using PS (instead of PDMAAm) as a control sample it was revealed that the thickness is a function of time, temperature and polymer MW. At higher temperatures, thicker films are achieved at shorter time; for instance, after 2 h heating at 120, 140, and 180 °C the thickness of the immobilized layer reached 2, 6, and 10 nm, respectively. Moreover, by increasing the MW, the thickness increased continually. Heating at 160 °C for 2 h using PS samples with MW of 3.0×10^4 and 3.0×10^6 g/mol resulted in the thicknesses of 1 and 12 nm, respectively.

In two similar reports, poly(2-ethyl-2-oxazoline) (PEOX) was tethered on the surface of perfluorophenyl azide (PFPA)-functionalized Si or Au substrates to improve the antifouling properties (Fig. 6d).^[36,40] Surfaces of Si and Au were first pre-treated with *N*-(3-trimethoxysilylpropyl)-4-azido-2,3,5,6-tetrafluorobenzamide (PFPA-silane) and 11,11'-disulfanediylbis(undecane-11,1-diyl)-bis(4-azido-2,3,5,6-tetrafluorobenzoate) (PFPA-disulfide), respectively. Spin-coating of a chloroform solution of PEOX on the surface of PFPA-functionalized substrate and exposing to UV light at 280 nm lead to the covalent tethering of a monolayer of PEOX. Upon UV-irradiation, nitrenes are produced which in turn attached to the PEOX chains *via* C–H insertion into the neighbouring polymer chains. Since the nitrene groups are available only on the substrate surfaces, therefore, the reaction and conjugation of nitrenes with the polymer chains mainly occur on the polymer-substrate interfaces without many crosslinking bonds between polymer chains. Accordingly, increasing the polymer concentration for spin-coating and increasing the time of the UV curing have no benefit for increasing the film thickness. However, the film thickness is a function of R_g of the polymer, which means polymers with higher molecular

weights create thicker layers. By increasing the thickness of PEOX layer the adsorption of bovine serum albumin (BSA) was decreased, which implies the improvement of the anti-fouling properties.

Photo-crosslinkable azidoaryl-derivative of pullulan was used for surface functionalization of PS, PE, and APTES-modified glass slides (Fig. 6e).^[41] Casting of an aqueous solution of azidophenyl-pullulan and exposing to the UV-irradiation with or without a photomask lead to the attachment of a continuous or micropattern hydrogel layer. PS and PE were used directly whereas the glass was pre-treated with APTES to create some C–H linkages on the glass surface. Adhesion of RAW264 macrophages cells to the micropatterned surfaces showed locations with the pullulan hydrogel layer had no adhered cell whereas sites without hydrogel were covered completely with a thick layer of the cells. Indeed pullulan can inhibit the attachment of macrophages cells.^[44] Similarly, azidophenyl derivative of dextran (Dex) was used for hydrogel layer immobilization on the surface of aminated-PET membranes,^[42] and O₂ plasma-treated PS and PU substrates^[43] under UV-irradiation (Fig. 6e). The Dex derivatives with DS < 0.31 were water-soluble whereas the ones with higher DS showed limited water solubility. Monitoring of hydrogel formation *via* FTIR showed that after 15 min irradiation, the bands of azide groups disappeared completely. Amination or plasma-pretreatment of substrates improved the polarity and wettability which in turn increased the interaction of the substrates with the aqueous solution of Dex and facilitated the attachment. The static contact angles of 82°, 24°, and 0° for PET, aminated-PET, and PET-*g*-Dex revealed the improved wettability. Also, the contact angles of the plasma-treated substrates were around 80° which after immobilization of the Dex hydrogels reduced to less than 10°. The presence of the Dex layer improved the antifouling behavior with almost no human albumin adsorption.

CROSSLINKING VIA TRIALKOXYSILANE GROUPS

Polymer chains bearing trialkoxysilane moieties enable another approach for surface grafting of polymer networks,^[45–49] which is especially useful for anchoring hydrogel layers on the surface of inorganic substrates such as glass, silicone, metal oxides and steel containing M–OH (M = Si or metal) on their surfaces. Condensation between Si–OR groups on polymer backbone and M–OH on substrate surface induces the Si–O–M linkages. Meanwhile, the formation of Si–O–Si linkages creates the crosslinking among polymer chains. Crosslinking and condensation reactions are usually triggered by the hydrolysis of siloxane groups upon heating or in the presence of acid/base catalysts. Additionally, nanocomposite hydrogels can be prepared by the addition of the nanoparticles of SiO₂ or other metal oxides to the polymer solution for casting. Indeed, in these types of tethered nanocomposite layers, the nanoparticles are not physically distributed in the hydrogel layer, but covalently linked with trimethoxysilyl (TMS) groups on polymer backbones.

Immersing of glass slides in a methanolic solution of P(TMSPMA-*co*-OEGMEMA) (TMSPMA = 3-(trimethoxysilyl) propyl methacrylate) led to the adsorption of a thin layer of polymer

(Fig. 7A) with thickness of 1.1 nm.^[50] The thickness of the adsorbed layer was independent of time and polymer concentration so that in the range of 1–48 h with polymer concentration of 5–50 mg, the same thickness of the adsorbed layer was observed. Indeed, the adsorbed polymer layer prevents further attachment of another polymer chain to the glass surface. Curing of the adsorbed polymer and its covalent attachment to the surface were achieved via 2 h heating at 120 °C or incubation in PBS (pH 7.4) at 37 °C for two weeks. The thickness remained constant before and after curing. The smoothness of the surface was highly dependent on the substrate quality. Pre-treatment of the glass surface with O₂ plasma led to the fabrication of a very smooth surface (RMS 0.13 nm) whereas in glass slides without plasma treatment some ag-

gregates were observed on the surface after polymer attachment. Plasma treatment increased the number of Si–OH groups and prevented self-condensation of polymer chains together, which result in undesired aggregation. Similarly, Dong *et al.* prepared quaternary derivative of poly(dimethyl-aminoethyl methacrylate) (PDMAEMA) bearing TMS groups via partial quaternization of its tertiary amino groups with 3-(iodopropyl)trimethoxysilane (IPTMS) followed by the full quaternization with bromoethane.^[51] Nanocomposite solutions of quaternized PDMAEMA with various contents of SiO₂ nanoparticles were used for spin-coating on the glass slides to fabricate the superhydrophilic surfaces (Fig. 7B). The hydrophilicity was a function of SiO₂ type and content. Formation of a tethered network of quaternized PDMAEMA created

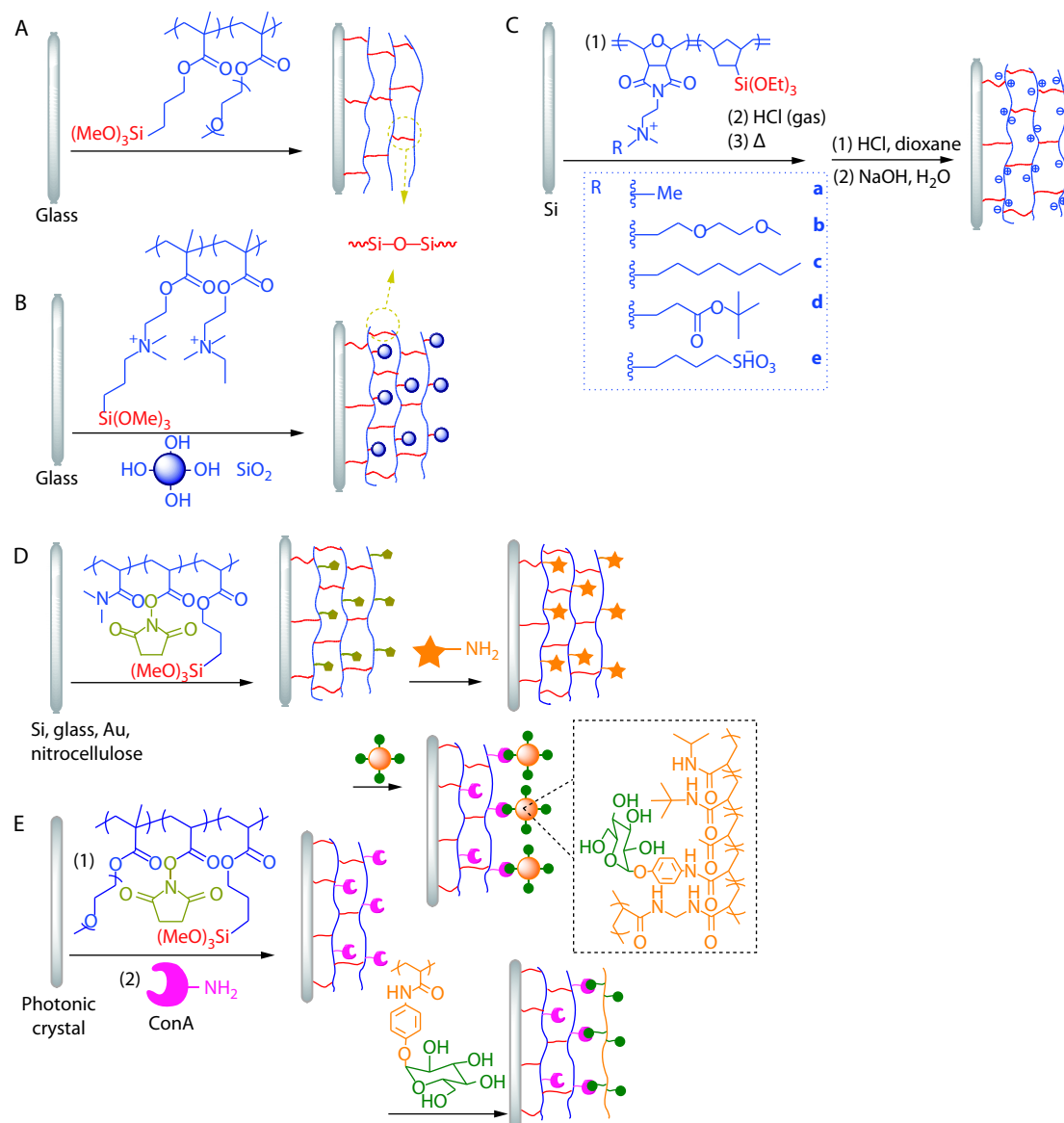


Fig. 7 Schematic descriptions for covalently tethering of (a) PEGylated hydrogels on the glass surface,^[50] (b) superhydrophilic nanocomposite hydrogels on the glass surface,^[51] (c) zwitterionic polyoxanorbornene hydrogels on the Si surface,^[46] (d) hydrogels with reactive N-hydroxy succinimide ester groups on various substrates and subsequent functionalization with biomolecules,^[47–49,53] and (e) hydrogels bearing mannose moieties on the surface of photonic crystal film for fabrication of lectin ConA selective biosensor.^[54]

a contact angle of 83° which decreased by incorporation of silica nanoparticles in the network structure. By the addition of 35 wt% and 50 wt% of dry fumed silica nanoparticles, the contact angle decreased to 14° and 5°, respectively, whereas the addition of 35 wt% and 50 wt% of colloidal silica nanoparticles reduced the contact angle to 43° and 42°, respectively. The dispersion state of the SiO₂ nanoparticles is the main point for the determination of the final surface roughness so that the roughness of bare glass increased from 3 nm to 63 nm by incorporation of 35 wt% of fumed silica nanoparticles in the coating structure.

Diverse types of cationic, carboxybetaine, and sulfobetaine norbornene-based monomers were copolymerized with triethoxysilane-norbornene derivative *via* a ring-opening metathesis polymerization (ROMP) and used for immobilization on the surface of Si wafer.^[46] Since kinetic of ROMP is drastically retarded by carboxylate groups,^[52] therefore, instead of directly using zwitterionic forms of norbornene derivatives, the cyclic maleimide derivatives of the monomers were used for polymerization; also the COOH group in monomer **d** (Fig. 7C) was protected with *tert*-butyl group. Spin-coating of organic solutions of norbornene-polymers on the Si surface and treatment by HCl and then heat treatment induced crosslinking of the polymer chains and attachment onto the silicon surface. Triethoxysilane groups did a dual function of crosslinking of polymer chains and anchoring of fabricated network on the surface. After immobilization of norbornene-based networks, the *tert*-butyl protecting group in repeating unit **d** was removed by treating with HCl to obtain carboxybetaine group and the cyclic maleimide rings in the repeating units **a**, **b**, **c** (Fig. 7C) were hydrolyzed by NaOH to obtain the zwitterionic hydrogels. The hydrogel thicknesses were tuned in the range of 20–200 nm by adjusting the concentration of polymer solution at 1 wt%–5 wt%. The increased thickness upon swelling in water was only 2–3 nm, which reveals the high density of crosslinking. The static contact angle was highly dependent on the polymer composition so that the lowest contact angle (32°) was for the hydrogel with OEG units and the highest one (70°) was for the hydrogel with octyl chains. Study of the protein adsorption for BSA, fibrinogen, Lys, myoglobin and cytochrome c showed that all silicon wafers coated with norbornene-based zwitterionic hydrogels (except the one with octyl chains) showed better anti-fouling properties than virgin Si wafer. Moreover, zwitterionic hydrogel with OEG units showed the lowest adsorption of BSA, fibrinogen, Lys, myoglobin, however, the adsorption of cytochrome c on the surface of zwitterionic hydrogel with C1 units (monomer **a** in Fig. 7C) was less than the one with OEG units. Moreover, converting the cationic surfaces to the zwitterionic ones by hydrolysis of maleimide units with NaOH improved the antifouling properties significantly.

There are several reports about the application of water-soluble terpolymers of DMAAm, TMSPMA, and *N,N*-acryloyloxysuccinimide (NAS) for modification of the surface of glass slides, Si wafer, silica capillaries, nitrocellulose and plasma-treated gold (Fig. 7D).^[47–49,53] The presence of TMS groups allows the surface attachment and crosslinking of polymer chains whereas *N*-hydroxysuccinimide esters provide active

sites for covalent conjugation with biomolecules. Conjugation of amino-modified DNA strands with coated layer *via* reaction with NAS units was used for the preparation of low-density DNA microarrays. Also, surface coating of fused silica capillaries with P(DMAAm-co-TMSPMA-co-NAS) and subsequent reaction of NAS groups with ethanolamine or PEG-NH₂ provide a powerful separation system that was used for separation of protein mixtures (Lys, cytochrome c, and ribonuclease A) *via* capillary electrophoresis. Due to the attachment to the surface *via* siloxane linkages, the immobilized layer remained stable in aqueous media in the presence of sodium dodecyl sulfate (SDS), urea, and salt even at boiling temperature. The dry thickness of the immobilized hydrogel was 2–7 nm which depends on the concentration of the applied polymer solution. Hydration and swelling of the hydrogel induced an increase of 7–20 nm in thickness. Similarly, P(OEG-MEMA-co-TMSPMA-co-NAS) was used to tether thin hydrogel layers on the surface of UV/O₃-treated photonic crystal films (Fig. 7E).^[54] The reactive *N*-hydroxysuccinimide ester groups were then reacted with amino groups of lectin ConA. Therefore, in the next step the crosslinked nanoparticles bearing mannose moieties were prepared *via* free radical copolymerization of NIPAm:TBAAm:AA:MBA:ManAm (TBAAm = *N*-*tert*-butyl acrylamide, ManAm = *p*-acrylamidophenyl- α -D-mannopyranoside) in the presence of SDS. Immersing of photonic crystal which has already been modified with hydrogel and ConA layer in a dispersion of mannose-bearing nanoparticles or in an aqueous solution of the homopolymer of poly(ManAm) induced attachment of a layer of NPs or poly(ManAm) on the surface of hydrogel layer *via* selective binding between mannose with ConA units. AFM images showed a flat surface with hole patterns for virgin photonic crystal films. The hole pattern remained during all modifications; however, the surface became rougher. Due to the presence of the mannose moieties on hydrogel surface, the obtained hybrid structure could act as a sensitive and selective biosensor for the detection of low concentrations of ConA. The detection limit was even lower than that of the surface plasmon resonance sensor.

CROSSLINKING VIA THIOL-ENE CLICK REACTION

There are two types of thiol-ene reactions:^[55,56] (1) addition of thiols to electron-rich or electron-poor alkenes triggered by radical initiator, UV light or heat, and (2) addition of thiols to electron-poor alkenes using a catalyst which usually is an amine or phosphine. This reaction has found great application in polymer and material chemistry.^[57,58] The reaction of hydrophilic polyenes and polythiols on the surface of substrates (bearing ene or thiol groups) has also been used to generate network layers covalently attached to the surfaces.^[59–63] UV-triggered thiol-ene reactions using electron-rich alkene moieties have been applied more than amine/phosphine catalyzed ones for surface tethering of hydrogel layers. This might be due to the fact that UV-triggered systems are more controllable than the amine/phosphine catalyzed ones. Indeed, the presence of the electron-poor alkene units for amine/phosphine catalyzed reactions leads to the instant initiation of the thiol-ene reaction even in the absence of catalysts, making the control more

difficult. Highly reactive polyenes based on electron-poor C=C bonds have been mostly used for layer-by-layer surface tethering of hydrogel layers^[64] or the fabrication of injectable hydrogels.^[65] On the contrary, the electron-rich units cannot react rapidly with thiols in the absence of UV light or without heat. This feature was utilized for the fabrication of interpenetrating polymer network (IPN) and double-network (DN) hydrogels.^[60]

Kurowska *et al.* used a combination of BPh-method and thiol-ene reaction for the immobilization of the oxanorbornene-based hydrogels on the surface of Si and Au substrates to improve the anti-fouling and antibacterial properties.^[66,67] Zwitterionic poly(amino/carboxylate) (PZI), zwitterionic polysulfobetaine (PSB), and polycationic (SMAMP) oxanorbornene polymers (Fig. 8b) were obtained *via* ROMP of *N*-Boc protected oxanorbornene monomers using Grubbs catalyst and subsequent deprotection of Boc group.^[66] Also,

copolymers of oxanorbornene monomer bearing *N*-Boc protected amino groups with an oxanorbornene-functionalized PEG (Fig. 8b) were prepared by ROMP and used for surface modification of Si and Au substrates.^[67] Spin-coating of a mixture of oxanorbornene polymers with pentaerythritoltetrakis(3-mercaptopropionate) crosslinker (Fig. 8a) on the surface of BPh-attached Si and UV-irradiation resulted in simultaneous crosslinking of oxanorbornene polymer *via* thiol-ene reaction and attachment of the generated hydrogel layer (dry thickness 70–150 nm) to the Si surface.^[66] The static contact angles of PZI, PSB, and SMAMP oxanorbornene polymers were 20°, 37°, and 70°, respectively, and the wet/dry swelling ratios were 1.9, 1.6, and 1.2. The presence of hydrophobic alkyl chains in polycationic hydrogel made it less hydrophilic than the other hydrogels. At pH 7.4, zeta potentials of PZI, PSB, and SMAMP hydrogels were −23, −2, and −34 mV, respectively. Due to the presence of NH₂ and COOH groups, the

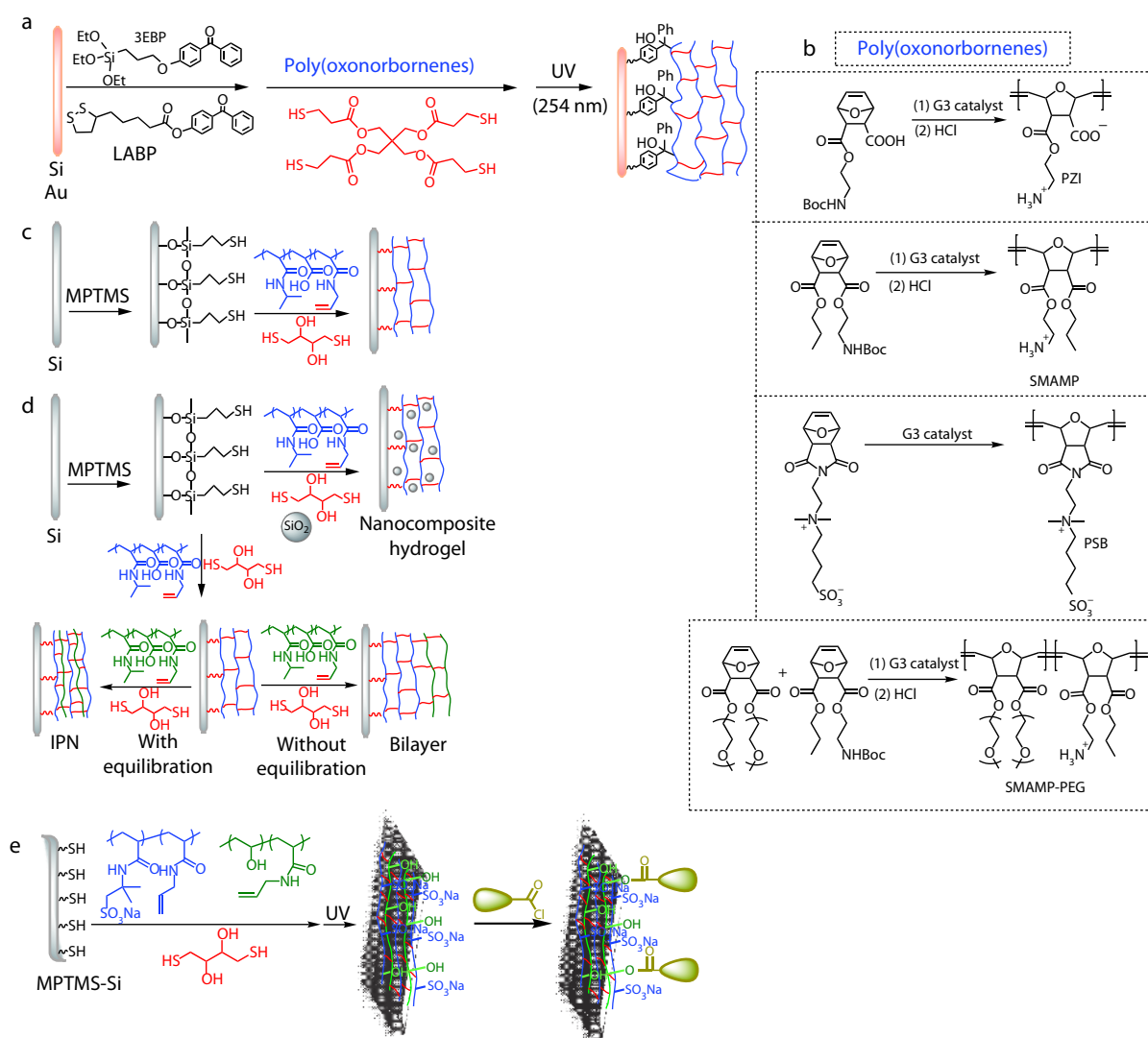


Fig. 8 (a, b) Synthesis of polyamino/carboxylate, polysulfobetaine, polycationic and polycationic-PEG poly(oxanorbornenes) and their tethering on the surface of benzophenone-functionalized Si or Au substrates in the presence of tetrathiol crosslinker *via* thiol-ene reactions.^[66,67] Thiol-ene click strategy for tethering of (c) thermosensitive hydrogels on the Si surface,^[59] (d) nanocomposite hydrogels, multilayer hydrogels, and IPNs on the Si surface,^[60] (e) hydrogels bearing conjugated drug on the surface of Si wafer.^[68]

zeta potentials of PZI and SMAMP hydrogels were a function of pH and became positive by decreasing pH. However, the surface charges of polysulfobetaine were almost independent of pH. Polycationic hydrogel layer was antibacterial but did not show antifouling behavior whereas the polysulfobetaine showed a contradict behavior with great antifouling and negligible antibacterial activity. On the other hand, PZI zwitterionic hydrogel combined both antibacterial and antifouling properties. Also, in the immobilized cationic-PEG oxanorbornene hydrogels on the Si surface, fibrinogen adsorption was decreased so that for samples with 0 mol% and 25 mol% of PEG-containing monomers the fibrinogen adsorption was 11 and 1 ng/mm², respectively. All the hydrogels regardless of PEG content could kill *E. coli* completely whereas for *S. aureus* less efficiency was observed.

Li *et al.* fabricated temperature-responsive surfaces via tethering of PNIPAm hydrogels on the surface of Si wafers (Fig. 8c).^[59] In P(NIPAm-co-AA) copolymers with different molecular weights, the AA groups were partially (~2 mol%) modified with allylamine. Spin-coating of a mixture of ene-P(NIPAm-co-AA) and dithiothreitol (DTT, crosslinker) on the surface of thiolated-Si (MPTMS-Si) and treatment at 120 °C resulted in hydrogel formation. The thickness of the hydrogel was controlled at 100–2500 nm by tuning the MW and polymer concentration. The thermal treatment for crosslinking was preferred to the UV treatment due to the uniform crosslinking of the polymer layer in the whole network structure. Wet/dry thickness ratio of immobilized hydrogel with dry thickness greater than 150 nm at $T < LCST$ was 4 whereas at $T > LCST$ it decreased to 1.5. The swelling ratio was independent of thickness, indicating the similar crosslinking densities in the whole structure of the hydrogel network for different thicknesses. However, at the thickness below 150 nm the swelling decreased significantly by decreasing the thickness. Since the distribution of the crosslinks is homogenous in the hydrogel structure, therefore, the reason for the drastic decrease in swelling for ultrathin films of the PNIPAm layer was attributed to the constraint effect due to the surface attachment.

Thiol-ene reaction was extended by Chollet *et al.* for immobilization of hydrogel multilayers, IPNs, and nanocomposite hydrogels on the surface of MPTMS-Si wafer or DTT-gold substrates (Fig. 8d).^[60] In the fabrication of multilayer hydrogels, each layer was prepared upon spin-coating of the ene-PAA or ene-(PNIPAm-co-AA) in the presence of DTT and curing at 120 °C or UV-irradiation at 254 nm. In IPN formation, before curing of the second layer a long term equilibration time between first immobilized hydrogel with DTT and ene-polymer mixture was required to assure the homogenous diffusion of the ene-polymer and DTT inside the first hydrogel. Therefore, the second spin-coated layer was kept under a saturated vapor atmosphere of methanol/butanol for 48 h and then followed by heat curing. Also, the immobilized nano-hybrid hydrogel was achieved *via* one-layer hydrogel formation in the presence of SiO₂ nanoparticles. Similar molecular weights of PAA and P(NIPAm-co-AA) yielded similar thickness indicating being independent of the polymer type. Curing with UV required shorter time (2 h) than thermal treatment

(12 h) and can be used for surface micropatterning by applying the desire photomasks during irradiation.^[61] In the fabrication of multilayer hydrogels, the thickness of the total multilayer structure was increased linearly by increasing the number of layers. The wet/dry swelling ratio of bilayer hydrogel was the same with the swelling ratio of the single hydrogel with a similar thickness, which means during the immobilization of the second layer, only a little interdiffusion has happened between layers. On the other hand, the swelling ratio of IPN was half of that in single hydrogel due to the fact the crosslinking density in IPN was doubled compared with that in the single hydrogel layer. Expectedly, in nanocomposite hydrogel layers the dry thickness of the layers increased by increasing the SiO₂ content. However, the swelling ratio decreased by increasing SiO₂ content so that in hydrogels with 0 wt% and 63 wt% the swelling ratio was 4 and 1.2, respectively. The reason for lower swellability was the topological constraints and H-bonding between nanoparticles with the polymers which act as a crosslinking agent and decrease the swelling of the hydrogels.

Hydrogel layer bearing conjugated indometacin (an antibacterial drug) was tethered on the surface of Si wafer *via* thiol-ene reaction (Fig. 8e).^[68] Ene-PVA and ene-P(AMSA-co-AA) were prepared by allylation of AA units of P(VA-co-AA) and P(AMSA-co-AA) with allylamine. Coating of mixed solutions of ene-PVA, ene-P(AMSA-co-AA) and DTT on the surface of MPTMS-modified Si wafer and exposing to UV-light induced hydrogel formation. By increasing the total polymer concentration from 2 wt% to 12 wt% the thickness increased from 0.4 µm to 3.5 µm. The reaction of the acyl chloride derivative of indometacin with hydroxyl groups of PVA segments in the immobilized hydrogel created the prodrug hydrogel layer. The hydrophilicity of the hydrogel was affected drastically by the hydrogel composition. The static contact angle of bare Si wafer was 76° which changed to 35° and 50° for hydrogels containing 30% and 70% of PVA segments. The higher contact angle of the samples bearing higher content of PVA was due to the lower hydrophilicity of PVA in comparison to PAMSA. Conjugation of hydrophobic indometacin to the PVA segment is another reason for increasing the contact angle of samples with higher PVA content. Approximately 80% of the drug was released after 2 days *via* hydrolysis of the ester bond at pH 7.4.

CROSSLINKING VIA CATECHOL UNITS

Polymers bearing catechol units have been used widely for surface anchoring of the thin layers.^[69,70] Mechanism and chemistry of bioinspired catechol-based coatings have been summarized in several reviews.^[71,72] Catechols can attach to various surfaces through diverse types of interactions (Fig. 9).^[73] The hydroxyl groups of catechol have a high affinity for attachment to the metal oxides *via* formation of charge-transfer complexes. Moreover, the phenyl ring enables catechol interaction with diverse types of polymeric substrates *via* π - π and van der Waals interactions. Also, H-bond formation between catechols and hydrophilic surfaces is another driving force for the attachment of catechol-bearing polymers to the substrates. The catechol units can be oxidized to quinones by air in weak basic medium

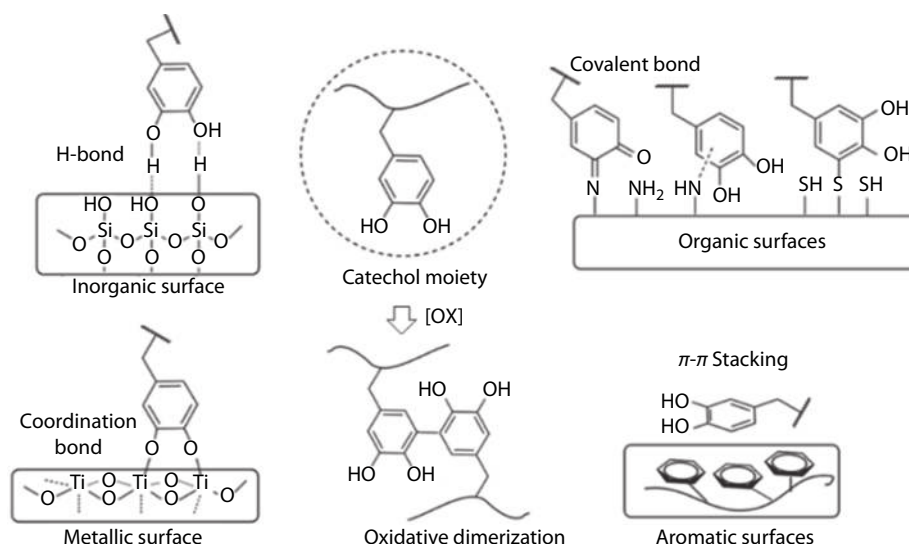


Fig. 9 Interactions of catechol-bearing polymers with different surfaces (Reproduced with permission from Ref. [73] with slight modifications; Copyright (2019) American Chemical Society).

and undergo crosslinking *via* dimerization. The quinones can further react with amines *via* Michael addition or Schiff base formation, and thiols through thiol-ene click reactions. Therefore, catechols are unique moieties for grafting versatile hydrogels on the surface of various organic and inorganic substrates. Generally, surface pretreatment is not required since the surface has at least one type of the interactions depicted in Fig. 9 for attaching catechol containing polymer layers.

Modification of the surfaces using catechol-bearing polymers usually is performed in a buffer medium with weak basicity. The selection of the buffer is important for different substrates since components of some buffers can interfere in the coating process. For instance, phosphate anions in PBS can adhere to the surface of inorganic oxides;^[74] primary amino groups in Tris buffer can react with catechols;^[75] and borate in boric buffer creates a complex with *cis*-diol of catechol and prevents its oxidation.^[76] Therefore, 3-(*N*-morpholino)propanesulfonic acid buffer is usually used for metal oxides; whereas PBS buffer for polymer substrates. Since catechols are very sensitive to oxidation in alkaline medium, the corresponding polymers need to be handled under protective conditions prior to forming hydrogels. Furthermore, a high amount of catechol units increase the hydrophobicity of surface, which is considered as a drawback for anti-biofouling application.

Four-arm PEG with terminal succinimidyl ester groups was conjugated with dopamine (Fig. 10a) and used for surface modification of plasma-treated TiO₂ and glass substrates.^[77] By using 0.5 mg/mL of the PEG-catechol derivative in aqueous buffer medium, incomplete coverage of the surface was obtained whereas in 2 mg/mL the surface was fully covered with a layer with a thickness of 3–4 μm. The surfaces coated with 2 mg/mL of PEG-catechol solutions showed a significant reduction (>98%) in protein adsorption from the whole bovine serum. A bifunctional PEG derivative (named as SBCEP) bearing catechol and sulfobetaine groups was prepared *via* reaction of PEG diglycidyl ether with dopamine followed by quaternization of tertiary amino groups with 1,3-

propanesultone (Fig. 10b).^[78] This derivative was used for anchoring of a thin hydrogel layer on the surface of SS, Si wafer and titanium substrates in aqueous medium at pH 7.5 to improve the anti-fouling behavior of the substrates. Self-attachment between catechol units created crosslinks between SBCEP chains; additionally, the *ortho*-phenolic hydroxyl groups of catechol acted as anchoring groups. The contact angles of surfaces modified with SBCEP and CaPEG (catechol-PEG) were in the range of 25°–45° with thickness of 9–11 nm. Adsorption of BSA and adhesion of bacteria and cells to the PEGylated surfaces were significantly lower than those for pristine SS. Moreover, the zwitterionic derivative exhibited slightly better antifouling performance than the PEGylated one.

Hyperbranched polyglycerol (hPG), as an excellent bioinert alternative for PEG,^[81] was functionalized with catechol groups (Fig. 10c) and used for immobilization of hydrophilic multilayer networks on the surface of TiO₂ and polystyrene.^[79] Three types of hPG-catechol derivatives were obtained *via* amination of terminal hydroxyl groups of hPG and then amidation with 3,4-dihydroxyhydrocinnamic acid: (i) hPG-Cat1: one catechol per each dendrimer molecule, (ii) hPG-Cat10: 10% of hydroxyl groups were functionalized with catechol moieties, and (iii) hPG(NH₂)Cat40: the degree of substitution of hydroxyl groups was 40% for catechol and 60% for amino groups. The surfaces of TiO₂ and polystyrene were modified by a dual-layer approach and a triple-layer approaches, respectively (Fig. 10d). For double-layer approach, the TiO₂ surface was coated first with hPG-Cat10 and then with hPG-Cat1 whereas in the triple-layer strategy, the surface of PS was coated sequentially with hPG(NH₂)Cat40, hPG-Cat10, and hPG-Cat1. The presence of free amino groups in hPG(NH₂)Cat40 can improve the crosslinking *via* Michael reaction and Schiff base formation with quinone forms of catechol.^[82] Coating of the substrates with only one of the hPG-catechol derivatives showed some drawbacks. Low content of catechol in hPG-Cat1 made it almost impossible to create stable

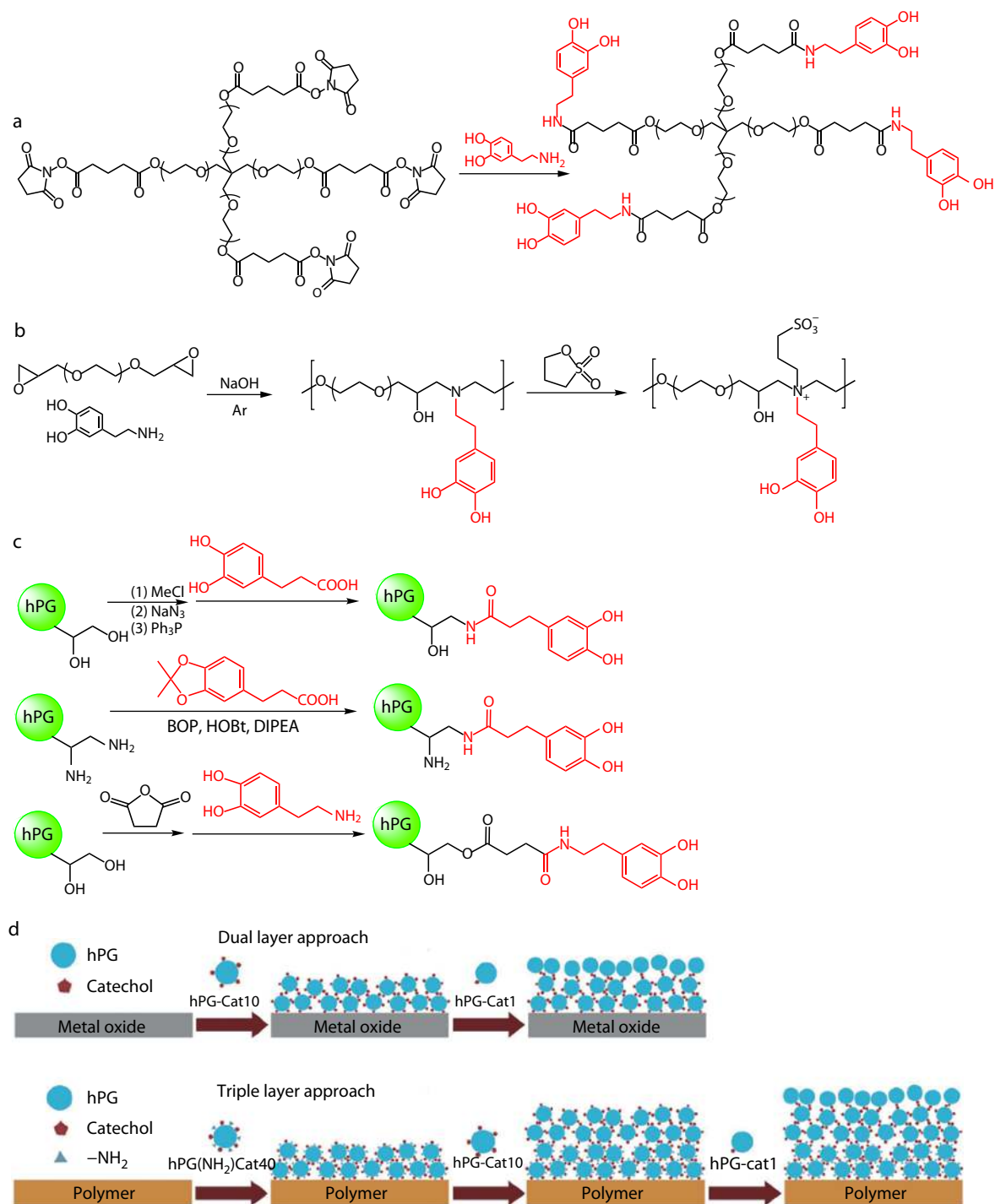


Fig. 10 Preparation of hydrophilic copolymers bearing catechol anchoring groups: (a) four-arm PEG with terminal catechol units,^[77] (b) zwitterionic PEG derivative with pendant catechol groups,^[78] and (c) hyperbranched polyglycerol (hPG) with partial functionalization with catechol units.^[79,80] (d) Fabrication of coatings with dual and triple layer architectures on the surface of metal oxides and polymer substrates. (Reproduced with permission from Ref. [79]; Copyright (2014) Wiley).

coating because three catechol per each macromolecule is the minimum required amount for the generation of a stable coating.^[83] However, hPG-Cat1 can create a stable connection with hPG-Cat10 layer. As comparison, more than 30% of the coated hPG-Cat1 monolayer was desorbed by washing the surface with SDS aqueous solution whereas no desorp-

tion was reported for dual-layer hPG-Cat1/hPG-Cat10 coating. Furthermore, the hPG-Cat40 can create a very stable layer on substrates and it contains a high number of reactive groups which can be shielded by further coating with hPG-Cat10. Again, the presence of a small number of catechol groups on the surface of the second layer can simply be shielded by

coating with hPG-Cat1. The static contact angle of TiO_2 was 67° which decreased to 28° after coating with hPG-Cat10 and to 22° by further coating with hPG-Cat1. The contact angle for triple layer immobilization was reduced to 19° . Indeed, surfaces with lower content of catechols are more hydrophilic, therefore, the hydrophilicities of polymers are in the order of hPG-Cat1 > hPG-Cat10 > hPG-Cat40. Accordingly, when the outermost layer is changed to hPG-Cat1, hydrophilicity is increased. The thickness of single layer coating of hPG-Cat1 and hPG-Cat10 were 1.7 and 4.0 nm, respectively, and the thickness for dual hPG-Cat1/hPG-Cat10 was 4.8 nm. The thickness of hPG-Cat40 was 15.1 nm which increased to 18.2 nm after triple layer formation.

In the extension of this work, the immobilization of hPG-Cat derivatives bearing various amounts of catechol group on various substrates was studied.^[80] Amino and carboxylic derivatives of hPG were used as precursors for reaction with 3,4-dihydroxyhydrocinnamic acid and dopamine, respectively, to obtain hPG-Cat samples with ester and amide linkages (Fig. 10c). By increasing the catechol content, the water solubility was decreased so that the sample in which 40% of hydroxyl groups have converted to catechol ones was only soluble in high polar organic solvents such as DMF. The obtained samples were coated on the surface of various substrates (TiO_2 , Al, PS, PP, SiO_2 , glass, Au) in aqueous medium with weak alkalinity (pH 7.5–8.5). The static contact angles by modification with hPG-Cat10 (with amide linkages) for TiO_2 , Au, Al, SiO_2 , glass, PS and PP substrates were 28° , 23° , 20° , 22° , 22° , 30° , and 38° , respectively. The higher contact angle for PP and PS was attributed to the weak van der Waals interaction between the substrate surface and the crosslinked hPG layer.^[84] Comparison of coating of the SiO_2 surface with hPG-Cat1, hPG-Cat5, hPG-Cat10, and hPG-Cat30 showed that by increasing the catechol content, some nanoaggregates are appearing on the coating surface due to the crosslinking of catechol units which increased the roughness. The formation of coating using hPG-Cat5 and hPG-Cat10 samples on the surface of TiO_2 at different pHs was studied by quartz crystal microbalance (QCM) technique. At pH 6.0, catechol units could not be oxidized in a short period, therefore no crosslinking was observed and only a monolayer of the hPG-Cat derivative on the surface of the substrate was produced. The grafting of hPG-Cat10 was 136 ng/cm^2 at pH 6.0. However, crosslinking of the catechol units at pH 7.5 led to the multilayer formation and achieving the grafting density of 194 and 1187 ng/cm^2 for hPG-Cat5 and hPG-Cat10 samples, respectively. The low grafting density of hPG-Cat5 even at pH 7.5 was due to the low content of catechol units (4–5 units per each dendrimer) which tend to attach to the surfaces of the substrates and only a few catechols are left for crosslinking and making multilayers. Additionally, it was determined that 50% of the catechol units are converted to quinones which act as crosslinking agents and the rest 50% act as anchoring agents. Moreover, the thicknesses of TiO_2 coated with hPG-Cat1, hPG-Cat5, hPG-Cat10 and hPG-Cat30 were 2.1, 2.7, 3.8, and 5.5 nm, respectively, which confirm the formation of thicker and multilayers for hPG samples with the higher catechol content. Samples with higher catechol content showed higher stabil-

ity. The decline in thickness for samples coated with hPG-Cat1, hPG-Cat10 and hPG-Cat30 after two weeks incubation at pH 7.4 was 33%, 13%, and 4%, respectively. The drawback of the samples with a high content of catechol was their high protein adsorption due to the presence of hydrophobic aromatic catechol units. Therefore, hPG-Cat10 was the best derivative to obtain high stability and high anti-fouling property. Moreover, the drawback of the hPG-Cat derivatives with ester bond was the weak long-term stability due to the hydrolysis of ester bonds.

Liu *et al.* functionalized various types of hydrophilic copolymers including P(SSNa-co-AA), P(SBMA-co-AA), P(OEGMEMA-co-AA), P(VP-co-AA), and P(MTAC-co-AA) with catechol units *via* coupling of AA units with the amino group of dopamine (Fig. 11a).^[85] Immobilization of catechol-containing derivatives of these polymers on the PES surface was performed by immersing PES films in aqueous solutions of the polymers at pH 8.5 to improve the anti-fouling and blood compatibility properties. The thickness of the inserted layers was 100 nm after 24 h which increased to 150 nm after 48 h. The static contact angle for virgin PES was 75° and reduced to 50° – 60° after immobilization of 100 nm of crosslinked layers. Interestingly, increasing the thickness to 150 nm led to the slight increase in contact angle which was attributed to the higher roughness for longer modification times. In three reports by Peng *et al.*, surfaces of silicon, PDMS and SS substrates were coated with a RAFT-made P(MAA-co-DPMAM-co-MAG) glycopolymer (DPMAM = *N*-dopamine methacrylamide and MAG = 2-(methacrylamido)glucopyranose) bearing dopamine as anchoring groups (Fig. 11b).^[86–88] In the obtained glycopolymers, dopamine units act as anchor groups for attachment of the glycopolymer to the substrate surface and the COOH units were used for complexation with Ag^+ ions to create antibacterial properties. The attachment of the glycopolymers to the surface of substrates was performed by *in situ* oxidation of dopamine units at pH 8.5. For P(MAA-co-DPMAM-co-MAG) glycopolymer, further incubation in AgNO_3 solution was performed for silver immobilization into the hydrogel structure. Glucose units of MAG and unreacted dopamine units reduced silver ions into Ag nanoparticles. The grafting degree and thickness of the P(MAA-co-DPMAM-co-MAG) glycopolymer was 0.0078 mg/cm^2 and 2 nm, respectively. The same thickness for P(DPMAM-co-MAG) was reported. The static contact angles of virgin silicon, PDMS, and SS were 55° , 105° , and 82° , respectively, which decreased respectively to 24° , 66° , and 54° after modification with P(MAA-co-DPMAM-co-MAG). Due to the presence of Ag nanoparticles, no *E. coli* bacteria could survive on the surface of the modified membrane.

Surface of PES membranes was coated with catechol-crosslinked hydrogels of heparin and poly(sodium 4-vinylbenzenesulfonate)-co-poly(sodium methacrylate) P(SSNa-co-MAANA) (heparin-like polymer, HepLP) (Fig. 11c) to improve the biocompatibility and bioactivity of the membranes.^[89] For derivatization with catechol moieties, 20 mol% and 30 mol% of carboxylic groups in heparin and HepPL were coupled with dopamine. Tethering of each polymer on the PES surface was simply performed *via* immersing the PES membranes in the

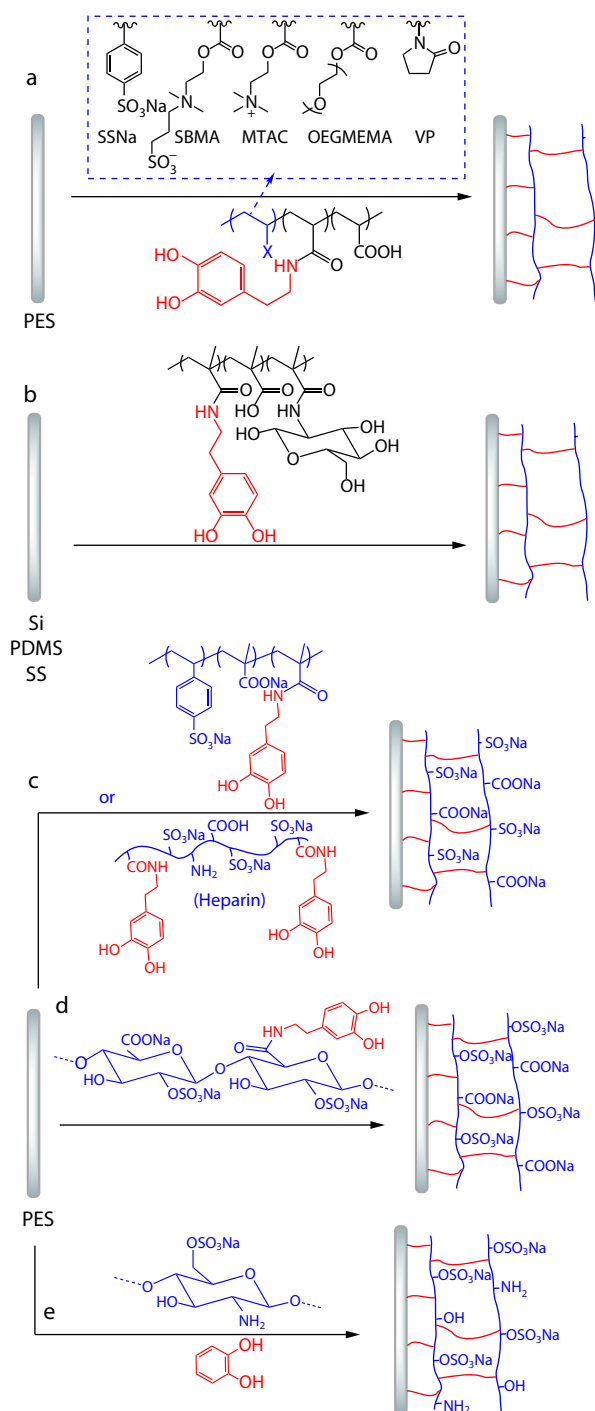


Fig. 11 Surface modification of (a) PES with copolymers of AA and SSNa, SBMA, MTAC, OEGMEMA, and VP bearing catechol groups,^[85] (b) Si, PDMS and SS substrates with P(MAA-co-DPMAM-co-MAG) glycopolymer bearing catechol units,^[86–88] (c) PES membrane with heparin or heparin-mimicking bearing dopamine moieties,^[89] (d) PES membrane with sulfated sodium alginate bearing pendant dopamine groups,^[90] (e) PES membrane with a mixture of sulfated chitosan with catechol molecules.^[91]

aqueous solution of polymer at pH 8.5. Self-oxidation polymerization of the catechol units induced hydrogel formation. TGA of the modified membranes showed a weight loss of 4%

at 220–490 °C which was attributed to the grafted hydrogel layers. Moreover, the cross-sectional SEM images revealed a thickness of more than 100 nm for the immobilized hydrogel layers. Additionally, the surface of PES was smooth shown by SEM but after modification, it showed a wrinkle-like structure and by increasing the coating time denser wrinkle-structure and finally, ridge structures were observed. Also, the wettability of the modified surfaces was improved relatively by increasing the coating time. The static contact angle for PES was 75° which decreased to 65° and 60° after 12 and 48 h of coating with hydrogels. Comparing the results for protein adsorption, platelet adhesion, and cell proliferation revealed that performance of HepLP is similar or in some cases even better than heparin layer indicating the great potential of HepLP to be used as an alternative for heparin.

Sulfated sodium alginate (SALS) with the anticoagulant property was tethered on the PES surface (Fig. 11d) to improve the biocompatibility.^[90] To enable the SALS for cross-linking and attachment to the PES surface, its carboxylate groups were partially functionalized with dopamine. AFM images showed the roughness of PES increased from 10 nm to more than 30 nm upon coating with SALS-DOP. The water contact angle for PES was 71° which reduced to 43° and 38° after coating with SALS-DOP derivatives with degrees of sulfation of 0.4 and 1.5, respectively. Due to the presence of a high number of carboxylate and sulfate groups, the SALS showed high anti-coagulation properties.^[90,92,93] Therefore, immobilization of such material on the PES surface enhanced the anti-coagulant performance of the membrane. In addition, the PES-g-SALS showed improvement in its antifouling property regarding protein and platelet adhesion. Similarly, Wang *et al.* used O-sulfated chitosan (CS) and N,O-sulfated derivatives of CS for coating the PES surface in the presence of free catechol as a crosslinker (Fig. 11e).^[91] The O-sulfated CS showed better solubility in water than N,O-sulfated CS did. Dip coating of an aqueous solution of a mixture of O-sulfated CS and catechol on the surface of PES membrane at pH 8.5 introduced a layer of crosslinked CS on the membrane surface. Air oxidation of catechol units and their subsequent Michael and Schiff base reactions with amino groups of sulfated CS were the driving force for hydrogel formation. Moreover, the addition of 1,6-hexadiazine to the coating mixture improved the coating stability due to the higher hydrophobicity of 1,6-hexadiazine in comparison to CS which increases the interaction with PES support. On the other hand, due to the low solubility of N,O-sulfated CS it was not used for direct immobilization on the PES membrane. Indeed, to mimic the structure of heparin which has $-\text{O}-\text{SO}_3^-$ and $-\text{N}-\text{SO}_3^-$ in its structure, the fabricated PES-g-(O-sulfated CS) was immersed in chlorosulfonic acid in formamide to generate N,O-sulfated CS on the PES surface. The average roughness of PES was 12 nm which increased to 16, 23, and 24 nm after coating with O-sulfated CS in the presence of 0, 3, and 6 $\mu\text{mol/mL}$ 1,6-hexadiazine. Higher content of 1,6-hexadiazine increased the crosslinking density and also increased the amount of the coated layer which in turn increased the roughness. However, after post sulfation the roughness decreased slightly due to the partial CS detachment of coating during the sulfation pro-

cess. The contact angle was 89° for PES and 55° for PES-g-(O-sulfated CS). For the samples bearing 1,6-hexadamine after post-sulfation the contact angle increased to the range of 60°–70° due to the hydrophobicity of 1,6-hexadamine and lower hydrophilicity of N,O-sulfated CS than O-sulfated CS. The PES membrane coated with sulfated CS derivatives showed heparin-mimicking behavior with significant blood compatibility and high anticoagulant activity.

CONCLUSIONS

Despite the fact that a variety of strategies have been developed to immobilize hydrogel layers on the surfaces of substrates, the preparation of hydrophilic polymers with desired functionalities and their subsequent crosslinking and tethering on the surfaces is one of the most promising approaches to achieve soft and hydrophilic surfaces. Much attention has been paid to the incorporation of photosensitizers, carbene and nitrene precursors, trialkoxysilanes, and catechol moieties on the surface of substrates and/or in the hydrophilic polymer structures, followed by the casting of polymer solutions on the surfaces and exposure to the curing conditions, thus inducing the crosslinking of polymer layers and surface attachment simultaneously. The crosslinking can be triggered by heat or UV-irradiation (for photosensitizers, carbenes, nitrenes, and trialkoxysilane) and adjusting medium pH (for catechols and trialkoxysilanes). Since the roles played by photosensitizers, carbenes and nitrenes are mainly based on C–H inserting reactions, therefore, the presence of C–H bonds is required on the surface. Polymeric membranes usually meet this criteria whereas in the case of inorganic surfaces (Si, Au, SS,...) the surface pretreatment with C–H containing molecules is essential. On the other hand, polymers bearing trialkoxysilanes can condense directly on the untreated inorganic surfaces *via* reaction with surface OH groups. Polymers containing catechols are applicable to most surfaces due to their high reactivity driven *via* charge-transfer complex, π - π stacking and van der Waals' forces for hydrophobic and aromatic surfaces, whereas hydrogen bonding interaction promotes their anchoring on polar surfaces. Other chemical reactions such as thiol-ene click reactions, boronate ester formation, esterification, and amidation have also been utilized for crosslinking and covalent attachment of hydrogels on the surface of substrates. In contrast, strong non-covalent dynamic interactions (such as cyclodextrin-based host-guest interaction^[94]) have been used occasionally for tethering self-healing hydrogel layers on the surfaces. We anticipate that the immobilization of hydrogels using host-guest assembly will attract enormous interest and become feasible soon due to its great potential in the fabrication of self-healing materials and encapsulation of various payloads. The immobilization process can be performed in one step to obtain a single hydrogel layer or in several sequential steps to generate multilayer hydrogels.

Surfaces grafted with a thin hydrogel layer have a broad spectrum of applications, including the hybrid materials with anti-fouling, anti-bacterial, antifogging and anticoagulating activities. Indeed, water adsorption of hydrogels creates a very soft and wet surface which prevents the proteins and platelets from settling down on the surfaces. Moreover, by incorporating different functionalities in the hydrogel structure,

the performance of hydrogel layers can be further improved. Specifically, the hydrogel layers bearing quaternary ammonium groups and Ag nanoparticles render the surface highly antimicrobial. The layers bearing zwitterionic groups usually are excellent anti-fouling agents whereas the hydrogels containing sulfate/carboxylate groups (heparin mimicking agents) are particularly useful for anticoagulating materials. Moreover, self-healing and responsive thin layers on the surfaces can be achieved by anchoring polymers bearing dynamic crosslinking groups, while the drug release can be manipulated by the conjugation of drugs as payloads to the hydrogel layers as carriers.

BIOGRAPHIES

Farzad Seidi obtained his PhD in Polymer Chemistry at the Sharif University of Technology (Iran) in 2011. In July 2016, he joined the newly established Vidyasirimedhi Institute of Science and Technology (VISTEC) in Thailand as a team leader in the research group led by Prof. Daniel Crespy. Currently, Farzad Seidi is an Associate Professor at Nanjing Forestry University in China. Prof. Farzad Seidi is a skilled polymer chemist with over 65 peer-reviewed journal papers with high impact (including Chemical Reviews and Progress in Polymer Science). He is an expert in the synthesis of functional polymers and hydrogels.

Hui-Ning Xiao, a Professor in Chemical Engineering at University of New Brunswick (UNB) and the Fellow of Canadian Academy of Engineering (FCAE), obtained his PhD in Chemical Engineering at McMaster University in Canada in 1995. Before joining the UNB in 2001, he was a Lecturer at the University of Manchester (formerly UMIST) in the UK from 1996 to 2001. He is the editor-in-chief of *Journal of Bioresources and Bioproducts*. His research areas mainly cover the polymers and nanoparticles for cellulose-based functional materials including antimicrobial/antiviral polymers for cellulose products, green-based and smart hydrogels and bioadsorbents, and biodegradable packaging with enhanced multi-barrier properties.

Chang-Sheng Zhao received his PhD in Biomedical Engineering from Sichuan University in 1998. From 2001 to 2003, he did research work in Hokkaido University (Japan) as a postdoctoral research fellow. Subsequently, he joined Sichuan University and became a professor in 2004. Prof. Chang-Sheng Zhao has published more than 250 papers in the international journals and held over 20 patents. Prof. Zhao's research interests are mostly focused on the development of hemodialysis materials with bioactive and anticoagulant properties; he has also been very dedicated to the design of heparin-inspired hydrogels and composite biomaterials for tissue engineering and regeneration medicine.

ACKNOWLEDGMENTS

This work was financially supported by Provincial Key Lab of Pulp and Paper Science and Technology and Joint International Research Lab of Lignocellulosic Functional Materials, Nanjing Forestry University, the National Nature Science Foundation of China (Nos. 31730106 and 31770623), and NSERC Canada.

REFERENCES

- Blaszczynski, C.; Sheikh, S.; Thompson, M. Surface chemistry to minimize fouling from blood-based fluids. *Chem. Soc. Rev.* **2012**, *41*, 5599–5612.
- Landolt, D. *Corrosion and surface chemistry of metals*. EPFL press, **2007**.
- Ching, H. A.; Choudhury, D.; Nine, M. J.; Abu Osman, N. A. Effects of surface coating on reducing friction and wear of orthopaedic implants. *Sci. Technol. Adv. Mater.* **2014**, *15*, 014402–014402.
- Howarter, J. A.; Youngblood, J. P. Self-cleaning and next generation anti-fog surfaces and coatings. *Macromol. Rapid Commun.* **2008**, *29*, 455–466.
- Lee, S. C.; Kwon, I. K.; Park, K. Hydrogels for delivery of bioactive agents: a historical perspective. *Adv. Drug Deliver. Rev.* **2013**, *65*, 17–20.
- Ahmed, E. M. Hydrogel: preparation, characterization, and applications: a review. *J. Adv. Res.* **2015**, *6*, 105–121.
- Yuk, H.; Lu, B.; Zhao, X. Hydrogel bioelectronics. *Chem. Soc. Rev.* **2019**, *48*, 1642–1667.
- Hoffman, A. S. Hydrogels for biomedical applications. *Adv. Drug Deliver. Rev.* **2012**, *64*, 18–23.
- Toomey, R.; Freidank, D.; Rühe, J. Swelling behavior of thin, surface-attached polymer networks. *Macromolecules* **2004**, *37*, 882–887.
- Pandiyarajan, C. K.; Prucker, O.; Zieger, B.; Rühe, J. Influence of the molecular structure of surface-attached poly(*N*-alkyl acrylamide) coatings on the interaction of surfaces with proteins, cells and blood platelets. *Macromol. Biosci.* **2013**, *13*, 873–884.
- Pandiyarajan, C. K.; Prucker, O.; Rühe, J. Humidity driven swelling of the surface-attached poly(*N*-alkylacrylamide) hydrogels. *Macromolecules* **2016**, *49*, 8254–8264.
- Li, K.; Pandiyarajan, C. K.; Prucker, O.; Rühe, J. On the lubrication mechanism of surfaces covered with surface-attached hydrogels. *Macromol. Chem. Phys.* **2016**, *217*, 526–536.
- Steinbach, T.; Wurm, F. R. Poly(phosphoester)s: a new platform for degradable polymers. *Angew. Chem. Int. Ed.* **2015**, *54*, 6098–6108.
- Becker, G.; Deng, Z.; Zober, M.; Wagner, M.; Lienkamp, K.; Wurm, F. R. Surface-attached poly(phosphoester)-hydrogels with benzophenone groups. *Polym. Chem.* **2018**, *9*, 315–326.
- Rendl, M.; Bönsch, A.; Mader, A.; Schuh, K.; Prucker, O.; Brandstetter, T.; Rühe, J. Simple one-step process for immobilization of biomolecules on polymer substrates based on surface-attached polymer networks. *Langmuir* **2011**, *27*, 6116–6123.
- Moschallski, M.; Evers, A.; Brandstetter, T.; Rühe, J. Sensitivity of microarray based immunoassays using surface-attached hydrogels. *Anal. Chim. Acta* **2013**, *781*, 72–79.
- Buller, J.; Laschewsky, A.; Wischerhoff, E. Photoreactive oligoethylene glycol polymers—versatile compounds for surface modification by thin hydrogel films. *Soft Matter* **2013**, *9*, 929–937.
- Christensen, S. K.; Chiappelli, M. C.; Hayward, R. C. Gelation of copolymers with pendent benzophenone photo-cross-linkers. *Macromolecules* **2012**, *45*, 5237–5246.
- Kommeren, S.; Dongmo, J.; Bastiaansen, C. W. M. Switchable surface structured hydrogel coatings. *Soft Matter* **2017**, *13*, 2239–2245.
- Yoshikawa, C.; Delalat, B.; Huang, F.; Braun, S.; Nishijima, N.; Voelcker, N. H.; Kingshott, P.; Thissen, H. Photo-crosslinked coatings based on 2-hydroxypropyl acrylamide for the prevention of biofouling. *J. Mater. Chem. B* **2019**, *7*, 3520–3527.
- Pidhatika, B.; Zhao, N.; Zinggeler, M.; Rühe, J. Surface-attached dual-functional hydrogel for controlled cell adhesion based on poly(*N,N*-dimethylacrylamide). *J. Polym. Res.* **2019**, *26*, 69.
- Kirmse, W. *Carbene chemistry*. Editor, Elsevier, **2013**, Vol. 1.
- Navarro, R.; Pérez Perrino, M.; Prucker, O.; Rühe, J. Preparation of surface-attached polymer layers by thermal or photochemical activation of α -diazoester moieties. *Langmuir* **2013**, *29*, 10932–10939.
- Ye, T.; McKervey, M. A. Organic synthesis with alpha-diazo carbonyl compounds. *Chem. Rev.* **1994**, *94*, 1091–1160.
- Osterwinter, G. J.; Navarro-Crespo, R.; Prucker, O.; Henze, M.; Rühe, J. Surface-attached polymer networks through carbene intermediates generated from α -diazo esters. *J. Polym. Sci., Part A: Polym. Chem.* **2017**, *55*, 3276–3285.
- Jørgensen, J. K.; Ommundsen, E.; Stori, A.; Redford, K. Synthesis, characterisation and decomposition of 1,3-benzene disulfonyl azide: a cross-linking agent for polyolefins. *Polymer* **2005**, *46*, 12073–12080.
- El-Sayed, R. A. Review on the chemistry of sulfonohydrazides and sulfonoazides. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179*, 237–266.
- Dequierez, G.; Pons, V.; Dauban, P. Nitrene Chemistry in organic synthesis: still in its infancy? *Angew. Chem. Int. Ed.* **2012**, *51*, 7384–7395.
- Wentrup, C. Carbenes and nitrenes: recent developments in fundamental chemistry. *Angew. Chem. Int. Ed.* **2018**, *57*, 11508–11521.
- Schuh, K.; Prucker, O.; Rühe, J. Tailor-made polymer multilayers. *Adv. Funct. Mater.* **2013**, *23*, 6019–6023.
- Raghuraman, G. K.; Schuh, K.; Prucker, O.; Rühe, J. Attachment of polymer films to solid surfaces via thermal activation of self-assembled monolayers containing sulphonyl azide group. *Langmuir* **2010**, *26*, 769–774.
- Liu, L.; Engelhardt, M. H.; Yan, M. Surface and interface control on photochemically initiated immobilization. *J. Am. Chem. Soc.* **2006**, *128*, 14067–14072.
- Liu, L.; Yan, M. A general approach to the covalent immobilization of single polymers. *Angew. Chem. Int. Ed.* **2006**, *45*, 6207–6210.
- Yan, M.; Ren, J. Covalent immobilization of polypropylene thin films. *J. Mater. Chem.* **2005**, *15*, 523–527.
- Wang, X.; Ramström, O.; Yan, M. A photochemically initiated chemistry for coupling underivatized carbohydrates to gold nanoparticles. *J. Mater. Chem.* **2009**, *19*, 8944–8949.
- Wang, H.; Li, L.; Tong, Q.; Yan, M. Evaluation of photochemically immobilized poly(2-ethyl-2-oxazoline) thin films as protein-resistant surfaces. *ACS Appl. Mater. Interfaces* **2011**, *3*, 3463–3471.
- Poe, R.; Schnapp, K.; Young, M. J. T.; Grayzar, J.; Platz, M. S. Chemistry and kinetics of singlet pentafluorophenyl nitrene. *J. Am. Chem. Soc.* **1992**, *114*, 5054–5067.
- Gritsan, N. P.; Gudmundsdóttir, A. D.; Tigelaar, D.; Zhu, Z.; Karney, W. L.; Hadad, C. M.; Platz, M. S. A laser flash photolysis and quantum chemical study of the fluorinated derivatives of singlet phenyl nitrene. *J. Am. Chem. Soc.* **2001**, *123*, 1951–1962.
- Schuh, K.; Prucker, O.; Rühe, J. Surface attached polymer networks through thermally induced cross-linking of sulfonyl azide group containing polymers. *Macromolecules* **2008**, *41*, 9284–9289.
- Bartlett, M. A.; Yan, M. Fabrication of polymer thin films and arrays with spatial and topographical controls. *Adv. Mater.* **2001**, *13*, 1449–1451.
- Hasuda, H.; Kwon, O. H.; Kang, I. K.; Ito, Y. Synthesis of photoreactive pullulan for surface modification. *Biomaterials* **2005**, *26*, 2401–2406.
- Bhat, V. T.; James, N. R.; Jayakrishnan, A. A photochemical method for immobilization of azidated dextran onto aminated poly(ethylene terephthalate) surfaces. *Polym. Int.* **2008**, *57*,

- 124–132.
- 43 Coll Ferrer, M. C.; Yang, S.; Eckmann, D. M.; Composto, R. J. Creating biomimetic polymeric surfaces by photochemical attachment and patterning of dextran. *Langmuir* **2010**, *26*, 14126–14134.
 - 44 Seidi, F.; Jenjob, R.; Phakkeeree, T.; Crespy, D. Saccharides, oligosaccharides, and polysaccharides nanoparticles for biomedical applications. *J. Control. Release* **2018**, *284*, 188–212.
 - 45 Xu, L.; Ma, P.; Yuan, B.; Chen, Q.; Lin, S.; Chen, X.; Hua, Z.; Shen, J. Anti-biofouling contact lenses bearing surface-immobilized layers of zwitterionic polymer by one-step modification. *RSC Adv.* **2014**, *4*, 15030–15035.
 - 46 Colak, S.; Tew, G. N. Dual-functional ROMP-based betaines: effect of hydrophilicity and backbone structure on nonfouling properties. *Langmuir* **2012**, *28*, 666–675.
 - 47 Sola, L.; Chiari, M. Modulation of electroosmotic flow in capillary electrophoresis using functional polymer coatings. *J. Chromatogr. A* **2012**, *1270*, 324–329.
 - 48 Ohlander, A.; Zilio, C.; Hammerle, T.; Zelenin, S.; Klink, G.; Chiari, M.; Bock, K.; Russom, A. Genotyping of single nucleotide polymorphisms by melting curve analysis using thin film semi-transparent heaters integrated in a lab-on-foil system. *Lab Chip* **2013**, *13*, 2075–2082.
 - 49 Petti, D.; Torti, A.; Damin, F.; Sola, L.; Rusnati, M.; Albisetti, E.; Bugatti, A.; Bertacco, R.; Chiari, M. Functionalization of gold surfaces with copoly(DMA-NAS-MAPS) by dip coating: surface characterization and hybridization tests. *Sens. Actuators B Chem.* **2014**, *190*, 234–242.
 - 50 Jon, S.; Seong, J.; Khademhosseini, A.; Tran, T. N. T.; Laibinis, P. E.; Langer, R. Construction of nonbiofouling surfaces by polymeric self-assembled monolayers. *Langmuir* **2003**, *19*, 9989–9993.
 - 51 Dong, H.; Ye, P.; Zhong, M.; Pietrasik, J.; Drumright, R.; Matyjaszewski, K. Superhydrophilic surfaces via polymer-SiO₂ nanocomposites. *Langmuir* **2010**, *26*, 15567–15573.
 - 52 Slugovc, C. The ring opening metathesis polymerisation toolbox. *Macromol. Rapid Commun.* **2004**, *25*, 1283–1297.
 - 53 Cretich, M.; Sadini, V.; Damin, F.; Pelliccia, M.; Sola, L.; Chiari, M. Coating of nitrocellulose for colorimetric DNA microarrays. *Anal. Biochem.* **2010**, *397*, 84–88.
 - 54 Terada, Y.; Hashimoto, W.; Endo, T.; Seto, H.; Murakami, T.; Hisamoto, H.; Hoshino, Y.; Miura, Y. Signal amplified two-dimensional photonic crystal biosensor immobilized with glyco-nanoparticles. *J. Mater. Chem. B* **2014**, *2*, 3324–3332.
 - 55 Hoyle, C. E.; Bowman, C. N. Thiol-ene click chemistry. *Angew. Chem. Int. Ed.* **2010**, *49*, 1540–1573.
 - 56 Sinha, A. K.; Equbal, D. Thiol-ene reaction: synthetic aspects and mechanistic studies of an anti-markovnikov-selective hydrothiolation of olefins. *Asian J. Org. Chem.* **2019**, *8*, 32–47.
 - 57 Kharkar, P. M.; Rehmann, M. S.; Skeens, K. M.; Maverakis, E.; Kloxin, A. M. Thiol-ene click hydrogels for therapeutic delivery. *ACS Biomater. Sci. Eng.* **2016**, *2*, 165–179.
 - 58 Sticker, D.; Geczy, R.; Häfeli, U. O.; Kutter, J. P. Thiol-ene based polymers as versatile materials for microfluidic devices for life sciences applications. *ACS Appl. Mater. Interfaces* **2020**, *12*, 10080–10095.
 - 59 Li, M.; Bresson, B.; Cousin, F.; Fretigny, C.; Tran, Y. Submicrometric films of surface-attached polymer network with temperature-responsive properties. *Langmuir* **2015**, *31*, 11516–11524.
 - 60 Chollet, B.; Li, M.; Martwong, E.; Bresson, B.; Fretigny, C.; Tabeling, P.; Tran, Y. Multiscale surface-attached hydrogel thin films with tailored architecture. *ACS Appl. Mater. Interfaces* **2016**, *8*, 11729–11738.
 - 61 Chollet, B.; D'Eramo, L.; Martwong, E.; Li, M.; Macron, J.; Mai, T. Q.; Tabeling, P.; Tran, Y. Tailoring patterns of surface-attached multiresponsive polymer networks. *ACS Appl. Mater. Interfaces* **2016**, *8*, 24870–24879.
 - 62 Khire, V. S.; Yi, Y.; Clark, N. A.; Bowman, C. N. Formation and surface modification of nanopatterned thiol-ene substrates using step and flash imprint lithography. *Adv. Mater.* **2008**, *20*, 3308–3313.
 - 63 Resetco, C.; Hendriks, B.; Badi, N.; Du Prez, F. Thiol-ene chemistry for polymer coatings and surface modification—building in sustainability and performance. *Mater. Horiz.* **2017**, *4*, 1041–1053.
 - 64 Seidi, F.; Zhao, W.; Xiao, H.; Jin, Y.; Zhao, C. Layer-by-layer assembly for surface tethering of thin-hydrogel films: design strategies and applications. *Chem. Rec.* **2020**, *20*, 1–26.
 - 65 Du, H.; Wang, Y.; Yao, X.; Luo, Q.; Zhu, W.; Li, X.; Shen, Z. Injectable cationic hydrogels with high antibacterial activity and low toxicity. *Polym. Chem.* **2016**, *7*, 5620–5624.
 - 66 Kurowska, M.; Eickenscheidt, A.; Guevara-Solarte, D. L.; Widyaya, V. T.; Marx, F.; Al-Ahmad, A.; Lienkamp, K. A Simultaneously antimicrobial, protein-repellent, and cell-compatible polyzwitterion network. *Biomacromolecules* **2017**, *18*, 1373–1386.
 - 67 Kurowska, M.; Widyaya, T. V.; Al-Ahmad, A.; Lienkamp, K. Surface-attached poly(oxanorbornene) hydrogels with antimicrobial and protein-repellent moieties: the quest for simultaneous dual activity. *Materials* **2018**, *11*, 1411.
 - 68 He, M.; Wang, Q.; Shi, Z.; Xie, Y.; Zhao, W.; Zhao, C. Inflammation-responsive self-regulated drug release from ultrathin hydrogel coating. *Colloids Surf. B Biointerfaces* **2017**, *158*, 518–526.
 - 69 Ye, Q.; Zhou, F.; Liu, W. Bioinspired catecholic chemistry for surface modification. *Chem. Soc. Rev.* **2011**, *40*, 4244–4258.
 - 70 Faure, E.; Falentin-Daudré, C.; Jérôme, C.; Lyskawa, J.; Fournier, D.; Woisel, P.; Detrembleur, C. Catechols as versatile platforms in polymer chemistry. *Prog. Polym. Sci.* **2013**, *38*, 236–270.
 - 71 Qiu, W. Z.; Wu, G. P.; Xu, Z. K. Robust coatings via catechol-amine coposition: mechanism, kinetics, and application. *ACS Appl. Mater. Interfaces* **2018**, *10*, 5902–5908.
 - 72 Saiz-Poseu, J.; Mancebo-Aracil, J.; Nador, F.; Busqué, F.; Ruiz-Molina, D. The chemistry behind catechol-based adhesion. *Angew. Chem. Int. Ed.* **2019**, *58*, 696–714.
 - 73 Lyu, Q.; Hsueh, N.; Chai, C. L. L. The chemistry of bioinspired catechol(amine)-based coatings. *ACS Biomater. Sci. Eng.* **2019**, *5*, 2708–2724.
 - 74 Tosatti, S.; Michel, R.; Textor, M.; Spencer, N. D. Self-assembled monolayers of dodecyl and hydroxy-dodecyl phosphates on both smooth and rough titanium and titanium oxide surfaces. *Langmuir* **2002**, *18*, 3537–3548.
 - 75 Lee, H.; Scherer, N. F.; Messersmith, P. B. Single-molecule mechanics of mussel adhesion. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 12999.
 - 76 Su, J.; Chen, F.; Cryns, V. L.; Messersmith, P. B. Catechol polymers for pH-responsive, targeted drug delivery to cancer cells. *J. Am. Chem. Soc.* **2011**, *133*, 11850–11853.
 - 77 Mizrahi, B.; Khoo, X.; Chiang, H. H.; Sher, K. J.; Feldman, R. G.; Lee, J. J.; Irusta, S.; Kohane, D. S. Long-lasting antifouling coating from multi-armed polymer. *Langmuir* **2013**, *29*, 10087–10094.
 - 78 Xu, L. Q.; Pranantyo, D.; Neoh, K. G.; Kang, E. T.; Teo, S. L. M.; Fu, G. D. Synthesis of catechol and zwitterion-bifunctionalized poly(ethylene glycol) for the construction of antifouling surfaces. *Polym. Chem.* **2016**, *7*, 493–501.
 - 79 Wei, Q.; Becherer, T.; Noeske, P. L. M.; Grunwald, I.; Haag, R. A universal approach to crosslinked hierarchical polymer multilayers as stable and highly effective antifouling coatings. *Adv. Mater.* **2014**, *26*, 2688–2693.
 - 80 Wei, Q.; Becherer, T.; Mutihac, R. C.; Noeske, P. L. M.; Paulus, F.; Haag, R.; Grunwald, I. Multivalent anchoring and cross-linking of mussel-inspired antifouling surface coatings. *Biomacromolecules* **2014**, *15*, 3061–3071.

- 81 Banerjee, I.; Pangule, R. C.; Kane, R. S. Antifouling coatings: recent developments in the design of surfaces that prevent fouling by proteins, bacteria, and marine organisms. *Adv. Mater.* **2011**, *23*, 690–718.
- 82 LaVoie, M. J.; Ostaszewski, B. L.; Weihofen, A.; Schlossmacher, M. G.; Selkoe, D. J. Dopamine covalently modifies and functionally inactivates parkin. *Nat. Med.* **2005**, *11*, 1214–1221.
- 83 Gillich, T.; Benetti, E. M.; Rakhmatullina, E.; Konradi, R.; Li, W.; Zhang, A.; Schlüter, A. D.; Textor, M. Self-assembly of focal point oligo-catechol ethylene glycol dendrons on titanium oxide surfaces: adsorption kinetics, surface characterization, and nonfouling properties. *J. Am. Chem. Soc.* **2011**, *133*, 10940–10950.
- 84 Kang, S. M.; You, I.; Cho, W. K.; Shon, H. K.; Lee, T. G.; Choi, I. S.; Karp, J. M.; Lee, H. One-step modification of superhydrophobic surfaces by a mussel-inspired polymer coating. *Angew. Chem. Int. Ed.* **2010**, *49*, 9401–9404.
- 85 Liu, X.; Deng, J.; Ma, L.; Cheng, C.; Nie, C.; He, C.; Zhao, C. Catechol chemistry inspired approach to construct self-cross-linked polymer nanolayers as versatile biointerfaces. *Langmuir* **2014**, *30*, 14905–14915.
- 86 Peng, L.; Luo, Y.; Zheng, Y.; Zhang, W.; Chen, G. Sunlight-induced raft synthesis of multifaceted glycopolymers with surface anchoring, *in situ* AgNP formation, and antibacterial properties. *ACS Appl. Nano Mater.* **2018**, *1*, 2219–2226.
- 87 Peng, L.; Li, Z.; Li, X.; Xue, H.; Zhang, W.; Chen, G. Integrating sugar and dopamine into one polymer: controlled synthesis and robust surface modification. *Macromol. Rapid Commun.* **2017**, *38*, 1600548.
- 88 Peng, L.; Zhou, S.; Yang, B.; Bao, M.; Chen, G.; Zhang, X. Chemically modified surface having a dual-structured hierarchical topography for controlled cell growth. *ACS Appl. Mater. Interfaces* **2017**, *9*, 24339–24347.
- 89 Ma, L.; Qin, H.; Cheng, C.; Xia, Y.; He, C.; Nie, C.; Wang, L.; Zhao, C. Mussel-inspired self-coating at macro-interface with improved biocompatibility and bioactivity via dopamine grafted heparin-like polymers and heparin. *J. Mater. Chem. B* **2014**, *2*, 363–375.
- 90 Ma, L.; Cheng, C.; Nie, C.; He, C.; Deng, J.; Wang, L.; Xia, Y.; Zhao, C. Anticoagulant sodium alginate sulfates and their mussel-inspired heparin-mimetic coatings. *J. Mater. Chem. B* **2016**, *4*, 3203–3215.
- 91 Wang, R.; Xie, Y.; Xiang, T.; Sun, S.; Zhao, C. Direct catechol conjugation of mussel-inspired biomacromolecule coatings to polymeric membranes with antifouling properties, anticoagulant activity and cytocompatibility. *J. Mater. Chem. B* **2017**, *5*, 3035–3046.
- 92 Arlov, Ø.; Aachmann, F. L.; Sundan, A.; Espevik, T.; Skjåk-Bræk, G. Heparin-like properties of sulfated alginates with defined sequences and sulfation degrees. *Biomacromolecules* **2014**, *15*, 2744–2750.
- 93 Dinoro, J.; Maher, M.; Talebian, S.; Jafarkhani, M.; Mehrli, M.; Orive, G.; Foroughi, J.; Lord, M. S.; Dolatshahi-Pirouz, A. Sulfated polysaccharide-based scaffolds for orthopaedic tissue engineering. *Biomaterials* **2019**, *214*, 119214.
- 94 Xu, G.; Pranantyo, D.; Xu, L.; Neoh, K. G.; Kang, E. T.; Teo, S. L. M. Antifouling, antimicrobial, and antibiocorrosion multilayer coatings assembled by layer-by-layer deposition involving host-guest interaction. *Ind. Eng. Chem.* **2016**, *55*, 10906–10915.