Temperature-Triggered Modification of Polymer-Solvent Interactions: From Fluid-to-Gel Transitions to Particle Capture

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Summary: Temperature-responsive polymers are of considerable interest in the literature. In this work the ability to combine temperature-responsive polymer-solvent interactions with architectural control to achieve a range of macroscopic effects is considered. The first part of the work considers poly(DEA) (*N,N*-dieth ylacrylamide) microgel particles. The particles exhibit temperature-triggered particle collapse at temperatures more than ca. 27 °C. As a consequence concentrated temperature-responsive microgel dispersions change from gels to fluids when heated. The opposite effect is observed when dispersions or emulsions are stabilised by temperature-responsive polymer surfactants. Recent results involving a gel-forming castor oil-in-water emulsion are considered. The gelled emulsion releases a model drug (lidocaine) according to first-order kinetics. We extend the principle of temperature-triggered control of particle-surface interactions to test a new approach for immobilising particles on surfaces. The method consists of electrodepositing Laponite particles onto a carbon surface, grafting of poly(NIPAM) (*N*-isopropylacrylamide) onto the deposited particles and then increasing the temperature of the modified surface to trigger capture of dispersed polystyrene particles. This new approach uses chemistry that is potentially applicable to any conductive surface.

Keywords: microgel; poly(diethylacrylamide); poly(NIPAM); polymer surfactant; polymer-solvent interactions; responsive emulsion

Introduction

Poly(NIPAM) (N-isopropylacrylamide) is one of the most widely studied members of polymers that are temperature-responsive.[1-4] Temperature-responsive polymers exhibit major conformational changes in response to changes in the balance between hydrogen bonding of the segments with water and segment-segment interactions. At temperatures greater than the lower critical solution temperature (LCST) attractive segment-segment interactions dominate causing chain collapse.[1] This temperature-triggered disruption of attractive polymer-water interactions results in large- scale, macroscopic changes for polymer solutions or hydrogels.

An important area of responsive polymer research involves controlling macroscopic behaviour through polymer architecture. There are a range of possible architectures. Microgels are cross-linked polymer particles that swell in a good solvent.[5] In these systems the responsive polymer is present throughout the particle. Poly(NIPAM) microgels exhibit a temperature-triggered decrease in particle size.[4] Particle contraction decreases the effective volume fraction of the microgel phase, which in turn lowers the viscosity.

An emerging area of research activity concerns using responsive polymer surfactants to confer responsiveness to otherwise

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non-responsive dispersions. Oil droplets containing adsorbed poly(NIPAM)-based temperature-responsive emulsions have been investigated.[6,7] Those dispersions show temperature-triggered gel formation. This behaviour has been shown to originate from the particles, as the parent polymer solutions do not exhibit gelation. The dispersed particle ‘‘interact’’ with the continuous phase via an adsorbed layer of polymer. A recent small-angle neutron scattering study suggested that polymer chains at the surface become adhesive-like and increase the extent of interparticle bridging. The same temperature-triggered gelation behaviour was also observed for dispersions of polymer particles.[8]

In this paper we present recent results from our group which illustrate the differing temperature-responsive behaviours that can be obtained from responsive polymers.

Experimental Part

Poly(DEA) microgel particles were prepared using surfactant-free emulsion polymerisation in water at 70 °C. The cross-linking monomer used was BA (N, N′-methylene bisacrylamide). The method used for synthesis has been described in detail elsewhere.[9] The microgels were prepared using 1 wt.% BA based on the total monomer mass employed. The microgel particles contained carboxylate groups from the initiator residues. The product was purified by extensive dialysis using water.

The emulsions were prepared by mixing castor oil with aqueous poly(NIPAM-*co*-PEGMa) solution (3.5 wt.%) followed by high-speed shearing at 9,400 rpm for 5 min using a Silverson L4R mixer. The synthesis of poly(NIPAM-*co*-PEGMa) is described elsewhere.[7] (PEGMa is poly(ethyleneglycol) methacrylate with $M_n = 360$ g mol^{-1}.) The volume fraction of castor oil was 0.30 unless otherwise stated. Controlled release measurements were conducted using emulsions contained within 12 kD molar mass cut off dialysis tube.

Particle capture experiments used a surface of poly(NIPAM) prepared using surface-initiated atom transfer radical polymerisation (ATRP). The synthetic method used to prepare the ATRP initiator is described elsewhere.[10] The conductive surface that was modified in this work was high surface area carbon foam. Laponite was electrodeposited onto the anode of the electrochemical cell (Figure 1) using a μAutolab potentiostat. No applied potential was used during the subsequent ATRP

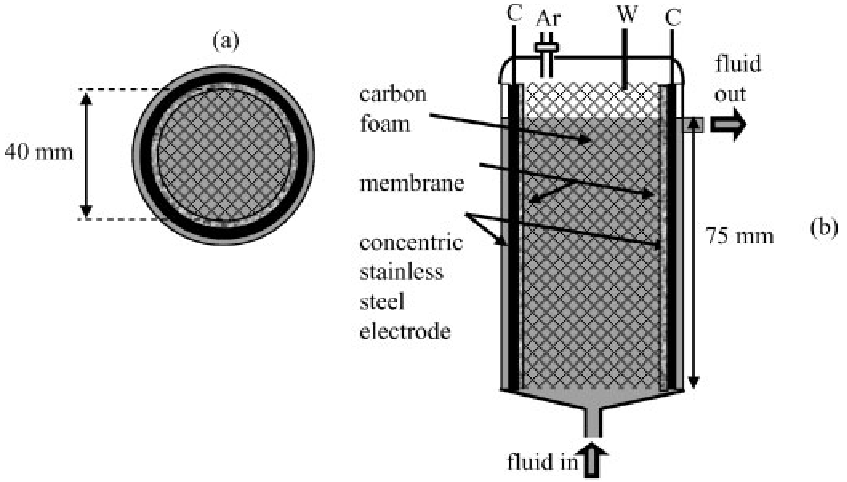


Figure 1.

Diagram showing (a) cross-section and (b) side view of the electrochemical cell. The connections to the working (W) and counter-electrodes (C) are labelled.

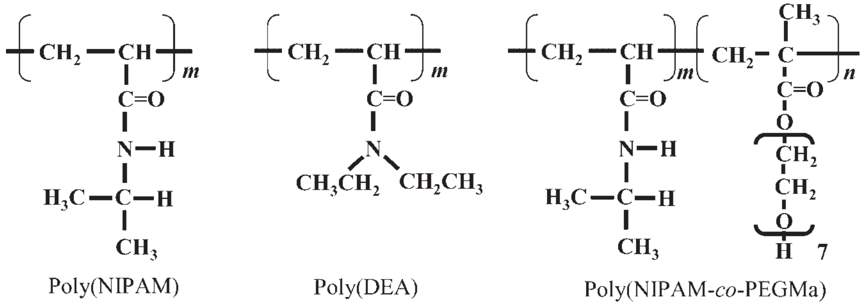


Figure 2.
Structures of the responsive polymers used in this study.

or particle capture stages. Following extensive rinsing of the electrodeposited Laponite, ATRP initiator was added to the cell to give 10^{-3} wt.% The initiator was adsorbed to the electrodeposited Laponite particles over a period of 24 h with constant recirculation. After a rinsing cycle using aqueous 1 mM $NaNO_3$, surface-initiated ATRP was conducted. (Scheme I – see below -shows the method.) The ATRP solution was re-circulated during the process. The electrochemical cell (Figure 1) was immersed in a temperature-controlled water bath during particle capture experiments. Polystyrene latex was used for these experiments with an average particle size of 500 nm.

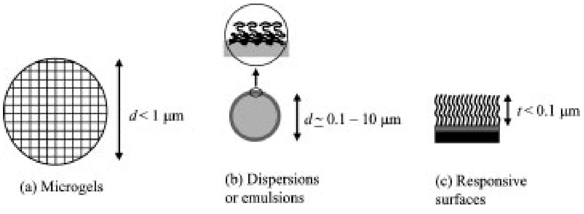
Results and Discussion

Figure 2 shows the structures of the three polymers used for this work. The substitution of hydrophobic groups on the amide groups confers temperature-responsiveness. Poly(DEA) (DEA is N,N diethylacrylamide) is more hydrophobic than poly(NIPAM). Poly(NIPAM-*co*-PEGMa) (PEGMa is poly(ethylene glycol) methacrylate) is temperature-responsive polymer surfactant. The poly(NIPAM-*co*-PEGMa) sample used in this work contained 86 mol.% of NIPAM. All of the polymers undergo temperature-triggered disruption of hydrogen bonding of the amide groups with water causing coil-to-globule transitions at the respective LCSTs.

This discussion considers three different structural arrangements of the responsive polymers (Figure 3). Microgel particles contain a responsive polymer network throughout the particles and at the particle surface. Responsive dispersions contain adsorbed, preformed, responsive polymer surfactant at the particle-water interface. Responsive surfaces contain grafted (or tethered) responsive polymer chains grown directly from the surface.

Temperature-Responsive Microgels

Figure 4 shows poly(DEA) microgel particles prepared using 1 wt.% of BA. The larger entities are due to partial coalescence



(a) Microgels
(b) Dispersions or emulsions
(c) Responsive surfaces

Figure 3.
Different geometries for responsive polymer colloids and surfaces.

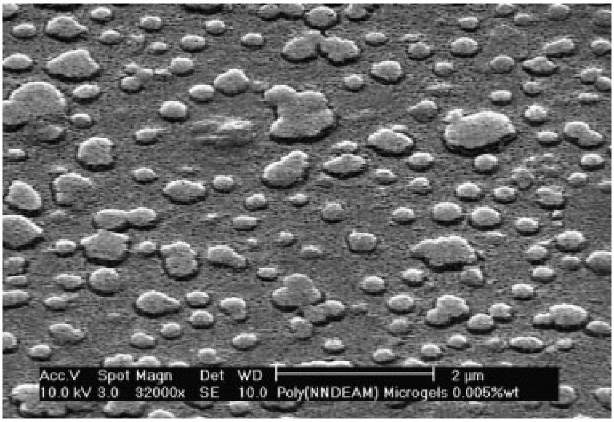


Figure 4.
SEM micrograph of poly(DEAM) microgels.

of neighbouring particles during specimen preparation. Although the glass transition temperature (T_g) for poly(DEA) has not been published to our knowledge, the T_g values for poly(NIPAM), poly(N, N-dimethyacrylamide), and poly(N,N-dibutylacrylamide) have been reported as 85–130, 89 and 60 °C, respectively.[11] It is likely that the T_g for poly(DEA) is lower than that of poly(NIPAM), which would aid film formation. The average size for the isolated poly(DEA) microgel particles is about 230 nm.

Figure 5 shows the variation of the hydrodynamic diameter with temperature for poly(DEA) microgel particles. Data for poly(NIPAM) microgel particles prepared using identical procedure are shown for comparison. In both cases an increase in the temperature causes the particles to undergo triggered particle collapse at the volume phase transition temperature (VPTT). (The VPTT is equivalent to the LCST in terms of the origin of the transition.) The triggered collapse is sharper in the case of the poly(D EA) microgels. The poly(DEA) microgel particles have a VPTT of about 27.5 °C. This is slightly lower than the VPTT for poly(NIPAM) microgels of ca. 32 °C that is apparent from Figure 5.

Poly(DEA) and poly(NIPAM) microgel dispersions have excellent colloidal stability in the swollen state ($T < \text{VPTT}$) due to a combination of three factors. Firstly, the particles contain residual carboxylate groups on the surface (from the initiator) which provide the dispersions with electrostatic stabilisation. Secondly, the particles contain more than about 95% water. This means that they have a very low effective Hamaker constant.[12] Finally, the outer periphery of the particles are believed to contain dangling chains which provide steric stabilisation.

An important consequence of the temperature-triggered particle contraction is that at temperatures greater than the VPTT dispersion stability is reliant on electrostatic stabilisation. (The effective Hamaker constant reaches maximum values and steric stabilisation is lost when $T > \text{VPTT}$.) In the presence of added salt poly(NIPAM) microgel dispersions flocculate.[9] However, in the absence of added salt the dispersions remain colloidally stable. It is important to note that under these circumstances concentrated microgel dispersions (e.g., containing at least 4 wt.% particles) change from gels to fluids at $T > \text{VPTT}$ directly as a result of particle contraction. The particles that were previously sterically trapped in the swollen state become able to move past one another at elevated temperatures. This behaviour

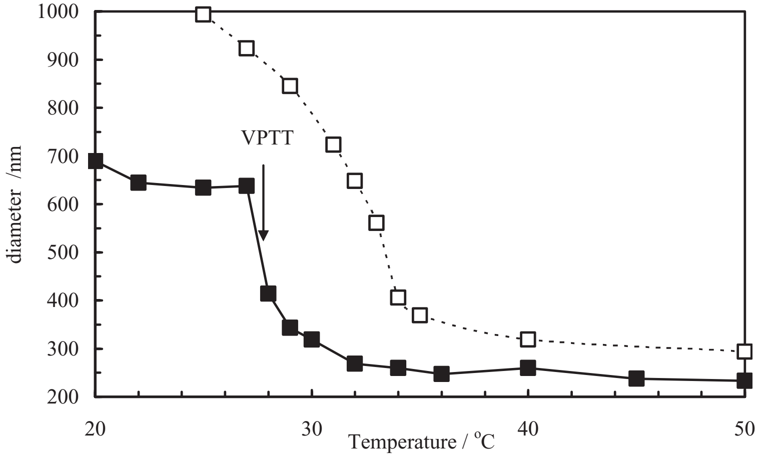


Figure 5.
Variation of hydrodynamic diameter with temperature for poly(DEA) (closed square) and poly(NIPAM) (open square) microgel particles dispersed in water. The curves are a guide for the eye.

contrasts to the temperature-responsive dispersions that are discussed in the next section.

Temperature-Triggered Dispersion Gelation

Figure 6 shows a gelation phase diagram for oil-in-water emulsions prepared in the presence of poly(NIPAM-*co*-PEGMa) (ie., Figure 3(b)). The gelation temperature (T_{gel}) is dependent on the oil phase volume fraction (ϕ_o) at low ϕ_o values. The droplets had a number area mean diameter of 4.2 μm. It is important to note that in the absence of a dispersed phase no gelation occurs at all. This implicates the droplets in the gelation mechanism. We treat the droplets as *interactive fillers*. The gelation mechanism for responsive emulsions has been probed[7] using SANS and involves temperature-triggered collapse of the poly(NIPAM-*co*-PEGMa) chains to form a ‘‘sticky’’ layer around the droplets and adsorption of neighbouring droplets to form a three-dimensional space filling structure. Copolymer from solution also aggregates and acts a ‘‘glue’’ to further bind

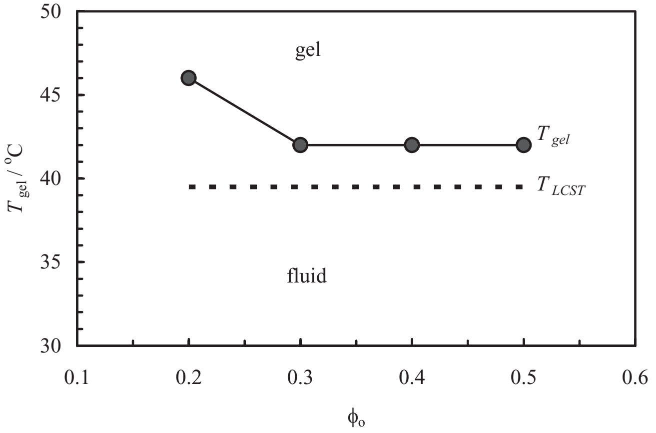


Figure 6.
Variation of emulsion gelation temperature with volume fraction of oil phase. The LCST of the copolymer is also shown for comparison.

the droplets. The T_{gel} values for emulsion gels can be controlled (and even predicted) by varying the copolymer concentration.[13] For the present work we wanted to demonstrate that release could occur from emulsion gels comprising droplets that themselves contained dissolved drug.

The release experiments were performed using a castor oil phase containing Lidocaine. The emulsions were contained within dialysis tubing and heated to below or above T_{gel}. The release data are shown in Figure 7. An analysis of the release data was performed using the following equation.

$$C_o(t) = C_o(0)\exp(-k_{o/w}t) \qquad (1)$$

The initial concentration of solute in the oil phase and that present at time, t, are given by $C_o(0)$ and $C_o(t)$, respectively. This equation was derived using Fick's law of diffusion and a simple geometric model in which the solute (dissolved in the oil phase) was considered to diffuse through a semi-permeable membrane (in this case the dialysis tubing interface) to the external water phase (w_1) via the internal water phase (w_2) of the O/W emulsion. The equation is identical to that for first order kinetics with a rate constant, $k_{o/w}$. The values for $k_{o/w}$ obtained for the emulsion fluid (at 30 °C) and emulsion gel (at 50 °C) were, 0.031 and 0.067 h^{-1}, respectively.

The data prove the concept of temperature-triggered release from gel-forming emulsions. In order to apply this approach more generally to the treatment of disease it would be necessary to replace the polymer with a FDA approved equivalent responsive polymer.

It is important to note that particulate dispersions can also be prepared that are stabilised by poly(NIPAM-*co*-PEGMa). Those dispersions also show temperature-triggered gelation.[8] Addition of ionic surfactant to the dispersions or latexes progressively increases the T_{gel} values in a predictable manner.

Temperature-Triggered Particle Capture

In this part of the discussion we extend the concept of temperature-triggered control of polymer-solvent interactions to modified planar surfaces. ATRP is a powerful method for producing functionalised surfaces. In this work we used surface-initiated ATRP to grow poly(NIPAM) chains from the surface of electrodeposited Laponite particles containing an adsorbed cationic initiator (I) (See Scheme 1). It is well known that tetra-alkyl ammonium cations have a strong affinity for the surfaces of

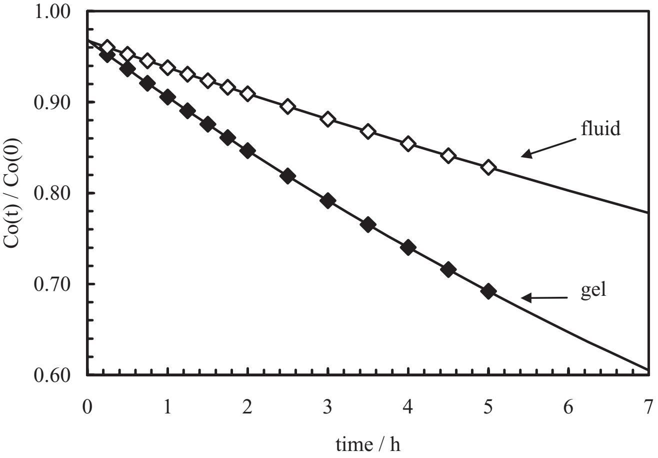
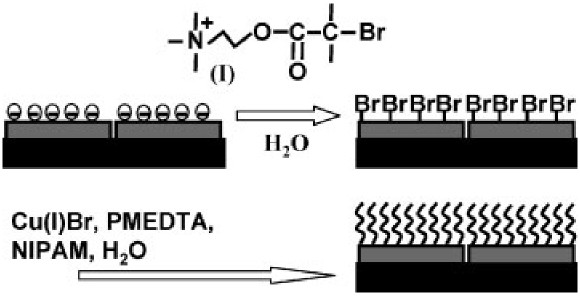


Figure 7.
Variation of fraction of lidocaine present in emulsion droplets as a function of time for an emulsion gel and fluid. The curves are fits using equation (1).



Scheme 1.
Temperature-responsive Laponite-poly(NIPAM) surface prepared using surface-initiated ATRP.

Laponite particles.[14] We combined these benefits to produce a grafting chemistry that is specific only to the clay.

Laponite is a nanometre-sized synthetic lithium magnesium silicate. The primary particles of Laponite RD are platelets with an average diameter and thickness of 20.4 and 1.2 nm, respectively.[15] For this work we selected Laponite RD because it has a strong tendency to exfoliate into primary particles with a fixed negative charge on the particle faces.

The first part of this study involved determining the conditions for achieving monolayer coverage of the carbon foam anode with the Laponite particles.[10] Surface-initiated ATRP of NIPAM was conducted as described elsewhere which yielded a poly(NIPAM) layer that was electrostatically bound to the electrodeposited Laponite particles. Surface-initiated ATRP of NIPAM in the presence of electrodeposited Laponite containing adsorbed (I) resulted in grafted chains as well as solution polymer. The washings were collected and polymer isolated. GPC analysis revealed that solution polymer had a M_n of 59,000 g mol^{-1} (PD = 6.5). The polydispersity is high. The M_n value considered above can be taken as an approximate measure of the molar mass of the grafted chains.

We then used turbidity measurements to determine the concentration of anionic polystyrene latex particles, which were used as a model system for the capture experiments. Figure 8 shows capture data for carbon foam containing Laponite-poly(NIPAM). The data show that the Laponite-poly(NIPAM) surface was able to prevent significant adsorption of the polystyrene particles for the first 24 h at room temperature. It was only once the temperature was increased to above 30 °C that triggered particle capture commenced. It follows that the nature of the interaction between the Laponite-poly(NIPAM) surface and the dispersed polystyrene particles changes from repulsive to attractive at higher temperatures.

The reversibility of particle capture was investigated by cooling the cell to room temperature and followed by another temperature ramp. Only a small fraction of the particles captured during the first heating cycle were released upon cooling and much less pronounced capture was observed during the second heating cycle. We propose that the lack of reversibility observed for this system was due to less than optimum grafted density being present. The effect of ATRP conditions on reversibility of particle capture is being investigated further at Manchester.

Figure 9 shows particle capture data as a function of temperature. The data show the ranges obtained from repeat experiments. Whilst there is significant scatter for these data it is clear that temperature-triggered particle capture becomes significant when the LCST of solution poly(NIPAM) (ca. 32 °C) is passed. The maximum particle

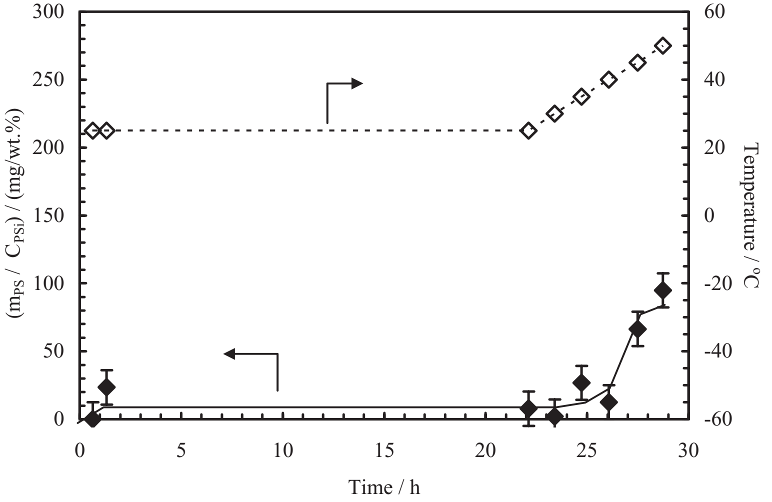


Figure 8.
Mass of polystyrene adsorbed divided by the initial dispersion concentration for a modified carbon electrode during temperature ramping. The lines are guides to the eye.

capture corresponded to a fractional coverage of ca. 0.05.

After a capture experiment the modified anode was rinsed thoroughly with water and then examined using SEM (Figure 10). Temperature-triggered particle capture occurred throughout the electrode. The particles adsorbed as single particles, strings and aggregates. The extent of particle coverage apparent on this electrode is equivalent to ca. 4×10^5 particles/mm^2.

This study has revealed that temperature-triggered particle capture at a modified electrode surface can be achieved using

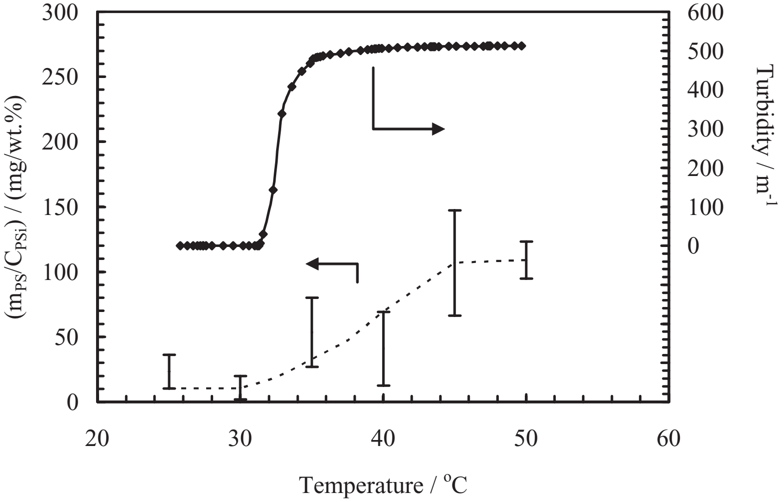


Figure 9.
Variation of the mass polystyrene particles adsorbed divided by the initial dispersion concentration as a function of temperature for modified electrodes. Turbidity data for solution poly(NIPAM) is also shown for comparision.

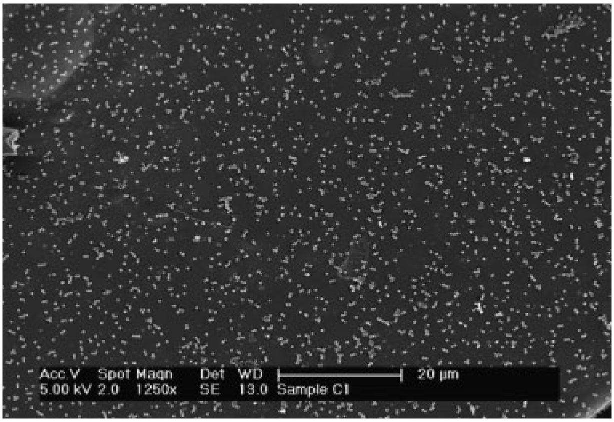


Figure 10.
Scanning electron micrographs of the modified carbon foam surface after triggered adsorption of polystyrene latex particles.

poly(NIPAM) which has been grafted on to electrodeposited Laponite particles. The use of nanometre-sized Laponite particles as a conditioning layer means that the smallest theoretical size of the modified surface is 10 nm. This could open up new opportunities for microarray fabrication or Janus particle construction if reversible capture is achieved and the approach is used in conjunction with localised heating.

Conclusion

Polymer-solvent interactions provide a very useful tool for controlling macroscopic behaviour. When combined with architectural control these interactions enable excellent opportunities for property manipulation. Electrostatically stabilised poly(NIP AM) microgel particles exhibit a temperature-triggered gel to fluid transition when heated. However, responsive dispersions (not electrostatically stabilised) exhibit the opposite behaviour, i.e., fluid-to-gel transitions due to particle collapse. The same interactions can be used to cause temperature-triggered particle capture at surfaces containing grafted poly(NIPAM).

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