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Synthesis of oligo(ethylene glycol) methacrylate polymer brushes

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Abstract

Here we report a study into controlling the polymerization of mono-hydroxy and mono-methoxy terminated oligo(ethylene glycol) methacrylates (HOEGMA and MeOEGMA, respectively) from functionalised, planar surfaces via atom transfer radical polymerization (ATRP). The effects of initiator structure, initiator density, temperature, and monomer ratios have been investigated for these polymerizations. The polymer brushes grown in this way were found to convey protein resistance to the underlying inorganic substrates, prone to facile protein adsorption in their native state.

Keywords: Poly(oligo(ethylene glycol) methacrylate) (POEGMA); Atom transfer radical polymerization (ATRP); Protein resistance

1. Introduction

Poly(ethylene glycol) (PEG) presents unique properties advantageous to biomedical and biotechnological devices [1]. In solution along with proteins, liposomes, cells, or other such biological structures, PEG can cause aggregation and precipitation (depletion attraction) or colloidal stabilisation, dependent on molecular weight and concentration [2]. PEG exhibits low toxicity, absence of antigenicity and immunogenicity, and an inherent ability to prevent protein adsorption. PEG–protein conjugates (made in the process called PEGylation) have shown to improve the performance and in vivo half-life of therapeutic agents such as antibodies and antibody fragments [3,4]. All these factors have resulted in various attempts to create surfaces presenting PEG to the environment. In recent years the use of oligo(ethylene glycol) terminated monolayers on gold and silicon have greatly expanded our basic knowledge of biocompatible surfaces [5]. Gold has been the substrate of choice owing to the relative ease of PEG–thiol synthesis [6,7] and the wide range of characterisation techniques possible on gold. It is, however, difficult to obtain good coverage of complex surfaces with gold using conventional deposition methods, as a result gold coating can become expensive. The recent move toward cheap polymeric substrates and the need to coat non-planar surfaces has turned attention toward surface tethered PEG from silicon: Via ring-opening polymerization of ethylene oxide [8], the synthesis of PEG-silanes for deposition onto silicon [9,10], or by photo-induced hydrosilylation of PEG-alkenes onto H–Si(1 1 1) surfaces [11]. These methods of surface modification can be applied to other

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oxidisable substrates, such as polymers or metals. Desai and coworkers [12] recently applied their silane chemistry to biosensors based on nanoporous alumina in order to minimise fouling within the sensors and improve their accuracy and shelf-life. These routes to surface modification require considerable synthetic effort and the resulting monolayers are prone to defects (especially when large areas need to be covered) which can counteract the surface properties required. The use of surface-tethered polymers, known as polymer brushes, created by a controlled *grafting-from* technique, such as ATRP [13], could help overcome these drawbacks by providing an easily accessible, homogeneous, defect free surface.

Recent research has documented considerable progress in the growth of surface-initiated polymer brushes using aqueous ATRP [14,15]. Chilkoti and coworkers [16] presented a route to create protein resistant surfaces based on poly(oligo(ethylene glycol) methacrylate) brushes (p(OEGMA)). These brushes are less well defined than self-assembled monolayers containing ethylene glycol moieties, but exhibit the same surface properties and provide mechanically and chemically robust protein resistant surfaces. ATRP has the versatility to create copolymers simply by varying monomer ratios. It should therefore be possible to incorporate specific binding sites within a p(OEGMA) background by using a mixed monomer feed for polymerization. If the non-PEG components of the surface were tailored to bind a specific analyte, such as an antibody fragment, the low protein binding of the PEG component would in theory improve the signal-to-noise ratio during analyte screening. In this paper, we present a detailed study of the controlled growth of p(OEGMA) brushes. The role of initiator density and structure, polymerization conditions (catalyst concentration and temperature), as well as the copolymerization of different monomers will be investigated.

2. Experimental

2.1. Materials

All chemicals were analytical reagent grade (unless otherwise stated) and were used as received from Aldrich, Fisher, or Lancaster. Monomethoxy oilgo(ethylene glycol) methacrylates (MeOEGMA) of molecular weights 400 (MW 400) and 200 (MW 200) were obtained from Polysciences Inc. Monohydroxy oligo(ethylene glycol) methacrylate of molecular weights 526 (MW 526) and 360 (MW 360) were obtained from Aldrich. Solvents were distilled prior to use except ethanol and methanol, which were analytical reagent grade and used as received. Deionised water with a resistance of 18.2 MΩ cm was obtained from a Millipore Simplicity 185 system. Triethylamine (Lancaster) was distilled from and stored over KOH before use. Inhibitors in the monomers were removed by elution through a neutral alumina plug before use. Copper(I) chloride (99+%) ($Cu^{I}Cl$), copper(II) bromide (99+%) ($Cu^{II}Br_2$) and 2,2′-dipyridyl (99+%) (bipy) were obtained from Aldrich. $Cu^{I}Cl$ was stored under vacuum until needed. Silicon wafers (Compart Technology Ltd, 100 mm diameter, boron-doped, ⟨1 0 0⟩ orientation, one side polished) were cleaned using an Emitech K1050X Plasma Asher in dry air plasma mode, 100 W for 10 min prior to use.

2.2. Instrumentation

Ellipsometric measurements were carried out on a DRE ELX-02C ellipsometer with a 632.8 nm laser at 70° from the normal. Refractive indices of 1.45 were used for initiator and polymer layers. Five measurements across each sample were taken, with their average and standard deviation used for analysis. When two or more samples were polymerized under identical conditions, but in separate experiments, the average and standard deviation of the combined ellipsometry data for those samples were used for analysis. Contact angle goniometry was performed using a homemade stage with a computer controlled microsyringe and digital camera. Infusion and withdrawal rates of 4 μL min^{-1} were used. Advancing (θ_{AW}) and receding (θ_{RW}) water contact angles were recorded.

2.3. ATRP initiator formation

Ester silane initiator (Scheme 1A). 2-Bromo-2-methyl-propionic acid 3-trichlorosilanyl-propyl ester. *Synthesis*: The synthesis of the trichlorosilane ATRP initiator (1) was adapted from published procedures [17] utilising allyl alcohol. *Monolayer deposition*: A plasma oxidised silicon wafer was placed in a crystallising dish and covered with a filtered (0.22 μm pore filter) solution of trichlorosilane initiator (1) (10 μL) in dry toluene (30 cm^3), followed by dry triethylamine (Et_3N) (50 μL). The dish was covered, sealed, and left at room temperature for 18 h. The wafer was washed with toluene, sonicated in toluene for 1 min, washed with acetone then absolute ethanol, and dried under a stream of N_2. The initiator coated wafer was kept under N_2 until needed. Ellipsometric thicknesses of 0.7–0.8 nm and contact angles of $\theta_{AW} = 76° \pm 4$ and $\theta_{RW} = 65 \pm 2$ were observed, which are reproducible and consistent with a full monolayer of the initiator (1).

Amide silane initiator (Scheme 1B). APTS monolayer: A plasma oxidised silicon wafer was placed in a desiccator with a vial containing a solution of aminopropyltrimethoxy silane (APTS) (5 drops) in hexane (2 cm^3). Placing the desiccator under vacuum for 20 min brought about vapour deposition of APTS onto