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Protein-resistant monolayers prepared by hydrosilylation of α-oligo(ethylene glycol)-ω-alkenes on hydrogen-terminated silicon (111) surfaces†

Chi Ming Yam, Juan Manuel Lopez-Romero,‡ Jianhua Gu and Chengzhi Cai*

Department of Chemistry, & Center for Materials Chemistry, University of Houston, Houston, Texas 77204, USA. E-mail: cai@uh.edu; Fax: +1 713 743 2709; Tel: +1 713 743 2710

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Atomically flat, homogeneous, and protein-resistant monolayers can be readily prepared on H–Si(111) surfaces by photo-induced hydrosilylation of α-oligo(ethylene glycol)-ω-alkenes.

Modification of silicon surfaces with a stable, uniform and ultrathin layer of biocompatible materials is of tremendous interest for the development of silicon-based bio-devices, including biochips, biosensors, microarrays, microfluidic systems, and implantable microdevices.[1,2] Grafting oligo- or poly(ethylene glycol)s (OEGs or PEGs)—well-known biocompatible materials—onto silicon oxide surfaces has been mostly based on siloxane chemistry using trichloro- or trialkoxylsilane derivatives.[2,3] Unfortunately, these reagents easily polymerize to form large aggregates and multilayers on the surfaces, and this is problematic particularly for coating on miniature devices. One way to circumvent this problem is to graft OH-terminated PEG onto Cl–Si surfaces, prepared by chlorination of hydrogen-terminated silicon surfaces,[4] to form Si–O bonds with the surfaces. We envisioned a more practical approach based on hydrosilylation[5] of α-OEG-ω-alkenes directly onto H-terminated silicon surfaces, forming Si–C bonds that are more stable towards hydrolysis than Si–O bonds. Also, the reaction can be induced by light, allowing for photopatterning on the surface.[5d] We were surprised that this seemingly obvious and very useful approach had not been reported, although hydrosilylation is widely used to prepare alkyl monolayers presenting a variety of surface functional groups including esters and amides.[5c] An uncertainty was the presence of multiple ethylene glycol units that might interfere with the reaction and trap a trace amount of water that facilitates the oxidation of the H–Si surface. While our initial interest in this approach was to modify silicon atomic force microscopic (AFM) tips,[6] two reasons prompted us to explore this approach also for the growth of OEG layers on flat silicon surfaces: (1) it is novel and potentially useful for the development of silicon-based biotechnology; in particular, we are interested in using such monolayers as atomically flat, robust, and protein-resistant platforms for patterning single protein molecules on such surfaces; (2) the films on flat silicon surfaces can be better characterized than those on AFM tips, whose existence cannot be verified.

Herein, we present the study of OEG layers grown by hydrosilylation of three alkenes with the general formula $CH_2{=}CH(CH_2)_9(OCH_2CH_2)_nOCH_3$ (n = 3,[3a] 6,[7] and 9, abbreviated as **EG$_3$**,[3a] **EG$_6$**,[7] and **EG$_9$**) on atomically flat H–Si(111) surfaces. We initially used the reported methods for thermally[5f] or photo-induced hydrosilylation,[5b] but the resultant films displayed a relatively high contact angle hysteresis (>5°) and a low protein resistivity (>20% monolayer adsorption of fibrinogen). We then developed a practical procedure for photo-induced surface hydrosilylation, in which only ~1 mg of the alkenes without solvent was used for coating a 1 × 1 cm^2 wafer under a 254 nm UV lamp. This procedure improves the quality of the EG films, probably due to the use of a small amount of EG derivatives which facilitates the removal of the trapped water even under a moderate vacuum (3 mTorr).

The advancing/receding contact angles (θ_a/θ_r) of water were 59°/56° for the **EG$_3$** films, substantially higher than the values of 49°/46° for both **EG$_6$** and **EG$_9$** films (Table 1). Both contact angles and hysteresis ($\Delta\theta$) of the **EG$_3$** films are lower than those of EG_3-terminated thiolate self-assembled monolayers (SAMs) on Au or Ag (θ_a/θ_r: 62°/52°).[8] The low $\Delta\theta$ (~3°) for all films indicate smooth and homogeneous surfaces. This is confirmed by the AFM images, *e.g.* **EG$_9$**, showing the atomic steps of the underlying substrate surface. The ellipsometric thicknesses (Table 1) of the **EG$_3$**, **EG$_6$**, and **EG$_9$** films are in good agreement with the estimated thicknesses of 22, 29 and 37 Å for the monolayers with all *trans* methylene chains tilted ~45° from the surface and helical OEG chains oriented normal to the surface,[5a,8b] although the EG region of our films are not helical (see below).

The FTIR-ATR absorbances for the EG films include those at ~2965 (CH_3 asymmetric stretch), ~2930 (OCH_2 asymmetric stretch), 2918 (alkyl CH_2 asymmetric stretch), ~2870 (OCH_2 symmetric stretch), 2849 (alkyl CH_2 symmetric stretch) and ~2810 cm^{-1} (CH_3 symmetric stretch), consistent with those for the EG-terminated thiolate films on Au and Ag.[8b] For the **EG$_3$** and **EG$_6$** films, both the alkyl CH_2 stretches at 2918 and 2849 cm^{-1} indicate a highly ordered environment for the methylene chains.[9] Interestingly, increasing the number of EG units from 6 to 9 results in broadening of all bands in the C–H stretching region, similar to those reported for poly(ethylene glycol) (PEG) films.[4] Vanderah *et al.* showed that, for the OEG thiolate SAMs on Au(111), broadening of bands in this region correlates with less ordered OEG chains.[10] The conformations (helical *vs.* nonhelical) and ordering of OEG chains can be proved by the bands in the 950–1400 cm^{-1} region for thiolate SAMs on Au or Ag.[8b,10] However, this method failed in our system due to the strong background absorption in this region. Nevertheless, the absence of an absorption band at ~2892 cm^{-1} that is characteristic to helical EG segments,[8b] indicates that the EG segments in our films did not adopt a helical structure.

The carbon 1s narrow-scan X-ray photoelectron spectra (XPS) of the EG films show two C 1s peaks (Fig. 1a). The one at a higher binding energy (~287 eV) is assigned to the carbon atoms that are adjacent to an oxygen atom, and the one at a lower binding energy

Table 1 Advancing and receding contact angles of water (θ_a, θ_r/deg) and ellipsometric thicknesses (T_e/Å) for **EG$_3$**, **EG$_6$**, and **EG$_9$** films on Si(111) before and after treatment with a fibrinogen solution

	Before protein adsorption		After protein adsorption	
Alkene	θ_a, θ_r/deg	T_e/Å	θ_a, θ_r/deg	T_e/Å
EG$_3$	59/56	23	80/20	65
EG$_6$	49/46	27	52/47	30
EG$_9$	49/46	33	50/46	34

† Electronic supplementary information (ESI) available: details of the synthesis of **EG$_6$** and **EG$_9$**, experimental setup and procedures for the surface hydrosilylation, AFM image of **EG$_9$**. See http://www.rsc.org/suppdata/cc/b4/b401499e/

‡ On leave from Dept. Quimica Organica, Universidad de Malaga, Malaga-29071, Spain

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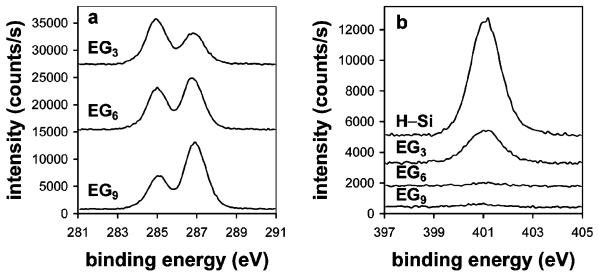

Fig. 1 XPS of films derived from **EG_3**, **EG_6**, and **EG_9** on Si(111): C 1s region before (a) and N 1s region after (b) immersion in protein solution.

(~285 eV) is assigned to the rest of the carbon atoms. The ratios of the integrated areas of the deconvoluted C 1s signals of the films between two types of carbon atoms—those adjacent to an oxygen atom (C–O, 287 eV) and those that are not (C–C, 285 eV)—are in good agreement with the expected ratios: 7 : 10 *vs.* 8 : 10 for **EG_3**; 13 : 10 *vs.* 14 : 10 for **EG_6**; 20 : 10 *vs.* 20 : 10 for **EG_9**. In addition, the relative intensity of C 1s peaks for **EG_3/EG_6/EG_9** is 0.7 : 0.9 : 1, close to the expected value (0.6 : 0.8 : 1).

To examine the protein adsorption properties, the films were immersed in a 0.1% solution of fibrinogen in 0.01 M phosphate-buffered saline (PBS) at pH 7.4 and at 20–25 °C for 1 h. The samples were then washed several times with Millipore water for removal of non-adsorbed protein and salts, followed by drying with a stream of N_2. For comparison, a freshly prepared H–Si(111) substrate was also subjected to the above conditions. As expected, fibrinogen readily adsorbed on the hydrophobic H–Si(111) surface, resulting in a film with an ellipsometric thickness of 60 Å and θ_a/θ_r (H_2O) of 80°/20°, corresponding to a monolayer of fibrinogen.[11] In contrast to the corresponding EG_3-terminated thiolate SAMs on Au that reduce adsorption of fibrinogen to 2% monolayer,[5] **EG_3** monolayers on silicon still adsorbed substantial amounts of the protein as shown by a large increase of water contact angles (Table 1) and ellipsometric thickness (~40 Å) corresponding to 60% monolayer. We also measured the surface density of the adsorbed protein by XPS (Fig. 1b) which is more sensitive than ellipsometry. Assuming a full monolayer adsorption of fibrinogen on H–Si(111), the ratio (I_{EG}/I_{HSi}) of the integrated areas of the N 1s peaks at ~401 eV arising from the adsorbed protein on the EG films (I_{EG}) and H–Si(111) (I_{HSi}) corresponds to the degree of protein adsorption on the OEG surfaces. This method gives 30% monolayer adsorption of fibrinogen on the **EG_3** films. The higher value measured by ellipsometry may be due to the errors associated with the adsorption of water and the change of reflective index of the films upon protein adsorption. The lower protein resistance for the corresponding **EG_3** films on Si(111) than on Au(111) surfaces may be due to the larger spacing between the alkyl chains on Si(111). Theoretical and experimental results have shown that the optimal packing density is 0.5–0.55 alkyl chains per surface silicon on a Si(111) surface.[5a,b,12] Using the XPS and thickness data and the reported equation,[5b] we estimate the coverage of our **EG_3**, **EG_6** and **EG_9** films to be about 0.37–0.39 molecules per surface Si-atom, substantially lower than that of the OEG thiolate SAMs on Au(111) (33.6 *vs.* 21.3 $Å^2$ per molecule).[5a,8b] The low density of the **EG_3** films on Si(111) may facilitate the penetration of the protein through the short OEG layer into the hydrophobic alkyl layer, thus increasing the adsorption of the protein. Prolonging the OEG chain should improve the protein resistance. Indeed, the **EG_6** and **EG_9** films almost completely resisted the adsorption of fibrinogen, as shown by the small increase of thickness (3 Å and 1 Å) and the nearly unchanged contact angles (Table 1). XPS measurements also show that both the **EG_6** and **EG_9** films on Si(111) resisted ~97% of protein adsorption, comparable to the EG-terminated thiolate SAMs on Au (111) which also displayed increasing protein resistance with longer OEG chain length.[8a,13]

In conclusion, atomically flat and homogeneous alkyl layers presenting OEG can be readily prepared on H–Si(111) surfaces by photo-induced hydrosilylation of OEG-terminated alkenes using our modified procedure. The coverage of the EG films was estimated to be about 0.37–0.39 molecules per surface Si-atom, substantially lower than that of the OEG thiolate SAMs on Au(111). The films with three EG units absorbed 30–60% monolayer of the model protein (fibrinogen), while the films with more than six EG units reduced the adsorption of fibrinogen to ~3% monolayer. We expect that the protein resistance of these films can be further improved by increasing the coverage of the films, accomplishable through reduction of the oxygen and water contents by increasing the vacuum of the system.

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