Developing 3D Printed Polymers for use as Ordered Media

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Introduction

Residual Dipolar Couplings (RDCs) are used to determine the three-dimensional structure of molecules in solution. This is very important for pharmaceuticals where their function depends on their three-dimensional structure. RDCs can be determined from spectra acquired with a Nuclear Magnetic Resonance (NMR) spectrometer. RDCs are not normally seen in NMR spectra. The random motion of molecules in solution causes them to average out. RDCs can only observe them by restricting the random motion of molecules in solution. Anisotropic media (also called ordered media) can be used to restrict random motion in solution.

Using this technique currently, however, can take weeks to develop (polymer swelling time), and there are limited suppliers for the gel, which can make it difficult to use. The development of a 3D printed anisotropic media—the subject of this experiment—could allow for reduced swelling times and widespread availability. Currently, this process is in its early stages; a file and washing method have been developed with high levels of success. Tests of these polymers have produced promising preliminary results. Various polymer printing sizes have also been tested with varying degrees of success.

Experimental

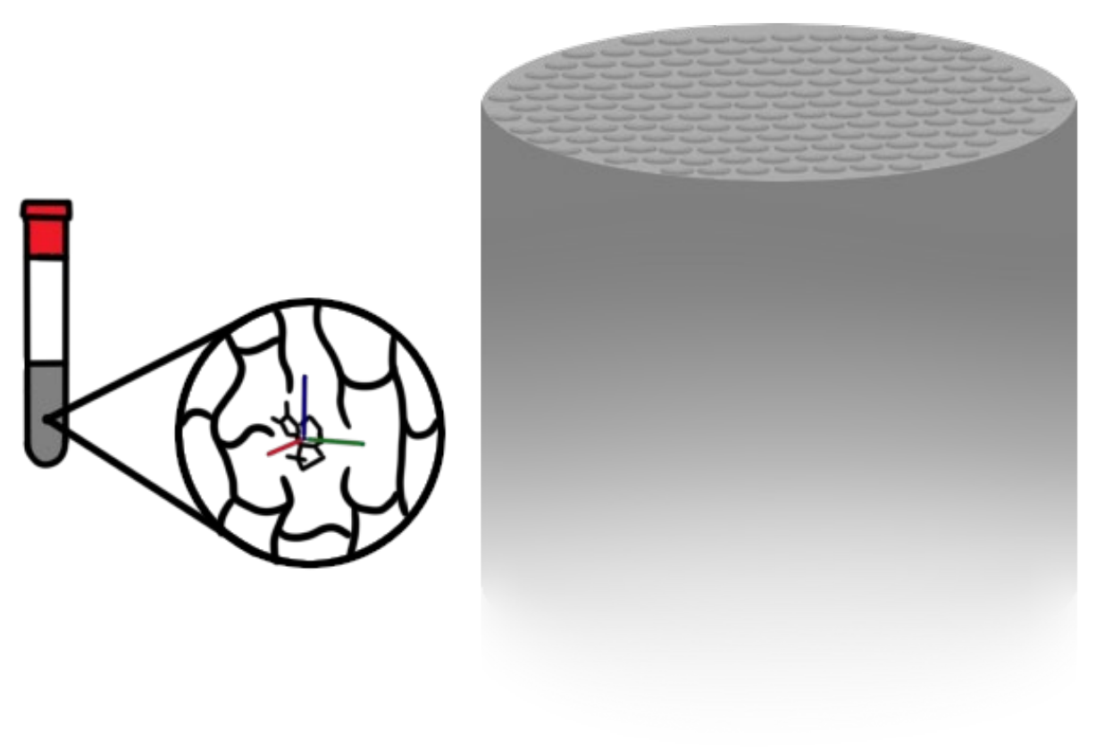
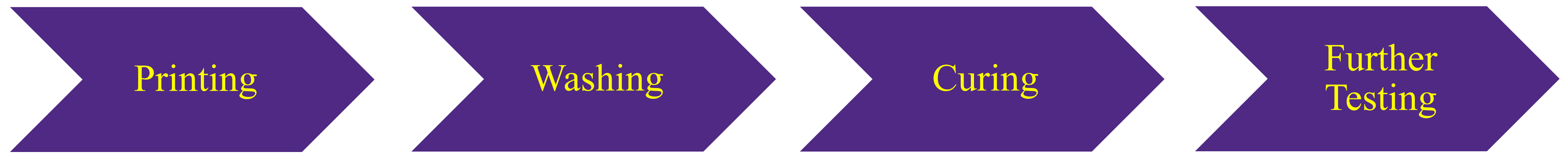


Figure 1 (left): An atomic view of the inside of a swollen ordered media holding an example molecule in place[2]
Figure 2 (right): A microscopic view of the channels in a 3D printed polymer

A polymer was modeled and 3D printed. Microscopic channels were incorporated into the design as shown in Figure 2. The channel size varies with each file. The ideal size has not yet been determined. The majority of the project this semester focused on the washing step detailed in Figure 3. This required finding the correct solvent. Some solvents can cause the polymer to over-swell and crack. Unfortunately, this destroys the polymer's delicate channels. As such, the solvent or solution needed to be able to dissolve some uncured polymer but not so much that the it would dissolve the fragile channels or cause it to crack. This pursuit gave rise to experiments based on wait times, solvents, solvent mixtures, and methods. For most versions of these experiments, polymers were placed inside a vial containing enough solution to cover them. This was typically about 6 mL. The polymers were left in the vials for varying amounts of time. Then, the polymer's swelling and cracking activity was recorded (Table 1) and analyzed.

Results

Figure 3: The basic process from polymer printing to testing



Printing	Washing	Curing	Further Testing
This step creates a fragile form of the polymer through use of a vat-polymerizing 3D printer	Vat-polymerization leaves resin inside of the microscopic channels (Fig. 2) that must be removed with the developed solvent	The fragile polymer is cured with a UV lamp to harden it into its final form	To use the polymer, it must swell in a solvent. It may be put directly into the solvent, or it may need an additional washing step

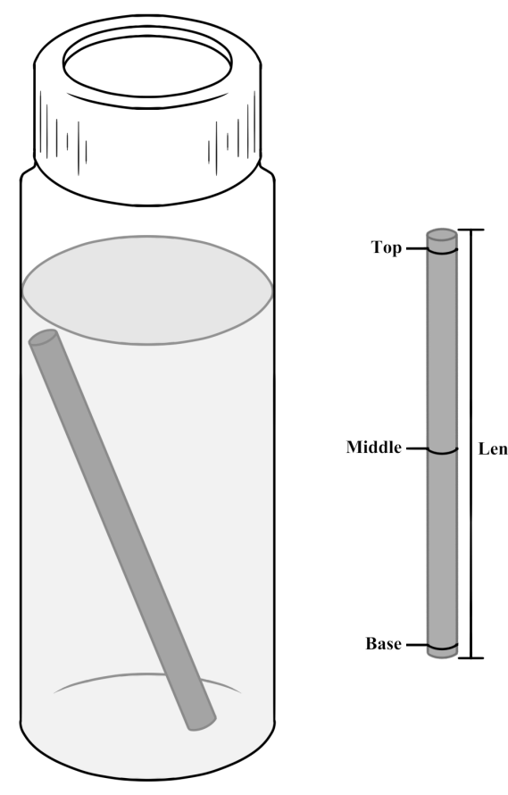


Figure 4 (left): An example vial
Figure 5 (right): A diagram showing the position of each measurement that was taken

Table 1: Percent Growth by Solvent

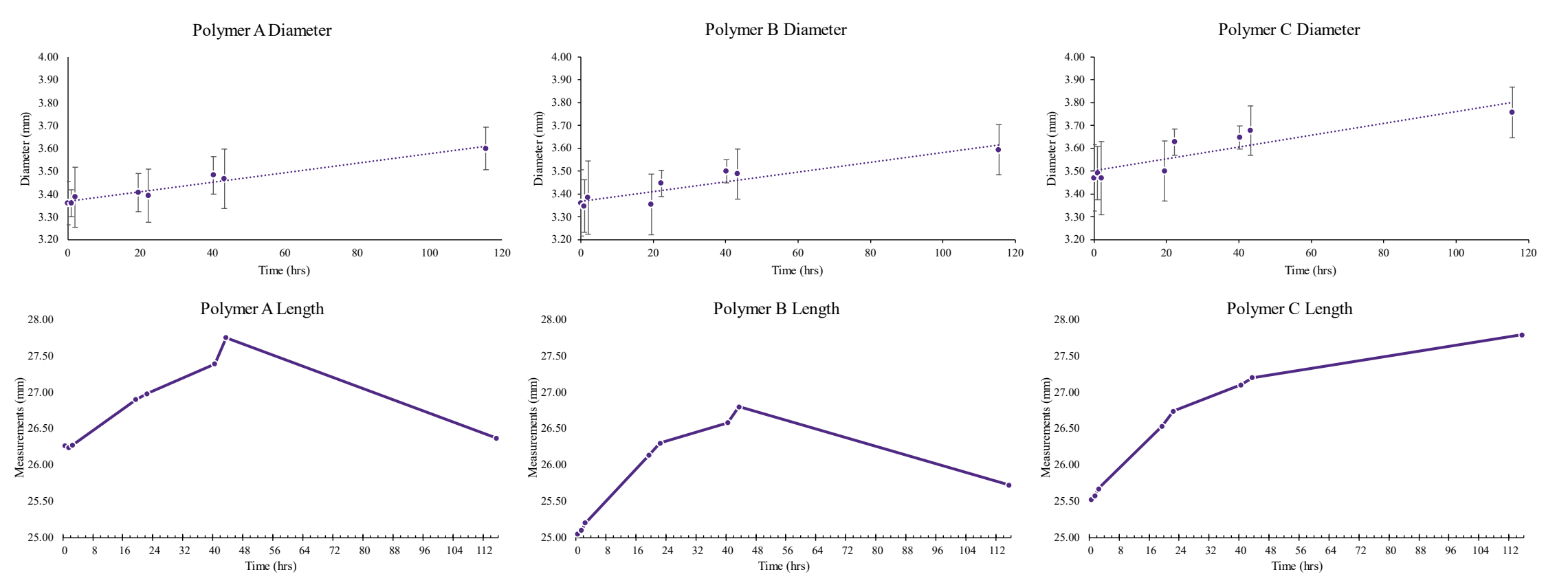
Solvent:	Percent Growth vs. Solvent				
	L	T	M	B	Ave. Diameter
MeCN	7.7%	2.2%	-0.7%	-1.7%	-0.1%
acetic acid	-	-	-	-	-
THF	13.2%	3.3%	-18.5%	9.7%	-1.8%
MeOH	7.9%	1.3%	-19.5%	5.7%	-4.2%
hexanes	0.1%	-1.0%	1.3%	1.0%	0.4%
water	0.8%	0.9%	2.4%	0.0%	1.1%
alconox, H_2O	-0.1%	9.6%	0.6%	-0.6%	3.2%
THF:hexanes Solutions					
100:0	-	-	-	-	-
75:25	-	-	-	-	-
50:50	6.2%	3.2%	4.8%	3.7%	3.9%
25:75	8.8%	3.0%	5.3%	1.5%	3.2%
0:100	-1.2%	-3.5%	-12.3%	10.7%	-1.7%
25:75 A	0.4%	7.2%	6.0%	8.3%	7.2%
25:75 B	2.7%	5.1%	7.8%	8.1%	7.0%
25:75 C	8.9%	6.0%	9.5%	9.5%	8.3%

Each polymer was left in a vial (Fig. 4) with 6 mL of solvent. It was then measured at varying increments of time. The polymer occasionally would crack beyond the ability to measure. This is indicated with a dashed row. THF typically had the greatest growth. Hexanes grew slowly and had very little cracking. These two were combined in various ratios to form T:H. A 25:75 ratio appeared to perform best when cleaning out the uncured polymer. Further testing was done on polymers A, B, and C with the same ratio of T:H.

Table Set 2 details the average diameter growth of each polymer submerged in the 25:75 T:H solution. A trend line and the points' standard deviations are also displayed for each plot.

Table Set 3 displays the length of the polymers each time they were measured. Unfortunately, polymers A and B broke during the last measurements. This led to the drastic decrease shown by the last point.

Tables 2A, 2B, and 2C (top row): Average polymer diameter over time
Tables 3A, 3B, and 3C (bottom row): Polymer length over time



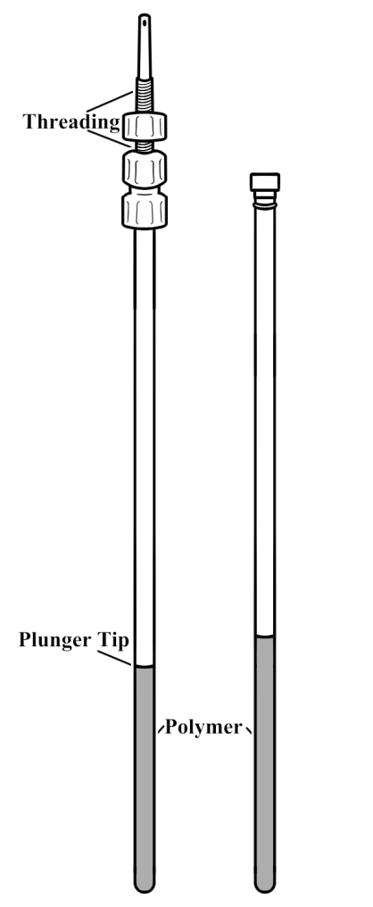
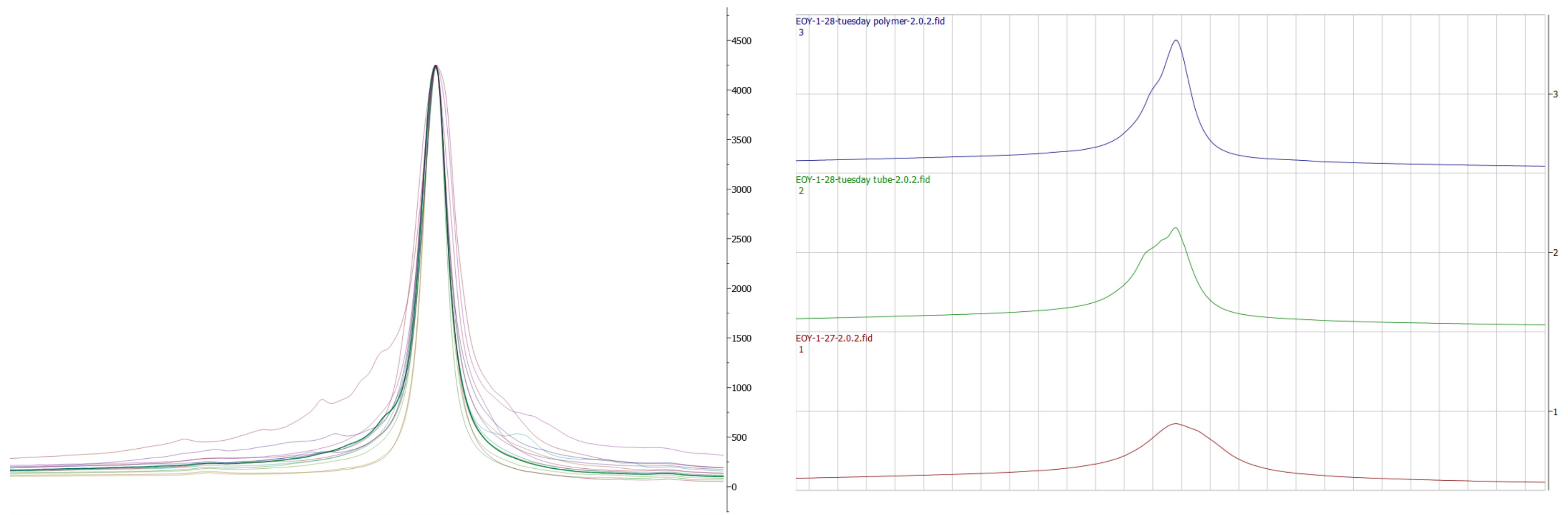


Figure 6: Two types of NMR tubes can be used: a compression tube (left) or the more standard tube (right)

The solution mixture's success allowed for NMR tests to be run. Deuterated chloroform (chloroform-D) was used as the sample and solvent. Deuterium and proton NMR spectra were taken. Cured polymers were typically placed once more into vials containing enough T:H solution to cover them and were left to sit for varying times (generally 30 minutes to an hour). They were then placed into a 50:50 mixture of chloroform-D and T:H. This process was repeated once more with a 75:25 mixture of the two. After this, the polymers were transferred into an NMR tube (Fig. 6) containing the appropriate amount of chloroform-D. Spectra were then taken under varying levels of compression (Spectra Set 1). Time-based data was also gathered (Spectra Set 2) over the course of about three days.



Spectra Set 1 (left): A set of compression-varied deuterium spectra of the same polymer superimposed over each other
Spectra Set 2 (right): A stacked set of deuterium spectra of the same polymer. The timeline starts with the bottom spectrum and ends with the top

Summary and Conclusions

- Hexanes was chosen because it swelled the slowest and allowed the polymer to remain mostly uncracked
- THF was chosen as a companion to hexanes because of its degree of swelling
- By combining the two, their properties created a solution that swelled the polymer relatively quickly but not so quickly that it cracked
- This was tested with polymers A, B, and C (Tables 1, 2, and 3). The polymers swelled well and lasted far longer than in previous tests
- When T:H was used for its intended purpose, it pulled the uncured polymer out of the channels to such a degree that it was able to be seen without any instrumentation

- Spectra Sets 1 and 2 are deuterium spectra of chloroform-D
- If the polymer is performing as intended, two distinct peaks will be shown
- While this has not yet been achieved, partial character is shown with both sets
- Set 1 indicates that compression appears to reduce the intended character; the largest splitting (in red) was the uncompressed polymer
- Set 2 displays the most recent information. Its peaks are split at the top, rather than at the base.
- Though the frame is enlarged, it indicates that with proper timing, the polymers have potential to perform as intended
- Overall, the polymers display promising results for the development of this technique

Future Work

In the future, it is anticipated that further adjustments to the model file and handling methods will be performed, with the end goal of obtaining high-quality spectra. This tests will likely include changes to the solvent-replacement method, polymer and channel size, and compression strength, as well as possible alterations to the washing method.

References

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