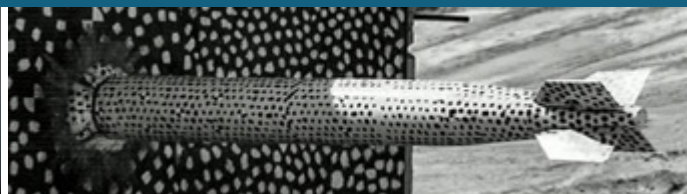
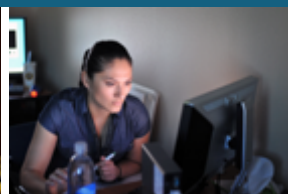




Tuning Poly(*N*-isopropylacrylamide) Surfactant Phase Behavior to Access Thermoresponsive Micelle Disassembly



Charles P. Easterling

ACS National Meeting Spring 2023

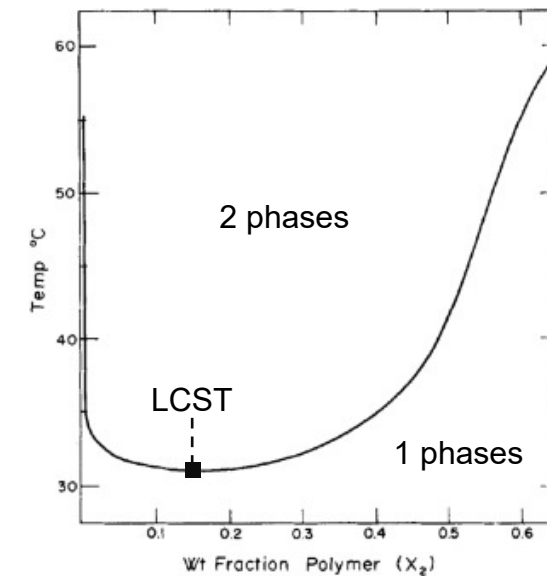
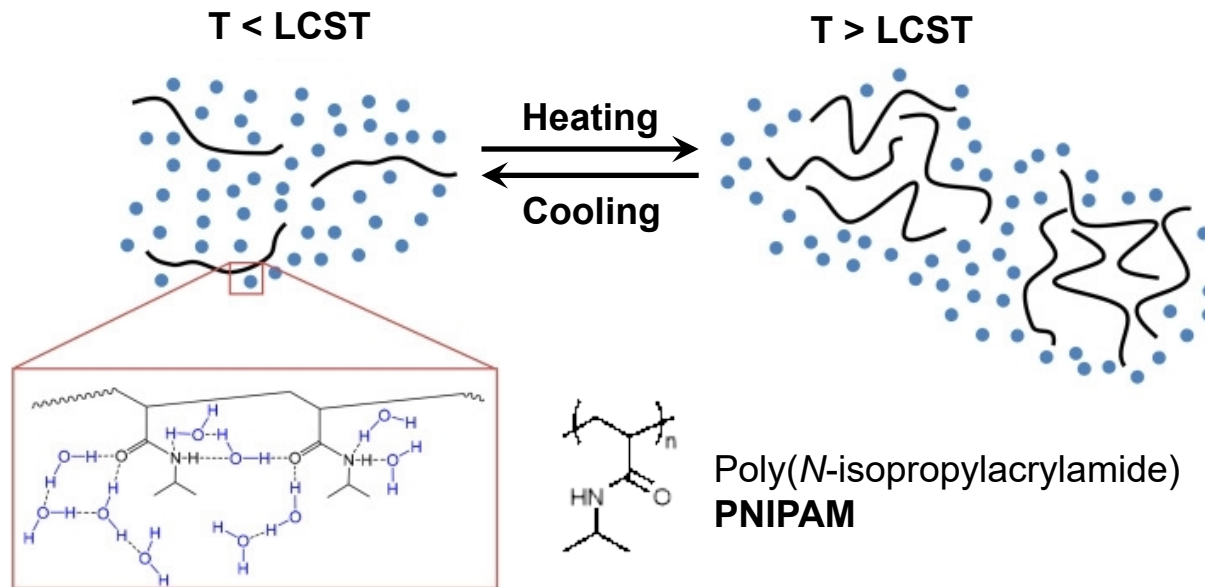
Introduction: Thermoresponsive Polymers



Temperature-dependent polymer-solvent and polymer-polymer interactions dictate solution properties

Fully hydrated & solubilized

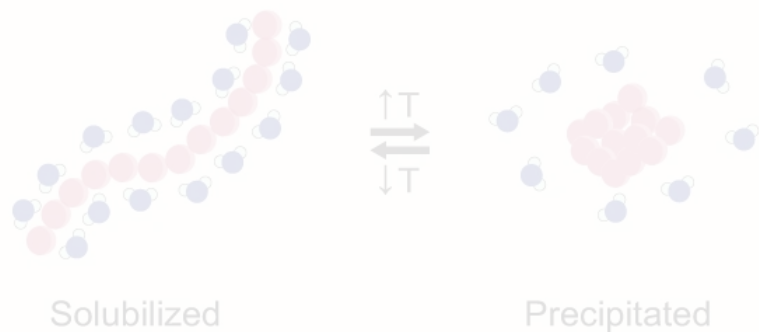
Deswelled polymer globule



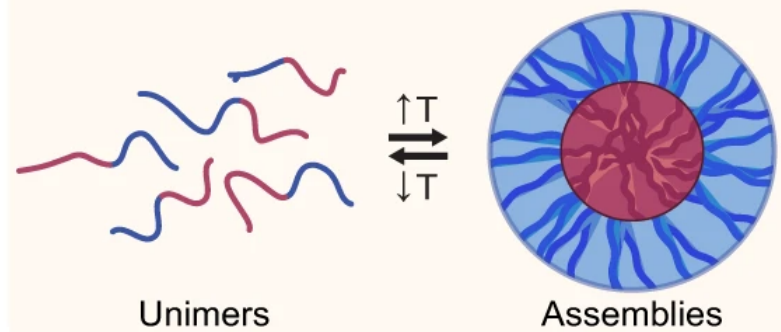
Thermoresponsive Polymers & Self Assembly



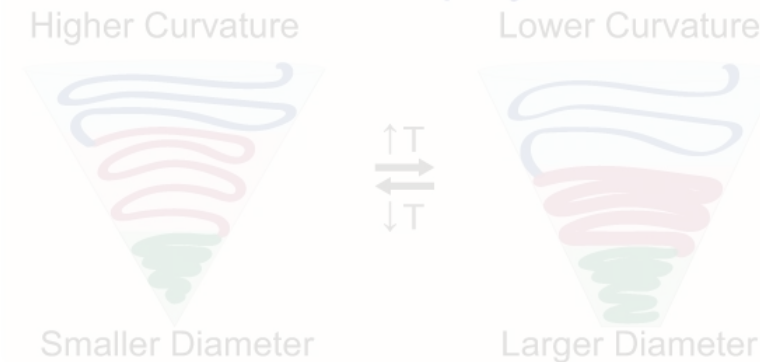
Homopolymer



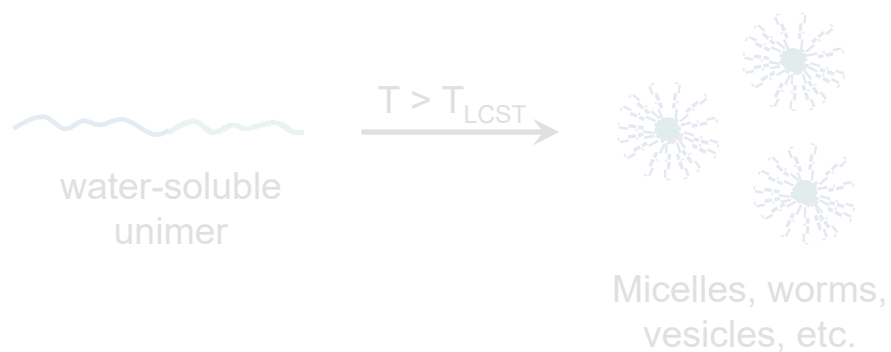
Diblock Copolymer



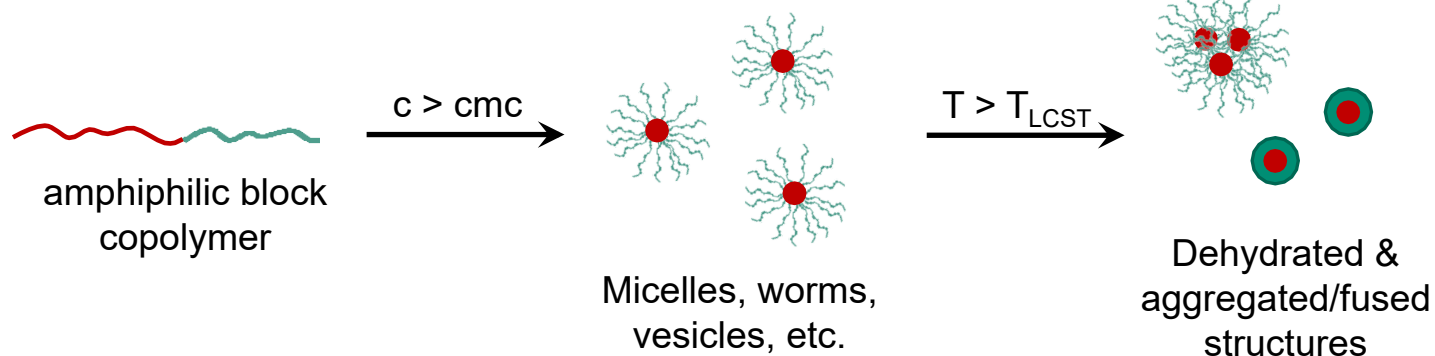
Triblock Copolymer



Hydrophilic-*b*-Thermoresponsive

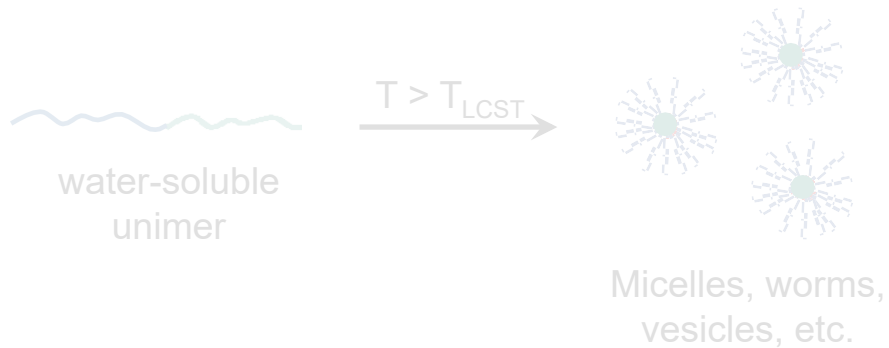


Hydrophobic-*b*-Thermoresponsive

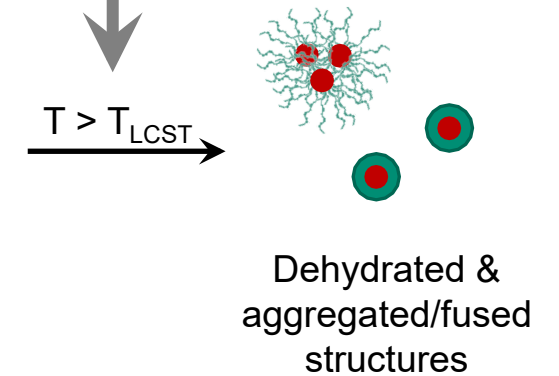
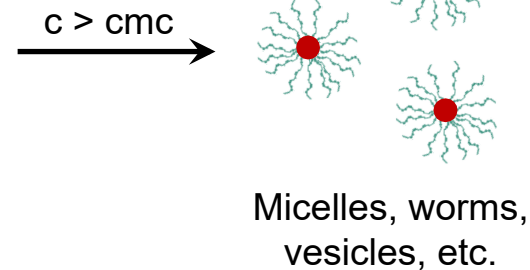


How does thermoresponsiveness correlate to cmc behavior and the micellization process?

Hydrophilic-*b*-PNIPAM



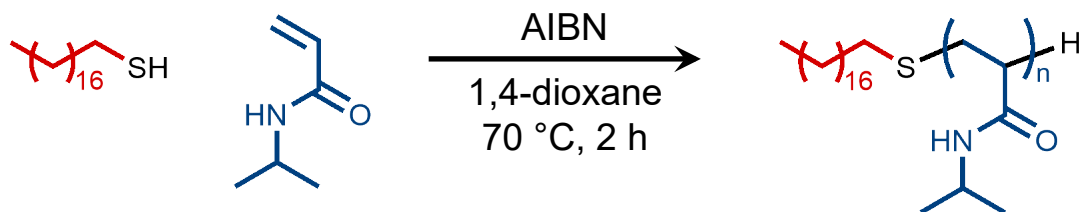
amphiphilic block copolymer



PNIPAM Surfactant Design & Synthesis

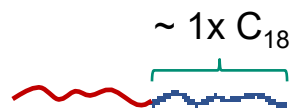


- Scalable synthesis using free-radical polymerization and thiol chain transfer agent
- PNIPAM block designed to have varied lengths relative to the C₁₈ hydrophobic tail



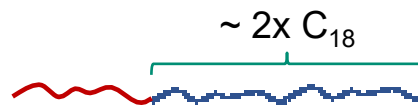
P8C18 (n = 8)

$M_n = 1.22 \text{ kg mol}^{-1}$, $\bar{D} = 1.50$



P20C18 (n = 20)

$M_n = 2.64 \text{ kg mol}^{-1}$, $\bar{D} = 1.95$

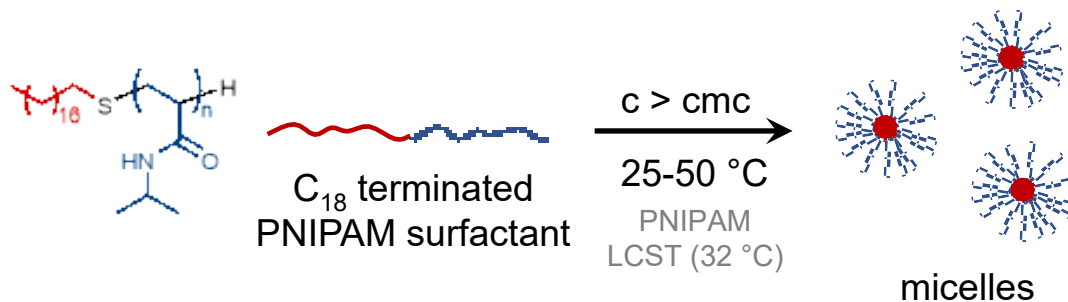


P34C18 (n = 34)

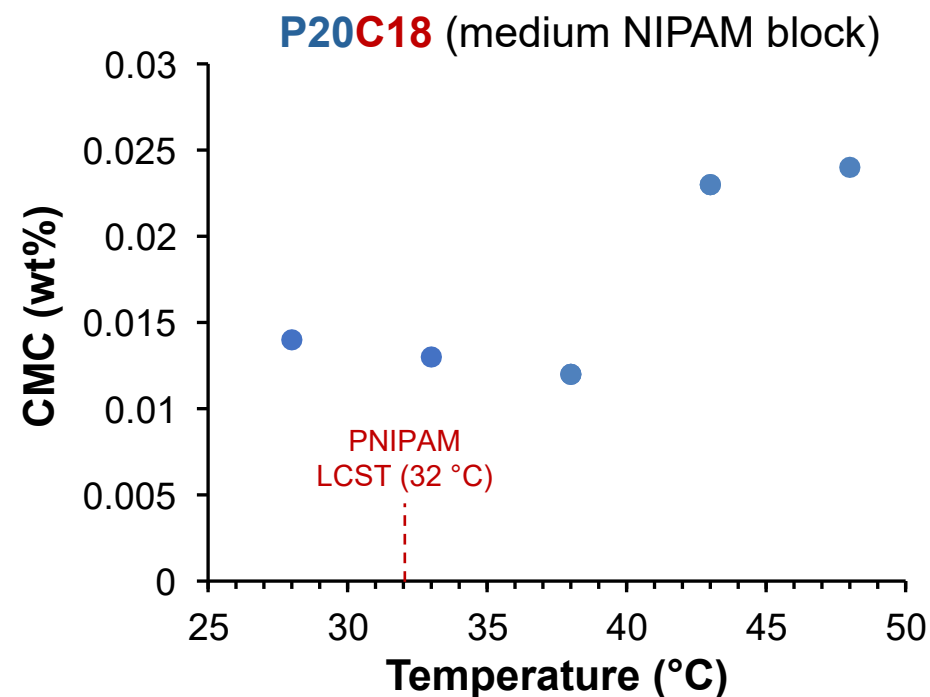
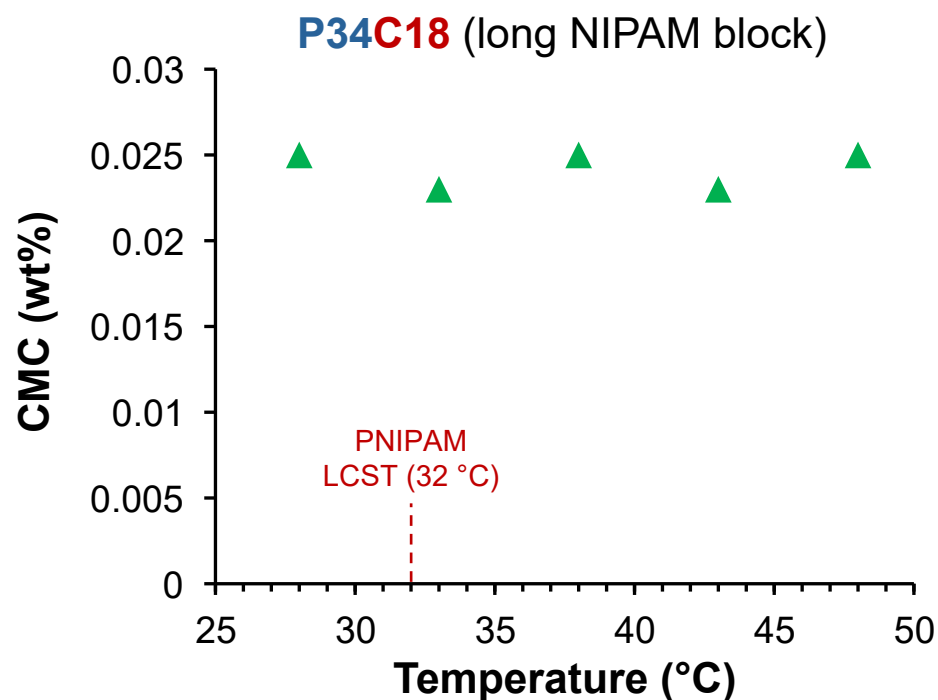
$M_n = 4.17 \text{ kg mol}^{-1}$, $\bar{D} = 2.52$



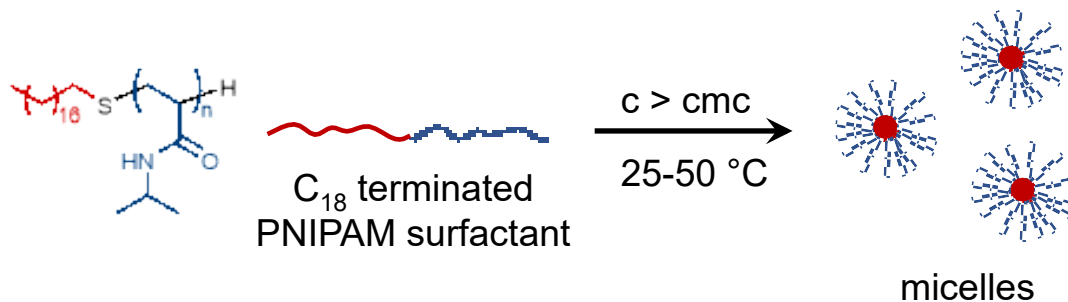
Critical Micelle Concentration of PNIPAM Surfactants



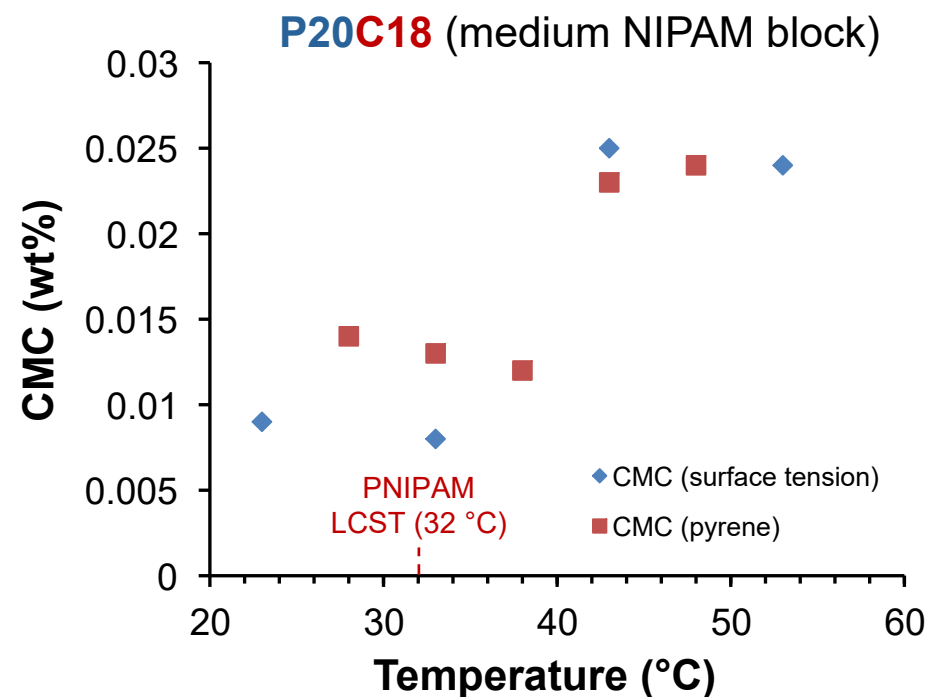
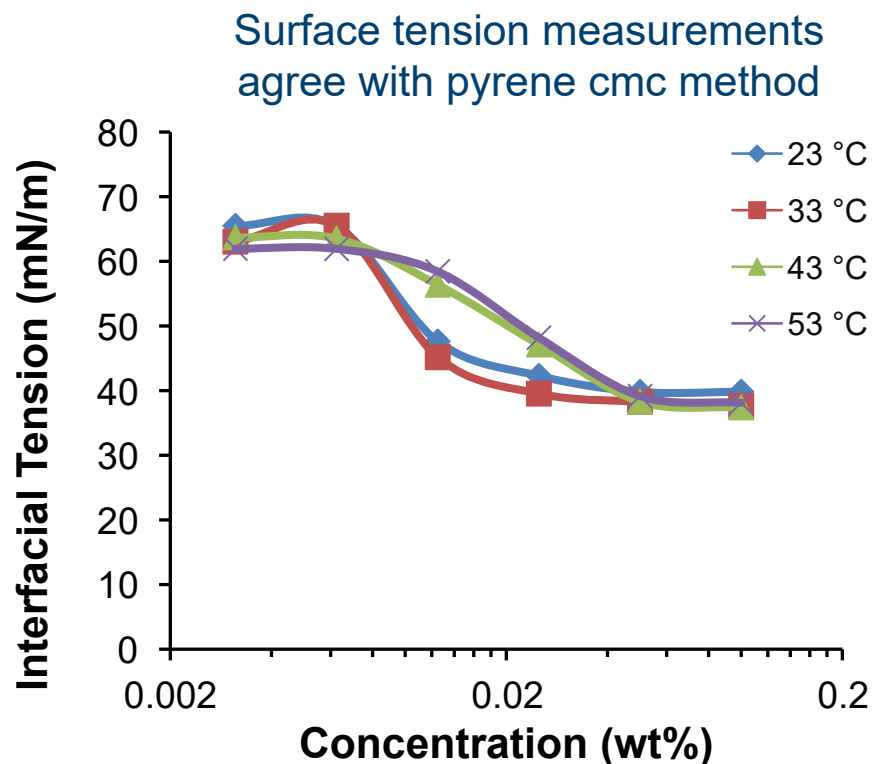
- **P34C18** PNIPAM surfactant shows consistent critical micelle concentration (cmc) of 0.025 wt.% from 25-50 °C.
- **P20C18** displays an increase in the CMC at temperatures above 40 °C (thermoreponsive regime).



Critical Micelle Concentration of PNIPAM Surfactants



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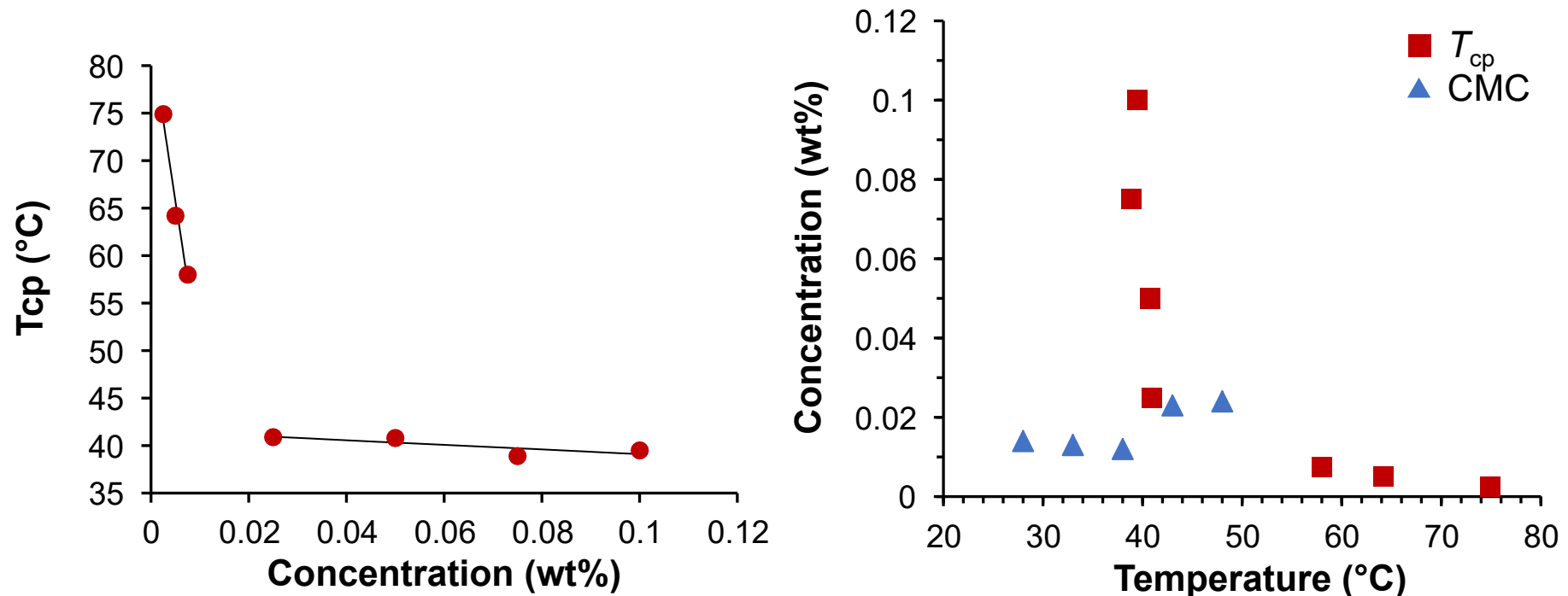


Correlating Thermoresponsiveness to CMC Behavior



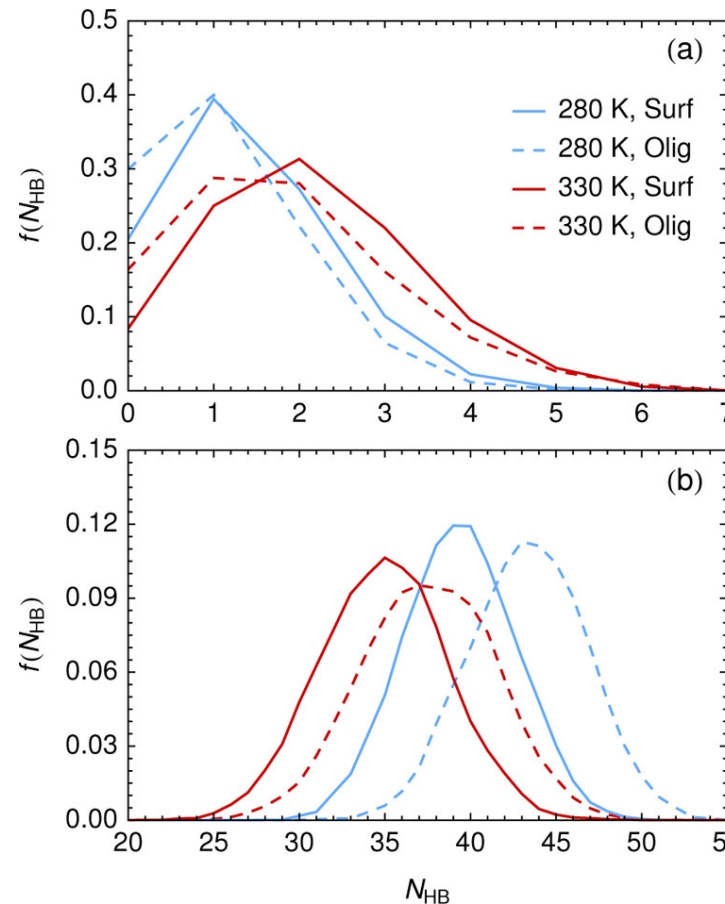
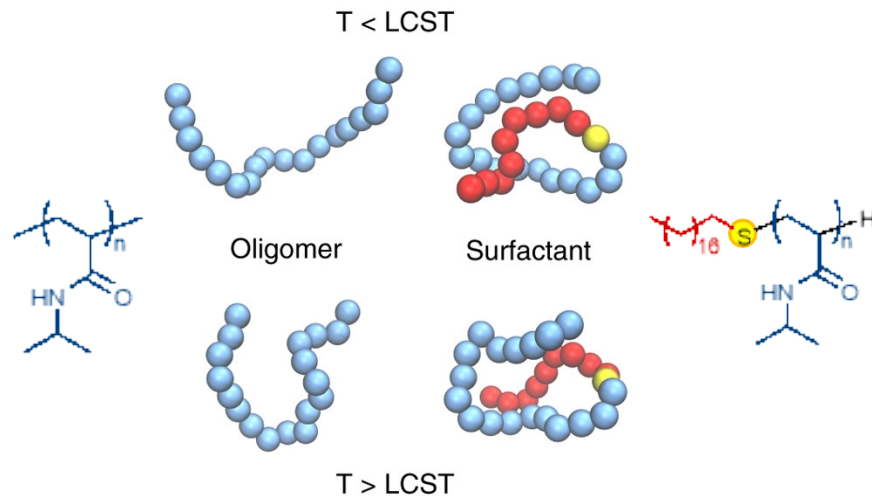
- Cloud point temperature (T_{cp}) is high (>55 °C) at low concentration but approaches ~40 °C between 0.02-0.1 wt%
- Overlaying T_{cp} and CMC reveals an increase in the CMC when the surfactant undergoes PNIPAM thermal transition

P20C18 (medium NIPAM block)

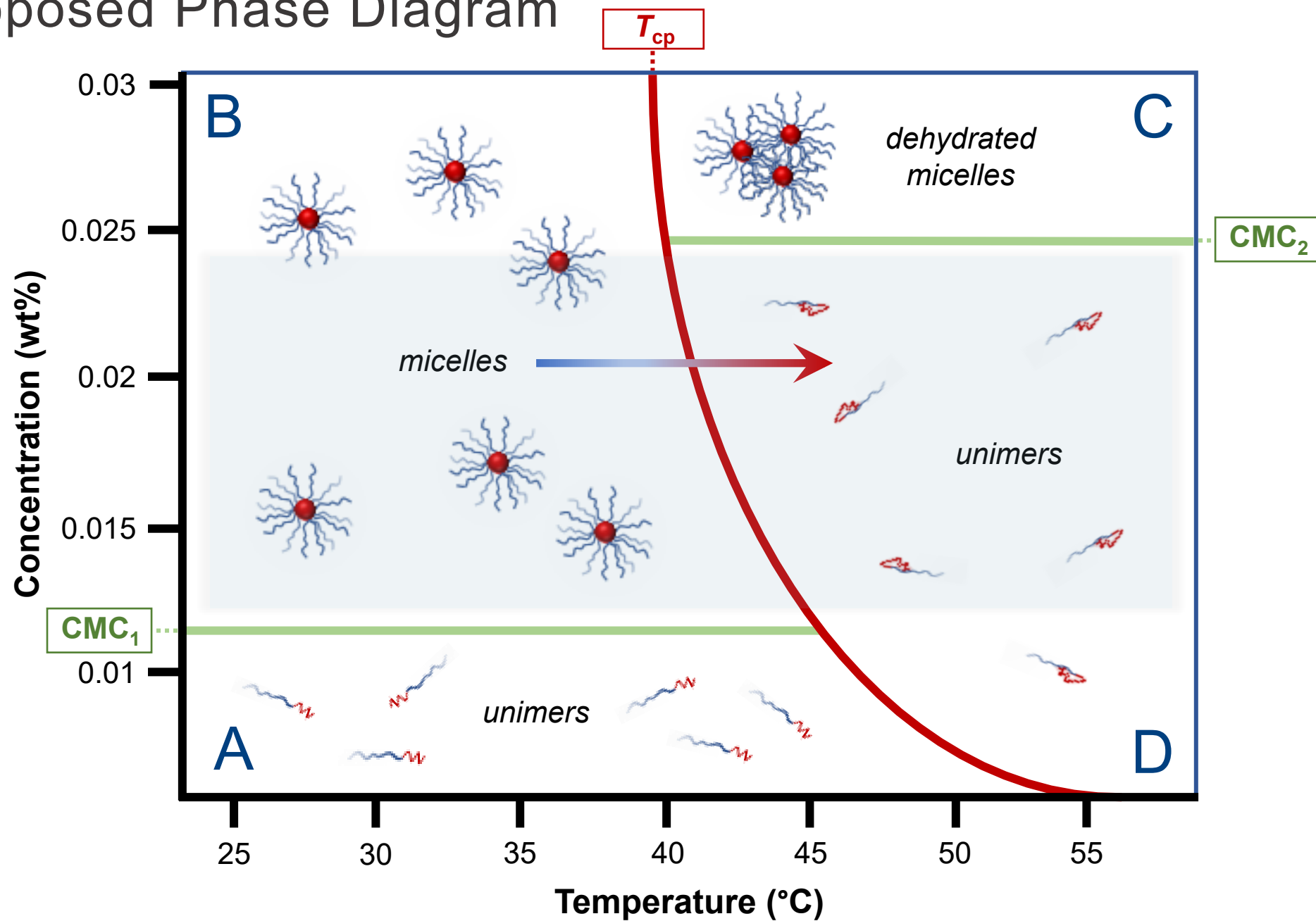


Atomistic Simulations Reveal Chain Folding for Stabilization

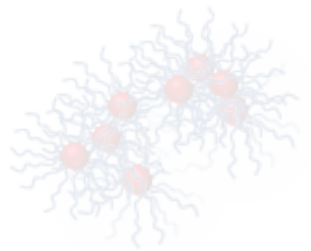
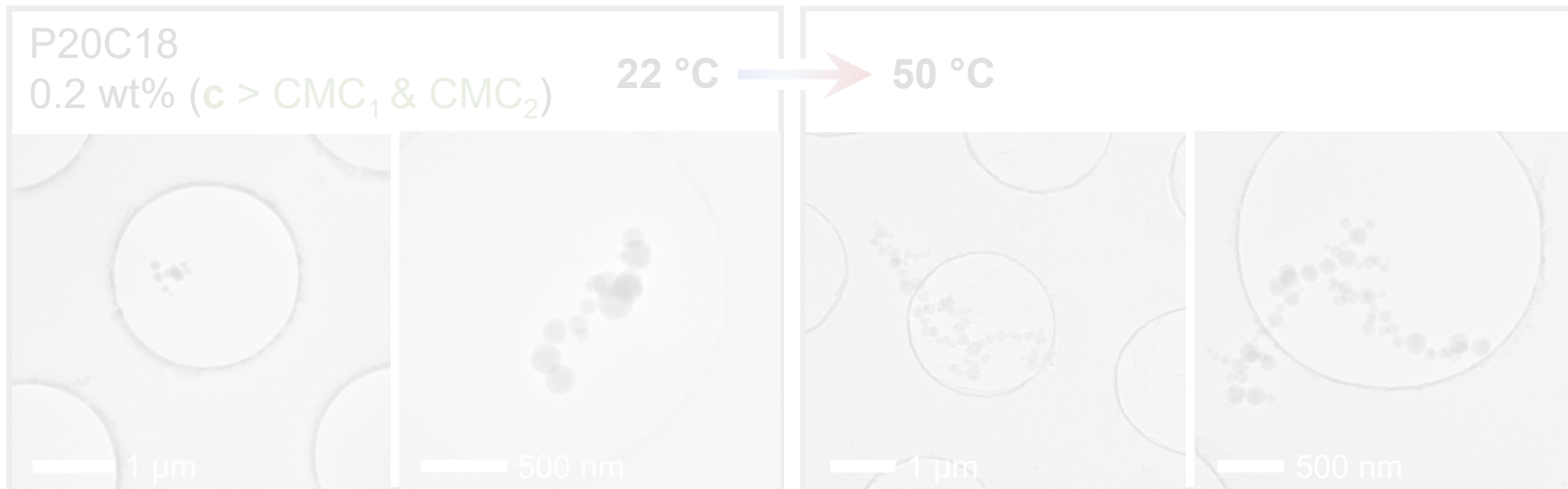
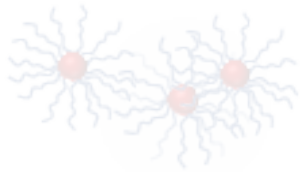
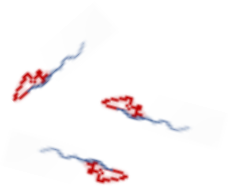
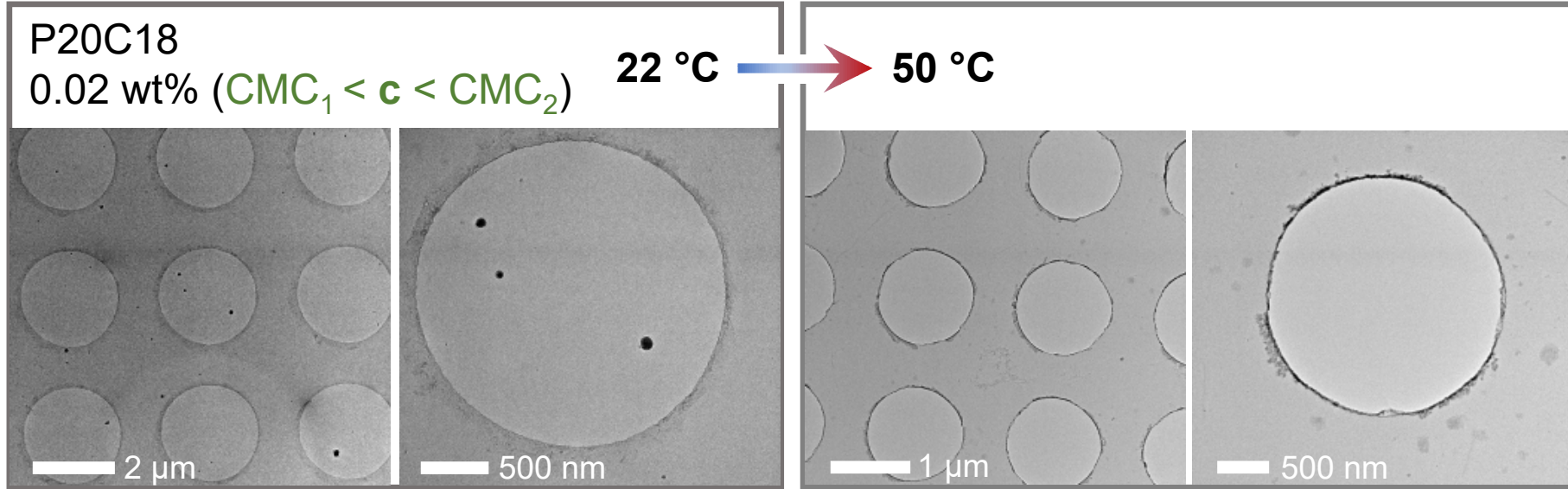
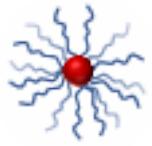
On the unimer level, **P20C18** collapses to bring the hydrophobic C₁₈ tail in contact with the PNIPAM backbone both below and above the transition temperature of PNIPAM



Proposed Phase Diagram



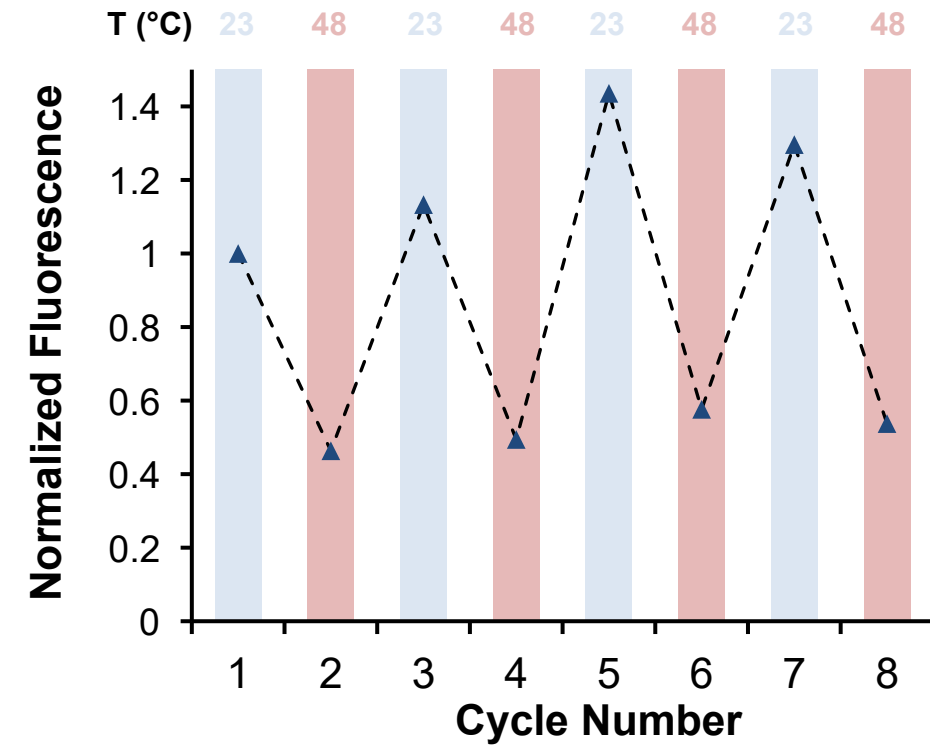
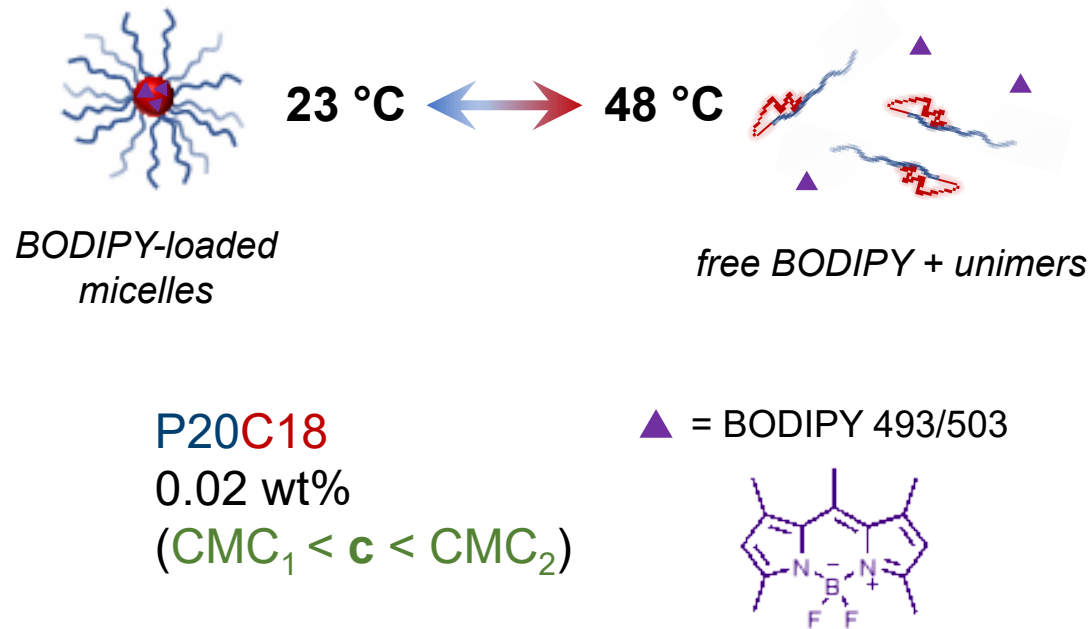
Cryo-EM Characterization of Phase Transitions



Reversible Release of Hydrophobe



- P20C18 micelles are capable of delivering hydrophobic payload through micelle disassembly
- Reversible BODIPY release of ~50% between heating/cooling cycles



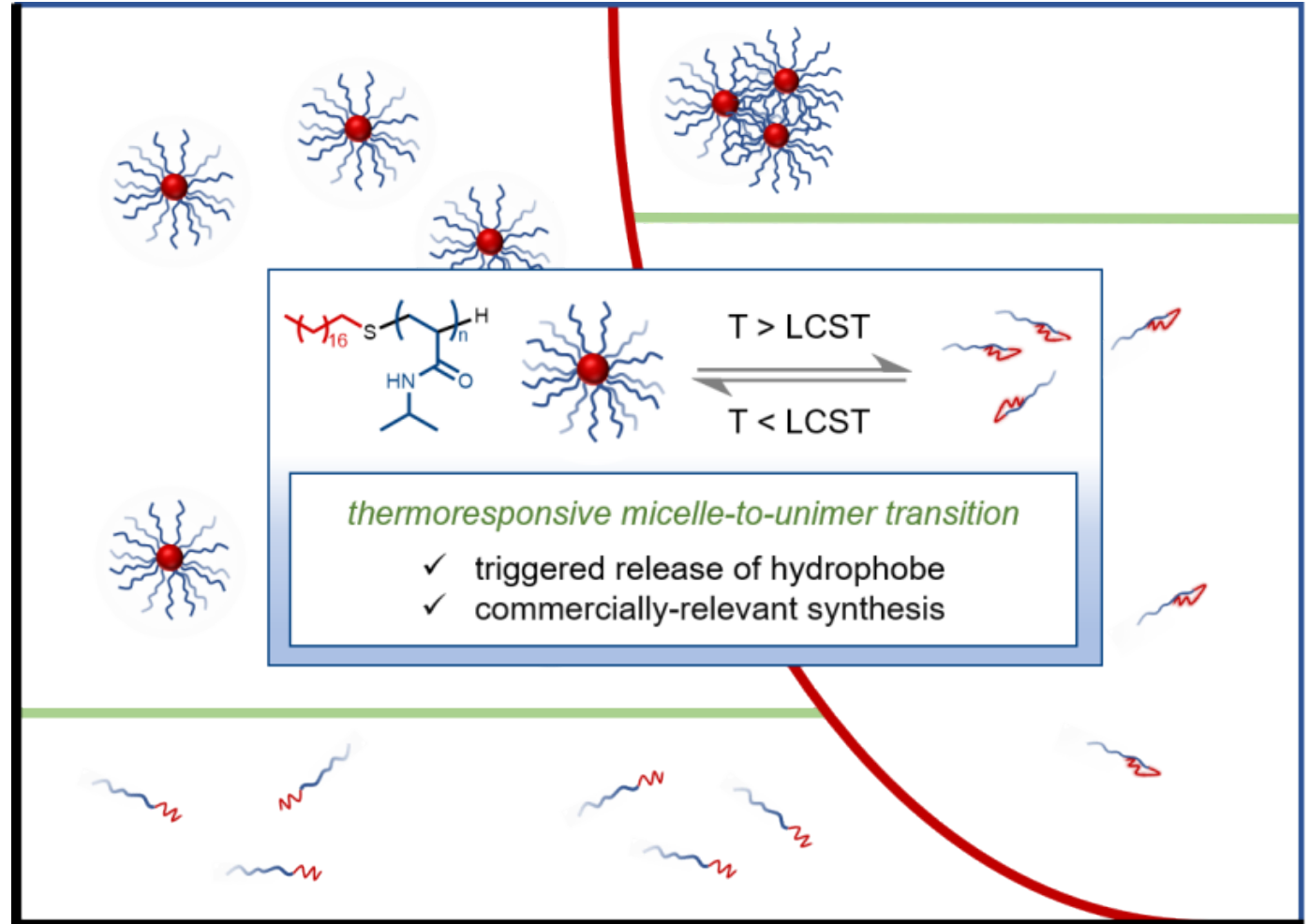
Summary and Future Directions



PNIPAM surfactants have a temperature-dependent critical micelle concentration that increases when $T > T_{\text{LCST}}$

First known report of thermally triggered micelle disassembly of a hydrophobic-*b*-LCST block copolymer micelle

Future work will study PNIPAM-based phospholipid surfactants in giant unilamellar vesicles





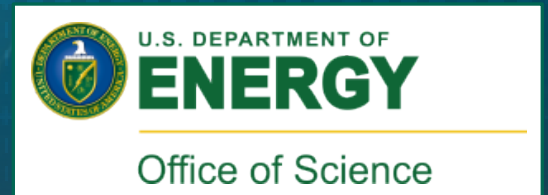
Acknowledgements

Students/Postdocs

Chet Simocko
Manish Singh
Lauren Abbott
Zachary Romero

Staff Scientists

John Watt
Mark Stevens
Dale Huber



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