Encapsulation of drugs during polymerization induced self-assembly

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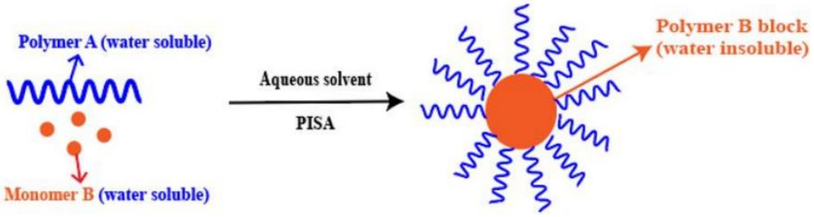
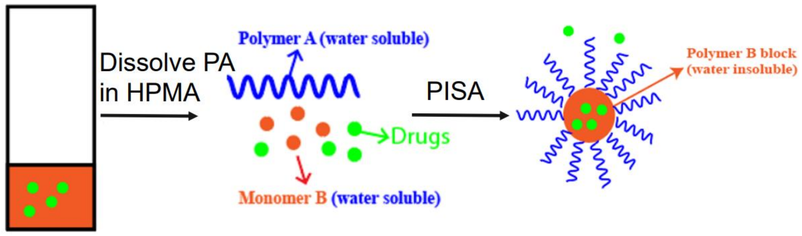
Introduction & Background

- Polymerization induced self-assembly (PISA) is a method of polymer synthesis that chain-extends an existing polymer through addition of a monomer. This creates a block copolymer that self-assembles into nanoparticles.



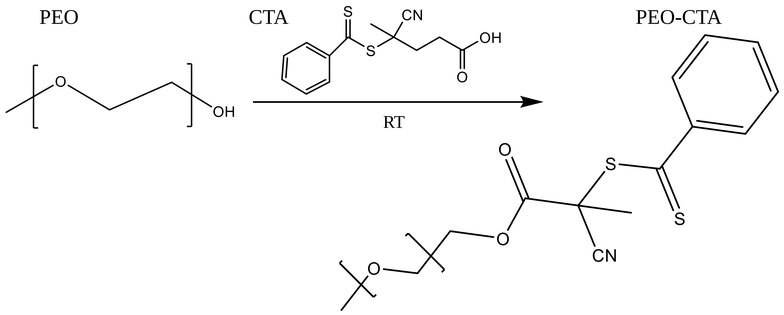
- PISA can be done in the presence of a hydrophobic drug, leading to physical entrapment of the drug within the nanoparticles. Polymerization, nanoparticle self-assembly, and drug encapsulation occur simultaneously.



- These encapsulation mechanisms are not well-understood. However, different drug loading mechanisms exist, producing different nanoparticle morphologies. Different morphologies can be targeted to optimize drug delivery to different parts of the body. Loading drug concentration and degree of polymerization are varied to produce the different morphologies.

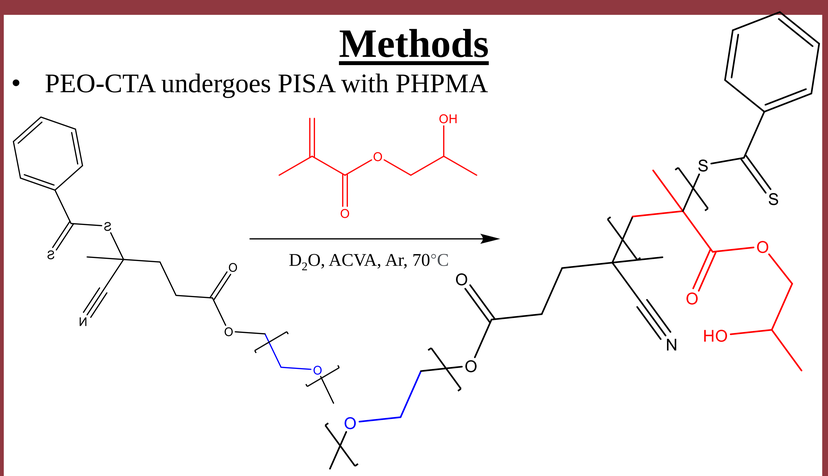
Methods

- Commercial-bought PEO is connected to a chain-transfer agent (CTA):



Methods

- PEO-CTA undergoes PISA with PHPMA



Results

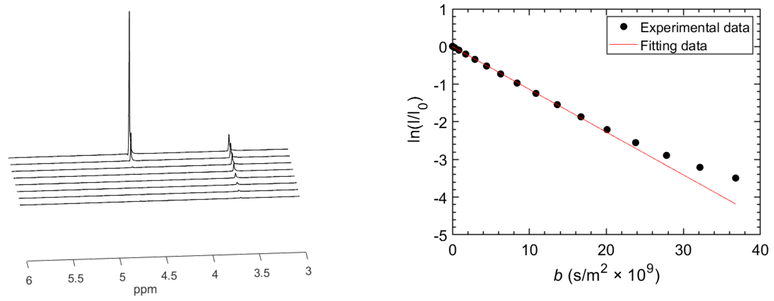


Figure 1. DOSY waterfall plot and Stejskal-Tanner plot for data GL-3-62A, PEO-PHPMA nanoparticles in D2O. [Diffusion coefficient will be reported here], and some further analysis will be given after consulting with Guanrui.

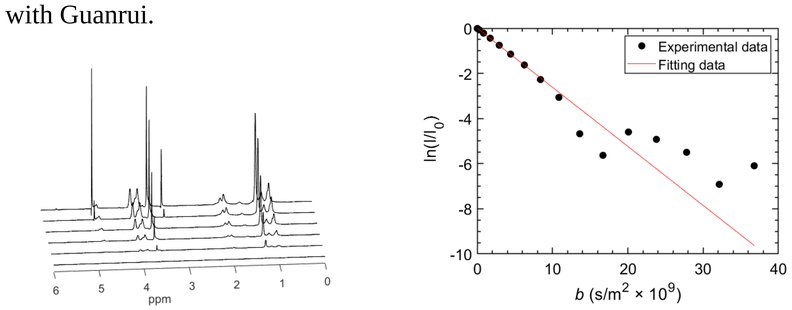


Figure 2. DOSY waterfall plot and Stejskal-Tanner plot for data GL-3-61B, PEO-PHPMA nanoparticles in D2O. [Diffusion coefficient will be reported here], and further analysis will be given after consulting with Guanrui.

Future Directions

- The present work confirms that PISA synthesis successfully produces polyethylene oxide-*b*-poly-(2-hydroxypropyl methacrylate) at various molecular weights.
- Increasing molecular weight indicates higher degrees of polymerization. These samples with varying molecular weights will be used in later synthesis of PEO-PHPMA block copolymer nanoparticles.
- Loading drug concentrations and targeted degrees of polymerization will be targeted as shown below:

Hydrophobic core block	N_{core}
2-hydroxypropyl methacrylate (HPMA)	90, 120, 160
Methyl methacrylate (MMA)	90, 120, 160

Drugs	C_{drugs} (mg/mL)
Phenylacetic acid (PA)	16, 24, 28, 32, 36

- NMR DOSY experiments will determine the diffusion coefficients of the various loading drug concentrations and targeted degrees of polymerization. The diffusion coefficients will be used to calculate the encapsulation efficiency of the drug, as shown below:

Encapsulation Efficiency Equation

$$D_{drug} = pD_{PNPs} + (1-p)D_{drug,aqueous}$$

D_{drug}	Drug diffusion coefficient dispersed in polymeric nanoparticles
p	Encapsulation efficiency
D_{PNPs}	Diffusion coefficient encapsulated in polymeric nanoparticles
$D_{drug,aqueous}$	Diffusion coefficient of drug in aqueous solvent

- Calculating the encapsulation efficiency will determine the effectiveness of PISA encapsulation in producing these drug-loaded delivery vehicles. Combining these findings with TEM, SEC, and SAXS testing will determine whether the hydrophilic corona is the locus of drug loading.