Feng Zhou *Editor*

Antifouling Surfaces and Materials

From Land to Marine Environment

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Preface

Fouling is the undesirable accumulation of material on a wide variety of objects such as medical devices, ship hulls, pipelines, membranes, as well as what is normally seen in most of the industries (paper manufacturing, food processing, underwater construction, and desalination plants etc.). The fouling material can either be living organisms or non-living substances (inorganic dusts, organic liquids). Fouling can occur almost anywhere and in almost all circumstances, especially where liquids are in contact with other materials, and is economically significant to the marine shipping, resulting in additional functional and monetary costs to various vessels which include reducing their fuel efficiency, increasing dry-dock maintenance costs, and reducing their hull strength and bio-corrosion. Now fouling has become a widespread global problem from land to oceans with both economic and environmental penalties. Fouling by living organisms such as in marine environment is especially problematic and complex: more than 1700 species comprising over 4000 organisms (microorganisms, plants algae, and animals) are responsible for biofouling, which is categorized into microfouling, biofilm formation and bacterial adhesion, macrofouling, and the attachment of larger organisms.

Antifouling is the process of removing or preventing the organism accumulation and growth. Bio-dispersants are usually used to take precautions against biofouling in industrial production processes. In less controlled environments, organisms can be killed or repelled with coatings containing biocides, thermal treatments, or pulses of energy. A variety of antifouling surfaces have been developed to overcome organism settlement, including choosing the surfaces or coating with low friction and low surface energies, creation of slippery antifouling surfaces or building ultra-low fouling polymeiric surfaces, creation of various micro/nano structural surfaces similar to the skin of sharks with less anchoring points, and antifouling hydrophilic surfaces (based on zwitterions, such as glycine, betaine, and sulfobetaine) with high hydration that increases the energetic penalty of removing water during the process of attachment of proteins and microorganisms.

Up to now, antifouling technologies have increased drastically in the last decades due to the advancement of bionic science and the longstanding challenge in search of viable and environmentally friendly alternatives of nonfouling surfaces, which is the focus of this book. In this book, we put together the self-cleaning function from

the land to the sea and try to tell readers the difference. For most terrestrial creatures, the hydrophobic surfaces based on surface morphology and chemical composition, which can lead to the self-cleaning for antifouling. The superhydrophobic surface (such as lotus leaves, rose petal, cicada wing, and pattern surface) can repel droplets of water and dust, and the large boundary slip occurs when water flows through the superhydrophobic surface because most of the "liquid-solid shear" is transferred to the "liquid-air shear" at the interface. However, the superhydrophobic surfaces existing on the land are not suitable for the underwater antifouling. Most of the aquatic organisms rather utilize hydrophilicity and softness to keep away the biological growth, such as shark's and whale's skin, nacre, etc. These soft surfaces also have drag reduction property due to the decrease of the vortex, the turbulent flow changing to laminar flow at the hydrophilic boundary layer, which also contributes to antifouling.

The book is highly interdisciplinary and covers the fields of nanotechnology, polymer science, surface science, coating technology, hydrodynamics, and marine biology. One area in which considerable research has been performed is self-cleaning and boundary slippage and is discussed in depth in the first and last part of the book. The other chapters are related to antifouling surfaces based on polymer brushes (PEGylated polymers, zwitterionic polymers, bioinspired polymers, and polymers incorporating antimicrobial agents), self-assemble monolayers, or layer-by-layer-assembled films, as well as an emerging research area focusing on micro/nano structural antifouling surfaces. There is also growing knowledge available on novel antifouling coatings and nontoxic green biocides such as ionic liquids and natural products. The future research about green antifouling surfaces should also be toward correlating molecular-level details of the functionalized surface, surface topography, and establishing a fundamental understanding of antifouling and fouling release mechanisms. It also requires to figuring out how mechanical properties of the coating surfaces affect fouling and fouling release and how the chemical composition of the adhesive matrices of organisms takes effect. Moreover, some fundamental work should be done in understanding the relationship between the structure, surface chemical composition, and properties of a coating and its biological performance.

In this book, we aim to provide an overview of antifouling techniques from land to marine environment and from natural to biomimetic technology, which allow readers to understand the antifouling approaches, the existing problems, and its perspectives. The book provides a reference source to scientists from the academic and industrial communities, as well as regulatory authorities.

Feng Zhou

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Chapter 3
Antifouling Surfaces Based on Polymer Brushes

Qian Ye and Feng Zhou

Abstract Biofouling is a crucial problem in the maritime industry for both military and commercial vessels. One promising approach to overcome the problem is creating a nonfouling surface with functional polymer brushes, which usually presents large exclusion volumes to inhibit protein and bacterial adhesion, or possess bactericidal functional groups. Previous studies show the increasing reports in creating an antifouling surface using polymer brushes via various techniques such as self-assembly through hydrophobic or electrostatic interactions, and covalent immobilization by means of either "grafting-to" or "grafting-from" strategy. These advances in techniques for surface modification and tailoring of polymer composition and architecture have resulted in many promising developments in the antifouling field. This chapter summarizes such recent research progress about polymer-brush-based antifouling surface, and focuses mainly on the development and application of nonfouling surfaces with anti-adhesive and/or bactericidal polymer brushes. Various types of polymer brushes (PEGylated polymers, amphiphilic copolymers, zwitterionic polymers, bioinspired polymers, bactericidal polymer, and polymers incorporating antimicrobial agents, etc.) are particularly suited for the preparation of functional bioactive surfaces, including anti-adsorption for cell and protein, antibacterial, and biomolecule-coupled and patterned surfaces.

3.1 Introduction

Biofouling, which is the undesirable growth of marine organisms on artificial surfaces including ship hulls, aquaculture cages, and pipelines, has become a widespread problem in the maritime industry for both military and commercial vessels.

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More than 4000 species of marine organisms (microorganisms, plants, and animals) are responsible for marine biofouling [1]. Various researches were performed to obtain antifouling surfaces—the developed methods are mainly based on two different strategies: (i) the immobilization of biocidal substances and (ii) grafting an antifouling coating on the surface to prevent proteins and cell adhesion. The methods employed to immobilize antifouling coating onto substrates are usually through chemical grafting, surface impregnation, or physical entrapment [2]. These species have different adhesion mechanisms due to their different adhesive compositions, and they can adapt to environmental changes; so the creation of effective antifouling surfaces is a very challenging task.

Recently, polymer brushes have attracted considerable attention as a way to tailor the surface properties of materials owing to their higher mechanical, chemical robustness, and higher long-term stability. The polymer brushes present large exclusion volumes to inhibit protein and bacterial adhesion or possess bactericidal functional groups, which is of great importance in antifouling fields [3]. The most common approach for creating a nonfouling surface involves the functionalization of surfaces with anti-adhesive and/or bactericidal polymer brushes, which could be grafted on surfaces via various techniques such as self-assembly through hydrophobic or electrostatic interactions, and covalent immobilization by means of either "grafting-to" or "grafting-from" strategy [4, 5].

3.2 PEG-Based Antifouling Surfaces

The nonadhesive coatings are mainly self-assembled monolayers (SAMs) or polymer brushes based on poly(ethylene glycol) (PEG) or its derivatives, the antifouling properties of PEG-based layers have been widely reported in the literature [6, 7]. PEG and oligo(ethylene glycol) (OEG) acted as the most commonly used antifouling materials due to their unique physical and biochemical properties, such as nontoxicity, nonimmunogenesis, nonantigenicity, excellent biocompatibility, and miscibility with many solvents [8, 9].PEG and its derivatives exhibit good antifouling effects to a wide variety of proteins, suppress platelet adhesion, and reduce cell attachment and growth [10, 11]. Although the mechanisms of inhibition have not been fully elucidated, it is generally believed that steric barrier, osmotic repulsion, excluded-volume effects, and the mobility or flexibility of highly hydrated PEG chains in water are the most probable explanations for protein resistance (Fig. 3.1; [12]). The presence of water molecules within the PEG layers for hydration is essential for protein resistance. Many methods were developed for immobilizing PEG coatings on surfaces, such as self-assembled PEG monolayer, graft polymerization of PEG monomers to a polymer backbone, adsorption of PEG block copolymers at multiple sites on the surface, and "grafting-from" approaches via surface-initiated polymerization (SIP) [13].

PEG or poly(ethylene oxide) (PEO), and their derivatives can act as highly hydrated polymer chain molecules and form the chemical basis of the most versatile

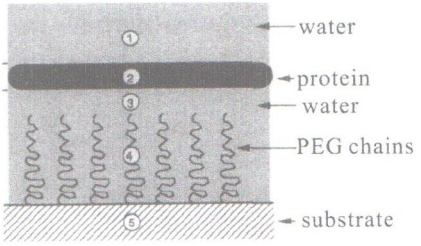

Fig. 3.1 Model picture for the theoretical study by Jeon et al. showing a protein of infinite size in water with a solid substrate having terminally attached PEG chains. PEG Poly(ethylene glycol). Reprinted from Ref. [12]. Copyright 1991, with permission from Elsevier)

approach to inhibit protein and bacterial adhesion, which altogether constitute what has probably been the single most studied/used class of antifouling materials over the years. Horbett et al. have studied the antifouling properties of tetraglyme coatings against human plasma via surface plasmon resonance (SPR; [14]). The results show that plasma deposited onto gold with a typical thickness of 100-nm tetraglyme coatings strongly resists protein adsorption even at low plasma dilution in phosphate-buffered saline (PBS). Even though SAMs with only a few ethylene glycol (EG) units per molecule, which have shown excellent resistance to adsorption of a variety of proteins. Chang et al. incorporated the OEG chain into a linear OEG-terminated alkanethiol molecule, which formed OEG-SAMs on gold exhibiting good antifouling properties against 20% human platelet-poor plasma [15, 16]. Heuberger and coworkers found that the water content inside the surface-grafted PEG chains is over 80 vol%, and it exhibits excellent protein-resistance properties due to a high degree of organization in the PEG–water complex [17].

The antifouling properties of PEGylated polymers are widely reported [18]. The polystyrene block copolymers with methoxyterminated PEG side chains have been reported and showed significantly weaker cell adhesion of *Navicula* diatoms compared to polydimethylsiloxane (PDMS) [19]. Tosatti et al. explored the triblock copolymer structures, in which the two external PEG chains were flanking a central block of polypropylene sulfide (PPS) [20]; the PEG–PPS–PEG can be directly anchored onto the gold surfaces via multisite polysulfide chemisorption of their central PPS block. The copolymer exhibits good anti-adsorption of protein from the whole human serum, measured using SPR [20, 21]. Robin and coworkers have reported another multidentate copolymeric chemisorbate with pendant PEG chains for the surface modification of titanium oxide [22, 23]. The terpolymer made of sodium decylphosphonate, PEG, and n-butyl side-chains branching out a central methacrylate backbone in a 1:1:8 ratio was able to self-assemble onto TiO_2 and granted this surface with excellent antifouling properties [22, 23]. Other approaches for creating PEGylated antifouling surfaces include the use of dendrimers and hyperbranched polymers. Zhao et al. have prepared functionalized membranes from blends of hydrophobic poly(vinylidene fluoride) (PVDF) and a hyperbranched polymer with hydrophilic PEG grafts, which showed excellent weaker protein adsorption than pure PVDF membranes [24]. Benhabbour et al. have obtained and researched the antifouling property of thiol-terminated PEG ($HS–PEG_{650}–OH$) functionalized with aliphatic polyester dendrons of generations 1–4 grafting substrate

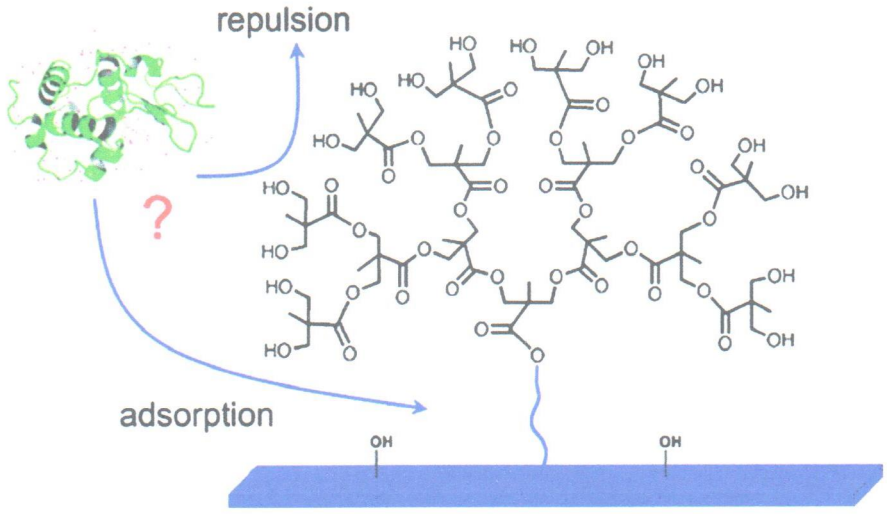

Fig. 3.2 Protein resistance of surfaces prepared via chemisorption of monothiolated poly(ethylene glycol) onto gold surfaces. (Reprinted with the permission from Ref. [25]. Copyright 2008, American Chemical Society)

surfaces (Fig. 3.2) [25]. They found that the dendronization of PEGylated surfaces can result in an increase in surface hydrophilicity, but protein adsorption increased. They thought that PEG chain flexibility is one of the key factors in the mechanism of protein resistance, and that the chain flexibility was impeded by the introduction of dendrons with multiple peripheral OH groups. The interaction of the OH groups with the underlying PEG is believed to lower the conformational flexibility of the PEG grafts [25]. Their long-term stability in a biological environment is crucial in practical applications as antifouling coatings. Sharma et al. have found that the PEG-modified silicon surfaces can retain their protein- and cell-repulsive properties even after at least 4 weeks of immersion in a PBS buffer solution [26]. Nowadays, alternatives to PEG-based antifouling coatings are still being widely researched. The effectiveness of each strategy for constructing a protein- and cell-resistant surface depends not only on the unique antifouling properties of PEG units but also the molecular structure and surface coverage [27]. In general, protein adsorption is expected to decrease with increasing graft density and chain length of PEG [28].

The effect of antifouling has been dependent on antifouling polymer surface density. So, the high polymer surface densities can provide better fouling resistance. High surface densities can be obtained through manipulation of such parameters as polymer design (chain length, anchoring chemistry, and antifouling polymer composition) and processing. Dense "nonfouling" polymer brushes grafting various substrate surfaces can be obtained via atom transfer radical polymerization (ATRP) growing various oligo(ethylene glycol) methacrylate (OEGMA) macromonomers. The thickness of the prepared polymer brushes (POEGMA) can be tunable, and the modification surfaces exhibited excellent antifouling effect to many

proteins. Moreover, the antifouling properties of the POEGMA brushes are stable under long-term cell culture conditions. Chilkoti et al. have reported that POEGMA brushes grafting substrates in situ via surface-initiated atom transfer radical polymerization (SI-ATRP) have showed to prevent nonspecific cell adhesion for up to 30 days [27]. Huck and coworkers have reported more systematic structural study in their influence on protein adsorption of various architectures of oligo-ethylene oxide (OEO) polymer brushes [29]. Brushes with regular, linear, and dendritic side-chain substructures were grafted on gold surfaces in situ via SI-ATRP of mono/oligoglycerol (meth)acrylate monomers (Fig. 3.3a–c), fouling from non-diluted human serum, and plasma was quantified by means of SPR. They found that the first-generation dendritic brushes with a thickness of 17 nm exhibit good resistance to serum adsorption. However, dendritic brushes with second-generation acrylate dendrimers (Fig. 3.3c-right) performed poorly. They have observed architectural dependence and trends of protein adsorption about polymer brushes using plasma, the highest resistance to protein adsorption still belonging to the first-generation dendritic brushes [29]. Regardless, all these polymer brushes exhibit excellent antifouling performance, against both non-diluted human serum and plasma, compared to bare gold or the SAM of ATRP initiator. Besides planar surfaces, SI-ATRP of OEGMA was carried out to tailor the magnetic nanoparticles (MNPs) with antifouling properties [30, 31]. The ability of the PEGylated MNPs to resist nonspecific adsorption of proteins and macrophage cells was higher than that of the pristine MNPs [30, 31]. The POEGMA brushes can also be grafted onto membrane surfaces via SI-ATRP to improve the performance of membranes in biomedical applications. The membranes modified with POEGMA brushes exhibited good resistance to protein adsorption and fouling under continuous-flow conditions, thus prolonging the useful lifetime of the filtration membranes [32].

Several groups also reported poly(HOEGMA) and poly(MeOEGMA) brushes with excellent antifouling properties. Chilkoti group prepared poly(MeOEGMA) brushes on silicon oxide via SI-ATRP and reported its excellent protein-resistance effect upon exposure to undiluted fetal bovine serum (FBS) for 60 min—the level of serum adsorption on these coatings is below the detection limit of ellipsometry [33]. They also integrated SI-ATRP with microcontact printing to create micropatterns of poly(OEGMA) on glass that can spatially direct the adsorption of proteins on the bare regions of the substrates [33]. Rodriguez-Emmenegger et al. reported the antifouling effect of two-type brush (HOEGMA and MeOEGMA) modification nylon, −6/6 adhesion films, zero fouling from single protein solutions, and a reduction of more than 90% in the fouling from blood plasma observed on the uncoated surfaces was achieved. The result showed that poly(MeOEGMA) brushes maintain their performance against both fluids upon storage in PBS for 5 months under dark condition [34].

Dense hydrophilic poly(2-hydroxyethyl methacrylate; PHEMA) brushes also possess excellent biocompatibility and physical properties and excellent protein repellency [35]. The PHEMA graft chains can become highly extended and oriented to physically exclude the protein molecules from the entire brush layer. Mei and coworkers have grafted well-defined density-gradient PHEMA brushes onto substrate

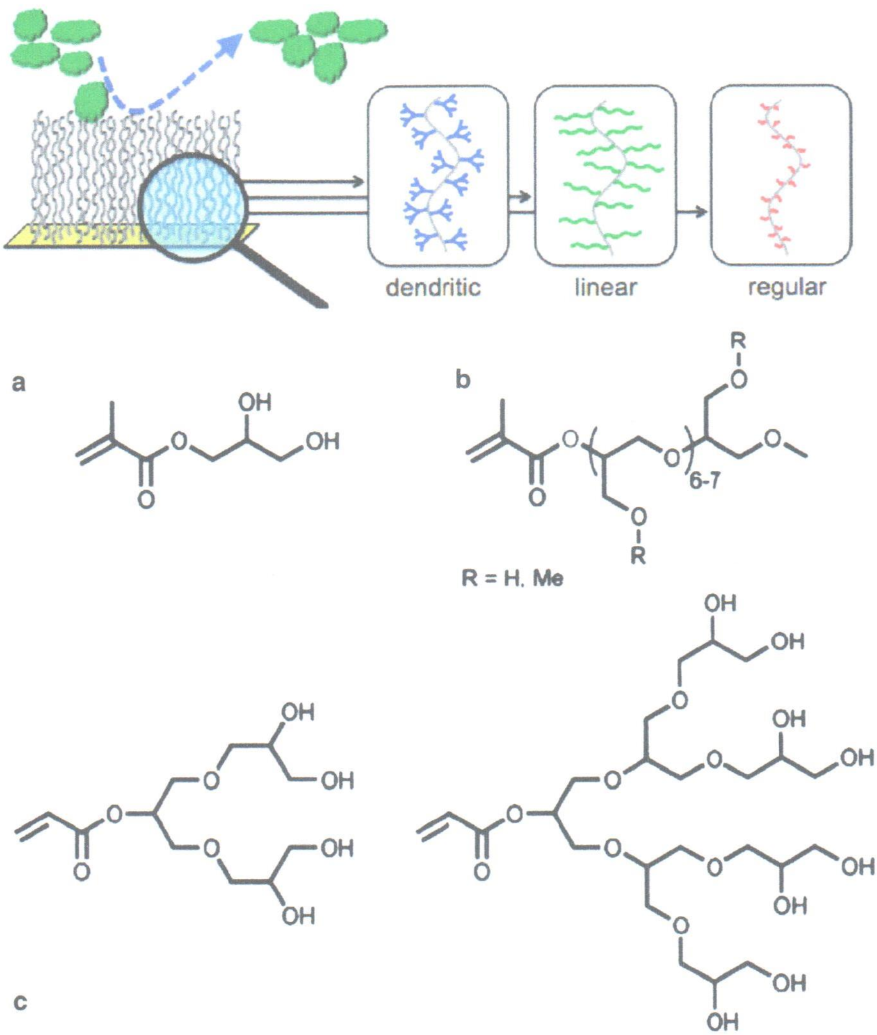

Fig. 3.3 The influence of polymer brush architecture on antifouling properties. Molecular structures of the **a** monoglycerol, **b** linear (hydroxylated and methoxylated) oligoglycerol methacrylates, and the **c** first (*left*) and second (*right*) generation dendritic oligoglycerol acrylates. (Reprinted with the permission from Ref. [29]. Copyright 2011, American Chemical Society)

surfaces via SI-ATRP for tuning cell adhesion [36]. They reported that fibronectin can adsorb onto the regions with low densities of PHEMA brushes, and be repelled at the high density regions. The PHEMA chain structure was in a "mushroom" regime at the low-graft density, while PHEMA chain was in a "brush" regime at high-graft density—the "mushroom" region could be made adhesive to cells by adsorbing adhesion proteins. Thus, cell adhesion could be tuned by controlling the grafting density of PHEMA brushes [36]. Highly hydrophilic polyacrylamide

(PAAm) brushes can also suppress the adsorption of proteins and inhibit cell growth [37]. PAAm brushes can be attached on electrophoretic microfluidic chips for improving protein separation [38]. It was shown that the dense PAAm brush layer reduced the attractive forces between the surface and microorganisms. Compared to the bare surface, a large reduction (70–92 %) was observed in microbial adhesion onto the PAAm brush's grafting surface [39]. Subsequently, they grafted PAAm brushes on silicon rubber via SI-ATRP using a three-step reaction procedure. PAAm brushes grown in water can reduce the adhesion of *Staphylococcus aureus* by 58 %, *Streptococcus salivarius* by 52 %, and *Candida albicans* by 77 %. The anti-adhesive properties of PAAm brush grown in *N,N*-dimethylformamide (DMF) are better due to the thicker polymer layer—the PAAm coating did not deteriorate even when exposed to PBS and saliva for 1 month at 37 °C [40].

3.3 Amphiphilic Polymer-Based Antifouling Surfaces

The highly hydrophilic (PEG-based) coatings show good effect for inhibiting attachment of proteins, bacteria, and marine organisms, but the hydrophobic polymer-based surfaces can possess excellent fouling-release property for attached species [41]. So, the amphiphilic copolymers with both hydrophobic and hydrophilic groups possess excellent antifouling- and fouling-release properties. Various designs for coatings that can resist the adsorption of marine organisms are based on the concept of "ambiguous" surfaces that present both hydrophobic and hydrophilic functionalities as surface domains.

The fluorinated block polymer preferentially segregates to the air–polymer interface owing to the low surface energy of the fluorinated groups. Gudipati and coworkers have synthesized fluorinated copolymers with optimal nanoscale heterogeneity in terms of composition and topography by adjusting the ratio of hyperbranched fluoropolymer and PEG [42]. The amphiphilic copolymer-functionalized surfaces exhibited excellent anti-adherence of proteins or glycoproteins via either hydrophobic or hydrophilic interactions, which weaken the interactions of the organism with the surface. The phase segregation between fluoropolymer and PEG can result in different topographical heterogeneity, which was believed to be driven by the swelling of the PEG domains onto the solid–water interface. At an optimal composition of fluoropolymer and PEG in the polymer, low protein adsorption and high fouling release were achieved [42]. Perfluoropolyether-based random terpolymers were synthesized and showed promising fouling-release performance of *Ulva*. These coatings exhibited good removal of *Ulva* spores after 1 h of contact with the coatings and exposure to water shear stress. But, when the spores were germinated for about a week to form sporelings, the release of sporelings was lower due to the blooming of polar groups on the interface of coating–water [43]. Recently, the hyperbranched fluoropolymers were prepared using atom transfer radical self-condensing vinyl homopolymerization—this hyperbranched fluoropolymers functionalized coating with surface heterogeneities, small enough in size, showed

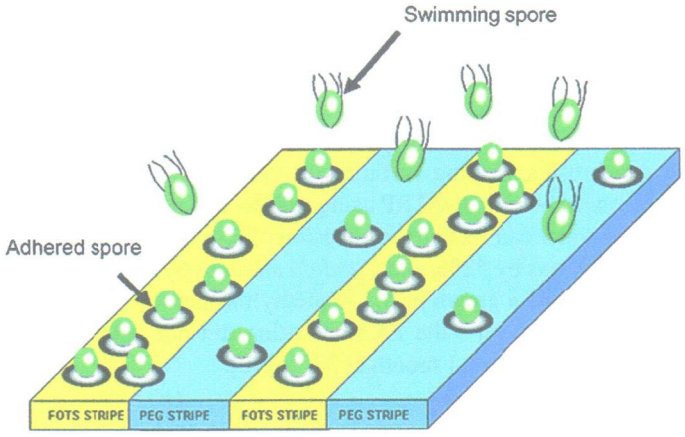

Fig. 3.4 The settlement of *Ulva* zoospores on patterned fluorinated and PEGylated surfaces. (Reprinted with the permission from Ref. [45]. Copyright 2008, American Chemical Society)

enhanced resistance to protein adsorption and cell adhesion, and the size of the heterogeneities must be below the size of the protein molecules, in the 1–10-nm range [44].

To facilitate the optimal design of "ambiguous" surfaces, Finlay and coworkers prepared different types of patterned surfaces containing alternating fluorinated and PEGylated stripes using standard lithographic techniques. *Ulva* spores were found to be selective in these surfaces, settling at higher densities on fluorinated stripes compared to PEGylated stripes (Fig. 3.4). The magnitude of the response was dependent on both the width of the stripes and the chemistry of the background, with settlement on fluorinated stripes narrower than 20 mm for the PEGylated background. However, the *Ulva* spores could not distinguish the difference between the fluorinated and PEGylated features when critical dimension was below 20 mm [45].

3.4 Zwitterionic Polymer-Based Antifouling Surfaces

Although PEG-based materials act as the most common antifouling materials, PEG is a polyether that undergoes oxidation in complex media readily, especially in the presence of oxygen- and transition-metal ions, and is not suitable for long-term use [46]. It is necessary to develop new antifouling materials for a wide range of biological applications. The zwitterionic polymers with a mixture of anionic and cationic terminal groups aroused much interest all over the world due to good antifouling properties, which can resist nonspecific protein adsorption via a bound hydration layer from solvation of the charged terminal groups, in addition to hydrogen bonding [47]. The zwitterionic polymer-grafted surfaces can become highly resistant to protein adsorption when the surface density and chain length of the

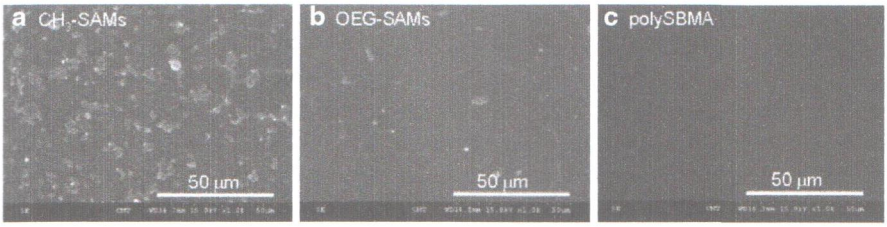

Fig. 3.5 SEM photographs of platelets adhered onto the surface of **a** CH_3-SAMs, **b** OEG-SAMs, and **c** poly(SBMA) surface. CH_3-SAMs self-assembled monolayers; OEG-SAMs oligo(ethylene glycol self-assembled monolayers; poly(SBMA) polysulfobetaine methacrylate. (Reprinted with the permission from Ref. [15]. Copyright 2008, American Chemical Society)

zwitterionic groups are well controlled. Phosphorylcholine (PC)-based zwitterionic polymers have been reported and showed good effectiveness for anti-adsorption of protein and cell due to hydration reaction. Most works related to PC materials have been performed with methacryloyloxyethyl phosphorylcholine (MPC)-based polymers, which can be successfully grafted onto various substrates via free-radical polymerization methods [48]. Iwata et al. have reported to graft PMPC brush onto substrate via SI-ATRP, when the thickness of the grafted PMPC brush layer was greater than 5.5 nm at a graft density of 0.17 chains/nm^2—the adsorption of serum protein and fibroblast on these surfaces was obviously reduced [49]. Zhu et al. have prepared various PMPC-grafted silicon surfaces with different graft-chain lengths via SI-ATRP, but similar graft densities. The adsorption of fibrinogen (Fg) was determined by both graft density and chain length of PMPC, and it showed a stronger dependence on graft density than on chain length. The Fg adsorption decreased significantly with increasing graft density and/or chain length and reached a level of < 10 ng/cm^2 at graft density ≥ 0.29 chains/nm^2 and chain length ≥ 100 units, compared to ca. 570 ng/cm^2 for the contrast samples [50].

MPC could not be widely used in the antifouling because it is moisture sensitive and difficult to synthesize and handle. So, other zwitterionic groups, such as sulfobetaine (SB) and carboxybetaine (CB), have been developed recently owing to good biocompatibilities and potential antifouling applications [51]. The PSBMA-grafted surface can reduce the adsorption of plasma protein for platelet-poor plasma solution to a level superior to that of adsorption on a tetra(ethylene glycol)-terminated surface. As shown in Fig. 3.5, we can see clearly that a lot of platelets have spread on CH_3-SAMs. However, there is still a small amount of slightly activated platelets on OEG-SAMs. The adhesion and activation of platelets from platelet-rich plasma solution were not observed on the PSBMA-grafted surface as compared with OEG-SAMs [15]. Chen et al. prepared PSBMA brushes about 7 nm thick, and found that it can limit protein adsorption [16]. Subsequently, Jiang and coworkers did a more systematic and deeper study—various-thickness (15–90-nm range) PSBMA brushes were screened via SPR to test their anti-adsorption ability for protein [52]. Although all of these surfaces exhibited high resistance to nonspecific protein adsorption from single Fg and lysozyme (Lyz) solutions, the protein adsorption

exhibits a minimum at a medium-film thickness, and the surface modified with 62-nm PSBMA brushes presents the best nonfouling property in 100% blood serum and plasma [52]. The Bailey group prepared PSBMA brushes via SI-ATRP onto the silicon surface of photonic microring resonators through precursor silane SAMs of undecyltrichlorosilane a-bromoisobutyrate; they found the modified surfaces have good antifouling properties against undiluted FBS in comparison to unmodified surfaces [53]. The residual amount of nonspecifically adhered serum proteins was evaluated after returning to the buffer solution, finding that PSBMA-modified surfaces were 260 pg/mm^2. By comparison, PLL-g-PEG and unmodified surfaces were fouled to extents of 1400 and 3000 pg/mm^2, respectively [53]. Chang et al. devised and prepared smart copolymer coatings with excellent antifouling properties using zwitterionic PSBMA and thermoresponsive poly(N-isopropylacrylamide) (PNIPAAm) [54]. Various statistical poly(SBMA-co-NIPAAm) copolymers were prepared and researched, the amount of adsorbed plasma proteins was found to be extremely low, even for copolymer coatings containing as little as 15 mol% of PSBMA [54].

Along with poly(SBMA) coatings, Jiang and coworkers have also prepared poly(CBMA) brushes, and found that the zwitterionic polymer brushes (PSBMA and PCBMA) grafting surfaces show clearly reduced Fg adsorption to a level comparable to that on par with PEG-based coatings [55]. The PSBMA or PCBMA-based surfaces also resisted adhesion of bovine aortic endothelial cells and prevented biofilm formation of Gram-positive and Gram-negative bacteria [56]. The thickness of 10–15-nm PCBMA brushes were grafted onto gold surfaces, which are able to resist fouling for 100% human plasma. The high plasma protein adsorption resistance of PCBMA, as well as its unique anticoagulant activity, makes PCBMA a candidate for blood-contacting applications [57]. More recently, the PCBMA-grafted surface exhibited an improved resistance to nonspecific protein adsorption from human serum and plasma over the POEGMA and PSBMA-grafted surfaces, which probably arises from the shorter distance between the charged groups on the CBMA monomer, resulting in a stronger hydration layer on the surface [51]. In addition, PCBMA brushes possess dual functionalities, such as resist protein adsorption/cell adhesion and immobilize proteins in the antifouling background through the abundant carboxyl functional groups [51].

Kitano and coworkers have prepared various pendent zwitterionic polymers (Fig. 3.6) using disulfide carrying *N, N*-diethyldithiocarbamoyl derivatives as chain transfer agents [58]. The nonspecific binding of proteins on various oligomer SAM surfaces was examined on gold using both electrochemical methods (cyclic voltammetry) and spectroscopic methods (localized surface plasmon resonance; LSPR absorption spectroscopy); the zwitterionic oligomer-based surfaces, in general, did not adsorb proteins significantly [58]. In contrast, the ionic groups and counterions of polyelectrolytes such as poly(sodium acrylate) and poly(sodium ethylenesulfonate) strongly perturbed the structure of water in their hydration shells. So, the existence of the native hydrogen-bonded network of water near the surface is necessary for antifouling and biocompatible properties [59]. Besides, Chen and Jiang have reported "non-zwitterionic" polymers (charge-balanced polyelectrolytes), such as

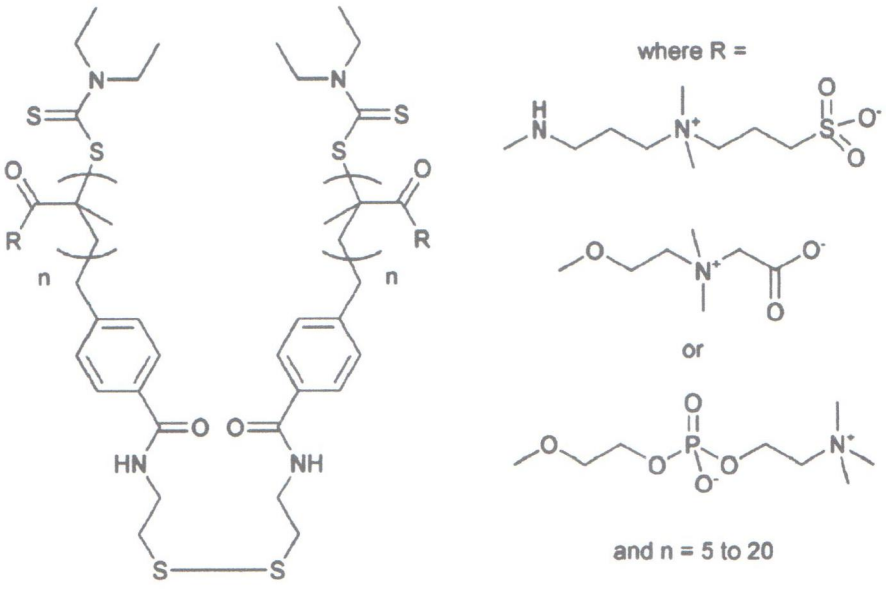

Fig. 3.6 Antifouling polymers with zwitterionic side chains and a disulfide group for attachment to gold substrates. (Reprinted from Ref. [58]. Copyright 2005, with permission from Elsevier)

copolymer hydrogels of positively charged aminoethyl methacrylate hydrochloride and negatively charged 2-carboxyethyl acrylate, which exhibited good resistance to protein adsorption, comparable to that on oligoethylene glycole surfaces [60]. They thought that the close proximity of amino and carboxylic acid groups in the copolymer makes it similar to a zwitterion in ionic character. So, their outstanding antifouling properties may be due to strong hydration of the copolymer through ionic solvation.

3.5 Bactericidal Polymer-Based Antifouling Surfaces

Infections caused by microorganisms remain a major problem, especially in the health-care sector [61, 62]. Various methods have been developed to concentrate the growing need for antibacterial surfaces. The antibacterial action results from the contact of the microorganisms with the biocidal surface without releasing the biocide into the environment. Antimicrobial surfaces can be successfully prepared via grafting antimicrobial polymers onto various substrates [63, 64]. These polymers usually contain cationic groups, such as alkyl pyridinium or quaternary ammonium moieties. While the exact bacteria-killing mechanism of these polymers is still debatable, it is generally thought that the interaction of the cationic sites of quaternized groups with the cell phospholipid membrane causes cell death by disrupting cell membranes allowing release of the intracellular contents.

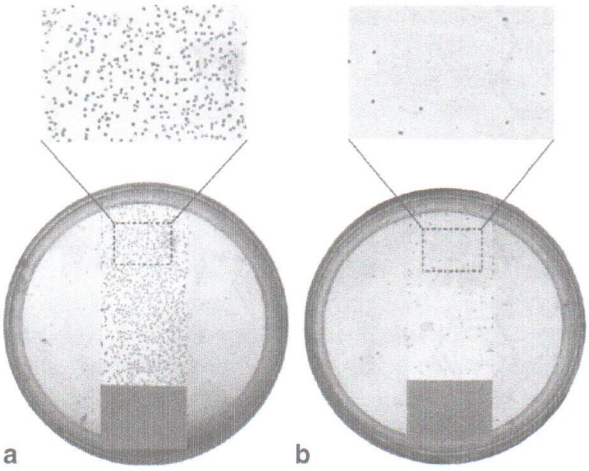

Fig. 3.7 Photographs of a plain NH_2 glass slide (**a**) and a hexyl-PVP-modified slide (**b**) onto which aqueous suspensions (~ 10^6 cells per mL of distilled water) of *S. aureus* cells were sprayed. Hexyl-PVP-modified slide hexyl-poly(4-vinylpyridine-modified slide; Reprinted with permission from Ref. [63]. Copyright 2001, National Academy of Sciences, USA)

The antibacterial surfaces can be prepared by the way of either classical free-radical polymerization or surface-initiated polymerization. Klibanov and coworkers prepared antibacterial polymers with vinyl pyridine group via aminopropyltrimethoxysilane-coated glass and N-alkylated with hexylbromide—the research results show that the coating surface can kill 94% of deposited *S. aureus* cells and more than 99% of deposited *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, and *Escherichia coli* [63]. Figure 3.7 a shows that numerous colonies of *S. aureus* grown on a plain NH_2 glass slide after spraying the bacterial suspension onto its surface are well distinguishable. The poly(4-vinylpyridine) (PVP)-functionalized glass slide was found to absorb approximately the same number of *S. aureus* cells. After *N*-alkylated by seven linear alkyl bromides, the hexyl-PVP-modified slides showed excellent ability to kill on contact with the *S. aureus* cells (Fig. 3.7b). The length of the alkyl group plays an important role in the bactericidal activity— the pyridine groups N-alkylated with alkylbromide with six carbon atoms (C6) showed the highest killing efficacy, followed by C3 and C4 chains, while the C8–C16 chains are obviously less effective. Besides the use of *N*-alkylated PVP, the long polyethylenimine chains were used for functionalization of various substrates, followed by N-alkylation displayed excellent antibacterial property towards both Gram-positive and Gram-negative bacteria [65, 66].

Chitosan acts as a cationic polysaccharide with antibacterial activity, which can be employed for producing antibacterial surfaces [67]. Kang and coworkers prepared hyaluronic acid–chitosan polyelectrolyte multilayers, and the antibacterial efficacy of the functionalized Ti substrates was assessed using *S. aureus* and *E. coli*. The studies showed that the number of adherent bacteria on Ti functionalized with hyaluronic acid–chitosan was up to an order of magnitude lower than that on the pristine Ti—the antibacterial properties were lasting without significant deterioration after 21 days of immersion in PBS owing to stability chemical cross-linking of the multilayers [68]. Another type of antimicrobial compound is the *N*-halamines,

which contains nitrogen–halide covalent bonds, and unlike the cationic bactericidal polymers, the antimicrobial action may be due to the transfer of the oxidative halogen to the bacterial cell [69]. Sun et al. reported that *N*-halamine-based tubing exhibits good antibacterial performance for *P. aeruginosa*. No bacteria could be recovered from the *N*-halamine-functionalized substrates after 1 week. Even four weeks later, the number of recovered bacteria was two orders of magnitude lower than on the contrast. When recharging with bleach, the antibacterial property was recovered, and repeated recharging does not seem to significantly affect its efficacy [70]. A similar method has been reported for functionalization of cotton cellulose with acyclic *N*-halamines, which displays good result in bactericidal properties towards both Gram-positive and Gram-negative bacteria; the *N*-halamines based cotton cellulose provided a total kill of 10^8–10^9 CFU/mL for *E. coli*, *S. aureus*, and *Candida tropicalis* in 3 min, and 10^6–10^7 spores/mL for *Bacillus subtilis* in 4 h [71].

To better control the composition, architecture, and functionalities of the bactericidal polymer, some monomers containing tertiary amino groups, such as 2-dimethylaminoethyl methacrylate (DMAEMA) and 4-vinyl pyridine, can be polymerized via ATRP, then quaternized, to obtain antibacterial polymer covalent attachment onto surfaces [72, 73]. Russell's group prepared the bactericidal polymer brushes via SI-ATRP of tertiary amine-containing DMAEMA from the filter paper and subsequent quaternization of 2-(dimethylamino)ethyl methacrylate (DMAEMA) by an alkyl halide to produce the biocidal functionality on the polymer-modified surfaces [72]. The modified surfaces showed substantial antimicrobial capacity against *E. coli* and *B. subtilis*. The permanence of the antimicrobial activity was demonstrated through repeated use of a modified glass without significant loss of activity. They investigated the relationship and regularity between bacterial-killing properties and polymer brush chain length and grafting density using a combinatorial screening method. Biocidal activity increased with surface charge density of quaternary groups, regardless of the thickness of the dry brush layer. At the same density of quaternary groups, the biocidal activity of surfaces prepared by the "grafting-to" technique was higher than those of surfaces prepared by the "grafting-from" technique [73]. The tertiary amino groups of PDMAEMA brushes were also quaternized via coupling with viologen [74]. In comparison with the alkyl halide-quaternized PDMAEMA brushes, the viologen-quaternized PDMAEMA brushes exhibited significantly enhanced antimicrobial capability, as well as the capability to effectively inhibit biofilm formation.

In addition, Detrembleur et al. prepared antibacterial surfaces using neutral poly(2-(*tert*-butylamino)ethyl methacrylate) (PTBAEMA) via SI-ATRP. PTBAEMA belongs to a novel class of water-insoluble neutral polymeric biocides. The antibacterial mechanism of PTBAEMA is thought to be the displacement of the Ca^{2+} and/or Mg^{2+} ions from the outer membrane of the bacteria, thus disrupting and compromising the membrane function [75, 76].

It is postulated that bacterial attachment on substrate can occur through a layer of adsorbed protein, and thus the anti-adsorption of protein surfaces should resist the attachment of bacteria [77]. Since PEG is widely known to possess good effect for protein resistance, the PEG-modified substrates have also been researched for anti-

adhesion of bacterial. Norde et al. investigated the relationship between the chain length of PEG brushes and the adhesion of different bacteria and yeast. In general, the higher molecular weight PEG and longer brushes showed more effective anti-adsorption of protein properties [78]. They also found that the relatively hydrophobic microbes (*P. aeruginosa* and *C. tropicalis*) adhered on surface more strongly than the hydrophilic microbes (*S. epidermidis* and *C. albicans)*, which is because hydrophobic interactions contributed to the attachment of the microbes on substrate surfaces. The microbes that adhered to the PEG brushes could be easily removed by the passage of an air bubble, indicating that the attachment force is weaker on the PEG-based surface [78]. Polyurethane surface was modified with PEG carrying different terminal groups (hydroxyl, amino, and sulfonate), which were investigated for bacterial adhesion using *E. coli* and *S. epidermidis* [79]. Park and coworkers found that the anti-adsorption of protein activity of substrates were dependent on media, functionalization, and molecular weight of PEG. It was seen that higher molecular weight PEGs showed greater antibacterial activity than the lower-molecular-weight ones, and surfaces functionalized with terminal sulfonate groups were most effective in reducing bacterial attachment [79]. Though PEG-functionalized surface is one of the most effective methods in fabricating anti-adsorption of protein surfaces, it is not very effective in reducing bacterial attachment, may be owing to the complex adsorbing mechanisms of bacteria on the surface [77].

3.6 Antimicrobial Polymer-Based Antifouling Surfaces

Polymer brushes could conjugate with agents such as antibiotics, antimicrobial peptides (AMPs), or complexes with silver for preparing an antimicrobial surface. The polymer brushes act as different roles such as providing an anti-adhesive surface, serving as a spacer for the tethered antimicrobial agent, etc.

There are some reports about the antibiotics-functionalized polymer brush to enhance antimicrobial activity [80]. The hybrid polymer with long PEG-3000 chain and antibiotic (vancomycin) was synthesized, which combines the anti-adhesive property of PEG with antibacteria of vancomycin. The long PEG linker should make the modified surfaces resistant to proteins and cells, and the vancomycin can inhibit the growth of bacteria. Thus, the hybrid polymer-grafting-titanium substrates exhibit cell-resistant properties and strong antimicrobial activity against *B. subtilis* [81]. Neoh et al. have reported antibiotics (gentamicin and penicillin)-tethered PHEMA brushes onto titanium surfaces via SI-ATRP of 2-hydroxyethyl methacrylate (HEMA). The antibacterial activity of the PHEMA and antibiotic-cofunctionalized substrates against *S. aureus* was equivalent to that of quaternized PDMAEMA. They thought that the bacterial proteases can help hydrolyze surface-attached antibiotics resulting in the gradual release of antibiotics [82].

AMPs have a good antimicrobial activity due to the interaction of the positively charged AMPs with the negatively charged bacterial cell membrane, which can cause cell disruption and lead to cell death. Bagheri and coworkers prepared

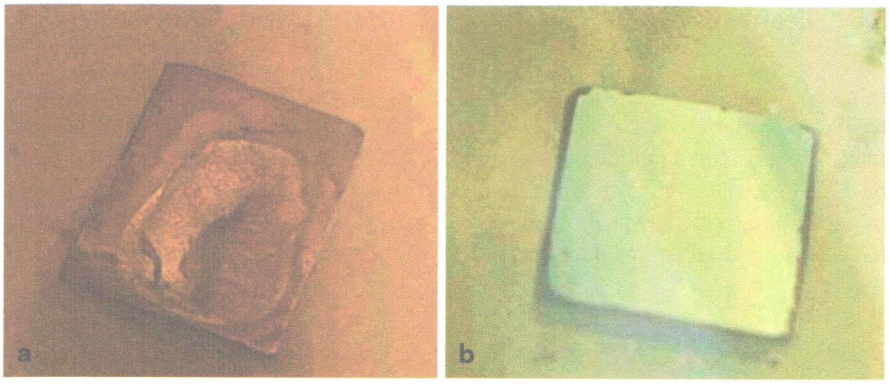

Fig. 3.8 **a** Growth of *S. aureus* on a piece of sulfonate brush-based silica wafer, **b** absence of growth of *S. aureus* on a silica wafer modified with silver-loaded sulfonate brushes. (Reprinted with the permission from Ref. [62]. Copyright 2007, American Chemical Society)

antibacterial surfaces with new hybrid polymer using AMP and different lengths of PEG and found that the peptide's antimicrobial activity decreases upon immobilization, and a shorter-length PEG will reduce the activity more [83]. Huck et al. have investigated and reported the nonfouling copolymer coating tethering AMP possessing high antibacterial activity against two different strains of Gram-positive bacteria *Listeria ivanovii* and *Bacillus cereus,* the nonfouling copolymer brush graft onto silicon wafers via SI-ATRP from 2-(2-methoxyethoxy)ethyl methacrylate (MEO_2MA) and hydroxyl-terminated oligo(ethyleneglycol) methacrylate (HOEGMA), which can be functionalized for attaching a natural antibacterial peptide due to the availability of the hydroxyl-reactive groups, the amount of hydroxyl group incorporated into the brushes can be varied by changing the ratio of the monomer mixture [2].

The good antibacterial activities of silver-based compounds were known for centuries [84, 85]. Although the antibacterial actions of silver nanoparticles on microorganisms are not fully understood, the good antibacterial effect of silver nanoparticles has stimulated great interests in potential and actual applications. Silver nanoparticles have been shown to cause pit formation in bacteria cell wall and increased membrane permeability [86]. In addition, silver also possesses excellent bactericidal activity via release of silver ions [87]. Anionic polyelectrolyte brushes bearing sulfonate groups have been used to trap silver ions. The anionic polyelectrolyte brushes of poly(3-sulfopropylmethacrylate) were prepared via SI-ATRP of 3-sulfopropylmethacrylate and used to load antibacterial silver ions inside of the polymer brush [62]. Figure 3.8a shows that bacterial growth and formation of a biofilm can take place on sulfonate-brush-based surface. The silver functional sulfonate brushes exhibit good effect for inhibiting the growth of both Gram-negative and Gram-positive bacteria (Fig. 3.8b). Furthermore, the brushes were able to retain the silver ions at the surface during leaching and also retard the leaching of silver ions in water and in the NaCl medium. Thus, the silver-loaded sulfonate brushes exhibited desirable antibacterial properties [62].

3.7 Bioinspired Polymer-Based Antifouling Surfaces

In recent years, a considerable amount of researches have been performed on antifouling polymer coatings (such as PEG, OEGMA, etc.) grafted onto substrate surfaces via catechol functional groups [19, 88, 89]. The adhesion of protein, cells, bacteria, and algae is significantly reduced with the increasing of the surface density of antifouling polymer. The thickness of coatings can range from a few nanometers to several hundred nanometers via "graft-to" or "graft-from" method.

3.7.1 Building Antifouling Surfaces Via "Graft-to" Approaches

Generally, the method for preparing antifouling surfaces via an antifouling polymer conjugated at one end to an adhesive moiety (amino acid or short peptide), then surface modification is accomplished via simple adsorption of functional polymer onto surfaces via the adhesive group. As a universal nonfouling polymer, PEGs were linked to surfaces using either single or multiple catecholic groups [88, 90] and showed excellent resistance to serum protein adsorption [91]. The first manifestation of this approach consisted of a PEG coupled to a decapeptide sequence that was derived from M. edulis foot protein 1(mfp-1). Messersmith et al. have researched cell attachment on the surfaces modified with PEGs end-functionalized consensus decapeptide repeat sequence of mfp-1 (mPEG-MAPD), and found that the substrate surfaces modified with mPEG-MAPD have good anti-adsorption for cell [92]. Figure 3.9 shows an image of cell attachment to an Au substrate partially coated with mPEG-MAPD. Fibroblasts are observed to adhere and spread only on the region that remains unmodified by polymer, while the polymer-modified area is entirely cell-free.

Lee et al. studied cell adhesion on PEG-g-catechol-modified surfaces, numerous fibroblast cells were attached to the bare Si surfaces after 6 h in the cell culture media. The average cell densities of each surface were 766 cells/mm^2 for Au and 838 cells/mm^2 for Si. By comparison, the cell density was only 16 cells/mm^2 for Au and 7 cells/mm^2 for Si on the PEGylated surfaces [93]. Textor and coworkers have grafted more complex oligo ethylene glycol dendritic structures onto titanium oxide surfaces via multidentate oligomers of L-DOPA/dopamine. The functionalized surfaces showed remarkable antifouling properties for full blood serum, and the resistance to protein adsorption was found to strongly depend on surface coverage of dendrimers [94]. PEG-DOPA$_3$ (three catechol groups) has a good effect for preventing bacterial absorbing, which can form biofilm on various substrate surfaces. [89] The mPEG-DOPA$_3$-grafted titanium surfaces have demonstrated a greater than 94% reduction in bacteria binding for six major uropathogenic bacterial strains for 24 h at 37 °C in human-pooled urine. The coatings of catechol-modified PEG also showed a significant reduction in bacteria adhesion.[89] Moreover, the strong correlation between the adsorbed PEG thickness and serum protein adsorption was demonstrated for mPEG-DOPA$_3$ with assembly time of more than 30 min and thick-

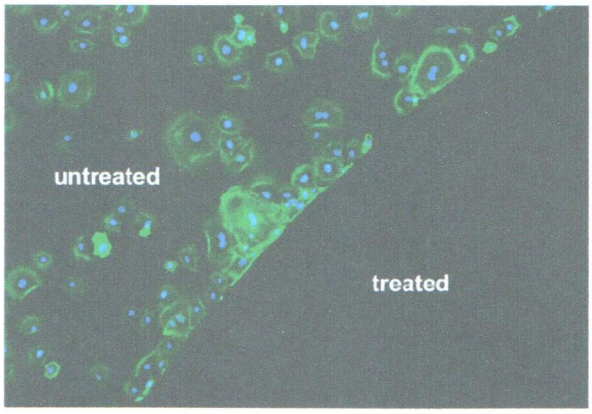

Fig. 3.9 Fluorescence microscopy image of fibroblast attachment (4 h) on Au substrate in which a circular portion of the surface was modified with mPEG-MAPD (treated), the remainder of the Au surface was unmodified (untreated). (Reprinted with the permission from Ref. [92]. Copyright 2003, American Chemical Society)

ness of adsorbed serum protein of less than the sensitivity limit of the technique (optical waveguide lightmode spectroscopy; <0.5 Å) [91]. The resistance to nonspecific blood serum adsorption were investigated using different types of PEG (5 kDa)-catechol derivatives, The mPEG-nitrodopamine showed a particularly attractive polymer resulting in higher PEG brush thickness and the best resistance of serum protein adsorption [95]. Gademann et al. investigated protein adsorption on the TiO_2 surfaces coated with the different catecholic anchors coupled to PEG and found that didopamine-PEG showed the highest adlayer thickness while displaying a large reduction in protein attachment [96]. The monodisperse PEG-Fe_3O_4 nanoparticles through catechol bonding exhibited negligible aggregation in cell culture condition and much reduced nonspecific uptake by macrophage cells, meaning that these nanoparticles can escape from the innate immune system [97].

Lee et al. have synthesized and evaluated the ability of poly[dopamine- methacrylamide-*co*poly(ethylene glycol)-methylether methacrylate] (DMAm–*co*–mPEG–MA) coated ureteral stents to resist bacterial adherence, infection development and encrustation in a rabbit model with uropathogenic *E. coli* cystitis, and found that p(DMAm–*co*–mPEG–MA)-coated devices showed decreased urine and stent bacterial counts compared to unmodified devices, eight of ten rabbits demonstrated sterile urine by day 3 in each control group, while stent-adherent organisms were decreased by more than 75%. The p(DMAm*co*-mPEG-MA) coating strongly resisted bacterial attachment, resulting in improved infection clearance over that of uncoated devices [98]. In addition, by conjugating bioactive functional groups to the end group of the DOPA-anchoring PEG chains, Miller et al. have developed surfaces that are conducive for the stable presentation of bioactive peptides and proteins in a background that resists nonspecific protein adsorption. Various biotinylated ligands can be incorporated into $DOPA_3$–PEG surfaces via biotinavidin interactions, opening the door to incorporate biospecific functional groups into such surfaces [99].

Furthermore, Jiang reported the synthesis of a zwitterionic polymer with two catecholic groups (pCB_2–$catechol_2$) that could graft onto an Au and SiO_2 surface.

The functionalized surface maintained excellent bioactivity for the detection of activated leukocyte cell adhesion molecule in complex blood media and excellent nonfouling properties—the surface has undetectable protein adsorption (<0.3 ng/cm^2) from single protein solutions, such as Lyz and Fg from SPR measurements [100]. The zwitterionic polymer-modified surfaces have the potential applications in implantable medical devices and for nanoscale sensors for medical diagnostics [101].

Wang and coauthors have investigated bacterial adhesion and osteoblast function on titanium surfaces with surface-grafted chitosan via a dopamine linker and immobilized Arg–Gly–Asp (RGD) peptide to the free NH_2 groups of chitosan [102]. This functionalized substrate exhibited a decrease in adhesion of *S. aureus* and *S. epidermidis* compared with the pristine substrate, a significant increase in osteoblast cell attachment, proliferation, and alkaline phosphatase activity was observed on the surface with the attachment RGD peptide on the chitosan, which is advantageous for combating biofilm-related infections and promoting tissue integration related to implants. Even immerging in PBS for 14 days, the immobilized substrates still remain good antibacterial properties [102].

Moreover, researchers have explored other antifouling polymers with catechol anchors and found they have a good antifouling performance. For example, the new kind of antifouling polymers [103, 104]-peptidomimetic polymer (PMP1) consisting of a short functional peptide domain forms robust adsorption to surfaces, coupled to an N-substituted glycine (peptoid) oligomer of variable length that provides excellent resistance to protein and cell fouling [104], PMP1-modified Ti surfaces show extremely good effect for anti-cell attachment over 5 months in spite of twice weekly challenges with new cells [104]. Investigators have explored the effect of adhesion resistance for protein, cell, and bacteria with a number of side-chain chemistries, including methoxyethyl, methoxypropyl, and hydroxypropyl. These new bioinspired antifouling polymers may provide long-term control of surface biofouling in the physiologic, marine, and industrial environments.

3.7.2 *Building Antifouling Surfaces Via "Graft-from" Approaches*

In recent years, more attention has been given to "graft-from" approaches, because the "graft-from" approaches theoretically have the advantage of achieving thicker and higher-density-layer polymer brush. The basic requirement for this approach is a bifunctional molecule containing an initiating group for initiating polymerization, and coupled to functional adhesion group for anchoring substrate surfaces. Messersmith et al. synthesized a biomimetic initiator that contains a catechol end group for surface anchoring and alkyl bromine to initiate ATRP [105]. Oligo (ethylene glycol) methyl ether methacrylate (OEGMEMA) brushes were grafted onto Ti or stainless steel. The grafted thickness of polymer (POEGMEMA) is many times greater than "graft-to" methods. Fibroblast cells readily attached on bare Ti and 316 L SS

after 4 h at average densities of approximately 40 and 50 cells/mm^2, respectively; POEGMEMA-grafted surfaces only supported the attachment of around 1 cell/mm^2 on Ti and no cells on 316 L SS [105].

Jiang and coworkers reported that nonfouling zwitterionic polymer brushes polysulfobetaine methacrylate (SBMA) were grafted via SI-ATRP from surfaces covered with an adhesive catechol initiator, which can be attached to both bare gold and amino-functionalized surfaces [106]. Ultralow protein adsorption from both single-protein solutions of Fg and Lyz and complex media of 10% blood serum and 100% blood plasma/ serum was achieved on polySBMA grafting substrates. Fouling from 10% human serum (measured by SPR after 15 min exposure) was low at 12 ± 3 ng/cm^2, even lower protein adsorption (1.1 ± 2.0 ng/cm^2) was achieved for polySBMA brushes grown from ATRP initiator immobilized onto pre-coated NH_2-terminated alkylthiol SAMs. These particular coatings maintained good performance (14.9 ± 6.0 ng/cm^2) against more challenging undiluted human serum. The research results showed that the zwitterionic coatings dramatically reduced the adhesion of *P. aeruginosa* by 99.5% as compared to a bare-glass contrast [106].

Another biomimetic catecholic initiator was designed for carrying out surface-initiated ring-opening metathesis polymerization (ROMP) [107].High-density poly(ionic liquid) brushes based on imidazolium salt were successfully grafted to surfaces via surface-initiated ROMPs from catecholic initiator (Fig. 3.10). Very uniform poly(ionic liquid)s coating with the thickness up to 80 nm was obtained on TiO_2. The poly(ionic liquid) brushes showed very good stability in an aqueous solution and provided significantly good antimicrobial function in comparison with conventional antibacterial ammonium-based polymer brushes. The evaluation of antibacterial and anti-biofouling properties of poly(ionic liquid) brushes show that poly(ionic liquid) brushes can obviously resist *chlorella* spores adhesion and the counter anions play a key role in the antimicrobial property. The poly(ionic liquid) s with hexafluorophosphate anions-coated TiO_2 nanomaterials have excellent antibacterial properties compared to pristine TiO_2 nanoparticles against both *E. coli* and *S. aureus*. The eco-friendly poly(ionic liquid)-TiO_2 nanomaterials can be applied to various antimicrobial applications ranging from light-activated systems to the dark sterilization approach [107].

This "graft-from" approach can be compatible with established photolithographic methods to pattern surfaces for spatial control of biointeractions. Molecular assembly/patterning by lift-off (MAPL) was used to produce nonfouling regions within a cell-adhesive Ti field [105, 108]. Figure 3.11a and b shows the TOF-SIMS chemical map of the patterned surface and the cell attachment to the patterned Ti surface on the patterned Ti surface with POEGMEMA, respectively. It is seen that one to four cells are confined within the circular regions of the bare Ti, while the grafted polymer region-resisted cell attachment in a spatially controlled manner. The method can combine "graft-from" strategy with simple patterning technique, which will have potential uses for creating antifouling surfaces for diagnostic cell-based arrays or other devices on metal substrates [105].

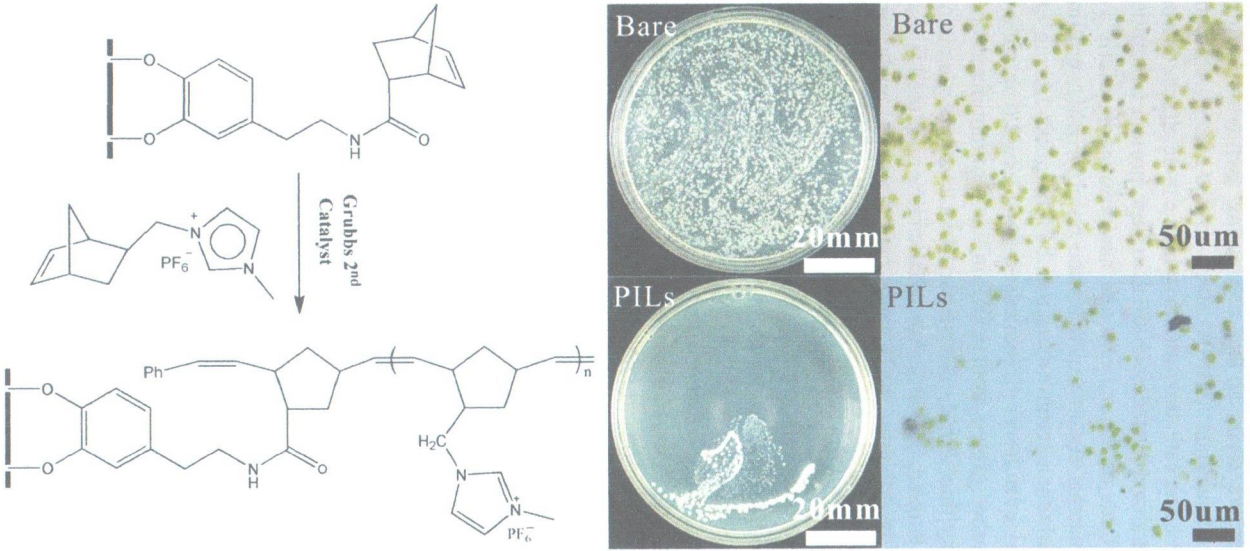

Fig. 3.10 Grafting poly(ionic liquid) brushes for antibacterial and anti-biofouling via surface-initiated ring opening metathesis polymerization. (Reproduced from Ref. [107] by permission of The Royal Society of Chemistry)

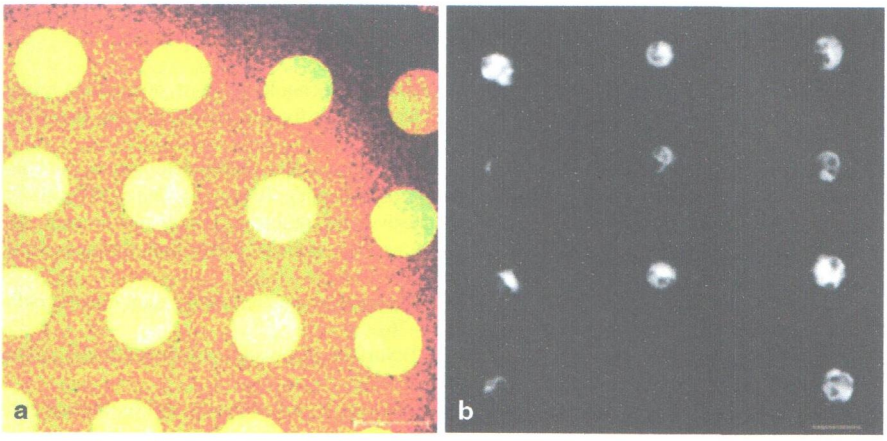

Fig. 3.11 **a** The time of flight secondary ion mass spectroscopy (TOF-SIMS) map of Ti+signal (m/z=47.89) collected from a patterned POEGMEMA thin film after a 12-h ATRP, with scale bar=100 mm; **b** The fluorescence microscopy image of fibroblast attachment (4-h culture) on the patterned POEGMEMA surface, with scale bar=50 mm. (Reprinted with the permission from Ref. [105]. Copyright 2005, American Chemical Society)

3.8 Conclusions and Perspectives

The development and application of antifouling surfaces based on polymer brushes are described in detail. Various types of polymer brushes (PEGylated polymers, amphiphilic copolymers, zwitterionic polymers, bioinspired polymers and polymers incorporating antimicrobial agents, etc.) are particularly suited for the preparation of functional bioactive surfaces, including anti-adsorption for cell and protein, antibacterial, biomolecule-coupled, and patterned surfaces. The advances in techniques for surface modification and tailoring of polymer composition and architecture in the past have resulted in many promising developments in antifouling field. Although a large number of different techniques for nonfouling polymer brush surfaces have been investigated in the past years, the creation of perfect antifouling surfaces is still a very challenging task because of the different adhesion mechanisms of various species and changeable environment, and the cost-effectiveness, long-term stability, and durability of nonfouling-polymer-brush-functionalized surfaces is also an indispensable part. These challenges indicate that much more work needs to be done in order to further develop polymer brushes-based antifouling surface via obtaining more effective nonfouling polymer and combining surface topography to create structural antifouling coatings. The future researches about polymeric antifouling surfaces should be also toward correlating molecular level details of the functionalized surface, and establishing a fundamental understanding of antifouling- and fouling-release mechanisms. So, it requires more knowledge on the role about mechanical properties of the coating on fouling release and the chemical composition of the adhesive matrices of organisms.

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