

# Thermo-Responsive Vesicles Based on Diblock Copolymers with Upper Critical Solution Temperature Under Physiological Conditions



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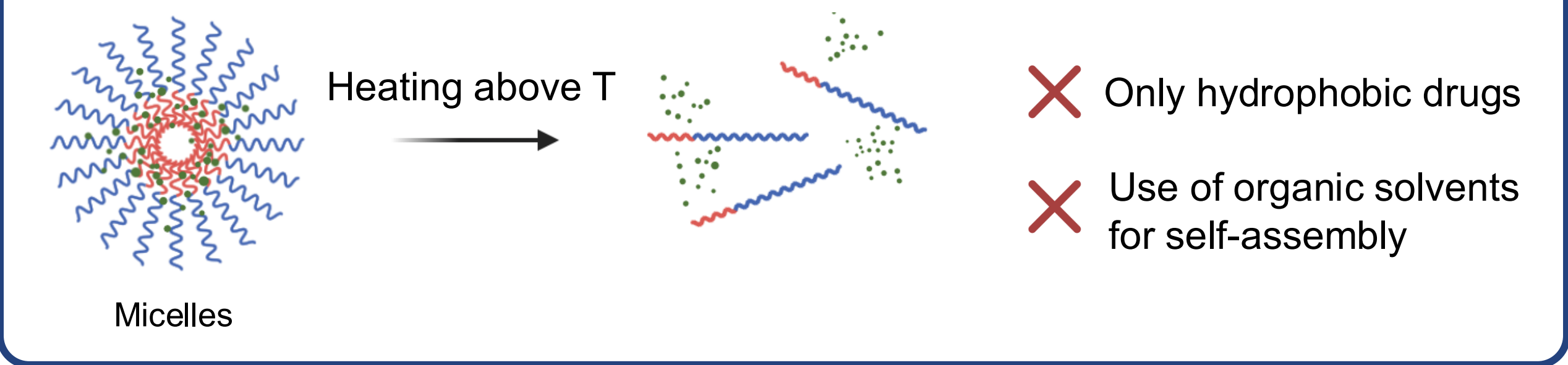
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## 1. “Smart” Polymers for Controlled Release

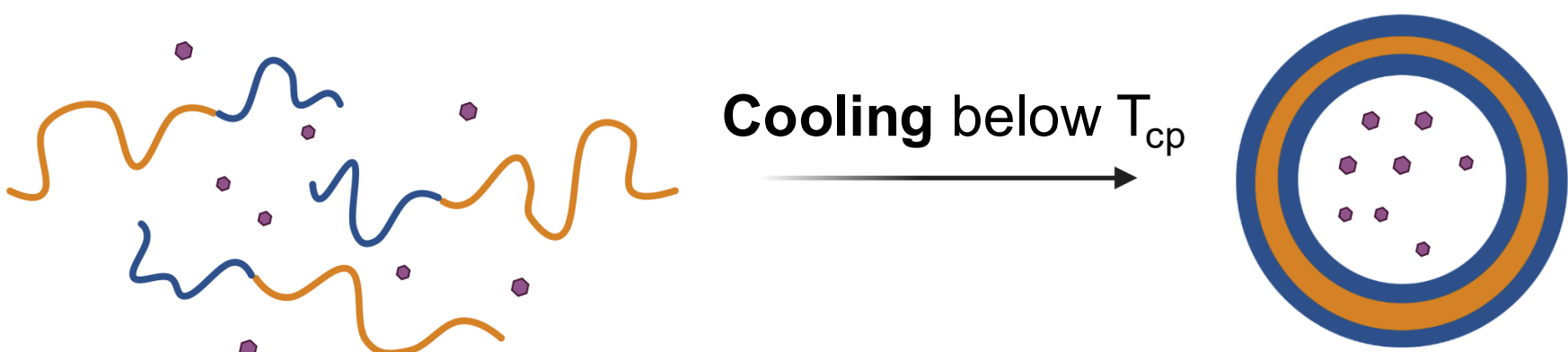
**Controlled release** of therapeutic cargo on “cue” according to specific cellular or extracellular stimuli triggered via **chemical, biochemical, or physical** means

### Previous Studies



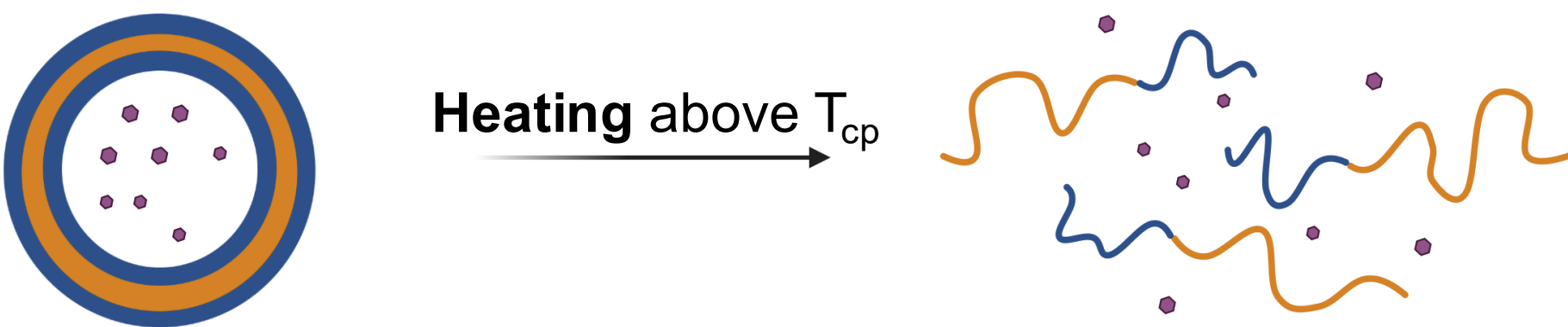
## 2. Objectives

➤ **Encapsulation** of hydrophilic active substances within thermo-responsive nanocarriers



● Active Substance

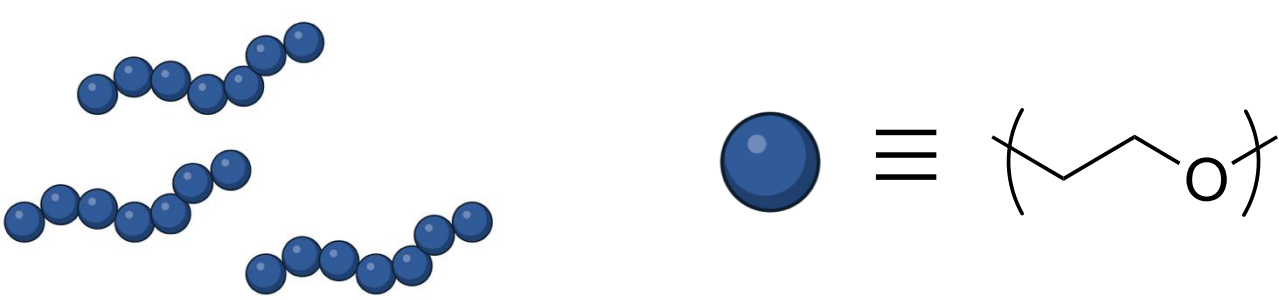
➤ **Temporally controlled** delivery of active substances



## 3. Our Approach

### First Block

- Hydrophilic polymer of choice: Poly(ethylene glycol) (PEG)
- ✓ Biocompatible
- ✓ FDA approved

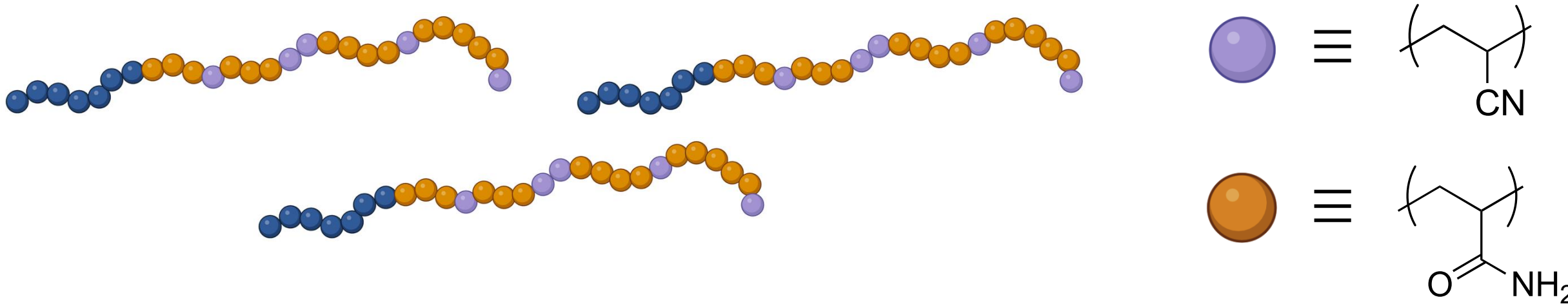


### Ratio of the Two Blocks

- Amphiphilic block copolymer with a hydrophilic weight fraction of ~ 20%, for forming vesicles via self-assembly.

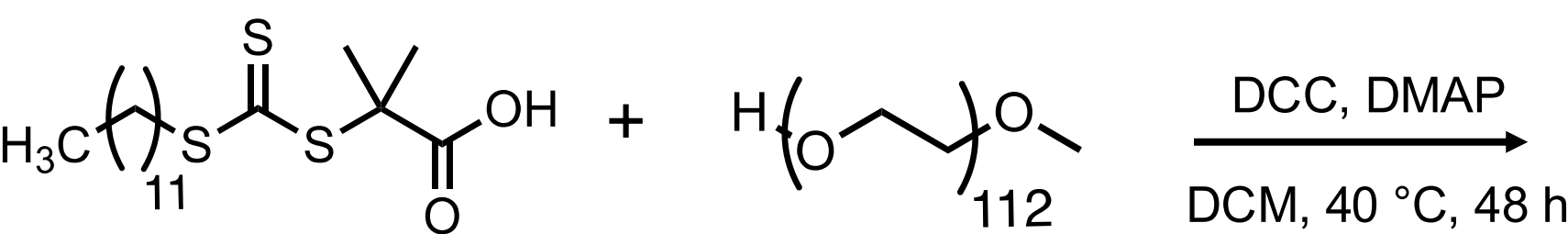
### Second Block

- Thermo-responsive copolymers of choice: Poly(acrylamide-co-acrylonitrile)
- ✓ UCST behaviour in aqueous solutions
- ✓ Tunable critical temperature by varying the acrylonitrile fraction

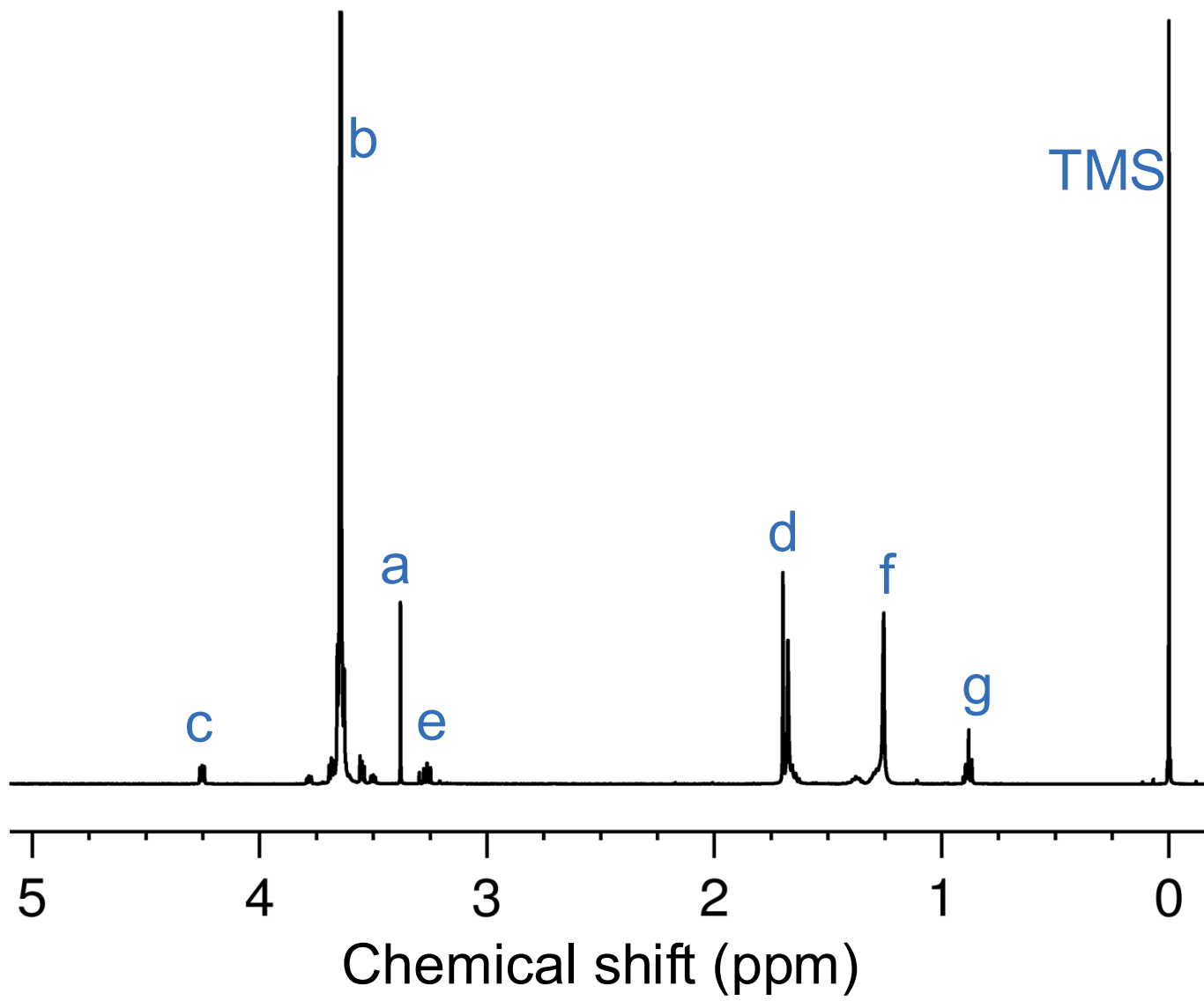


## 4. Synthesis

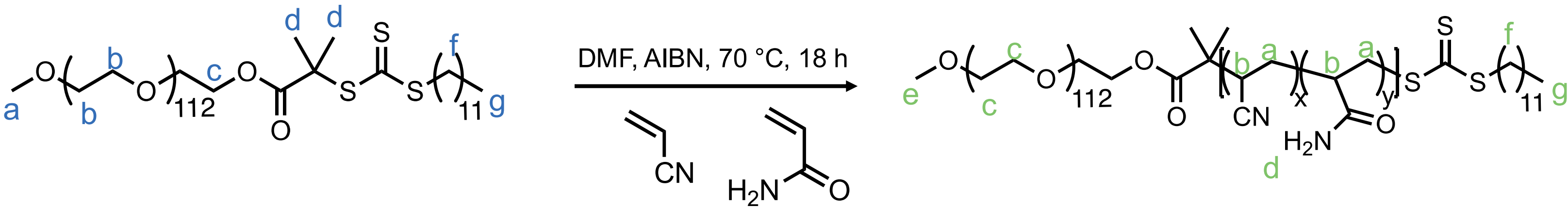
### A. Synthesis of a hydrophilic segment as the macro-chain transfer agent



- <sup>1</sup>H NMR (500 MHz) spectrum of the PEG macro-chain transfer agent in CDCl<sub>3</sub>.



### B. Synthesis of thermo-responsive diblock copolymers with UCST-type behavior by RAFT polymerization



- <sup>1</sup>H NMR (500 MHz) spectrum of PEG-*b*-P(AAm-co-AN) in DMSO-d<sub>6</sub>.

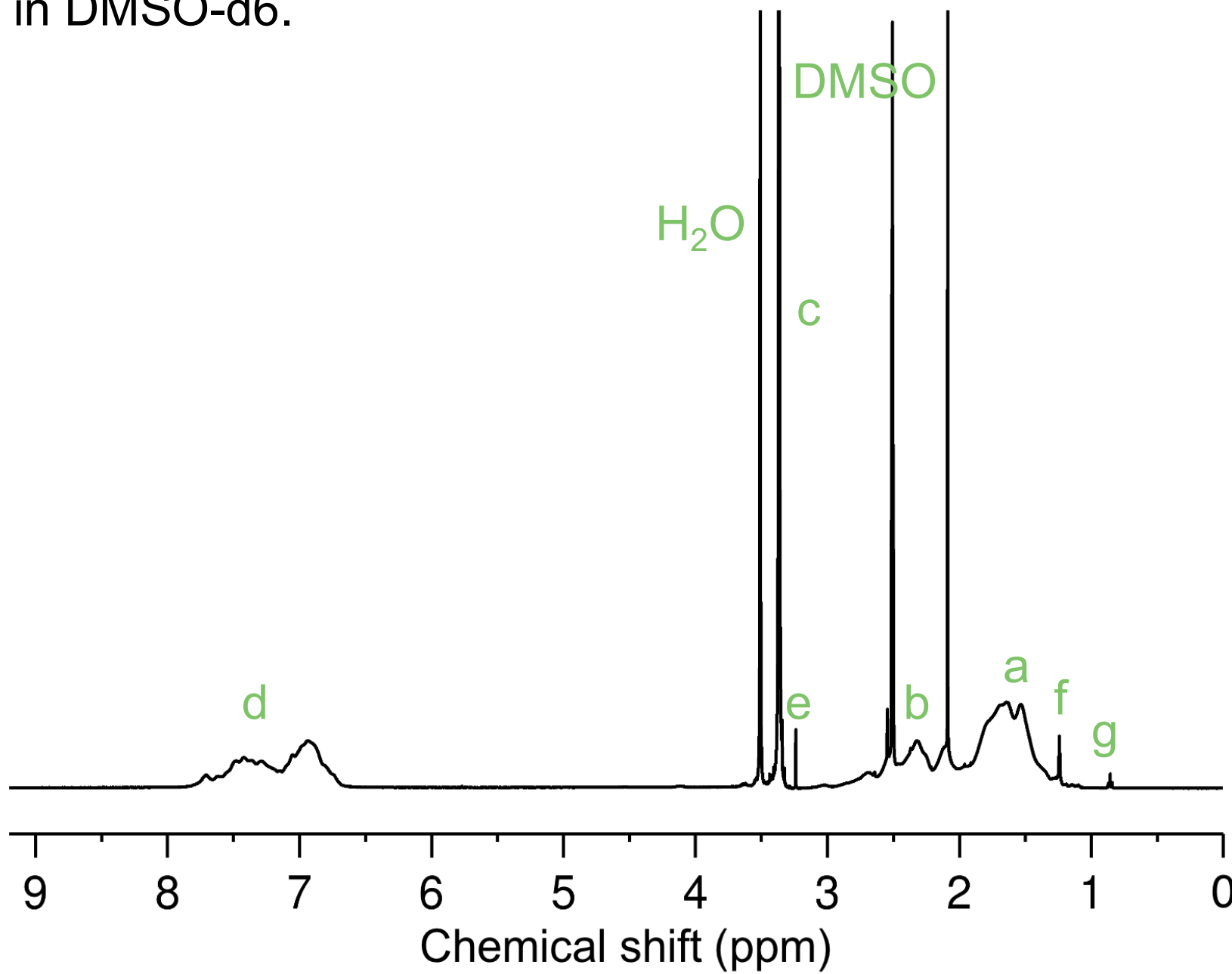


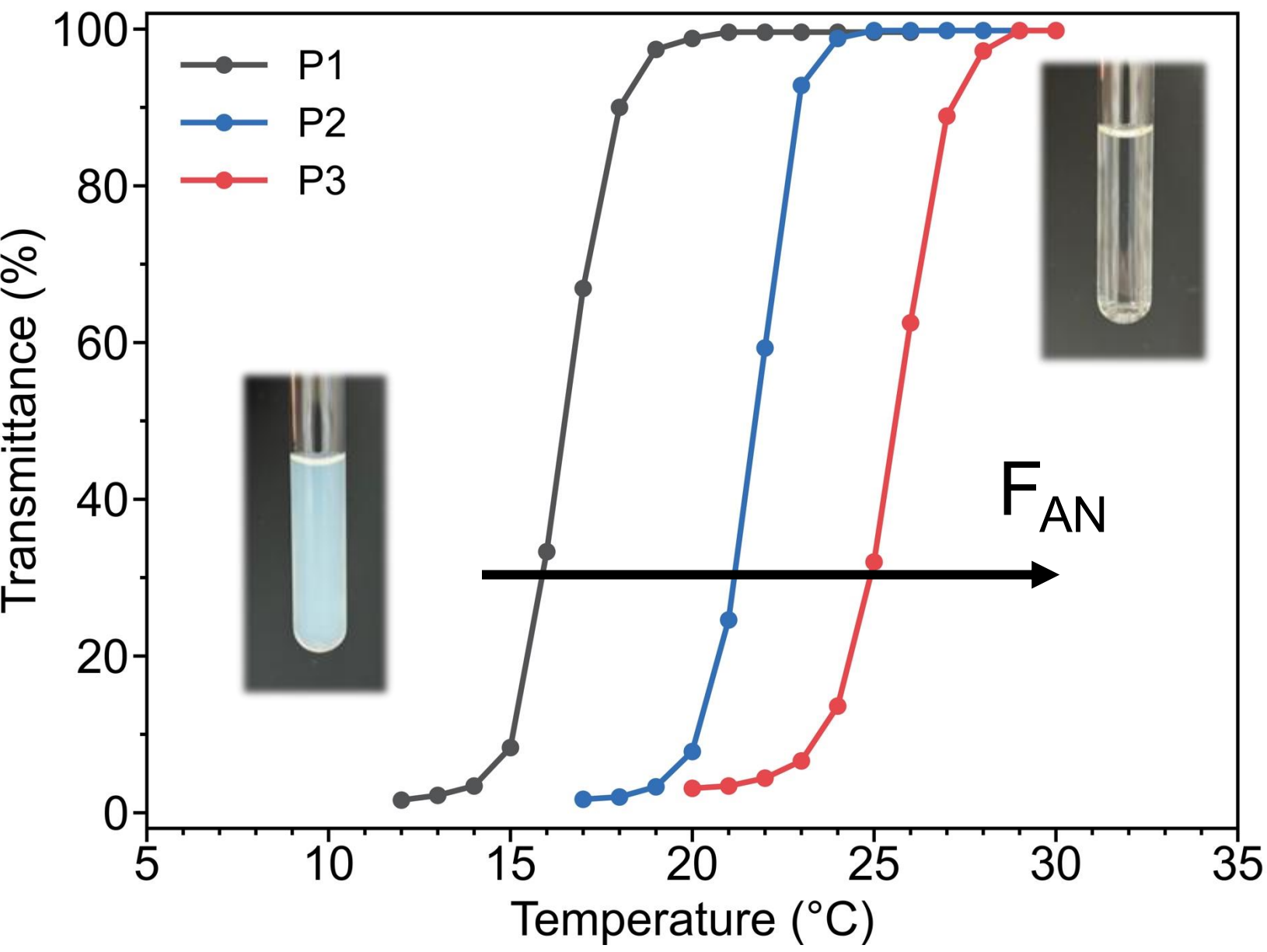
Table 1: Macromolecular characteristics determined by SEC

Entry	AN (% in feed)	<i>M<sub>n</sub></i> (kg mol <sup>-1</sup> )	<i>M<sub>w</sub></i> (kg mol <sup>-1</sup> )	<i>M<sub>w</sub>/M<sub>n</sub></i>
P1	25	23.3	29.9	1.28
P2	26	22.7	29.1	1.28
P3	27	21.8	28.5	1.29

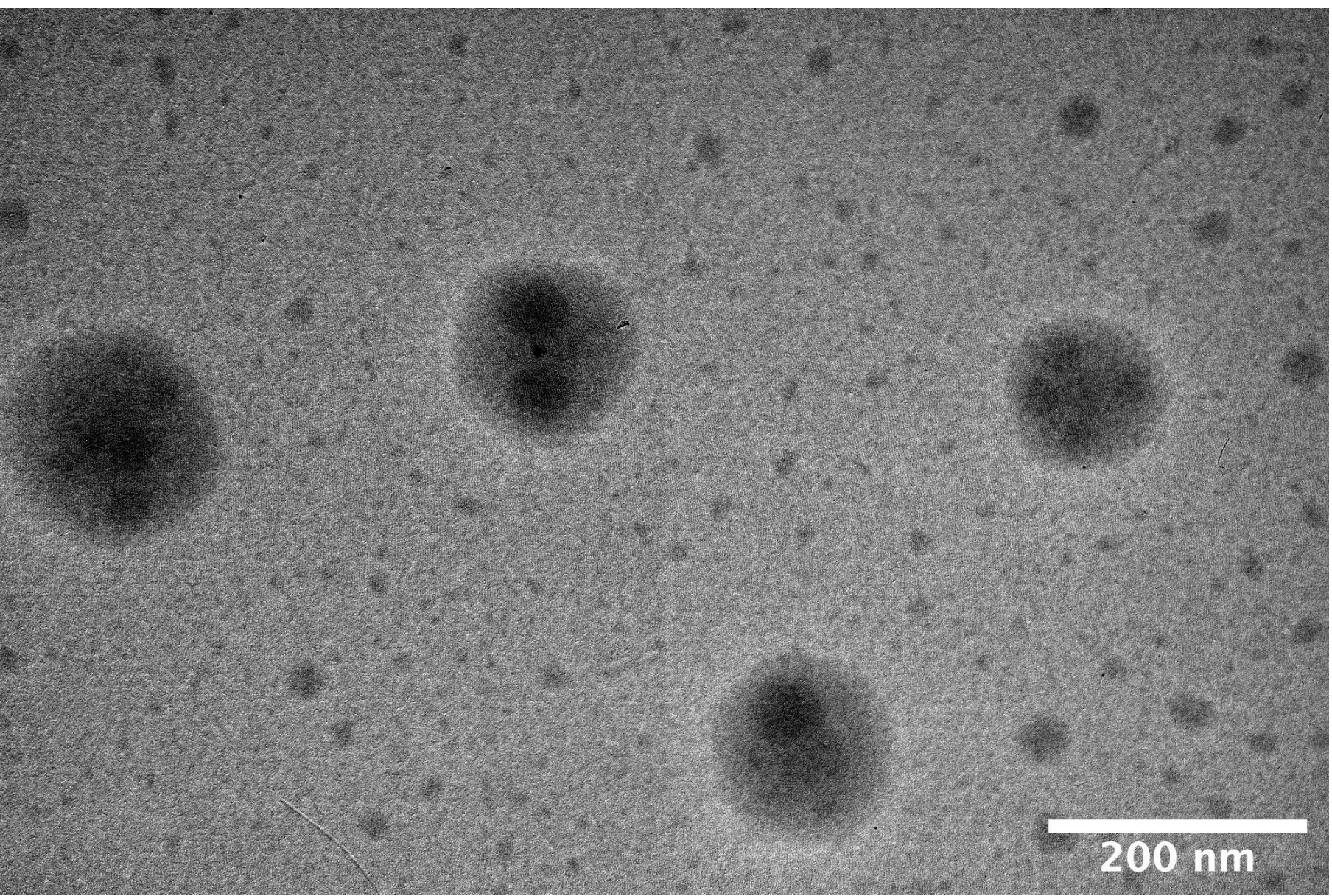
\* DMF eluent, PMMA standards

## 5. Self-Assembly

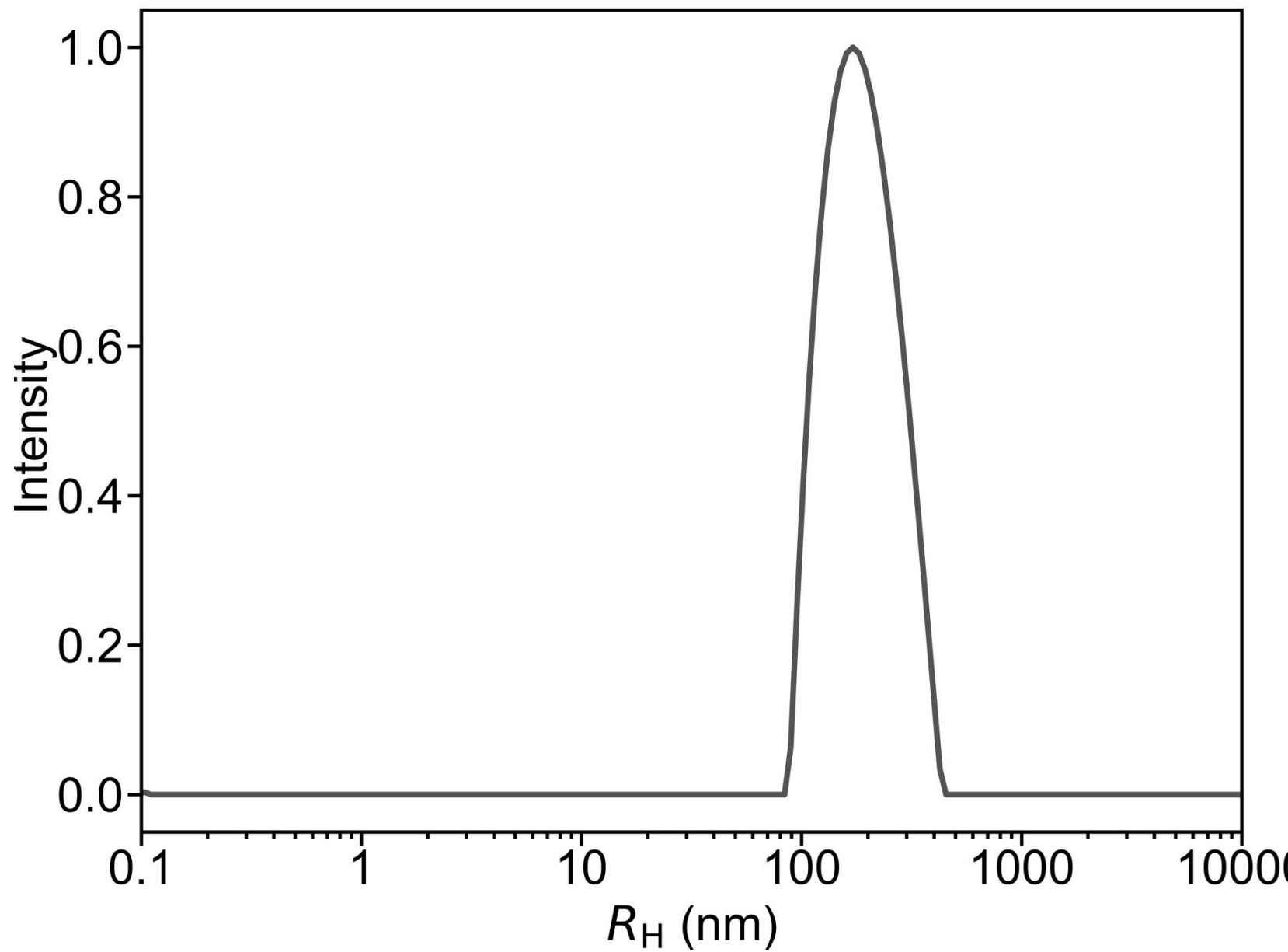
- Turbidimetry measurements at 500 nm in **PBS solution** upon cooling



- TEM measurements of **P2** aqueous solution at 19 °C



- DLS measurements in **PBS solution at 19 °C**



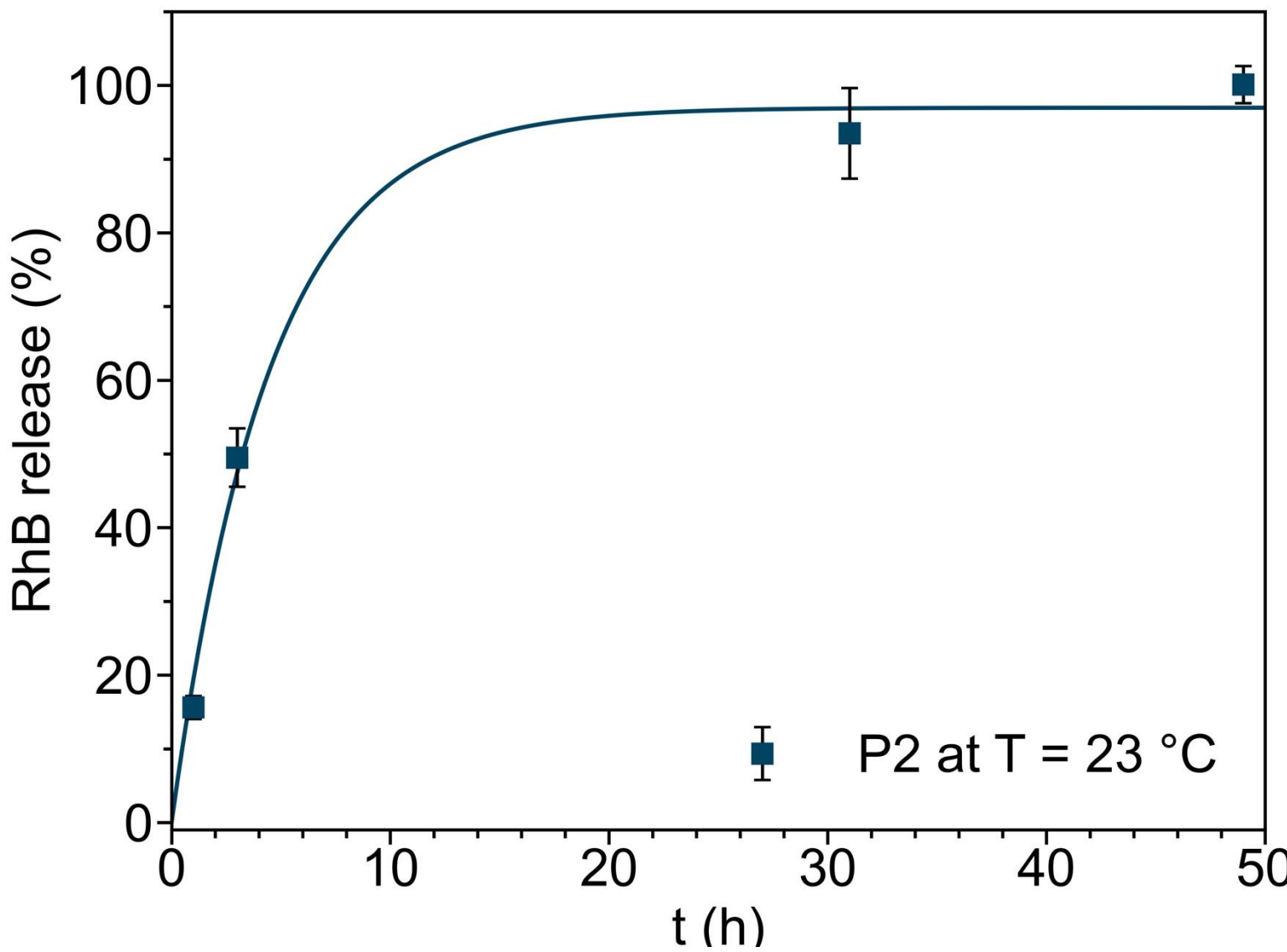
❖ The *T<sub>cp</sub>* of the diblock copolymers **was tuned** by the acrylonitrile mole fraction

## 6. Encapsulation and Release

- **Rhodamine B** was encapsulated by simply cooling a pre-heated PBS solution containing a UCST-type diblock copolymer and the model dye.

$$\text{DLC (\%)} = \frac{(\text{weight of RhB encapsulated}) \times 100}{(\text{weight of diblock copolymer})} = 0.2 \%$$

$$\text{DLE (\%)} = \frac{(\text{weight of RhB encapsulated}) \times 100}{(\text{weight of RhB initially used})} = 9.5 \%$$



## 7. Acknowledgments

The research project was supported by the Hellenic Foundation for Research and Innovation (H.F.R.I.) under the “2nd Call for H.F.R.I. Research Projects to support Faculty Members & Researchers” (Project Number: HFRI-FM17-3346).

