

Article

Synthesis of Environmentally Responsive Polymers by Atom Transfer Radical Polymerization: Generation of Reversible Hydrophilic and Hydrophobic Surfaces

Vikas Mittal^{1,2}

- ¹ Department of Chemistry and Applied Biosciences, Institute of Chemical and Bioengineering, ETH Zurich, Zurich, Switzerland; E-Mail: vikas.mittal@chem.ethz.ch
- ² BASF SE, Polymer Research, 67056 Ludwigshafen, Germany

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Abstract: Environmentally responsive poly(N-isopropylacrylamide) brushes were grafted from the surface of polymer particles or flat surfaces in order to generate reversible hydrophilic and hydrophobic surfaces. The use of atom transfer radical polymerization was demonstrated for the grafting of polymer brushes as it allows efficient control on the amount of grafted polymer. The polymer particles were generated with or without surfactant in the emulsion polymerization and their surface could be modified with the atom transfer radical polymerization (ATRP) initiator. The uniform functionalization of the surface with ATRP initiator was responsible for the uniform grafting of polymer brushes. The grafted brushes responded reversibly with changes in temperature indicating that the reversible responsive behavior could be translated to the particle surfaces. The particles were observed to adsorb and desorb protein and virus molecules by changing the temperatures below or higher than 32 °C. The initiator functionalized particles could also be adsorbed on the flat surfaces. The adsorption process also required optimization of the heat treatment conditions to form a uniform layer of the particles on the substrate. The grafted polymer brushes also responded to the changes in temperatures similar to the spherical particles studied through water droplets placed on the flat substrates.

Keywords: atom transfer radical polymerization; poly(*N*-isopropylacrylamide), grafting, hydrophobic; hydrophilic; reversible; latex particles; flat substrates; microscopy; crosslinking; polystyrene

1. Introduction

Surface properties of polymer particles or flat surfaces have been one of the most important contributors to their application, especially when the application involves the interaction of these surfaces with foreign media or entities. As an example, the surface properties are of tremendous importance in the chromatographic separations of proteins, polymers or any mixtures. There is always a requirement or desire to achieve extra functionalization on the surface by controlling the surface properties, which can be used for either one application or another or a combination of a few [1,2]. These functionalized surfaces represent a novel class of materials, which at the forefront of technology can lead to revolutionary changes in conventional processes. In one such approach, environmentally responsive character has been generated on the surfaces. Generation of this property on the surface of the materials leads to functionalized materials in which their nature e.g., hydrophobicity or hydrophilicity can be finely controlled by environmental stimulants like temperature, salt, pH, *etc*. This property translates into the use of these materials in a number of applications like temperature controlled adsorption and desorption of biomolecules, temperature controlled drug delivery processes, *etc*.

Different ways to generate the thermal responsive behavior on the surfaces have been developed, different materials to generate thermal responsiveness have been used and different substrates on which thermal responsive character has been achieved have been used. Many techniques to functionalize the surfaces have been reported in the literature, like physical adsorption of oligomeric or polymeric chains on the surface [3-5], grafting of polymer chains 'to' the surface [6,7] and grafting of polymer chains 'from' the surface [8,9]. Though physical adsorption has an advantage that it can lead to the adsorption of long polymer chains of well defined length, molecular weight distribution and composition to the surface, this approach suffers from the limitations of steric hindrance posed by the long polymer chains, thus seriously limiting the final surface density of the grafts. Apart from that, as the chains are only physically bound to the surfaces, the efficiency of these linkages for load transfer or resistance towards washing or cleaving off may not be sufficient. Grafting of polymer chains 'to' the surface approach focuses on chemical immobilization of end-functionalized polymer chains to the surface by reacting the ends with the reactive groups already immobilized on the surface. It can also be achieved either by attaching a monomer on the surfaces and subsequently polymerizing the monomer in the presence of externally added monomer and initiator. In both the cases, as the preformed long chains approach the surfaces, therefore, the steric hindrance concerns may still hinder the generation of high density grafts on the surface. The generated grafts may also not be very uniform in terms of molecular weight and chain lengths etc. owing to the uncontrolled nature of the process which is generally achieved by non-living conventional free radical polymerization.

Another important and extensively studied approach is the grafting of polymer chains 'from' the surface. In this approach, an initiator is covalently bound to the surface which is subsequently polymerized with the external monomer without the external addition of any further initiator. This approach has enjoyed more success because of its ability to generate densely packed polymer functionalities in the absence of any kinetic hindrance along with the advantage of covalently bound polymer chains on the surface [8-11]. Such structures are referred to as polymer brushes, when the distance between the grafted chains is less than twice the radius of gyration of the unperturbed polymer

chain [12]. A number of different polymerization modes have been used to graft polymer chains on the surfaces like non-living free radical polymerization [13], controlled polymerization techniques such as ionic polymerization [14,15], nitroxide mediated polymerization [13], atom transfer radical polymerization (ATRP) [11,16-18] and reversible addition fragmentation transfer (RAFT) [19-21] *etc*. Conventional polymer systems suffer from unwanted bimolecular termination reactions thereby leading the grafting process to an abrupt end. However, the growth of living polymer chains from the surfaces generated by controlled living polymerization techniques ensures better control over the molecular weight distribution and the amount of grafted polymer. ATRP has been particularly useful technique because of ease of operation, good control on the properties of the grafts, and possibility of polymerization in aqueous phase [3-10,16,17,19,22-39].

As mentioned earlier, environmental responsiveness means reversible changes in the hydrophobicity and hydrophilicity, dimension and density of the polymer chains owing to changes in the intramolecular interactions stimulated by changes in stimulants like temperature, salt concentration, pH, electrical potential *etc*. Out of a number of known polymers known to exhibit this behavior, water soluble poly(*N*-isopropylacrylamide) (PNIPAAM) is a very common and extensively studied material. It has a lower critical solution temperature (LCST) of about 32 °C [40-45] and below this temperature, the chains exhibit chain extended conformations and random coil structure. The intermolecular hydrogen bonding with the water molecules due to the chain extended morphology generates the hydrophilic nature of the chains. The chains transform into more collapsed globular form above the lower critical solution temperature owing to the domination of intramolecular bonding between the CO and NH groups over the external hydrogen bonding. The highly reversible responses of PNIPAAM chains to temperature as well as other stimulants have led to its extensive use for the synthesis of stimulus sensitive surfaces. Due to these characteristics, PNIPAAM chains grown on various surfaces have been used for protein adsorption, responsive gels, biological separations *etc.* [46-56].

The goal of the reported study was to graft environmentally responsible PNIPAAM brushes on the surface of spherical and flat surfaces by using ATRP and to demonstrate the applications of these surfaces. Crosslinked polystyrene particles containing a thin shell of ATRP initiator on the surface were prepared using emulsion polymerization reactions (with and without the use of surfactant) and were subsequently used for the grafting of environmentally responsible PNIPAAM brushes.

2. Experimental

2.1. Materials

Monomer styrene (S, \geq 99.5%), crosslinker divinylbenzene (DVB, \geq 80%), free-radical initiator potassium peroxodisulphate (KPS, \geq 99.0%) were purchased from Fluka (Buchs, Switzerland). Atom transfer radical polymerization initiator end capped with acrylic monomer unit *i.e.*, 2-(2-bromo-propionyloxy)ethyl acrylate (BPOEA) was synthesized as reported in literature [57]. *N*-isopropyl-acrylamide (NIPAAM, 97%) and other reagents to run the ATRP polymerization, namely 1,1,4,7,10,10-hexamethyltriethylenetetramine (HMTETA, 97%), copper(I) bromide (CuBr, 99.99%), copper(II) bromide (CuBr₂, 99.99%) and powder copper (Cu, 99%, 200 mesh) were

2.2. Synthesis of ATRP Initiator Functionalized Crosslinked Polystyrene Particles and PNIPAAM Grafting

Synthesis of crosslinked polystyrene particles was carried out by using either surfactant-free emulsion polymerization or emulsified emulsion polymerization, as reported in earlier studies [58,59]. The molar ratio of styrene to divinylbenzene in the seed latex was ~50. The second batch of monomers containing BPOEA (the molecule containing the ATRP initiator), styrene and divinylbenzene was added to the polymerization system either after a conversion of 70% of the monomer was achieved in the seed latex or after 100% conversion. A molar ratio of styrene to divinylbenzene of ~40 was used in the shell forming monomers. The generated particles were then subsequently grafted with PNIPAAM brushes. The latex particles, especially the particles obtained by using surfactant, were washed by multiple sedimentation and resuspension cycles so as to avoid unwanted interaction of the ATRP catalyst with the surfactant or other residual molecules. For PNIPAAM grafting by using ATRP, NIPAAM, HMTETA, CuBr, CuBr₂ and Cu powder were carefully measured and stirred with functionalized polystyrene particles, which was then carefully degassed by applying alternative vacuum and nitrogen cycles. The reaction was kept under stirring for 24 h using a magnetic stirrer (400 rpm). The latex particles were washed off any free polymer formed in the solution by centrifugation and resuspension in Millipore water.

2.3. Adsorption of Surface Functionalized Crosslinked Polystyrene Particles on Flat Sapphire Disks and PNIPAAM Grafting

To study the generation of environmentally responsive flat surfaces, crosslinked polystyrene particles functionalized with ATRP initiator were adsorbed on flat sapphire disks. To obtain this, positively charged sapphire discs, freshly etched by charged oxygen plasma (10 s, 100 mV, 5 mbar of O_2) in Balzers GEA-003-S glow-discharge apparatus (Balzers), were placed on the droplet of particle latex for 2 min and dried on filter paper. The disks were then placed on the heating plates for 60 s equilibrated at room temperature or 100 °C and 150 °C. The PNIPAAM brushes were subsequently grafted on the surface of the discs by placing them in an aqueous solution of NIPAAM, HMTETA, CuBr, CuBr₂ and Cu powder followed by degassing and purging with nitrogen. The disks were kept immersed in the monomer solution overnight and were subsequently placed 5–7 times in Millipore water to wash off any unreacted monomer.

2.4. Electron Microscopy

For transmission electron microscopy of particles, carbon coated 400-mesh copper grids were freshly glow discharged and were placed on the droplets of particle suspensions for 20 s followed by washing with distilled water. Adsorption trials of IgG protein supported on gold particles or tobacco mosaic virus were performed by stirring the protein or virus solution in water with the latex at 37 °C

overnight. Desorption studies were carried out by stirring the same latex sample at 4 °C overnight. For scanning electron microscopy studies, carbon/collodium-coated 400-mesh copper grids, freshly etched by charged oxygen plasma (10 s, 100 mV, 5 mbar of O_2) in Balzers GEA-003-S glow-discharge apparatus (Balzers), were placed on the droplets of particle suspension for 2 min, dried on filter paper followed by sputter-coating with 3 nm platinum.

3. Results and Discussion

Generation of environmentally reversible behavior on the surface can lead to a number of exciting applications of both spherical as well as flat substrates. In order to control the properties of the surfaces efficiently, it is important to control the surface functionalization processes, first with ATRP initiator and subsequently with PNIPAAM polymer brushes. In the case of functionalization of surfaces with ATRP initiator, it is important that a uniform distribution of the initiator is obtained on the surface of the particles. It was also reported earlier that a number of factors like presence of crosslinker, presence of surfactant, mode of addition of monomers, colloidal characteristics of the system etc. can influence the initiator distribution on the surface of the particles [58]. The functionalization of surfaces with PNIPAAM is directly proportional to the quality of the ATRP initiator distribution on the surface of the particles. In the case of grafting of PNIPAAM from the flat surface, it is also important to ensure that the particles adsorbed on the flat surface form a uniform layer so that the dead-spaces between them are minimized as such spaces do not contribute towards the environmentally responsive behavior. The use of ATRP for polymer grafting is advantageous as it allows an efficient control on the amount or molecular weight of the polymer grafted on the surface. The density of the initiator on the surface can also be varied by varying the molar ratio of monomers in the shell forming monomer batch, thus again allowing control on the extent of surface grafting according to the requirement.

The particle synthesized without the use of surfactant were earlier reported and the grafting of PNIPAAM chains on the surface of these particles was also successful [58,59]. The synthesis of the particles without the use of surfactant was achieved by homogenous nucleation where the micelles are absent in the absence of any additionally added surfactant and the negative charges on the surface of forming particles owing to the initiator residues provide partial colloidal stability. The non-emulsified polymerization conditions were used because the commonly used ionic surfactants in emulsified systems can poison the ATRP catalyst thus hindering control over the molecular characteristics of the grafted chains. The absence of surfactant thus allows better control on the grafted polymer properties, but on the other hand, also leads to much larger particles as compared to emulsified systems owing to lesser number of particles formed during polymerization. Also, the colloidal instability of the particles formed by emulsifier free conditions poses problems during the surface functionalization. Therefore, it was observed that the functionalization of such particles with ATRP initiator was significantly affected by minor changes in the polymerization system. The addition of small amount of divinylbenzene crosslinker to the system was observed to be beneficial as it destabilizes the particles forming due to secondary nucleation and as a result, these particles collapsed on the seed particles thus allowing the better functionalization of seed particles with the ATRP initiator as compared to the case where there is generation of secondary particles thus causing the division of ATRP initiator molecules in the latex and secondary particles. Figure 1a,b, respectively, shows the scanning and transmission electron

micrographs of the crosslinked polystyrene particles functionalized with a thin copolymer layer of styrene, BPOEA and divinylbenzene. The surface of the particles was not completely smooth or spherical owing to the collapse of smaller secondary particles on the surface during the course of polymerization. Figure 1c,d represents the transmission electron micrographs of the particles after grafting with PNIPAAM. The polymer brushes can be clearly seen protruding out from the surface of the particles. Here it is important to notice that though the brushes seem not to be uniformly grafted from the surface, but such an effect arises from the microscopy analysis and depending on the staining of particles or placement of particles on the microscope grids, the same particles with more uniform grafting were also observed. It was also observed that the particles were partially aggregating after the polymer grafting.

Figure 1. (a,b) SEM and TEM micrographs of the latex particles functionalized with a copolymer layer carrying ATRP initiator and (c,d) the grafted brushes of poly(*N*-isopropylacrylamide) from the surface of the functionalized particles using ATRP [58,59].



As mentioned earlier, the use of surfactant was avoided in the process owing to the poisoning of the ATRP catalyst with the surfactant, but the process then leads to the generation of larger particles. Smaller particles are important substrates owing to different applications and it is of interest to achieve the grafting of environmentally responsive polymer on the surface of these particles too. To avoid the

negative interactions of ATRP catalyst and surfactant, the particles were extensively washed before the PNIPAAM grafting reaction. Figure 2a shows the crosslinked polystyrene particles synthesized with emulsified polymerization conditions. Figure 2b is the micrograph depicting the particles after surface functionalization with a thin layer of copolymer of styrene, BPOEA and divinylbenzene. The particles were smoother in morphology as compared to the particles generated without the use of surfactant (Figure 1). The particles were grafted with PNIPAAM and the grafted particles are shown in Figure 2c,d. The particles can be seen covered with thick layers on PNIPAAM, which are visibly lighter in color owing to non-compact nature as compared to polystyrene particles owing to their higher thickness as well as compact nature. The amount of grafted polymer could also be controlled by changing the initial amount of *N*-isopropylacrylamide added during grafting reaction. This confirms the successful generation of polymer grafts by using atom transfer radical polymerization on the surface of smaller particles also, thus expanding the applicability of ATRP on the substrates generated by two different polymerization methods. Similar to the case of grafted particles of Figure 1, the particles in the case of emulsified conditions were also observed to have some extent of aggregation after grafting.

Figure 2. (a) Crosslinked polystyrene latex particles generated by the use of surfactant, (b) particles of Figure 2a surface modified with ATRP initiator and (c) and (d) are the particles of Figure 2b after grafting with poly(*N*-isopropylacrylamide) brushes.



As observed in Figures 1 and 2, partial aggregation of the particles was observed after PNIPAAM grafting, probably owing to the sticky surface of the polymer particles. Further studies were also carried out to confirm this phenomenon. Figure 3a shows the cryo scanning electron micrograph of the grafted particles. Cryo SEM allows better investigation of the structural features of the grafted polymer layer as the instantaneous freezing of the system in this case eliminates any shrinkage of the grafted polymer brushes on the surface of the particles. It was observed in the micrograph that PNIPAAM brushes around the particles formed a homogenous layer and aggregated the particles together owing to long brushes of sticky nature. It should also be noted that the latex were thoroughly washed after PNIPAAM grafting, therefore, the observed layer in the micrograph is not free polymer but is bound to the polymer particles. Figure 3b also shows the behavior of the latex particles when pulled away from each other. The homogenous grafting of the polymer around the surface of the polymer particles does not allow quick separation owing to the entanglement of the grafted brushes as well because of their sticky nature. The extent of aggregation of the particles was observed to increase on increasing the amount of polymer grafting on the surface of particles, thus, further confirming the above mentioned findings. It was also necessary to confirm that the particles also have environmentally reversible behavior after the grafting of environmentally responsive PNIPAAM brushes from their surface. Therefore, the microscope grids were prepared at high temperature (37 °C) as at temperatures higher than the lower critical solution temperature, the PNIPAAM chains are hydrophobic in nature and collapse on the surface of the particles.

Figure 3. (a) Cryo-SEM micrograph of the polymer particles after PNIPAAM grafting and (b) TEM micrograph demonstrating the pulling of two grafted particles apart.



Figure 4 shows the TEM micrograph of the particles adsorbed on the microscope grids at 37 °C. The brushes observed in the case of Figures 1 and 2 were observed to collapse completely on the surface of the particles owing to their hydrophobic nature. The collapsed bushes on the surface were partially visible in the voids between the particles. The brushes were observed to gain extended morphology when the particles were adsorbed at 10 °C confirming the translation of environmentally responsive behavior to the particles also. Figure 5 also represents this phenomenon schematically. At temperature below the lower critical solution temperature (LCST) of PNIPAAM, the nature of the particles is hydrophilic owing to extended morphology of the polymer brushes and hydrogen bonding

formed between the polymer chains and water molecules. When the temperature is higher than the lower critical solution temperature of PNIPAAM, the nature of the particles reverses to hydrophobic as in this case the polymer chains tend to form hydrogen bonds between CO and NH groups in the chains and thus coil or collapse on the surface of the particles. This reversible process is also quite fast and thus the functional surfaces can be used for different applications like temperature controlled adsorption and desorption of proteins, viruses *etc.*, thermal filters, responsive textiles *etc.*

Figure 4. TEM micrograph of the PNIPAAM grafted particles, when the grids were prepared at 37 °C.



Figure 5. Representation of reversible hydrophilic and hydrophobic nature of the polymer particles grafted with PNIPAAM brushes.



To demonstrate the application of the PNIPAAM grafted polymer particles for the temperature controlled adsorption and desorption of proteins and viruses, IgG protein supported on gold particles and tobacco mosaic virus were chosen. The particles mixed with either protein or virus at 10 °C (lower than the LCST), were observed to have extended morphology of the brushes on the particles and no adsorption of protein or virus molecules as shown in Figure 6a. However, when the mixture were equilibrated at 37 °C (higher than LCST), the brushes collapse and the nature of the surface becomes suitable for the adsorption of the biological entities. As observed in Figures 6b,c, the particles tend to aggregate owing to hydrophobic interactions and the protein supported gold particles (observed as tiny dots around the particles in the micrograph) or virus (seen as long tubes in the micrograph) molecules

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(a)

adsorb on the surface of the particles. The same mixture when re-cooled to 10 °C showed desorption of the protein or virus molecules and the brush morphology was again extended as shown in Figure 6a. Similar behavior has also been quantitatively shown for Human Serum Albumin (HSA) protein [60]. This behavior confirms the potential of these polymer materials in advanced applications.

Figure 6. (a) Micrograph of the particles at 10 °C, (b) and (c) micrographs depicting the adsorption of protein and virus molecules respectively at 37 °C.





As mentioned above, not only spherical but also flat macro-surfaces are of tremendous interest for different applications. To study the environmentally responsive behavior of flat surfaces, sapphire discs were chosen and the particles which have been functionalized with ATRP initiator were adsorbed on the surface of these discs. The particles were then used to graft PNIPAAM brushes from the surface of the flat surfaces. It should be noted that a number of other sophisticated methods for the generation of responsive flat surfaces exist, but they are extremely cost-intensive owing to the requirement of laser etching and other similar processes. The process of adsorption of particles and subsequent grafting of polymer brushes is very cost-effective and does not require any complex processing of the surfaces. Figure 7 shows the process of adsorption of the latex particles on the flat substrates to make a uniform film once the water contained in the latex is evaporated. The generation of uniform film on the substrate is important as the uniform film is directly responsible for the uniform grafting of polymer brushes to film on the substrate is a lot of empty or dead space between the polymer particles, this space

would not contribute to any functional behavior of the surface. To generate a uniform film, heat treatment to the particles is generally provided so that they diffuse with each other optimally forming a thin layer. However, it is very important to optimize the heat treatment as too high a temperature or heating for too long may lead to complete melting of the polymer particles on the surface of discs and in this process, the ATRP initiator may be embedded deep into the melt and thus may not be accessible for the grafting reaction.

Figure 7. Process of film formation of polymer particles on a flat substrate and top view of the uniform film.



Figure 8a shows the particles adsorbed on the positively charged sapphire discs at room temperature. By the generation of positive charges on the surface of discs, the negatively charged particles were observed to have much better adsorption on the surface of the discs as compared to the case of negatively charged discs. However, the surface coverage of the substrate with the particles was

still not optimum and the discs were heated at 100 °C and 150 °C for roughly 10 s. Figure 8b,c shows the particles after heat treatment at 100 °C. The coverage of the surface was observed to be much better as compared to room temperature. In Figure 8c, even two layers of particles were observed to be formed on the surface. The disc treated at 150 °C is shown in Figure 8d and it is clear that the temperature was too high as the particles were observed to be completely molten. Complete loss of identity of the particles may also affect the presence of ATRP polymer on the surface of the particles, thus affecting the grafting of PNIPAAM from the surface.

Figure 8. (a) Latex particles adsorbed on positively charged sapphire disc at room temperature, (b) and (c) adsorption of particles at 100 $^{\circ}$ C and (d) adsorption of particles at 150 $^{\circ}$ C.



Figure 9 shows the behavior of the PNIPAAM grafted sapphire discs (which were treated at 100 °C). At 10 °C, the droplet of water placed on the disc spread out quickly indicating the hydrophilic nature of the surface. On the other hand, when the disc was heated to 37 °C, the droplet of water did not spread out at all, indicating the change in the nature of the surface with temperature. The hydrophilic hydrophobic transition was also observed to be reversible thus confirming the successful translation of reversible behavior to the flat surface also. It should be noted that though the observed behavior is not superhydrophobic and superhydrophilic, the surfaces could be modified efficiently by

following a very simple and cost-effective technique. Further refinement of synthetic processes can be expected to improve the reversible hydrophobic and hydrophilic behavior of the surfaces.

Figure 9. Behavior of the water droplets on the PNIPAAM grafted sapphire discs at (a) 37 °C and (b) 10 °C.



(a)

(b)

4. Conclusions

Atom transfer radical polymerization of *N*-isopropylacrylamide for the generation of polymer grafts on the surface of either spherical latex particles or flat surfaces has been demonstrated. The grafting of thermally responsive behavior of poly(*N*-isopropylacrylamide) also led to the generation of thermal repsonsivity to the bulk surfaces. The use of controlled living polymerization conditions allowed the control on the molecular characteristics of the polymer grafts. Increasing the amount of *N*-isopropyl-acrylamide in the grafting reaction led to corresponding increase in the extent of grafting or molecular weight of grafts on the surface. The graft density was also observed be controllable by varying the monomer ratios. The grafted particles were observed to have slight aggregation owing to the sticky nature of the grafted polymer and the extent of aggregation was also related to the extent of polymer grafting. The grafted particles were shown to successfully adsorb or desorb protein or virus molecules by changing the temperature from 10°C to 37°C and *vice versa*. The flat surfaces were also observed for their thermal responsive potential by studying the behavior of water droplets paced on them. At 10°C, the droplet spreads out quickly, which is totally opposite of what is observed at 37 °C.

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