Freie Universität Berlin

# Mussel-Inspired Polyglycerols as Universal Bioinert and Multifunctional Coatings

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The work presented herein was carried out in the research group of Prof. Dr. Rainer Haag from July 2011 until December 2014 at the Institute of Chemistry and Biochemistry of the Freie Universität Berlin, and in collaboration with the Fraunhofer-Institut für Fertigungstechnik und Angewandte (IFAM) in the research group of Prof. Dr. Andreas Hartwig.

Hereby I certify that the work presented in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text.

I also certify that the thesis has been written by me. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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Date and Signature

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Dedicated to my wife

人生得意须尽欢，
莫使金樽空对月。
天生我材必有用，
千金散尽还复来。
—《将进酒》（李白，701 年－762 年）

Do enjoy life while in prime you run high;
Not to the moon just your empty cup ply.
So born by heaven we must be of use;
Spend all the money and more will come up.
—*Drinking Revelry* (Author: Bai Li, A.D. 701-762, China)
translated by Yanchun Zhao

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# Table of Contents

# 1 Introduction

## 1.1 Universal Polymer Coatings

Polymer coatings on solid materials play an increasingly important role in modern physical, chemical, and medical science.[1-2] Thiol and siloxane chemistry are commonly used to modify noble metal and hydroxylated surfaces, respectively.[3-4] Besides the widely used self-assembled monolayer (SAM) and chemical surface immobilization that are induced by these and other anchor groups, Langmuir-Blodgett deposition,[5] layer-by-layer assembly,[6] irradiation,[7] and electrostatic or hydrophobic adsorption[8-9] are well established. However, most of these technologies require specific chemical or physical substrate properties, and thus have failed to become substrate-independent universal coatings.

Chemical specificities like a covalent binding between polymeric modifiers and surfaces must be avoided in order to modify a wide range of substrates, because no anchor can be active on all of the different surface compositions. Although, some of the irradiation technologies can activate many kinds of surfaces, the efficiency and the density of the active sites are relatively low on some surfaces. Therefore, they should be treated by other methods, e.g., polymerization, to obtain dense surface coatings.[10-11] On the other hand, noncovalent interactions like electrostatic interaction, hydrogen bonding, hydrophobic attraction, and van der Waals interaction occur on nearly all types of interfaces. Thus multiple noncovalent interactions can be recognized as the driving force for constructing polymer coatings on different kinds of surfaces. Admittedly, most of the noncovalent interactions in interfaces are not strong enough to tether polymer coatings for practical applications. Therefore additional intra-layer interactions, i.e., physical and chemical crosslinking must take place to enhance the stability of the coatings.

Crosslinking can either be initiated while anchoring the coating, or in the interior of precast layers (**Figure 1**). In the former case, one-pot coating is easy and rapid. However, spontaneous crosslinking may cause the polymeric modifiers to aggregate,

which makes the surface morphology less controllable. In the latter case using precast layers, further crosslinking procedures like heating or irradiation are required, which must be well designed to avoid decreasing the performance of the coatings.

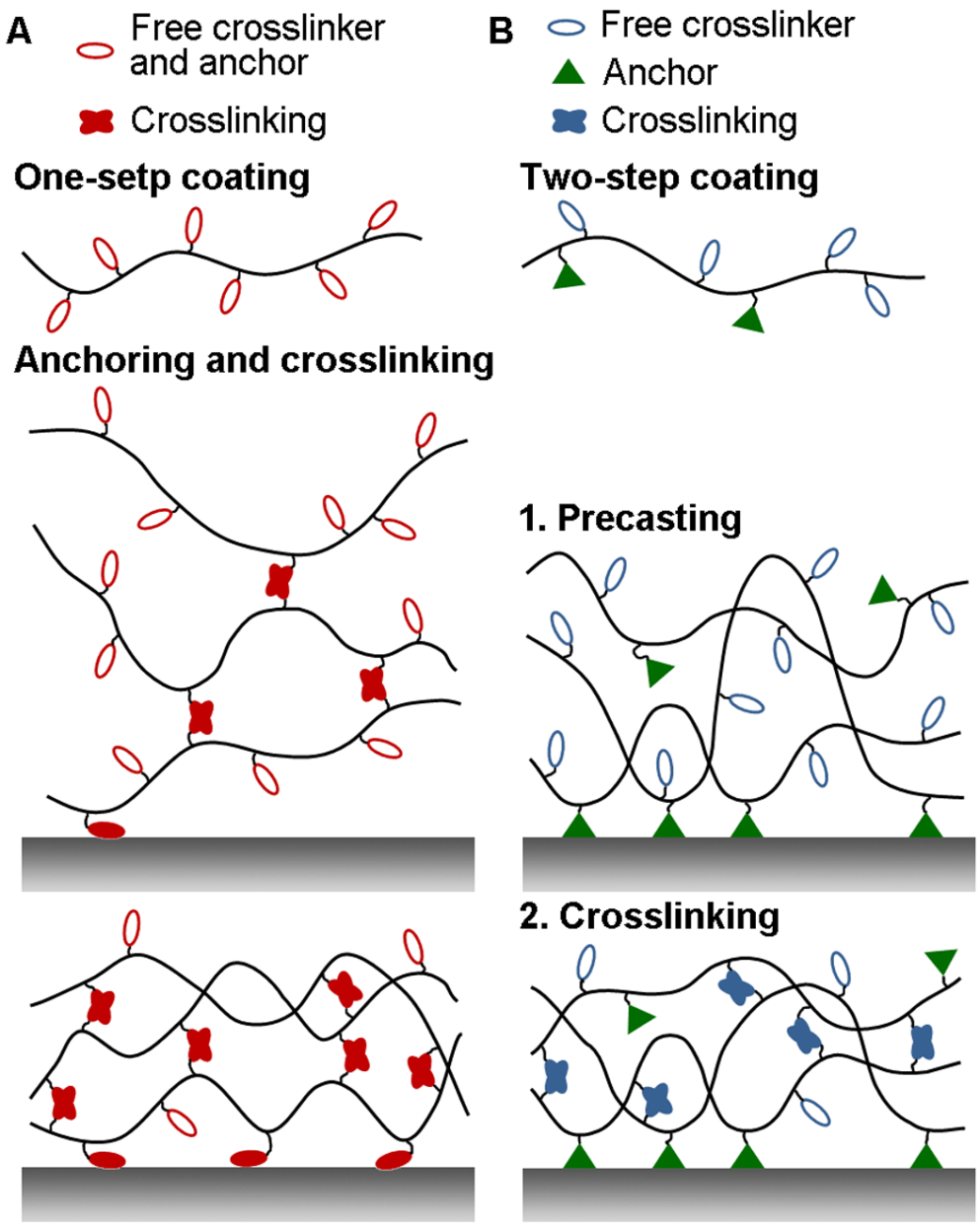



**Figure 1.** Universal coatings can be stabilized on different kinds of surfaces by interior crosslinking, which can be achieved either (A) by initiating crosslinking together with anchoring or (B) by crosslinking a precast layer.

A secondary functionalization of these universal coatings is normally required to achieve specific surface characteristics. Thus, there must be enough active groups remaining in the coatings for further modification. The most important surface coatings in biomedical applications include bioinert, biospecific, and antibacterial coatings. A bioinert surface requires dense and stable coatings to prevent protein adsorption on the molecular level and to further repel cell adhesion.[2] These coatings must be hydrophilic and electrically neutral, and contain hydrogen bond accepting groups but not hydrogen bond donating groups.[12-13] Biospecific surfaces, which contain cell recognition motives, are another approach to modulate cell interaction on the surface of a biomedical device.[1] A relatively low density of functionalization is sufficient to trigger cell adhesion. In the case of arginylglycylaspartic acids (RGDs), a minimum density as low as 1 fmol per $cm^2$ was reported for cell spreading and 10 fmol per $cm^2$ for forming focal contacts and stress fibers on a surface.[14] Inspired by a cell membrane that contains bioactive carbohydrates and proteins in the bioinert background of a phospholipid bilayer, biospecific molecules can be combined with bioinert coatings to increase the efficacy of the biological communication.[1-2] As a result, implanted surfaces would only integrate with, for example, endothelial cells, and prevent leukocyte and other cells. When constructing such combined coatings, it is important to achieve multifunctionalization on universal coatings. Antibacterial agents are usually immobilized for antibacterial surfaces.[15] Bioinert materials are often combined with antibacterial agents to repel bacteria adhesion and improve the biocompatibility of the coatings. Besides these three kinds of coatings, multiple functional surfaces, e.g., infection-resistant, anticoagulated, self-cleaning surfaces, can be developed by immobilizing different functional molecules[16-17] on the active universal coatings.

Summarizing and understanding the present universal coating systems is a good way to identify common features and general rules for developing universal polymer coatings and to reveal drawbacks that still need to be improved. Some perspectives on future development will be also raised.

## 1.2 Irradiative Chemisorption

High energy ionizing radiation can directly generate initiation sites by liberating electrons from atoms or molecules near the material surfaces. These positively charged initiation sites can immediately react with other molecules to generate functional groups for further surface modifications. Different radiation methods, including plasma, ultraviolet (UV), gamma ray, microwave, laser, electron beam, etc., have been employed to active correspondingly material surfaces.[18]

Plasma exposure is the most common radiation method. However, plasma, which can easily activate organic surfaces, does not do equally well with inorganic surfaces.[10] Thus, plasma polymerization of monomers with vinyl groups has become a general way to functionalize different solid surfaces.[10, 19-20] As a result, highly crosslinked polymer films can be stably deposited on substrates via polyvalent anchoring.[19] Various chemical surface functionalities like anhydride-,[10] amino-,[19] epoxide-,[21] and perfluoroalkyl- groups,[22] can be achieved by employing different monomers (**Figure 2**).

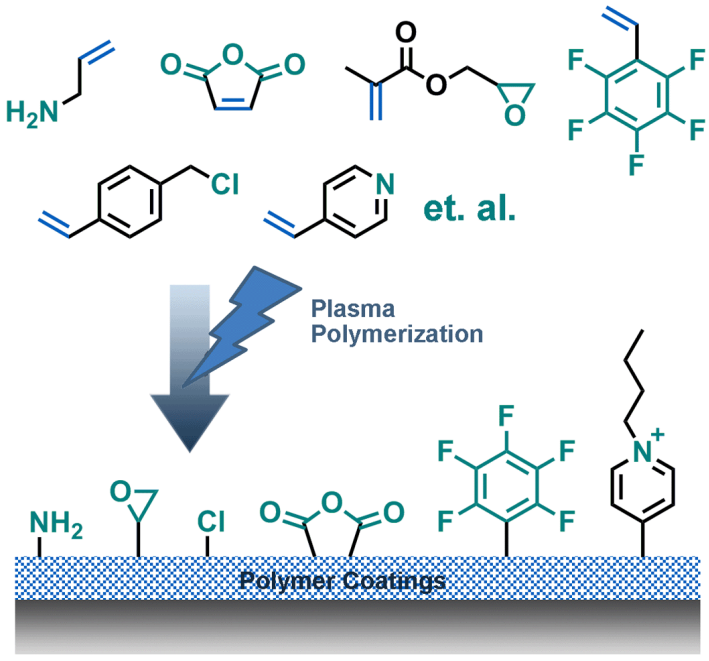



**Figure 2.** Various functional universal coatings can be achieved by plasma polymerization with different monomers.

Long-term irradiation may change the properties of the functional groups of the monomers. Pulsed plasma with short on-periods and long off-times was proven to deposit polymer films with a higher degree of molecular specificity than traditional continuous wave plasma.[10] The active sites in gas phase and at the growing film surface could be generated in the short plasma duty cycle on-period (microseconds), which initiated polymerization during the longer plasma off-period (milliseconds).[23]

Alternatively, polymeric targets, such as polytetrafluoroethylene (PTFE), polyimide, and polyolefin, have been sputtered to form coatings by radio frequency (RF) magnetron sputtering.[24] Powerful magnets cause the emission of volatile fragments from the polymeric targets. These fragments take part in the plasma polymerization process and line up on the substrates to form thin films. Since the polymeric targets are provided in a solid state, fewer safety precautions are required than handling the gas of monomers in plasma polymerization.[25] To achieve the secondary modification, amino-rich thin films were prepared by sputtering Nylon 6,6 target in a mixture of $N_2/H_2$ or $N_2$/Ar. As a result, a high $NH_2$/C ratio in the coatings was achieved.[25]

The amino groups presented in the plasma polymerized polyallylamine coatings and RF magnetron sputtered nylon coatings are suitable for immobilization of atom transfer radical polymerization (ATRP) initiators via amide linkages.[11, 19] Bioinert polymer brushes of poly(oligoethylene glycol methacrylate) or poly(carboxybetaine acrylamide) can be subsequently initiated from the functional surfaces, which has resulted in dramatically decreased protein adsorption on the solid surfaces.[11]

The plasmachemical functionalization of surfaces with poly(4-vinyl pyridine) coatings yielded bactericidal activity towards *Staphylococcus aureus* (Gram positive) and *Klebsiella pneumoniae* (Gram negative), after quaternization of the pyridine moieties with bromobutane.[26]

Patterned functional surfaces were developed by depositing two separate functional nanolayers, including an active bottom layer of poly(glycidyl methacrylate)

and a passive release top layer of poly(pentafluorostyrene) on the substrates. A selective lift-off of the top layer by a prepatterned adhesive template resulted in the exposure of the underlying active layer.[27]

Surface irradiation methods are easy control methods for film growth on different substrates. In many cases, solvent is not required and the coating processes are suitable for large-scale film deposition. However, the irradiation may change the property of the substrates, especially the ultrathin substrate layers. Additionally, irradiation or deposition can be limited by the shape of the substrates. Thus, physisorbed universal coatings can be considered as alternatives.

## 1.3 Physisorption

Typical physisorption methods to prepare surface coatings include electrostatic attraction, van der Waals force, and hydrophobic interaction. Based on these universal interactions, some technologies, including layer-by-layer (LbL) assembly, spin coating, and chemical vapor deposition (CVD), have been developed to achieve some universal coating systems.

### *1.3.1 Electrostatic Attraction*

Polyelectrolytes are the candidates to anchor the substrate surface via electrostatic attraction. Monolayer brushes of block copolymers, which can be adsorbed through the polyionic block onto the surface and prevent further adsorption via the other flexible block, only work on inorganic oxide surfaces.[28] The layer-by-layer (LbL) assembly technique is more universal, because it does not dependent the nature, size, and topology of the substrate so much.[6] Some LbL assembly systems indeed successfully fabricate multicomponent thin films on a wide range of surfaces by consecutive adsorption of polyanions and polycations. The electrostatic attraction between oppositely charged and flexible polymers has the least steric demand of all

the chemical bonds building and stabilizing fuzzy layered LbL assembled multilayers.

An alternate electrostatic assembly of cationic poly(allylamine hydrochloride) (PAH) and anionic poly(sodium 4-styrenesulfonate) (PSS) has been deposited on a variety of material surfaces, including glass, gold, mica, silicon, and polymer. The properties of the different underlying surfaces were completely converted to the surface properties of the polyelectrolyte coatings.[29] This chemically active scaffold can be further utilized to fabricate protein microarrays. Mouse IgG has been immobilized on PAH-capped polyelectrolyte coatings. The rest of the surface was then blocked with bovine serum albumin (BSA). The nearly identical specific signal intensities of anti-mouse IgG with low nonspecific binding can be observed on the tested dissimilar substrates.[29]

The LbL assembly is however a time-consuming process, especially for fabrication of thick films.[30] Large dimensional building blocks with fast adsorption kinetics can realize a rapid fabrication and have been built with mesoporous silica ($MSiO_2$) nanoparticles were employed with cationic poly(diallyldimethylammonium chloride) (PDDA) to assemble a substrate-independent thick coating with only three coating cycles.[31] This coating exhibited both antireflection and antifogging properties, because the rough surface morphology and nanopores in the $MSiO_2$ nanoparticles resulted in superhydrophilic surface performance. A maximum transmittance of 99.9% was achieved in the visible spectral range, under optimal conditions.

### *1.3.2 Van der Waals and Hydrophobic Interactions*

The relatively weak van der Waals and hydrophobic interactions can also be used to anchor universal coatings, if the intra-coating crosslinking is well designed.

A mixture of hydrophilic amine- and epoxy-terminated four-arm polyethylene glycols (PEGs) was spin-coated on a flat substrate. After chemically crosslinking these macromonomers under gentle heating, a hydrogel-like coating with tunable film

thicknesses of 4-200 nm was fabricated on a broad variety of solid substrates. Because of its controllable swelling behavior, this coating was able to adsorb a high density of citrate-stabilized gold nanoparticles (AuNP) from aqueous solution and resulted in PEG/AuNP composite films.[32]

In a similar approach, hydrophobic benzocyclobutene-functionalized random copolymers of styrene and methyl methacrylate [P(S-r-BCB-r-MMA)] were spin coated on a wide variety of metal, metal oxide, semiconductor, and polymeric surfaces to produce thin films.[33] The styrene moieties of the copolymers induced balanced interfacial interactions on the surfaces.[34] After heating under 200-250 ℃, the reactive benzocyclobutene (BCB) moieties resulted in the crosslinking reactions. These crosslinked films were resistant to solvents and formed a robust coating on the substrates. By the same way, a hybrid polymer composed of poly(methylsilsesquioxane) (PMSSQ) block and poly(pentafluorophenyl acrylate) (PFPA) blocks has been employed to coat different materials.[35] PMSSQ blocks initiated crosslinking after spin coating, while the PFPA blocks enabled a variable secondary functionalization of the coatings.

In the above crosslinkable PEGs, the coating mainly interacted with substrates by van der Waals force. Keeping this kind of hydrophilic coating stable in water solution for long term is a big challenge, because water can shear off the whole coating, which makes it preferable to use hydrophobic coatings. Nonpolar substances tend to aggregate or adsorb on solid surfaces in aqueous solution and repel water molecules. Since water is the most common solvent in our daily life, the hydrophobic interactions have successfully generated a set of universal coatings including chemical vapor deposition (CVD) of poly(*p*-xylylenes).

Chemical vapor deposition (CVD), which is often used in the semiconductor industry to produce thin films, can also fabricate hydrophobic coatings of poly(*p*-xylylenes) and derivatives for a wide range of substrates including PTFE (**Figure 3**).[36] In the CVD polymerization process, diradicals of [2.2]paracyclophane or its derivatives have been obtained during vaporization under heating and vacuum.

The diradicals are then deposited on the substrate during polymerization. It has been reported that these CVD polymers strongly anchor on substrate surfaces and are insoluble in common organic solvents.[37] It is reasonable to speculate that the chain transfer in such radical-rich polymerizations may have resulted in chemical crosslinking, which highly stabilized the deposited coatings as well as intermolecular hydrophobic interactions and π-stacking. The copolymers of [2.2]paracyclophane and its functionalizal derivatives have generated multifunctionalizal CVD coatings, which can be widely used in biomedical applications. Using a vacuum deposition overcomes the limitations caused by solvents and additives in dip coating procedures,[37] so that highly pure coatings can be obtained. However for production every CVD step requires a vacuum chamber.

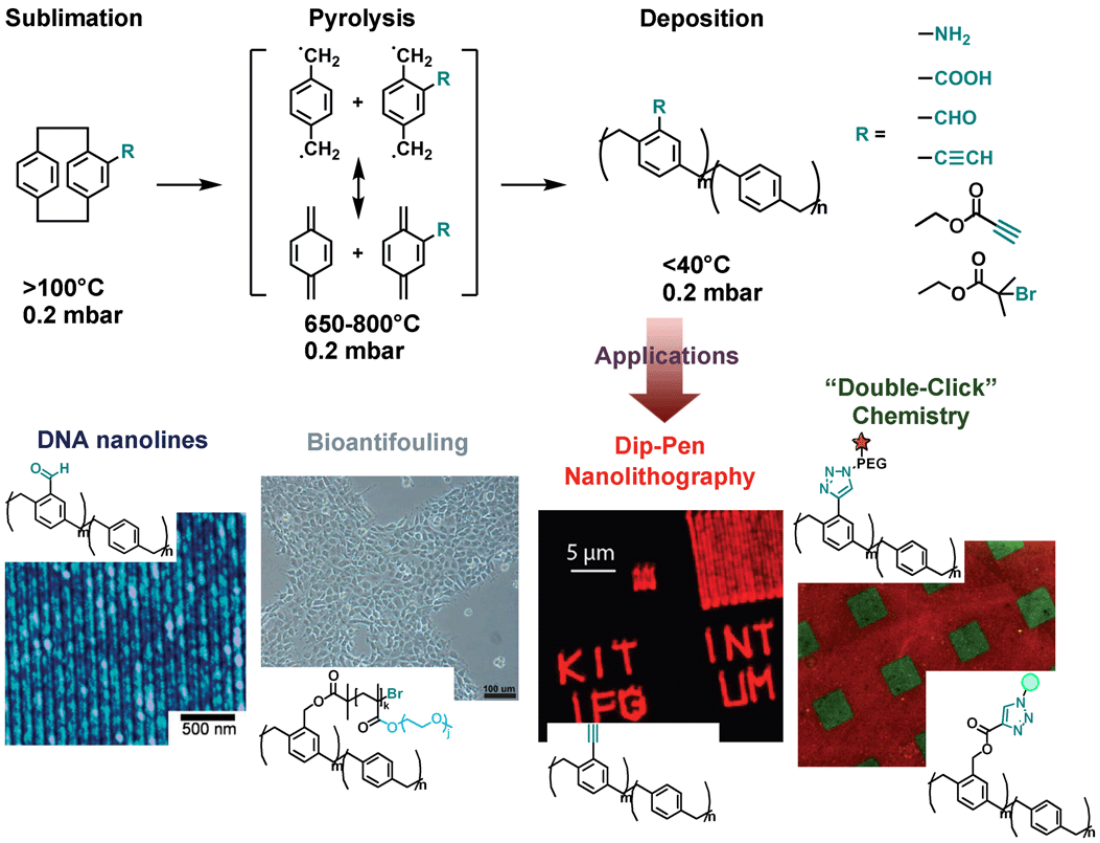



**Figure 3.** Chemical vapor deposition (CVD) polymerization with various monomers to achieve multifunctional universal coatings. Reprinted from Ref. [38-41] with kind permission of Wiley and The American Chemical Society.

Bioactive surface CVD coatings are good platforms for immobilizing biomolecules and even mammalian cells. The anhydride-rich coating of poly(p-xylylene-2,3-dicarboxylic anhydride) can immobilize amino-terminated biotin ligands which selectively bind to streptavidin. The biotin-conjugated human anti-$\alpha_5$-integrins were then immobilized on the streptavidin and specifically interacted with endothelial cells.[42] Surfaces that "click" have been developed by alkyne-containing vapor deposited polymer coatings. The polymers with monoalkyne grafted [2.2]paracyclophane have generated excellent adhesion and stability, even at 680 ℃ and in many organic solvents. On the other hand, enough alkynes were exposed on the surfaces to react with azide-containing biotin-based ligands[43] or support the dip-pen nanolithography by "click chemistry".[40] In a further development, a bioorthogonal immobilization of biotins and streptavidins was carried out with a copper-free click reaction on the CVD coatings.[41] A propiolate moiety, which contained a electron-withdrawing group in proximity of the alkyne, was identified for copper-free click reaction with azide groups. Moreover, this propiolate moiety modified [2.2]paracyclophane derivative was compatible with the processing conditions during CVD polymerization without decomposition or side reactions. With alkynyl moiety for copper-catalyzed reactions, a two-step cascade of bioorthogonal reaction sequentially immobilized different biomolecules on separate areas of the same surface.[41] Additionally, aldehyde functionalized CVD coatings could link to 5' amine modified complementary DNA sequences by forming imine bonds. Thus, poly(4-formyl-*p*-xylylene-co-*p*-xylylene) was deposited on different substrates to serve as a "replica" to collect DNA microarrays from microcontact printing.[38]

Besides the immobilization of biomolecules, initiators for atom transfer radical polymerization (ATRP) can be directly immobilized to the CVD monomers and be polymerized and deposited on the different kinds of substrates including stainless steel, glass, silicon, poly(dimethylsiloxane), poly(methyl methacrylate), poly(tetrafluoroethylene), and polystyrene.[39] This polymeric initiator coating

initiated ATRP of oligo(ethylene glycol) methyl ether methacrylate to produce a bioinert polymeric coating as thick as 300 nm. Both protein adsorption and cell adhesion were significantly inhibited on this bioinert coating.

Overall, versatile physisorption based universal coatings have been developed that overcome many problems in irradiated chemisorptions. The inherently weak anchoring interactions of the physisorbed coatings, however, can become thermally unstable. These coatings may also be displaced by other solutes in solution.

## 1.4 Bioinspiration

Nature has a tendency to excellently and precisely solve problems from which many artificial systems are suffering. Learning from nature is an endless source of inspiration. In the present section, the universal coatings that have been inspired or directly collected from the natural biological systems of blood proteins, mussel foot proteins, and plant phenols will be described and discussed.

### *1.4.1 Blood Proteins*

It is well known that blood proteins nonspecifically adsorb on blood contact surfaces within seconds via multiple interactions such as van der Waals force, ionic or electrostatic attraction, hydrogen bonds, and hydrophobicity.[2] An approach involving blood proteins to modify both flat and nonwoven substrates has been reported.[44] A set of proteins, including α-lactalbumin, lysozyme, fibrinogen, and soy globulins (glycinin and β-conglycinin), were denatured at their isoelectric point (pI). Under these conditions, a maximum amount of proteins could be adsorbed onto the substrates, because the electrostatic repulsion among protein molecules was limited.[45] Denaturation helped the hydrophobic domains of the proteins be adsorbed on the substrates with the result that the hydrophilic amino and hydroxyl groups could be exposed on the surface for secondary modification. To stabilize the coatings, the

adsorbed protein layers were crosslinked with glutaraldehyde in the presence of sodium borohydride. The ATRP initiator molecules could then be immobilized on the amino and hydroxyl groups, from which poly(2-hydroxyethyl methacrylate) (PHEMA) polymer brushes were grown. By combining the fluorinating moieties, these amphiphilic polymer brushes efficiently prevented further nonspecific protein adsorption.[46] Although these protein based coatings were only reported for modifying polyolefin surfaces, it is possible to apply these coatings on a wide range of material surfaces because of the nonspecific adsorption of proteins quite general on solid surfaces. The main problem for this coating system may be long-term stability, since protein layers can be degradable in physiological environments.

### *1.4.2 Mussel Foot Proteins*

#### *1.4.2.1 Dopamine*

Mussels adhere to virtually all types of material surfaces with byssus as the holdfast. The byssus contains 25-30 kinds of mussel foot proteins (mfps), which are the keys for fast solidification and strong adhesion.[47] Inspired by the most two abundant functional groups of catechol and amine in mfps, dopamine has been recognized as a new and efficient precursor for developing active universal coatings with just a simple immersion (**Figure 4**).[48] To initiate the coating process, the catechol in dopamine must first be oxidized to quinone in alkaline solution or in the presence of an oxidant.[48-49] Although the mechanism for further polymerization of dopamine is still being debated,[50-52] it is widely agreed that dopamine forms oligomers up to the tetramer level[51] which then aggregate to form coatings via hydrogen bonding and π-stacking.[50, 52] Many mechanistic details of surface anchoring have already been revealed. Either a charge-transfer complex can form between the catechol and metal oxide surface[53] or a hydrogen bond between the catechol and a mica or silica surface.[54-55] Covalent bonds on nucleophile containing surfaces have also been reported.[56] The hydrophobic interaction, π-stacking, and van der Waals interaction

between the catechol and inert polymer surfaces have been discussed as well.[57-58] Whereby, the high crosslinking by both covalent and noncovalent bonding definitely enhances the stability of the polydopamine coatings.

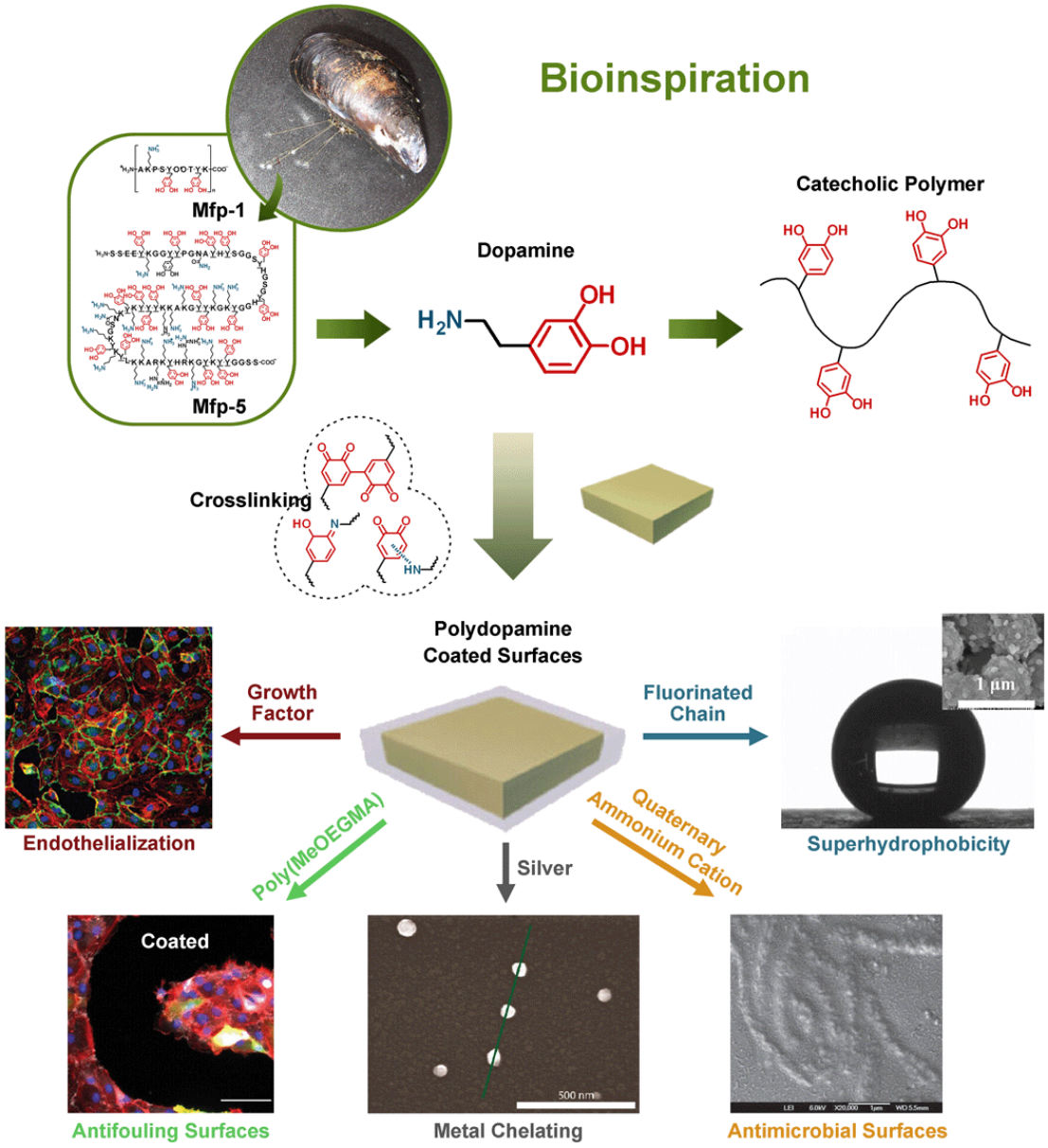



**Figure 4.** Mussel-inspired polydopamine as universal mltifunctional coatings. The structures of Mfp-1 and Mfp-5 were extracted from Ref. [47]. Reprinted from Ref. [59-63] with kind permission of Wiley and The American Chemical Society.

Native polydopamine coatings already show low cytotoxicity and can promote the

adhesion of osteoblasts[64] and endothelial cells,[65] because the critical surface tension of polydopamine (39.2 dynes/cm) is in the suitable range for cell adhesion (35-40 dynes/cm).[66] Furthermore, a number of secondary modifications can be applied by immobilizing different functional molecules to polydopamine coatings via the residual free amines and catechols.[17] Bioinert polymer layers have been created by both "grafting to" and "grafting from" approaches, as well as by LbL assembly on polydopamine coatings to achieve substrate-independent surface modification.[60, 67-68] Biospecific molecules, such as vascular endothelial growth factor,[59] adhesion peptides,[69] and glycosaminoglycan,[70] have been easily immobilized onto polydopamine coatings with an one-step immersion, and have resulted in specific cell adhesion. The metal chelating ability of the catechol groups in the coatings can cause in situ deposition of silver nanoparticles.[61] The silver nanoparticles or the grafted quaternary ammonium groups[62] on the coatings have exhibited strong and broad-spectrum antimicrobial activities. Moreover, the combination of bioinert layers with antibacterial moieties produced the dual fouling resistance and antibacterial properties of the coatings, which significantly improved the antibacterial performance of the surfaces.[61-62] The deposited silver nanoparticles on polydopamine coated microparticles resulted in a hierarchical structure similar to the micromorphology of lotus leaf. These composite particles became extremely water repellence after fluorination.[63] Although synthetic polydopamine coatings were just identified in 2007 by the Messesmith group,[48] it has already become one of the most widely applied universal coating due to its facile procedure and chemical versatility.

### *1.4.2.2 Dopamine Derivatives*

Several dopamine derivatives have been also identified that form different functionalized coatings. 3,4-Dihydroxyphenylalanine (DOPA) contains one more carboxylic group than dopamine. During the coating formation, the deprotonated carboxyl groups may repel the noncovalently bonded polyDOPA aggregates by

electrostatic repulsion, thus more covalently bonded DOPA molecules can be incorporated into the coatings. As a result, the polyDOPA coating showed better stability in strongly acidic and alkaline solutions.[71] A smoother coating can be developed by norepinephrine.[72] Norepinephrine represents the intermediate of 3,4-dihydroxybenzaldehyde (DHBA), which deactivates the amino group of norepinephrine by forming DHBA-norepinephrine. The deactivated amino group results in less crosslinking and obviously suppresses the aggregation of the coating. Polynorepinephrine can be used as an NO-loading scaffold for biomedical applications. NO can be stored as diazeniumdiolates which react with aliphatic secondary amino groups in the coatings. In addition, the extra hydroxyl group allows an efficient ring-opening polymerization of biodegradable monomers like ε-caprolactone.[73] The presence of the electron-withdrawing nitro group in the *p*-position lowers the pK of the nitrocatechol. This enhances the acidity and hydrogen bond donor character of catechol and increases its stability against oxidation.[74] The other significant feature is that the *o*-nitrophenyl ethyl moiety can be photocleavable.[75] Furthermore, chloro-catechol prevents microbial fouling due to its toxicity. The appropriate polymer-bound chloro-catechol groups showed effective antibacterial activity and were not toxic for the attached cells.[76] Functional molecules can also be immobilized onto the amine group of dopamine to obtain synthetic derivatives. A lysine-dopamine coating improved cell adhesion, promoted cell growth, accelerated endothelialization on the substrate surface, and provided plasma clot lysis activity.[77] The copolymerization of dopamine and ATRP initiator bearing dopamine (1:2) resulted in a colorless coating. Surface-initiated ATRP of 2-hydroxyethyl methacrylate (HEMA) can be performed from this coating.[78] A fluorinated dopamine derivative was developed by conjugating perfluorinated chains to the carboxyl group of DOPA.[79] The remaining amine and catechol groups resulted in a structurally rough film with the static water contact angles larger than 150 ° as a superhydrophobic surface.

*1.4.2.3 Catecholic Polymers*

Polymers with the appropriate amount of catechol groups can be directly coated onto material surfaces as functional universal coatings. Catechol-grafted PEG with 4-5 catechol side groups per polymer chain was employed for PEGylation on many different substrates.[80] Catechol-grafted poly(ethoxyethyl glycidyl ether-co-allyl glycidyl ether) with around 70 catechol side groups per polymer chain was also successfully coated on many types of substrates including PTFE.[81] This polymeric coating prevented cell attachment without further modification. After the coating was immobilized with 3-mercaptopropionic acid in a thiol-ene reaction, it exhibited excellent cell adhesion. Thus, it is possible to design and adjust cell adhesion with this universal coating.

Systematic studies, on how the grafting amount of catechol groups affects the coatings on different types of surfaces also have also been reported.[82] The thickness and stability of the polymer coatings can be controlled by catechol groups which work as both anchors and crosslinkers. In the case of metal oxide surfaces, although even one catechol group can tether the polymer chain, multiple catechol units are required in the anchor group to prevent the oxidative detachment.[83] In the case of inert polymeric substrates, such as PTFE, polystyrene, and polyolefin, the interaction between the catechol group and these surfaces is relatively weak.[57, 84] Besides weak anchoring, the other role of catechol as a crosslinker is important to stabilize the coatings on inert substrates. Therefore, a relatively large amount of catechol groups is required to achieve universal coatings. For the design of bioinert surface coatings, however, an overrepresentation of catechol groups leads to protein adsorption and cell adhesion. Only a well-balanced amount of catechol groups can supply coatings with both good stability and bioinertness.

Although catechol is a powerful anchor for surface coating, its effectiveness has been somewhat over praised in some previous publications, in which catecholic polymers were employed to coat inert surfaces. Actually, many multiple catechol functionalized polymers hardly reached a very high surface coverage on inert

surfaces.[82] The hydrophobic effect of the polymer itself has often been ignored, which may be the reason why effective coatings are obtained rather than catechol anchoring. Control experiments should be well designed to explore the further role of catechols in these cases.

Besides catechol induced surface adhesion, mussels limit the auto-oxidation of catechols on the surface of byssal plaques to enhance the adhesion by the thiol-rich mfp-6.[85] Other hydrophobic amino acid residues, mainly in mfp-3 “slow”, can retard oxidation of catechols by shielding them from the solvent and, more importantly, compensate the adhesion by hydrophobic interactions.[86] The adhesion of mussel byssus, however, is more complicated than a simple catechol-mediated recipe. There is still a long way to go in chemistry and materials science to really mimic mussel foot proteins to generate the best universal coatings.

### *1.4.3 Plant Phenols*

Tea cups are often stained by tea water. Inspired by this phenomenon, a number of phenolic biomolecules that are present in tea, red wine, chocolate, and many other plants have been identified for versatile universal coatings. These biomolecules possess abundant and dense catechol (1,2-dihydroxyphenyl) and gallol (1,2,3-trihydroxyphenyl) functional groups and thus exhibit strong solid-liquid interfacial properties. A plant polyphenol of tannic acid (TA) and a simple phenolic mimic of pyrogallol were deposited from buffered saline (0.6m NaCl, pH 7.8) to form polydopamine-like films.[87] These phenolic films retained most of the advantages of polydopamine films as multifunctional universal coatings, but they were low cost and colorless. In addition, these coatings could scavenge radical and non-radical reactive oxygen species. In a subsequent work, a library of about 20 kinds of natural and synthetic phenolic molecules was screened.[88] Among them, eight catechol-, gallol-, and resorcinol-rich molecules were identified to form excellent universal coatings. Besides TA and pyrogallol, the other six precursors were epigallocatechin gallate

(EGCG), epigallocatechin (EGC), catechin, catechol, hydroxyhydroquinone (HHQ), and Morin (**Figure 5A**). As the polymerization and deposition of dopamine could be accelerated by oxidant,[49] the laccase-catalyzed polymerization of plant phenols also resulted in a rapid coating formation.[89] In fact, the research on oxidant-induced polydopamine coatings and the enzymatic polymerization of phenols can be unified with each other.

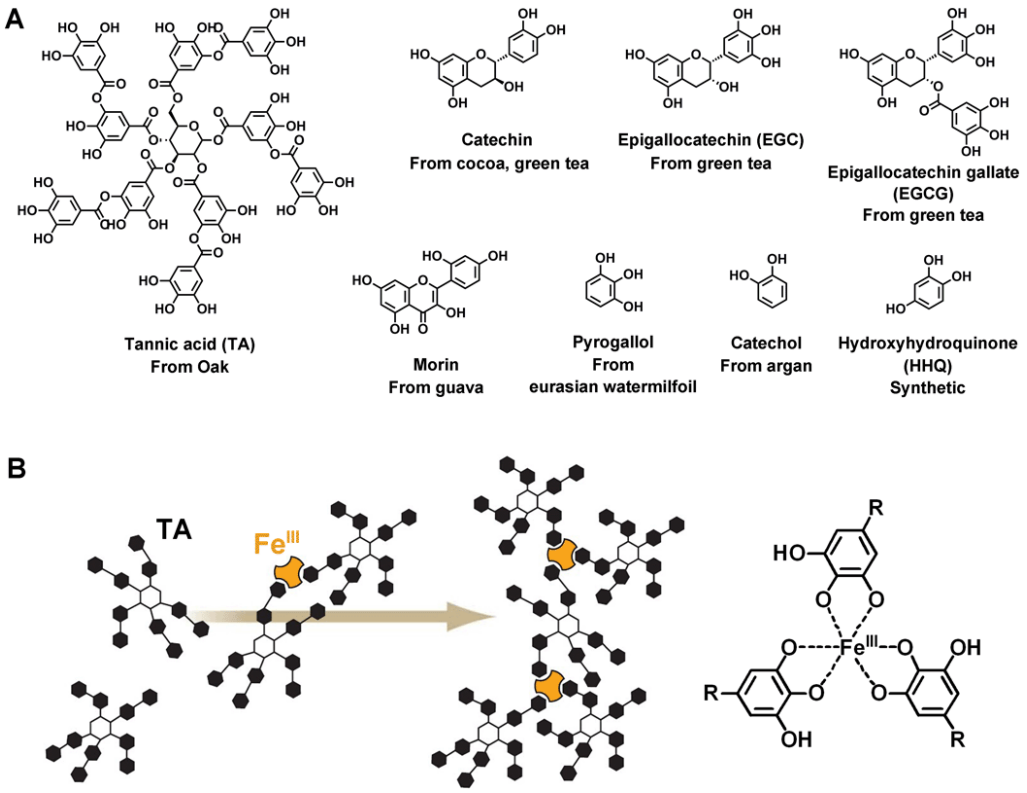



**Figure 5.** (A) Chemical structures of the natural and synthetic phenols that were identified to form universal coatings.[88] (B) Scheme of the assembly of iron-based coordination complexes. Reprinted from Ref. [90] with kind permission of AAAS.

Besides polydopamine type crosslinking, another self-assembly process based on polyphenols for surface modification was explored. Phenolic moieties are weakly acidic and can donate an electron or electron pair to chelate metal ions.[90] Thus, polyphenols like TA can be crosslinked by coordination with iron, e.g. Fe(III) (**Figure 5B**), then deposited and bound to substrates to form versatile coatings with negligible cytotoxicity.[91] This coordinative crosslinking is pH responsive. At low pH, the

hydroxyl groups should be protonated, which leads to a destabilization of crosslinking and disassembly of the coatings.[92] In the case of a coordination between TA and Fe(III), only mono-complexes formed at pH < 2.0, with the result that the coating disassembled. Even at 3 < pH < 6, when bis-complexes existed, the coatings could not be kept stable. Only when tris-complexes formed at pH > 7, the coatings showed good long-term stability. A library of functional TA-metal networks showed that this pH sensitivity was controllable by changing the metal species and feed concentrations.[93] Moreover, varying the feed concentration of the lanthanide metals allowed control over the fluorescence intensity of the coatings. Therefore, this new type of coatings is a potential candidate for biomedical applications.

In summary, all three types of bioinspired universal coating systems, i.e., blood proteins, mussel foot proteins, and plant phenols, bind to substrate surfaces by combined multiple interactions, besides simple chemisorption or physisorption. Natural systems, e.g., mussel byssus, can even adjust the balance of each interaction to reach optimal adhesion on different kinds of surfaces. The joint surface anchoring interactions, together with the high degree of intra-coating crosslinking, resulted in several stable universal coatings which were presented above.

## 1.5 Conclusion and Perspective

An ancient Chinese proverb says “A single chopstick can be gently broken, a pillar of ten chopsticks firmly holds dough”. Both intra-coating crosslinking and the polymerization process let all of the monovalent anchorings (one root chopstick) on the substrate surface group together to reach the multi-/polyvalent anchoring (pillar of ten chopsticks) level. Thus, the coating can be indeed stabilized to reach a universal coating, even if the force of the monovalent anchoring is relatively small. Therefore, the common features of the presented universal coatings can be summarized, and the general rules for developing new universal coatings can be proposed that: (1) There must be some interaction between the coating materials and the substrate surfaces,

even though the interaction is relatively weak; (2) Intra-coating crosslinking, either covalent or noncovalent, must be present; (3) A coating should be prepared with the available functions or it can be further functionalized. Stronger interfacial interaction and a higher degree of crosslinking can result in more stable coatings, especially on chemically inert surfaces.

Among the large family of surface modification systems, however, still only a few universal coatings can be successfully used for practical applications. More importantly, it is necessary to further establish a mechanistic understanding of the stabilization of universal coatings and the theoretical guidelines for developing such coatings. Therefore, future research should be focused on the following points:

- Quantitative studies are needed to figure out the crosslinking's contribution in stabilizing coatings.
- Mechanisms for the adsorption of materials onto different surfaces should be further explored.
- A set of theories to guide the development of universal coatings must be established.
- New interactions for anchoring, especially on the chemical inert surfaces, can be explored.
- New *in situ* crosslinking technology, especially in the area of "green chemistry", should be investigated.
- The stability of the universal coatings, especially in harsh environments, should be enhanced.
- A set of universal coatings with similar chemistry but different properties, e.g., stiffness, hydrophilicity, color, should be developed.
- Universal coatings with well-defined coating structures, like monolayer coatings, hierarchical coatings, and patterned coatings, are of great interest for applications.

Overall, it remains a big challenge to further develop a family of universal coatings to become a real universal tool in our daily lives, however, universal polymer coatings have already added a new page to materials surface modification.

# 2 Scientific Goals

In the previous work, polyglycerol (PG) and its derivatives were identified as excellent bioinert polymers,[94-95] which were successfully immobilized on both gold and silica surfaces via thiol and silane chemistry for bioinert coatings.[96-98] However, universal PG coatings that can be applied to all surfaces using the same chemistry still remains a challenge.

In this work, nature's amazing bioadhesive catechol groups will be combined with hyperbranched polyglycerols (hPGs) (**Figure 6**) to achieve universal coatings under mild conditions for bioinert surfaces and other biomedical applications.

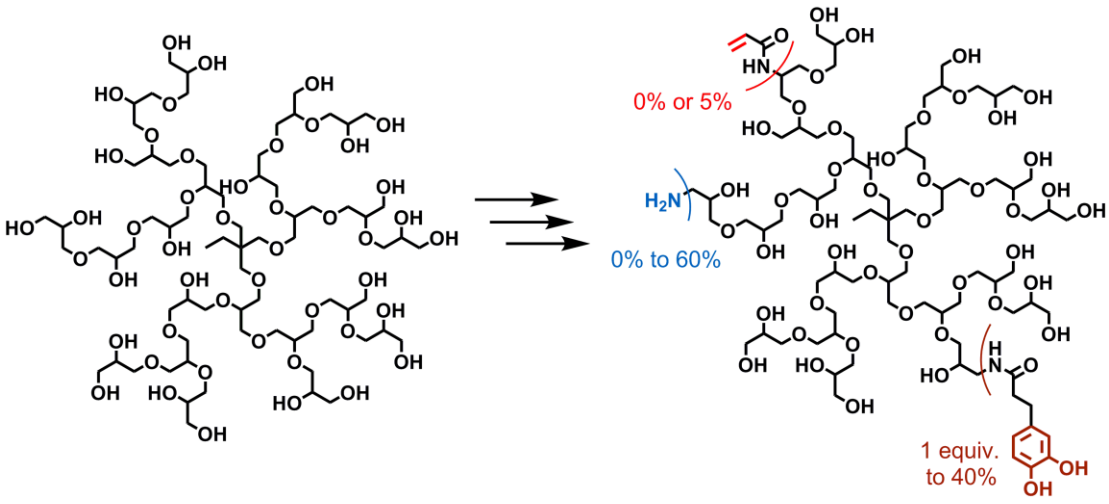



**Figure 6.** Functional hyperbranched polyglycerols (hPGs)

The effect of the catechol multiplicity on the immobilization, surface morphology, stability, and antifouling performance of the coatings shall be studied. When the catechol groups on the hPG polymers are underrepresented, the tethering of the coating may be not effective; while an overrepresentation of catechol groups may lead to nonspecific protein adsorption and cell adhesion. An optimized amount of catechol groups to supply the coatings with both good stability and antifouling ability on various material surfaces will be explored.

Coatings with different architecture can be fabricated by simply controlling the

pH values of the coating solution, as well as by introducing extra crosslinkers (**Figure 7**). The bioinertness and stability of monolayer, crosslinked monolayer, and multilayer coatings will be compared to reveal how multivalent anchoring and crosslinking enhanced the stability of the coatings.

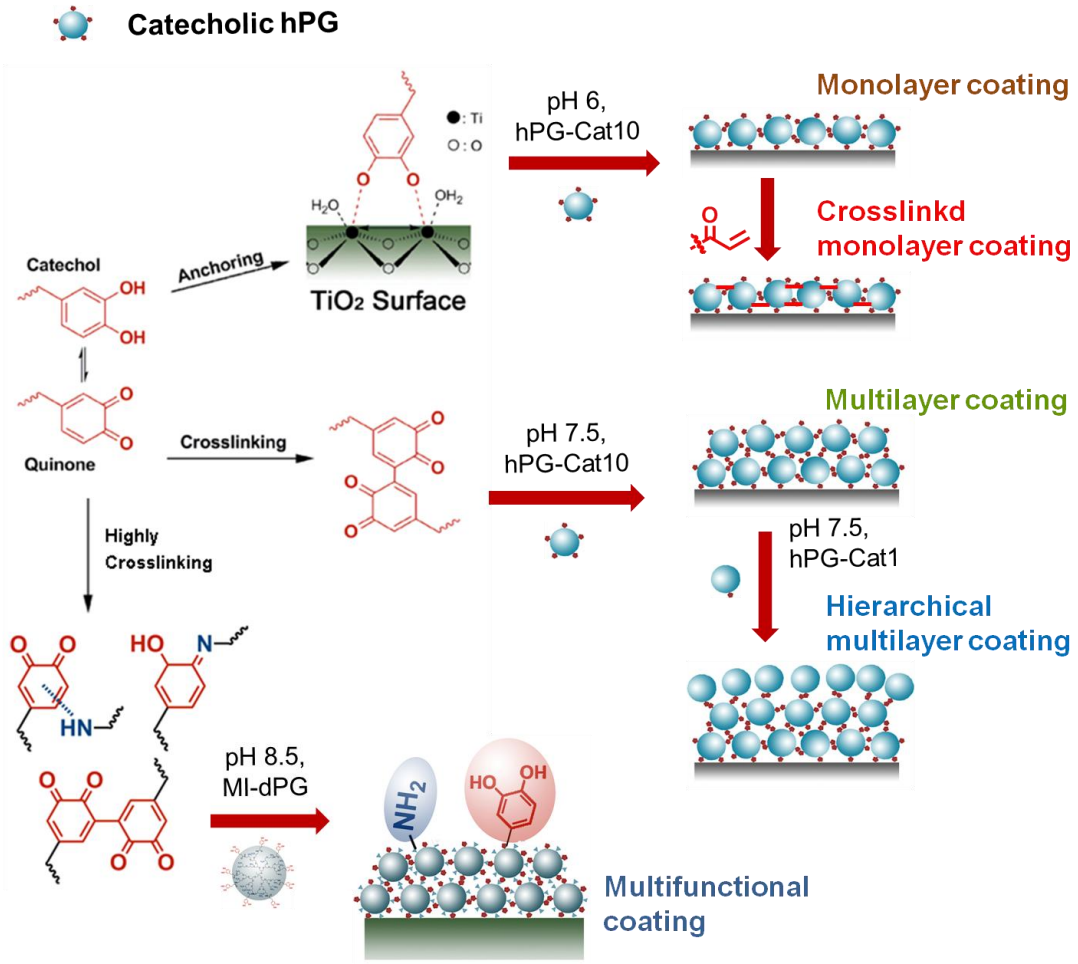



**Figure 7.** Catecholic hyperbranched polyglycerols (hPGs) for different coating architectures. Under acidic conditions, the oxidation of catechols can be avoided, thus catechol groups can only serve as anchors to result in monolayer coatings. The vinyl groups in the monolayer coatings can further initiate the intra-layer crosslinking to generate crosslinked monolayer coatings. Under weak basic conditions, parts of catechols can be oxidized to quinones. The crosslinking of the quinones can cause multilayer formation. The free catechols that are exposed on the surface of the multilayer coatings can be terminated by single catechol functionalized hPG to

achieve surface bioinert hierarchical multilayer coatings. Moreover, a heteromultivalent catechol and amine functionalized hPG can generate universal multifunctional coatings.

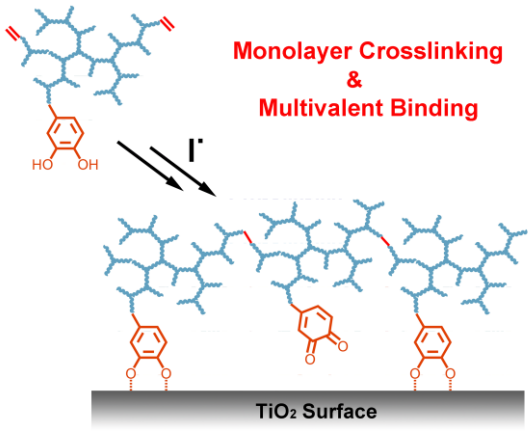
The free catechol groups that exposed on the surface of the coatings still initiate some protein adsorption. The new coating architecture of hierarchical multilayer will be developed to exhibit the optimized surface bioinertness in the meanwhile to show high stability even on chemical inert substrates. hPGs with different catechol functional degree will be employed to achieve this goal.

Furthermore, a heteromultivalent catechol and amine functionalized hPG can mimic mussel foot proteins (mfps) from three aspects: functional groups, molecular weight, and molecular structure. A rapid and universal coating is expected to be prepared by this new mfp inspired polymer. Versatile secondary functionalization will be developed for multiple applications.

Overall, the mechanism of the generation of universal coatings will be explored. The new biomedical applications based on the universal coatings will be developed.

# 3 Publications

## 3.1 Multivalent Anchored and Crosslinked Hyperbranched Polyglycerol Monolayers as Antifouling Coating for Titanium Oxide Surfaces




**Qiang Wei**, Stefanie Krysiak, Katharina Achazi, Tobias Becherer, Paul-Ludwig Michael Noeske, Florian Paulus, Hendrik Liebe, Ingo Grunwald, Jens Dernedde, Andreas Hartwig, Thorsten Hugel, Rainer Haag

*Colloids Surf. B* **2014**, *122*, 684-692.

DOI: 10.1016/j.colsurfb.2014.08.001

http://www.sciencedirect.com/science/article/pii/S0927776514004238

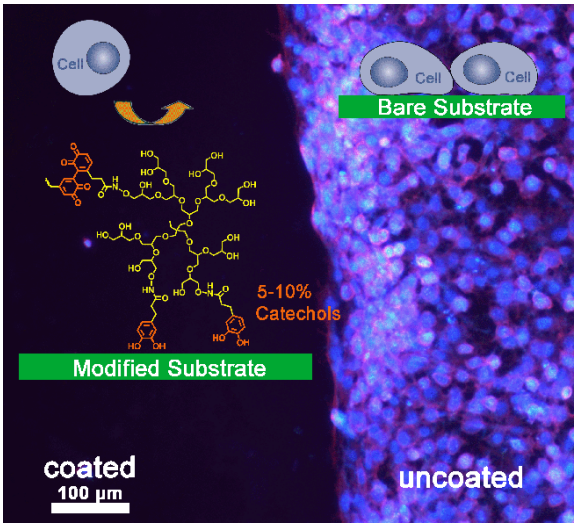
**Author contributions**

**Qiang Wei** conceived the project, performed the main experiments, and wrote the manuscript.

Stefanie Krysiak performed AFM measurements. Katharina Achazi prepared cells for cell adhesion tests and supported the biological experiments. Tobias Becherer supported the synthesis and coating. Paul-Ludwig Michael Noeske performed XPS measurements. Florian Paulus synthesized hPG. Hendrik Liebe supported the synthesis.

Ingo Grunwald, Jens Dernedde, Andreas Hartwig, Thorsten Hugel, and Rainer Haag supervised and discussed this project, as well as corrected the manuscript.

## 3.2 Multivalent Anchoring and Cross-Linking of Mussel-Inspired Antifouling Surface Coatings




**Qiang Wei**, Tobias Becherer, Radu-Cristian Mutihac, Paul-Ludwig Michael Noeske, Florian Paulus, Rainer Haag, Ingo Grunwald

*Biomacromolecules* **2014**, *15*, 3061-3071.

DOI: 10.1021/bm500673u

http://pubs.acs.org/doi/abs/10.1021/bm500673u

### Author contributions

**Qiang Wei** conceived the project, performed the main experiments, and wrote the manuscript.

Tobias Becherer supported the synthesis, coating and QCM measurements.

Radu-Cristian Mutihac performed AFM measurements.

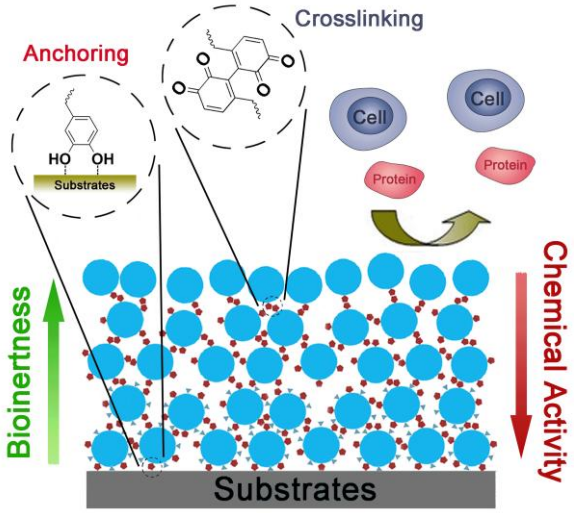
Paul-Ludwig Michael Noeske performed XPS measurements.

Florian Paulus synthesized hPG.

Rainer Haag conceived, discussed, and supervised the project, as well as corrected the manuscript.

Ingo Grunwald supervised this project and corrected the manuscript.

## 3.3 A Universal Approach to Crosslinked Hierarchical Polymer Multilayers as Stable and Highly Effective Antifouling Coatings




**Qiang Wei**, Tobias Becherer, Paul-Ludwig Michael Noeske, Ingo Grunwald, Rainer Haag

*Adv. Mater.* **2014**, *26*, 2688-2693.

DOI: 10.1002/adma.201304737

http://onlinelibrary.wiley.com/doi/10.1002/adma.201304737/abstract

**Author contributions**

**Qiang Wei** conceived the project, performed the main experiments, and wrote the manuscript.

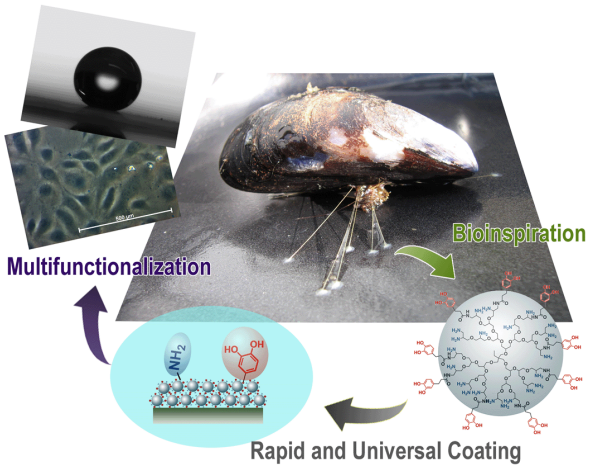
Tobias Becherer supported the synthesis, coating and QCM measurements.

Paul-Ludwig Michael Noeske performed XPS measurements.

Ingo Grunwald supervised this project and corrected the manuscript.

Rainer Haag conceived, discussed, and supervised the project, as well as corrected the manuscript.

### 3.4 Mussel-Inspired Dendritic Polymers as Universal Multifunctional Coatings




**Qiang Wei**, Katharina Achazi, Hendrik Liebe, Andrea Schulz, Paul-Ludwig Michael Noeske, Ingo Grunwald, Rainer Haag

*Angew. Chem. Int. Ed.* **2014**, *53*, 11650-11655.

DOI: 10.1002/anie.201407113

http://onlinelibrary.wiley.com/doi/10.1002/anie.201407113/abstract

**Author contributions**

**Qiang Wei** conceived the project, performed the main experiments, and wrote the manuscript.

Katharina Achazi supported the biological experiments.

Hendrik Liebe supported the synthesis and performed infrared measurements.

Andrea Schulz performed SEM and AFM measurements.

Paul-Ludwig Michael Noeske performed XPS measurements.

Ingo Grunwald and Rainer Haag supervised and discussed this project, as well as corrected the manuscript.

# 4 Conclusions and Outlook

In this thesis, a set of universal polymer coatings with tunable chemical activity and bioinertness were developed by mussel-inspired catecholic hyperbranched polyglycerols (hPGs) via simple dip coating. A wide range of material surfaces, including metal oxides, noble metals, ceramics, and polymers, were successfully modified by these new coatings to achieve versatile biomedical applications.

Under weak basic condition, parts of the catechol groups in the catecholic hPGs can be spontaneously oxidized to quinones which can crosslink with each other. The remaining catechol groups still anchored the polymers to the substrates, while the crosslinking of the quinones caused the formation of multilayer coatings. In the case of acidic conditions, the oxidation can be avoided, thus catechol groups can only serve as anchors to result in monolayer coatings. However, monolayer coatings are only stable on metal and metal oxide surfaces, on which catechols form coordinative bonds with the surface metal atoms. Moreover, a single catechol group even failed to efficiently anchor hPG molecules on metal oxide surface due to the oxidative detachment. Therefore, it is necessary to employ multivalent anchoring for long-term stable coatings. As a result, only the multivalently anchored and crosslinked multilayer coatings can be stabilized on various surfaces.

Bioinert surface coatings can be directly prepared by catecholic hPGs with appropriate amount of catechol groups. Thirty percent of catechol functionalization switched the bioinert hPG to a protein-adhesive molecule, because quinones strongly interact with amine and thiol groups in proteins. As mentioned above, single catechol anchor group suffers oxidative detachment. Our results revealed that hPGs with 5 to 10 percent of catechol functional degree showed an excellent antifouling performance, and at the same time, can generate stable multilayer coatings. However, there were still a few free catechol groups exposed on the surface of the coatings. In order to generate perfect bioinert hPG surfaces, hierarchical hPG multilayer coatings were developed. In this case, mono-catecholic hPGs were used to terminate all of the free

catechol groups and to construct a flexible bioinert top layer via quinone crosslinking. In addition, an extra chemically active catecholic hPG foundation layer can stabilize coatings even on chemically inert substrates including polytetrafluoroethylene (PTFE). This foundation layer can be further shielded by the above mentioned bioinert catecholic hPGs, and the mono-catecholic hPG terminal layer via the same chemistry. As a result, the chemical activity of this new type of coatings gradually decreases and the bioinert property gradually increases from bottom to top. With these characteristics, this new architecture was employed to form a highly stable material-independent surface coating with outstanding antifouling properties.

The highly adhesive catecholic hPG that used as foundation layer contains 40% of catechol groups and 60% of amine groups. Both two kinds of functional groups are abundant in mussel foot proteins (mfps) and play key roles in the rapid formation of mussel byssus. Furthermore, the molecular weight of this catecholic hPG reaches 10 kDa, which is similar to the most adhesive mussel foot protein mfp-5 (about 9 kDa). Also, the dendritic structure, exhibits a relatively distinct “interior”, and exposes its functional groups on the surface of the polymer, while natural proteins exhibit important domains on the surface as well. Based on the mimicry of functional groups, molecular weight, and molecular structure, this new mussel-inspired hPG formed a considerably stable coating on virtually any type of material surface within 10 min or a micrometer scale coating in hours, which is comparable to the formation of mussel byssal threads in nature. Functional molecules, like collagen A and rhodamine B, can be post-functionalized or pre-functionalized to the coatings to generate different kinds of functional biosurfaces. Additionally, the controllable surface roughness resulted in superhydrophilic or superhydrophobic surface properties for self-cleaning applications.

This bioinspired copy of mussel foot proteins reaches a new level of functional mimicry. What more can we learn from these proteins to design synthetic molecules for material surface modification? Mussels employ thiol-rich mfp-6 to reduce quinones in the adhesive interface back to catechols to enhance its adhesion, while

inside catechols can be oxidized to quinones to enhance cohesion. How to achieve controllable redox balance of catechol groups in coatings remains a tremendous challenge and can be a direction to develop next generation of mussel-inspired coatings. Besides catecholic surface chemistry, mussels also employ hydrophobic aromatic sequences, mainly present in mfp-3 “slow”, on the one hand to retard oxidation of catechols by shielding the groups from aqueous solution, on the other hand to increase the hydrophobic interaction which is not pH dependent. Combining this hydrophobic interaction with catecholic chemistry, universal polymer coatings with well defined thickness and surface morphology may be achieved.

# 5 Zusammenfassende Bewertung und Ausblick

Die vorliegende Arbeit beschreibt neuartige Polymerbeschichtungen mit einstellbaren chemischen und bioinerten Eigenschaften, welche durch einfaches Eintauchen in von Muscheln-inspirierten brenzcatechinhaltigen, hyperverzweigten Polyglycerinen (hPG) hergestellt werden können.

Eine große Anzahl von Materialoberflächen, wie zum Beispiel die von Metalloxiden, Edelmetallen, Keramiken und Polymeren können mit Hilfe dieser neuartigen Beschichtung modifiziert werden, wobei unterschiedlichste biomedizinische Anwendungsfelder adressierbar sind.

Unter leicht basischen Reaktionsbedingungen gelingt es Teile der Brenzcatechingruppen der hyperverzweigten Polyglycerine (hPG) spontan zu Chinonen zu oxidieren, welches zu einer Vernetzung innerhalb der Moleküle führt und hierdurch eine Multilagenbeschichtungen entsteht. Die übrig gebliebenen Brenzcatechingruppen dienen als stabile Anker für das hPG an die Substratoberfläche.

Im Fall von sauren Reaktionsbedingungen wird die Oxidation vermieden und die vorhandenen Brenzcatechingruppen können hierdurch als Anker dienen, wobei nur Monolagen des hPG ausgebildet werden. Solche Monolagenbeschichtungen sind nur stabil auf Metall- und Metalloxidoberflächen, bei welchen die Brenzcatechingruppen koordinative Bindungen mit den Metallatomen an der Oberfläche ausbilden können.

Anzumerken ist hierbei, dass eine einzelne Brenzcatechingruppe nicht in der Lage ist das hPG Molekül fest an die Metalloxidoberfläche anzukoppeln, da es hier zu einer oxidativen Ablösung kommen kann. Vor diesem Hintergrund müssen für eine feste Oberflächenankopplung auf unterschiedlichsten Substraten multivalente und vernetzte Multilagenbeschichtungen verwendet werden.

Bioinerte Oberflächenbeschichtungen können direkt durch die Verwendung von hPGs mit entsprechend eingestellten Brenzcatechingruppenanteilen erzeugt werden. Hierdurch können vorher bioinerte hPGs durch die Funktionalisierung mit 30% Brenzcatechingruppen zu für Proteine adhäsive Moleküle umgewandelt werden. Dies

beruht auf den nun vorhandenen Chinongruppen, welche mit den Amino- und Thiolgruppen der Proteine reagieren können.

Wie oben erwähnt, haben einzelne Brenzcatechingruppen den Nachteil, dass diese als Ankergruppen oxidativ abgelöst werden können. Die erhaltenen Daten belegen, dass hPGs mit fünf bis zehn Prozent Brenzcatechinfunktionalisierung exzellente Antifouling-Eigenschaften aufweisen und stabile Multilagenbeschichtungen generieren. Nur wenige freie Brenzcatechingruppen sind hierbei an der Oberfläche vorzufinden.

Zur Herstellung perfekter bioinerter hPG Oberflächen wurden in dieser Arbeit eine neue hierarchische hPG Multilagenbeschichtungen entwickelt. Hierfür wurden für den Aufbau einer flexiblen bioinerten äußeren Schicht die freien Brenzcatechingruppen mit monobrenzcatechinhaltigen hPGs über Chinonvernetzung terminiert. Zusätzlich kann mit Hilfe einer weiteren chemisch aktiven brenzcatechinhaltigen hPGs Grundschicht eine stabile Beschichtung selbst auf inerten Materialien, wie z. B. Polytetrafluorethylen (PTFE), erreicht werden.

Im Ergebnis führte die Kombination der Grundschicht mit einer äußeren Schicht dazu, dass die chemische Reaktivität graduell abnahmen und die bioinerten Eigenschaften graduell zunahmen – dies von der Grundschicht zur äußeren Schicht. Hierdurch konnte eine neue Schichtarchitektur erzeugt werden, die sich durch eine hochstabile und materialunabhängige Beschichtung mit hervorragenden Antifouling-Eigenschaften auszeichnete.

Dieses hochreaktive brenzcatechinhaltige hPG-Schicht enthält 40% Brenzcatechin- und 60% Aminogruppen. Diese beiden funktionellen Gruppen sind auch in den mfp Proteinen des Muschelfußes (Muschelfußprotein = mfp) vorzufinden und spielen hier eine entscheidende Rolle bei der Ausbildung des Byssusklebapparates der Muscheln.

Die in dieser Arbeit vorgestellten brenzcatechinhaltigen hPG weisen mit etwa 10 kDa eine molekulare Masse auf, welche sehr ähnlich zu der des Muschulfußproteins mfp-5 ist (ungefähr 9 kDa). Weiterhin ist festzustellen, dass die dendritische Struktur

der hPG ein kompaktes Inneres aufweist und die funktionellen Gruppen an der Oberfläche des Polymers zu finden sind – eine weitere Ähnlichkeit zu natürlichen Proteinen, die ebenfalls wichtige Bindungsdomänen an der Oberfläche tragen.

Auf Basis der biomimetisch funktionalen Gruppen, der molekularen Masse und der molekularen Struktur ist das hier beschriebene von Muscheln inspirierte hPG in der Lage, innerhalb von 10 Minuten auf nahezu allen Oberflächen stabile Beschichtungen auszubilden, die sogar nach wenigen Stunden Dicken im Mikrometerbereich ausmachen können. Hierdurch ist das neue hPG Polymer vergleichbar mit dem Byssussystem der Muschel.

Die beschriebenen brenzcatechinhaltigen hPG Beschichtungen können anschließend mit unterschiedlichen bioaktiven Fähigkeiten mit Biomolekülen wie Kollagen A oder Rhodamine B ausgestattet werden. Zusätzlich kann die Oberflächenrauheit gezielt eingestellt werden, um z.B. superhydrophobe oder superhydrophile Oberflächeneigenschaften zu erhalten. Dieses kann u.a. für das Design von selbstreinigenden Oberflächen genutzt werden.

Die hier vorgestellten Daten tragen dazu bei, die biomimetischen Ansätze im Bereich der Muschelfußproteine auf eine neue Entwicklungsstufe zu bringen. In diesem Kontext stellt sich die Frage, welche weiteren chemische Zusammenhänge von diesen Muschelproteinen gelernt werden können, um innovative Materialien für synthetische Oberflächenfunktionalisierungen zu generieren. So nutzen zum Beispiel die Muscheln das thiolgruppenhaltige Protein mfp-6, um Chinone an der Adhäsionsgrenzschicht zu Brenzcatechingruppen zurück zu reduzieren und hierdurch die Adhäsion zu verbessern. Im Inneren des Proteinklebstoffes werden dahingegen die Brenzcatechine zu Chinonen oxidiert, um hierdur die Kohäsion des Klebstoffes zu verbessern.

Die Kontrolle des Redox-Gleichgewichtes der Brenzcatechingruppen in einer Muschel-inspirierten Beschichtung bleibt bis heute eine Herausforderung, könnte aber eine Richtung für nachfolgende Forschungsarbeiten darstellen. Neben der brenzcatechinbasierten Oberflächenchemie, nutzen Muscheln hydrophobe

aromatische Sequenzen – vor allem im Protein mfp-3, zum Einen, um die Oxidation der Brenzcatechingruppen zu verlangsamen, wobei hier die Abschirmung der Gruppen von der wässrigen Umgebung im Vordergrund steht. Zum Anderen werden hierdurch, in einem pH unabhängigen Prozess, die hydrophoben Interaktionen im Klebstoff erhöht.

Die Kombination der hydrophoben Interaktionen mit der Brenzcatechinchemie könnte genutzt werden, um eine neue Generation von biomimetischen Beschichtungen von Polymeren zu erzeugen, wobei die Schichtdicke und die Oberflächenmorphologie gezielt eingestellt werden kann.

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# 7 Appendix

## 7.1 Publications and Patent Applications

### Publications

**Q. Wei**, C. Schlaich, S. Prévost, A. Schulz, C. Böttcher, M. Gradzielski, Z. H. Qi,* R. Haag,* C. A. Schalley,* Supramolecular Polymers as Surface Coatings: Rapid Fabrication of Healable Superhydrophobic and Slippery Surfaces. ***Adv. Mater.*** 2014, 26, 7358-7364.

**Q. Wei**, K. Achazi, H. Liebe, A. Schulz, P.-L. M. Noeske, I. Grunwald, R. Haag,* Mussel-Inspired Dendritic Polymers as Universal Multifunctional Coatings. ***Angew. Chem. Int. Ed.*** 2014, 53, 11650-11655.

**Q. Wei**, S. Krysiak, K. Achazi, T. Becherer, P.-L. M. Noeske, F. Paulus, H. Liebe, I. Grunwald, J. Dernedde, A. Hartwig, T. Hugel, R. Haag,* Multivalent Anchored and Crosslinked Hyperbranched Polyglycerol Monolayers as Antifouling Coating for Titanium Oxide Surfaces. ***Colloids Surf. B*** 2014, 122, 684-692.

**Q. Wei**, T. Becherer, R.-C. Mutihac, P.-L. M. Noeske, F. Paulus, R. Haag,* I. Grunwald,* Multivalent Anchoring and Cross-Linking of Mussel-Inspired Antifouling Surface Coatings. ***Biomacromolecules*** 2014, 15, 3061-3071.

**Q. Wei**, T. Becherer, S. Angioletti-Uberti, J. Dzubiella, C. Wischke, A. T. Neffe, A. Lendlein, M. Ballauff, R. Haag,* Protein Interactions with Polymer Coatings and Biomaterials. ***Angew. Chem. Int. Ed.*** 2014, 53, 8004-8031.

**Q. Wei**, T. Becherer, P.-L. M. Noeske, I. Grunwald,* R. Haag,* A Universal Approach to Crosslinked Hierarchical Polymer Multilayers as Stable and Highly Effective Antifouling Coatings. ***Adv. Mater.*** 2014, 26, 2688-2693.

K. Höger, T. Becherer, **W. Qiang**, R. Haag, W. Frieß, S. Küchler,* Polyglycerol Coatings of Glass Vials for Protein Resistance. ***Eur. J. Pharm. Biopharm.*** 2013, 85, 756-764.

**Q. Wei**, B. J. Li, Y. Nan, Z. H. Yin, F. L. Zhang, J. Li, C. S. Zhao,* Improving the Blood Compatibility of the Material Surfaces via Biomolecule-Immobilized Mussel-Inspired Coatings. ***J. Biomed. Mater. Res. Part A*** 2011, 96A: 38-45.

**Q. Wei**, F. L. Zhang, J. Li, B. J. Li, C. S. Zhao,* Oxidant-Induced Dopamine Polymerization for Multifunctional Coatings. ***Polym. Chem.***, 2010, 1, 1430-1433.

**Q. Wei**, J. Li, B. S. Qian, B. H. Fang, C. S. Zhao,* Preparation, Characterization and Application of Functional Polyethersulfone Membranes Blended with Poly(acrylic acid) Gels. ***J. Membr. Sci.*** 2009, 337, 266-273.

**Patents**

R. Haag, **Q. Wei**, I. Grunwald, T. Becherer, M. Weinhart, European patent application 2013, EP2013/184328, Multischicht-Architektur als Antifouling-Beschichtung für vielfältige Substrate.

**Oral Presentations**

**Q. Wei**, R. Haag
Mussel-Inspired Dendritic Polymers as Universal Multifunctional Coatings
Polydays 2014: Beyond Self Assembly - Making Polymeric Materials More Versatile, Berlin, Germany, 2014

**Poster Presentations**

**Q. Wei**, T. Becherer, R. Haag
Hierarchical Polymer Multilayers as Highly Antifouling Coatings
12th International Conference on Polymers for Advanced Technologies, Berlin, Germany, 2013

**Q. Wei**, R. Haag
Hierarchical Polymer Multilayers as Highly Antifouling Coatings
BSRT PhD Symposium “Regeneration is Communication: Fireside Chats between Cells & Matrices”, Berlin, Germany, 2013

**Q. Wei**, R. Haag
Hierarchical Polymer Multilayers as Highly Antifouling Coatings
Makromolekulares Kolloquium 2014 - HVI-Sponsored Session on Bioengineering and Multifunctional Biomaterials, Freiburg, Germany, 2014

**Q. Wei**, R. Haag
Mussel-Inspired Dendritic Polymers as Universal Multifunctional Coatings
3nd International Symposium of the Collaborative Research Center (Sonderforschungsbereich) 765 on "Multivalency and Chemistry and Biochemistry", Berlin, Germany, 2014

## 7.2 Curriculum Vitae

For reasons of data protection,

the curriculum vitae is not included in the online version