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Energetics of Association in Poly(lactic acid)-based Hydrogels with Crystalline and Nanoparticle-Polymer Junctions

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Abstract

We report the energetics of association in polymeric gels with two types of junction points: crystalline hydrophobic junctions and polymer-nanoparticle junctions. Time-temperature superposition (TTS) of small-amplitude oscillatory rheological measurements was used to probe crystalline poly(L-lactide) (PLLA)-based gels with and without added laponite[®] nanoparticles. For associative polymer gels, the activation energy derived from the TTS shift factors is generally accepted as the associative strength, or energy needed to break a junction point. Our systems were found to obey TTS over a wide temperature range of 15–70°C. For systems with no added nanoparticles, two distinct behaviors were seen, with a transition occurring at a temperature close to the glass transition temperature of PLLA, T_g . Above T_g , the activation energy was similar to the PLLA crystallization enthalpy, suggesting that the activation energy is related to the energy needed to pull a PLLA chain out of the crystalline domain. Below T_g , the activation energy is expected to be the energy required to increase mobility of the polymer chains and soften the glassy regions of the PLLA core. Similar behavior was seen in the nanocomposite gels with added laponite[®]; however, the added clay appears to reduce the average value of the activation enthalpy. This confirms our SAXS results and suggests that laponite[®] particles are participating in the network structure.

1. Introduction

Soft materials based on associative polymer gels, both with and without added nanoparticles, have long been explored for applications in personal care products, foods, and paints. More recently, there has been renewed interest in these types of materials for tissue engineering, drug delivery, and soft nanocomposites. Physically-associating polymers have been the subject of several studies due to their ability to form networked gels. The “stickiness” or associative strength of the functional group that forms the network junction points can often be manipulated to modify and control the properties of the physical gel. Common examples of such physical gels are amphiphilic block copolymers in selective solvents,¹ hydrophobically-modified polymers,^{2–4} and gels with crystalline domains formed by freeze-thaw procedures.⁵ These materials often have interesting nanoscale structure and rheological properties that can be controlled by small changes in the polymer chemistry or polymer interaction with the surroundings (e.g., through modifying the solvent, adding

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surfactant or salt, changing temperature or pH, etc.), allowing for the design of materials optimized for a variety of applications.

A common architecture for block copolymer-based physical gels is that of ABA triblock copolymers, or analogously telechelic modified polymers, in a solvent selective for the midblock.^{1–4} In dilute solution, the polymers typically assemble into flowerlike micelles. However, at higher concentrations the midblocks bridge between micelles, leading to formation of a three-dimensional network and gelation. The junction points formed are temporary and reversible, and therefore they may break and reform frequently over the time scales of a typical rheological experiment. We have previously studied solutions and gels formed by ABA triblock copolymers in which the A block is crystallizable. Our systems are aqueous gels of poly(lactic acid)-poly(ethylene oxide)-poly(lactic acid) (PLA-PEO-PLA) triblock copolymers. The neat polymer forms associative micelles with hydrophobic PLA cores. Our work distinguishes itself from previous studies through controlled stereochemistry of the PLA blocks and crystallinity of the PLA domains.^{6,7} We can create gels with crystalline junctions through use of copolymers in which the PLA block is poly(L-lactic acid) (PLLA), or amorphous junctions through copolymers in which the PLA blocks contain a racemic mixture of D-lactic acid and L-lactic acid (PRLA).⁶ The crystalline junctions in the PLLA-based gels cause a significant increase in the elastic modulus over the PRLA gels, allowing us to create gels with elastic moduli that are an order of magnitude higher than previously reported with PLA-based associative gels. Using these polymers we were able to design stiff hydrogels with elastic moduli in the range of 1–10 kPa, by changing the crystallinity and molecular weight of the hydrophobic PLA block.

To increase the number of elastically effective chains in these systems, we have previously explored incorporation of nanoparticles into the gels. Specifically, we have used laponite[®],⁸ a synthetic disk-shaped clay that is roughly 1 nm thick and 25 nm in diameter. PEO chains are known to adsorb strongly onto the surface of laponite[®] particles. Thus, the resulting gels have both PLLA-based hydrophobic junctions and PEO-clay junctions. The gels containing laponite[®] show an enhanced elastic modulus with very small amounts of added solid.⁸ SAXS measurements confirm that the clays are participating in the polymer network, and not merely acting as fillers in the system.

Time-temperature superposition (TTS) has frequently been used to obtain information about the rheological behavior of materials at conditions outside the measurement range of a conventional rheometer.⁹ Although the most commonly-known use of time-temperature superposition is investigation of dynamics in polymer melts, it has also been applied to block copolymers^{1,10–13} and polymer nanocomposites^{14,15} in the presence of a solvent. In the present work we have studied the temperature dependence of the rheological behavior of gels formed by PLLA-PEO-PLLA triblock copolymers in water, both with and without added nanoparticles (figure 1). In these systems PLLA is crystalline and thus the junctions formed in the gels by PLLA are crystalline in nature.⁶ The rheological data for the gels at different temperatures was found to obey TTS by shifting the data along the frequency axis to yield master curves that could be used to predict the rheological behavior of the gels over very small frequencies or very long time scales. We use these data to understand the activation enthalpies of junction points in the hydrogels. Furthermore, TTS has been performed on PLLA-PEO-PLLA hydrogels with added laponite[®] and the activation enthalpies obtained for these systems have been compared with that for the neat polymer gels.

2. Materials and Methods

2.1. Materials

L-lactide ((3S)-cis-3,6-dimethyl-1,4-dioxane-2,5-dione) from Aldrich was purified by recrystallization in ethyl acetate and then sublimated prior to polymerization. The α,ω dihydroxy polyethylene glycol macroinitiator with molecular weight 8000 g/mol (PEG 8K, Aldrich) was dried at room temperature under vacuum for two days prior to polymerization. MALDI (matrix assisted laser desorption/ionization) and GPC (gel permeation chromatography) showed this polymer to be 8,900 g/mol in weight. Stannous (II) 2-ethyl hexanoate (Alfa Aesar) was used without further purification. Laponite® XLG used in this study was obtained from Southern Clay Products, Inc. (Gonzales, TX).

2.2. Synthesis of PLLA-PEO-PLLA triblock copolymer

Solution-synthesized PLLA-PEO-PLLA copolymers were prepared as previously reported⁷. Telechelic PEO macroinitiator was weighed into a dry 3-neck round bottom flask with a stir bar and attached to a condenser. The PEO was stirred and heated at 130 °C under nitrogen flow. Tin (II) 2-ethylhexanoate was added to the PEO, followed by immediate addition of lactide. The condenser was turned on and toluene was added to the reaction mixture. The mixture was refluxed for 24 hours under nitrogen flow, then diluted with THF, and precipitated using hexanes. The recovered precipitate was dried under vacuum at room temperature. The polydispersity indices were typically less than or equal to 1.1 as compared to narrow polystyrene standards using N,N-dimethylformamide (0.01 M LiCl) at 50°C as the eluent.

The polymers used in our study are listed in Table 1, where DP_{PLLA} is the total degree of polymerization of PLLA (both endblocks), DP_{PEO} is the degree of polymerization of the PEO midblock, and M_n is the number-average molecular weight of the entire triblock in kDa. The sample names indicate the total length of PLA block followed by a letter indicating the stereospecificity of PLA block, e.g., 58L refers to the polymer $PLA_{29}PEO_{202}PLA_{29}$ which is made using semi-crystalline PLLA blocks. The gels prepared by addition of laponite® nanoparticle solution to the polymers have been referred to as nanoparticle-reinforced gels in this study. Since the same concentration of laponite® solution (2 wt%) was added to all the polymers to make a 25 wt% gel, the nanoparticle reinforced gels have been named individually as “polymer sample name + lap.” For example at 58L + lap refers to a nanoparticle-reinforced 58L gel.

2.3. Rheology

PLLA-PEO-PLLA hydrogels were prepared by simple addition of a known quantity of nanopure water to the polymer to prepare a 25 wt% dispersion of the polymer in water. For preparing the nanoparticle-reinforced hydrogels, a dispersion of laponite® in water was first prepared for addition to the polymer. Laponite® XLG clay was added to nanopure water to make a 2 wt% dispersion. The system was then homogenized in a T25 Basic Ultra-Turrax homogenizer for ~ 2 minutes till the lumps of clay at the bottom of the vial broke and dispersed completely in water eventually forming a clear, homogeneous and stable dispersion. The dispersion was then kept at equilibrium for about half hour before addition to the hydrogel. This process was followed to ensure that we could get good exfoliation of clay. Hydrogels were prepared by slow addition of the laponite® dispersion to a measured amount of dried polymer sample in order to make samples with total concentration of solids, defined as

$$w_s = \frac{m(\text{polymer}) + m(\text{laponite})}{m(\text{polymer}) + m(\text{laponite}) + m(\text{water})} \times 100, \text{ fixed at 25 wt\%.} \quad (1)$$

All the hydrogel samples were kept at equilibrium for 1 day at room temperature and then heated at 80°C for 20 hours. The gels were again allowed to sit for 2–4 days. The final gels obtained were macroscopically homogeneous and translucent in appearance.

For rheology, gels were transferred to a TA Instruments AR2000 stress-controlled rheometer. Rheological measurements were performed using the cone and plate geometry (40 mm diameter cone with a 2° cone angle). To prevent the evaporation of water, a layer of corn oil was applied to surround the gels on the outside and in the gap between the cone and the plate. Another physical solvent trap was also used to cover the cone-plate assembly and water evaporation was not found to be significant for the temperatures and timescales investigated. Frequency sweep tests over a frequency range 0.01 Hz to 100 Hz, were done at constant strain amplitudes of 0.1% to measure G' and G'' (storage and loss moduli, respectively) at all the temperatures investigated. We know from our previous rheology experiments that the material behavior remains in the linear viscoelastic regime at the small strain amplitudes of 0.1% at which we probe the gels. A dynamic time sweep test at a strain amplitude of 0.1% and frequency of 1 Hz, was performed on the gels before each frequency scan to ensure that the gel systems have reached equilibrium. Also, after initial loading, the samples were allowed to equilibrate for 20–30 min before starting any tests in order to avoid any effects of shear during sample loading. The IRIS Rheology Platform (IRIS Development, LLC) was used to aid in performing the TTS analysis of the rheology data. While the original experiments were performed with the frequency in Hz, in performing the TTS analysis using IRIS we converted the frequency units to rad/s.

2.4. Small Angle X-Ray Scattering

SAXS measurements were performed on the hydrogels on a Molecular Metrology SAXS instrument in the W.M. Keck Nanostructures Laboratory at UMass Amherst. The instrument generates X-rays with a wavelength of $\lambda = 1.54 \text{ \AA}$ and 2-D multiwire detector with a sample to detector distance of 1.5 m. The same hydrogel samples as that used for rheology were used for SAXS characterization. The gel samples used for SAXS experiments were sandwiched between kapton films and this enclosed in an airtight sample holder. This assembly was then put in the X-ray beam path and the data was collected on the samples for 30 minutes.

3. Results and Discussion

Previous studies have shown that TTS can be performed on polymer melts and solution systems for which there are no temperature dependent structural changes or phase transitions in the system over the temperature range where TTS is performed.¹⁶ This has been found to be possible for polymer melts and/or amorphous single component polymer systems away from the glass transition temperature of the system.^{16,17} However, for more complex systems such as solutions and gels of block copolymers, TTS is frequently not possible due to morphological transitions and/or changes in polymer-solvent interactions with temperature. In particular, in physically gelling polymer systems, the physical processes that lead to junction formation in the gels evolve with time, because of which rheological measurements for such systems at very low frequencies or long time scales cannot be performed.

Below, we report the rheological response of PLLA-PEO-PLLA triblock copolymer gels in water, which behaves as a good solvent for PEO and a non-solvent for PLA, at temperatures

ranging from 15°C to 70°C. In these systems the PLLA blocks are semi-crystalline and therefore gelation in these copolymer systems occurs because of crystallization of the PLA block in addition to phase separation of the hydrophobic PLA blocks to form micellar aggregates. The latter reason is more commonly the cause of aggregation and gelation in ABA triblock copolymers in a solvent compatible for mid B block.^{18–21} We have shown in earlier publications^{22,23} that because of the presence of crystalline PLLA domains forming the network junction points in the gel, these systems form stiff gels and do not show a power-law terminal relaxation behavior at low frequencies as is commonly seen for associative network gels.^{4,18,19,24,25} Instead these systems show a viscoelastic solid-like behavior with G' and G'' displaying a relationship $G' \sim G'' \sim \omega^n$ over the entire frequency range. Such a relationship between the elastic and loss modulus is characteristic of dynamic mechanical behavior of a system at the gel point and has been seen previously for other physically gelling systems with crystalline physical junctions.^{26,27} The power law frequency dependence of these gels show that the junctions formed by these polymers do not relax over the time scales of the experiment and have a long lifetime, giving the appearance of 'permanent' junctions formed by chemically crosslinked systems.

In order to determine the effect of temperature on the nanoscale morphology of the PLLA-PEO-PLLA hydrogels, we performed small angle X-ray scattering experiments on 25 wt% gels of these polymers. The scattering spectra for 71L and 71L + lap systems at different temperatures are shown in figure 2. For clarity, spectra at higher temperatures have been shifted in intensity. We have shown previously that these systems form non-spherical "disk-like" micelles, (figure 1), with the PLLA blocks forming a crystalline core and PEO chains attached on the faces of PLLA disks forming the corona.^{28,29} The random orientation of these disk-like aggregates may lead to smearing of any peaks in the spectra, which is what we see in figure 2. Gelation in these systems occurs due to bridging between the aggregates caused by the two hydrophobic PLLA blocks on the same polymer chain attaching to PLLA cores of different aggregates. Figure 2 shows that the scattering spectra of the 71L and 71L + lap gels at temperatures ranging from 25°C to 80°C are nearly indistinguishable. Without shifting data at higher temperatures, the spectra overlap nearly perfectly (not shown). This demonstrates that the PLLA-PEO-PLLA systems do not show any significant change in the nanoscale morphology with increase in temperature and the three-dimensional network of the gel formed by crystalline PLLA junctions remains preserved. We observed the same behavior for other polymer gels having a different molecular weight of the PLLA block (data not shown).

Since the structure of the gels was found to be invariant upon change in temperature, TTS could be applicable to these materials. Frequency sweeps, measured isothermally at different temperatures, were superposed onto a master curve by shifting the curves in the x (frequency) direction through multiplication with a temperature dependent shift factor a_T to obtain final master curves with a reference temperature of 25°C. Master curves obtained for 66L, 71L and 89L systems are shown in figure 3. The superposition was done by matching the high frequency range of G' to that for the next lower temperature. As can be seen from the figure 3, the G' data overlaps very well for the entire range of temperatures and frequencies. The G'' data show some deviation from the master curve at higher frequencies. Similar TTS behavior has been observed in several types of physical gels, including thermoreversible gels based on poly(2-vinyl pyridine)-poly(ethyl acrylate)-poly(2-vinyl pyridine)/poly(4-hydroxysytrene) in ionic liquids,³⁰ borax-crosslinked polysaccharide gels,³¹ and associative gels of polyhedral oligomeric silsesquioxane (POSS)-containing copolymers.³² In our system, since this effect was seen for all three polymer gels and did not seem to vary with changes in temperature, we believe that it may be due to instrument effects or possibly due to some slippage of the gels during the rheological tests at high frequency. Interestingly, the final TTS master curves obtained for all the samples show the

dependence $G' \sim G'' \sim \omega^n$ over the entire frequency range. The values for the power law exponent (n) obtained upon fitting the curves are shown in table 2 and are found to be very low and in the range 0.04 – 0.06, indicating that the PLLA-PEO-PLLA hydrogel systems behave as stiff viscoelastic solids.³³

Another distinctive feature of the TTS curves obtained for the various hydrogel systems is that using this method we are able to obtain combined rheological information about these systems for almost 11 decades in frequency whereas a traditional rheological measurement gives us information about the rheological properties of a system for only 3–4 decades in frequency. The master curves also provide us information about the behavior of the system under small stress at very long time scales corresponding to small frequencies. We see that the hydrogels display a viscoelastic solidlike behavior with $G' \sim G'' \sim \omega^n$ and $G' \gg G''$ even at very small frequencies, which correspond to long timescales, even though they tend to soften with time leading to a decrease in their elastic modulus value. This information is particularly important for possible applications of these materials as cell scaffolds for soft tissue engineering, since it shows that these materials remain stable under a small constant stress for very long periods of time. The decrease in the elastic modulus of the polymer gels with increasing temperature can be ascribed to the glass transition and melting of the PLLA core and is discussed below.

In analyzing our data via TTS, we deliberately chose to superpose the data by only applying a horizontal shift factor, setting the vertical shift factor to unity. Because the data follow a power law dependence over a large frequency range, it is easy to see that superposition could also be achieved with both a horizontal and vertical shift. Classical theories of the linear viscoelasticity of polymer solutions and melts relate the vertical shift factor to thermal expansion,^{34,35} whereby the vertical shift factor b_T is approximately $\rho_0 T_0 / \rho T$. For water (recall that our systems are hydrogels), this ratio varies between 1.03–1.17 for the temperature range we have considered. Although the system density will vary with addition of polymer and with nanoparticles, the contribution of this effect is relatively minor, particularly given the experimental errors in rheological testing (discussed below). Thus, while applying a vertical shift factor that accounts for thermal expansion will change the horizontal shift factors we report, the impact will be small and likely within the experimental uncertainty.

Important details about the energetics of junction formation and the molecular processes that lead to gelation in the system that undergoes time-temperature superposition can be obtained by studying dependence of the shift factor a_t with temperature. Figure 4 shows the temperature dependence of the shift factors in an Arrhenius representation for 66L, 71L and 89L polymer gels. It was seen that in this representation, the slope of all the straight-line curves obtained broke abruptly between the temperatures of ~40°C and ~55°C. Thus, we performed fits on the sections of the curves before and after the point of change of the slope for all the systems to the Arrhenius equation;

$$a_t = \exp \left[-\frac{\Delta H_{app}}{R} \left(\frac{1}{T} \right) \right] \quad (2)$$

An apparent activation enthalpy (ΔH_{app}) for all the systems was thus computed for the two regions of the curve, the values for which have been tabulated in table 2.

The break in the slopes for all the curves occurs in the region 40–55°C, however there is clearly uncertainty in the values reported in Figure 4, and one could argue that the transition is not distinct for the highest molecular weight, 89L. The occurrence of the transition of

slopes in this temperature window is particularly interesting since it is very close to the glass transition temperature (T_g) of PLLA, which for PLA-PEO block copolymer systems has been reported to be 53–64°C.^{36–40} In the presence of PEO and water in the system, which may act as a plasticizer even though it is expected to interact negligibly with PLLA, T_g of PLLA is expected to be lower than the above value, which overlaps well with the transition region we observe. Therefore we believe that the transition region seen for all the polymer systems represents the apparent glass transition temperature ($T_{g,app}$) of the semi-crystalline cores formed by PLLA. The decrease in elastic modulus with temperature of the hydrogels below $T_{g,app}$ (region 1) is due to softening of the glassy regions of the PLLA semi-crystalline micellar cores that form the junction points in the network. As the temperature of the system is increased beyond $T_{g,app}$, a much faster decrease in the modulus of the gels is seen because of the increased mobility of the PLLA chains. This is an interesting result since it is not possible to detect the glass transition of the PLLA domains in the gel through DSC because of the evaporation of water. Additionally, even though a decrease in the modulus of the gels takes place with temperature due to increase in mobility of the PLLA blocks, the absolute value of the elastic moduli of all the systems still remains much greater than 1000 kPa, showing that the original crystalline junctions that contribute to the high strength of the network are still supporting the gel network. This is also consistent with the fact that the structure of the gels does not change with increasing temperature as seen through SAXS (figure 2). Because of this, superposition of the thermorheological data is possible at all temperatures even though the systems go through a transition zone in shift factors.

The description of the dependence of shift factors on temperature has commonly been described by an Arrhenius equation (eqn. 2) only far away from the T_g of the polymer system.¹⁴ We see however, that for our data, equation 2 fits the data very well separately for regions both above and below T_g . The activation enthalpy values obtained for both region 1 and region 2 are somewhat larger than that reported for many other ABA triblock copolymer systems in selective solvents. Examples include aqueous solutions of PEO capped with long chain alkanols^{18,41} with $\Delta H_{app} = 67\text{--}70$ kJ/mol and styrenic triblock copolymers⁴² with $\Delta H_{app} = 200$ kJ/mol. However, ΔH_{app} values of 400–500 kJ/mol have been reported for physical gels of poly(methyl methacrylate)-poly(tert-butyl acrylate)-poly(methyl methacrylate) by Inomata et al.¹. Activation energies obtained for associative triblock copolymer systems have been related to the activation energy for pullout of the terminal A block from the core of the aggregate, thereby breaking the junction formed by the polymer chain^{1,18,19,25}. Effectively this is the energy cost for transferring the terminal block from the aggregate core to the solvent. Since the PLLA chains in our triblock copolymer systems are associated not only because of the hydrophobic interactions but also because of the crystallization of PLLA, the energy required for junction pullout is expected to be on the order of and greater than the crystallization enthalpy of PLLA, which has been reported to be 146 kJ/mol for completely crystalline PLLA.³⁸ This value is of the same order but smaller than the ΔH_{app} we obtain for region 2, which is above $T_{g,app}$. For region 1 however, the ΔH_{app} are expected to be the energy required to increase the mobility of the polymer chains and soften the glassy regions of the PLLA polymer core. Overall, the large values for ΔH_{app} obtained shows that the PLLA chains interact strongly with each other and agrees with our previous observation that these polymer gels have very strong and ‘permanent’ junction points, which are responsible for the viscoelastic ‘solidlike’ rheological behavior of the physical gel network as described earlier.

A similar TTS analysis was performed on PLLA-PEO-PLLA hydrogels with added laponite[®] nanoparticles. We have shown previously⁸ that addition of laponite[®] aids in building new junctions in the gel because of adhesion of PEO chains from different aggregates on the same nanoparticles. At the same time the original junctions formed in the material due to the segregation of the hydrophobic PLLA chains and their crystallization

remain intact. This effect leads to an increase in G' of the gels due to an overall increase in the number of elastically effective chains in the network. It is notable that this occurs even through the total weight fraction of solids in the systems remains constant at 25 wt%.⁸

SAXS on the 71L laponite[®] reinforced gels at different temperatures in the range 28–75°C again shows that the internal structure of the hydrogels does not change due to the effect of temperature (figure 2). Similar data was obtained for all the other polymers as well. Hence TTS can also be performed on the nanoparticle-reinforced systems. The rheology of the nanoparticle-reinforced gels also shows viscoelastic solidlike behavior with G' and G'' showing a power law frequency dependence and follow the relation $G' \sim G'' \sim \omega^n$. The TTS master curves obtained for the nanoparticle reinforced 66L, 71L and 89L systems are shown in figure 5. The superposition achieved is again seen to be very good and the final master curves again show the power law frequency dependence as described above over nearly 8 decades in frequency. The power law exponents (n) obtained for all the systems are tabulated in table 3 and are seen to be very similar to the gels without added laponite[®].

In order to better understand the energetics of junction formation in the nanoparticle-reinforced gels and nature of the junctions formed by the nanoparticles with polymer, the temperature dependence of the shift factors a_T was fitted to equation (2), in a way similar to the neat polymer gels as done earlier. The graphs and the fits are depicted in figure 6 for nanoparticle-reinforced 66L, 71L and 89L gels. All systems again showed a break in the slope of the curves in the range 40–55°C. The slope of the curves obtained are different than those found for the neat polymer gels earlier, and the ΔH_{app} are tabulated in table 3. For region 2, the shift factors do not obey an Arrhenius relationship for the 71L+lap system, and so no value is reported for ΔH_{app2} . It is difficult to speculate on why this occurs; however, this conclusion is based on a very limited number of data points. Any error in the rheology for the temperatures corresponding to region 2 (55°C–70°C) could result in this deviation from Arrhenius behavior. The values of ΔH_{app1} for all the nanoparticle-reinforced polymer gels below T_g (region 1) are significantly lower than ΔH_{app1} for the corresponding neat polymer gels. This may be because ΔH_{app1} represents some type of averaged value of the junction strength that includes both the PLLA junctions and the PEO-laponite[®] junctions. Daga et al.¹⁴ recently reported values of ΔH_{app} for laponite[®]-PEO aqueous systems of 26.4 ± 0.8 kJ/mol. Since this value of ΔH_{app1} for PEO-laponite[®] bond formation is much lower than the ΔH_{app1} obtained for neat polymer gels (table 2), the average value of ΔH_{app1} for nanoparticle reinforced gels is expected to be much smaller than that of the neat polymer gels because of the presence of laponite[®]-PEO bonds in the system. The observation also supports our previous hypothesis that the addition of laponite[®] to the gels leads to formation of new laponite[®]-PEO bonds rather than laponite[®] just acting as a filler in the polymer matrix.

The values of ΔH_{app} we report are based on a limited number of data points, and as noted above, a small error in the rheology at one temperature can impact the apparent activation energies derived from fitting the shift factors. Thus, from the values of ΔH_{app} alone, it is difficult to discern trends in the energetics upon addition of nanoparticles or with different molecular weight endblocks. To aid in determining these types of trends, we have plotted the TTS shift factors for samples with and without nanoparticles together on an Arrhenius-type plot (Figure 7). While all of the data series show some curvature, we can consider the first derivative of these curves to represent some type of overall temperature-dependent activation energy. When plotted in this manner, we can see two trends emerge. First, for systems both with and without nanoparticles, the overall apparent activation energy increases as the molecular weight of the PLLA block increases. This is not unexpected, as we would expect the strength of association of the PLLA junctions to increase with PLLA molecular weight, regardless of whether the junctions are crystalline or glassy.

Second, in comparing samples with and without nanoparticles, it becomes apparent that samples with nanoparticles have a lower overall activation energy than samples without nanoparticles. This is likely due to the fact that the junctions formed from laponite[®]-PEO associations are weaker than those formed by association of the PLLA domains. As noted above, the strength of the laponite[®]-PEO has been estimated as approximately 26 kJ/mol,¹⁴ where the association strength of the PLLA junctions is likely 150–250 kJ/mol. This trend may not extend to other associative gels with nanoparticles and clearly depends on the relative strength of any polymer-nanoparticle associations as compared to the polymer-polymer associations. Thus, if the nanoparticles are used that adsorb polymer very strongly, it is likely that the activation energy of the system would increase upon addition of nanoparticles, rather than decrease. A more complicated question to consider is the effect of concentration of nanoparticles. If the overall activation energy represents some averaging of the effect of polymer-polymer junctions versus polymer-nanoparticle junctions, then clearly the effect of the polymer-nanoparticle junctions should become more pronounced as concentration increases. However, at some point the presence of nanoparticles will alter self-assembly of the polymer, likely leading to a sharp decrease in the apparent activation energy.

4. Conclusions

The energetics of association in PLLA-PEO-PLLA triblock copolymer gels with and without added nanoparticles was explored using TTS on small-amplitude oscillatory rheological measurements. SAXS shows that the nanoscale structure of these systems remains invariant over a temperature range of 25–70°C. Good superposition was achieved for these materials, and important information about the energetics of bond formation in the hydrogels was obtained by fitting the temperature dependence of the shift factors used for TTS to an Arrhenius equation. A break in the slope of the shift factors was seen in a temperature region that overlaps with $T_{g,app}$ for PLLA. Below $T_{g,app}$ we observe a decrease in G' with temperature, which we believe is due to an increase in mobility of the glassy regions of the PLLA junctions. Above $T_{g,app}$ the activation enthalpies obtained using the Arrhenius equation fits were similar to the PLLA crystallization enthalpy. This confirms that PLLA junction points in the hydrogel are semi-crystalline. Finally, addition of laponite[®] nanoparticle to the hydrogel system led to a reduction in the average value of the activation enthalpy for the gels. We believe the origin of this is the lower activation enthalpies for laponite[®]-PEO junctions, which reduces the average value of activation enthalpy for flow for the nanoparticle-reinforced polymer gels. Thus, laponite[®] nanoparticles are not simply acting as filler in the polymer matrix but adhesion of PEO on laponite[®] is taking place, which leads to formation of additional junction in the hydrogel thus contributing to enhancement in its mechanical properties.

Our results on the energetics of association of these somewhat unconventional disklike PLLA-PEO-PLLA micelles may yield insight into the assembly and rheology of related hydrogels of nonspherical micelles, for example, the novel “super-strongly segregated” disklike and sheetlike micelles recently described by Taribagil et al.,⁴³ comprising poly(perfluoropropylene oxide) (PFPO)-*b*-PEO-*b*-PFPO copolymers in water. We have also quantified the association enthalpy of the polymer-particle junctions in our gels. Understanding the interactions between PLA-based copolymers and inorganic nanoparticles is becoming increasingly relevant, as PEG-PLA polymers have recently been explored in the creation of dense gold nanoclusters for bioimaging⁴⁴ and in the fabrication of iron-polymer nanocomplexes for biological delivery.⁴⁵ Finally, we note that the use of PLA-PEO-PLA triblock gels in biomaterials applications continues to expand, from delivery of anti-cancer agents⁴⁶ to paclitaxel-eluting coatings for stents⁴⁷ to substrates for tissue engineering.⁴⁸ As

such, fundamental studies on the physics and rheology of PLA-PEO-PLA systems, such as ours, are important to the large-scale processing of these triblock gels for clinical use.

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Figure 1. Schematic of PLLA-PEO-PLLA triblocks forming associative disklike micelles with crystalline PLLA cores and PEO coronas, and addition of laponite[®] particles that adsorb PEO chains and form additional polymer-particle junction points.

Figure 2.

SAXS spectra for (a) 71L hydrogel sample and (b) 71L + lap hydrogel sample, obtained at temperatures ranging from 25°C–80°C. No changes in micellar assembly or structure occur over this temperature range. For clarity, the scattered intensities have been shifted by factors of 2 (45 C and 40 C data), 5 (55 C and 50 C data), 10 (65 C and 60 C data), and 20 (80 C and 75 C data). Without this shifting, the spectra overlap completely (not shown), again reflecting no change in the micellar structure with temperature.

Figure 3. TTS master curves for hydrogels of (a) 66L, (b) 71L, and (c) 89L polymers, with no added nanoparticles. TTS curves have a reference temperature of 25°C.

Figure 4. Arrhenius plots derived from TTS over 15–70°C for hydrogels of (a) 66L, (b) 71L, and (c) 89L polymers, with no added nanoparticles.

Figure 5. TTS master curve for (a) 66L+lap, (b) 71L+lap, and (c) 89L+lap hydrogels at a reference temperature of 25°C.

Figure 6. Arrhenius plots derived from TTS over 15–70°C for (a) 66L+lap, (b) 71L+lap, and (c) 89L+lap hydrogels.

Figure 7.
Comparison of TTS shift factors for samples with and without nanoparticles. Lines are guides for the eye.

Table 1

Characteristics of PLA-PEO-PLA triblock copolymers synthesized.

Sample	DPPLLA	DPPEO	M _n (kDa)
66L	66	202	13.5
71L	71	202	13.9
89L	89	202	15.2

Table 2

Values of power law exponent n for PLLA-PEO-PLLA hydrogels obtained by fitting the TTS master curve data, and activation enthalpies calculated from the temperature-dependence of the frequency shift factors to equation 2. Activation enthalpies in J/g are computed by dividing values in kJ/mol with the total molecular weight of the PLLA block used. Errors reported in fitted parameters are based on experimental uncertainty in the rheological measurements of 5% and on the uncertainty derived from the goodness-of-fit.

Sample	$N (G')$	$N (G'')$	$\Delta H_{app1} (kJ/mol)$	$\Delta H_{app1} (J/g)$	$\Delta H_{app2} (kJ/mol)$	$\Delta H_{app2} (J/g)$
66L	0.061 ± 0.003	0.065 ± 0.003	280 ± 30	59 ± 5	440 ± 30	93 ± 5
71L	0.054 ± 0.003	0.060 ± 0.003	240 ± 10	47 ± 2	610 ± 30	119 ± 6
89L	0.042 ± 0.002	0.042 ± 0.002	380 ± 30	60 ± 5	480 ± 20	75 ± 4

Table 3

Values of power law exponent n for the nanoparticle-reinforced PLLA-PEO-PLLA hydrogels from the TTS master curve data and H_{app} calculated from the temperature dependence of the frequency shift factors to equation 2. Activation enthalpies in J/g are computed by dividing the values in kJ/mol with the total molecular weight of the PLLA block used. Errors reported in fitted parameters are based on experimental uncertainty in the rheological measurements of 5% and on the uncertainty derived from the goodness-of-fit.

Sample	$N (G')$	$N (G'')$	$\Delta H_{app1} (kJ/mol)$	$\Delta H_{app1} (J/g)$	$\Delta H_{app2} (kJ/mol)$	$\Delta H_{app2} (J/g)$
66L+lap	0.052 ± 0.003	0.062 ± 0.003	109 ± 6	23 ± 1	146 ± 7	31 ± 2
71L+lap	0.054 ± 0.003	0.051 ± 0.003	190 ± 10	38 ± 2	-	-
89L+lap	0.043 ± 0.002	0.043 ± 0.002	230 ± 10	36 ± 2	50 ± 10	81 ± 4