

Effects of Confinement on Crystallization of Molecular Glasses

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Primary CNF Tools Used: Woollam Ellipsometer

Abstract:

Investigations were conducted comparing indomethacin crystal growth rates in bulk films and nanocomposites as a function of temperature. It was found that nanoconfinement slowed the crystal growth rates, but these effects were diminished as temperature increased above the glass transition temperature. Ellipsometry was used to characterize the films, but this characterization faced challenges.

Summary of Research:

There is growing interest in applications of small molecular amorphous solids, which necessitates improving the stability of such systems against crystallization. Nanoconfinement has been promising in this regard^{1–4}. As far we are aware, literature has been limited to studies of crystallization occurring below the glass transition temperature, where many molecules exhibit “diffusionless” growth, characterized by growth faster than would be predicted by diffusion⁵. Above the glass transition, by contrast, crystal growth rates are limited by diffusion.

In this investigation, the well-studied pharmaceutical glass-former indomethacin (glass transition temperature, $T_g=42^\circ\text{C}$) was confined in nanoparticle composites via a method known as Capillary Rise Infiltration (CaRI) by first spin coating a silica nanoparticle (10-nm or 100-nm) film onto a substrate and then spin coating indomethacin on top of the nanoparticle film^{6,7}. For comparison, indomethacin was also coated directly onto the bare substrate. All films were then annealed allowing for infiltration into the nanoparticle films. Films were then monitored for crystal growth by polarized light microscopy during storage at 25°C , 50°C , 75°C .

Figure 1 shows images under polarized light of typical crystals seen on each type of sample when stored at room temperature, which could be measured over time to give crystal growth rates. Growth was linear over several data points. Figure 2 shows $\log(\text{growth rate})$ as

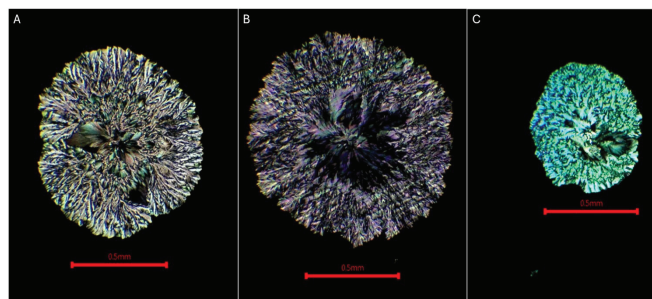


Figure 1: Indomethacin crystals under polarized light grown after storage under ambient temperature in a desiccator on bulk film (A), 100-nm nanoparticle nanocomposite (B), and 10-nm nanoparticle nanocomposite (C).

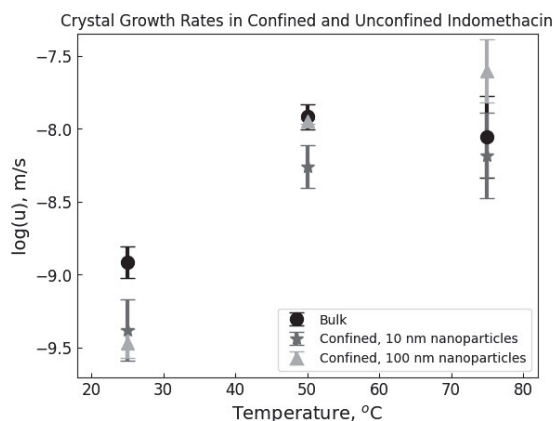


Figure 2: Log of growth rate (m/s) versus temperature ($^\circ\text{C}$) for crystal growth in indomethacin bulk films and films confined to 10-nm and 100-nm nanocomposite films. Error bars represent standard deviations of at least five repeat measurements per data point.

a function of temperature for each of the three sample types (unconfined, confined in 100-nm nanoparticle film, and confined in 10-nm nanoparticle film). At low temperatures, the data shows the expected result of a decreased growth rate as a result of confinement, but this effect is eliminated as the temperature is increased.

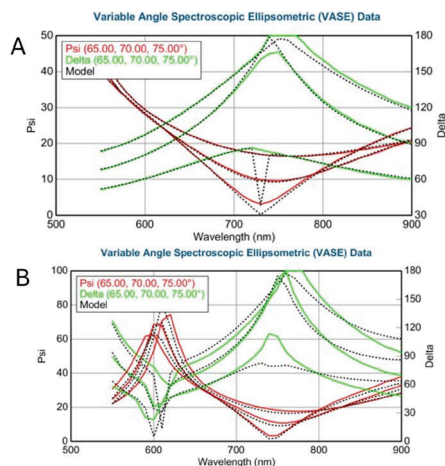


Figure 3: Psi and Delta data for variable angle data showing experimental data and Cauchy model fits for bulk indomethacin film (A) and annealed nanocomposite of indomethacin infiltrated into 10-nm nanoparticles. While figure A shows a unique fit, B shows one of many results that is relatively well-fit to data by varying the fit parameters of interest.

Figure 3 shows the data collected with the Cornell NanoScale Science and Technology Facility Woollam Variable Angle Ellipsometer. These were modeled using CompleteEase software and a Cauchy model. Unfortunately, as the samples became more complicated by the addition of more layers the addition of fit parameters (Cauchy A, B, and thickness for indomethacin, nanoparticle, and mixed layers) sufficiently complicated the analysis so that a unique fitting difficult to find. Figure 3 does show a fitting consistent with successful infiltration of indomethacin into the nanoparticle packing, modelling bulk indomethacin (3A) to a very low mean squared error (MSE) with unique fitted parameters and the confined sample (3B) with the same Cauchy A and B for indomethacin, where a relatively good fitting is achieved when the thickness for the indomethacin layer is close to zero and most of the thickness is in the mixed indomethacin/nanoparticle layer, but other fits do an equally good job (as measured by MSE). Efforts to overcome this challenge included analysis of samples of nanoparticle layers alone, indomethacin layers alone, and nanocomposites prior to the annealing step in order to better determine parameter values. Careful analysis of further samples may improve the analysis, including repeating the nanoparticle only samples but annealing these (which was not done previously), or a model other than Cauchy may be more appropriate to fit these samples. Given the experimental difference between samples it seems likely that the method was successful in confining the indomethacin, but it remains essential to appropriately characterize this confinement using a tool like ellipsometry, so this work will continue.

Conclusions and Future Steps:

This study revealed that, in indomethacin, confinement in nanoparticle composites does slow crystallization growth as expected, but in a manner dependent on temperature, suggesting a possible dependence on crystallization mode. Characterization of the films using ellipsometry was challenging due to the number of fit parameters involved, but a number of potential next steps to improve fitting are identified.

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