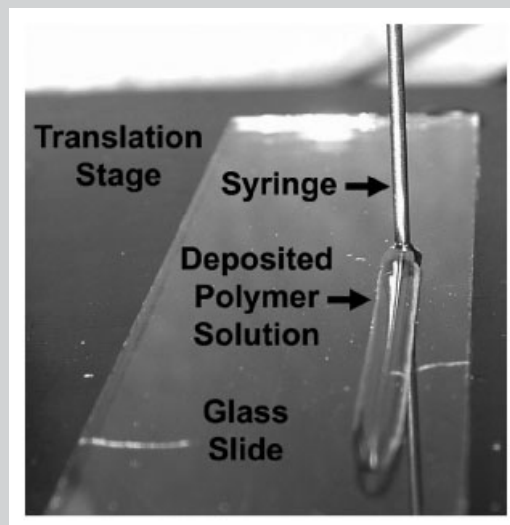


Summary: A method for rapidly determining the modulus of polymer blends was developed. A polymer blend gradient library of poly(L-lactic acid) (PLLA) and poly(D,L-lactic acid) (PDLLA) was created in the form of a strip-shaped film and characterized with FTIR microspectroscopy. Nanoindentation measurements were made along the gradients to obtain modulus data over a wide range of PLLA-PDLLA blend compositions. This novel, high-throughput approach to material characterization provides engineers with a technique to accelerate the development of materials.

Deposition of the polymer composition gradient.



High-Throughput Method for Determining Modulus of Polymer Blends

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Introduction

Manufacturing industries have a history of using polymer blending as an efficient method to create new materials with desirable properties and nearly one quarter of polymers are used in blends.^[1,2] Blending can be used to optimize modulus, strength, morphology and crystallinity and for these reasons blending is also receiving attention from the tissue engineering community.^[3–6] In order to accelerate

the development of polymer blends, we have developed a high-throughput method for determining their modulus. The basic premise of this new approach is to make nanoindentation measurements upon polymer composition gradients.

Using a three-syringe pump system and a mixing vial,^[6] PLLA and PDLLA were mixed to create a composition gradient in the barrel of a syringe. The polymer solution was deposited from the syringe in a line onto a flat substrate (Figure 1). Previously,^[6] the bead was spread with a knife into a wider, thinner film, but here we let the bead dry into a thicker “strip” film (thickness 4 μm). We chose to make thicker films since determining the modulus of sub-micrometer thin films can be challenging.^[7] High-resolution, automated FTIR microspectroscopy was used to resolve the composition of the gradients and automated

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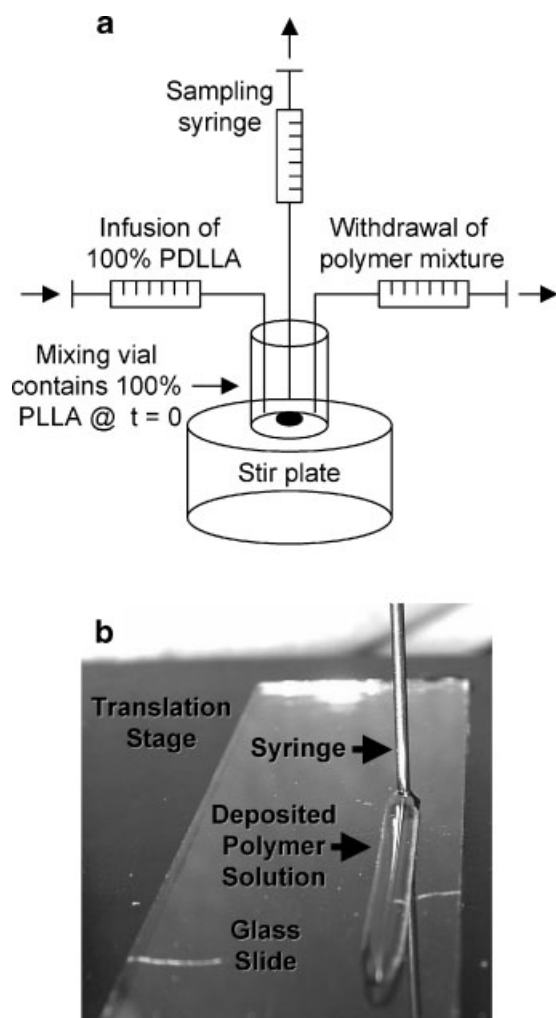


Figure 1. a) Diagram of the syringe system used to create the polymer composition gradients. Starting with 2 mL of pure PLLA solution in the mixing vial, pure PDLLA solution is pumped in at $2 \text{ mL} \cdot \text{min}^{-1}$ from the left and mixed with the PLLA. The mixture is removed by the pump on the right at a rate of $4 \text{ mL} \cdot \text{min}^{-1}$ and the composition of the mixing vial goes from 100% PLLA at $t=0$ to nearly 100% PDLLA at $t=2$ min. The overhead syringe samples the mixing vial during the 2 min to create a composition gradient in the barrel of the sampling syringe which is then deposited onto the substrate; b) The polymer blend gradient being deposited onto the reflective glass substrate as a strip film is shown. An automated syringe pump and an automated translation stage were used for this procedure.

nanoindentation was used to determine their modulus. Combining these data yields a final plot of modulus versus PLLA-PDLLA blend composition and provides a high-throughput method for determining the modulus of polymer blends.

Experimental Part

Six composition gradients were made from PLLA and PDLLA using a modification of published methods^[6] by depositing 1% mass fraction solutions in chloroform (PDLLA: $\bar{M}_w =$

330 000–600 000; PLLA: $\bar{M}_w = 300 000$; Polysciences, Warrington, PA) onto a flat substrate. Briefly, PDLLA was infused from a syringe ($1 \text{ mL} \cdot \text{min}^{-1}$) into a mixing vial containing PLLA (2 mL) while a second syringe removed the polymer mixture ($2 \text{ mL} \cdot \text{min}^{-1}$). Meanwhile, a third syringe sampled the mixing vial (0.075 mL per 2 min), creating a gradient along the barrel of the syringe (Figure 1a). The gradient was deposited in a line onto a reflective glass slide^[8] (Kevley Technologies, Chesterland, OH) using an automated syringe and a motorized stage (Figure 1b). Previously,^[6] the bead was spread with a knife into a wider, thinner film, but here we let the bead dry into a thicker “strip” film ($4 \mu\text{m}$ approximate thickness) making it more amenable to automated nanoindentation measurements. The strip films dried in air within 30 s after being deposited.

In addition, five discrete blend strip films (0, 25, 50, 75 and 100% mass fraction PLLA) were made for calibrating the FTIR measurements^[8] and five discrete “thick droplet” specimens were made to verify the accuracy of nanoindentation on the gradients. The thick droplet specimens (profilometry thickness $13 \mu\text{m}$) were made in triplicate by allowing droplets ($200 \mu\text{L}$) of polymer solutions to dry on glass slides. All gradients and control films were melted at 200°C for 5 min (above T_m for PLLA) and then annealed at 120°C for 8 h (between T_g and T_m) under nitrogen to remove residual solvent and induce crystallization of the PLLA. The strip films were approximately $4 \mu\text{m}$ thick after melting and annealing as determined by profilometry (Dektak 8 Stylus Profilometer, Veeco, Woodbury, NY).

The PLLA-PDLLA gradients and control discrete blends were mapped with FTIR reflection-transmission microscopy (FTIR-RTM)^[8] using a Nicolet Magna-IR 550 FTIR spectrophotometer (Madison, WI) interfaced with a Nic-Plan IR microscope with an automated stage (Spectra-Tech, Inc., Shelton, CT, USA) and the Atlus mapping software (Thermo Electron Corp., Madison, WI). Matrices of spectra (between 4000 cm^{-1} to 650 cm^{-1} (spectral resolution 8 cm^{-1} , 32 scans per spectrum, spot size $0.2 \text{ mm} \times 0.2 \text{ mm}$) for each film. The 1270 cm^{-1} peak area (ester C–O stretch)^[9] is dependent on PDLLA concentration whereas the 1450 cm^{-1} peak (methyl asymmetrical bending)^[9] is constant and thus serves as an internal standard.^[8] The maps were processed as ratios between the areas of the 1270 cm^{-1} and the 1450 cm^{-1} peaks ($1246\text{--}1286 \text{ cm}^{-1}$ and $1420\text{--}1500 \text{ cm}^{-1}$ spectral regions, respectively) and presented as color contour maps in Figure 2a. The color thresholds for these maps were adjusted manually to achieve optimal color contrast between the ends of the gradients. Using the same thresholds for all maps enables direct visual qualitative comparison between the six gradients.

For quantitative determination of the compositions of the gradients (Figure 2b), the maps of the control discrete blends and maps of the gradients were imported into the ISys software package (Spectral Dimensions Inc., Olney, MD). The ratios between the 1270 cm^{-1} and the 1450 cm^{-1} peak areas were calculated for all spectra in the same spectral regions used in processing the color contour maps. A calibration curve (linear regression, $R^2 = 0.998$) was constructed from the discrete blend strip films (25, 50, 75 and 100% PLLA) by plotting the peak ratios (ratio of 1270 cm^{-1} peak and the 1450 cm^{-1} peak) versus the fraction of PLLA in each discrete film. This cali-

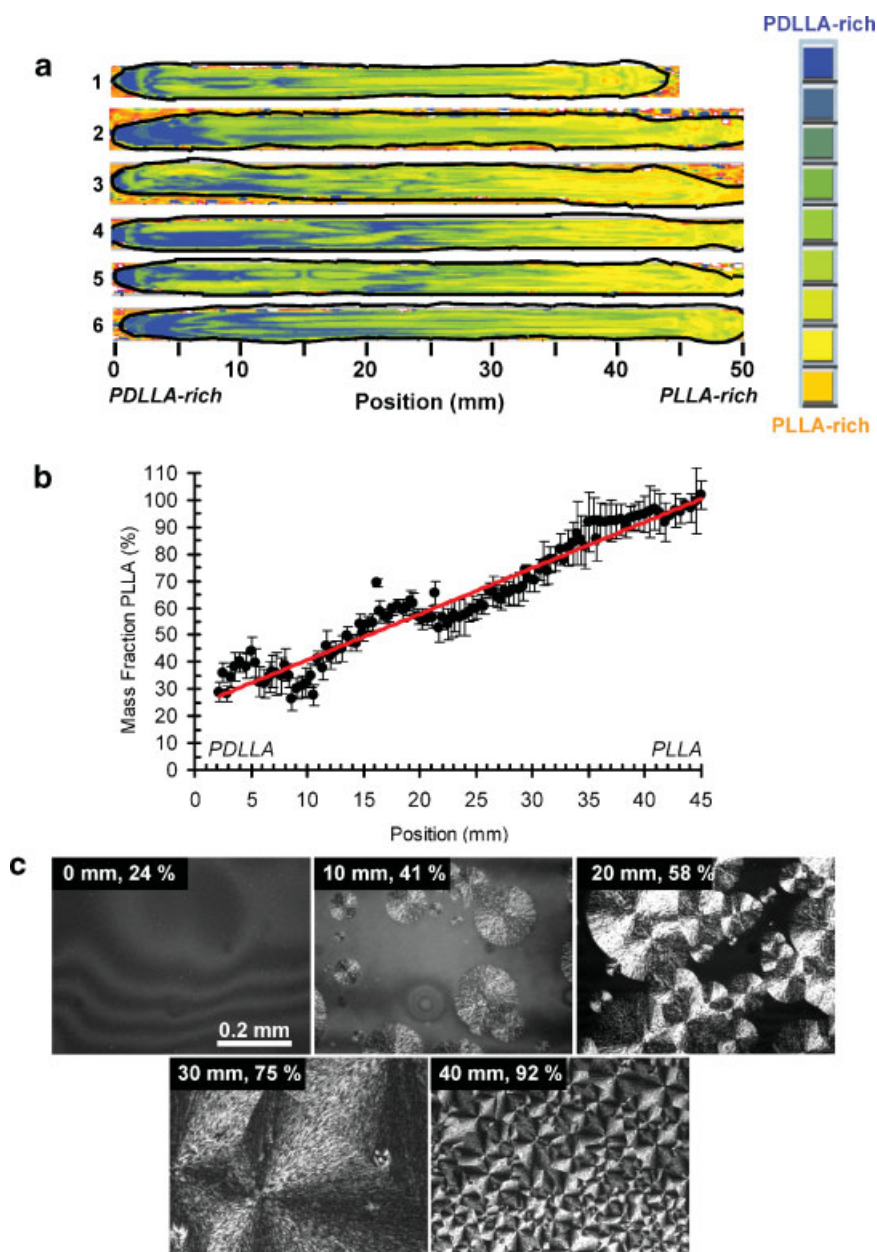


Figure 2. a) FTIR-RTM maps of the six PLLA-PDLLA composition gradients used in this study. The strip films have been outlined with a black line and numbered 1 to 6. Qualitative gradients in colors are seen in all films, with blue corresponding to PDLLA-rich regions and orange corresponding to PLLA-rich regions. Pixels located outside the black borders represent artifactual data from bare regions on the slides and were not included in the composition calculations; b) The compositions of the six PLLA-PDLLA gradients determined with FTIR-RTM were averaged along the short axis of the film and plotted versus position along the gradient. Error bars are S.D. of the mean (taken as an estimate of the standard uncertainty) and lines were fitted by linear regression. Each data point was derived from 72 spectra; c) Transmitted light micrographs taken through crossed polarizers show the change in spherulite morphology across the gradients. The position (mm) and composition (mass fraction PLLA) are given in the top left corner of each image.

ration curve was used to determine the composition of the gradients as previously described.^[8]

All measurements of modulus were determined by nanoindentation (Nanoindenter II, Nano Instruments, Knoxville, TN)

using a three-sided pyramidal diamond tip (Berkovich). The loading segment was controlled to have a constant ratio of load rate to load of 0.15/s, and a small dynamic oscillation was superimposed over the loading segment (45 Hz frequency, 2 nm

amplitude). Modulus was calculated using procedures described in detail elsewhere.^[10] For each test, the indentation modulus was calculated throughout the loading segment using instantaneous values of force, displacement and contact stiffness.^[10] The continuous measurement of contact stiffness throughout the loading segment is based on a dynamic model of the indentation system and the response of the material to the oscillatory loading. The contact area was determined from a knowledge of the indenter tip shape, which was calibrated from indentation tests on a fused silica reference sample.^[10] Indentations were made to a depth of 1 μm and data from the depth range 200 nm to 400 nm (maximum contact diameter approximately 3.5 μm) was used in modulus calculations to avoid substrate effects. Automated measurements were made using the instrument's software in a 6×10 matrix on each of the six PLLA-PDLLA gradients. Each measurement takes approximately 10 min and the instrument was calibrated once per week. As a control, six measurements (using nanoindentation) were also made on each of 3 discrete blend thick droplet samples for each of 5 compositions (0, 25, 50, 75 and 100% mass fraction PLLA).

Results and Discussion

Composition gradients were made from PLLA and PDLLA, two degradable polymers used for biomaterials which differ in tacticity and modulus.^[11] In addition, separate sets of control films were prepared for the FTIR-RTM measurements and the nanoindentation measurements, and all films (including gradients) were annealed as described in the Experimental Part.

FTIR-RTM^[8] was used to map the composition of the PLLA-PDLLA gradients (Figure 2a). The maps showed that gradients in composition were present in the films which were PDLLA-rich on one end and PLLA-rich on the opposite end. A plot of averaged data from the 6 maps (Figure 2b) demonstrated that the gradients were approximately linear (linear regression, solid line, $R^2 = 0.94$) and ranged from 25% to 100% PLLA. Transmitted light micrographs taken through crossed polarizers every 10 mm across a gradient showed that spherulites were present on the PLLA-rich end but were absent from the PDLLA-rich end (Figure 2c). In the 10 mm and 20 mm panels, part of the volume was spherulitic while part of it was amorphous. These morphologies were observed in discrete PLLA-PDLLA blends in previous studies^[12] and in the control films of the present work (strips and thick droplets, data not shown). These data serve as an additional indicator that our specimens contain gradients in polymer composition.

The modulus of the gradients (circles, Figure 3) and of the control discrete blend thick droplet specimens (triangles, Figure 3) was determined with nanoindentation. A plot of averaged modulus values from the gradients (circles) versus position (top x -axis in Figure 3) showed that modulus varied linearly with position (linear regression, solid line, $R^2 = 0.98$). Modulus of the gradients ranged from 4.9 GPa

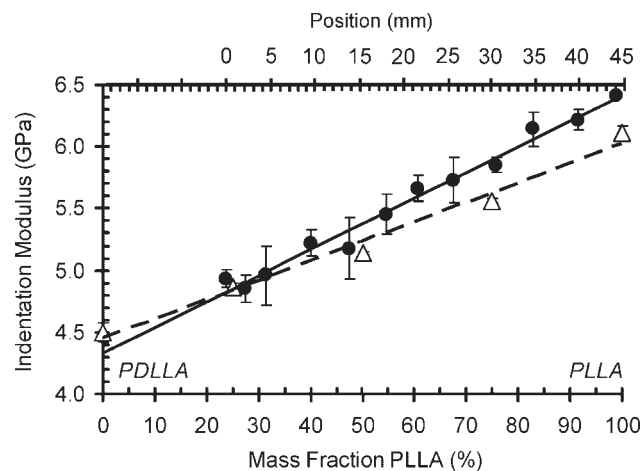


Figure 3. Modulus was measured across the six gradients using nanoindentation and average values (circles) were plotted against position (top x -axis) and composition (bottom x -axis). Triangles are the modulus (measured by nanoindentation) from discrete blend thick droplet specimens (0, 25, 50, 75 and 100% mass fraction PLLA) plotted against composition only (bottom x -axis). Error bars are S.D. of the mean (taken as an estimate of the standard uncertainty) and lines were fit by linear regression.

(PDLLA-rich end) to 6.4 GPa (PLLA-rich end). The equation describing the linear fit to the composition plot in Figure 2b (solid line) was used to calculate the composition at each position along the gradients yielding the plot of modulus versus composition depicted by solid circles in Figure 3 with the bottom x -axis. Modulus values (measured by nanoindentation) of control PLLA-PDLLA discrete thick droplet blends ranged from 4.5 GPa (PDLLA) to 6.1 GPa (PLLA) (Figure 3, triangles using bottom x -axis). These control measurements closely agreed with measurements made on gradients, and the average difference between controls and gradients was only 3.9%.

The modulus values measured by nanoindentation shown herein are somewhat higher than those obtained by tensile testing for pure PLLA and for pure PDLLA.^[11] These discrepancies may result from differences in molecular weight and processing. In addition, nanoindentation of polymers typically yields values that are higher than tensile tests^[13–15] making the technique appropriate for relative comparisons between samples rather than absolute measurements. As such, the present results from nanoindentation and those from tensile tests^[11] followed the same trend in that the modulus of PLLA was approximately 30% greater than for PDLLA.

As mentioned above, there were regions in the gradients which were partly amorphous and partly crystalline (Figure 2c, 10 mm and 20 mm). Given that the lateral diameter of the indentations (3.5 μm) was smaller than that of the spherulites (Figure 2c), it is possible that some modulus measurements landed within the bounds of a spherulite while others landed in amorphous zones. Since the

nanoindenter was equipped with a microscope, the modulus from a spherulite was compared to that of an amorphous region but the difference in modulus was not significant (data not shown). Even so, the data from the 6 gradients was averaged and any small differences between measurements made within and outside of a spherulite are not likely to affect the results. As can be seen in Figure 3, the variation in modulus with composition along the gradients is linear.

High-throughput methods have recently been applied to polymer science.^[16–21] As for blends, two general approaches for high-throughput methods have emerged: discrete and gradient. The discrete approach aims to develop a rapid method for creating of a library of discrete polymer blends.^[22–24] The gradient approach aims to create a specimen containing a continuous gradient in composition spanning the length of the sample.^[6,8,25–28] We chose the gradient approach since a vast number of compositions can be tested on a single specimen. There are also a number of high-throughput methods for determining the mechanical properties of materials.^[7,26,29–32] However, our novel combination of nanoindentation with polymer composition gradients described herein is the only one that has been applied to measuring modulus of polymer blends in a high-throughput fashion with high spatial resolution.

Conclusion

We have combined nanoindentation with gradient creation technology to yield a high-throughput method for determining the modulus of polymer blends. This rapid approach to materials characterization provides a tool to enable accelerated materials development.

Disclaimer

Certain equipment and instruments or materials are identified in the paper to adequately specify the experimental details. Such identification does not imply recommendation by the *National Institute of Standards and Technology*, nor does it imply the materials are necessarily the best available for the purpose.

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