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# Colloidal force probe study of poly(di(ethylene glycol)methylether methacrylate) homopolymer brush layers in aqueous media at different temperatures

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ABSTRACT

This study reports on the property changes of thermoresponsive layers of end-grafted poly(di (ethylene glycol) methyl methacrylate) (PDEGMA) on gold studied by atomic force microscopy (AFM) in aqueous medium as a function of thickness and temperature. The changes in interaction forces between a hydrophobized colloidal AFM probe and PDEGMA brushes as well as the mechanical properties and swelling of the PDEGMA layers below and above the reported lower critical solution temperature (LCST) of PDEGMA brushes of 32 °C were analyzed. This work corroborates independently acquired data on thermally triggered changes in protein and cell adsorption and release of these brush layers. While the adherence between colloidal probe and PDEGMA showed a monotonic and reversible increase from 27 °C to 60 °C, the work of adhesion increased sigmoidally with increasing temperature. For layer thicknesses from 5 nm to 27 nm, the apparent transition temperature, determined from the corresponding inflection point, varied linearly from 35 °C to 49 °C. These transition temperatures match the transition temperatures determined by the irreversible adsorption of bovine serum albumin via surface plasmon resonance (SPR). Additionally it was concluded from the AFM force-displacement and indentation data that the layers were swollen to three times their dry thickness below the LCST. When the temperature was increased, they collapsed and became progressively more adhesive and stiffer. The interplay of polymer collapse and balanced interactions with the underlying substrate in very thin layers allows one to tune the efficient transition temperature to temperatures above the LCST. Therefore such “smart materials” with unique features can be exploited to fabricate thermoresponsive surfaces with finely tunable collapse temperatures located in the physiological range.

## 1. Introduction

Polymer brushes have garnered increasing attention in the past decades and their role has evolved from academic curiosity in polymer physics to application in various advanced fields, including responsive systems and biointerfaces [1–4]. Polymer brushes are defined as polymer chains grafted at one end to a solid surface with appropriately high grafting density. This results in chains overlapping and therefore stretching away from the surface. These polymeric systems can be synthesized under controlled conditions by various sophisticated techniques [5,6]. Stimulus-responsive polymer brushes allow one to reversibly switch between different

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defined states of surface properties [7–10] and hence polymer brushes are excellent candidates for soft nanotechnology [11,12]. In polymer based bionanotechnology, the reversibly adjustable surface properties [13], non-fouling properties or the local alteration of e.g. wettability or friction [10,14], afforded by polymer brushes, are key features.

Poly(*N*-isopropyl acrylamide) (PNIPAM) is one of the most studied temperature-responsive polymers with a transition temperature of 32 °C close to the physiological temperature [15–18]. The temperature-induced collapse of PNIPAM has been for instance utilized to afford temperature-gated switching of pores from the closed to the open state [19]. PNIPAM brushes have in particular been utilized in cell sheet engineering applications by the group of Okano, who avoided the traditional but detrimental methods of mechanical dissociation and trypsinization for the removal of cells from culture substrates, by replacing these *brute-force* methods with a mild temperature-triggered cell desorption step [20–22]. The simple decrease in temperature to below the LCST leads to a pronounced hydration and swelling of the thermoresponsive PNIPAM chains, which allows the recovery of cell monolayers as connected living cell sheets and retains the extracellular matrix (ECM) beneath cell sheets and also the cell-cell junctions [20–22].

In the past decade alternative materials exhibiting thermoresponsive properties like PNIPAM have moved into the focus of (bio) interface science. This work has been in parts motivated by reports that indicate potential cytotoxicity of PNIPAM as an acrylamide-based polymer and showed the activation of platelets upon contact with blood [23,24]. In addition, PNIPAM unfortunately does not eliminate protein adsorption completely and is not a bio-inert material [25]. Among the alternatives for PNIPAM are methacrylates, which possess oligo(ethylene glycol) side grafts. Poly(ethylene glycol) (PEG) itself is one of the most studied and well known protein resistant materials [26–28]. Neat PEG based polymers show transition temperatures beyond the physiological range and therefore are unsuitable for biomedical applications. However, PEG containing copolymers and copolymer brushes of oligo(ethylene glycol) macromonomers of different side chain lengths allow the precise adjustment of LCST [29,30]. The LCST was found to be increased for poly(di(ethylene glycol)methyl ether methacrylate) (PDEGMA) from 26 °C (for bulk PDEGMA in water) [31,32] to 32 °C (for brushes) [33]. Related poly(tri(ethylene glycol) ethyl ether methacrylate) brushes showed according to Dworak et al. LCST- like cell release behavior, when the solution temperature was dropped from 37 °C to 17.5 °C [34]. In addition, there is also evidence that the transition temperature may depend on the brush thickness. Theoretical and experimental work showed that the conformation of brushes depends on brush-surface interactions [35–37].

We have reported before that the effective or apparent transition temperature observed in 5 ± 1 nm thin PDEGMA layers may deviate from the brush LCST value of 32 °C. The irreversible adsorption of the soft protein bovine serum albumin (BSA) was shown by surface plasmon resonance (SPR) to depend sigmoidally on temperature [38]. The apparent transition temperature determined from the inflection point increased linearly with layer thickness from 35 °C at 5 nm (dry) thickness to 48 °C at 23 nm thickness. While PDEGMA layers with a dry ellipsometric thickness ≥10 nm are protein and cell resistant, 5 ± 1 nm thin PDEGMA layers were shown to allow cells to adhere [39], and similar to the work by Okano, Duschl and many others to release them by decreasing the temperature to room temperature [15,20–22,25].

Such a thermally stimulated switching should coincide with the collapse of the polymer layer and a profound change in nanomechanical and other properties. In earlier work, these phenomena have been addressed for related LCST systems. Syntytska et al. investigated the effect of the AFM tip radius on the adhesion force and the adhesion energy of brushes made of poly(NIPAM), poly(OEGMA-co-DEGMA) and poly(OEGMA-co-OPGMA) and could prove that an increasing of the AFM tip radius led to an increase of adhesion force and a decrease of the measured adhesion energy, respectively [40]. Latter decrease was attributed by the authors to an altered penetration depth. Not only the adhesion force, but also the work of adhesion is a function of temperature, as was shown for the work of adhesion of silica probes and probes coated with fibronectin on PNIPAM microgel surfaces [41]. In another study, higher molar mass brushes of polydimethylsiloxane (PDMS), polystyrene (PS), and a poly(propylene glycol)–poly(ethylene glycol) block copolymer (PPG/PEG) were reported to exhibit higher friction forces than polymer brushes of lower molar mass in air [42]. These forces were also influenced similarly by changes in the grafting density.

Previous reports on the temperature-dependent swelling of a PDEGMA brush with a dry film thickness of 105 nm in water by Jonas et al. clearly indicated that the thickness of PDEGMA brushes in water, as assessed by AFM, decreased with increasing temperature [30,43]. While we analyzed in earlier work the nanomechanical properties of OEGMA-derived homopolymer brushes in the dry and in aqueous medium at room temperature [44], we studied in the work reported here, the thermoresponsive behavior of PDEGMA layers with a thickness of 5–27 nm in aqueous solution *in situ* at different temperatures. The data were acquired in AFM force-distance experiments using hydrophobically modified colloidal force probes to unravel the origin of the previously observed phenomena [38,39] (Scheme 1).

## 2. Experimental section

### 2.1. Materials

Di(ethylene glycol) methyl ether methacrylate (DEGMA) was purchased from Sigma Aldrich Germany. Methanol (99.8%) was purchased from J.T. Baker. The Copper bromide (CuBr) and the initiator ω-mercaptoundecyl bromoisobutyrate were synthesized as reported previously [38,39]. Gold was purchased from Allgemeine Gold- und Silberscheideanstalt AG (Pforzheim); 99.99% (granules), Titanium from Chempur; 99.998% (pieces: 1–6 mm). Hexamethyldisilazane (HMDS) was purchased from Sigma Aldrich and distilled before usage. Ethanol 97%, denaturated: purchased from Fischer Scientific, chloroform 99% p. A.: purchased from Roth, methanol 99.8%: purchased from J.T. Baker, aluminum oxide neutral, for column chromatography: purchased from Macherey-Nagel, bipyridine (2,2′-bipyridyl) 99%: purchased from Sigma Aldrich, hydrogen peroxide ($H_2O_2$): purchased from Roth; 30%, sulfuric acid ($H_2SO_4$): purchased from Riedel de Haën, toluene: purchased from Sigma Aldrich. Milli-Q water from a Millipore Direct Q8 system