Thermo-Responsive Polymer Brushes with Tunable Collapse Temperatures in the Physiological Range

**Alain M. Jonas,*,† Karine Glinel,‡ Ron Oren,
Bernard Nysten,† and Wilhelm T. S. Huck***

*Melville Laboratory for Polymer Synthesis; Department of
Chemistry; University of Cambridge; Lensfield Road,
Cambridge CB2 1EW, U.K.*

Stimuli-responsive polymers[1] have attracted considerable interest for applications such as actuation,[2] drug delivery,[3] affinity control,[4] fabrication of materials of tunable shape and surface properties,[5] or stimuli-gated filtration.[6] Among these systems, hydrogels,[7] brushes,[8] and micro- or nanopatterned brushes[9] of poly(*N*-isopropylacrylamide) (PNIPAM) and of related copolymers have been studied extensively, because these polymers exhibit a lower critical solution temperature (LCST) in water at about 32 °C, which means that they undertake a reversible change in surface properties and swelling in water at temperatures close to physiological ones. Recently, the predominance of PNIPAM as the paradigmatic example of thermoresponsive polymer was challenged by the discovery that random copolymers of 2-(2-methoxyethoxy)ethyl methacrylate (MEO$_2$MA) and oligo(ethylene glycol) methacrylate (OEGMA) exhibit a LCST in water, which can be finely tuned anywhere between 26 and 90 °C depending on OEGMA content,[10] and which is almost independent of molar mass, concentration, and ionic strength, contrarily to PNIPAM.[10c] In addition, in contrast with PNIPAM which was recently shown to be moderately cytotoxic at 37 °C,[11] these poly(ethylene glycol)-based copolymers are expected to be nontoxic and non-immunogenic, since the addition of oligo(ethylene oxide) sequences to responsive polymers was also shown to decrease cytotoxicity.[11] Here, we exploit the unique features of these copolymers to prepare novel thermoresponsive surfaces with finely tunable collapse temperatures located in the physiological range. By measuring the temperature derivative of their equilibrium water contact angles, we succeed in obtaining thermodynamically relevant collapse transition temperatures, in stark contrast with previously reported attempts on thermoresponsive surfaces, which were devoid of thermodynamic meaning as shown below.

The thermoresponsive surfaces were obtained by growing brushes of P(MEO$_2$MA-*co*-OEGMA) copolymers from plasma-cleaned silicon wafers modified with a silane ATRP initiator, using surface-initiated aqueous atom transfer radical polymerization (ATRP) (full experimental details given in the Supporting Information).[12] Figure 1 is a plot of brush thickness vs polymerization time for different MEO$_2$MA:OEGMA ratios. The polymerization is well-controlled, with typically 100 nm thick pure MEO$_2$MA brushes or 20 nm thick OEGMA brushes obtained in 3 h, with the copolymers somewhere between these limits.

The temperature-responsiveness of the brushes was assessed by water contact angle measurements in the captive bubble
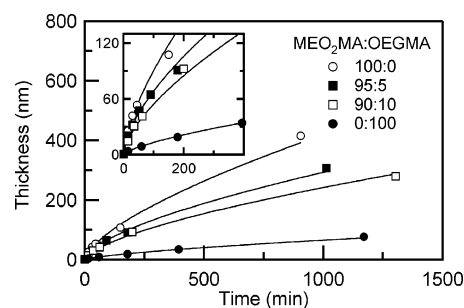
* Corresponding authors : E-mail: (W.T.S.H.) wtsh2@cam.ac.uk; (A.M.J.) alain.jonas@uclouvain.be.
† Permanent address: CeRMiN, Université catholique de Louvain, Louvain, Belgium.
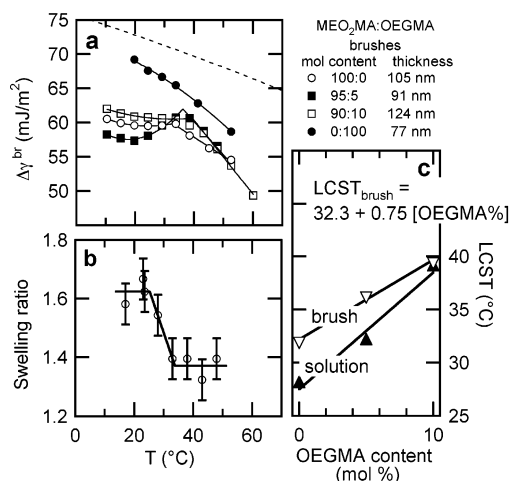‡ Permanent address: PBM-UMR 6522, CNRS−Université de Rouen, Rouen, France.

Figure 1. Thickness vs polymerization time of P(MEO$_2$MA-*co*-OEGMA) brushes grown by ATRP from silicon surfaces. The molar ratio of the two monomers in solution is indicated in the figure. The inset is a zoom for short times. The lines are power law fits and are drawn as support for the eye.

configuration. In this configuration, an air bubble is trapped below the tested surface which is immersed face down in water, and the strongly hydrophilic brush can attain equilibrium, which is rarely the case for usual contact angle measurements. Here, the samples can be equilibrated until the chemical potential of water vapor in the vapor-saturated air bubble equals the one of liquid water, and until the chemical potentials of the brush below the vapor-saturated bubble and below liquid water are equal.

The curves of equilibrium water contact angle vs temperature, $\theta(T)$, are presented in the Supporting Information for a series of copolymer brushes. From these curves, we computed the difference between the interfacial tensions of the brush in saturated water vapor and in liquid water, $\Delta\gamma^{\text{br}}$, using the Young-Dupré equation:[13]

$$\Delta\gamma^{\text{br}} = \gamma^{\text{br,vap}} - \gamma^{\text{br,liq}} = \gamma^{\text{w}} \cos(\theta) \qquad (1)$$

where γ^{w} is the surface tension of water,[14] and $\gamma^{\text{br,liq}}$ (respectively $\gamma^{\text{br,vap}}$) is the interfacial tension of the swollen brush in liquid water (respectively water vapor). Since interfacial tensions are excess free energies per unit area,[15,16] $\Delta\gamma^{\text{br}}$ obeys specific thermodynamic rules. For instance, its variation follows a Gibbs adsorption equation:[15,17]

$$\mathrm{d}\Delta\gamma^{\text{br}} = -\Delta s^{\text{br}}\, \mathrm{d}T - \Delta\Gamma_{\text{w}}\, \mathrm{d}\mu_{\text{w}} - \Delta\Gamma_{\text{br}}\, \mathrm{d}\mu_{\text{br}} \qquad (2)$$

where Δs^{br} is the difference of excess surface entropy between the brush/vapor and brush/liquid interfaces, μ_{br} (respectively, μ_{w}) is the chemical potential of the brush (respectively, water), and $\Delta\Gamma_{\text{br}}$ (respectively, $\Delta\Gamma_{\text{w}}$) is the difference of excess concentration in monomer segments (respectively, water) between the brush/vapor and brush/liquid interfaces. Since chemical potentials are continuous functions of temperature, eq 2 indicates that the interfacial tensions (and therefore the equilibrium contact angles) are continuous functions of temperature as well, even across a first order thermodynamic transition such as a LCST. In most previous works on thermoresponsive brushes, sudden jumps of the contact angles were reported to occur at the LCST;[8a,18] however, eq 2 shows that this may only arise for out-of-equilibrium contact angles, which obviously cannot be used to determine the location of a thermodynamic transition.[19] The temperature derivatives of $\Delta\gamma^{\text{br}}$ and of $\theta(T)$ can however be discontinuous at the LCST. Indeed, since $\Delta\Gamma_{\text{br}}$ is nonzero for a swollen brush,[20] eq 2 shows that the temperature variation of $\Delta\gamma^{\text{br}}$ partly reflects the temperature variation of the chemical potential of the brush, μ_{br}, which changes slope across

Figure 2. (a) Temperature dependence of the difference between the interfacial tensions of P(MEO$_2$MA-*co*-OEGMA) brushes in liquid water and saturated water vapor. The dashed line is the surface tension of water. (b) AFM-determined temperature-dependent swelling of a poly-(MEO$_2$MA) brush in water (105 nm dry thickness). (c) Comparison between the LCST of P(MEO$_2$MA-*co*-OEGMA) chains in solution (from ref 10b), and their collapse temperature in brushes.

a first-order transition.[21] The other right-hand terms of eq 2 may also contribute to changing the slope of $\Delta\gamma^{br}(T)$ through a sudden variation of excess entropy or water adsorption at the LCST. A complete assessment of the balance between these three contributions may only be obtained from a microscopic model, which is not required for our purposes.

Figure 2a presents the $\Delta\gamma^{br}(T)$ curves of selected copolymer brushes, which indeed exhibit a sudden and reversible change of slope at the expected[10] collapse transition of the brushes. To support this interpretation, we have measured by AFM in water the swelling of a poly(MEO$_2$MA) brush of 105 nm dry thickness, scanning across a scratch in the layer. The average swelling of the brush, expressed as the ratio of swollen to dry thickness, is reported in Figure 2b vs temperature. The collapse of the brush occurs over a ~10 °C wide temperature interval, with the collapsed state being reached at ~33 °C, coinciding with the kink in the corresponding curve of $\Delta\gamma^{br}(T)$ (open circles, Figure 2a).

The temperatures corresponding to the collapse of the copolymer brushes are plotted in Figure 2c, together with the literature LCST values determined for the copolymers in solution.[10b] Both vary linearly with the OEGMA content (the consistently lower bulk values are probably due to differences in the method of determination of the LCST). From Figure 2c we can estimate that, starting from ~32 °C and 0% OEGMA, every increase by 1% in OEGMA content results in a finely tunable shift of the brush collapse transition by 0.75 °C toward higher temperatures. The linear dependence of the collapse temperature probably extends toward higher OEGMA contents, as was shown for the LCST of the copolymers in solution;[10c] however, higher OEGMA contents would result in brushes of collapse temperature outside the physiological range, which are not investigated here. Finally, it should be noted that brushes much thinner than 50 nm showed a significantly higher LCST (e.g., 26 nm thick poly(MEO$_2$MA) brushes exhibited a LCST value of 40 °C).

Summing up, we have shown that finely tunable temperature-responsive surfaces can be easily obtained by growing P(MEO$_2$-MA-*co*-OEGMA) brushes by surface-initiated ATRP, and demonstrated how equilibrium contact angle measurements allow us to obtain thermodynamically relevant collapse transition

temperature. PEO-based polymers are nontoxic and non-immunogenic and extensively used for biomedical applications; we therefore expect our brushes to replace the traditional PNIPAM-based approaches for the fabrication of novel bio-compatible responsive surfaces of tunable set point in the physiological range.

Supporting Information Available: Text giving full experimental and analytical details and figures showing a typical image of a captive air bubble, complete contact angle data and AFM height images. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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