

Interaction between a Hydrophobic Probe and Tri(ethylene glycol)-Containing Self-assembled Monolayers on Gold Studied with Force Spectroscopy in Aqueous Electrolyte Solution

Christian Dicke[†] and Georg Hähner*

Department of Physics and Astronomy, University College London, Gower Street, London WC1E 6BT, U.K.

Received: October 15, 2001; In Final Form: January 25, 2002

Methoxy-tri(ethylene glycol)-terminated self-assembled monolayers of alkanethiols adsorbed on gold were investigated by force spectroscopy with hydrophobic probes under electrolyte solution. Various ions from the Hofmeister series dissolved in the electrolyte, which are known to have different influence on water structure and to be able to react specifically with ethylene glycol based molecules, were employed in order to test the hypothesis of a *structured* long-range (several nanometers) water interface and to elucidate the type of (repulsive) force that is experienced by hydrophobic probes. This force is expected to play an important role in the resistance of these films to protein adsorption. Further analysis by photoelectron and mass spectroscopic techniques was employed to test for a specific interaction between the ions and the organic film. Our experiments support the significance of an electrostatic component in the interaction between hydrophobic probes and the organic film and corroborate earlier studies.

Introduction

Surface coatings that resist the nonspecific adsorption of proteins are of utmost importance in biomedicine and related areas. The engineering and preparation of such functional coatings with high reliability and reproducibility is, for example, a prerequisite for the tailoring of biosensor surfaces. It requires, however, a fundamental understanding and knowledge of the type of relevant forces and of the processes underlying the inertness.

The polymer poly(ethylene glycol) (PEG) has been recognized for some time for its protein-repelling properties.^{1–3} These are due to the high conformational freedom of the chains and tightly bound water, summarized in so-called “steric repulsion”.^{4,5} More recently it has been found that self-assembled monolayers (SAMs) containing oligo(ethylene glycol) (OEG) can also resist the adsorption of biomolecules.^{6,7} SAMs are easy to prepare while offering at the same time some flexibility toward functionalization and have therefore attracted a lot of interest over the last 2 decades. The mechanism responsible for the repulsion of proteins by OEG-containing monolayers, however, is different from that of the polymer. In a densely packed film the conformational freedom of the OEG tails is strongly restricted and other mechanisms than those relevant in the case of the PEG must become effective.

Different suggestions have been made in order to explain the ability of the ultrathin films to resist nonspecific adsorption. Ethylene glycol units are known to interact strongly with the surrounding aqueous environment: For a methoxy-tri(ethylene glycol)-terminated (EG₃-OMe) SAM on gold, for example, a helical to amorphous conformation was found in a vacuum,⁷ while under water, the order present in the OEG tail diminishes.⁸ In another study it was observed that water molecules penetrate into micrometer-thick PEG films in ambient and finally form

dimers and trimers with other water molecules.⁹ IR–visible sum-frequency generation spectroscopy at the water/PEG interface revealed the presence of water molecules that are strongly bonded to the O atoms of the ethylene glycol entities and of further water species located in the vicinity of the PEG surface organized in an “ice-like” film.¹⁰ The maximum hydration number per EG monomer for PEG molecules has been determined experimentally to vary between 1.6 and 3.3, depending on the molecular weight of the polymer.^{11,12} Some attention has also been given to the interface of EG functional groups and a hydrophobic backbone under water, for PEG modified with alkane chains.¹³ A very low hydration of the PEG units near the PEG/hydrocarbon interface was found, which increased toward the outer region of the PEG tail.

Due to the strong interaction of EG units with water it has been hypothesized that water might establish a transition layer at the film/liquid interface of the OEG-functionalized SAMs, which is different from the bulk solution.¹⁴ A “thick water interface (several nm) with unusual properties” might be responsible for the inertness toward the adsorption of proteins. This could be a water layer that is structured or has reduced density compared to the bulk. Similarly, it has been suggested that hydrophobic interactions are due to the influence of the surface on the water structure.¹⁵ The surface is assumed to induce order into the water molecules in close proximity. This order decays into the liquid and gives rise to a long-range interaction with the same decay length as the order profile.

Apart from the strong affinity between OEG and water molecules, it has also been reported that a specific interaction of certain (cat)ions with EG units is possible. Ab initio calculations performed for 1:1 complexes of triglyme (triethylene glycol dimethyl ether) with different cations revealed several stable complexes for different metal ions, with Li⁺ forming the most stable and energetically most favorable one.¹⁶ All four ether oxygens are involved in complexing the cation,

* Corresponding author. E-mail: g.haehner@ucl.ac.uk. Phone: +44 20 7679 3496. Fax: +44 20 7679 1360.

[†] Also at the Department of Materials, ETH Zurich, Switzerland.

which can lead to different configurations. However, in all of them the ethylene glycol units "encage" the cation.

Complexation has also been studied in connection with electrochemical devices such as rechargeable batteries. Small alkali ions are in particular of high interest. Several studies were concerned with PEG/alkali salt complexes, where Li^+ , Na^+ or K^+ ions form stable crystalline complexes with PEG via coordination of the cations to the ether oxygens.^{17–20} In general, 5:1 complexes, where five ether oxygens are coordinated to one cation, are most stable, while several PEG chains can cooperatively contribute oxygens to the constituted complex. Due to the complexing properties, poly(ethylene glycol) has been considered to form "flexible crown ethers".²¹

Alkanethiols functionalized with different crown ethers have been shown to react specifically with cations depending on their size and can be utilized for recognition.^{22–26}

$\text{EG}_3\text{-OMe}$ SAMs have been investigated in view of their resistance to polyelectrolyte adsorption at ion concentrations between 1 mM and 0.1 M. It was concluded that resistance is caused by a swelling of the EG interface, and the hydrated brush structure of the EG repeat units is stabilized by small ions.²⁷ In addition it was found that Li^+ ions in particular "fit" into the hydrated structure of the EG brushes giving them additional stability. Na^+ ions showed a similar but weaker tendency to support the hydrated brush, as did K^+ ions.

An incorporation of certain cations into the OEG tail of the molecules in the monolayer can therefore not be excluded a priori.

To test the hypothesis of a long-range *structured* water interface and to explore the affinity of different ions to the EG units in more detail, we have performed the present investigation. In an earlier study we found repulsive forces with a decay length depending on ionic strength between a hydrophobic AFM probe and the monomolecular EG_3 film on gold in electrolyte solution.²⁸ The experiments suggested that there is an electrostatic component involved.

In the present study we have employed ions from the so-called Hofmeister or lyotropic series.^{29,30} This series emerges from a combination of a general effect of cosolutes on solvent structure and of specific interactions between the cosolutes and the solute.^{29–34} Cations and anions are known to have influence on both water structure and the solution behavior of (bio)-molecules.^{34,35} The ability of the ions in the lyotropic series to disturb the hydrogen bond network between the water molecules varies. While some of them effectively "break" water structures (so-called chaotropes such as Cs^+ or Li^+), others are water structure "supporting" (so-called polar kosmotropes, e.g., NH_4^+ or $\text{N}(\text{CH}_3)_4^+$).

The different ions employed shall give us an idea about the order profile of an extended *structured* water interface, if present, as well as an indication of a specific interaction with the OEG tails.

Experimental Section

Materials. (1-Mercaptoundec-11-yl)tri(ethylene glycol) ($\text{EG}_3\text{-OMe}$) methyl ether was prepared according to the literature.⁶ The oligomer was dissolved in ethanol (>99.8%, p.a., Merck AG, Dietikon, Switzerland) at a concentration of approximately 2 mM for the preparation of the organic monolayers.

Electrolytes employed in the present study were LiNO_3 (>99.5%, purchased from Fluka Chemie AG, Buchs, Switzerland), NaNO_3 (>99.5%, p.a., Fluka), KNO_3 (>99.5%, p.a., Merck), CsNO_3 ($\geq 99\%$, Aldrich Chem. Co., Milwaukee, WI), NH_4NO_3 (>99.5%, p.a., Fluka), and $\text{N}(\text{CH}_3)_4\text{NO}_3$ ($\geq 96\%$,

Aldrich) for cation-dependent measurements and KF ($\geq 99\%$, Fluka), KCl ($\geq 99\%$, Fluka), KI ($\geq 99\%$, Fluka), KNO_3 ($\geq 99\%$, Fluka), and K_2SO_4 ($\geq 99\%$, Fluka) for anion-dependent measurements. All salts were used without further purification. Aqueous solutions of the salts were prepared with ultrapure water (18 M Ωcm), with concentrations ranging from 0.1 mM to 0.1 M.

SAM Preparation. Plasma-cleaned single-polished silicon (100) wafers (MEMC Electronic Materials, Inc., St. Peters, MO) were coated with 5 nm of chromium as adhesion promoter by electron beam evaporation, followed by the deposition of 80-nm-thick layers of polycrystalline gold (99.99%, Balzers Materials, Liechtenstein) via thermal evaporation. Coating was performed in a Balzers BAE 370 coating system at a base pressure of $\sim 5 \times 10^{-7}$ mbar at a rate of 0.5 to 1 nm/s. The substrates were immersed into a 2 mM solution of $\text{EG}_3\text{-OMe}$ molecules in ethanol (>99.8%, p.a., Merck) immediately after metal coating. After an extended period (typically 24 h) they were removed from the solution, rinsed with the pure solvent, put into an ultrasonic ethanolic bath for 1 min, and dried in a stream of nitrogen.

Instrumentation and Probes for SFM Measurements. All measurements were performed with a commercially available scanning probe microscope, Nanoscope IIIa (Digital Instruments, Inc., Santa Barbara, CA), equipped with a liquid cell. All electrolyte solutions were introduced into the liquid cell by using low protein binding PTFE filters (Semadeni AG, Ostermundigen, Switzerland) with 0.2- μm pore size. Oxide sharpened tips from DI with nominal force constants of 0.12 N/m and nominal radii of curvature of ~ 30 nm were coated simultaneously with the substrates with chromium (5 nm) and gold (80 nm). Subsequently, gold samples and AFM tips were covered with $\text{EG}_3\text{-OMe}$ by immersion or hydrophobized by a "vapor-phase-type" deposition of a monolayer of hexadecanethiol (Aldrich) in a metal desiccator.²⁸ Static contact angle, XPS and ToF-SIMS measurements were performed on selected oligo(ethylene glycol) coated gold samples to ensure the quality of the films.

SFM Measurements. Force vs distance measurements were collected with a cycle frequency of 0.3–0.5 Hz. At least 64 force curves per sample over an area of $2 \times 2 \mu\text{m}$ were recorded. During a force–distance cycle, the measured experimental parameters were the deflection of the cantilever, obtained from the voltage of the four-quadrant photodiode, and the displacement of the piezo scanner, indicated by the applied voltages. Piezo displacement vs cantilever deflection curves were converted into force–distance curves according to a procedure described in the literature.³⁶ "Zero distance" corresponds to a hard-wall potential.

XPS. X-ray photoelectron spectroscopy experiments were carried out on an PHI 5700 XPS instrument (Physical Electronics, Eden Prairie, MN), equipped with an Al $\text{K}\alpha$ source and operated at 350 W during the measurements. The base pressure in the chamber was $< 2 \times 10^{-9}$ mbar. Survey spectra were recorded with only moderate resolution. The takeoff angle during acquisition was set to 30° . Electron binding energies were calibrated with respect to the C 1s line at 284.8 eV.

ToF-SIMS. Secondary ion mass spectra of SAM-covered gold substrates and of SAM-covered samples that were immersed into electrolyte solution were recorded on a PHI 7200 time-of-flight secondary ion mass spectrometer in the mass range 0.2–500 m/z for positive ions and 3–300 m/z for negative ions. The total ion dose of the 8 kV Cs^+ primary ion beam (diameter: 200 μm) was typically 2×10^{12} ions cm^{-2} , corresponding to a value below the static limit. Time per data

TABLE 1: Hofmeister Series^a

anions	cations	kosmotropic					chaotropic				
		F ⁻	PO ₄ ³⁻	SO ₄ ²⁻	CH ₃ COO ⁻	NO ₃ ⁻	Cl ⁻	Br ⁻	I ⁻	CNS ⁻	CF ₃ SO ₄ ⁻
		(CH ₃) ₄ N ⁺	(CH ₃) ₂ NH ₂ ⁺	NH ₄ ⁺	K ⁺	Na ⁺	Cs ⁺	Li ⁺	Mg ²⁺	Ca ²⁺	Ba ²⁺

^a Kosmotropic ions are water structure supporting while chaotropic ions are assumed to be structure breaking.

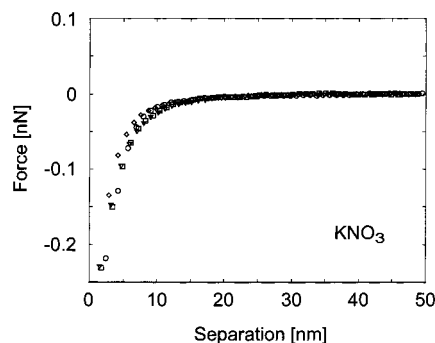


Figure 1. Advancing force vs distance curves (averaged) for a hydrophobic hexadecanethiol-covered probe and a hexadecanethiol SAM on gold in aqueous KNO₃ solution for different concentrations (◇, 0.1 M; ○, 0.01 M; ▽, 1 mM; □, 0.1 mM).

point was 0.625 ns. Mass resolution $M/\Delta M$ was typically 7500 in the positive and 2000 in the negative mode (mass 59 and 16, respectively). To calibrate the mass scale, the whole mass range was first calibrated by using a single standard set of low ion masses (CH, C₂H₃, C₃H₅, C₃H₇O and CH, OH, C₂H, Au for positive and negative ions, respectively) followed by the assignment of species in the whole mass range using the PHI software TOFPAK.

Results

Force Measurements with Hydrophobic Probes. To check the chemical quality and stability of the hydrophobized probes that were employed for the force measurements on OEG-terminated films during and after exposure to electrolyte solution, we first measured a system consisting of two hydrophobic alkanethiol films adsorbed on both probe and counter-surface. Figure 1 shows advancing force vs distance curves recorded under KNO₃ solution for hexadecanethiol films adsorbed on gold.

The concentration was varied between 0.1 mM and 0.1 M, the same range as used for the measurements on the EG₃ system. The measurement cycle was started with the lowest concentration, which was then increased stepwise by factors of 10.

For all concentrations an attractive interaction was found as displayed in Figure 1. This attractive interaction showed a constant range, independent of the ionic strength. Finally, the measurement with the lowest concentration of 0.1 mM was repeated to check for a possible alteration of the tip or the surface. No difference to the first measurements with the same concentration was detectable.

The retracting parts of the force curve cycles, which are not displayed in the figure, showed high adhesion forces (~50 nN), which remained rather constant for all electrolyte concentrations, as has been reported earlier in the literature.^{37,38}

The forces between a hydrophobic probe and an EG₃-OMe-terminated alkanethiol film adsorbed on a gold substrate were also recorded in KNO₃ solution and for different ionic strengths (see Figure 2).

Aqueous KNO₃ solution was chosen as “standard electrolyte” for the force distance measurements. According to the Hofmeister series the K⁺ and the NO₃⁻ ion are both supposed to be

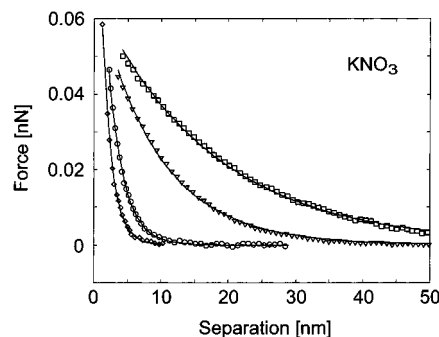


Figure 2. Advancing force vs distance curves (averaged) for a hydrophobic probe and a EG₃-OMe-terminated SAM on gold in aqueous KNO₃ solution for different concentrations (◇, 0.1 M; ○, 0.01 M; ▽, 1 mM; □, 0.1 mM). The solid lines represent exponential fits to the experimental data. See text for details.

TABLE 2: Comparison between Experimentally and Theoretically Determined Decay Lengths for the Force between a Hydrophobic Probe and an OEG-Containing SAM Recorded under KNO₃

ionic strength, mM	debye length (theor), nm	1/ κ (exptl), nm
0.1	30.7	17.3
1	9.6	9.1
10	3.1	2.4
100	1.0	1.5

“neutral”; i.e., they are neither structure breaking nor structure supporting (see Table 1). The interaction displayed in Figure 2 shows an exponentially decaying repulsive force for low ionic strength. At a concentration of 0.1 mM a decay length of 17.3 nm was observed. Increasing the concentration resulted in lower values for the decay length: we found 9.1 nm for 1 mM and 2.4 nm for 10 mM solutions. For the highest concentration (0.1 M) investigated a value of 1.5 nm was observed.

The strong dependence of the decay length on the concentration of the solution suggests an electrostatic contribution and a DLVO type force, although there are no free charges associated with the organic films involved per se. According to DLVO theory, the decay length, i.e., the so-called Debye length, scales with the inverse of the square root of the concentration.³¹

Table 2 summarizes the values determined for the theoretical Debye length and the experimental decay lengths of the repulsive forces, depending on the ionic strength. They are in reasonable agreement except for the lowest concentration of 0.1 mM.

One possible source for error in our measurements is the concentration of the solution. The preparation process itself as well as contamination during the measurement cycles might lead to deviations from the nominal concentration. We estimate this error to be on the order of 5%, resulting in an error of the same magnitude for the decay length. Other (systematic) errors such as unknown tip radius or spring constant of the probe do not affect the decay length, since they do not change during the measurement. Errors of the theoretical fit have been determined based on least-squares fits of an exponential function of the form $f(x) = a \cdot \exp(-bx)$ to the experimentally determined curves. Noise in single force curves was found to be <0.01 nN. Parameter b , corresponding to the decay length, showed

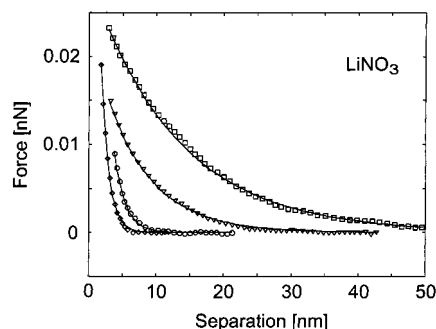


Figure 3. Advancing force vs distance curves (averaged) for a hydrophobic probe and a EG₃-OMe-terminated SAM on gold in aqueous LiNO₃ solution for different concentration (◇, 0.1 M; ○, 0.01 M; ▽, 1 mM; □, 0.1 mM). The solid lines represent exponential fits to the experimental data. For details see text.

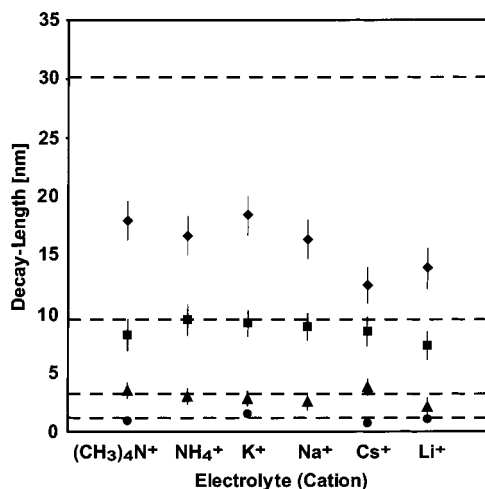


Figure 4. Measured decay lengths for different cations from the Hofmeister series depending on the ionic strength (●, 0.1 M; ▲, 0.01 M; ■, 1 mM; ◆, 0.1 mM). Dashed lines correspond to values expected on the basis of the DLVO theory.

an error in the range 5–10% for a fixed concentration. The overall error in the decay length can then be estimated to be below 15%.

A rigorous quantitative analysis of the absolute values of the forces acting between probe and sample surface is not possible, because force constants and radii of curvature of the probes were not determined after functionalization. Note, however, that the decay length is independent of both of these parameters.

To test the hypothesis of a long-range (several nanometers) structured water layer adjacent to the EG₃ interface, force–distance measurements were performed under different electrolyte solutions. These experiments were targeted to a determination of the influence of various dissolved ions on the resulting force between tip and sample surface.

We have employed both chaotropic as well as kosmotropic ions from the lyotropic series (see Table 1). Keeping the anion, NO₃[−], measurements with various cations were performed in order to investigate their influence on water structure and interaction with the ethylene glycol units of the SAM. Figure 3 shows examples of the force distance curves recorded under LiNO₃.

Figure 4 summarizes the experimentally determined decay lengths for the different cations employed, depending on the solution concentration.

In another series, the cation, K⁺, was kept, while the influence of different anions was investigated. Figure 5 summarizes these force measurements, displaying the observed decay lengths of

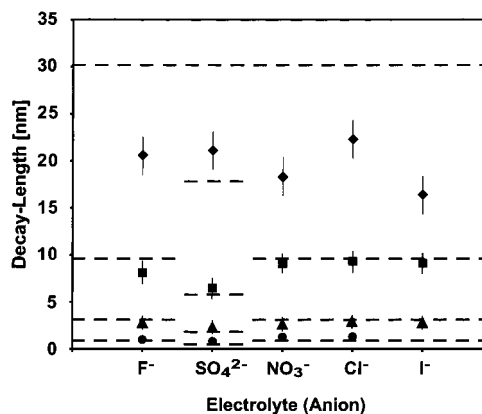


Figure 5. Measured decay lengths for different anions from the Hofmeister series depending on the ionic strength (●, 0.1 M; ▲, 0.01 M; ■, 1 mM; ◆, 0.1 mM). Dashed lines correspond to values expected on the basis of the DLVO theory.

the repulsive force curves depending on the ionic strength and the anion dissolved.

For a fixed ion concentration all different electrolytes show a similar force distance behavior as was also observed for the “standard” KNO₃ solution. For all ions the values of the experimental decay lengths and the theoretical Debye lengths are in reasonable agreement within the error bars, with the exception of the lowest concentration.

XPS and TOF-SIMS Analysis. Different cations can have different affinity to the OEG part. The incorporation of cations into the OEG interface might result in a charge separation and a dipolar field could be established. To test the possibility of ion incorporation of some of the cations from electrolyte solution into the OEG tail of the SAM films, additional XPS and ToF-SIMS measurements were performed. After preparation of the SAM surface, samples were immersed into 10 mM solutions of the different electrolytes for 12 h. Subsequently the samples were removed and rinsed with ultrapure water, dried with nitrogen, and immediately introduced into the vacuum chamber. All XPS survey spectra recorded showed the same characteristics as was found for the untreated, freshly prepared sample with the same elemental ratios and species. No additional peaks indicative of the various electrolytes investigated were observable.

The TOF-SIMS measurements also did not reveal any indication of a strong affinity between the cat- and/or anions and the SAM surface for most of the salts. There was, however, a slight increase in the oxysulfur peaks and the potassium intensity observable after immersion of the films into the according electrolyte (K₂SO₄). Figure 6 shows the positive mass peaks in the range 0.2–100 amu. Some of the peaks that can be assigned to the SAM are labeled with the corresponding fragments. Negative mass peaks in the range 3–100 amu are displayed in Figure 7. No evidence for specific complexation of cations with the EG entities was found.

Discussion

The measurements described above were performed in order to explore the influence of different ions from the Hofmeister series on the repulsive interaction between hydrophobic probes and OEG-terminated monolayers. The interactions in electrolyte solutions are mediated by water. Cosolutes can influence both the structure of the liquid and the surfaces of the solids by specific adsorption or dissociation processes.^{32–35,39–41}

The reference measurement showed an attractive interaction between two methyl-terminated alkanethiol films at ~pH 6,

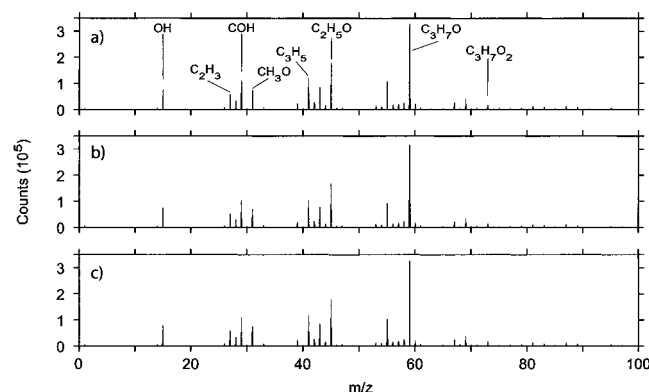


Figure 6. Positive static ToF-SIMS spectra of (a) a freshly prepared EG₃-OMe SAM, (b) an EG₃-OMe SAM after 12-h exposure to 10 mM aqueous KNO₃ solution, and (c) an EG₃-OMe SAM after 12-h exposure to 10 mM aqueous K₂SO₄ solution. Some of the species related to the SAM are labeled.

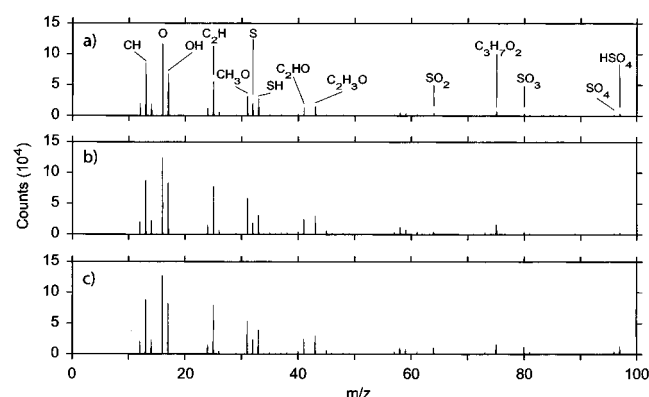


Figure 7. Negative static ToF-SIMS spectra of (a) a freshly prepared EG₃-OMe SAM, (b) an EG₃-OMe SAM after 12-h exposure to 10 mM aqueous KNO₃ solution, and (c) an EG₃-OMe SAM after 12-h exposure to 10 mM aqueous K₂SO₄ solution. Note the increase in intensity of the oxy-sulfur species for the latter.

independent from the ion concentration of the solution. The observed force–distance curves resembled those published in the literature for the same system and reflect a “typical hydrophobic” interaction.³¹ Replacement of the hydrophobic film on the gold substrate by an EG₃-OMe terminated film, however, resulted in a completely different behavior. A repulsive force, strongly dependent on ion concentration, was found under KNO₃ solution, as was reported earlier.²⁸

Replacing the, according to the Hofmeister series, neutral K⁺ ion in the electrolyte by more kosmotropic ions such as NH₄⁺ and N(CH₃)₄⁺, which are supposed to be water structure breaking, or by more chaotropic ions such as Cs⁺ and Li⁺, which are considered to be structure supporting, resulted in very similar force–distance curves to those observed under KNO₃, showing a strong dependence on ionic strength. Fitting exponential curves to the experimental data revealed decay lengths very close to those expected on the basis of DLVO theory, except for the lowest concentration. There was no clear trend observable for the measured decay lengths within the Hofmeister series for constant ionic strength. A similar observation was made for the different anions investigated. The determined decay lengths do not show a clear trend with increasing chaotropic or kosmotropic character.

In the case of a pronounced network of organized water molecules at the interface between organic surface and bulk electrolyte, different ions from the Hofmeister series are expected to have a different effect on the *order profile* of the

network, which should reflect itself in the observed force profile and range of the repulsive interaction. Addition of polar kosmotropes to the electrolyte should break an extended water structure more efficiently than chaotropic ions and reduce the range of the repulsion experienced by the AFM tip for a fixed ionic strength, if it is due to an order profile. However, as evidenced by Figures 4 and 5, no clear trend was found in our experiment within the experimental error bars. Instead, a typical DLVO-like behavior was observed, independent of the type of ion, with the exception of the lowest concentration. For higher concentrations the repulsive force between the hydrophobic probe and the EG₃-OMe coated sample surface strongly depends on the ion concentration and scales approximately with the Debye length. We interpret this as a strong hint for a significant electrostatic contribution to the interaction force between the hydrophobic tip and the EG₃-OMe surface, suggesting that there is no long-range (> 2 nm) highly ordered water interface.

We have no final answer for the deviation of the force from DLVO behavior in the case of 0.1 mM solutions. It has been reported in the literature, however, that for such low concentrations and low surface charging an additional attractive component is expected in colloidal systems.⁴² The latter is due to an increase in ion concentration between the two surfaces when approaching each other.⁴³ This effect might also be responsible for the consistently observed shorter decay lengths in our system.

The origin of the charges in the case of an electrostatic interaction, however, remains to be resolved. It has recently been reported that hydrophobic alkanethiol films on gold display a negative ζ potential in electrolyte solution at pH 7 and below.⁴⁴ Our probe will similarly acquire a negative charge. Consequently, the OEG-terminated films must be also negatively charged, because a repulsive interaction was observed. The charge density can be estimated to be on the order of -0.01 C/m², based on our experiments described in ref 28.

Since the observed interaction appears to be of electrostatic nature, the question of whether there is some contribution from a specific interaction between certain cations and the OEG tails arises. An incorporation of ions into the OEG tails, for example, might lead to an effective charge separation and result in a dipolar field. In such a case “high” surface charge density should be established for ions with higher affinity to EG, in contrast to those which do not show any preferred reaction with EG units. A possible complexation should then reflect itself in higher absolute force values between probe and surface.

All probes were prepared following an identical procedure. Therefore it appears reasonable to assume that all force constants are affected similarly by the functionalization process. However, for a fixed ion concentration, the force curves showed values within the same order of magnitude for all different ions (see Figures 4 and 5). Strongly hydrated cations such as Li⁺ and Na⁺ which can complex with EG units,^{16,45,46} showed no hint for specific interaction with the EG tails by displaying significantly higher repulsive force values within our limited resolution. As a consequence, we suggest that ion binding and the specific interaction with ions do not play a major role for the observed interaction. This is supported by the X-ray photoelectron spectroscopy and TOF-SIMS analysis. These measurements did not show a clear indication of an irreversible ion incorporation into the films, supporting that specific adsorption or coordination of various ions to the ethylene glycol tail do not play a major role. However, difficulties in detecting salt ions in these systems with XPS have been reported earlier.^{27,47} The ions are removed during the rinsing process with high probability. It should also be borne in mind that both XPS and

TOF-SIMS measurements were performed under vacuum conditions, while the interaction was probed under aqueous solution. However, a strong and irreversible interaction between the ions and the organic film seems unlikely at least.

A possible complexation between the EG units and a cation requires a certain amount of space, which might not be available in the densely packed SAMs. There will be, however, defects in the films, which create less densely packed regions where ions might preferentially interact with the film and the substrate. This view is supported by the TOF-SIMS measurements, where no ions except traces of oxysulfur related species and the counterion were found in the films, which we attribute to the high affinity of the sulfur to the gold and a penetration of the ions into the film. This is most likely to occur at defect sites and has been reported in previous SIMS studies.^{48–50}

We do not, however, assign the origin of the effective negative charge to the ions from the salt in the solution, since no difference was observed for different electrolytes. In addition, methyl-terminated alkanethiol films are also not free of defects. If adsorbing ions from the electrolyte would be responsible for the charging, this effect should have also been observable for the pure hexadecanethiol films. In that case the ion concentration should have had a similar effect on the force–distance curves of the “reference system” to the one observed for the EG films.

We have no final explanation for the effective negative charge that appears to be established at the EG₃ interface. It is possible, however, that the conformation of the OEG tails in connection with water is responsible for it. The charges associated with the EG₃ monolayer might, for example, be due to the interaction of hydroxyl and/or hydronium ions with the EG interface or the oriented water molecules in the OEG tail. It has recently been reported that weakly interacting interfacial water molecules can be oriented by interactions with an organic phase.⁵¹ A similar effect might play a central role in the interaction observed here.

Our studies underline the strong interaction between EG units and water and its importance for the resulting chemical and physical properties of the films. The observed repulsive force appears to be mainly of electrostatic nature and is in high need of further investigation. The described interaction is likely to play also some role in the protein-repelling properties of EG terminated films. Additionally, a water interface of lower density as has been suggested earlier could also contribute to the overall repulsive behavior. Also, a short-range structured water interface (<2 nm) cannot be excluded. A long-range structured water interface or a specific interaction of ions with the OEG tails, however, appear to be less important.

Conclusions

Force–distance curves between OEG containing SAMs and hydrophobic probes were recorded under different electrolyte solutions and for varying ionic strength. The force curves showed no indication of a long-range (≥ 2 nm) order profile due to a structured water interface or a preferred “reaction” with or higher affinity of some of the cations to the ethylene glycol interface. The latter is supported by XPS and TOF-SIMS analysis. Instead it appears that a significant electrostatic component is involved in the repulsive force observed. The effective negative surface charge established on the OEG SAM might be due to oriented water molecules and/or the interaction with hydroxyl and hydronium ions from solution.

Acknowledgment. We thank Professor N. Spencer, ETH Zurich, for instrument time and I. Klingenfuss, ETH Zurich,

for XPS and TOF-SIMS measurements. We are grateful to S. Herrwerth, Dr. W. Eck, and Professor M. Grunze, University of Heidelberg, Germany, for providing the (1-mercaptopundec-11-yl)tris(ethylene glycol) methyl ether. Financial support by ETH Zurich under Grant 0-20778-00 is also gratefully acknowledged.

References and Notes

- (1) Taunton, H. J.; Toprakcioglu, C.; Fetters, L. J.; Klein, J. *Nature* **1988**, 712.
- (2) Jeon, S. I.; Andrade, J. D. *J. Colloid Interface Sci.* **1991**, 159.
- (3) Harris, J. M. *Poly(Ethylene Glycol) Chemistry*; Plenum: New York, 1992.
- (4) Sleifzer, I. *Curr. Opin. Solid State Mater. Sci.* **1996**, 2, 337.
- (5) Halperin, A. *Langmuir* **1999**, 15, 2525.
- (6) Prime, K. L.; Whitesides, G. M. *J. Am. Chem. Soc.* **1993**, 115, 10 714.
- (7) Harder P.; Grunze, M.; Dahint, R.; Whitesides, G. M.; Laibinis P. E. *J. Phys. Chem. B* **1998**, 102, 426.
- (8) Zolk, M.; Eisert, F.; Pippert, J.; Herrwerth, S.; Eck, W.; Buck, M. Grunze, M. *Langmuir* **2000**, 14, 5849.
- (9) Ide, M. I.; Yoshikawa, D.; Maeda, Y.; Kitano, H. *Langmuir* **1999**, 15, 926.
- (10) Dreesen, L.; Humpert, C.; Hollander, P.; Mani, A. A.; Ataka, K.; Thiru, P. A.; Peremans, A. *Chem. Phys. Lett.* **2001**, 333, 327.
- (11) Huang, L.; Nishinari, K. *J. Polymer Sci. Part B* **2001**, 39, 496.
- (12) Kjellander, R.; Florin, E. *J. Chem. Soc., Faraday Trans* **1981**, 77, 2053.
- (13) Caldararu, H.; Caragheorheopol, A.; Schlick, S. *Bull. Pol. Acad. Sc. Chem.* **2000**, 48, 367.
- (14) Wang, R. L. C.; Kreuzer, H. J.; Grunze, M. *J. Phys. Chem. B* **1997**, 101, 9767.
- (15) Kokkoli, E.; Zukoski, C. F. *Langmuir* **1998**, 14, 1189.
- (16) Johansson, P.; Shridhar, P. G.; Tegenfeldt, J.; Lindgren, J. *Solid State Ionics* **1996**, 86–88, 297.
- (17) Spevacek, J.; Dybal, J. *Macromol. Rapid Commun.* **1999**, 20, 435.
- (18) Banka, P. A.; Selser, J. C.; Wang, B.; Shenoy, D. K.; Martin, R. *Macromolecules* **1996**, 29, 3956.
- (19) MacGlashan, G. S.; Andreev, Y. G.; Bruce, P. G. *Nature* **1999**, 398, 792.
- (20) Annis, B. K.; Kim, M.-H.; Wignall, G. D.; Borodin, O.; Smith, G. D. *Macromolecules* **2000**, 33, 7544.
- (21) Harris, J. M.; Hundley, N. H.; Shannon, T. G.; Struck, E. C. in *Crown Ethers and Phase-Transfer Catalysis in Polymer Science*; Mathias, L.; Carreher, C. E. Eds.; Plenum: New York, 1984, 371.
- (22) Bandyopadhyay, K.; Liu, H.; Liu, S.-G.; Echegoyen, L. *Chem. Commun.* **2000**, 141.
- (23) Liu, H.; Liu, S.; Echegoyen, L. *Chem. Commun.* **1999**, 1493.
- (24) Flink, S.; van Veggel, F. C. J. M.; Reinhoudt, D. N. *J. Phys. Chem. B* **1999**, 103, 6515.
- (25) Manege, L. C.; Takayanagi, T.; Oshima, M.; Iwachido, T.; Moto-mizu, S. *Bull. Chem. Soc. Jpn.* **1999**, 72, 1301.
- (26) Talanova, G. G.; Elkarim, N. S. A.; Talanov, V. S.; Hanes, R. E.; Hwang, H.-S.; Bartsch, R. A.; Rogers, R. D. *J. Am. Chem. Soc.* **1999**, 121, 11 281.
- (27) Clark, S. L.; Montague, M. F.; Hammond, P. T. *Organic Thin Films, ACS Symp. Ser. 695* **1997**; Chapter 15.
- (28) Feldman, K.; Hähner, G.; Spencer, N. D.; Harder, P.; Grunze, M. *J. Am. Chem. Soc.* **1999**, 121, 10 134.
- (29) Hofmeister, F. *Arch. Exp. Natur. Pharmacol.* **1888**, 24, 247.
- (30) Hofmeister, F. *Arch. Exp. Natur. Pharmacol.* **1890**, 27, 395.
- (31) Israelachvili, J. *Intermolecular and Surface Forces*, 2nd ed.; Academic Press: San Diego, CA, 1992.
- (32) Napper, D. H. *J. Colloid Interface Sci.* **1970**, 33, 384.
- (33) Collins, K. D.; Washabaugh, M. W. *Quart. Rev. Biophys.* **1985**, 18, 323.
- (34) Cacace, M. G.; Landau, E. M.; Ramsden, J. J. *Quart. Rev. Biophys.* **1997**, 30, 241.
- (35) Vogler, E. A. *Adv. Colloid Interface Sci.* **1998**, 74, 69–117.
- (36) Ducker, W. A.; Senden, T. J.; Pashley, R. M. *Nature* **1991**, 353, 239.
- (37) v. d. Vegte, E. W.; Hadzioannou, G. *J. Phys. Chem. B* **1997**, 101, 9563.
- (38) Vezenov, D. V.; Noy, A.; Rozsnyai, L. F.; Lieber, C. M. *J. Am. Chem. Soc.* **1997**, 119, 2006.
- (39) Franks, F. *Water: a matrix of life*, 2nd ed.; Cambridge: Royal Society of Chemistry, 2000.
- (40) Klose, M. *Wasser: Struktur und Dynamik*, Berlin: Akademie Verlag; 1986.

- (41) Vogler, E. A. J. *Biomater. Sci. Polymer Ed.* **1999**, *10*, 1015.
- (42) Knott, M.; Ford, I. *J. Phys. Rev. E* **2001**, *6303*, 1403.
- (43) Knott, M. *J. Phys. Rev. E*, submitted for publication.
- (44) Schweiss, R.; Welzel, P. B.; Werner, C.; Knoll, W. *Langmuir* **2001**, *17*, 4304.
- (45) Rogers, R. D.; Bauer, C. B. *J. Chromatogr. B* **1996**, *680*, 237.
- (46) MacGlashan, G. S.; Andreev, Y. G.; Bruce, P. G. *Nature* **1999**, *398*, 792.
- (47) Lvov, Y. M.; Decher, G. *Crystallography Reports* **1994**, *39*, 628.
- (48) Hutt, D. A.; Cooper, E.; Leggett, G. J. *J. Phys. Chem. B* **1998**, *1*, 174.
- (49) Cooper, E.; Leggett, G. J. *Langmuir*, **1998**, *14*, 4795.
- (50) Rading, D.; Kersting, R.; Benninghoven, A. *J. Vac. Sci. Technol. A* **2000**, *18*, 312.
- (51) Scatena, L. F.; Brown, M. G.; Richmond, G. L. *Science* **2001**, *292*, 908.