Nonsolvent-induced morphological changes and nanoporosity in poly(l-lactide) films†

P. Shaiju,ab N. Sanjeeva Murthy b,c and E. Bhoje Gowd ab†

The role of a nonsolvent in controlling the crystallization and morphology of solvent-crystallized poly-(l-lactide) (PLLA) films was investigated using various microscopy techniques and small- and wide-angle X-ray scattering (SAXS/WAXS). PLLA films crystallized in THF and acetone had 40–80 μm spherulites. When water was present in the solvent, a completely different morphology was observed with nanosized voids and the surfaces of the films were smooth. In contrast, SEM studies revealed that the films crystallized in acetone and THF which had macroporous structures, had larger voids and film surfaces were rough because of the presence of globular structures. Voids appeared within the spherulites in the THF/water treated film, whereas crystals nucleated at the surface of the nanosized voids in acetone/water treated PLLA films. The formation of such voids is attributed to the interface-enhanced crystal nucleation in a solvent/nonsolvent system where the nonsolvent increases the polymer crystal nucleation and the subsequent evaporation of the nonsolvent. The method described in this work can be extended to other polymers to control the morphologies of polymer films during solvent-induced crystallization.

Introduction

Solvent-induced crystallization of polymers is an important subject from both scientific and technological perspectives. In many advanced polymer applications that rely on processing techniques such as spin-casting, electrospinning, and wet spinning, a solvent is required. There have been significant efforts carried out to understand the solvent-induced crystallization of semicrystalline polymers.1–7 Solvents enhance the segmental mobility of polymer chains by lowering the glass transition temperature (Tg) of the polymer, and as a result, the polymer chains can rearrange themselves to a lower free energy state.5,7 Depending on the nature of the interaction between the polymer and solvent molecules, in some cases, the solvent molecules cocrystallize with polymer chains.5,8–10 Extensive studies have been carried out to understand the solvent-induced crystallization behavior of polymers such as syndiotactic polystyrene (sPS),1,4,5,7,8,11–14 poly(ethylene terephthalate),10 poly(ethylene imine).6 Poly(l-lactide) (PLLA), the most common stereoisomer of polylactide, is a widely used biobased polymer obtainable from renewable natural resources. In addition to being a commodity plastic used to make fibers and packaging films, PLLA is used in biomedical applications such as implants, surgical sutures, coronary stents and bone fixation devices.15–19 PLLA is known to crystallize in different polymorphic forms in the presence of solvents.5,20–23 The solvent-induced crystallization of PLLA is well understood both in bulk and thin films in the presence of organic solvents. Based on the theoretical studies, it has been predicted that poorer solvent enhances crystal nucleation and the nucleation occurs at the interfaces only when the solvent becomes sufficiently poor.24 In order to understand the crystal nucleation process in the presence of poor solvents, water was chosen as a nonsolvent to study the crystallization behavior of PLLA. Vyavahare et al. studied the crystallization behavior of poly(lactic acid) in water and demonstrated that water molecules residing in the amorphous phase play a significant role in enhancing the PLLA crystallization rate.25 However, a detailed investigation of the role of water molecules in the nucleation, structure and morphology of PLLA has not yet been conducted.

In the present work, we study the solvent-induced crystallization of PLLA under ambient conditions using aqueous miscible organic solvents such as acetone and THF, and their water mixtures. We investigated the morphologies at different length scales using polarized light microscopy, atomic force microscopy, scanning electron microscopy and wide-angle and small-angle X-ray scattering. It was found that water plays a significant role in determining the crystal nucleation and morphology of the solvent-crystallized PLLA films.
Results and discussion

Crystallization of amorphous PLLA films was induced by direct immersion of films into various solvents at 30 °C for three days and the PLLA films were characterized after drying the crystallized films at room temperature. Fig. 1 shows the POM images of PLLA thin films crystallized in THF, acetone, THF/water, and acetone/water mixtures. The volume percentages of the solvents in THF/water and acetone/water mixtures were kept as 50/50 (v/v). The PLLA film crystallized in THF and acetone shows spherical particles (spherulites) with diameters between 40 and 80 μm [Fig. 1(a and b)]. Unlike the melt-crystallized spherulites, irregular growth of the highly disordered spherulitic crystallites was observed. On the other hand, PLLA films crystallized in the THF/water mixture show smaller distorted spherulites [Fig. 1(c)] and PLLA films crystallized in the acetone/water mixture show uniformly sized tiny crystallites [Fig. 1(d)] in the nanometer size range. The increase in the number of spherulites and the decrease in the average diameter of the spherulites indicate that water enhances the nucleation in PLLA films. Since it is difficult to identify the boundaries, and hence the spherulite sizes from the POM images, AFM measurements were carried out on thin films of PLLA crystallized in various solvents to gain more insight into the size and morphology of the spherulites.

AFM images of PLLA films crystallized in acetone and the acetone/water mixture are shown in Fig. 2 (dried films). Consistent with the POM results, the PLLA film crystallized in acetone showed larger spherical particles (~30 μm) with high surface roughness [Fig. 2(a)]. The dark areas around the spherulites in Fig. 2(a) are not voids but are spaces inaccessible to the tip; these are due to the height difference among the spherulites [see Fig. S2(b), ESI†]. Unlike the melt-crystallized spherulites, irregular growth of the highly disordered spherulitic crystallites was observed. On the other hand, PLLA films crystallized in the THF/water mixture show smaller distorted spherulites [Fig. 1(c)] and PLLA films crystallized in the acetone/water mixture show uniformly sized tiny crystallites [Fig. 1(d)] in the nanometer size range. The increase in the number of spherulites and the decrease in the average diameter of the spherulites indicate that water enhances the nucleation in PLLA films. Since it is difficult to identify the boundaries, and hence the spherulite sizes from the POM images, AFM measurements were carried out on thin films of PLLA crystallized in various solvents to gain more insight into the size and morphology of the spherulites.

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Marubayashi et al. reported the formation of a rod-like lamellar morphology in PLLA thin films crystallized under high-pressure carbon dioxide.23 However, their study did not show the pathways of the formation of the rod-like lamellar morphology. Here in our work, the presence of a nonsolvent, water, enhances the nucleation during solvent evaporation and brings about liquid–liquid phase separation. Even though acetone and water are miscible, when amorphous PLLA is dipped in an acetone/water mixture, the PLLA film swells by selectively absorbing acetone. As a result, water molecules phase separate from the swollen polymer domains due to the immiscibility, and form small droplets within the PLLA films. When the sample is taken out from the solvent mixture, acetone evaporates rapidly due to its low boiling point, and the water droplets present in the sample act as an impurity that initiates the crystal nucleation. With time, water will also evaporate forming tiny voids on the surface of the film. Generally, heterogeneous nucleation requires less energy and occurs preferentially at phase boundaries, surfaces, impurities, etc. since the effective surface energy will be lower at such sites. The lower surface energy reduces the free energy barrier and facilitates the nucleation.26 As is evident from the AFM image [Fig. 2(b)], the nucleation occurs at the interfaces of water in PLLA films swollen in the acetone/water mixture and upon drying these nuclei grow to form lamellae that give rise to the observed rod-like lamellar morphology. Evaporation of water results in the formation of nanovoids in polymer films. These results revealed that the presence of water molecules induces the rapid nucleation and faster growth rate of crystals.

Another feature of the morphology is porosity that occurs in crystalline polymer films obtained by solvent evaporation.27,28 SEM images were obtained to understand the surface morphology and surface roughness of PLLA films crystallized in various solvents. In agreement with the POM results, spherical aggregates are observed in PLLA films crystallized in THF and acetone [Fig. S2(a) and (b), ESI†]. These spheres are similar to the polyethylene “globs” observed by quenching the polyethylene solutions in xylene.29 Such globules are formed due to the precipitation/phase separation process occurring during the solidification process, and are packed with crystalline lamellae as evidenced by the strong birefringence in POM images [Fig. 1(a) and (b)] and by the crystalline features in the WAXS patterns (Fig. S3, ESI†). These samples had large porosity and high surface roughness. In contrast, no such globular structures were observed in PLLA films crystallized in THF/water and acetone/water mixtures, and the films had negligible surface roughness. It is also worth mentioning here that the films crystallized in organic solvents (acetone and THF) were opaque due to the larger spherulite sizes and high surface roughness of the
crystallized films. On the other hand, the films crystallized in the mixture of solvents (THF/water and acetone/water) are translucent. Further, the transparency of PLLA film is varied with the nature of the solvent used for the crystallization of PLLA in the solvent/water mixture. The transparency of the PLLA film crystallized in acetone/water mixture is almost comparable with the melt-quenched amorphous PLLA. The PLLA film crystallized in the THF/water mixture is less transparent compared to the film crystallized in the acetone/water mixture.

In solvent-induced crystallization, several factors including solvent evaporation rate, interfacial tension between the polymer and the solvent, viscosity, degree of supercooling ($\Delta T$), and rate of film shrinkage control the rates of nucleation and growth. In both acetone and THF crystallized films, the solvent evaporates quite rapidly (in about 30 s) because of their low boiling points, and crystal nuclei are generated as a consequence of supersaturation, similar to crystallization from a melt with different cooling rates, and this results in the formation of spherulites. Upon drying the swollen film, the solvent molecules are expelled out from the crystal growth front to the adjacent amorphous region and the fast evaporation of these agglomerated solvent molecules from the constrained amorphous region leads to the formation of porous structures and surface roughness. However, the presence of water created a different scenario for the crystallization of PLLA. Upon exposure of the swollen film to air, unlike the organic solvents, the solvent evaporation rate in PLLA films in the presence of water is slow because of the interactions between the solvent and water. The crystal growth rate $G$ is diffusion-controlled and it is linearly proportional to supercooling $\Delta T$ in solution grown crystals.\textsuperscript{23,20} DMA results, which will be discussed later, revealed that PLLA films immersed in water mixtures have sufficiently high mobility (lower $T_g$) and, as a result, high supercooling ($\Delta T$). In addition, the slower evaporation of acetone or THF from the PLLA matrix with the water mixture and the residence time of these solvents might also influence the supercooling ($\Delta T$). As a result different morphologies are observed in water mixtures.

SAXS measurements were carried out to further understand the morphology related to the lamellar structure. Fig. 3(a) shows that the central diffuse scattering decreases considerably when water is added to either THF or acetone. Upon immersing in silicone oil, the intensity of the diffuse scattering decreased further [Fig. 3(b) and (c)], and almost disappeared in the acetone/water mixture [Fig. 3(c)], suggesting that the central diffuse scattering arises from the voids. The central part of the diffuse scattering was used to estimate the size of the voids using Guinier analysis (Fig. S4, ESI\textsuperscript{+}).\textsuperscript{3,12} Although diffuse scattering from the nanometer sized crystallites occurs in the same regions as the voids, the contrast between the crystallites and the surrounding amorphous matrix is much smaller than that between the void and the surrounding polymer (crystalline and amorphous PLLA densities are 1.29 and 1.25 g cm\textsuperscript{-3}).\textsuperscript{3} Hence, central diffuse scattering can be, for the most part, attributed to the voids. In all the samples, with the exception of acetone/water and THF/water crystallized samples immersed in silicone oil, the approximate diameter of the voids is $23.4 \pm 2.8$ nm. Larger voids that are seen in SEM images are not accessible with the SAXS data. Fig. S5 (ESI\textsuperscript{+}) shows the Lorentz-corrected SAXS patterns of THF and acetone treated samples before and after immersing in silicone oil, where a clear SAXS peak was observed after immersing in silicone oil.

The WAXS patterns (Fig. S3, ESI\textsuperscript{+}) of solvent-crystallized, dried PLLA films show well-defined X-ray reflections at $2\theta = 12.5^\circ$, $14.8^\circ$, $16.8^\circ$, $19.1^\circ$, and $22.5^\circ$ irrespective of the solvent used for the crystallization and these reflections were assigned to the $\alpha$ form.\textsuperscript{34} The absence of the characteristic reflection of the $\alpha'(\beta)$ form at $2\theta = 24.6^\circ$ indicates that the amorphous PLLA directly crystallized exclusively into the $\alpha$ form in the presence of solvents.\textsuperscript{15–37} It should be noted here that the treatment of amorphous PLLA with THF at sub-ambient temperatures yields $\varepsilon$ cocrystals.\textsuperscript{9,20,21} However, in the present study, the crystallization in THF was carried out at $30^\circ$ C, which favoured the formation of the $\alpha$ form. It is also worth mentioning here that Rizzo \textit{et al.} observed uniplanar orientations of cocrystalline phases in solvent crystallized PLLA films prepared at lower temperatures;\textsuperscript{20} such uniplanar orientation was not observed in the present study. It is possible that this could be because the polymer crystallized in the $\alpha$ form, and did not cocrystallize after the solvent induced crystallization of the amorphous PLLA films at room temperature.

Solvents are also known to affect the $T_g$ of polymers. For example, Tashiro and co-workers measured the $T_g$ of sPS in different solvent environments and showed that the $T_g$ was shifted to sub-ambient temperatures depending on the solvent used for the

![Fig. 2](image-url) AFM height images of PLLA films crystallized in (a) acetone and (b) acetone/water mixture.
swelling experiments. To identify the variation in the $T_g$, DSC measurements were carried out for the solvent-crystallized PLLA samples (dried films). Fig. 4(a) shows the DSC thermograms obtained during the first heating. The scans show the endotherm at $\sim 177^\circ C$ corresponding to the melting of the $\alpha$ form of PLLA. No other transitions corresponding to the $\gamma'(\delta)$-to-$\alpha$ or $\epsilon$-to-$\alpha$ are present in the DSC thermograms indicating that all the solvent-crystallized samples directly crystallized into the $\alpha$ form.

Unlike the cocrystals, in the $\alpha$ form, the residual solvents mainly reside in the amorphous phase. In addition to the

![DSC thermograms obtained for PLLA films crystallized in various solvents at 30 °C for three days. (b–d) tan$\delta$ curves measured using DMA. (b) Amorphous PLLA, (c) PLLA films crystallized in THF and THF/water mixture, and (d) in acetone and acetone/water mixture.](image-url)
melting peak, broad endotherms were observed in each thermogram in the temperature range of 30–120 °C. These endotherms are due to the evaporation of residual solvents as shown in TGA (Fig. S6, ESIF). TGA measurements show that 13, 15, 8, and 10 wt% of residual solvents were present in THF, THF/water, acetone and acetone/water crystallized PLLA samples, respectively. These broad endotherms prevent us from using the DSC scans to measure the \( T_g \). The re-heat scans, which would have eliminated the contribution to the DSC traces and which could have been used to obtain the \( T_g \) were not used because we were interested in the influence of the solvents on the thermal behavior. Therefore, the \( T_g \) values of the PLLA films were measured by dynamic mechanical analysis (DMA). The \( T_g \) calculated from the tan \( \delta \) plot for the amorphous PLLA is ~62 °C [Fig. 4(b)], which is in good agreement with the DSC value. Among the solvent-crystallized PLLA films, the film from the acetone/water mixture had the lowest \( T_g \) (~47 °C) [Fig. 4(d)] and the film crystallized in THF showed the highest \( T_g \) (~60 °C) [Fig. 4(c)], almost similar to that of amorphous PLLA, even though there was 13 wt% of residual solvent in the sample (Fig. S6, ESIF). On the other hand, the \( T_g \) of PLLA crystallized in acetone was found to be ~55 °C [Fig. 4(d)], even though the amount of residual solvent with acetone is lower than that with THF (8% vs. 13%) and the \( T_g \) was ~50 °C for the sample crystallized in the THF/water mixture [Fig. 4(c)]. This reduction of \( T_g \) is due to the plasticization effect and it depends on the strength of interaction between the amorphous PLLA chains and solvent.\(^7\)

Recently, by studying the crystallization behavior of PLLA ultrathin films induced by dichloromethane, acetone, and chloroform, Wu et al. showed that the solvent-specific competition between solvent-induced crystallization and dissolution plays an important role in determining the crystallization rate and morphology of PLLA.\(^3\) These effects were explained by the solubility parameters. The solubility parameter of PLLA is similar to that of acetone and is slightly higher than that of THF (\( \delta_{\text{PLLA}} = 9.7 \text{cal}^{1/2} \text{cm}^{-3/2} \), \( \delta_{\text{acetone}} = 9.8 \text{cal}^{1/2} \text{cm}^{-3/2} \) and \( \delta_{\text{THF}} = 9.1 \text{cal}^{1/2} \text{cm}^{-3/2} \)). Thus, PLLA is expected to interact more strongly with acetone than with THF. This is consistent with the conclusions of Naga et al. who investigated the crystallization of PLLA in various organic solvents including acetone and THF, and found that acetone was the effective solvent for expediting the crystallization of PLA.\(^5,39\) Thus, based on the present study and the published literature, it is clear that the segmental mobility of PLLA chains and crystallization rate are higher in acetone than in THF.

Water is a nonsolvent that brings about the liquid–liquid phase separation. TGA data (Fig. S6, ESIF) show that the samples crystallized in the acetone/water mixture and the THF/water mixture contain ~2 wt% more residual solvent compared to the samples crystallized in acetone and THF. Since solvent is not likely to be present in the crystalline domains, we speculate that this 2 wt% excess residual mass is due to water molecules in the amorphous phase of PLLA. Absorption of water by PLLA, a hydrophobic polymer, is far lower than that of organic solvents. Vyawahare et al. showed that the equilibrium water uptake in PLLA was small in the solid state (~1 wt%).\(^25\) From the DMA results, it is evident that the 2 wt% of residual water molecules present in the amorphous phase exerts a significant influence on the segmental mobility of PLLA: \( T_g \) of PLLA crystallized from water mixtures is ~8 °C lower than those from the organic counterparts. A similar observation has been reported and it was attributed to the plasticizing effect of water.\(^25,40\) These findings indicate that the presence of water significantly enhances the segmental mobility of PLLA chains.

Conclusions

The nonsolvent, water, appears to interfere with the unimpeded crystal growth processes. While PLLA films crystallized in acetone and THF were spherulitic, the spherulitic morphology was disturbed in the THF/water mixture, and absent in the acetone/water mixture. The surface morphology was found to have a strong correlation with the nature of solvent used for the crystallization. Both acetone and THF treated films showed larger spherical particles with high surface roughness. On the other hand, the surface roughness was comparatively less in THF/water and negligible in acetone/water treated films. AFM results revealed the formation of nanosized voids in the films treated with water mixtures. The solvent evaporation rate, interfacial tension between the polymer and the solvent, viscosity, degree of supercooling (\( A_T \)), and film shrinkage rate upon the removal of the solvent from the films affect the formation of different morphologies.

Experimental

Materials

PLLA, having \( \text{M}_{\text{w}} \sim 260,000 \), and \( D \sim 1.5 \) was purchased from Sigma-Aldrich. Acetone (purity \( \geq 99% \)) was supplied by SD Fine Chemicals Limited. THF (purity \( \sim 99.9% \)) was purchased from Merck. The solvents were used as received.

Sample preparation

Amorphous films were prepared by melting PLLA pellets by keeping at \( \sim 200 \) °C, followed by sudden quenching in liquid nitrogen. Such obtained films were directly dipped in various organic solvents such as THF, acetone, THF/water, and acetone/water mixtures for three days. Even after the immersion of PLLA films in THF and acetone for three days, no dissolution of films was observed. However, it was observed that PLLA films were swollen in these solvents. In the case of very thin films used for some of the measurements, the dissolution was controlled by reducing the immersion time. In THF/water and acetone/water mixtures, the volume percentages of the solvents were maintained as 50/50 (v/v). After removing from the solvents, the films were wiped gently with a dry tissue and kept at room temperature for 5 min before the measurements. Dried films thus obtained were used for all the measurements.

Characterization

Polarized optical microscopy (POM) measurements. The spherulitic morphology of the samples (thickness \( \sim 100 \mu \text{m} \))
was analyzed using a Leica DFC 490 polarized light optical microscope.

**Atomic force microscopy (AFM) measurements.** The surface morphology of solvent-crystallized PLLA films was probed using a Bruker Multimode AFM-3COCF in the tapping-mode at room temperature. Antimony doped silicon cantilever tips with a resonance frequency of 300 kHz and a spring constant of 40 N m\(^{-1}\) were used. Films (thickness ~200 \(\mu\)m) pasted on a silicon wafer substrate were used for the imaging.

**Scanning electron microscopy (SEM) measurements.** The surface morphology of the PLLA films was analyzed with the help of a scanning electron microscope (Zeiss EVO 18 cryo SEM). The film (thickness ~1 mm) was directly pasted onto a stub using a double face adhesive tape and subjected to a thin gold coating before the analysis. The measurements were carried out at an accelerating voltage of 20 kV.

**X-ray measurements.** Wide- and small-angle X-ray scattering (WAXS/SAXS) measurements were performed using a XEUS SAXS/WAXS system from Xenocs (operating voltage: 50 kV and current: 0.60 mA). The source of X-ray was Cu K\(_\alpha\) radiation with wavelength \(\lambda = 1.54 \text{ Å}\). The measurements were taken in the transmission mode geometry. The thickness of the films used for the X-ray measurements was ~1 mm. The 2D images were recorded on a Mar 345 detector (Image plate), and the obtained images were azimuthally averaged using the Fit2D software. Silver behenate and silicon powder were used to calibrate the sample to detector distance for SAXS and WAXS, respectively. The detector was set at 1050 mm and 221.75 mm from the sample to detector distance for SAXS and WAXS, respectively. The detector was set at 1050 mm and 221.75 mm from the sample to detector distance for SAXS and WAXS, respectively.

Guinier analysis was carried out to estimate the pore sizes.\(^\text{31,32}\) The diameter \((D)\) was determined from the radius of gyration \((R_g)\) assuming that the pores were spherical.

\[
I(q) = I(0) \exp \left(-\frac{R_g^2 q^2}{3}\right) \\
D = 2 \times \sqrt{\frac{5}{3}} R_g
\]

The linearity of the Guinier plot at \(q < 0.2 \text{ nm}^{-1}\) indicates that the pores can be considered as widely dispersed in the sample.

**Differential scanning calorimetry (DSC).** DSC measurements were carried out using a TA Instruments DSC Q2000 model equipped with a refrigerated cooling system. The solvent-crystallized samples were heated from 0 to 200 °C at a heating rate of 10 °C min\(^{-1}\), under a nitrogen atmosphere.

**Dynamic mechanical analysis (DMA).** Amorphous samples for the DMA measurements were prepared by melting the PLLA pellets by keeping between two aluminium plates at ~200 °C, followed by sudden quenching in liquid nitrogen. These samples were dipped in various solvents for three days. The measurements were performed in the tension mode at a frequency of 1 Hz with an amplitude of 5 μm. The samples, having the dimension \(35 \times 4 \times 1 \text{ mm}^3\), were heated from room temperature to 150 °C at a heating rate of 2 °C min\(^{-1}\).

**Thermogravimetric analysis (TGA).** The solvent content in the PLLA films (thickness ~1 mm) treated with various solvents was measured using a TA Instruments TGA Q50. The measurements were carried out under a nitrogen atmosphere, at a heating rate of 10 °C min\(^{-1}\).

**Conflicts of interest**

The authors declare no competing financial interest.

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