

Investigation of Interpolymer Complexation in Swollen Polyelectrolyte Networks Using Solid-State NMR Spectroscopy

ANTHONY M. LOWMAN,^{1,2} BRETT A. COWANS,² NIKOLAOS A. PEPPAS²

¹Chemical Engineering Department, Drexel University, Philadelphia, Pennsylvania 19104

²Polymer Science and Engineering Laboratories, School of Chemical Engineering, Purdue University, West Lafayette, Indiana 47907-1283

Received 16 May 2000; revised 2 August 2000; accepted 14 August 2000

ABSTRACT: Copolymer networks of poly(methacrylic acid) (PMAA) and poly(ethylene glycol) (PEG) exhibit large changes in their swelling behavior over a narrow pH range due to the reversible formation/dissociation of interpolymer complexes between the polymer chains. Intepolymer complexation occurs in copolymer gels of PMAA and PEG due to hydrogen bonding between protonated acid groups and the ether groups of the PEG. Because of their nature, these gels have been identified for use as delivery vehicles for macromolecular drugs. In this work, solid-state, nuclear magnetic resonance nuclear Overhauser enhancement (NOE) experiments were performed to detect the molecular level complexation between PMAA and deuterated PEG in copolymer blends and crosslinked networks. For gels swollen in acidic media at room temperature or at 37 °C, strong enhancements were detected in the ¹³C resonance of the PEG carbons. The NOE was generated due to energy transfer between the rapidly rotating methyl group protons and the deuterated PEG carbons. The presence of the NOE was indicative of close packing of the polymer chains and was evidence of the presence of the intermacromolecular complexes. In basic solutions, no NOE was detected in the PEG, as the complexes were dissociated and the chains were separated in space. © 2000 John Wiley & Sons, Inc. *J Polym Sci B: Polym Phys* 38: 2823–2831, 2000

Keywords: hydrogels; solid-state NMR; interpolymer complexation; nuclear Overhauser enhancement

INTRODUCTION

Polymer complexes, also known as polycomplexes, are insoluble, macromolecular structures formed by the noncovalent association of polymers with the affinity for one another. The complexes form due to association of repeating units on different chains (interpolymer complexes) or on separate regions of the same chain (intrapoly-

mer complexes). Polymer complexes are classified by the nature of the association. The major classes of polymer complexes are stereocomplexes, polyelectrolyte complexes, and hydrogen bonded complexes.^{1–3}

In our work, we are interested in investigating the formation of interpolymer complexes stabilized by hydrogen bonds. The complexes form between polymers containing electron donating protons, typically poly(carboxylic acids), and polymers containing electron-donating groups such as poly(ethylene glycol) (PEG),^{4,5} poly(pyrrolidones),^{6,7} or poly(vinyl alcohol).⁸ Because of their nature, these associations generally

Correspondence to: A. M. Lowman (E-mail: alowman@cbis.ece.drexel.edu)

Journal of Polymer Science: Part B: Polymer Physics, Vol. 38, 2823–2831 (2000)
© 2000 John Wiley & Sons, Inc.

form in aqueous media within a narrow range of solvent composition, pH, and ionic strength. Additionally, complexation stability is strongly dependent on the composition and structure of the polymers, as well as hydrophobic interactions. Typically, the polymer complexes are enhanced slightly by changes in temperature.^{1,2}

One of the most widely studied pairs of complexing polymers is PMAA and PEG. In this system, complexation occurs due to the formation of hydrogen bonds between the PMAA carboxyl protons and the PEG ether group. These complexes are highly sensitive to the pH of the environment, and only form in solutions in which the pH is low enough to allow for substantial protonation of the PMAA acid group. The behavior of these polymers has been investigated in solution and in polymer networks.

The complexation behavior of copolymer solutions of PMAA and PEG has been investigated using a wide variety of techniques such as viscometry,^{5,9,10} calorimetry,¹¹ and light scattering.¹² In acidic media, complexes formed between PMAA and PEG. This complexation behavior was found to be strongly dependent on the length of the interacting chains.^{5,9-11}

The study of complexation in polymer networks was initiated by Osada.¹³ Researchers have investigated the swelling/deswelling behavior of PMAA networks in the presence of linear PEG.¹³⁻¹⁵ They found that in acidic media, PMAA networks collapsed in the presence of PEG. No network collapse occurred in neutral or basic conditions. Additionally, the permeability of PMAA membranes in the presence of PEG was found to be reduced in acidic media.¹³

Our group has developed a class of novel gels of PMAA grafted with PEG (P(MAA-g-EG)). We synthesized these gels and observed their pH-dependent swelling behavior.¹⁶⁻²⁰ Additionally, solute permeability studies were performed using complexed and uncomplexed membranes. Solute permeability was significantly hindered in complexed gels.^{17,19} More recently, rubber elasticity measurements were used to elucidate information about the structure of P(MAA-g-EG) networks in the uncomplexed and complexed states.^{18,20} Increased degrees of crosslinking were detected in networks swollen in acidic solutions due to the presence of physical crosslinks consisting of complexes.

Researchers have attempted to observe complexation between PMAA and PEG on the molecular level using NMR spectroscopy.^{21,22} We used

homonuclear ^1H - ^1H NMR nuclear Overhauser enhancement experiments to study complexation in dilute solutions of PMAA and PEG.²¹ In this work, enhancements were observed in the PEG ethylene protons following saturation of the α -methyl protons of the PMAA when the polymers were dissolved in acidic solutions. The observed enhancement, an indication of interpolymer complexation between the polymer chains, was significantly greater in the graft copolymers. No enhancement was detected for polymers in basic solutions. However, these interactions were only studied in dilute solutions of the polymers not hydrogels.

Miyoshi²² used cross-polarization experiments to study complexation in dried polymers of PMAA and PEG. They attributed a change in the peak shape of the carbonyl resonance to the presence of interpolymer complexes. However, experiments in our labs have shown that the peak shape of the carbonyl was the same for swollen PMAA/PEG networks in acidic (complexed gels) and basic media (uncomplexed gels).

In this work, we propose the use of one-dimensional ^{13}C - ^1H NMR-NOE experiments to observe complexation in hydrogels of PMAA/PEG. Enhancement in the PEG carbon resonance following saturation of the protons can be detected if complexation occurs in the gels. To detect the true intermacromolecular interactions, deuterated PEG must be used in the NOE experiments. The combination of the large dipolar interactions with the nearby protons and the rapid chain mobility causes a rapid relaxation of the PEG carbons. This relaxation occurs so rapidly that it is virtually impossible to detect crossrelaxations with other nuclei. In the deuterated PEG, the protons are replaced with deuterons, and there are no crossrelaxations between the PEG carbon and the deuterons following proton saturation. Therefore, intermolecular interactions can be detected between the deuterated PEG and PMAA by the presence of an enhancement to PEG carbon due to crossrelaxations between PEG carbon and the PMAA protons that are close in space (less than 5 Å). In these gels, the dipolar relaxations for the PEG carbons, as well as the other nuclei, are dominated by molecular motion of the α -methyl group rotation, and these crossrelaxations would occur only in nuclei along PEG chains that are hydrogen bonded to the PMAA chains.

EXPERIMENTAL

Preparation of Physically Crosslinked Gels

A 20% wt solution of PMAA (molecular weight $\sim 100,000$, Polysciences Inc., Warrington, PA) in pH = 8 deionized water and NaOH was prepared. A 20% wt solution of PMAA in pH = 8 deionized water and NaOH was prepared. A 20% wt solution of dPEG ($M_w = 10,162$, $M_n = 3768$, Cambridge Isotopes, Andover, MA) in deionized water was also prepared. The two solutions were mixed in ratios to yield an MAA/EG molar ratio of 1, and cast into films and dried under vacuum for 48 h at 50 °C. The dry copolymers were ground into particles and washed with D₂O/DCl (pH = 2) to ensure that the acid groups of the PMAA were deuterated. Following the washing, the particles were dried under vacuum for an additional 24 h.

The dried particles were swollen in either D₂O/NaOD of pH = 8 to form a gel with a swelling ratio (q) of 4, or in D₂O/DCl of pH = 2 to form a gel with $q = 2$. The degree of swelling in the base was significantly below the equilibrium value, however, only specific amounts of swelling fluid were added to the particles to keep the volume of the samples within a factor of 2. The samples were allowed to swell for 24 h following addition of the swelling agent.

The ensuing hydrogels were loaded into Pyrex® magic angle spinning (MAS) rotor inserts (Wilmad Glass Co., Buena, NJ) and sealed using epoxy resin. The sealed inserts were used to prevent the loss of any swelling agent during the high-speed spinning.²³ This was important, because if the sample dried out during the experiment (the typical experiment lasted approximately 17 h), the NOE was strongly affected. The inserts were cut to the required length to fit into the MAS rotors using a diamond saw, and the ends were smoothed with additional epoxy resin and polished using a diamond blade.

Preparation of Chemically Crosslinked Gels

Chemically crosslinked polymer samples of PMAA and dPEG were also prepared. Vacuum distilled MAA and dPEG were mixed in appropriate ratios to yield a MAA/EG ratio of 1. The mixture was diluted to 50% weight with a 1 : 1 by weight mixture of ethanol and water. Tetraethylene glycol dimethacrylate was added as the crosslinking agent in the amount of 0.75% mol per mol MAA. Following complete dissolution of the

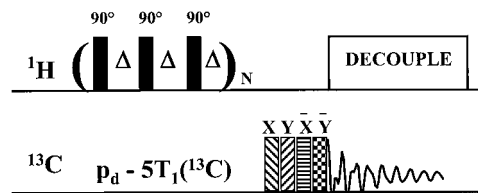


Figure 1. Pulse sequence for the solid-state heteronuclear (¹³C-¹H) NOE measurement.

monomers and the dPEG, nitrogen was bubbled through the mixture for 30 min to remove any dissolved oxygen, a free radical scavenger.

DMPA (Sigma Chemical Co., St. Louis, MO) was added to the mixture in the amount of 1% weight of MAA. The reaction mixture was poured between flat plates to form films of 0.9 mm thickness. The films were sealed under nitrogen and exposed to UV light at 1 mW/cm² at 365 nm and allowed to react for 30 min. The ensuing hydrogels were removed from the glass plates and dried under vacuum for 24 h.

The dried copolymer network was ground into particles and washed in deionized water for 24 h. The particles were rinsed with D₂O/DCl solutions to ensure protonation of the acid groups along the backbone of the network. Following rinsing, the particles were dried under vacuum. The dried crosslinked particles were swollen in either D₂O/NaOD of pH = 8 to form a gel with a $q = 4$ or in D₂O/DCl of pH = 2 to yield a gel with $q = 2$. After equilibrating for 24 h, the hydrogels were loaded into the Pyrex rotor inserts and sealed.

NMR-NOE Experiments

NMR measurements were performed on a GE Instruments Omega Solid-State Spectrometer at a carbon resonance frequency of 100.6 MHz. A Doty double-resonance MAS probe was used with 5-mm Zirconia rotors. The experimental spinning speed was ~ 5.5 kHz. The experiments were performed with the probe at room temperature and at 37 °C.

The NOE spectra were obtained using the pulse sequence^{24,25} shown in Figure 1. Initially, the sample was subjected to a series of 90° proton pulses (5 μs) separated by a time delay, $\Delta = 5$ ms. The sequence of 90° pulses was used to saturate the proton resonances. The observed NOE was strongly dependent on the total number of cycles used, N , or total saturation time, τ . The steady-

state or maximum NOE value was normally observed for saturation times greater than 10 s.

Following the proton saturation pulse train, a composite 90° carbon pulse was applied for detection. The four-pulse composite 90° pulse was used to suppress the carbon background signal from the probe.²⁶ The 90° pulse time for carbons was $3.4 \mu\text{s}$. Following the carbon pulse, the signal was acquired with high-power proton decoupling.

Between carbon pulses, a delay was required to allow the carbon magnetization to return to equilibrium. This delay consisted of an initial pulse delay, p_d , between the end of the composite carbon pulse and the beginning of the proton pulses, and the proton saturation time. The initial pulse delay, p_d , was selected so that the total delay between composite carbon pulses was at least five times the relaxation time, T_1 , of the slowest relaxing carbon species.^{24,25,27-29} The total delay period was kept constant for all of the experiments with a particular material. The necessary pulse delay was determined as equal to the initial pulse delay, p_d , plus the total number of cycles used times delta. To accurately select the pulse delay, the carbon T_1 values were determined by an inversion recovery experiment.²⁹ Based on the carbon T_1 values, the total delay time between composite carbon pulses was 60 s for all the samples.

RESULTS AND DISCUSSION

Peak Assignment

A typical ^{13}C (MAS) spectrum of a PMAA/PEG gel (1 : 1 molar ratio of MAA/EG) without proton saturation is shown in Figure 2(a). The four peaks were attributed to the PEG ethylene carbons (69 ppm), the PMAA methyl carbons (16 ppm), the PMAA methylene carbons (45 ppm), and the PMAA carbonyl carbon (184 ppm).^{21,22} The peak for the quaternary carbon was very broad, and only a weak resonance was observable in highly swollen gels. The relative peak intensities confirmed that the gel contained approximately a 1 : 1 MAA/EG molar ratio.

Calculation of the NOE

For each sample, ^{13}C spectra were acquired with varying proton saturation times and without proton saturation. In these experiments, the pulse delay was sufficiently long so that no NOE

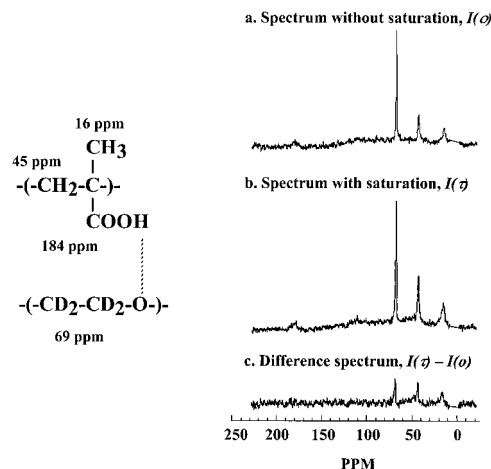


Figure 2. Sample spectra for the PMAA/PEG gels and the assignments of the individual resonances of interest.

buildup due to high-power proton decoupling during signal acquisition was observed. To observe the NOE for a given degree of proton saturation, a difference spectrum was obtained by subtracting the spectrum obtained in the absence of proton saturation from the spectrum obtained with proton saturation for a specified time (Fig. 2). The intensities were determined by fitting the peaks from the spectra with proton saturation ($I(t)$) and without proton saturation ($I(0)$) to Lorentzian curves. The enhancements were calculated using eq. (1).

$$\eta = \frac{I(t) - I(0)}{I(0)} \quad (1)$$

The enhancements for the PEG carbon peaks, the PMAA methylene peak, and the PMAA methyl peaks were calculated as a function of the proton saturation time. No enhancement was calculated for the the PMAA quaternary carbons, as these peaks were generally not observed due to the extremely long T_1 for the nuclei.

Physical Mixtures of PMAA and PEG

To observe the NOE in mixtures of PMAA and PEG without the possibility of complexation occurring, physical mixtures of the homopolymers were prepared. PMAA was mixed with both deuterated and protonated PEG. The mixtures contained EG/MAA molar ratios of 1. For each sample, spectra were acquired with and without pro-

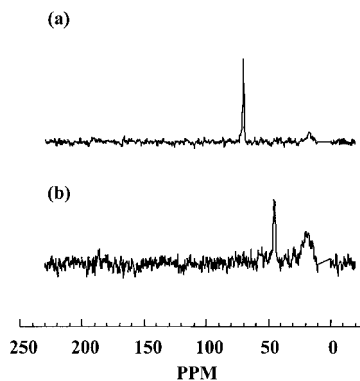


Figure 3. Difference spectra ($\tau = 20$ s) for physical mixtures of PMAA and (a) protonated and (b) deuterated PEG.

ton saturation, and the difference spectra were obtained by subtracting the two.

The difference spectrum for the mixture of PMAA and protonated PEG is shown in Figure 3(a). The peaks in the difference spectrum represent the enhancements due to crossrelaxations. In this mixture, no interpolymer complexation occurred. However, a strong NOE was observed to the PEG carbon due to intramolecular interactions. In this mixture, the NOE was due to crossrelaxations between the PEG carbon and its directly bonded protons. In this case, the NOE was calculated to be 1.17 for the PEG carbon. An NOE was also observed in the methyl carbon due to crossrelaxations with its directly bonded carbons.

The difference spectrum for the mixture of PMAA and dPEG is shown in Figure 3(b). For this mixture, no enhancement was detected in the dPEG carbon because of the lack of efficient dipolar crossrelaxations between the carbon and its directly bonded deuterons following proton saturation. In this mixture, the absence of the NOE was also evidence that there was not hydrogen bonding between the two polymers in the dry state.

In our experiments, the goal was to detect the presence of an NOE in PEG carbon due the presence of intermolecular interactions between the PEG hydroxyl groups and the PMAA. Therefore, for the remainder of the experiments, gels were prepared using deuterated PEG (dPEG). For the gels containing dPEG, the presence of an enhancement in the ethylene resonances could only result due to crossrelaxations between the PMAA protons and the PEG carbons when the polymers were in the complexed state.

Complexation Between Linear Homopolymers

Copolymer gels of PMAA and dPEG were prepared by physically crosslinking the linear polymers. Each of the homopolymers was dissolved in deionized water (10% by weight) and mixed together. After mixing, the pH of the solution was adjusted to 2.0 with the addition of 0.1 N HCl, and gelation occurred due to interpolymer complexation between the homopolymers. The gels were removed from solution and dried under vacuum. The dry polymers were swollen in deuterated water of pH = 2 or 8.

The difference spectrum for gels swollen in pH = 8 solutions is shown in Figure 4. In this case, no enhancement was detected in the ethylene resonance (dPEG). For these gels, no enhancements were observed in the ethylene resonances due to the absence of interpolymer complexes. Under these conditions, the complexes dissociated due to ionization of the pendant acid groups along the PMAA chains. Enhancements due to intramolecular interactions in the PMAA were observed in these spectra.

The difference spectra for the complexed gels swollen in pH = 2 solution are shown in Figure 5. For the shortest saturation or NOE time, no enhancements were observed for any of the peaks. However, as the proton saturation time was increased to 2.5 s, strong enhancements were detected in all of the resonances, including the dPEG-ethylene resonance. The presence of the NOE of the dPEG resonance was due to energy transfer from the PMAA (most likely the rapidly relaxing methyl protons) to the PEG carbons. This energy transfer could only occur if the groups were very close in space (intermolecular distances of 5 Å or less). This enhancement clearly verified the presence of interpolymer complexation between physically crosslinked gels of PMAA and PEG in acidic media.

Complexation between Crosslinked PMAA and PEG

Chemically crosslinked gels consisted of PMAA crosslinked with PEGDMA. The dPEG was phys-

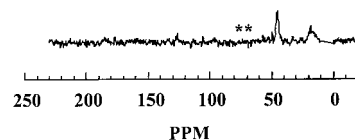


Figure 4. Difference spectrum ($\tau = 20$ s) for a physically crosslinked gel of PMAA/d-PEG swollen in $D_2O/NaOD$ (pH = 8) at 20 °C.

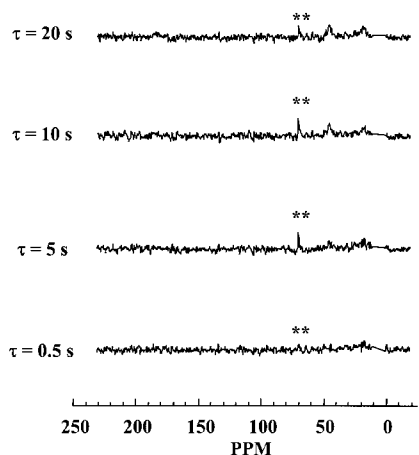


Figure 5. Difference spectra for different proton saturation times for physically crosslinked gels of PMAA/d-PEG swollen in D_2O/DCI ($pH = 2$) at $20\text{ }^\circ\text{C}$.

ically entrapped in the gel during the polymerization process. The polymer gels were swollen in solutions of $pH = 2$ and 8 , and the time-dependent NOE experiments were performed at ambient conditions ($20\text{ }^\circ\text{C}$) to determine under which conditions the complexes formed.

It is significant to note that complexation is dependent on environmental temperature as the stability of the complex decreases with increasing temperature.¹ For complexing gels of PMAA and PEG to function in biomedical applications, it is vital that complexation occurs in these gels at temperatures mimicking physiological conditions. Therefore, the NOE experiments were also performed at $37\text{ }^\circ\text{C}$.

The time-dependent difference spectra for the gels swollen in $pH = 8$ at ambient conditions are shown in Figure 6. At the longest NOE times, a

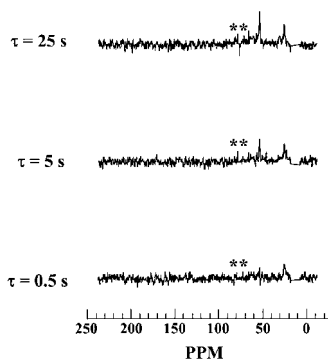


Figure 6. Difference spectra for different proton saturation times for chemically crosslinked gels of PMAA and d-PEG swollen in $D_2O/NaOD$ ($pH = 8$) at $20\text{ }^\circ\text{C}$.

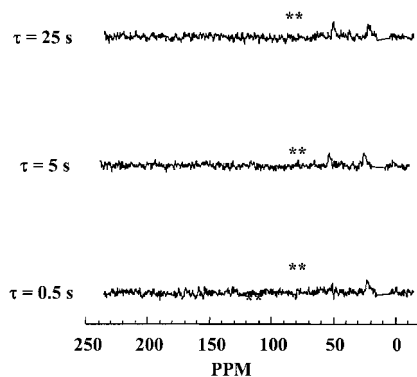


Figure 7. Difference spectra for different proton saturation times for chemically crosslinked gels of PMAA and d-PEG swollen in D_2O/DCI ($pH = 2$) at $20\text{ }^\circ\text{C}$.

very small NOE was detected to the PEG. The value for the enhancement was less than 0.01 , significantly less than what was observed in complexed gels. The small NOE appeared in the PEG resonance due to the protonated ethylene peaks contained in the crosslinking agent. This resonance overlapped the resonance of the ethylene groups of the deuterated PEG chain. It is clear that no complexation occurred in these gels in the high pH fluid due to ionization of the acid groups.

The time-dependent spectra for the gels swollen in $pH = 8$ at $37\text{ }^\circ\text{C}$ are shown in Figure 7. Again, a small NOE was detected to the PEG resonance due to the crosslinking agent. However, no complexation occurred under these conditions as the ionization of the pendant acid groups prevented the formation of hydrogen bonds between the polymers.

Interpolymer complexation did occur in the chemically crosslinked gels swollen in $pH = 2$ solutions at ambient conditions and at $37\text{ }^\circ\text{C}$. The difference spectra for gels swollen at $pH = 2$ and $20\text{ }^\circ\text{C}$ are shown in Figure 8. A significant enhancement was observed in the PEG carbon resonance for all of the saturation times used. The steady-state or maximum NOE value of 0.275 was substantially greater than what was observed in the uncomplexed gel. The presence of the PEG NOE was indicative of the presence of interpolymer complexes stabilized by hydrogen bonds for the gels swollen under acidic conditions.

Spectra for the gels swollen in $pH = 2$ solutions at $37\text{ }^\circ\text{C}$ are shown in Figure 9. For all saturation times, a significant NOE of the PEG resonance was observed. The presence of the NOE verified the presence of interpolymer complexes in chemically crosslinked PMAA/PEG gels swollen in

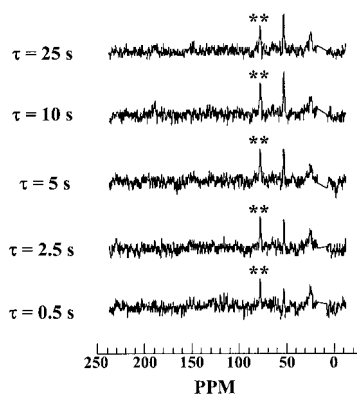


Figure 8. Difference spectra for different proton saturation times for chemically crosslinked gels of PMAA and d-PEG swollen in $D_2O/NaOD$ (pH = 8) at 37 °C.

acidic media at temperatures simulating physiological conditions. The steady-state PEG NOE for these gels was 0.27.

The NOE was strongly dependent on the proton saturation time. As the proton saturation time was increased, the energy transfer due to crossrelaxations of spins also increased. For long proton saturation times, steady-state enhancements were observed. This steady-state value can be described by the following equation.²⁵

$$\eta = \left(\frac{\gamma_S}{\gamma_I} \right) \frac{W_{2IS} - W_{0IS}}{W_{0IS} + 2W_{II} + W_{2IS}} = \frac{\sigma}{\rho} \quad (2)$$

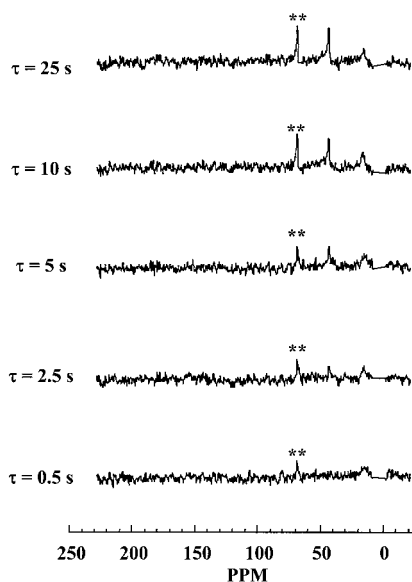


Figure 9. Difference spectra for different proton saturation times for chemically crosslinked gels of PMAA and d-PEG swollen in D_2O/DCl (pH = 2) at 37 °C.

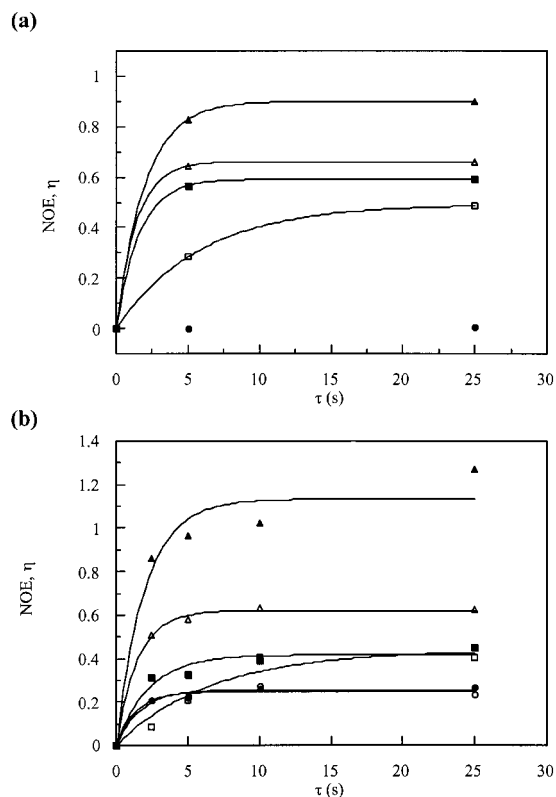


Figure 10. Noe growth curves for the (Δ, \blacktriangle) α -methyl carbon, (\square, \blacksquare) methylene carbon, and (\circ, \bullet) ethylene carbon for crosslinked PMAA gels containing d-PEG swollen in (a) $D_2O/NaOD$ (pH = 8) and (b) D_2O/DCl (pH = 2) at 20 °C (open symbols) and 37 °C (filled symbols).

where σ is the crossrelaxation rate and ρ is the dipolar longitudinal relaxation rate. The steady-state NOE is dependent on the nature and strength of the interaction. Accordingly, intermolecular NOE values are much less than intramolecular values. In our crosslinked gels, the maximum observed NOE observed in the PEG carbons, intermolecular enhancement, was 0.28 while intramolecular NOE values were 1.30 for the methyl carbons and 0.43 for the methylene carbons.

The time-dependent NOE is dependent on the molecular dynamics of the system. By assuming a single correlation function model for the dynamics of the chains,²⁵ the time dependent NOE can be expressed as:

$$\eta = \frac{\sigma}{\rho} (1 - e^{-\rho\tau}) \quad (3)$$

where τ is the proton saturation time. The rate at which the time-dependent enhancement grows is

Table I. Maximum Observed NOE to the PEG Carbons and Relaxation Rate Constants in Acidic and Basic Solutions

Sample	pH	T ($^{\circ}\text{C}$)	Crossrelaxation Rate, σ	Dipolar Relaxation Rate, ρ	Maximum NOE, η_{max}
Linear PMAA/dPEG	2.0	20	0.18	0.83	0.21
Linear PMAA/dPEG	8.0	20	—	—	0.00
Crosslinked PMAA/dPEG	2.0	20	0.18	0.71	0.28
Crosslinked PMAA/dPEG	2.0	37	0.15	0.58	0.27
Crosslinked PMAA/dPEG	8.0	20	—	—	0.00
Crosslinked PMAA/dPEG	8.0	37	—	—	0.01

governed by the crossrelaxation rate, σ . This rate is dependent not only on the nature of the interaction but also the distance between the interacting spins.²⁵

The NOE growth curves for the uncomplexed and complexed gels are shown in Figure 10. In both cases, the NOE values for the PMAA carbons (methyl and methylene) were higher at elevated temperatures due to increased molecular mobility. However, the intermolecular NOE observed in the complexed gels was not dependent on the environmental temperature. This was most likely due to the rigid structure of the hydrophobic complexes.

To compare the complexation phenomena in the gels, the growth curves for the PEG were fit to eqs. (2) and (3) to determine the relaxation rates. These rates along with the steady-state NOE values are indicative of the strength of the interactions. These data are summarized in Table I for all of the polymers studied. For the chemically crosslinked, complexed gels, the increased NOE was indicative of increased hydrogen bonding in these materials. As more units were bound, a greater NOE was observed between the polymers. This is in good agreement with previous work with this system.^{21,30} However, the crossrelaxation rates for both types of gel were nearly identical. These values were the same because this rate, σ , is strongly dependent on the distance between the crossrelaxing nuclei. Because this rate was similar for both gels, we can conclude that the length scale for the interaction (i.e., hydrogen bonding between the polymer) the two gels were the same. This was expected because while the total number of complexes in the gels differed, the length scale of the hydrogen bond was the same.

CONCLUSIONS

The presence/absence of interpolymer complexes in PMAA/PEG gels was verified using one-dimensional, heteronuclear NMR-NOE experiments. Physically and chemically crosslinked copolymer gels were prepared and swollen in acidic (pH = 2) and basic (pH = 8) media. In acidic media, a strong PEG NOE was observed due to crossrelaxations between the PMAA protons and the PEG carbon, and was strong evidence of the presence of interpolymer complexes between the polymers. In basic media, the complexes dissociated due to ionization of the pendant acid groups. As a result, the distance between the chains was increased and no intermolecular NOE was observed between the polymers.

The NOE enhancement observed for the PEG carbons for the chemically crosslinked gels swollen in acidic media was greater than that observed for the physically crosslinked gels swollen under the same conditions. This was due to the fact that a greater number of complexes formed in the chemically crosslinked gels. However, the length scale of the interpolymer complexes was shown to be similar for both gels.

This work was supported by the National Institutes of Health, Grant No. GM 43337.

REFERENCES AND NOTES

- Kabanov, V. A.; Papisov, I. M. *Vysokomol Soedin* 1979, A21, 243.
- Bekturov, E. A.; Bimendina, L. A. *Adv Polym Sci* 1981, 43, 100.
- Tsuchida, E.; Abe, K. *Adv Polym Sci* 1982, 45, 1.
- Antipina, A. D.; Aronovsky, V. Yu.; Papisov, I. M.; Kabanov, V. A. *Vysokomol Soyed* 1972, A14, 941.

5. Osada, Y.; Sato, M. *J Polym Sci Part C Polym Lett* 1976, 14, 129.
6. Bimendina, L. A.; Roganov, V. V.; Bekturov, E. A. *Vysokomol Soedin* 1974, A16, 2810.
7. Ohno, H.; Abe, K.; Tsuchida, E. *Makromol Chem* 1978, 179, 755.
8. Bel'nikovich, N. G.; Budtova, T. V.; Ivanova, N. P.; Panarin, Ye. F.; Panov, Yu. N.; Frenkel, S. Ya. *Vysokomol Soedin* 1989, A31, 1691.
9. Antipina, A. D.; Baranovsky, V. Yu.; Papisov, I. M.; Kabanov, V. A. *Vysokomol Soyed* 1972, A14, 941.
10. Papisov, I. M.; Baranovsky, V. Yu.; Sergieva, Y. I.; Antipina, A. D.; Kabanov, V. A. *Vysokomol Soedin* 1974, A16, 1133.
11. Osada, Y. *J Polym Sci Part A Polym Chem* 1979, 17, 3485.
12. Hemker, D. J.; Frank, C. W. *Macromolecules* 1987, 23, 4404.
13. Osada, Y. *J Polym Sci Part C Polym Lett* 1980, 18, 281.
14. Philippova, O. E.; Starodubtzev, S. G. *J Membr Sci Pure Appl Chem* 1995, A32, 1893.
15. Karybants, N. S.; Philippova, O. E.; Starodubtzev, S. G.; Khoklov, A. R. *Macromol Chem Phys* 1996, 197, 2373.
16. Bell, C. L.; Peppas, N. A. *J Biomater Sci Polym Ed* 1996, 7, 671.
17. Bell, C. L.; Peppas, N. A. *Biomaterials* 1996, 17, 1203.
18. Lowman, A. M.; Peppas, N. A. *Macromolecules* 1997, 30, 4959.
19. Lowman, A. M.; Peppas, N. A. *J Biomater Sci Polym Ed* 1999, 10, 999.
20. Lowman, A. M.; Peppas, N. A. *Polymer* 2000, 41, 73.
21. Klier, J.; Scranton, A. B.; Peppas, N. A. *Macromolecules* 1990, 23, 4944.
22. Miyoshi, T.; Takegoshi, K.; Hikichi, K. *Polymer* 1996, 37, 11.
23. Giammatteo, P. J.; Hellmuth, W. W.; Ticehurst, F. G. *J Magn Reson* 1987, 71, 147.
24. Findlay, A.; Harris, R. K. *J Magn Reson* 1990, 87, 605.
25. White, J. L.; Mirau, P. M. *Macromolecules* 1993, 26, 3049.
26. White, J. L.; Beck, L. W.; Ferguson, D. B.; Haw, J. F. *J Magn Reson* 1992, 100, 336.
27. Neuhaus, D.; Williamson, M. *The Nuclear Overhauser Effect in Structural and Conformational Analysis*; VCH Publishers: New York, 1989.
28. Brevard, C.; Ganger, P. *Handbook of High Resolution Multinuclear NMR*; Wiley: New York, 1981.
29. Derome, A. E. *Modern NMR Techniques for Chemistry Research*; Pergamon Press: New York, 1987.
30. Scranton, A. B.; Klier, J.; Peppas, N. A. *J Polym Sci Part B Polym Phys* 1991, 29, 211.