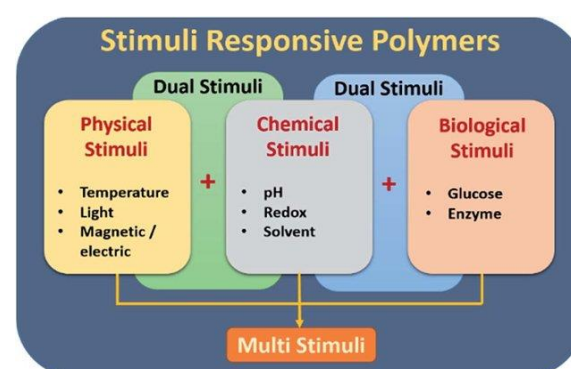


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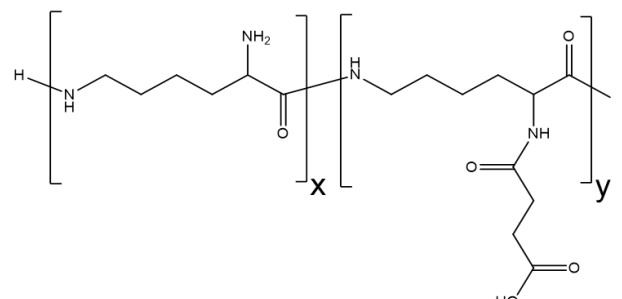
INTRODUCTION

Stimuli-responsive polymers have attracted great attention in recent years. They respond to small changes in the surrounding environment, which makes them suitable candidates for applications in nanotechnology and biomedicine, for use as drug carriers and smart surfaces, and for protein separation.



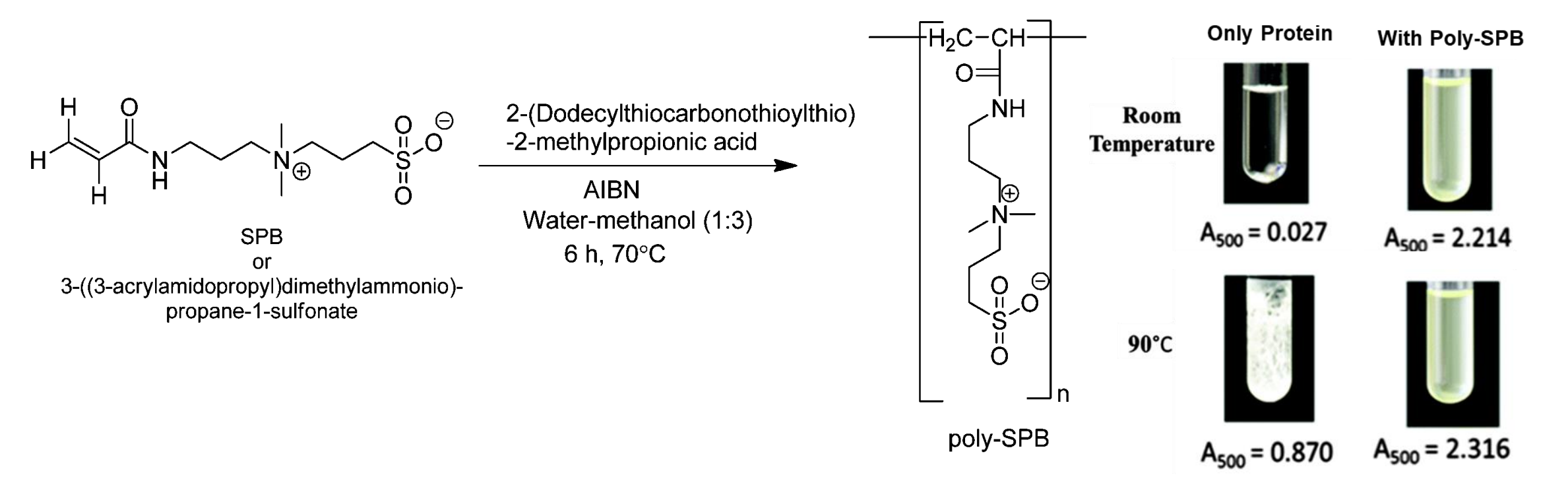
As the field of applications expands, a single stimuli-responsive polymer can no longer fulfill the demands of the growing industry, so dual-stimuli responsive systems are attractive options.

Our group reported that carboxylated poly-L-lysine (PLLSA) exhibits LCST-type thermo-responsive and pH-responsive property.

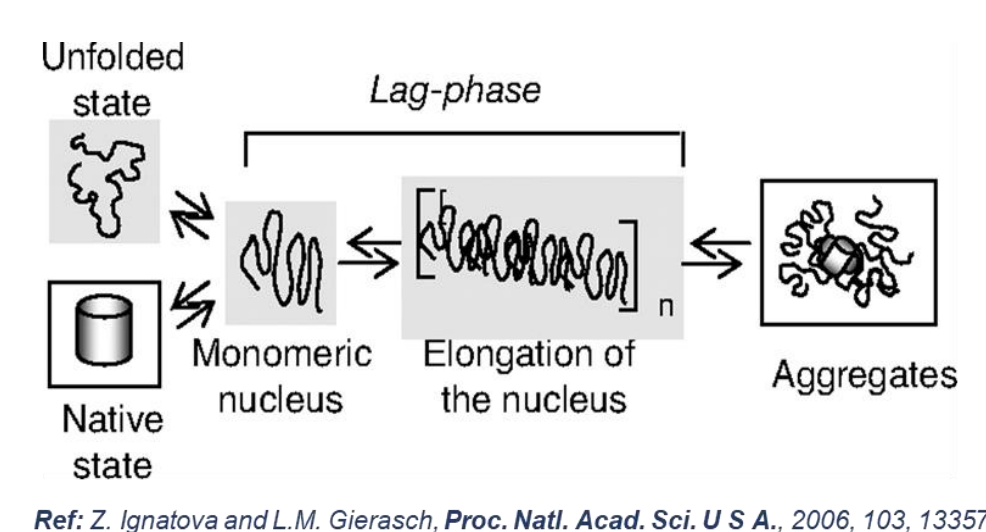


Another polymer, poly-sulfobetaine (poly-SPB) is known to exhibit UCST-type phase transition.

In our other studies, we had developed various poly-SPB polymers, which could protect proteins against denaturation.

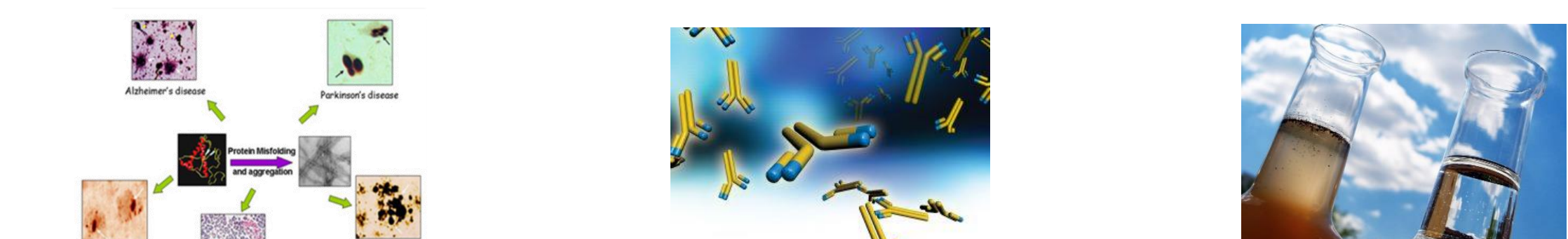


Protein Aggregation is the process by which misfolded proteins adopt a conformation that cause its polymerization into aggregates and organized fibrils.



Ref: Z. Ignatova and L.M. Gierasch, Proc. Natl. Acad. Sci. U S A, 2006, 103, 13357

Problems associated with protein aggregation



Neurodegenerative disease

Protein Biopharmaceutics: Protein Drugs

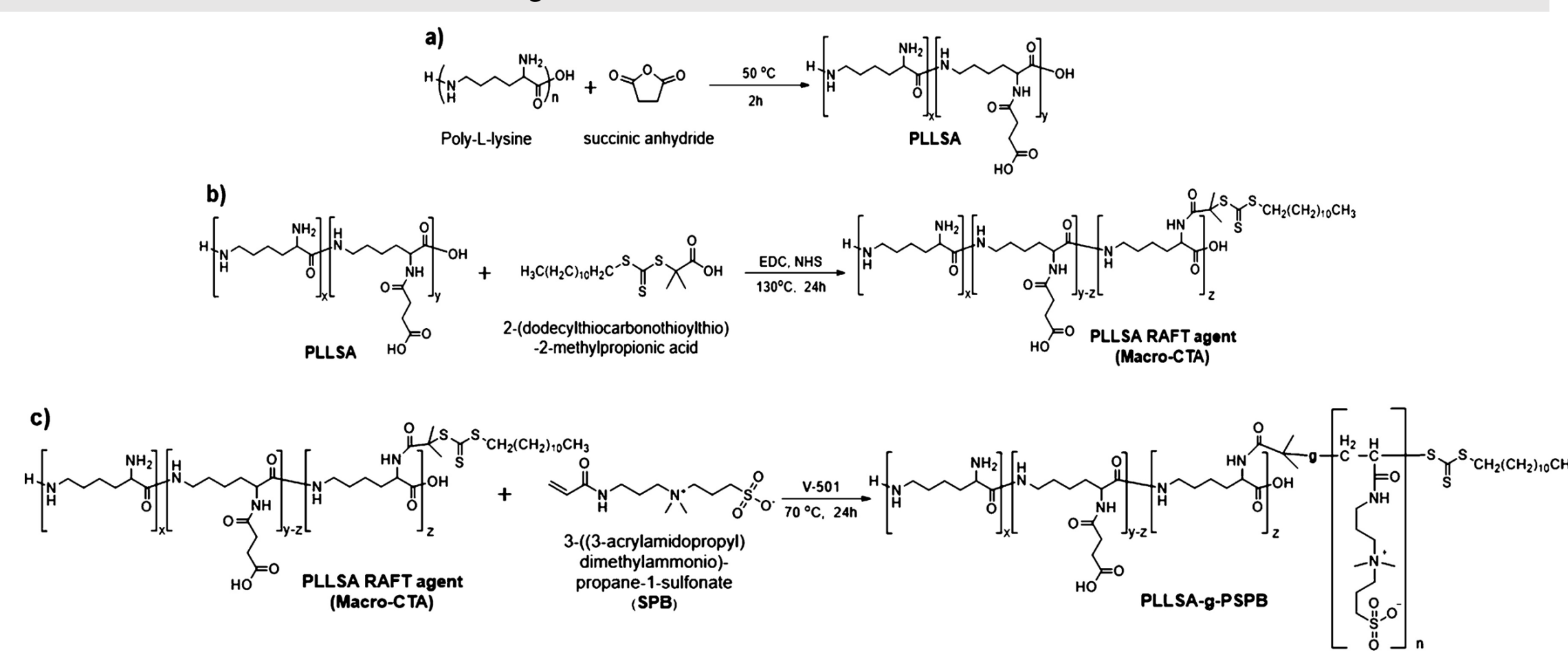
Purification of Proteins and storage

AIM

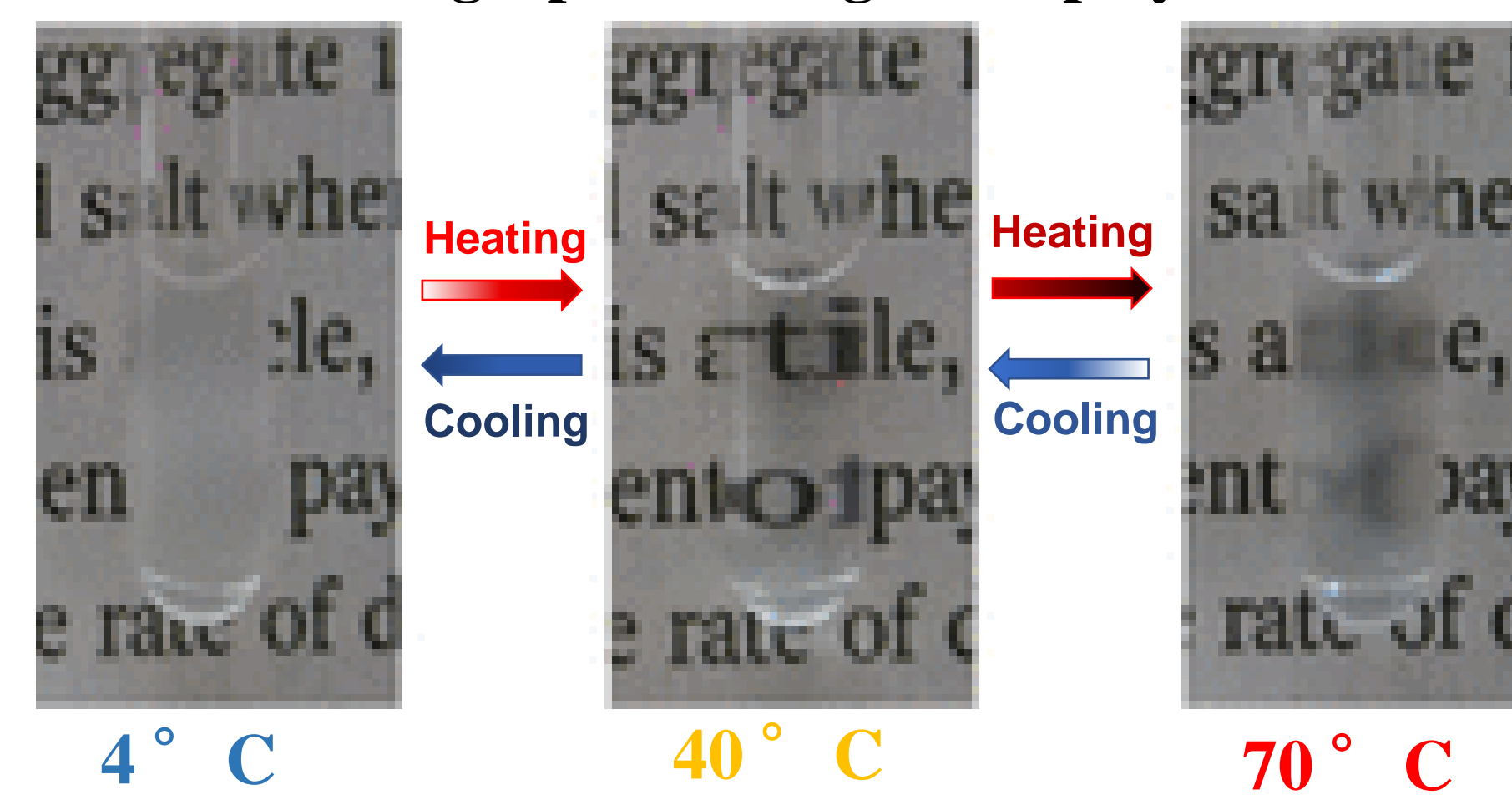
- In the first part, we developed graft copolymers consisting of two zwitterionic blocks, that is, PLLSA-g-PSPB. The presence of the PLLSA segment allows these graft copolymers to exhibit LCST and pH responsive properties, and the PSPB block allows for UCST-type transition.
- We analyzed the protein aggregation inhibition property of these graft copolymers and the stimuli responsive capture and delivery of proteins. The presence of the PSPB segment is expected to impart this property
- We transform the linear copolymer into a self-assembled micelle and analyze their structure at the molecular level and use this system a delivery vehicle. By incorporating cholesterol to the copolymer.

RESULTS

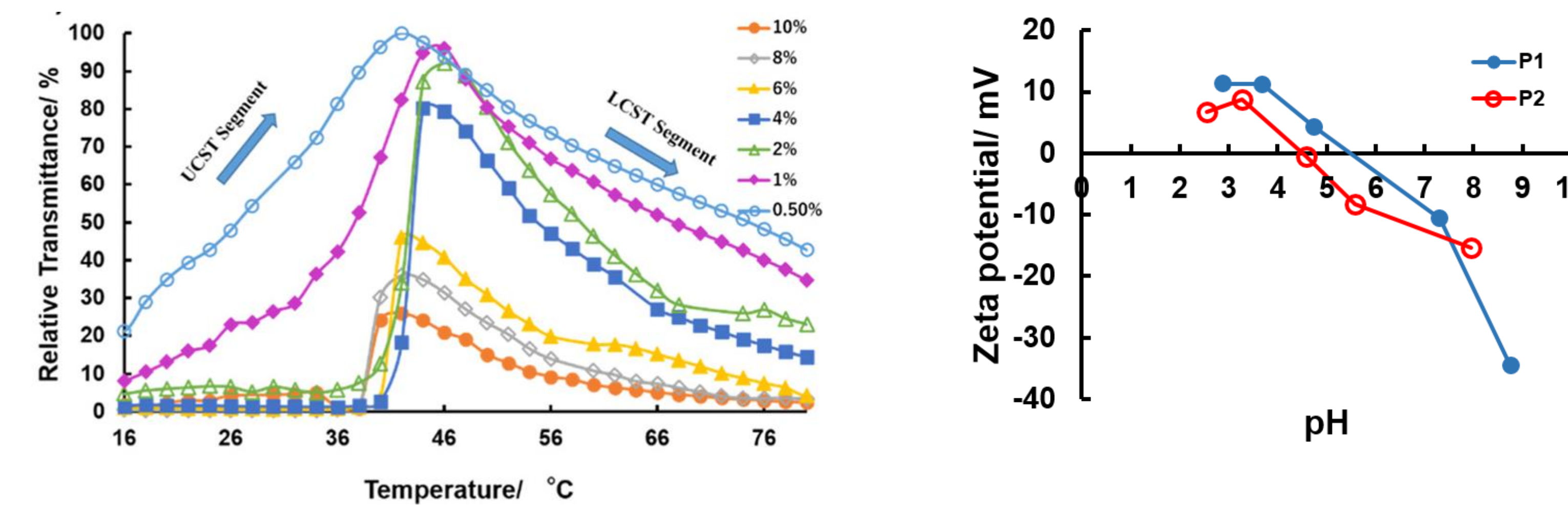
Synthetic Scheme



Photographs of the graft copolymer

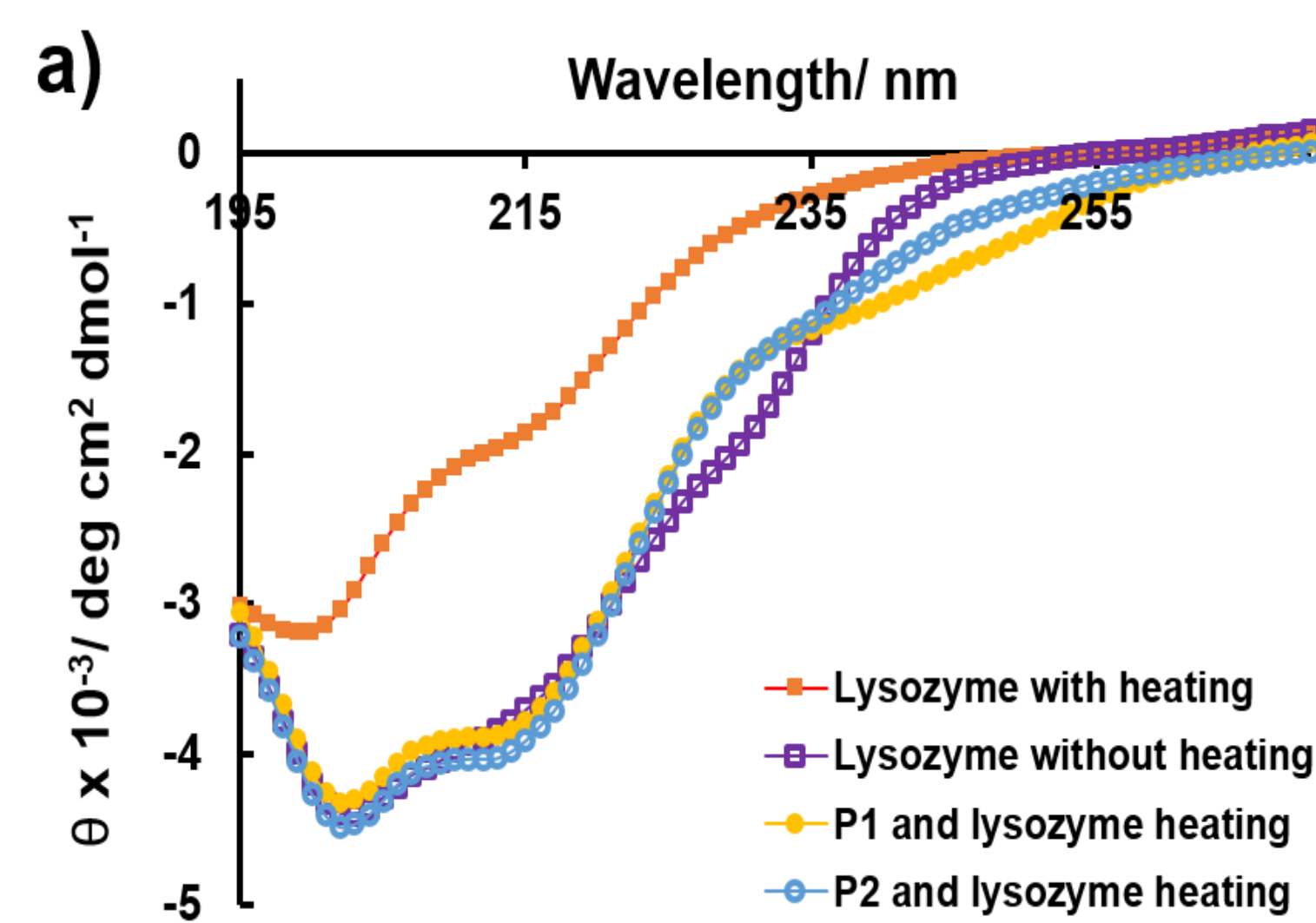


Dual thermoresponsive and pH-responsive property



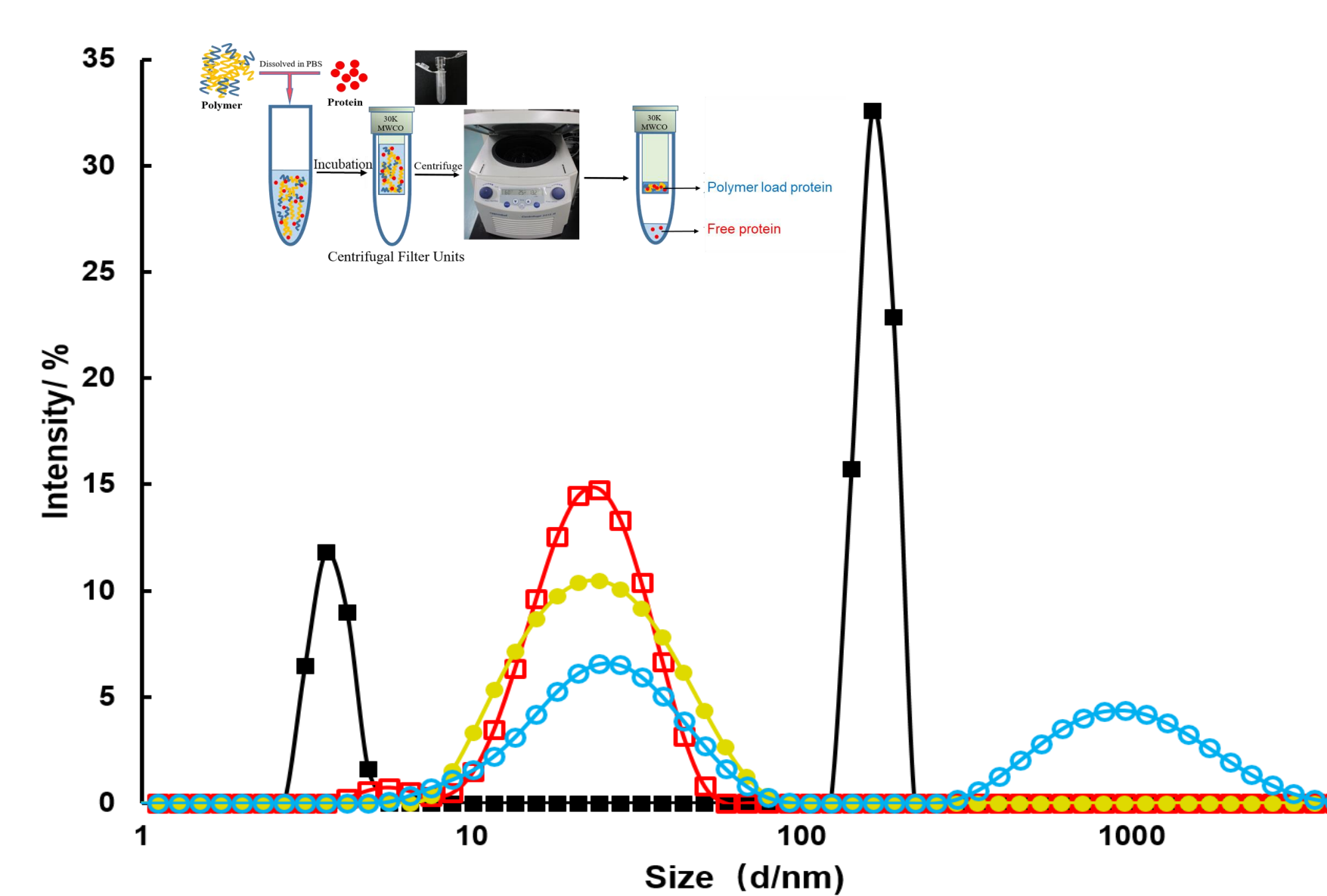
Protein Study

Protein Protection (CD Spectroscopy)



Graft polymers stabilize higher-order structure of proteins.

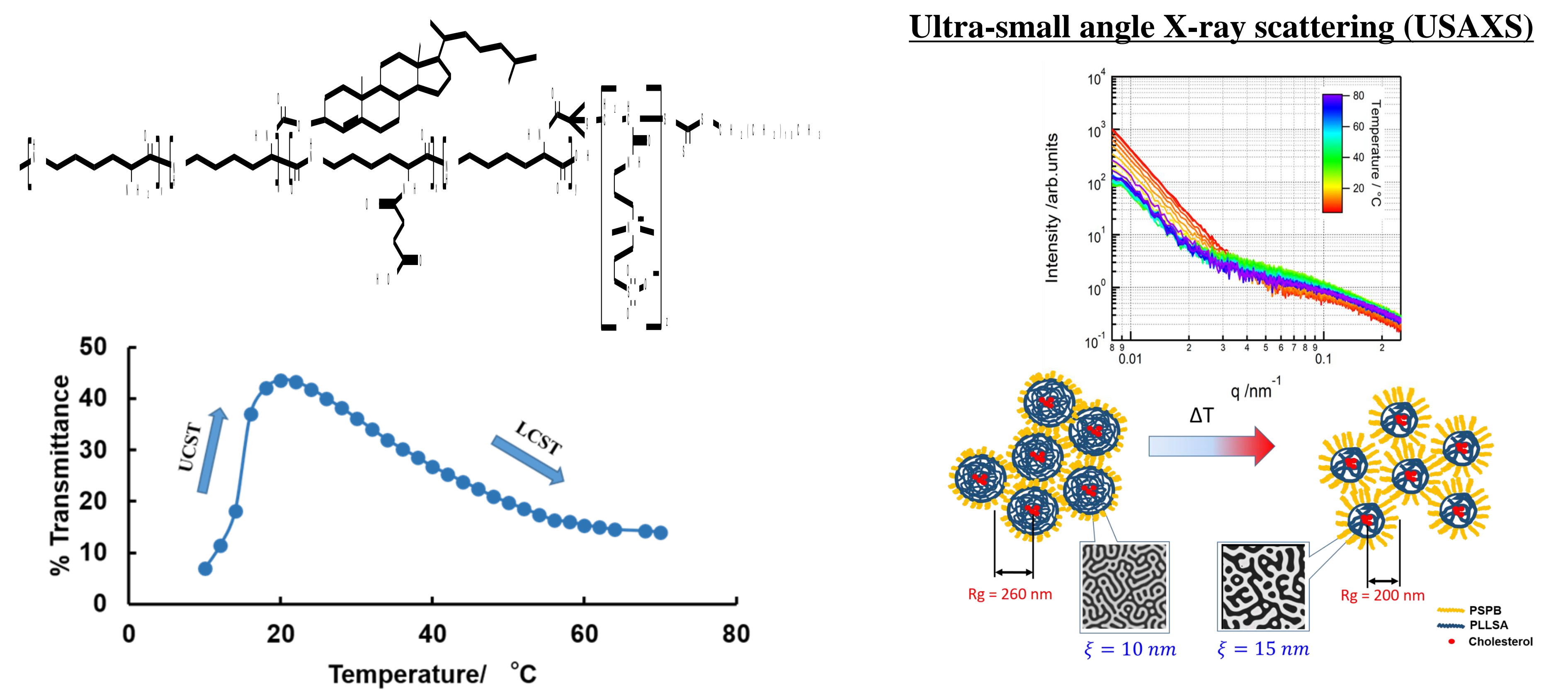
pH responsive protein delivery



These polymers can bind lysozyme (90%) spontaneously at neutral pH and release it on changing the pH.

Self-assembled Micelle

Ultra-small angle X-ray scattering (USAXS)



CONCLUSIONS

- Zwitterionic polymers can be easily synthesized in a RAFT polymerization.
- These polymers exhibit dual thermo-responsive and pH responsive behavior and can be used as a protein delivery vehicle.
- This polymer can suppress protein aggregation at high temperature and allow the protein to maintain its higher order structures.
- The thermoresponsive polymeric micelles modified with cholesterol were fabricated. These micelles were formed by self-assembly in an aqueous solution.

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