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Poly(ethylene oxide) surfactant polymers

KATANCHALEE VACHEETHASANEE^{1,*}, SHUWU WANG², YONGXING QIU^{2,†}, and ROGER E. MARCHANT^{1,2,‡}

¹ Department of Macromolecular Science, Case Western Reserve University, Cleveland, OH 44106, USA

² Department of Biomedical Engineering, Wickenden Building, Case Western Reserve University, Cleveland, OH 44106, USA

Abstract

We report on a series of structurally well-defined surfactant polymers that undergo surface-induced self-assembly on hydrophobic biomaterial surfaces. The surfactant polymers consist of a poly(vinyl amine) backbone with poly(ethylene oxide) and hexanal pendant groups. The poly(vinyl amine) (PVAm) was synthesized by hydrolysis of poly(*N*-vinyl formamide) following free radical polymerization of *N*-vinyl formamide. Hexanal and aldehyde-terminated poly(ethyleneoxide) (PEO) were simultaneously attached to PVAm via reductive amination. Surfactant polymers with different PEO : hexanal ratios and hydrophilic/hydrophobic balances were prepared, and characterized by FT-IR, ¹H-NMR and XPS spectroscopies. Surface active properties at the air/water interface were determined by surface tension measurements. Surface activity at a solid surface/water interface was demonstrated by atomic force microscopy, showing epitaxially molecular alignment for surfactant polymers adsorbed on highly oriented pyrolytic graphite. The surfactant polymers described in this report can be adapted for simple non-covalent surface modification of biomaterials and hydrophobic surfaces to provide highly hydrated interfaces.

Keywords

Nonionic surfactant polymers; poly(ethylene oxide); poly(vinyl amine); surface tension; atomic force microscopy

INTRODUCTION

Surface modification provides a practicable and economic route for achieving significant improvements to the interfacial properties of materials. In the context of materials used for biomedical applications, considerable effort has been devoted to surface modification of polymer biomaterials in order to reduce the clinical problems of surface-induced thrombosis and infection [1–4]. Highly hydrated polymers may serve the purpose of effective surface modifying agents, by providing a physical steric barrier that suppresses non-specific cellular and molecular adhesions. Examples of this approach include poly(ethylene oxide) (PEO) [5, 6], polyacrylamide [7] and ethoxylated cellulose [8]. In living systems, however, adhesive and non-adhesive interactions are controlled and directed by the cell-surface-glycosylated molecules, known as glycocalyx [9]. In following this biological perspective, glycocalyx-like oligosaccharide-rich surfaces have been designed in our laboratory as a potential solution to the medical-device-related problems of thrombosis [10–12].

[‡]To whom correspondence should be addressed at the Department of Biomedical Engineering. Tel.: (1-216) 368-3005. Fax: (1-216) 368-4969. E-mail: rxm4@po.cwru.edu.

^{*}Current address: National Metal and Materials Technology Center, NSTDA Building, 73/1 Rama VI Road, Rajdhevee, Bangkok 10400, Thailand.

[†]Current address: CIBA Vision Corporation, BIT, 11460 Johns Creek Parkway, Duluth, GA 30097, USA.

Non-covalent adsorption and assembly of hydrated molecules on biomedical device surfaces is a promising modification strategy for hydrophobic biomedical polymers which typically contain no labile functional groups required for covalent immobilizations [13]. Previously we have designed glycocalyx-like surfaces using comb-like oligosaccharide surfactant polymers, poly(*N*-vinyl dextran aldonamide-*co-N*-vinyl hexanamide) [10]. The oligosaccharide surfactant polymers consist of flexible poly(vinyl amine) (PVAm) with multiple hexanoyl and dextran side chains randomly spaced along the polymer backbone. The hexanoyl chains serve to anchor the polymer surfactant to the substrate through entropic hydrophobic interactions, while the hydrophilic dextran chains orient into the aqueous environment to provide a glycocalyx-like steric barrier. The surfactant polymers are surface active at both the air/water interface, as determined by significant decreases in water surface tension; and at the solid/water interface, as determined by spontaneous adsorption onto highly oriented pyrolytic graphite (HOPG) [11] and polyethylene [12] observed by AFM. Furthermore, oligosaccharide surfactant polymers-modified surfaces showed approximately 90% reduction in non-specific adsorption of plasma proteins [11,12].

For designing a bacterial-resistant interface for a solid surface, oligosaccharides may not be the optimum choice, since bacteria contain numerous enzymes capable of degrading glycosidic bonds. One possibility for manipulating the surfactant polymer design for developing bacteria-resistant surfaces, is to replace the dextran side chains with synthetic hydrated polymer molecules. Apart from its hydrolytic stability, PEO has conformational flexibility and high chain mobility, that can be exploited to create a repulsive barrier to prevent adsorption of other macromolecules or particles [14]. Therefore, we prepared PEO surfactant polymers having a similar architecture to the dextran surfactant polymers, in order to investigate the influence of PEO conformational flexibility and chain mobility on surface active properties. Although the bacterial resistant properties of PEO surfactant polymers have been reported [15], we have not reported on the synthesis and surface active properties.

In this report, we describe the synthesis, characterization, and surface active properties of a series of well-defined, comb-like surfactant polymers derived from PVAm. Aldehyde-terminated PEO molecules and hexanal side chains were incorporated into PVAm via reductive amination using various feed ratios. The molecular composition of the surfactant polymers was determined by FT-IR, ¹H-NMR and XPS spectroscopies. Surface active properties at the air/water interface were determined by surface tension measurements, while AFM was used to investigate the surface activity of PEO surfactant polymers at the HOPG/water interface.

MATERIALS AND METHODS

Materials

N-vinylformamide, monomethoxypoly(ethylene glycol) (M_n 2000), 2,5-difluorobenzaldehyde, sodium cyanoborohydride (NaBH₃CN) and 2,2' azobisisobutyronitrile (AIBN) were purchased from Aldrich and used as received. Acetic anhydride, used as received, was obtained from Fisher Chemical. Dimethylsulfoxide (DMSO; Fisher Chemical) was freshly distilled before use. Amberlite IRC-50, strong anionic exchange resin, was purchased from Sigma and rinsed with distilled Millipore water before use. All other reagents and solvents were used as received unless otherwise specified.

Methods

The products obtained from each step were characterized by proton nuclear magnetic resonance (¹H-NMR) and Fourier transform infrared (FT-IR) spectroscopies. ¹H-NMR spectra were obtained from a 200 MHz Varian Gemini-200 spectrometer using DMSO-*d*₆ as a solvent and a reference at 2.45 ppm. Transmission FT-IR spectra in the wavelength range of 400–4000

cm^{-1} were obtained using a Bio-Rad FTS-575C FT-IR spectrometer. The materials were ground with KBr and pressed into pellets under reduced pressure. The spectrum of each sample was then collected from 100 scans for with a resolution of 8 cm^{-1} .

X-ray photoelectron spectroscopy (XPS) was carried out using a Perkin Elmer PHI-5400 XPS system, equipped with a 400 W anode and 15 V Al K_{α} X-ray source (1487 eV). The spectra were charge referenced to the C_{1s} peak of C–C at binding energy 285 eV. The take-off angle was fixed at 45° . For each sample, five survey spectra were recorded from 0 to 1100 eV, using a fixed pass energy of 93.9 eV. Atomic compositions were calculated using Phi analysis software, which utilizes peak areas and pre-programmed atomic sensitivity factors. The XPS samples were prepared by coating PEO surfactant polymers on low density polyethylene sheets (PE; NHLBI primary reference; Abiomed) from 1 mg/ml aqueous solutions.

Gel-permeation chromatography (GPC) was carried out using a Waters 2690 Alliance HPLC system equipped with a HEMA-BIO100 GPC column, a reflective index detector (Waters 410) and a light scattering detector (Mini Dawn, Wyatt Technology). The flow rate was 1.0 ml/min using deionized water as eluent.

Surface active properties of the surfactant polymers at an air/water interface were determined from water surface tension measurements. Surface tensions of aqueous surfactant polymer solutions were measured at 25°C and ambient pressure, using a Sigma 703 ring tensiometer. The tensiometer was calibrated with Millipore water before use. The platinum ring was cleaned by flaming, while all glassware was cleaned with strong basic solution and rinsed with Millipore water. A saturated solution of surfactant polymer was freshly prepared, as a starting solution and then diluted to the desired bulk concentration for each measurement. Surface tension was measured three times at each bulk concentration.

Surface active properties of surfactant polymers at a solid surface/water interface were examined using AFM operating in fluid tapping mode. Images of surfactant polymers adsorbed on highly oriented pyrolytic graphite (HOPG) were obtained using a Nanoscope III multimode AFM (Digital Instruments) equipped with a glass fluid cell attachment. Silicon nitride (Si_3N_4) cantilevers with integrated Si_3N_4 tips (Nanoprobes, Digital instruments) were used. Freshly cleaved HOPG was imaged in water, before injection of surfactant solution ($0.5\text{--}100 \mu\text{g/ml}$) into the fluid cell. This was done without withdrawing the AFM probe, so that the images before and after adsorption of surfactant molecules were scanned in the same region of the HOPG surface.

Synthesis of poly (N-vinyl monomethoxy poly(ethylene oxide) ethylamine-co-N-vinyl hexanamine) (PVAm/PEO : Hex)

A series of comb-like surfactant polymers, PVAm/PEO : Hex, were synthesized using a three step procedure as shown in Scheme 1A: (i) synthesis of poly(vinyl amine) (PVAm), (ii) preparation of monoaldehyde terminated poly(ethylene oxide) (PEO-CHO) and (iii) coupling of PEO-CHO and hexanal side chains to PVAm using reductive amination.

Synthesis of poly(vinyl amine).—Poly(vinyl amine) (PVAm) was synthesized from poly (N-vinyl formamide) and characterized as previously described [10]. Poly(N-vinyl formamide) was synthesized by free radical polymerization using AIBN as initiator. The poly(N-vinyl formamide) was hydrolyzed to form poly(vinyl amine) salt, using aqueous NaOH solution. The amine salt was converted to free amine by ionic exchange using a strong anionic resin.

Synthesis of aldehyde-terminated poly(ethylene oxide).—PEO-CHO was prepared by oxidation of the terminal hydroxy group on monomethoxypoly(ethylene glycol) using a modification of the method published by Harris *et al.* [16,17]. Monomethoxypoly(ethylene

glycol) (10 g, 5 mmol) was dissolved in DMSO (17 ml). Acetic anhydride (10.2 g, 20 : 1 mol ratio of anhydride to hydroxyl) was added to this mixture and stirred for 8 h at room temperature. At the end of the reaction, the solution was precipitated in a 20-fold excess of diethyl ether. The precipitate was redissolved in minimum methylene chloride and then reprecipitated three more times in a 10-fold excess of diethyl ether. The product obtained was vacuum dried overnight at room temperature to yield 8.8 g (88%) of PEO-CHO. IR: 2887 cm^{-1} ($\nu(\text{C-H})$ of CH_2), 1737 cm^{-1} ($\nu(\text{C=O})$ of CHO), 1467 cm^{-1} (deformation of C-H in R- CH_3) and 1117 cm^{-1} ($\nu(\text{C-O-C})$). $^1\text{H-NMR}$ (ppm): 3.2–3.6 ($-\text{CH}_2\text{CH}_2\text{O}-$) and 2.0 (CH_3-O). No characteristic peak of aldehyde was detected by $^1\text{H-NMR}$, possibly because of its extremely low atomic concentration per PEO group.

Coupling aldehyde-terminated poly(ethylene oxide) and hexanal side chains to poly(vinyl amine).—PVAm/PEO : Hex surfactant polymers were synthesized by reacting

amino groups on PVAm with terminal aldehyde groups on PEO-CHO and hexanal simultaneously in the presence of sodium cyanoborohydride, using the method of reductive amination [18]. Polymer surfactants with five different feed ratios of PEO-CHO to hexanal (1 : 0, 1 : 1, 1 : 2, 1 : 4, 1 : 8) were prepared. To prepare PEO surfactant with 1 : 1 feed ratio, hexanal (36.14 μl , 0.3 mmol aldehyde groups) was added to a methanol solution (6 ml) containing PVAm (25.8 mg, 0.6 mmol amino groups) and PEO-CHO (0.75 g, 0.375 mmol). The amount of PEO-CHO used in the reaction was calculated based on the findings of others that approx. 80% aldehyde end-groups were found in the PEO-CHO product obtained from the oxidation of the terminal hydroxy group on PEO [16,17,19]. A methanol solution (1 ml) containing NaBH_3CN (37.7 mg, 0.6 mmol) was added to the mixture and the pH was adjusted to 5–6 using 4 M HCl. After stirring for 24 h at room temperature, the solution was precipitated in diethyl ether. Recovery of the product was accomplished by centrifugation at $800 \times g$ at 5°C to give 0.42 g (64.5%) of raw product. The precipitates were dried under vacuum at room temperature overnight. Purification was performed by dialysis against water to remove unreacted PEO-CHO and hexanal, using Spectra Pro 3 regenerated cellulose membrane with a 25 kDa molecular mass cut-off (Spectrum). The sample was dehydrated by lyophilization and the product was dried further under vacuum at room temperature overnight to give 0.28 g (42% yield) raw product. PEO surfactant polymers with 1 : 0, 1 : 2, 1 : 4 and 1 : 8 feed ratios were prepared using similar procedures, providing 31, 42, 41 and 45% yields, respectively. IR: 2887 and 2930 cm^{-1} ($\nu(\text{C-H})$ of CH_2 and CH), 1467 cm^{-1} (deformation in C-H of R- CH_3) and 1117 cm^{-1} ($\nu(\text{C-O-C})$). $^1\text{H-NMR}$ (ppm): 3.2–3.6 ($-\text{CH}_2\text{CH}_2\text{O}-$ of PEO ligands and CH groups on PVAm backbone), 2.6 (NH and NH_2 on PVAm backbone), 2.0 (CH_3-O), 1.1–1.5 ($-(\text{CH}_2)_4\text{CH}_3$ of hexanal side chains and CH_2 groups on PVAm backbone) and 0.84 ($-\text{CH}_3$ of hexanal groups). XPS: C (1s, 285 eV), N (1s, 398 eV) and O (1s, 532; 2s, 23 eV; Auger-KLL, 977 eV).

Fluorination of unreacted amino groups on poly(vinyl amine)

Unreacted amino groups on the PVAm backbone of surfactant polymers were quantified by fluorination of the amino groups, followed by XPS analysis. The unreacted amino groups were capped with 2,5-difluorobenzaldehyde (DFB) via reductive amination in the presence of NaBH_3CN (Scheme 1B). The protocol for fluorination was analogous to the PVAm/PEO : Hex synthesis with the following reactants: methanol solution (6 ml) containing PEO surfactants (15 mg), DFB (150 μl , 1.4 mmol), NaBH_3CN (7 mg, 0.1 mmol). Purification of raw product was performed by dialysis against methanol to remove unreacted DFB, using Spectra Pro 3 regenerated cellulose membrane with a 3 kDa molecular mass cut-off (Spectrum). The solution was then added to water (10 ml), purged with N_2 to remove methanol and lyophilized. The final product was dried under vacuum at room temperature overnight to give approx. 8 mg (approx. 54% yield) raw product. XPS: C (1s, 285 eV), N (1s, 398 eV), O (1s, 532; 2s, 23 eV; Auger-KLL, 978 eV) and F (1s, 685; 2s, 30 eV; Auger-KLL, 832 eV).

RESULTS AND DISCUSSION

Synthesis of poly(*N*-vinyl monomethoxy poly(ethylene oxide) ethylamine-co-*N*-vinyl hexanamine)

Synthesis of comb-like PEO surfactant polymers, PVAm/PEO : Hex, required 3 reaction steps (Scheme 1A). The first step was to prepare PVAm using an existing, well-defined method [10]. Polymerization of commercially available *N*-vinyl formamide yielded poly(*N*-vinyl formamide) with average molecular weights: M_n approx. 52 300 and M_w approx. 87 800 as determined by GPC. The poly(*N*-vinyl formamide) was hydrolyzed and passed through a strong anionic exchange column, yielding PVAm with M_n approx. 31 700 and M_w approx. 53 100, as calculated from the molecular weight averages of the poly(*N*-vinyl formamide). FT-IR and ^1H -NMR results were similar to those published previously [10]; however, molecular weights of PVAm obtained in the present study were approximately 3-times greater.

The PVAm/PEO : Hex surfactant polymers were prepared by simultaneous attachment of hydrophilic PEO-CHO and hydrophobic hexanal chains to PVAm backbone via reductive amination in the presence of NaBH_3CN catalyst. The extent of coupling for the 1 : 4 feed ratio surfactant polymer was followed by monitoring the relative decrease in absorbance of the carbonyl stretching vibration in aldehyde groups at 1737 cm^{-1} from normalized ATR-IR spectra. An initially rapid reaction was observed, reaching a plateau after about 12 h. To assure that the reaction was complete, a reaction time of 24 h was chosen for preparing PVAm/PEO : Hex with four different molar feed ratios of PEO-CHO to hexanal (1 : 1, 1 : 2, 1 : 4 and 1 : 8).

The IR spectrum of PVAm/PEO : Hex obtained after 24 h reaction time showed similar absorption peaks to that of PEO-CHO (Fig. 1, top spectrum). However, the peak area of the CH_2 stretching in PVAm/PEO : Hex at 2887 cm^{-1} (Fig. 1, bottom spectrum) has increased compared with PEO-CHO, due to the contributions from methyl and methylene groups in PVAm and hexanal. The aldehyde (1737 cm^{-1}) in PEO-CHO decreased after reaction and product purification.

The ^1H -NMR spectrum of the purified surfactant polymer is shown in Fig. 2. The spectrum shows proton peaks derived from PVAm, PEO and hexanal groups, qualitatively demonstrating that the desired composition of the surfactant polymers was achieved. Table 1 lists the estimated compositions for surfactant polymers from four molar feed ratios, based on integration of ^1H -NMR spectra and atomic percentages obtained from XPS analysis. Characteristic proton peaks in PEO and hexanal were found at 3.2–3.6 and 0.84–1.5 ppm, respectively. Using the integrals of these two characteristic peaks, the measured molar ratio of PEO to hexanal in PVAm/PEO : Hex, represented by x/y in the scheme, was estimated as the X/Y value, where X = (integral of peaks f and f')/179 (i.e. 178 protons from PEO and 1 from $-\text{CH}-$ of PVAm); and Y = (integral of peaks a and b)/15 (i.e. 13 protons from hexanal and 2 from CH_2 of PVAm). The measured molar ratios of PEO to hexanal in surfactant polymers synthesized from feed ratios 1 : 1, 1 : 2, 1 : 4 and 1 : 8 were calculated to be 1 : 1.4, 1 : 2, 1 : 5 and 1 : 9.8, respectively. Unfortunately, the proton environments for reacted secondary amine groups and unreacted primary amine groups are not sufficiently distinct to be detected by ^1H -NMR. Therefore, an alternative characterization technique was needed. Quantification of unreacted amino groups on the PVAm backbone was achieved by chemically capping free amino groups with 2,5-difluorobenzaldehyde (DFB), followed by XPS analysis of the extent of fluorination.

XPS provided complementary data on the hydrophilic/hydrophobic ligand ratios in surfactant polymers, using PE and PEO surfactant polymers as controls (spectra not shown). Only carbon atoms were detected in PE, whereas the PEO surfactant polymers showed carbon, nitrogen, and oxygen. The results indicated no contamination by fluorine or nitrogen containing compounds in either PE or surfactant polymers. Figure 3 shows the XPS spectra obtained from

survey scans of PVAm/PEO : Hex, showing carbon, nitrogen, oxygen and fluorine as the atomic constituents in the surface. The percentages of PEO, hexanal and unreacted amino groups on the PVAm backbone, designated as x , y and z , respectively, were estimated from the % atoms detected by XPS. Letting $X = \%O/45$ (i.e. 45 oxygen atoms from PEO with M_W 2000), $Z = \%F/2$ (i.e. 2 fluorine atoms from DFB) and $A = \%N/1$ (i.e. 1 nitrogen atom from amine groups in the PVAm backbone). Thus, $x = (X/A) \times 100\%$; $z = (Z/A) \times 100\%$ and $y = 100 - (x + z)$. Based on these calculations, the molar content of PEO in the surfactant polymers decreased from approx. 23% to 8% to 5% to 4%, which corresponding to PEO weight percentages of approximately 88.9, 74%, 63% and 53%, or alternatively, 169, 73, 36 and 32 PEO molecules per surfactant chain (Table 1). Accordingly, the calculated molar ratios for PEO: hexanal for surfactant polymers synthesized from feed ratios of 1 : 1, 1 : 2, 1 : 4 and 1 : 8 were determined to be 1 : 1.4, 1 : 2.5 : 1 : 4.6 and 1 : 10.7, respectively. The ligand molar ratios estimated independently from XPS and 1H -NMR results were similar, which demonstrate successful synthesis of comb-like PEO surfactant polymers, and the feasibility of adjusting the hydrophilic (PEO)/hydrophobic (hexanal) balance. For clarity, the molar ratio determined from XPS (1 : 1.4, 1 : 2.5, 1 : 4.6 and 1 : 10.7) will be used here to identify the different surfactant polymers.

PVAm/PEO : Hex 1 : 1.4, 1 : 2.5 and 1 : 4.6 are soluble in water, methanol, DMSO and dimethylformamide (DMF), whereas PVAm/PEO : Hex 1 : 10.7 is only partially soluble in water, but is soluble in methanol, DMSO and DMF. The PVAm/PEO : Hex 1 : 10.7 can be dissolved in water at low concentration (approx. 1 mg/ml) after vigorous sonication (≥ 30 min).

A three-dimensional molecular model of PVAm/PEO : Hex 1 : 10.7 is shown in Fig. 4. PEO molecules have a large molecular exclusion volume and high degree of hydration. During synthesis, steric hindrance between PEO molecules already attached to the PVAm backbone prevents approach of free PEO molecules toward unreacted amino groups. This resulted in a significant number of unreacted amino groups (50–70%) along the polymer chain, although the unreacted amino groups were completely blocked by the much smaller DFB.

Surface active properties at the air/water interface

Insight into the surface active properties of surfactant polymers at an air/water interface can be gained from surface tension measurement. Surface tension measurements were conducted with aqueous solutions of pure PEO ($M_n = 2000$), PVAm/PEO : Hex 1 : 0, 1 : 1.4, 1 : 2.5 and 1 : 4.6. The surface tension of PVAm/PEO : Hex 1 : 10.7 could not be determined due to its relatively poor solubility in water. For clarity, Fig. 5 shows only plots of surface tension vs. log PEO concentration (mol/l) in bulk solution of (A) pure PEO control, (B) PVAm/PEO : Hex 1 : 0 and (C) PVAm/PEO : Hex 1 : 4.6.

All polymers exhibited similar surface tension curves as the PEO control, which could be divided into two regions, Region I (low concentration) and Region II (high concentration). For all polymers, the surface tension in Region I decreased linearly and then became relatively constant. This plateau was followed by a sudden decrease in surface tension as the polymer concentration increases, designated Region II. No plateau for Region II was observed over the entire concentration range tested. Note that the highest concentration employed for all tested PEO surfactant polymers was limited by their water solubility. The surface tension plots are similar to those reported for pure PEO, AB and ABA-type PEO surfactants [20–23]. The minimum surface tensions in Region I for all tested polymers were similar (63.5–61 dyne/cm) to that of pure PEO, indicating that the decreases in surface tension were primarily dictated by the PEO ligands. However, increased slopes in surface tension plots were observed in Region I for all polymers containing PVAm, indicating that the PVAm increased surface activity at the air/water interface. At the inflection point identifying Region II, the bulk concentration increases sufficiently to change the conformation of polymers at the interface, causing them to occupy less surface area by extending into the water phase. Thus, more polymer molecules

assemble at the interface as the polymer concentration increases, resulting in a decrease in surface tension with increasing polymer concentration. In addition, the width of plateau region decreases as the hexanal content in PVAm/PEO : Hex increases from 1 : 0 to 1 : 4.6. This indicates that hexanal ligands provide additional driving force for polymers to assemble at the air/water interface, resulting in the conformational transition at the lower bulk concentration.

Surface tension data indicate that the surface activity of PEO surfactant polymers at the air/water interface has contributions from all segments of the polymer, including the PVAm backbone, and PEO and hexanal ligands. However, the surface excess of surfactant polymer cannot be calculated from the Gibbs adsorption isotherm, since the assumption of an activity coefficient of 1.0 is not valid for polymer adsorption phenomenon [24]. The Langmuir–Blodgett technique is capable of collecting such quantitative information, and we recently have used this method to determine surface active properties of the polymer surfactants. Our results show the presence of two transitions of which only the first one is observed in the range of surface pressure covered by surface tension measurement. Further details have been described in a separate report that focuses on the molecular orientation of the PEO surfactant polymer, and surface pressure dependence on molecular area [25].

Surface active properties at the solid/water interface

The surface tension data provide insight into the behavior of the PVAm/PEO : Hex at the water/air interface. However, as a potential surface modifying agent, the behavior at the solid/fluid interface is of significant interest. For this purpose, AFM was used to examine surfactant polymer adsorption from aqueous solution onto highly oriented pyrolytic graphite. Adsorption of PVAm/PEO : Hex surfactants at the graphite/water interface occurs rapidly even at low solute concentrations. At a concentration of 0.1 mg/ml for PVAm/PEO : Hex 1 : 4.6, the HOPG was fully covered before the first AFM scan was completed (image not shown). At 0.5 μ g/ml, the adsorption kinetics of was sufficiently slow to be observed by AFM. The initial adsorption appeared to be Langmuirian, with adsorbing molecules filling empty surface sites, with no apparent preference for aligning with previously adsorbed molecules (Fig. 6A). Surface coverage increased slowly, and after 16 h adsorption, the surface appeared to be fully covered by surfactant molecules.

AFM images for the adsorption of PEO surfactant polymer (PVAm/PEO : Hex 1 : 10.7) from approx. 0.03 mg/ml are presented in Fig. 6. The first AFM scan obtained after injecting the polymer solution showed that the surfactant polymer adsorbs rapidly in enlarging domains in three directions, with a preferential adsorption at the edge of previously adsorbed surfactant polymer molecules (Fig. 6B). A uniformly coated surface was obtained after only a few scans.

The differing adsorption behavior for the surfactant polymers is indicative of the role of the hexanal ligands in the adsorption process [11]. Preferential adsorption adjacent previously adsorbed surfactant polymer, observed with PVAm/PEO : Hex 1 : 10.7, results from intermolecular interdigitation of the hexanal side chains, which minimizes the energy of the adsorbed molecule [11]. This results from extending the polymer backbone and drawing the adjacent chains closer together to form domains of aligned chains. Epitaxial adsorption of alkyl side chains confines the polymer backbone to the substrate allowing the hydrophilic side chains to protrude into the aqueous phase.

The epitaxial alignment of the surfactant polymer is unique to the highly ordered graphite substrate, although interdigitation of the polymer side chains, which stabilizes the adsorbed assembly, can feasibly occur on any hydrophobic solid surface, such as polymer biomaterials. However, AFM currently lacks sufficient resolution to obtain visual confirmation of this mechanism on synthetic polymer substrates. Confirmation of the stability of surfactant polymer

adhesion on synthetic polymer substrates can be obtained by testing under an applied shear stress followed by conventional surface analysis methods [12,15].

The synthetic approach reported here offers a promising route to prepare a wide range of surfactant polymers that undergo surface- and self-induced interdigitating assembly on solid hydrophobic surfaces, creating a highly hydrated biomaterial interface. Such highly hydrated interfaces exhibit effective non-adhesive properties, that can suppress non-specific adsorption of biological macromolecules and cells, such as proteins, blood cells and bacteria. For example, we have examined PVAm/PEO : Hex surfactants as potential surface-modifying agents with bacterial resistant properties [15,26]. Briefly, we found that bacterial adhesion on graphite or polyethylene is decreased significantly by the PEO surfactant polymer. Further, the bacterial adhesion decreases with increasing PEO content in the surfactant polymer. However, decreased hexanal content leads to less stability in the presence of applied shear forces. The hydrophobic/hydrophilic balance of the surfactant polymer can be adjusted to optimize both anti-adhesion and stability characteristics. For example, one can use fewer, but longer alkyl groups. In the case of dextran surfactants [10,11], surface stability under shear is achieved with a feed ratio of dextran : lauryl at 1 : 1.5, as compared with dextran : hexanoyl of 1 : 4. The longer alkyl side chains increase surface stability under applied shear stress, while the anti-adhesion properties are not significantly affected.

CONCLUSIONS

A series of comb-like poly(ethylene oxide) surfactant polymers with well-defined structural compositions were synthesized by simultaneous incorporation at different feed ratios of hydrophilic poly(ethylene oxide) (PEO) and hydrophobic hexanal groups on poly(vinyl amine). The PEO surfactant polymers demonstrate surface active properties at an air/water interface, as shown by surface tension measurement; and exhibit surface activity at a solid surface/water interface, as visualized by AFM imaging of adsorbed surfactant polymers on graphite.

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Figure 1. Transmission FT-IR spectra. (Top) PEO-CHO and (bottom) PVAm/PEO : Hex (1 : 4).

Figure 2.

^1H -NMR spectrum of PVAm/PEO : Hex in DMSO-d_6 , where x , y and z are the percentages of PEO, hexanal and unreacted amino groups, respectively. The number of unreacted amino groups cannot be estimated from the ^1H -NMR spectrum.

Figure 3.

XPS spectrum of polyethylene modified with PVAm/PEO : Hex after capping reaction. The unreacted amino groups on PVAm/PEO : Hex were capped by 2,5-difluorobenzaldehyde. The percentages of PEO, hexanal and unreacted amino groups, designated as x , y and z , respectively, were estimated from the % atoms (N_{1s} , O_{1s} and F_{1s}).

Figure 4.

Molecular model of poly(ethylene oxide) (PEO) polymer surfactant with a 1 : 2.5 molar ratio PEO to hexanal. The surfactant polymer consists of flexible poly(vinyl amine) (PVAm) with multiple hexanal and PEO side chains randomly spaced along the backbone. In the limited model shown, 2 PEO molecules (upper) and 5 hexanal groups (lower) are grafted onto the PVAm backbone. The predicted conformation for the PEO molecules is based on the distance between PEO grafting points (D) and the Flory radius ($R_F = 29 \text{ \AA}$, the size of one PEO coil in bulk solution). The D value of $25 \text{ \AA}$ was estimated from the surfactant polymer composition (Table 1) and the theoretical distance between adjacent amino groups along the PVAm chain ($2.5 \text{ \AA}$). The similarity of D and R_F implies that PEO molecules maintain random conformation.

Figure 5.

Plots of surface tension vs. log molar concentration of PEO molecules in aqueous solutions of pure PEO, and PVAm/PEO : Hex 1 : 0 and 1 : 4.6. Surface tension curves for all polymers can be divided into two regions. Regions I and II are represented by thin and thick lines, respectively.

Figure 6.

AFM images of adsorbed PEO surfactant polymers onto the basal plane of HOPG. PVAm/PEO : Hex 1 : 4.6 (A) and 1 : 10.7 (B) were imaged in 5 $\mu\text{g/ml}$ and 0.1 mg/ml polymer solutions, respectively. (A) Initial adsorption of PVAm/PEO : Hex 1 : 4.6 appears random and disordered. (B) The first scan after injection of PVAm/PEO : Hex 1 : 10.7 solution shows epitaxial adsorption of additional polymer along previously adsorbed chains, as observed by the enlarging adsorbed domain.

Scheme 1.

Synthetic pathways of (A) uncapped and (B) 2,5-difluorobenzaldehyde-capped PEO surfactant polymer.

Table 1Compositions for PNVPEO-*co*-PVNH

PEO/Hexanal molar feed ratio	1 : 0	1 : 1	1 : 2	1 : 4	1 : 8
Calculated molar ratio					
¹ H-NMR	—	1 : 0.8	1 : 2	1 : 5	1 : 9.8
XPS	—	1 : 1.4	1 : 2.5	1 : 4.6	1 : 10.7
Composition (mol%)					
PEO chains	35.3 ± 2.7	23.0 ± 2.6	7.7 ± 0.3	4.9 ± 0.4	4.3 ± 0.4
hexanal groups	0	30.48 ± 5.6	19.1 ± 1.0	22.1 ± 4.5	46.2 ± 3.0
amino groups	64.7 ± 2.7	46.49 ± 3.4	73.2 ± 1.1	73.0 ± 4.5	49.5 ± 2.9
Composition (wt%)					
PEO chains	96.3	88.9	73.8	62.6	52.6
hexanal groups	0	7.3	11.4	17.7	34.8
amino groups	3.7	3.8	14.8	19.7	12.6
Branch groups/surfactant					
PEO chains	260	169	73	36	32
hexanal groups	0	224	140	163	340
amino groups	476	342	539	537	364
Estimated M_w (× 1000)	551	389	157	117	124

Compositions were calculated from at% obtained from XPS analysis. Values are mean±standard deviation. Number of branch groups was calculated from the average molar compositions and 736 amino groups per PVAm molecule, estimated from molecular weight of PNVF. Molecular weights were estimated from the average number of groups per surfactant molecule and molecular weight of PVAm.