

Grafting of Poly(*N*-isopropylacrylamide) Onto Nylon and Polystyrene Surfaces by Atmospheric Plasma Treatment Followed with Free Radical Graft Copolymerization

Xiaoling Wang,^{1,2} Marian G. McCord^{1,2}

¹Joint Department of Biomedical Engineering, North Carolina State University, Raleigh, North Carolina 27695-7115

²Textile Engineering, Chemistry, and Science Department, North Carolina State University, Raleigh, North Carolina 27695-8301

Received 24 September 2005; accepted 16 December 2006

DOI 10.1002/app.26081

Published online in Wiley InterScience (www.interscience.wiley.com).

ABSTRACT: Stimuli-responsive polymer materials (SRPs) have potential uses in drug delivery, tissue engineering, bioreactors, and cell-surface adhesion control. Temperature-responsive surfaces were fabricated by grafting poly(*N*-isopropylacrylamide) (PNIPAM) onto nylon and polystyrene surfaces via a new procedure, i.e., He atmospheric plasma treatment followed by free radical graft copolymerization. The atmospheric plasma exhibits the activation capability to initiate graft copolymerization. The procedure is suitable for integration into a continuous manufacturing process. To reduce homopolymerization and enhance graft yield, Mohr's salt was added. The graft of PNIPAM was confirmed by

Fourier transform infrared spectroscopy and atomic force microscopy. Dramatic water contact angle increase was found for PNIPAM-grafted polymers at about 32°C, indicating the temperature sensitivity of the grafted surface, i.e., the change of surface from hydrophilic to hydrophobic when temperature increases above the lower critical solution temperature (LCST). The addition of Mohr's salt enhances the grafting reaction and the magnitude of temperature sensitivity. © 2007 Wiley Periodicals, Inc. *J Appl Polym Sci* 104: 3614–3621, 2007

Key words: polystyrene; hydrogels; biomaterials; graft copolymers; plasma polymerization

INTRODUCTION

Polymer materials have been widely used in the tissue engineering and biomaterials fields because of their good resilience, low density, and low cost. However, due to problems including nonselective protein adsorption and nonselective cell adhesion, polymer biomaterials are limited in their applications. Hence, surface modification of polymers to improve their biocompatibility has been a significant issue in this field.¹ It is desirable for biomaterials to direct or participate in specific biomaterial/biological tissue interfacial responses. Biomaterials with responsive surfaces can meet this requirement, since they may exhibit remarkable property changes in response to stimuli, such as temperature, pH, liquid composition, photo, electric stimulation, etc. This response can be used to regulate the activity of biological tissues, for example, the automatic cell detachment from the substrate.

A responsive biomaterial surface can be made by grafting stimuli-responsive polymers (SRPs) onto another polymer surface. SRPs can react, adjust, or modulate their physicochemical characters, i.e., in most

cases, their water-solubility, in response to an external stimulus. The environmental stimulus can be pH, temperature, ions, solvents, electrical field, magnetic field, light, pressure, or chemical/biochemical compounds.² Poly(*N*-isopropylacrylamide) (PNIPAM) is one kind of thermoresponsive polymer among SRPs. It shows remarkable changes in aqueous swelling with a change in temperature. The thermoresponsive polymer shows fully hydrated and extended conformation below 32°C. Above 32°C, however, it extensively dehydrates and exhibits a compact chain conformation.³ Grafting thermoresponsive polymers, such as PNIPAM, onto a surface endows the surface with considerable thermoresponsive properties—hydrophilic below the LCST and hydrophobic above it.⁴ Novel applications that have been indicated for these surfaces include smart and thermally responsive cell culture substrates that control the attachment and detachment of cells,¹³ temperature responsive membranes,²⁷ controlled release of drugs and growth factor,²⁸ and temperature responsive chromatography.^{25,26} Thus, PNIPAM-grafting of surfaces is an enabling technology that can facilitate experiments and applications that were previously difficult or impossible.⁵

Because of the wide range of biomedical applications of PNIPAM-grafted surfaces, grafting of PNIPAM on polymer biomaterial surfaces has been the subject of numerous recent experimental studies. Methods

Correspondence to: M. G. McCord (mmccord@ncsu.edu).

reported for surface grafting of PNIPAM include ultraviolet (UV) irradiation,^{6–8} vacuum plasma treatment,^{5,8–10} ozone treatment,^{11,12} electron-beam^{3,13,14} and γ -irradiation,¹⁵ and chemical treatment.¹⁶ Irradiation results in the formation of active species on the substrate surface, which are capable of initiating the copolymerization of NIPAM monomer. In one study, PNIPAM was grafted onto a polypropylene membrane surface using a vacuum plasma technique to activate the surface, resulting in thermoresponsive membrane permeability.¹⁰ Polyamide has also been activated by ozone treatment and then grafted with PNIPAM.¹²

Among the many irradiation methods, vacuum plasma treatment has been widely used because of its commercial advantages. It offers flexibility, effectiveness, safety, and environmental friendliness. The vacuum plasma is effective at near-ambient temperature without damage to most heat-sensitive biomaterials. Vacuum plasma treatment modifies only the near surface of treated substrates and does not change the bulk material properties. It can be used to modify any kind of substrate geometry. In spite of its advantages, costs associated with maintaining a vacuum and the constraint of batch processing have limited the acceptance of this technique.¹⁷

In contrast, atmospheric plasmas maintain the positive aspects of vacuum plasma treatment, without the limitations. Compared with conventional vacuum plasma treatment, atmospheric plasma treatment costs less and may be integrated into a continuous manufacturing process.¹⁸ In this investigation, atmospheric plasma treatment with subsequent graft copolymerization was used to graft PNIPAM onto nylon and polystyrene (PS) surfaces. The PNIPAM-grafted surfaces were investigated by FTIR, contact angle, and AFM.

EXPERIMENTAL

Materials

Nylon 6,6 (McMaster-Carr) film and 60-mm nontissue culture-treated polystyrene (PS) plates (Corning, NY) were used as the substrates for graft polymerization. Nylon and PS were cut into 3×3 cm² samples, washed with acetone, dried in an oven at 60°C, and weighed. *N*-isopropylacrylamide (NIPAM) was generously provided by Kohjin, Tokyo, Japan. It was recrystallized using hexane prior to grafting. Mohr's salt [Fe(NH₄)₂(SO₄)₂·6H₂O, EM Science] and hexane (95%, Acros Organic) were used without further purification after purchase.

Atmospheric plasma treatment

The atmospheric pressure plasma treatment system used in these experiments is located in the Atmos-

pheric Plasma Laboratory in the College of Textiles at North Carolina State University. It is an atmospheric pressure glow discharge (APGD) device. Figure 1 shows a schematic drawing of the experimental facility. It is a capacitively-coupled chamber and contains two horizontal parallel copper electrodes. The radio frequency power is coupled to the plasma via electrodes through an oscillating electric field. Each electrode is covered with a dielectric material to limit the current in the discharge and force the charge to spread out over a large area instead of constricting to an arc. The dielectric barrier prevented the transition of the discharge to an arc when the acoustic frequency voltage signal was applied.

The device has two chambers: an inner plasma chamber is for batch treatment and an outer chamber equipped with a fabric rolling system for continuous fabric modification treatments. Therefore, the device is capable of batch treatment of fabric/film pieces using a test cell, as well as continuous operation using the roller feed system for large fabric rolls or continuous filaments and yarns. The device produces uniform plasma at atmospheric pressure.

In this investigation, PS and nylon were treated for 1 min in the batch chamber with atmospheric plasma generated from 100% He. The distance between sample and electrode was 1 in. The power level used was 4.8 kW. The frequency was 5 kHz. The flow rate of He was 10.18 L/min.

Graft polymerization of NIPAM onto Nylon and PS

After He plasma treatment, the samples were immediately immersed into a NIPAM aqueous solution (5% wt) in a reaction kettle. The monomer solution was degassed with N₂ for 30 min to remove the existing O₂. The kettle was then sealed under N₂ and placed in a 60°C shaking water bath to begin the graft copolymerization. After 24 h, the PNIPAM-grafted films were washed by agitating in ultrapure water at

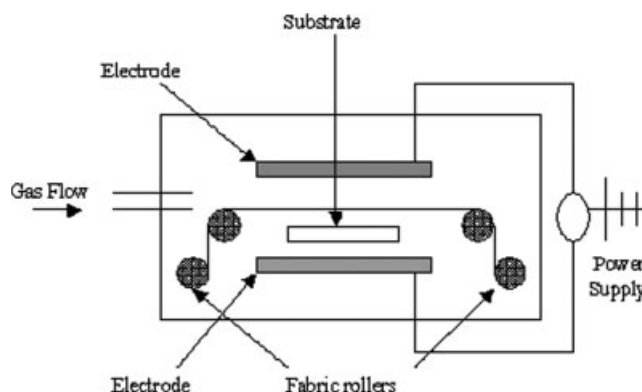


Figure 1 A Schematic of the atmospheric pressure plasma system.

room temperature for 24 h to remove unreacted monomer and ungrafted homopolymer. The samples were then dried at 60°C for 3 h and weighed. Mohr's salt was added into the monomer solution before reaction at a concentration of 0.345 mM in half of the reactions to adjust the degree of grafting.

Graft yield

The graft polymerization of PNIPAM was evaluated by weighing the nylon and PS samples before and after the graft polymerization. The amount of PNIPAM grafted on any PS surface was calculated using

$$\text{Graft yield (mg/cm}^2\text{)} = (W_1 - W_0)/A,$$

where W_0 is the weight of untreated film, W_1 is the weight of grafted film, and A is the film surface area.

FTIR measurement

Fourier transform infrared spectroscopy (Nicolet 510P FTIR spectrometer) was used to examine the surface chemistry of the grafted nylon and PS. The spectra were collected at 4 cm^{-1} resolution with an FTIR microscopic spectrometer over 32 scans. The sampling area was coupled with an attenuated total reflection accessory and a 45° KRS-5 crystal.

Atomic force microscopy

Surface topography of original, plasma-treated, and PNIPAM-grafted nylon and PS was examined using atomic force microscopy (JEOL JSPM-5200) under tapping mode in air. Measurements were carried out with a silicon probe (Olympus AC-160) at a scan area of 5 μm^2 .

Water contact angle measurement

The water contact angle of PNIPAM-grafted nylon and PS was measured in air at 20, 25, 30, 32, 37, and 42°C using the sessile drop method with a goniometer (Model A-100, Ramé-Hart). The temperature of the test cell of the goniometer was controlled by a circulating water bath. Ultrapure water (12 μL) was placed on the sample surfaces using a syringe. The contact angle was read after 1 min. The contact angle reported was an average of eight readings at different places on the same sample.

RESULTS AND DISCUSSION

Nylon has been widely used in artificial joints, blood vessels, and kidney dialysis. PS is commonly used in cell culture plates. Neither of these materials exhibits any surface thermal responsiveness. PNIPAM under-

goes a reversible phase transition in response to temperature; hence, graft copolymerization of PNIPAM makes nylon and PS surfaces smart and temperature sensitive. The PNIPAM-grafted nylon and PS will have applications in bioreactors, drug delivery, tissue scaffolds, and cell detachment control.

The process for grafting PNIPAM onto nylon and PS surfaces consists of a He atmospheric plasma treatment of nylon and PS and subsequent graft copolymerization in NIPAM monomer solution. A schematic presentation of the grafting method is depicted in Figure 2. The atmospheric plasma treatment activates the substrate surface and forms free radicals on the substrate surface. Since the plasma chamber is not sealed, there is always oxygen in the system, and the free radicals react with oxygen to form hydrogen peroxide groups either inside the chamber during plasma treatment or upon removal and exposure to the ambient environment. The hydrogen peroxide groups are thermally labile in nature and initiate the graft copolymerization of NIPAM to introduce graft brush layers on the surface.¹

Fourier transform infrared spectroscopy

FTIR spectra of original PS and PNIPAM-grafted PS are shown in Figure 3. Absorption bands of 1540, 1650, and 3350 cm^{-1} , attributed to the secondary amide C=O stretching and secondary amide N—H stretching of PNIPAM chains,⁹ respectively, are found in both PNIPAM-grafted PS samples, indicating that PNIPAM has been successfully grafted onto the PS surface. The addition of Mohr's salt increases the intensity of the absorption bands at 1650 and 3350 cm^{-1} of PNIPAM-grafted PS, indicating that the Mohr's

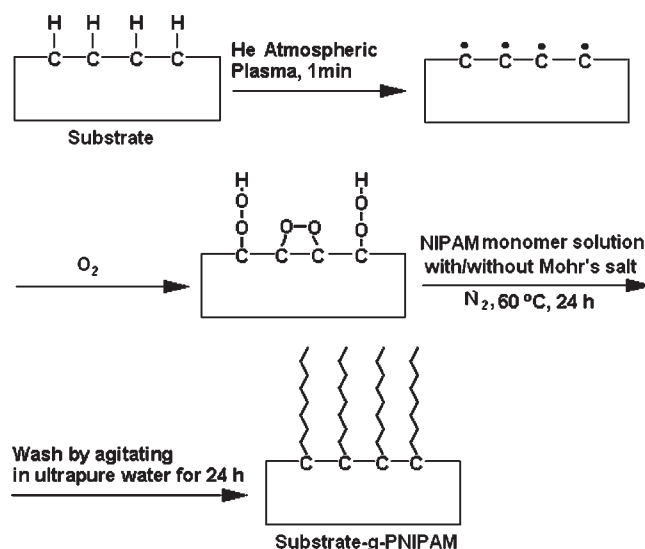


Figure 2 The schematic of graft copolymerization of NIPAM on PS and nylon surfaces.

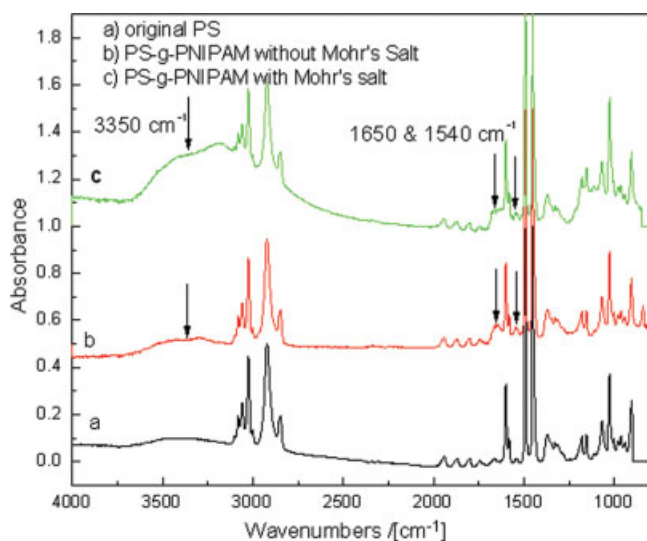


Figure 3 FTIR spectra of original and PNIPAM-grafted PS. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

salt enhances the graft copolymerization and increases the PNIPAM chain density on the PS surface.

Figure 4 shows FTIR spectra of original nylon and PNIPAM-grafted nylon. Since there is a —NHCO— group in both nylon and PNIPAM structure, the absorption bands of 1540, 1650, and 3350 cm^{-1} cannot be used to detect PNIPAM chains on the nylon surface. Therefore, the absorption band of 2970 cm^{-1} , attributed to the —CH_3 asymmetric stretching of PNIPAM chains, is used to monitor the grafting of PNIPAM on nylon. The 2970 cm^{-1} peak is present in both PNIPAM-grafted nylon surfaces with or without Mohr's salt, which confirms the grafting of PNIPAM

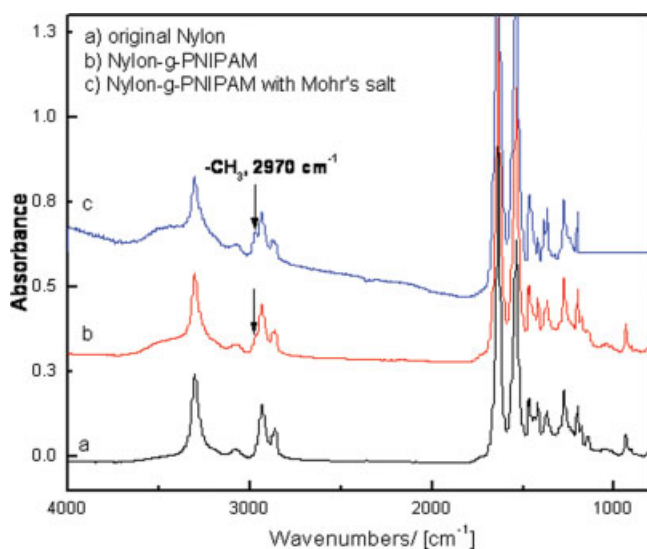


Figure 4 FTIR spectra of untreated and PNIPAM-grafted nylon. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

on the nylon surfaces. The intensity of this absorption band increases with the addition of Mohr's salt, indicating that Mohr's salt can enhance graft copolymerization of PNIPAM on nylon.

In the atmospheric plasma system at NC State University, the discharge is a nonequilibrium ionized gas that has many of the beneficial characteristics of low-pressure plasma treatment at increased pressure without the potentially damaging thermal energy.¹⁹ Hence, atmospheric plasma may be used as an alternative to vacuum plasma to initiate graft copolymerization. In atmospheric plasma, the surface is activated by free radicals formed on the surface during plasma treatment, which initiates the graft copolymerization.

Effect of Mohr's salt on the grafting of PNIPAM

Graft yields of PNIPAM-grafted nylon and PS are shown in Table I. The He atmospheric plasma-induced graft copolymerizations of PNIPAM onto PS and nylon resulted in graft yields of 0.056 and 1.67 mg/cm^2 , respectively. Generally, the graft copolymerization competes with homopolymerization. If the surfaces were not atmospheric plasma pretreated, grafting copolymerization was minimal and the reaction was dominated by homopolymerization. However, as in studies using vacuum plasma, atmospheric plasma produced free radicals on the substrate surfaces, which induced graft copolymerization. The graft yield for nylon is 20 times higher than that for PS. This is due to their different chemical structures. Nylon has many N—H and C=O bonds, which are more susceptible to chain scission and free radical formation under atmospheric plasma.

Although atmospheric plasma is used to activate the surface, the grafting of PNIPAM onto nylon and PS surfaces is still generally accompanied by the formation of PNIPAM homopolymer. This leads to large-scale monomer waste and may adversely affect the kinetics of the grafting process. As anticipated, the addition of Mohr's salt [$\text{Fe}(\text{NH}_4)_2(\text{SO}_4)_2 \cdot 6\text{H}_2\text{O}$] suppressed the homopolymerization and enhanced graft copolymerization. It was found (Table I) that the addition of Mohr's salt increased the graft yield for PS from 0.056 to 0.087 mg/cm^2 , and graft yield for

TABLE I
Graft Yields of PNIPAM-Grafted Nylon and PS by Atmospheric Plasma-Induced Graft Copolymerization with or without Addition of Mohr's Salt

Samples	Graft yield (mg/cm^2)
PS-g-PNIPAM	0.056
PS-g-PNIPAM with Mohr's salt	0.087
Nylon-g-PNIPAM	1.67
Nylon-g-PNIPAM with Mohr's salt	1.93

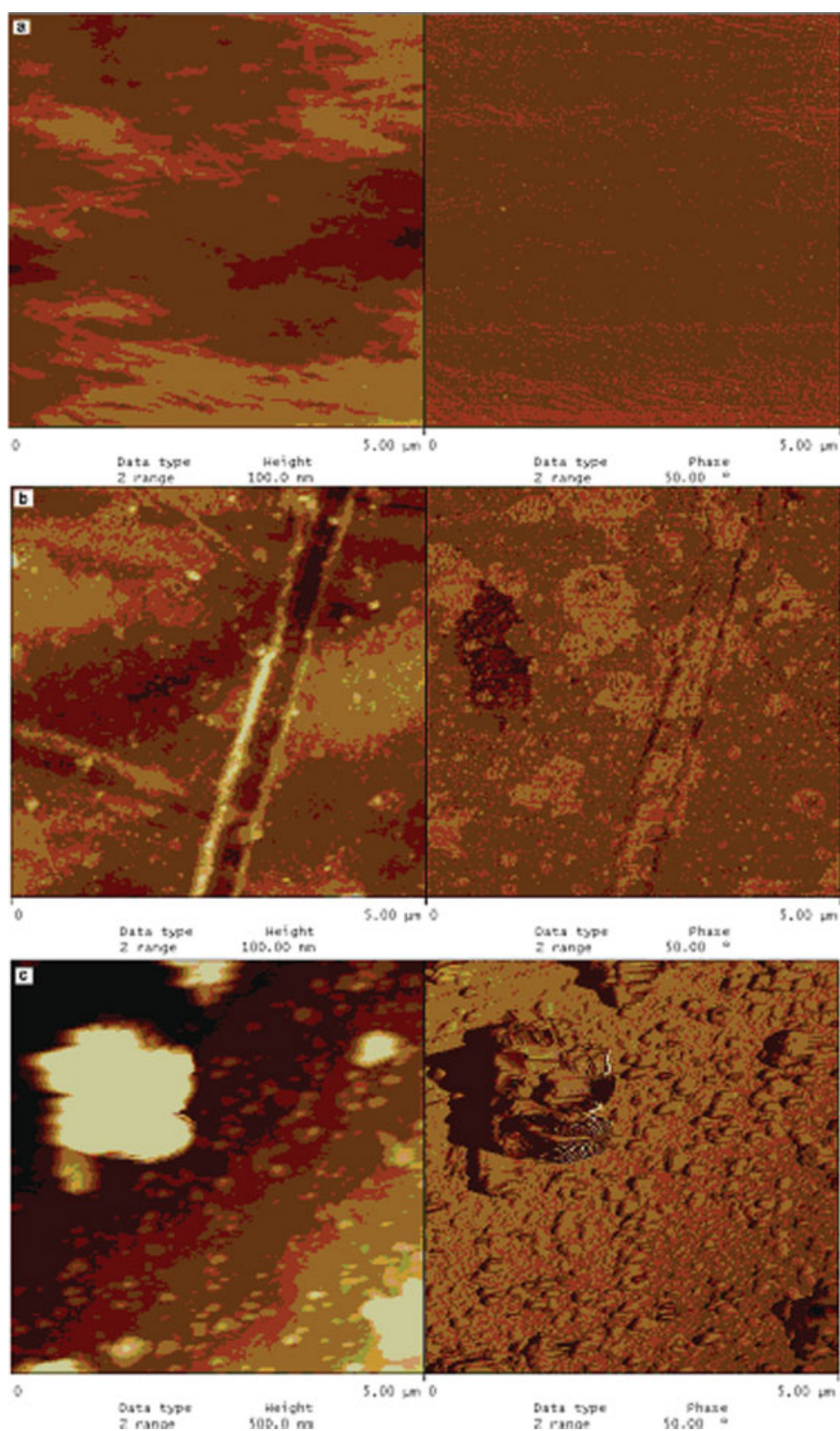


Figure 5 AFM images of PS (left images are topography while the right ones are phase): (a) untreated PS; (b) plasma-treated PS; (c) PNIPAM-grafted PS. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

nylon from 1.67 to 1.93 mg/cm². Hsiue and Wang²³ also found that the presence of Mohr's salt in the plasma grafting of vinyl monomers increased the graft yields. This was further supported by Hirotsu's

results²⁴ in the plasma grafting of different monomers onto polypropylene films.

The mechanism can be explained as follows. Mohr's salt, by virtue of its reducing nature, modifies

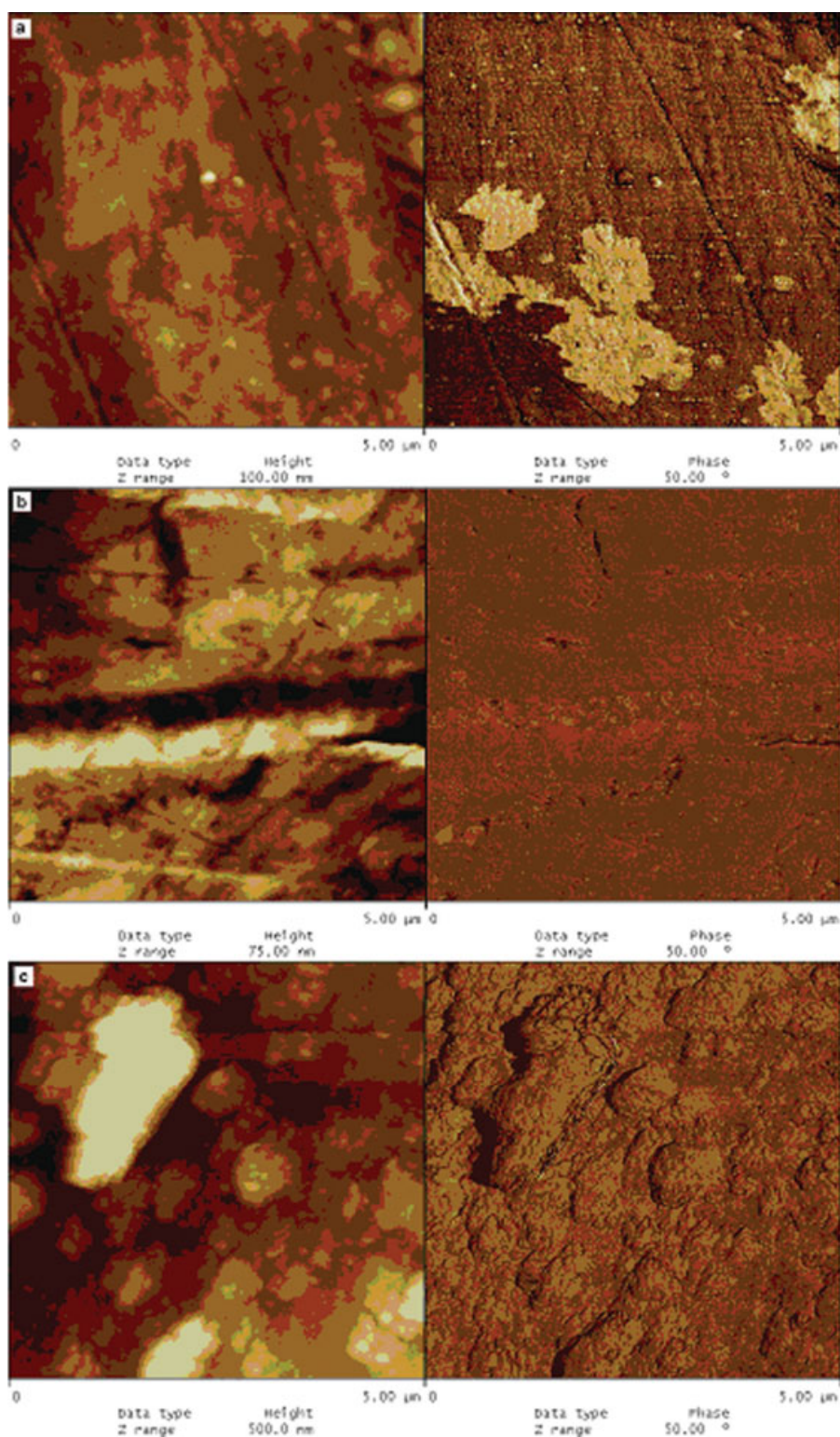


Figure 6 AFM images of nylon (left images are topography while the right ones are phase): (a) untreated nylon; (b) plasma-treated nylon; (c) PNIPAM-grafted nylon with Mohr's salt. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

the usual thermal decomposition of hydrogen peroxide and suppresses the formation of hydroxyl radicals. Hydroxyl radicals [eq. (1)] are partly responsible for homopolymerization during the grafting reaction.

In the presence of Mohr's salt, the hydrogen peroxide group is transformed to a hydroxyl ion and primary radical PO, which initiates the grafting reaction [see eq. (2)]:¹

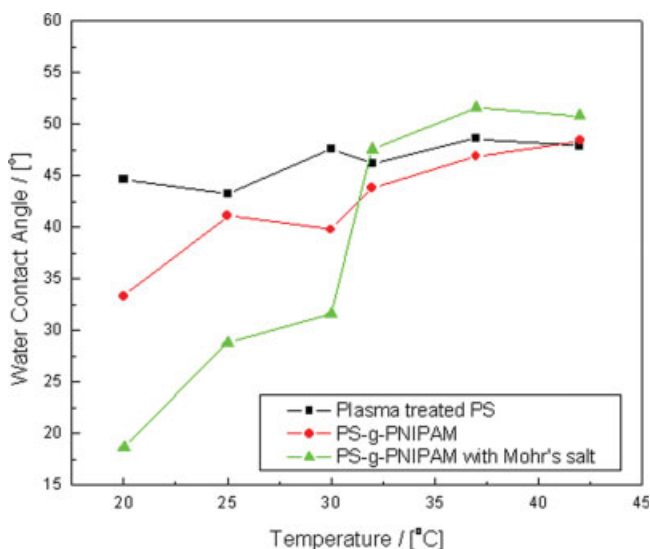
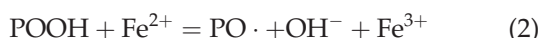


Figure 7 Contact angles of PNIPAM-grafted PS. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]



Therefore, Mohr's salt can suppress homopolymerization [eq. (1)] and results in a higher degree of grafting.

AFM images of PNIPAM-grafted surface

Figure 5 shows AFM images of untreated, plasma-treated, and PNIPAM-grafted PS with Mohr's salt. Ungrafted PS has a flat surface, while the topography changes after the surface treatment. The plasma-treated PS becomes less flat and has many isolated rough spots due to the irradiation. Hwang et al.²⁰ also found that atmospheric plasma treatment changes the morphology and roughness of polyester film due to the etching and redeposition effects of plasma. PNIPAM-grafted PS in the presence of Mohr's salt contains a large amount of projections ($\sim 0.2 \mu\text{m}$), which were also found by Curti et al.²¹ on a PNIPAM-grafted polyester surface. The remarkable topography change is attributed to the grafting of PNIPAM chains on the PS surface.

AFM images of untreated, plasma-treated, and PNIPAM-grafted nylon with Mohr's salt are shown in Figure 6. Like PS, untreated nylon also has flat surface, which becomes rougher after the plasma treatment. PNIPAM-grafted nylon in the presence of Mohr's salt shows many isolated rough spots (ca. $0.6 \mu\text{m}$), which are even larger than those found on PNIPAM-grafted PS. This corresponds with the

higher (about 20 times) graft yield of nylon than the one of PS.

Temperature sensitivity

PNIPAM alone undergoes reversible phase transition in response to temperature; hence, graft copolymerization of PNIPAM makes a surface smart and temperature sensitive. There are several methods to test the temperature sensitivity of PNIPAM-grafted surface, including swelling, permeability, and contact angle evaluation at low and high temperatures.

Here, the temperature sensitivity of PNIPAM-grafted PS and nylon was investigated using water contact angle measurement at various temperatures and the results are shown in Figures 7 and 8, respectively. Contact angles for plasma-treated PS and nylon are about 46 and 47°C , respectively. The contact angle for the plasma-treated samples remains almost constant between 20 and 42°C . However, all the PNIPAM-grafted PS and nylon surfaces show a temperature-responsive behavior, i.e., the contact angle increases dramatically at a temperature around 32°C , which is the lower critical solution temperature (LCST) of PNIPAM. This indicates that PNIPAM undergoes a phase change on the nylon and PS surfaces after being grafted. The grafted surfaces are hydrophilic at low temperatures and become relatively hydrophobic at temperatures higher than 32°C . In addition, the magnitude of contact angle increase is affected by the grafting method. The contact angle increases are in the range of 10 – 40° . Samples grafted in the presence of Mohr's salt show a larger difference in contact angle between the tested ranges of temperature than the samples grafted without Mohr's salt.

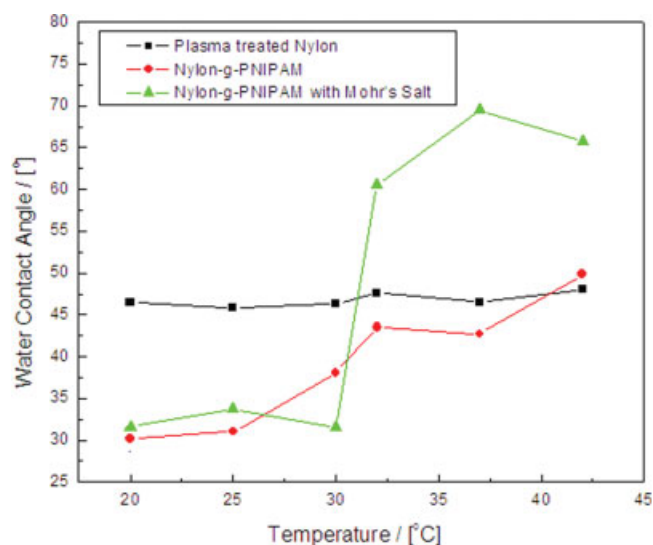


Figure 8 Contact angles of PNIPAM-grafted nylon. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Temperature response of the PNIPAM-grafted surface is partly attributed to conformation changes of the grafted PNIPAM chains. The temperature-responsive polymer chains have fully-hydrated and extended conformation at low temperatures. However, the PNIPAM polymer is essentially dehydrated and has compact chain conformation at temperatures higher than 32°C. The temperature response is believed to be due to the change of hydrogen bonding between polymer segments and water molecules.² In general, the efficiency of hydrogen bonding decreases with the increasing temperature. As a result, PNIPAM can form sufficient hydrogen bonding with water molecules at lower temperatures. However, at temperatures higher than 32°C, the efficiency of hydrogen bonding becomes insufficient to maintain the solubility of PNIPAM polymer in water, and the polymer chains collapse and form an aggregation/precipitation.

However, Wu et al.²² believe that both hydrophobic interactions of PNIPAM segments and polymer-water hydrogen bonding are involved in the phase transition of PNIPAM at ~ 32°C. They claimed that hydrogen bonding on its own is unlikely to be significant, because polyacrylamide (PAAm), a polymer that has no hydrophobic N-alkyl groups, is soluble in water at all temperatures. Furthermore, poly-N-alkylacrylamides with more hydrophobic N-alkyl groups exhibit lower LCSTs, again suggesting that polymer-water H-bonding may not be the only factor. It appears that both hydrophobic interactions of PNIPAM segments and polymer-water hydrogen bonding play roles in the phase change. At some point, the hydrophobic interactions between polymer molecules become more favorable than polymer-water interactions and the polymer molecules collapse.

CONCLUSIONS

Atmospheric plasma treatment is capable of activation of polymer surfaces and induction of graft copolymerization. PNIPAM was successfully grafted onto nylon and PS surfaces by atmospheric plasma-induced grafting copolymerization. The grafting of PNIPAM was confirmed by FTIR and atomic force microscopy. The temperature sensitivity of the PNIPAM-grafted surface was demonstrated by water contact angle measurement at different temperatures. Addition of Mohr's salt in the graft copolymerization of NIPAM suppressed the homopolymerization of NIPAM and enhanced the graft copolymerization. It also increased the magnitude of water contact angle changes of PNIPAM-grafted surface around 32°C. PNIPAM-grafted surfaces have many potential uses

in biomedical field, such as drug delivery, bioreactors, tissue engineering, and cell detachment control.

The authors thank Dr. Suzanne Matthews and Dr. Mohamed Bourham for assistance in plasma treatment, Dr. Sam Hudson and Dr. David Jenkins for assistance in the grafting, Dr. Jan Genzer for assistance with contact angle measurement, and Chuck Mooney for assistance with AFM.

References

- Gupta, B.; Hilborn, J. G.; Bisson, I.; Frey, P. *J Appl Polym Sci* 2001, 81, 2993.
- Galaev, I. Y.; Mattiasson, B. In *Synthetic Polymers for Biotechnology and Medicine*; Freitag, R., Ed.; Landes Bioscience: Texas, 2003; pp 116–129.
- Yamada, N.; Okano, T.; Sakai, H.; Karikusa, F.; Sawasaki, Y.; Sakurai, Y. *Macromol Chem Rapid Commun* 1990, 11, 571.
- Galaev, I. Y.; Mattiasson, B. *Trends Biotechnol* 1999, 17, 335.
- Schmaljohann, D.; Oswald, J.; Jorgensen, B.; Nitschke, M.; Beyerlein, D.; Werner, C. *Biomacromolecules* 2003, 4, 1733.
- Chen, S.; Tsai, J.; Chou, C.; Yang, M.; Yang, J. *Mater Sci Eng C* 2002, 20, 203.
- Yang, B.; Yang, W. *J Membr Sci* 2003, 218, 247.
- Lee, Y. M.; Ihm, S. Y.; Shim, J. K.; Kim, J. H. *Polymer* 1995, 36, 81.
- Pan, Y. V.; Wesley, R. A.; Luginbuhl, R.; Denton, D. D.; Ratner, B. D. *Biomacromolecules* 2001, 2, 32.
- Kim, S. Y.; Kanamori, T.; Shinbo, T. *J Appl Polym Sci* 2002, 84, 1168.
- Karlsson, J. O.; Gatenholm, P. *Polymer* 1999, 40, 379.
- Wang, W. C.; Ong, G. T.; Lim, S. L.; Vora, R. H.; Kang, E. T.; Neoh, K. G. *Ind Eng Chem Res* 2003, 42, 3740.
- Okano, T.; Yamada, N.; Okuhara, M.; Sakai, H.; Sakurai, Y. *Biomaterials* 1995, 16, 297.
- Yamato, M.; Utsumi, M.; Kushida, A.; Konno, C.; Kikuchi, A.; Okano, T. *Tissue Eng* 2001, 7, 473.
- Mazzei, R.; Smolko, E.; Tadey, D.; Gizzi, L. *Nucl Instrum Methods Phys Res B* 2000, 170, 419.
- Xie, J.; Hsieh, Y. L. *J Appl Polym Sci* 2003, 89, 999.
- Loh, I. H. *AST Technical J* 2004. Available at www.astp.com.
- Hwang, Y. J. Characterization of atmospheric pressure plasma interactions with textile/polymer substrates, Dissertation, North Carolina State University, 2004.
- Bures, B. L. Rapid mortality of pest arthropods by direct exposure to a dielectric barrier discharge, Dissertation, North Carolina State University 2004.
- Hwang, Y. J.; Matthews, S.; McCord, M.; Burnham, M. *J Electrochem Soc* 2004, 151, C495.
- Curti, P. S.; De Moura, M. R.; Radovanovic, E.; Rubira, A. F.; Muniz, E. C.; Moliterno, R. A. *J Mater Sci Mater Med* 2002, 13, 1175.
- Wu, X. Y.; Zhang, Q.; Arshady, R. In *Introduction to Polymer Biomaterials*; Arshady, R., Ed.; Citus: London, UK, 2003, p 157.
- Hsiue, G.; Wang, C. *J Polym Sci Part A: Polym Chem* 1993, 31, 3327.
- Zubaidi, A.; Hirotsu, T. *J Appl Polym Sci* 1996, 61, 1579.
- Kanazawa, H.; Kashiwase, Y.; Yamamoto, K. *Anal Chem* 1997, 69, 823.
- Hosoya, K.; Kimata, K.; Araki, T. *Anal Chem* 1995, 67, 1807.
- Li, Y.; Chu, L. Y.; Zhu, J. H.; Wang, H. D.; Xia, S. L.; Chen, W. M. *Ind Eng Chem Res* 2004, 43, 2643.
- Klumb, L. A.; Horbett, T. A. *J Control Release* 1992, 18, 59.