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1 Introduction

Polymers composed of oligo(ethylene glycol) (OEG) macromonomers are attractive materials for bio-medical applications due to their biocompatibility¹ and ability to suppress nonspecific interactions with biomaterials.²⁻⁴ Moreover they have, for instance, been implemented as constituents for sensing applications,⁵⁻⁹ for "smart" surfaces with the capability of controlling cell adhesion,10-12 and, if appropriately functionalized, they are even capable of reacting to the presence of biomacromolecules.13 A particularly useful property of the poly(OEG) copolymer system is the facile tunability of the phase transition temperature. It can be adjusted at will by simply varying the ratio of comonomers with different oligo(ethylene glycol) chain lengths.¹⁴⁻¹⁶ Despite these interesting properties, it seems that their temperature dependent swelling behaviour on surfaces has exclusively been studied for brush architectures,17-19 and there are no reports about nanoscale oligo-(ethylene glycol) thin films.

Photoreactive oligoethylene glycol polymers – versatile compounds for surface modification by thin hydrogel films†

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Solid surfaces are modified using photo-crosslinkable copolymers based on oligo(ethylene glycol) methacrylate (OEGMA) bearing 2-(4-benzoylphenoxy)ethyl methacrylate (BPEM) as a photosensitive crosslinking unit. Thin films of about 100 nm are formed by spin-coating these *a priori* highly biocompatible copolymers onto silicon substrates. Subsequent UV-irradiation assures immobilization and crosslinking of the hydrogel films. Their stability is controlled by the number of crosslinker units per chain and the molar mass of the copolymers. The swelling of the hydrogel layers, as investigated by ellipsometry, can be tuned by the crosslinker content in the copolymer. If films are built from the ternary copolymers of OEGMA, BPEM and 2-(2-methoxyethoxy) ethyl methacrylate (MEO₂MA), the hydrogel films exhibit a swelling/deswelling transition of the lower critical solution temperature (LCST) type. The observed thermally induced hydrogel collapse is fully reversible and the onset temperature of the transition can be tuned at will by the copolymer composition. Different from analogously prepared thermo-responsive hydrogel films of photocrosslinked poly(*N*-isopropylacrylamide), the swelling-deswelling transition occurs more gradually, but shows no hysteresis.

Crosslinking of polymers *via* benzophenone groups is a long established strategy for the preparation of polymer networks.²⁰ It also offers the possibility of tethering polymers to surfaces.²¹⁻²⁴ Benzophenone excited by UV light undergoes a rapid intersystem crossing to a reactive triplet state often being represented as a diradical. As such it easily abstracts aliphatic hydrogens from virtually any organic compound. Therefore if organic substrates are used, radicals are readily formed on the surface and may subsequently react with the polymer layer on the top. Consequently, the copolymer gets immobilized onto the substrate. The application of polymer attached benzophenone units is thus especially convenient as radicals generated on the copolymer simultaneously lead to crosslinking.

When efficient crosslinking is ensured, hydrogel layer properties can be conveniently controlled by the crosslinker content and/or irradiation time.²³ Yet the efficiency of crosslinking is strongly related to the reactivity of hydrogens in the copolymer toward abstraction.²⁵ Considering this, OEGMA copolymers represent an ideal material for benzophenone crosslinking: the hydrogens of the α -methylene group next to the ether moieties within the side chains are known to be particularly prone to radical attack. Thus, radical formation should be facilitated at this position.²⁶⁻²⁸

In this paper we apply polymerizable 2-(4-benzoylphenoxy) ethyl methacrylate (BPEM) as photocrosslinker (Fig. 1). BPEM and its closely related derivatives have been investigated occasionally as monomeric and polymeric photoinitiators.^{29,30} However,

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investigations have so far mainly been focused on the photochemistry and photophysics of this compound,^{30,31} while reports dealing with the use as a crosslinker seem to be virtually absent. We report here the synthesis and characterization of poly(OEG) methacrylates incorporating the benzophenone bearing monomer, BPEM, and their use for stabilized thermo-responsive coatings. The properties of such films were investigated and relationships to experimental parameters were established.

2 Experimental

2.1 Materials

4-Hydroxybenzophenone (98%, Aldrich), 2-bromoethanol (98% for synthesis, Merck), potassium carbonate (Riedel-de-Haën), potassium iodide (Acros), dimethylformamide (DMF), triethylamine, 4-dimethylaminopyridine, methacryloyl chloride (97%, Aldrich) and ethanol (99.8%, Chem Solute) were used as received. Dichloromethane (analytical grade, J.T. Baker) was dried over calcium chloride prior to use. 2-(2-Methoxyethoxy) ethyl methacrylate (MEO₂MA, 95%, Aldrich) and oligo(ethylene glycol) methylether methacrylate (OEGMA, Aldrich, average $M_r = 475$ g mol⁻¹) were passed through a basic alumina column before use to remove inhibitors. 2-2'-Azobisisobutyronitrile (AIBN, 98%, Acros) was recrystallized from methanol before use.

Single side polished silicon wafers with an oxide layer of 1.0 nm thickness (Si-Mat, Kaufering, Germany) were cut into square pieces of 2 cm \times 2 cm.

2.2 Synthesis of 2-(4-benzoylphenoxy)ethyl methacrylate (BPEM)

The benzophenone monomer was synthesized following a strategy similar to that reported by Zvara *et al.*³¹ First 4-hydroxybenzophenone (10.0 g, 50.44 mmol) was dissolved in dry DMF (150 mL). K₂CO₃ (13.82 g, 100 mmol), KI (3.98 g, 24 mmol) and 2-bromoethanol (5.3 mL, 74 mmol) were added and the solution was stirred at 65 °C overnight. As thin film chromatography showed incomplete conversion, two additional portions of K₂CO₃ (7.0 g, 50 mmol) and 2-bromoethanol (4.4 mL, 62 mmol) were added and the solution was stirred for further 18 h. The yellowish reaction mixture was poured into 1.5 L of ice-water and the precipitate was separated by centrifugation. The collected product was dried in a vacuum at room temperature over CaCl₂ to give 10.7 g of colourless shiny platelets (86% yield).



Fig. 1 Chemical structures of the monomers used.

In a second step, a mixture of 10.0 g of the as-prepared intermediate 2-(4-benzoylphenoxy)ethanol (41.2 mmol), triethylamine (11.4 mL, 82.5 mmol) and 4-dimethylaminopyridine (0.25 g, 2.1 mmol) in dichloromethane (225 mL) was cooled to 0 °C. Methacryloylchloride (4.6 mL, 45.4 mmol) in dichloromethane (20 mL) was added drop wise. After stirring for additional 2 h at 0 °C, the reaction mixture was allowed to warm to room temperature and stirred overnight. The mixture was then poured into a saturated aqueous NaHCO₃ solution. The organic phase was separated, washed with additional saturated aqueous NaHCO₃ and NaCl, dried by Na₂SO₄ and filtered through a column filled with silica gel and evaporated to give 7.5 g of monomer BPEM as colourless crystalline solid (yield 60%).

2.3 Synthesis of copolymers

The copolymers were synthesised according to a standard procedure. In a round bottom flask protected from ambient light appropriate amounts of 2-(2-methoxyethoxy) ethyl methacrylate (MEO₂MA), oligo(ethylene glycol) methylether methacrylate (OEGMA, average molar mass 475 g mol⁻¹) and 2-(4benzoylphenoxy)ethyl methacrylate (BPEM) were dissolved in ethanol (15 wt% monomers for copolymers of moderate molar mass; 20 wt% monomers for copolymers of elevated molar mass). The initiator azobisisobutyronitrile (AIBN, 0.5 equivalents) was added, the flask was sealed with a rubber septum and the mixture was purged with argon for 30 min. The mixture was heated to 60 °C in an oil bath for 20 h. The reaction was stopped by opening the flask and allowing contact with air. The mixture was diluted with deionized water and subsequently purified by dialysis against deionized water for at least 3 days (Roth, ZelluTrans membrane, molecular weight cut off: 4000-6000). The polymer was isolated by freeze drying. All operation and purification steps were carried out under careful protection from light.

2.4 Film preparation

Silicon substrates were washed and hydrophilised for 20 h in a solution of 100 mg of potassium permanganate in 40 mL of concentrated sulphuric acid. The substrates were washed three times with water, then with ethanol and finally with toluene. To provide an organic surface for the immobilization of the copolymer, samples were immersed in 1 vol% solutions of (3-aminopropyl) dimethylethoxysilane in toluene, resulting in the silanization of the substrates. After 6 h the substrates were taken out of the solutions, washed with toluene and ethanol and dried under air flow. Solutions of the copolymers in ethyl acetate were spincast onto the pre-treated substrates with a standard spin-coater (KL-SCV, Schaefer technologies, Langen/Germany). About 5 droplets of a 1–2 wt% solution were dispensed on the wafer at zero rotation, and then the copolymer was cast at 50–70 rotations per second for 30 s.

2.5 UV radiation chamber

UV irradiation was carried out in a UVACUBE 100 radiation chamber (Hönle, Gräfelfing/Germany) with a 100 W iron doped mercury vapour lamp equipped with sheet glass as a filter (cut off 310 nm). The distance of the sample from the light source was 20 cm.

2.6 Characterisation methods

Cloud points of the aqueous polymer solutions were measured in 3.0 g L⁻¹ solutions in ultrapure water on a thermostatted TP1 photometer (Tepper, Mainz/Germany).³² Transmittance at 670 nm was monitored as a function of temperature with heating/cooling cycles at rates of 1 °C min⁻¹ (cell path length 12 mm). ¹H NMR spectra were recorded in CDCl₃ using a Bruker Avance 300 spectrometer. Size exclusion chromatography (SEC) was run at 50 °C in DMF (flow rate 1 mL min⁻¹) using a Spectra Physics Instruments apparatus equipped with a UV-detector SEC-3010 and a refractive index detector SEC-3010 from WGE Dr Bures (columns: guard (7.5 × 75 mm), PolarGel-M (7.5 × 300 mm)), and calibrated with linear polystyrene standards (PSS/Germany). For samples with a thickness exceeding 300 nm, a Dektak 150 Profilometer (Veeco Instruments Inc.) was used for surface film thickness measurements.

2.7 Ellipsometry

Ellipsometry used a Multiscope apparatus from Optrel GbR (Kleinmachnow/Germany) equipped with a HeNe laser (632.8 nm wavelength), in a null ellipsometer configuration, with an angle of incidence of 60° . Dry film thicknesses were calculated by the software "Elli", version 5.2 (Optrel GbR, Kleinmachnow/Germany), using a four-layer model with the following parameters: layer 1: air (n = 1.000, k = 0), layer 2: organic layer (n = 1.4800, k = 0), layer 3: SiO₂ (d = 1.0 nm, n = 1.4580, k = 0), layer 4: silicon (n = 3.8858, k = -0.0200). The samples for ellipsometry were prepared on pieces cut from silicon wafers.

2.8 Swelling experiments

Samples were placed into a fluidic cell (Optrel GbR, Kleinmachnow/Germany) filled with deionized water at ambient temperature. The basis for the calculation of the thickness and the refractive index of the swollen film by the software "Elli" was a 4-layer system with fixed parameters for layer 1: (water n = 1.332, k = 0), layer 3: (SiO₂ d = 1.0 nm, n = 1.4580, k = 0) and layer 4: (silicon n = 3.8858, k = -0.0200). The hydrogel layer (layer 2) was considered as a homogenous mixed layer of polymer and water. This layer was calculated in the "n variable" mode, in which the software searches for points on the Delta, Psi-trajectories,³³ which match best the experimentally determined values.

2.9 Temperature dependent measurements

The fluidic cell was connected to a Julabo F32-MH refrigerated heating circulator filled with water. Layer thicknesses were determined at 5 °C intervals and the cell was allowed to equilibrate for 20 min after each temperature step.

3 Results and discussion

3.1 Synthesis of the UV-crosslinker monomer

The synthesis of the monomer was carried out in two steps. Briefly an ethylene glycol group was first attached to 4-hydroxy

benzophenone via a Williamson ether synthesis, then the resulting functional alcohol was coupled with methacryloyl chloride. The UV-sensitive benzophenone group is thus attached to a polymerizable methacrylic unit via an ethylene glycol spacer. This specific design, differing from other benzophenone functionalized monomers,23,25 was selected for two reasons. First, compared to the direct coupling via a phenolic ester bond, the aliphatic ester of the polymerizable moiety in combination with the phenol ether link introduced by the short ethyl spacer should provide superior stability of BPEM against hydrolysis. Secondly, the introduction of the ethylene glycol spacer results in close electronic and steric similarity of BPEM to the other comonomers used. Accordingly, their copolymerisation behaviour should be close to the ideal azeotropic case. This implies that the benzophenone monomers are incorporated into the copolymer with nearly the same probability as the other comonomers, independent of monomer a)



Fig. 2 UV-vis spectra of BPEM monomers and copolymers produced. (a) BPEM monomer in *n*-hexane (--- 10-fold magnification) and (b) absorption of a copolymer layer of 800 nm thickness on a quartz window after different periods of UV-irradiation (solid line 0 min, --- 1 min, --- 2 min, --- 4 min, --- 6 min, --- 10 min, and --- 16 min). Inset: decrease of the maximum absorption peak at 287 nm with duration of UV-irradiation.

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conversion. Consequently, the copolymers are expected to be chemically more homogeneous than analogous materials prepared with 4-methacryloyloxy-benzophenone, and their composition should be close to the one of the monomer feed, with a fairly even distribution of crosslinking sites. The UV-spectrum of purified BPEM exhibits the typical absorption pattern of a donor substituted benzophenone, namely an intense $\pi \rightarrow \pi^*$ -transition at 277 nm and a much weaker n $\rightarrow \pi^*$ -transition at 342 nm (see Fig. 2). For photo-activation of the BPEM units, both wavelength ranges are equally useful.³⁴

3.2 Synthesis of UV-crosslinkable copolymers

The BPEM monomer was used as a comonomer in free radical copolymerization with 2-(2-methoxyethoxy) ethyl methacrylate (MEO₂MA) and oligo(ethylene glycol) methylether methacrylate (OEGMA, $M_n = 475$ g mol⁻¹). The content of incorporated benzophenone moieties in the copolymer was calculated by ¹H-NMR spectroscopy. The integrated signals in the aromatic range from 7.0 ppm to 7.9 ppm (m, 9H of aromatic group) were compared to the integrated signals of the methylene protons at the α -position to the ester group at 4.0 ppm (broad signal, 2H). Keeping in mind the effective accuracy of quantitative NMR spectroscopy, the calculated benzophenone content and the feed ratio, within the precision range of the method, are the same.

Binary copolymers of photoreactive BPEM with MEO₂MA and ternary copolymers of BPEM, MEO₂MA and moderate fractions of OEGMA are thermosensitive in aqueous media, showing a lower critical solution temperature (LCST) type transition. The cloud point of these copolymers can be easily adjusted by varying the comonomer composition.³⁵ In contrast, binary copolymers of BPEM with OEGMA did not show thermoresponsive behaviour (cloud point beyond 90 °C). Cloud points of the different copolymers can be taken from Table 1. Characteristically, the cloud points of such ternary copolymers are

markedly lower than those of analogous binary copolymers of the same MEO_2MA : OEGMA ratio without BPEM,¹⁵ even if only small amounts of benzophenone comonomer are incorporated. For example, the cloud point of tercopolymer T-5 containing 1 mol% of BPEM is about 8 °C lower than that of the binary copolymer of the same MEO_2MA -OEGMA composition. For copolymer T-2 containing 0.5 mol% of BPEM, the cloud point still is lowered by 2 °C compared to the equivalent copolymer containing no BPEM. This is explained by the hydrophobic character of the benzophenone moiety, decreasing the cloud point of the ternary copolymers. In order to maintain a specific phase transition temperature, this effect can be easily counterbalanced by adjustment of the comonomer ratio, *i.e.* by incorporating more OEGMA into the copolymer.

3.3 Characterisation of the hydrogel layers

For immobilisation of the copolymers onto silica substrates, silica wafers were treated with (3-aminopropyl) dimethylethoxysilane. This pre-treatment provides organic groups, which can react with the benzophenone moieties upon UV-irradiation, ensuring the covalent immobilisation of the polymer onto the surface.27 The pre-treated silica wafers were spin-coated with different copolymers. Film thicknesses from 10 nm to nearly 1 µm are accessible with this technique. The thickness of the layers is adjusted by the choice of the copolymer concentration and the spinning speed. The best results regarding homogeneity of the films were obtained with ethyl acetate as a solvent for coating. Other solvents such as toluene, THF, chloroform, ethanol or water did either lead to inhomogeneous layers, or were only useful for layers thinner than 100 nm. As the final layer thickness after rinsing is affected by the molar mass of the copolymers used, the formation of a given thickness requires slightly different spin-coating conditions for different molar mass analogues of the same copolymer. Higher

Table 1 Characterization of the copolymers synthesised by free radical polymerization									
Polymer	OEGMA/ MEO ₂ MA in the feed	BPEM in the feed (mol%)	BPEM incorporated into the copolymer ^a (mol%)	$M_n^{\ b}$ (kg mol ⁻¹)	DP_n^c	BPEM units per polymer chain ^d	Cloud point ^e (°C)	Turbidity transition midpoint (°C)	Expected transition for analogous OEGMA/ MEO ₂ MA copolymers ^f (°C)
POEGMA	100:0	0	0	79	166	0	_	_	<100
B-1	100:0	0.1	0.1	138	291	0.3	_	_	<100
B-2a	100:0	0.25	0.26	91	192	0.5	_	_	<100
B-2b	100:0	0.25	0.25	292	615	1.5	_	_	<100
B-3a	100:0	0.5	0.5	80	169	0.9	_	_	<100
B-3b	100:0	0.5	0.8	350	738	3.7	_	_	<100
B-4	100:0	1.0	1.3	49	104	1.0	_	_	<100
T-1	0:100	0.5	0.7	125	664	3.3	24.8	25.7	28.0
T-2	10:90	0.5	0.6	84	385	1.9	35.5	36.1	38.4
T-3	21:79	0.5	0.7	130	529	2.6	49.2	50.8	49.8
T-4	33:67	0.5	0.7	147	536	2.7	56.6	57.9	62.3
T-5	3:97	1.0	1.0	68	344	3.4	22.3	23.1	31.0
PNIPAM-x	NIPAM	0.5	0.5	23	201	1.0	32.0	33.2	_

^{*a*} Determined by ¹H-NMR spectroscopy. ^{*b*} Apparent number average molecular weight M_n determined by SEC in DMF, calibrated by polystyrene. ^{*c*} Calculated from SEC results and monomer feed. ^{*d*} Average number calculated from NMR and SEC results. ^{*e*} Onset of turbidity. ^{*f*} The midpoint of turbidity transition of equivalent binary copolymers with the same MEO₂MA/OEGMA ratio but without BPEM, according to ref. 15. molar masses require lower polymer concentrations. As a film thickness of 100 nm was targeted, according to the molar mass of the copolymer, a copolymer concentration of 1 wt% in ethyl acetate was used for high molar mass compounds B3-b and B2-b and a copolymer concentration of 2 wt% in ethyl acetate was used for all other lower molar mass compounds. The spinspeed for every copolymer solution was 50 rotations per second.

The thicknesses of the silane monolayer and the spin-cast copolymer layer were determined by ellipsometry, assuming a refractive index of 1.48 for both compounds (the refractive index for bulk POEGMA was determined as $n_{\rm D}$ (ref. 20) = 1.480). All spin-coated layers showed a specific interference colour. As the refractive index of POEGMA is quite similar to that of silicon dioxide (silicon dioxide $n_{\rm D}$ (ref. 20) = 1.458 and POEGMA $n_{\rm D}$ (ref. 20) = 1.480), the interference colours of layers of the same thickness for both materials should match well. Thus with the help of a colour chart for thermally grown silicon dioxide, the colour of the coated copolymer layer could be attributed to a certain thickness.^{36,37} The thickness values determined by ellipsometric measurements were in good agreement with thicknesses estimated with the colour chart for SiO₂ coatings.

3.4 Kinetics of UV-crosslinking

The photoreaction of the benzophenone moiety is monitored *via* UV-spectroscopy after spin-coating a thin copolymer film onto a quartz window. In order to get a sufficiently high absorbance value, the layer thickness was chosen to be relatively thick (900 nm as determined by a profilometer). The absorbance maximum at 287 nm was measured for the coated windows irradiated with UV-A radiation for distinct time intervals (see Fig. 2b). With ongoing photoreaction, the absorbance band decreases gradually. Under the given conditions, the half life time of the benzophenone moiety is found to be in the range of 1 min by UV/Vis spectroscopy. The reaction is almost complete after 10 min, and the residual absorption reaches a plateau value. Accordingly, samples were irradiated for 15 min to ensure maximum conversion of the photoreactive groups in the experiments.

3.5 Stability of the crosslinked layers

Highly swollen hydrogel systems are desirable in some bioapplications. In such systems, the high liquid content imitates conditions close to the ones in biological fluids. Furthermore, the higher mesh size enables effective diffusion of small and medium sized biological compounds, like proteins, inside the network structure. The use of oligo(ethylene glycol)-based copolymers in this context seems to be quite suitable, as they are known to suppress unspecific interactions and thus prevent fouling.

According to Flory–Rehner theory,³⁸ swelling is inversely proportional to the crosslinker content. Thus for highly swollen systems, a low crosslinker content is desirable. Still an infinite reduction of the crosslinker content is not feasible, as it is limited by the practical preparation of a stable network structure. In order to achieve a maximum swelling, we thus tested the stability of crosslinked hydrogel layers with the minimized crosslinker content.



Fig. 3 Stability of the UV-cured hydrogel layers against washing/extraction: remaining layer thickness on silicon substrates after washing – (a) remaining layer thickness for different benzophenone contents in the copolymer, and (b) comparison of the remaining layer thickness for copolymers of different molar masses and benzophenone contents. Striped grey bars: lower molar mass copolymers ($M_n = 50-140$ kg mol⁻¹, copolymers B-1, B-2a, B-3a, and B-4), checkered white bars: higher molar mass copolymers ($M_n = 290-350$ kg mol⁻¹, copolymers B-2b and B-3b).

For stability tests, the copolymers were crosslinked and immobilized by exposing the samples to UV-A radiation for 15 min. The unbound copolymer was then rinsed off, and remaining traces were removed by washing in water overnight. The thusleached hydrogel layer showed resistance to phosphate buffer saline solution (PBS) with a pH of 7.4 and to various organic solvents, such as chloroform, ethyl acetate and ethanol. When immersed in these liquids for 1 week, the thicknesses of the polymer layers remained constant. The extent of the elutriated sol fraction was strongly related to the molar fraction of the crosslinker in the copolymer (see Fig. 3a, binary copolymers B-1 to B-4). While the main part of spin-coated copolymer B-4 with 1 mol% of crosslinking benzophenone groups was robustly immobilized onto the surface (85% layer thickness after washing), most of the spin-coated copolymer B-1 containing just 0.1% crosslinker was washed away despite the UV-crosslinking step: only 32% layer thickness remained after all washing steps. This finding is easily rationalised. Every polymer chain has to be connected to other

chains by at least two crosslinking points for creating a stable network. For a stable binding of a single copolymer chain to the network, at least one connection per chain is necessary. For benzophenone bearing copolymers, Hayward et al. investigated the possible reaction routes towards these crosslinks.²⁵ After UV activation, benzophenone moieties abstract one hydrogen from adjacent polymer chains and thus create two radicals, one at the benzophenone site and one at the activated carbon. They found that recombination of the benzophenone radical with the radical on the polymer chain is the most probable reaction. Thus, every benzophenone moiety can create one link at best. Consequently, the absolute minimum for a completely interconnected system is one benzophenone unit per polymer chain. Obviously in copolymers B-1, B-2a and B-3a the number of BPEM units per chain is below this critical value. Thus, not all copolymer chains can be immobilized, and the stability of the spin-coated layers decreases with decreasing content of benzophenone moieties. Though copolymer B-4 on average bears one benzophenone unit per copolymer chain, not all polymer chains may in fact contain a benzophenone moiety due to a statistical distribution of the benzophenone in the copolymer chains. Moreover, due to loop formation, not every activated BPEM unit may contribute to crosslinking. Consequently also in copolymer B-4 not every polymer chain is covalently connected to the hydrogel. For a given crosslinker content, more stable layers can be assembled with copolymers of an elevated molar mass. Longer polymer chains contain more BPEM units than copolymers of lower molar mass, and hence, crosslinking and immobilisation onto the substrate is more efficient. The highly effective crosslinking for higher molar mass copolymers is readily demonstrated by the behaviour of the pure copolymer in solution. When exposed to daylight, the higher weight copolymers rapidly gelled and could not be dissolved any more, whereas the lower molar mass copolymers tolerated brief contact with daylight.

Hydrogel layers built of copolymers with different molar masses also differ in their stability (see Fig. 3b, copolymers B-2b and B-3b). In copolymer B-2a with a molar mass of 90 kg mol⁻¹ containing 0.25 mol% benzophenone comonomer, a polymer chain only contains 0.5 benzophenone units on average; therefore, it is not surprising that almost 50% of the layer thickness is washed away in the rinsing procedure. In a copolymer with a higher molar mass of 300 kg mol⁻¹ and the same benzophenone content (B-2b), every copolymer chain contains 1.5 benzophenone units per chain. The photo-crosslinked layer is thus more stable. Indeed about 80% of the originally deposited material remains immobilized onto the substrate after rinsing. Copolymers with a higher benzophenone content of 0.5 mol% generate even more stable networks. Here, the higher molar mass copolymer B-3b contains 3.7 benzophenone units per chain on average. This polymer remains on the substrate almost completely after rinsing, whereas films made of copolymers B-3a with the same crosslinker content but a lower molar mass of around 80 kg mol⁻¹ still lose about 30% of the original layer thickness upon rinsing. These findings highlight the importance of using high molar mass compounds, when stable coatings with low crosslinking density are desired.



Fig. 4 Swelling ratios SR determined by ellipsometric measurements under water. Crosslinked films of binary copolymers with different BPEM contents are examined (B-1, B-2a, B-3a, and B-4).

3.6 Swelling behaviour of the hydrogel layers at room temperature

The thickness and the refractive index of the swollen hydrogel films in pure water were determined by ellipsometry in a flow cell (Fig. 4). The optical values of water as surrounding medium were considered for the calculation of the swollen film. The refractive index of the swollen layers determined by ellipsometry was in a range between 1.345 and 1.355. Since water is the main constituent of the hydrogel in the swollen state, its refractive index is near the value of pure water (which is 1.332).

In theory, it is possible to determine the volume fraction of the copolymer in the swollen hydrogel layer and thus the swelling ratio from the mixed refractive index of the layer, since the refractive indices of the pure copolymer and pure water are known.³⁹ However, in highly swollen systems even small deviations in the measured refractive index result in large variations in the swelling ratio. Thus, we determined the swelling ratio exclusively from the thickness in the swollen and in the dry state. As the film may only swell in one dimension, the swelling ratio SR can be calculated from the thicknesses according to

$$SR = d_{swollen}/d_{dry}$$

in which d_{swollen} is the equilibrium layer thickness of the swollen hydrogel layer under water at a given temperature and d_{drv} is the dry layer thickness.

We investigated first the swelling behaviour of binary oligo(ethylene glycol methacrylate) copolymers with different molar fractions of BPEM. Copolymers of this kind are soluble in water at temperatures from 0–100 °C. The layer thicknesses determined under water were considerably higher than the dry layer thicknesses. The swelling ratio SR of these swollen hydrogels was inversely proportional to the BPEM content, as expected.³⁸ When decreasing the BPEM ratio from 1% to 0.1%, the swelling ratio increased by a factor of 4.5 (see Fig. 4). Therefore, the volume fraction of water in the swollen hydrogel can be easily adjusted in a wide range *via* the molar fraction of benzophenone units, incorporated into the copolymer.

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Fig. 5 Thermo-responsive collapse of a film formed from T-2, followed by ellipsometry. Filled squares (\blacksquare) refer to the layer thickness and open triangles (Δ) refer to the refractive index.

3.7 Thermo-responsive hydrogel layers

The thermal behaviour of thermo-responsive hydrogel layers was studied by temperature dependent ellipsometric measurements. To exclude systematic errors caused by temperature effects, a control experiment was performed first: a blank silicon wafer with an oxide layer of the known thickness was mounted in the flow cell and the optical values were determined to be in the range from 20 to 60 °C. In the whole temperature range, values for Δ and Ψ did not change more than 0.8° and 0.2° , respectively. For the considered hydrogel layers, the addition of these \varDelta and Ψ values to the determined layer thickness at elevated temperature would result in a slight overestimation of the layer thickness (i.e. 4 nm for an 88 nm thick layer). However, this uncertainty has only a minor influence on the thickness values and would, if at all, counteract the observed extent of shrinking of the layer caused by the phase transition. In the following, this baseline effect is therefore neglected.

The temperature induced deswelling of a layer of the thermoresponsive hydrogel is shown in Fig. 5. Upon heating, the thickness of the hydrogel layer decreases markedly, while simultaneously the refractive index increases. Similar to the hydrogel layers that do not exhibit thermoresponsivity, the refractive index of the highly swollen hydrogel is close to the refractive index of pure water. During the phase transition, more and more water is expelled from the hydrogel network.

Thus the volume fraction of organic polymer in the hydrogel gets larger, and the averaged refractive index approaches the value of the pure polymer of approximately 1.48. At temperatures below the onset of the collapse, the layer thickness seems to increase by about 10%. As in this temperature range, the difference between the refractive index of the aqueous medium and of the hydrogel layer is low, the observed differences however may be still within the experimental precision and therefore cannot be considered significant.

The thermal transition of the oligo(ethylene glycol)-based films is rather broad and covers a temperature range of about 20 °C. This finding is in agreement with a report on the same copolymer system immobilised in a brush architecture, as



Fig. 6 Thermo-responsive collapse of various copolymers in water. Filled symbols: swelling ratios SR of crosslinked copolymer films in water determined by ellipsometry; and open symbols: turbidity measurements of copolymers in aqueous solution. (a) Ternary copolymers of MEO₂MA, OEGMA and BPEM. Upside triangles (\blacktriangle , Δ) for copolymer T-4, circles (\blacklozenge , \bigcirc) for copolymer T-3, and downside triangles (\blacktriangledown , ∇) for copolymer T-1. (b) Swelling ratios SR (\blacksquare) and turbidity (\square) of the binary copolymer PNIPAM-*x* (NIPAM and BPEM).

analysed by a quartz crystal microbalance (QCM).¹⁷ To verify whether the broad transition is indeed a characteristic feature of the oligo(ethylene glycol)-based copolymers, we synthesised an analogous PNIPAM copolymer also bearing the benzophenone unit. The ellipsometric data of the photocrosslinked PNIPAM were collected and mathematically treated in the same way as the data of the oligo(ethylene glycol)-based films. In contrast to the OEG containing films, the PNIPAM films show a sharp thermal transition (Fig. 6b). Similar results have already been reported for the comparison of thin films made of poly-(diethyl acrylamide) (PDEAAm) and PNIPAM.⁴⁰ Schmaljohann *et al.* attributed the gradual transition in the PDEAAm-films to different hydrogen bonding properties of PDEAAm compared to PNIPAM.

Similar to PDEAAm-copolymers, OEG-based copolymers can only act as hydrogen bond acceptors, whereas PNIPAM additionally acts as a hydrogen bond donor. Increased intra- and interchain interactions may thus sharpen the transition for PNIPAM, while OEG-based copolymers in accordance with this explanation show a gradual transition.^{41,42} In fact, physically crosslinked thin polymer films of hydrophobically end-capped PNIPAM have been shown by GISAXS experiments to undergo a



Fig. 7 Switching cycles of a thermo-responsive copolymer film prepared from T-1.

much narrower thermal transition in a water-saturated atmosphere in comparison to thin films of analogously designed polymers, which have a short oligo(ethylene glycol)methylether side chain, namely poly(methoxy diethylene glycol acrylate).^{42–44} Even if the chemical structures of our polymer hydrogel films differ from these examples in various variables, and our study has been done in contact with liquid water, the observed distinctions between PNIPAM and OEG-side chain polymers during the thermal transition suggest a general pattern.

The different hydrogen bonding interactions of PNIPAM are also held responsible for the observed hysteresis between the phase transition in heating and cooling cycles in PNIPAM-based polymers. In contrast, OEG-based polymers virtually do not exhibit a hysteresis.^{15,45,46} In accordance with this observation for the linear polymers in solution, all investigated films formed from OEG copolymers did not reveal any notable differences in heating and cooling cycles. Even after multiple switching cycles the films swelling ratio did not change (see Fig. 7).

For some applications this quality and a more gradual transition could be favourable over a sharp transition. For instance a slower transition potentially could favour a rapid transport of water out of the hydrogel, as skin formation at the film surface is reduced. Moreover, a more gradual change may be advantageous for different sensing applications as here often a quantitative statement is preferred to a simple yes/no signal. In any case, our results demonstrate that the precise chemical structure of thermo-responsive hydrogels has more implications than simply defining the transition temperature.

A special interest in the use of oligo(ethylene glycol) based copolymers lies in the easy tunability of the phase transition temperature. Hence we also verified that the temperature response of the prepared films can be adjusted to certain temperatures. We therefore prepared films of different comonomer compositions (copolymers T-1, T-3 and T-4) and followed the phase transition by temperature dependent ellipsometric measurements. Fig. 6a illustrates the transition curves for copolymers with different ratios of longer oligo(ethylene glycol) side chains. The higher the OEGMA content, the higher the phase transition temperatures. Likewise, the swellability of the hydrogel film is enhanced with increasing OEGMA content. This finding is well consistent with similar investigations for these types of bulk hydrogels.47 Looking at the shape of the transition curve, it is obvious that the collapse neither follows a sigmoidal curve, as is typical for cloud point measurements of polymer solutions, nor a steady decrease. For copolymers with higher OEGMA contents of 21% and 33%, the transition curve can be separated into two distinct ranges. At temperatures below the transition temperature, the hydrogel gradually repels water from the network, whereas above a specific temperature, a steeper decrease of the water content is visible. The corresponding onset temperature increases with the OEGMA content: for the film made of T-3, it is in the range of 30 °C, whereas for the film made of T-4, it is around 40 °C. The steeper decay is attributed to the thermo-responsive collapse of the hydrogel film. Consistent with this observation, a minor decrease in swellability was also found for a film of pure OEGMA polymer B-3a. Upon heating from 20 °C to 60 °C, the swelling degree drops from 5.9 to 5.6. This is putatively attributed to the degeneration of solvent quality for oligo(ethylene glycol)s in water with temperature.48 Still, the hydrogel film remains highly hydrated even at high temperatures.

For the thermo-responsive copolymer films, the phase transition temperatures are qualitatively comparable to those of the copolymers in solution. However, the onset temperature for the transition is shifted towards lower temperatures. Possibly this is due to the higher copolymer concentration in the hydrogel as the transition temperature depends notably on the weight fraction of the copolymer in water.⁴¹ Yet, for a given weight fraction the transition temperature is easily adjustable by the copolymer composition, so that thin polymer hydrogel films of any desired transition temperature can be prepared.

4 Conclusions

Oligo(ethylene glycol) copolymers bearing benzophenone units provide an easy and versatile access to biocompatible polymer coatings on organic surfaces. We demonstrate that applicationrelevant film parameters, such as thickness, crosslinking density, swelling and phase transition behaviour can be adjusted at will, by appropriate choice of copolymer composition, crosslinker content, molar mass of the parent polymers and spin coating conditions. Compared to the frequently used thin films of PNI-PAM, the thermally induced swelling-deswelling transition is broadened, but shows no hysteresis. Thus, the new photoreactive oligo(ethylene glycol) copolymers represent an interesting basis for coatings with potential application in the bio-medical field.

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Notes and references

- 1 J.-F. Lutz and H. G. Börner, Prog. Polym. Sci., 2008, 33, 1-39.
- 2 J. M. Harris, *Poly(ethylene Glycol) Chemistry: Biotechnical and Biomedical Applications*, Plenum Press, New York, USA, 1992.
- 3 H. Ma, M. Wells, T. P. Beebe and A. Chilkoti, *Adv. Funct. Mater.*, 2006, **16**, 640–648.
- 4 D. Sung, S. Park and S. Jon, Langmuir, 2009, 25, 11289-11294.
- 5 G. R. Hendrickson and L. A. Lyon, Soft Matter, 2009, 5, 29-35.
- 6 A. Hucknall, S. Rangarajan and A. Chilkoti, *Adv. Mater.*, 2009, **21**, 2441–2446.
- 7 J. Trmcic-Cvitas, E. Hasan, M. Ramstedt, X. Li, M. A. Cooper, C. Abell, W. T. S. Huck and J. E. Gautrot, *Biomacromolecules*, 2009, **10**, 2885–2894.
- 8 I. Tokarev and S. Minko, Soft Matter, 2009, 5, 511-524.
- 9 C. Pietsch, R. Hoogenboom and U. S. Schubert, Angew. Chem., Int. Ed., 2009, 48, 5653-5656.
- 10 E. Wischerhoff, K. Uhlig, A. Lankenau, H. Börner, A. Laschewsky, C. Duschl and J.-F. Lutz, *Angew. Chem., Int. Ed.*, 2008, 47, 5666–5668.
- 11 J. E. Gautrot, B. Trappmann, F. Oceguera-Yanez, J. Connelly, X. He, F. M. Watt and W. T. S. Huck, *Biomaterials*, 2010, 31, 5030–5041.
- 12 E. Wischerhoff, N. Badi, J.-F. Lutz and A. Laschewsky, *Soft Matter*, 2010, **6**, 705–713.
- 13 J. Buller, A. Laschewsky, J.-F. Lutz and E. Wischerhoff, *Polym. Chem.*, 2011, 3, 352–361.
- 14 J. F. Lutz, O. Akdemir and A. Hoth, J. Am. Chem. Soc., 2006, 128, 13046–13047.
- 15 J. F. Lutz and A. Hoth, Macromolecules, 2006, 39, 893-896.
- 16 C. Weber, R. Hoogenboom and U. S. Schubert, *Prog. Polym. Sci.*, 2012, **37**, 686–714.
- 17 X. Laloyaux, B. Mathy, B. Nysten and A. M. Jonas, *Langmuir*, 2010, **26**, 838–847.
- A. Synytska, E. Svetushkina, N. Puretskiy, G. Stoychev,
 S. Berger, L. Ionov, C. Bellmann, K.-J. Eichhorn and
 M. Stamm, *Soft Matter*, 2010, 6, 5907–5914.
- 19 H. Kitano, T. Kondo, H. Suzuki and K. Ohno, *J. Colloid Interface Sci.*, 2010, 345, 325–331.
- 20 S. Tocker, US Patent 3062784, 1963.
- 21 O. Prucker, C. A. Naumann, J. Rühe, W. Knoll and C. W. Frank, *J. Am. Chem. Soc.*, 1999, **121**, 8766–8770.
- 22 N. Griep-Raming, M. Karger and H. Menzel, *Langmuir*, 2004, 20, 11811–11814.
- 23 R. Toomey, D. Freidank and J. Rühe, *Macromolecules*, 2004, 37, 882–887.
- 24 M. E. Nash, W. M. Carroll, P. J. Foley, G. Maguire, C. O. Connell, A. V. Gorelov, S. Beloshapkin and Y. A. Rochev, *Soft Matter*, 2012, 8, 3889–3899.
- 25 S. K. Christensen, M. C. Chiappelli and R. C. Hayward, Macromolecules, 2012, 45, 5237–5246.
- 26 J. W. McGinity, T. R. Patel, A. H. Naqvi and J. A. Hill, Drug Dev. Ind. Pharm., 1976, 2, 505–519.

- 27 G. Dorman and G. D. Prestwich, *Biochemistry*, 1994, 33, 5661–5673.
- 28 V. Kumar and D. Kalonia, *AAPS PharmSciTech*, 2006, 7, E47–E53.
- 29 D. Ruhlmann, K. Zahouily and J. P. Fouassier, *Eur. Polym. J.*, 1992, 28, 1063–1067.
- 30 A. M. Rufs, A. Valdebenito, M. C. Rezende, S. Bertolotti,
 C. Previtali and M. V. Encinas, *Polymer*, 2008, 49, 3671–3676.
- 31 P. Hrdlovič, I. Lukáč and I. Zvara, *Eur. Polym. J.*, 1981, **17**, 1121–1126.
- 32 J. Weiss, A. Li, E. Wischerhoff and A. Laschewsky, *Polym. Chem.*, 2012, **3**, 352–361.
- 33 H. G. Tompkins and W. A. McGahan, Spectroscopic Ellipsometry and Reflectometry: A User's Guide, John Wiley & Sons, New York, USA, 1999.
- 34 N. J. Turro, Modern Molecular Photochemistry, University Science Books, Sausalito, USA, 1991.
- 35 J.-F. Lutz, J. Polym. Sci., Part A: Polym. Chem., 2008, 46, 3459– 3470.
- 36 W. A. Pliskin and E. E. Conrad, *IBM J. Res. Dev.*, 1964, **8**, 43–51.
- 37 S. Franssila, in *Introduction to Microfabrication*, John Wiley & Sons, Ltd, New York, USA, 2010, pp. 503–504.
- 38 P. J. Flory and J. Rehner, J. Chem. Phys., 1943, 11, 521-527.
- 39 M. Born and E. Wolf, Principles of Optics: Electromagnetic Theory of Propagation, Interference and Diffraction of Light, Cambridge University Press, Cambridge, UK, 2011.
- 40 D. Schmaljohann, D. Beyerlein, M. Nitschke and C. Werner, *Langmuir*, 2004, **20**, 10107–10114.
- 41 V. Aseyev, H. Tenhu and F. Winnik, *Adv. Polym. Sci.*, 2011, 242, 29–89.
- 42 Q. Zhong, E. Metwalli, G. Kaune, M. Rawolle, A. M. Bivigou-Koumba, A. Laschewsky, C. M. Papadakis, R. Cubitt and P. Müller-Buschbaum, *Soft Matter*, 2012, 8, 5241–5249.
- 43 W. Wang, K. Troll, G. Kaune, E. Metwalli, M. Ruderer, K. Skrabania, A. Laschewsky, S. V. Roth, C. M. Papadakis and P. Müller-Buschbaum, *Macromolecules*, 2008, **41**, 3209– 3218.
- 44 Q. Zhong, W. Wang, J. Adelsberger, A. Golosova,
 A. M. B. Koumba, A. Laschewsky, S. S. Funari, J. Perlich,
 S. V. Roth, C. M. Papadakis and P. Müller-Buschbaum, *Colloid Polym. Sci.*, 2011, 289, 569–581.
- 45 Ö. Akdemir, N. Badi, S. Pfeifer, Z. Zarafshani, A. Laschewsky,
 E. Wischerhoff and J.-F. Lutz, ACS Symp. Ser., 2009, 1023, 189–202.
- 46 A. Miasnikova and A. Laschewsky, J. Polym. Sci., Part A: Polym. Chem., 2012, 50, 3313-3323.
- 47 R. París and I. Quijada-Garrido, *Eur. Polym. J.*, 2009, 45, 3418–3425.
- 48 E. A. Bekturov and Z. K. Bakauova, *Synthetic Water-Soluble Polymers in Solution*, Hüthig & Wepf, Basel, Switzerland, 1986.