

REU Project Proposal: Complex Coacervation**Jonathan K. Whitmer****November 13, 2015**

A host of interesting phenomena, both biological and technological, involve the complexation of charged polymers; these may be long polymers with well-defined secondary structure, such as proteins¹, linear polyelectrolytes, or multi-branched species². A particularly interesting phenomenon within polyelectrolyte solutions is coacervation^{3,4}, a liquid–liquid phase separation where polymer-enriched liquid droplets are formed within a dilute phase⁵. Coacervation is a puzzling process where two primarily aqueous phases become immiscible⁶. Aggregates (coacervates) formed in mixtures of oppositely charged polyelectrolytes are known as complex coacervates^{5,7,8}. Coacervates occur in many natural systems^{9,10}, and have found application in microencapsulation^{11,12} and extraction¹³ processes, as their ultra-low surface tension allows them to readily assimilate nanoparticles or drug payloads within aqueous suspension. Coacervation is intimately related to the process of layer-by-layer deposition, where films up to micrometers in thickness are built by iterative surface adsorption of polyelectrolytes. These films are of interest as solid electrolytes in lightweight batteries^{14,15}, fuel-cell electrodes^{14,16}, protective coatings¹⁶, and drug micro-encapsulation¹⁷. Solvation and electrostatic forces bind the layers, with hydrodynamics relevant to the histories of the nonequilibrium layers. Coacervation is further related to the phase separation of charged colloidal mixtures^{18,19}, and molecular ionic liquids—organic salts whose balance of hydrophobic and electrostatic interactions renders them liquid near room temperature^{20,21}. As these systems exhibit common thermodynamic features, a primary goal of this research is the development of a unified theoretical and modeling framework capable of representing each system with arbitrary detail from continuum phase separation to the molecular conformations.

This topic inspires two REU projects involving characterization of coacervates through molecular dynamics simulation. In each, there will be focus on utilizing coarse-grained modeling to understand the phase diagram of complex coacervates, as well as the structure and dynamics of coacervate phases. While some recent work has shown mean-field²² and PRISM²³ theories capture the primary features of coacervate phases, limited simulation²⁴ and structural characterization data exist. Thus, precise description of the phase remains elusive. In the first project, a student will utilize an open-source simulation package, such as LAMMPS²⁵ to characterize the structure of coacervates formed by oppositely charged linear polyelectrolytes at varying compositions of added salt. Salt acts as an artificial temperature in these systems, weakening electrostatic interactions between the chains and disrupting the coacervate phase. As such, a combination of salt and temperature variation will enable precise tuning of the strength of polyelectrolyte complexation for engineering applications. In the second project, the student will examine the intriguing limit of polyelectrolyte solutions with highly-valent polyoxometalate ions. Molecular simulations here will provide important information about the phase diagram, internal structure, and relaxation dynamics important for material applications.

It is preferable (but not required) for students interested in this project to have prior experience with writing computer code (C++ preferred) and with scripting languages to facilitate running computations on the Whitmer group cluster and CRC machines.

References

1. S. L. Perry, L. Leon, K. Q. Hoffmann, et al. “Chirality-selected phase behaviour in ionic polypeptide complexes.” *Nature Communications*, 6, 2015.
2. D. Priftis, X. Xia, K. O. Margossian, et al. “Ternary, tunable polyelectrolyte complex fluids driven by complex coacervation.” *Macromolecules*, 47(9):3076–3085, 2014.
3. S. L. Turgeon, C. Schmitt, and C. Sanchez. “Protein–polysaccharide complexes and coacervates.” *Curr. Opin. Colloid Interface Sci.*, 12(4-5):166–178, 2007.
4. J. R. Nixon, A. H. Khalil, and J. E. Carless. “Phase relationships in the simple coacervating system isoelectric gelatin : Ethanol : Water.” *J. Pharm. Pharmac.*, 18:409–416, 1966.
5. D. Priftis and M. Tirrell. “Phase behaviour and complex coacervation of aqueous polypeptide solutions.” *Soft Matter*, 8(36):9396, 2012.
6. F. M. Menger and B. M. Sykes. “Anatomy of a coacervate.” *Langmuir*, 14(15):4131–4137, 1998.

7. R. A. Riggelman, R. Kumar, and G. H. Fredrickson. "Investigation of the interfacial tension of complex coacervates using field-theoretic simulations." *J. Chem. Phys.*, 136:024903, 2012.
8. C. G. de Kruif, F. Weinbreck, and R. de Vries. "Complex coacervation of proteins and anionic polysaccharides." *Curr. Opin. Colloid Interface Sci.*, 9(5):340–349, 2004.
9. N. Pawar and H. B. Bohidar. "Statistical thermodynamics of liquid–liquid phase separation in ternary systems during complex coacervation." *Phys. Rev. E*, 82(3):36107, 2010.
10. A. E. Smith, F. T. Bellware, and J. J. Silver. "Formation of nucleic acid coacervates by dehydration and rehydration." *Nature*, 214(5092):1038–1040, 1967.
11. C. I. Onwulata. "Encapsulation of new active ingredients." *Annu. Rev. Food. Sci. Technol.*, 3:183–202, 2012.
12. S. R. Bhatia, S. F. Khattak, and S. C. Roberts. "Polyelectrolytes for cell encapsulation." *Curr. Opin. Colloid Interface Sci.*, 10(1-2):45–51, 2005.
13. F.-J. Ruiz, S. Rubio, and D. Pérez-Bendito. "Water-induced coacervation of alkyl carboxylic acid reverse micelles: Phenomenon description and potential for the extraction of organic compounds." *Anal. Chem.*, 79:7473–7484, 2007.
14. J. L. Lutkenhaus and P. T. Hammond. "Electrochemically enabled polyelectrolyte multilayer devices: from fuel cells to sensors." *Soft Matter*, 3(7):804, 2007.
15. D. M. DeLongchamp and P. T. Hammond. "Highly ion conductive poly(ethylene oxide)-based solid polymer electrolytes from hydrogen bonding layer-by-layer assembly." *Langmuir*, 20(13):5403–11, 2004.
16. P. R. Van Tassel. "Polyelectrolyte adsorption and layer-by-layer assembly: Electrochemical control." *Curr. Opin. Colloid Interface Sci.*, 17(2):106–113, 2012.
17. D. B. Shenoy, A. A. Antipov, G. B. Sukhorukov, and H. Möhwald. "Layer-by-layer engineering of biocompatible, decomposable core-shell structures." *Biomacromol.*, 4(2):265–72, 2003.
18. M. E. Leunissen, C. G. Christova, A.-P. Hynninen, et al. "Ionic colloidal crystals of oppositely charged particles." *Nature*, 437(7056):235–40, 2005.
19. G. A. Chapela, F. del Río, and J. Alejandre. "Liquid-vapor phase diagram and surface properties in oppositely charged colloids represented by a mixture of attractive and repulsive Yukawa potentials." *J. Chem. Phys.*, 138(5):054507, 2013.
20. K. Iwata, H. Okajima, S. Saha, and H.-o. Hamaguchi. "Local structure formation in alkyl-imidazolium-based ionic liquids as revealed by linear and nonlinear Raman spectroscopy." *Acc. Chem. Res.*, 40:1174–1181, 2007.
21. H. Weingärtner. "Understanding ionic liquids at the molecular level: Facts, problems, and controversies." *Angew. Chem. Int. Ed.*, 47:654–670, 2008.
22. J. Qin, D. Priftis, R. Farina, et al. "Interfacial tension of polyelectrolyte complex coacervate phases." *ACS Macro Letters*, 3(6):565–568, 2014.
23. S. L. Perry and C. E. Sing. "Prism-based theory of complex coacervation: Excluded volume versus chain correlation." *Macromolecules*, 2015.
24. Z. Ou and M. Muthukumar. "Entropy and enthalpy of polyelectrolyte complexation: Langevin dynamics simulations." *J. Chem. Phys.*, 124(15):154902, 2006.
25. S. Plimpton. "Fast parallel algorithms for short-range molecular dynamics." *J. Comp. Phys.*, 117(1):1–19, 1995.