

Self-Assembled Microparticles for Targeted Protein Delivery to Sites of Internal Hemorrhage

Janet Kang

Allan Hancock College

Biochemistry

Mentor: April Sawvel

Faculty Advisor: Prof. Galen D. Stucky

UCSB, Department of Chemistry and Biochemistry

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A New Approach to Treating Internal Hemorrhage



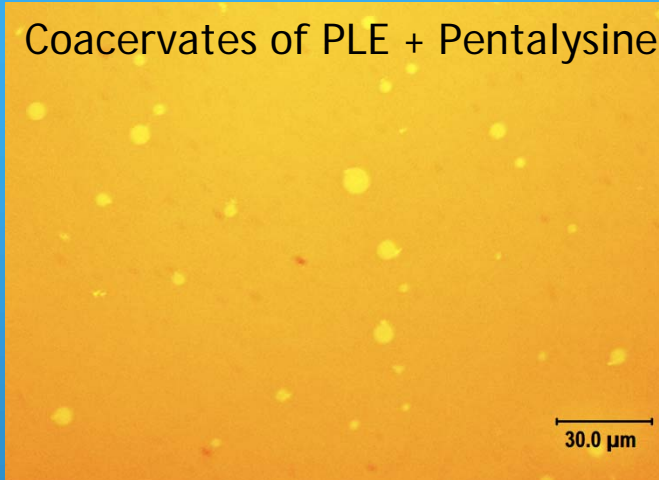
- Uncontrolled hemorrhage is the leading cause of battlefield mortalities and second leading cause of death in civilian traumas
- There is no effective method for treating internal hemorrhage

Our Approach

- Create a microparticle carrier:
 - biocompatible
 - synthetic
 - can be targeted to deliver the coagulation protein, thrombin, to the site of injury
- Will significantly advance the current technology available for targeted protein delivery in general.

Research Goals

Coacervates of PLE + Pentalysine



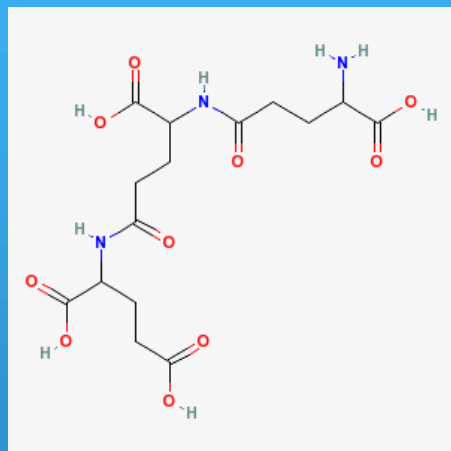
- Synthesize poly-L-glutamate (PLE) microparticles via simple coacervation
- Investigate the effects of polyelectrolyte concentration, pH, and ionic strength

- Produce stable, solid-like microparticles by applying a cross-linking agent.

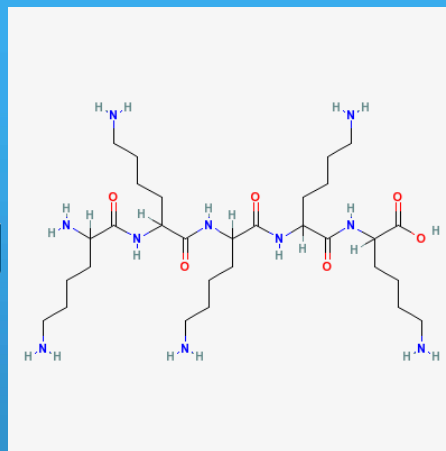
Significance

- Determine optimal conditions for microparticle formation
- Optimize microparticle porosity, size, quantity
- Microparticle properties = carrier effectiveness

Coacervate Synthesis



Poly-L-glutamate

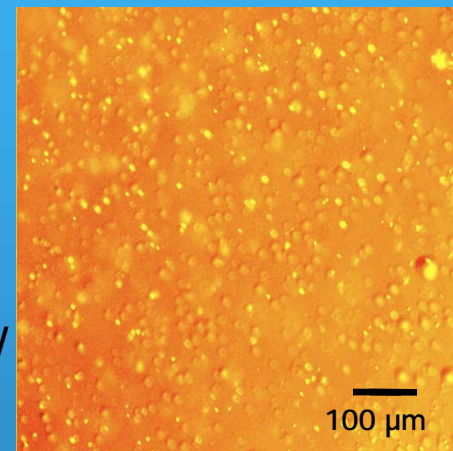


Pentalysine

10 mins



Self-assembly



Coacervates

Assembly Conditions:

- pH
- Ionic strength
- Polyelectrolyte concentrations

<http://pubchem.ncbi.nlm.nih.gov>

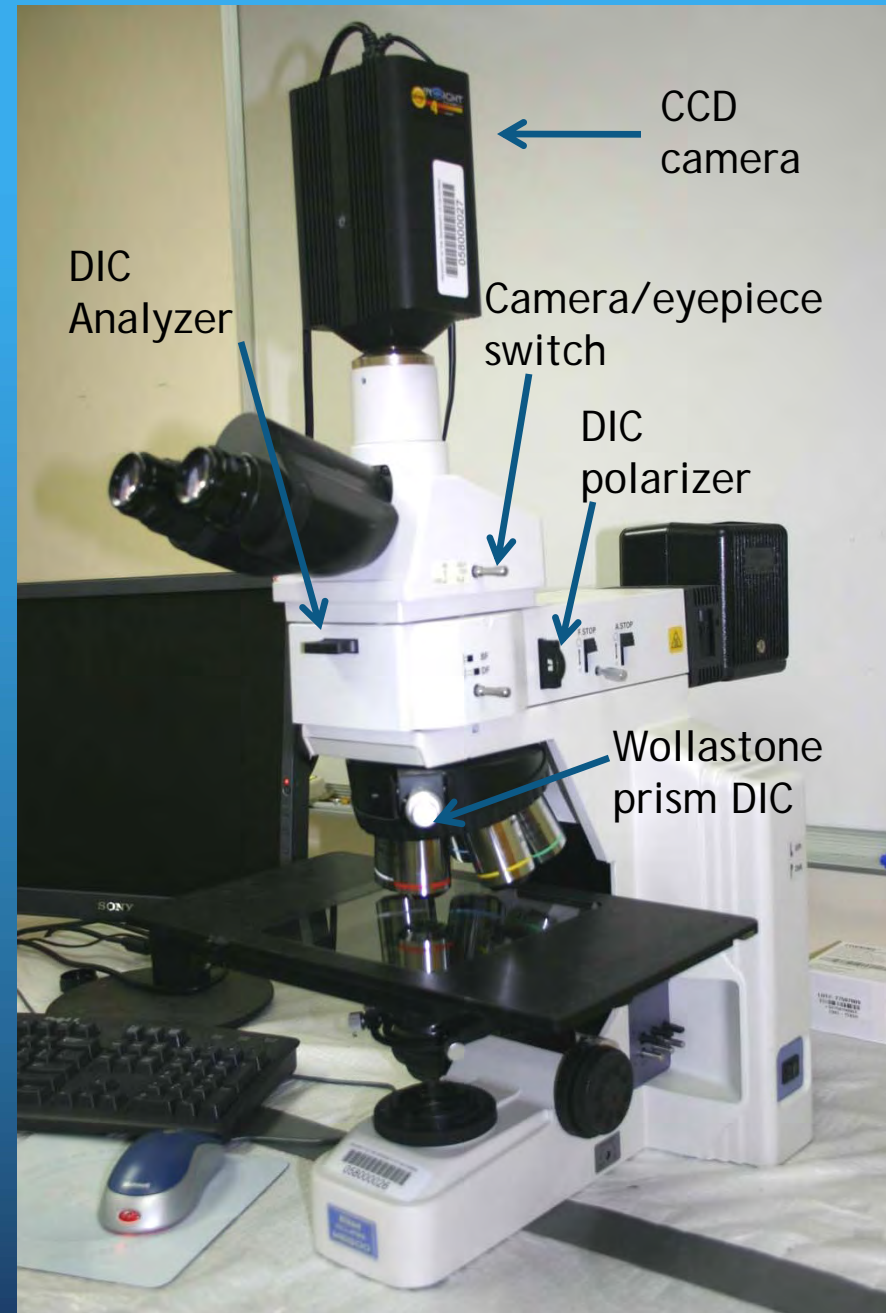
Optical Microscope

Advantages

- Qualitative and quantitative observations (size, quantity, shape, etc)
- Visually identify the type of substance in solution

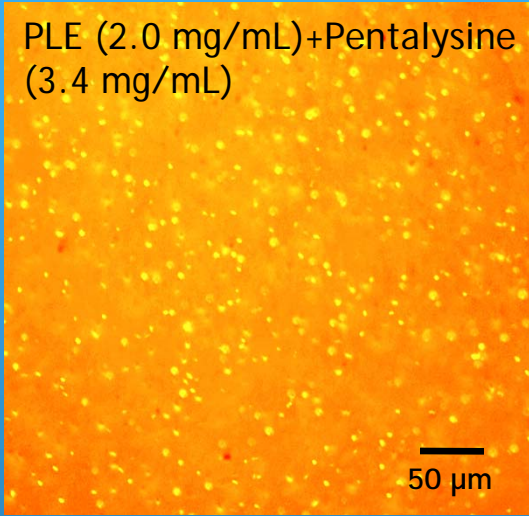
Disadvantages

- Time-consuming
- Wrong adjustments → miss coacervate formation

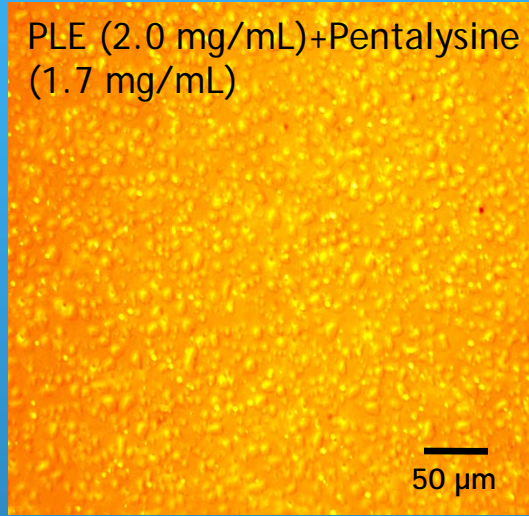


Coacervates Optical Microscopy Images

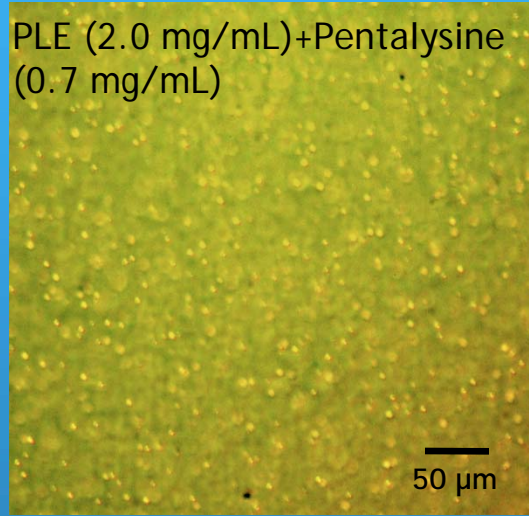
PLE (2.0 mg/mL)+Pentalysine
(3.4 mg/mL)



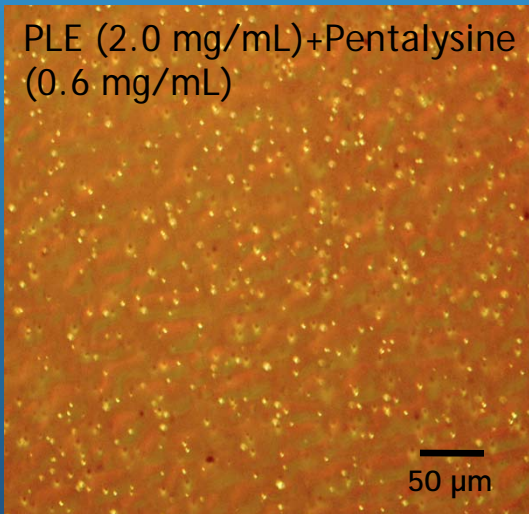
PLE (2.0 mg/mL)+Pentalysine
(1.7 mg/mL)



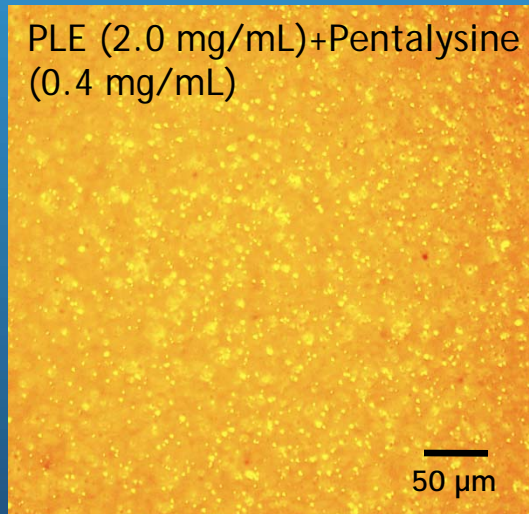
PLE (2.0 mg/mL)+Pentalysine
(0.7 mg/mL)



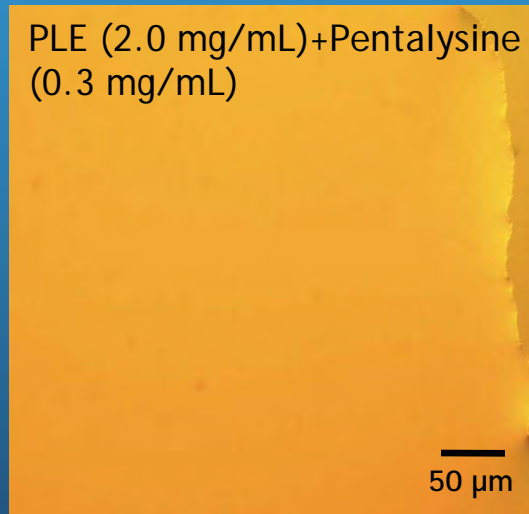
PLE (2.0 mg/mL)+Pentalysine
(0.6 mg/mL)



PLE (2.0 mg/mL)+Pentalysine
(0.4 mg/mL)



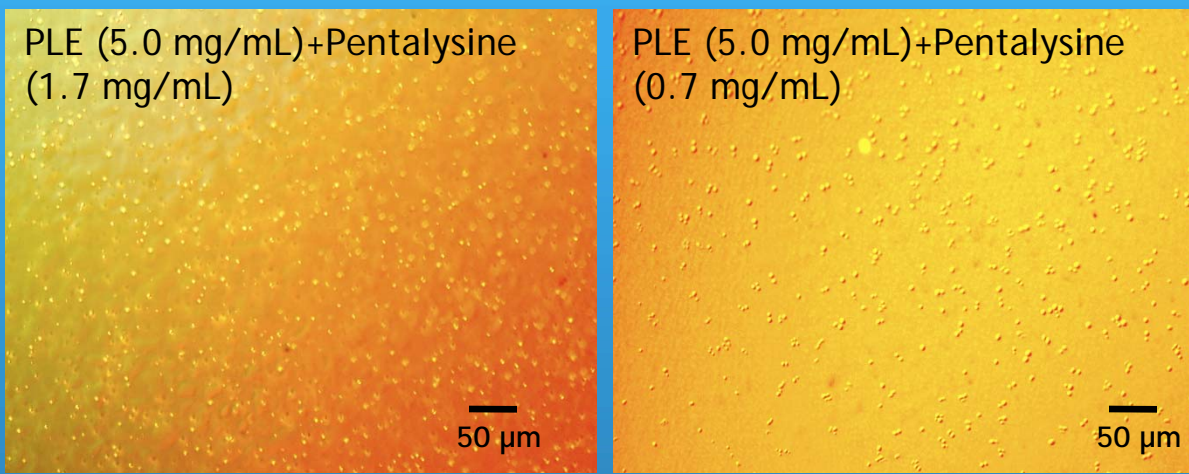
PLE (2.0 mg/mL)+Pentalysine
(0.3 mg/mL)



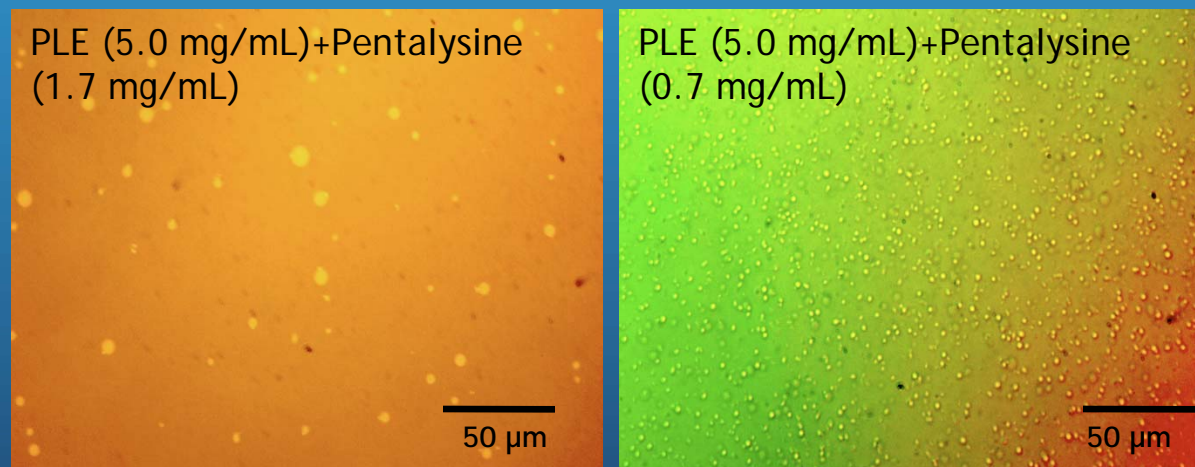
2.0 mg/mL PLE with various pentalysine concentrations

➤ No coacervate formation at pentalysine concentrations below 0.3 mg/mL

Coacervate Optical Microscopy Images (cont.)



20x magnification



50x magnification

5.0 mg/mL PLE with two different pentalysine concentrations

Summary and Future Plans

- Size of coacervates increases and quantity slightly decreases with increasing pentalyisine concentration
- Immediate plans:
 - Test more pentalyisine concentrations with 5 mg/mL PLE to verify conclusion
 - Analyze images with ImageJ software for quantitative results
 - Explore effects of pH and ionic strength
 - Cross-link coacervates under different conditions to determine how solution conditions influence microparticle properties
- Long-term plans:
 - Encapsulate thrombin in microparticle carriers and quantify thrombin-loading capacity
 - Develop a thrombin release mechanism that is specific to the site of injury
 - Develop a particle anchor that is specific to the site of injury

Acknowledgements

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Thank You!

Any Questions?