Using Molecular Dynamics to Model the Structure of Polyelectrolyte Micelles

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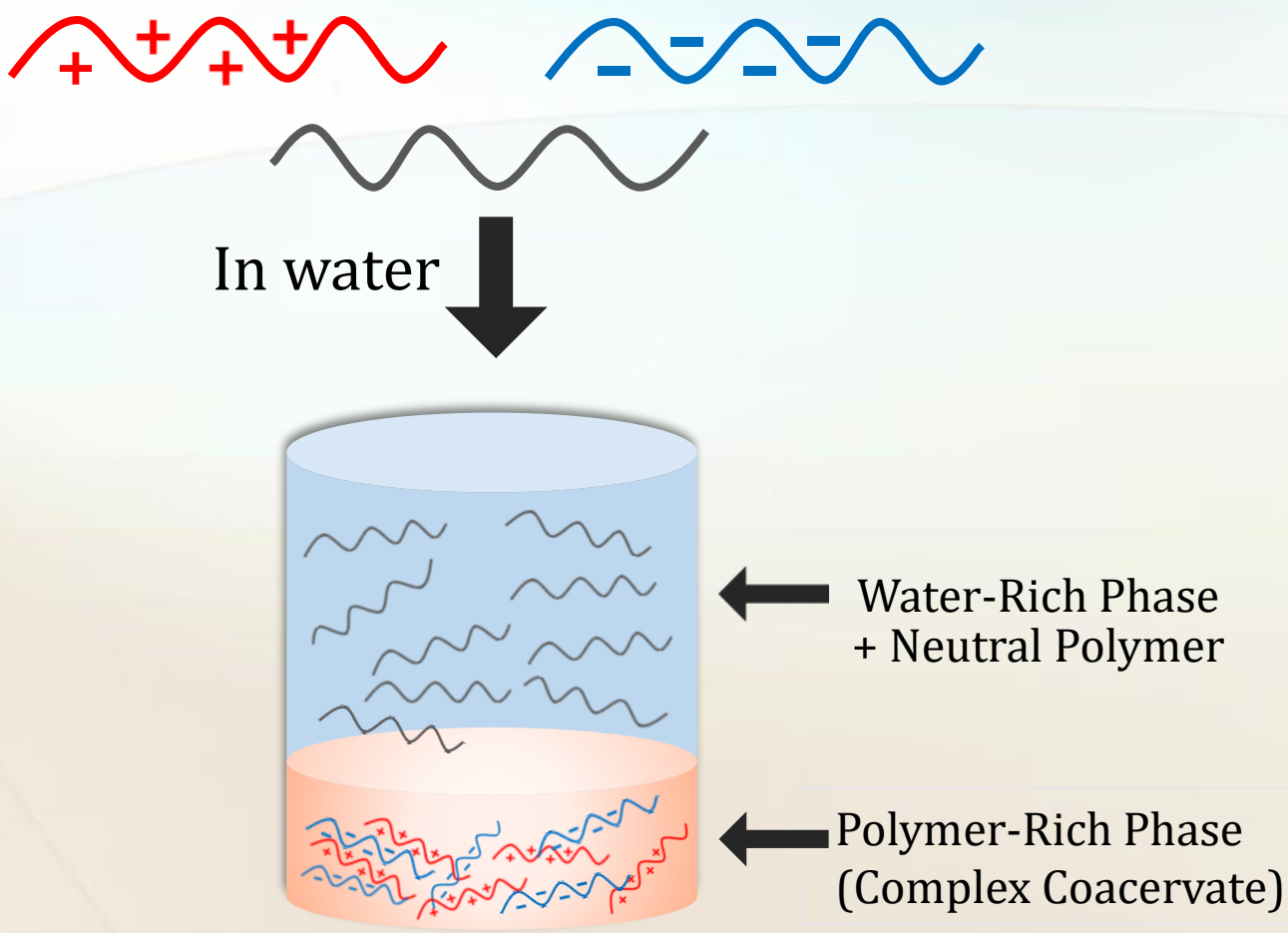
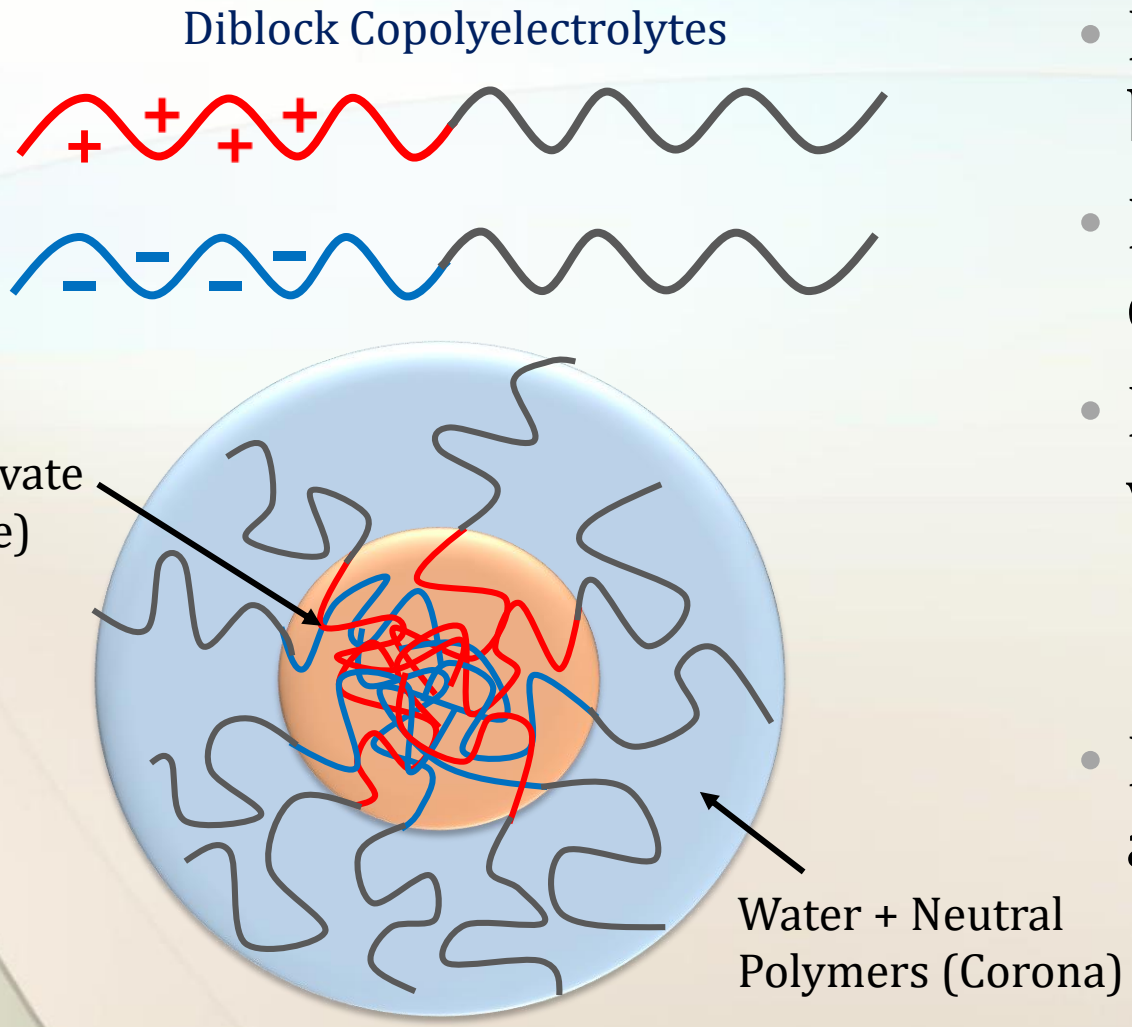
Complex Coacervation



- Oppositely charged polymers attract
- Form a coacervate
- Liquid-liquid phase separation
- Hydrophilic neutral polymer goes to water phase

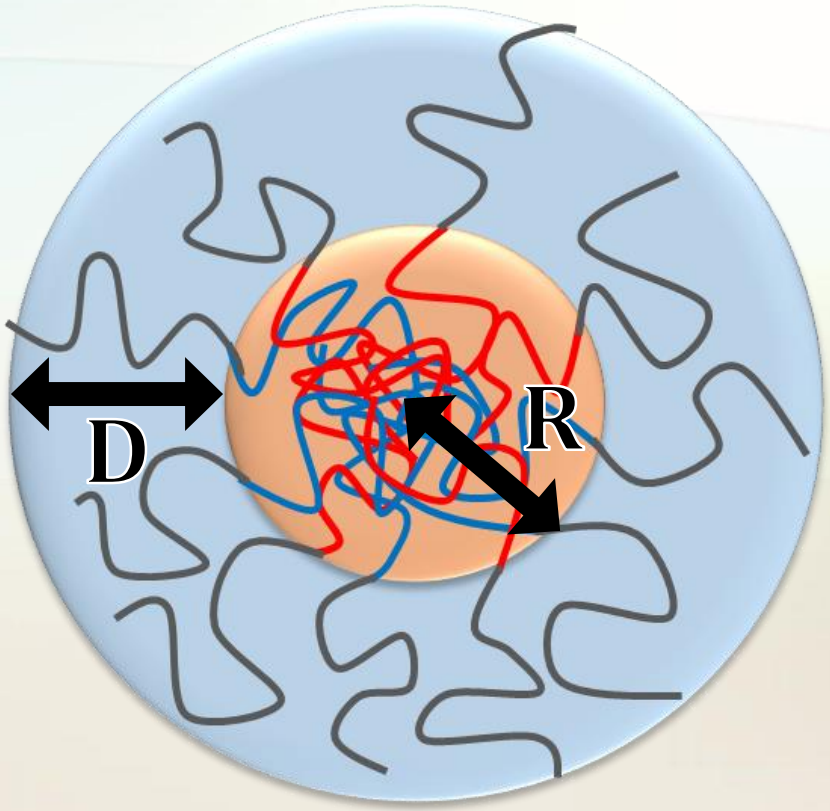
Complex Coacervation



- Hydrophilic neutral polymers bonded to a charged polymer
- Form spherical micelles at low concentrations
- Micelles are responsive to a variety of stimuli
  - pH, salt concentration, among others
- Potential as drug delivery agents

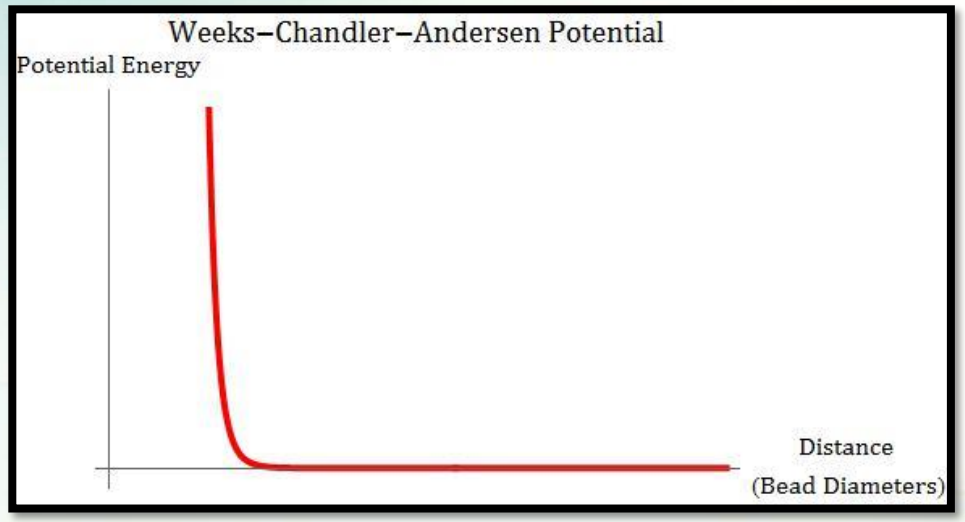
Micelle Structural Properties

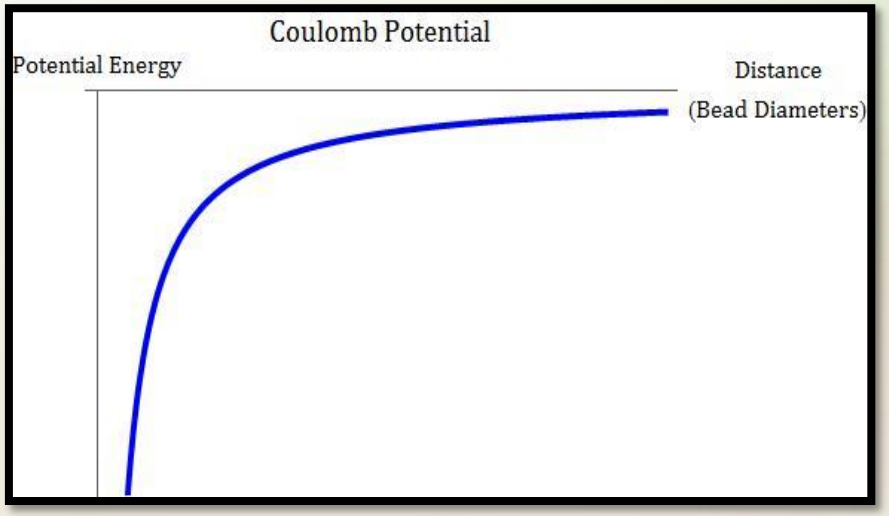
- Other molecules can be encapsulated in the core
- Helpful to know size
- R – Radius of the core
- D – Size of the corona
- C – Concentration in the core
- n – The number polymers in the micelle, or the aggregation number



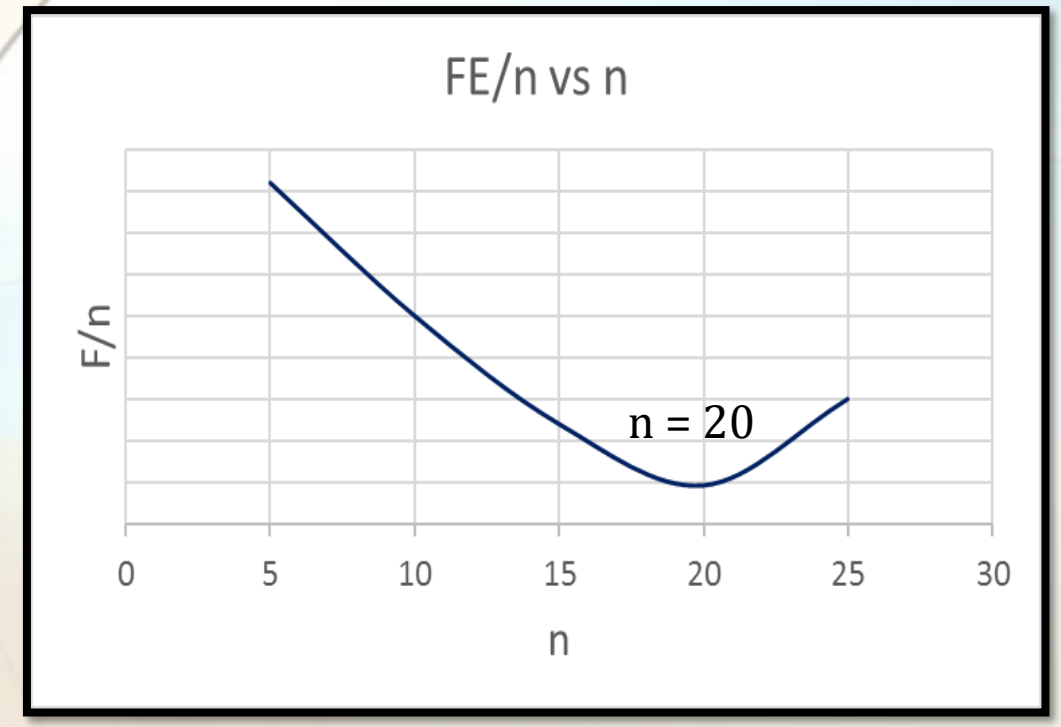
Molecular Dynamics

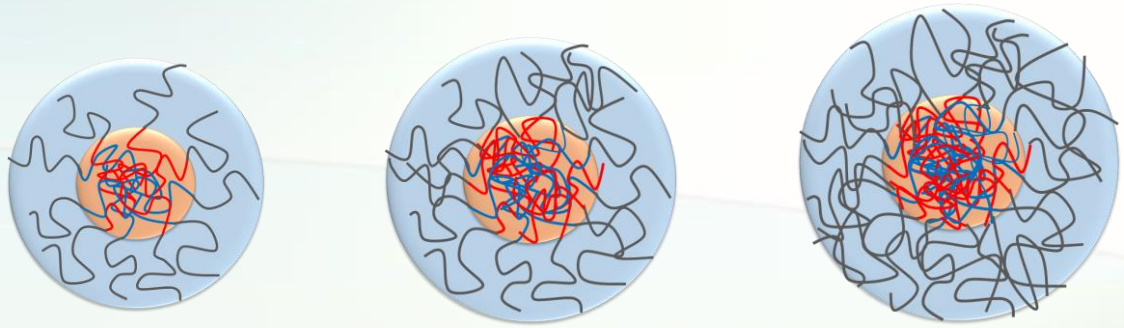
- Method of computer simulation
- Uses Newton's equations of motion to determine positions of atoms
  - LAMMPS
- Coarse-grain simulations – 'necklace beads'
  - Charge of ±1 on charged beads (Coulomb interactions)
  - Repulsive interactions models a good solvent
- Why not just throw a bunch of polymers in a box, wait for it to equilibrate, and take the average micelle size?
  - Many molecules in a very large box → Extremely long computational time





Finding the Aggregation Number





n = 10 n = 20 n = 30

- Model with different numbers of polymers
- Find free energy per chain minimum
- Lowest free energy per chain → most favorable energy state → most common/accurate aggregation number
- Free energy cannot be directly measured from a single simulation

Thermodynamic Integration

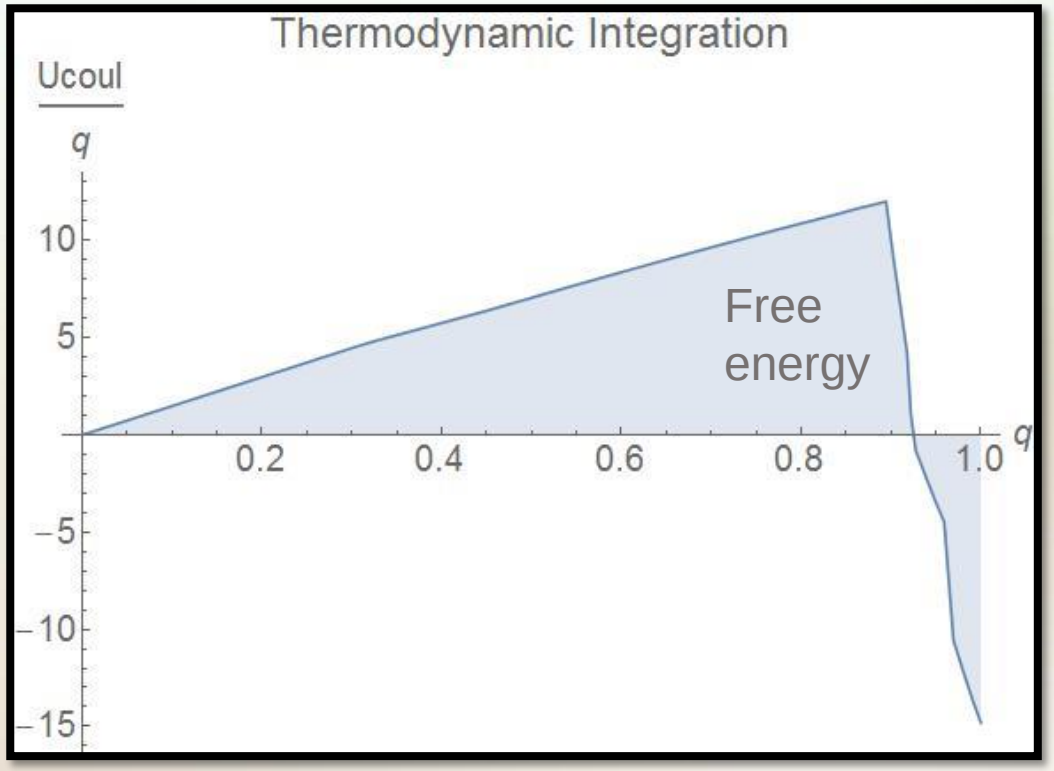
- Free energy is found with thermodynamic integration
- Relate free energy to coulomb potential energy (energy due to charged beads)
- Plot from known state (neutral, q=0) to desired state (micelle, q=1)

$$\Delta F = F_{\text{final}} - F_{\text{ref}} = 2\int_0^1 dq \left\langle \frac{U_{\text{coul}}}{q} \right\rangle$$

Change in free energy

Charged system

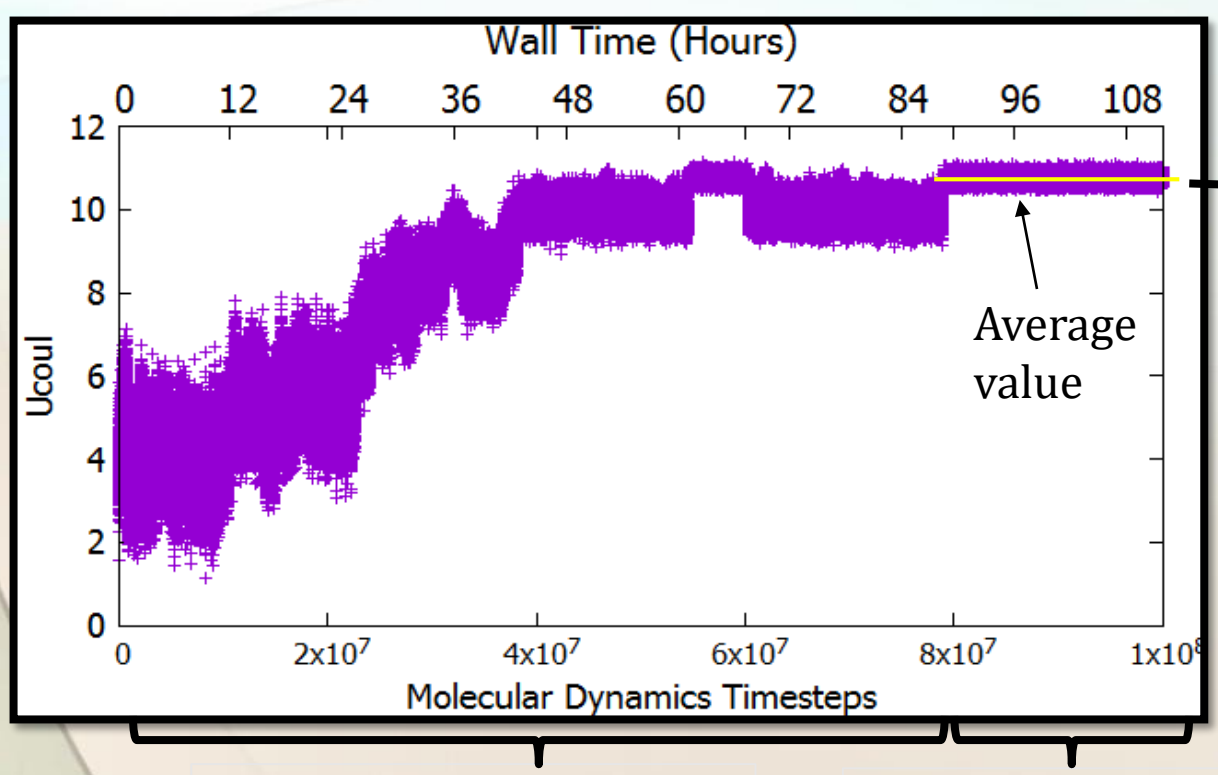
Neutral system

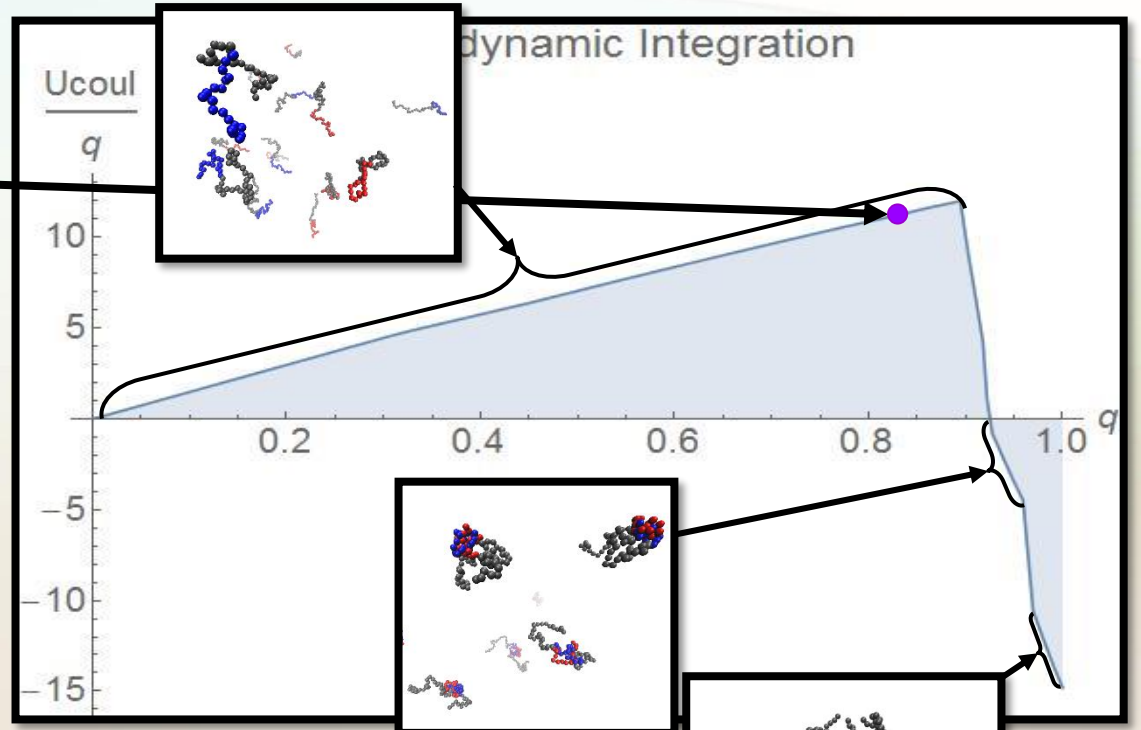


- Free energy is the area under the curve

Equilibrium Coulomb Energy

- Generate thermodynamic integration curves using coulomb energy
- Simulations record coulomb potential energy through time
- Once the system equilibrates, find the mean → one point on TI curve





Equilibration

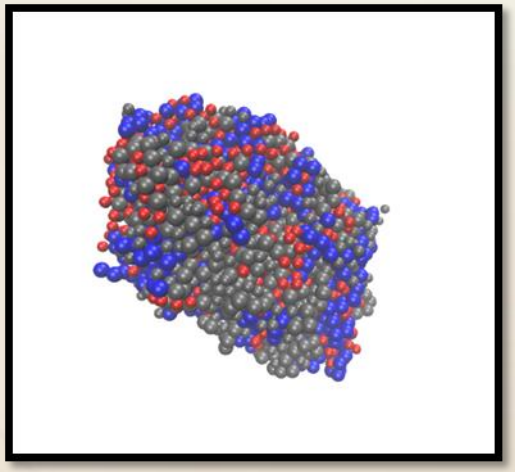
Data collection

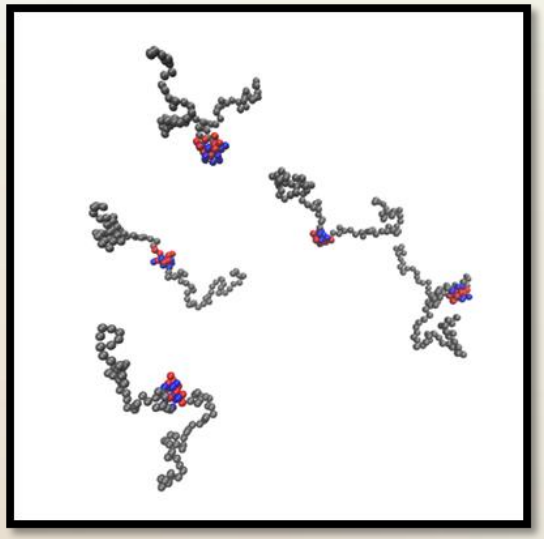
Micelle Conditions

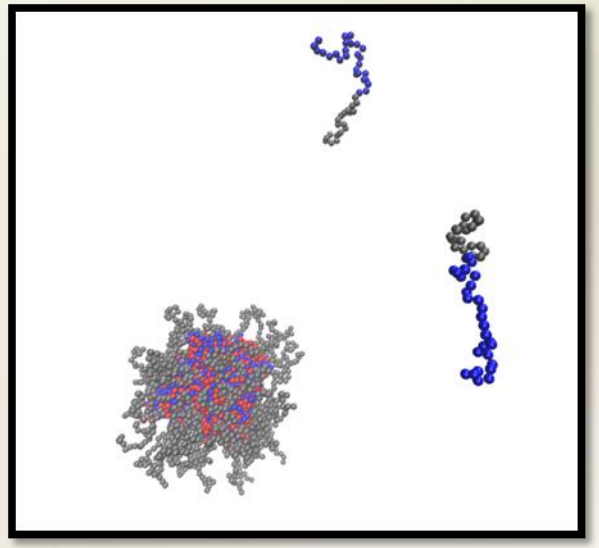
- Not all polymers make micelles
- Too many charged beads → macro-phase separation
- Too few charged beads → paired polymers/unstable micelles
- Significantly too many or too few polymers also tend to break apart

	= Micelle		= No Micelle

Nc ↓	Nn →	40	35	30	25	20	10
10							
15							
20							
25							
30							
40							

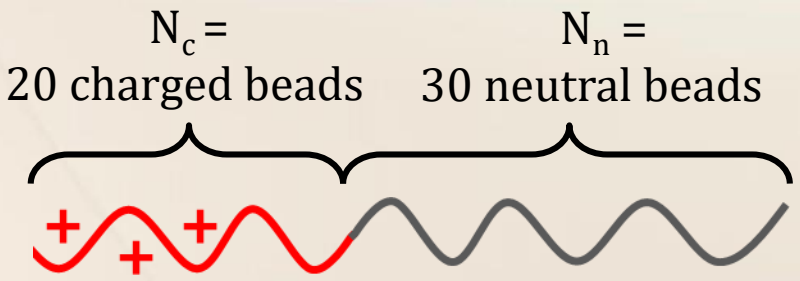


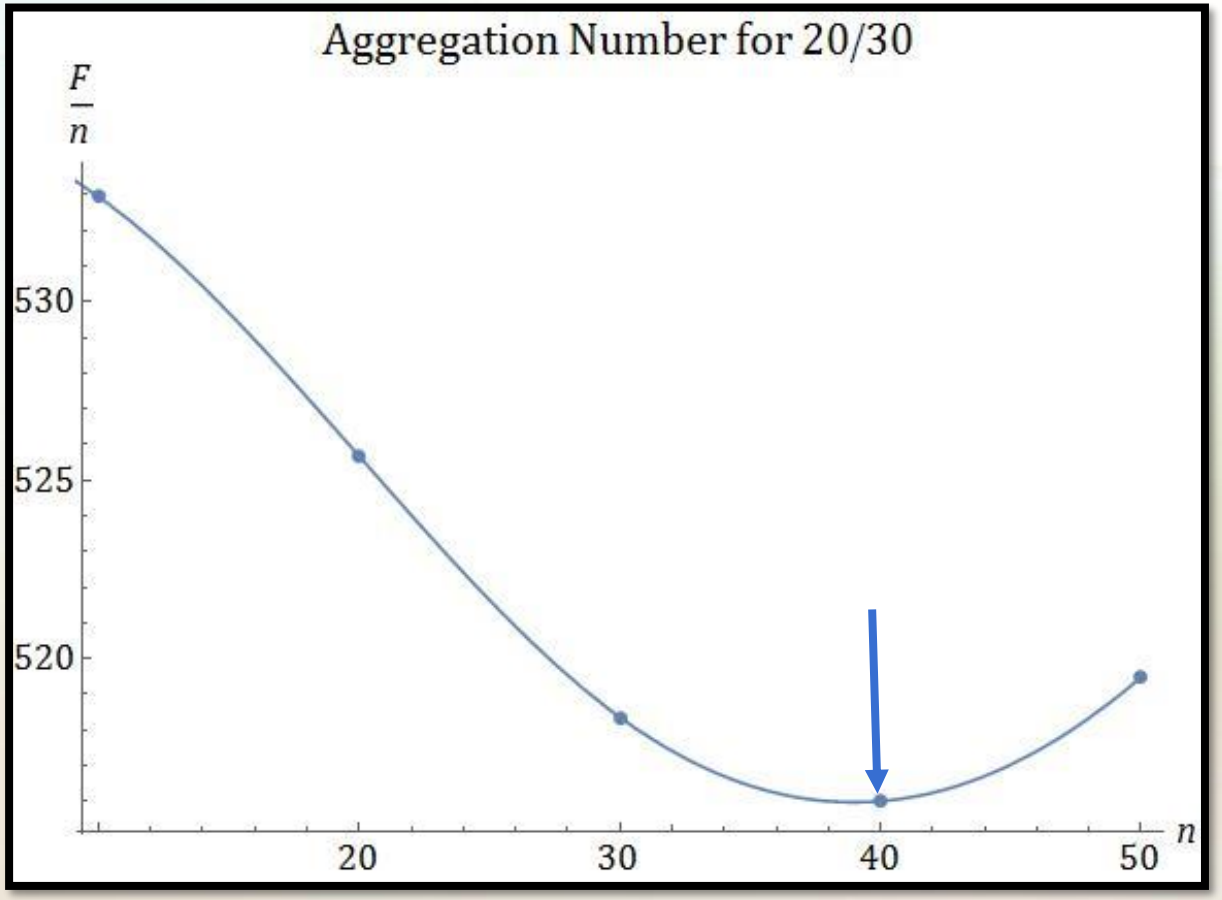




n Results

- Polymer with 20 charged and 30 neutral beads
- n ≅ 40
- Additional points between 30 and 50 can be tested to improve accuracy

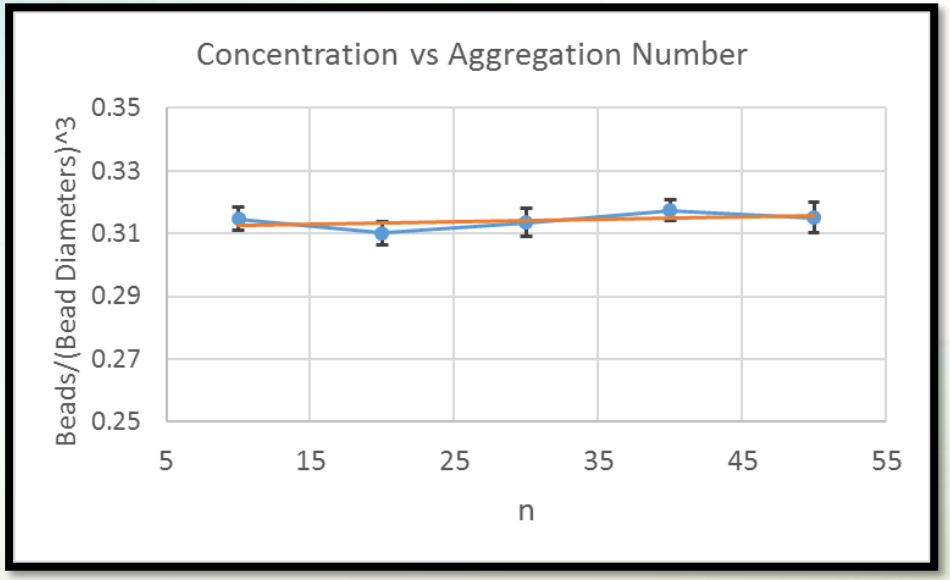


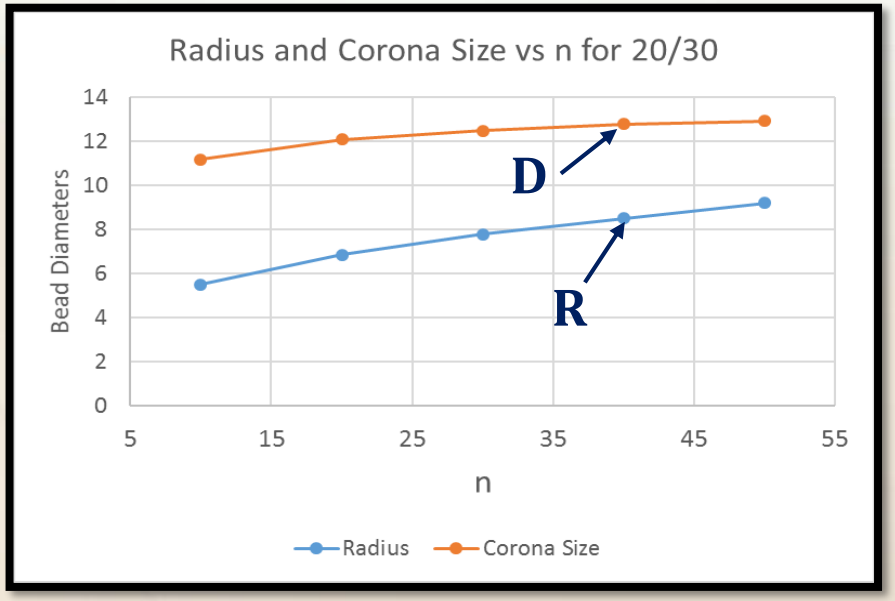


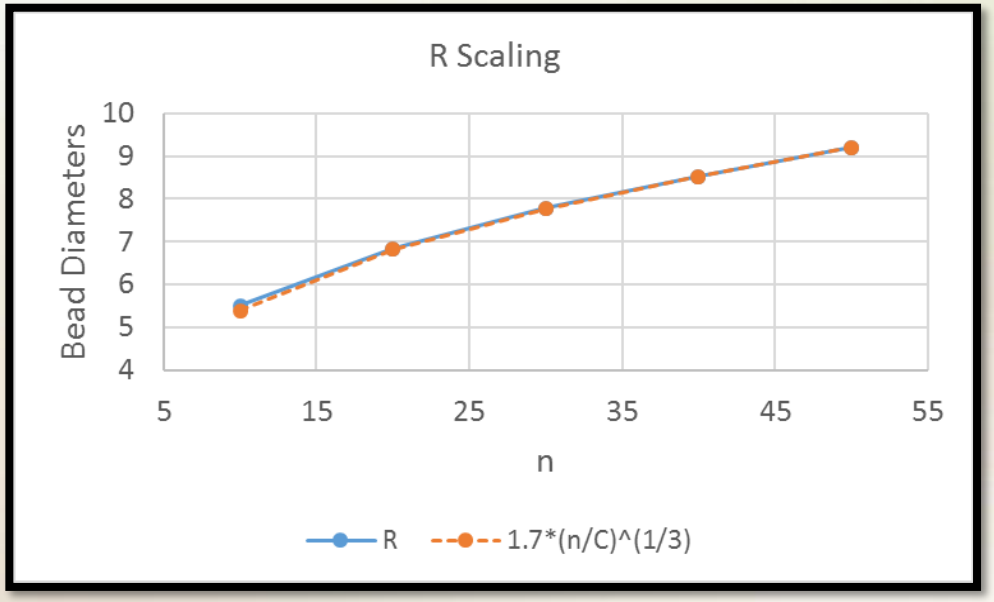
Structural Results & Relations

- Concentration does not depend on knowing the aggregation number
  - Controlled by interactions
  - Agrees with a theoretical prediction
- Since C is constant, we know the scaling of R

$$R \propto \left(\frac{n}{C}\right)^{\frac{1}{3}}$$

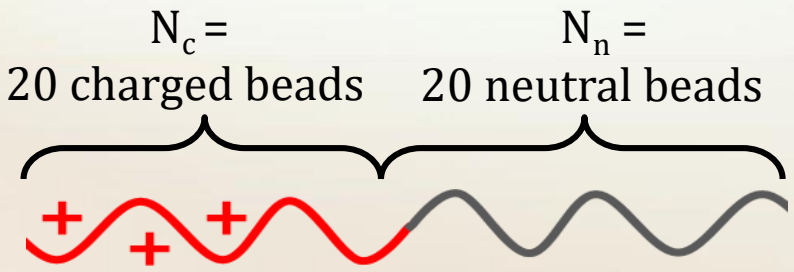


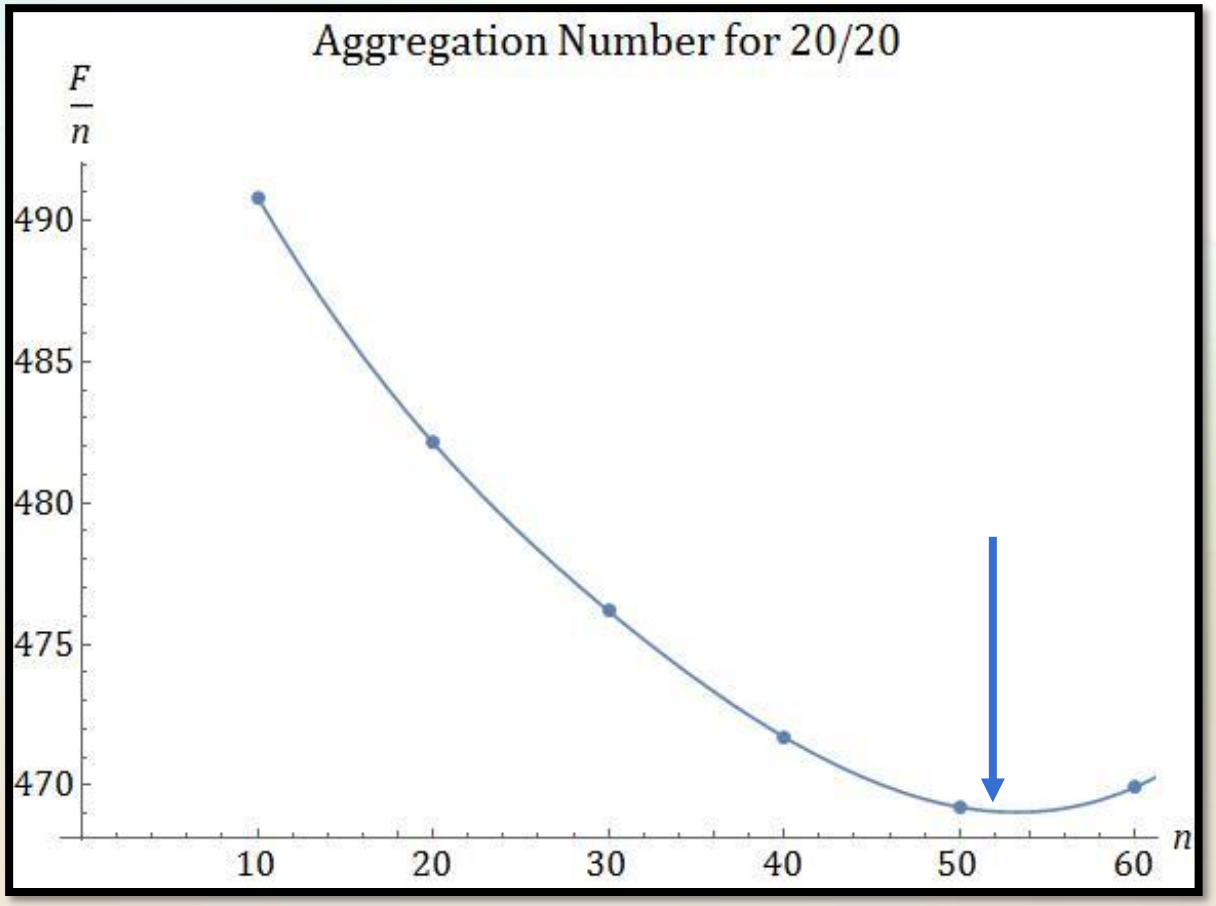




n Results

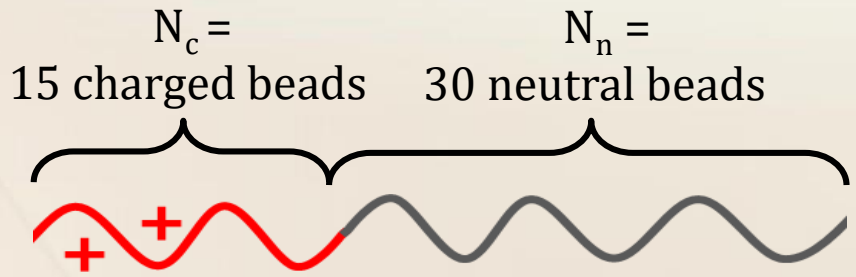
- Polymer with 20 charged beads and 20 neutral beads
- n ≅ 52

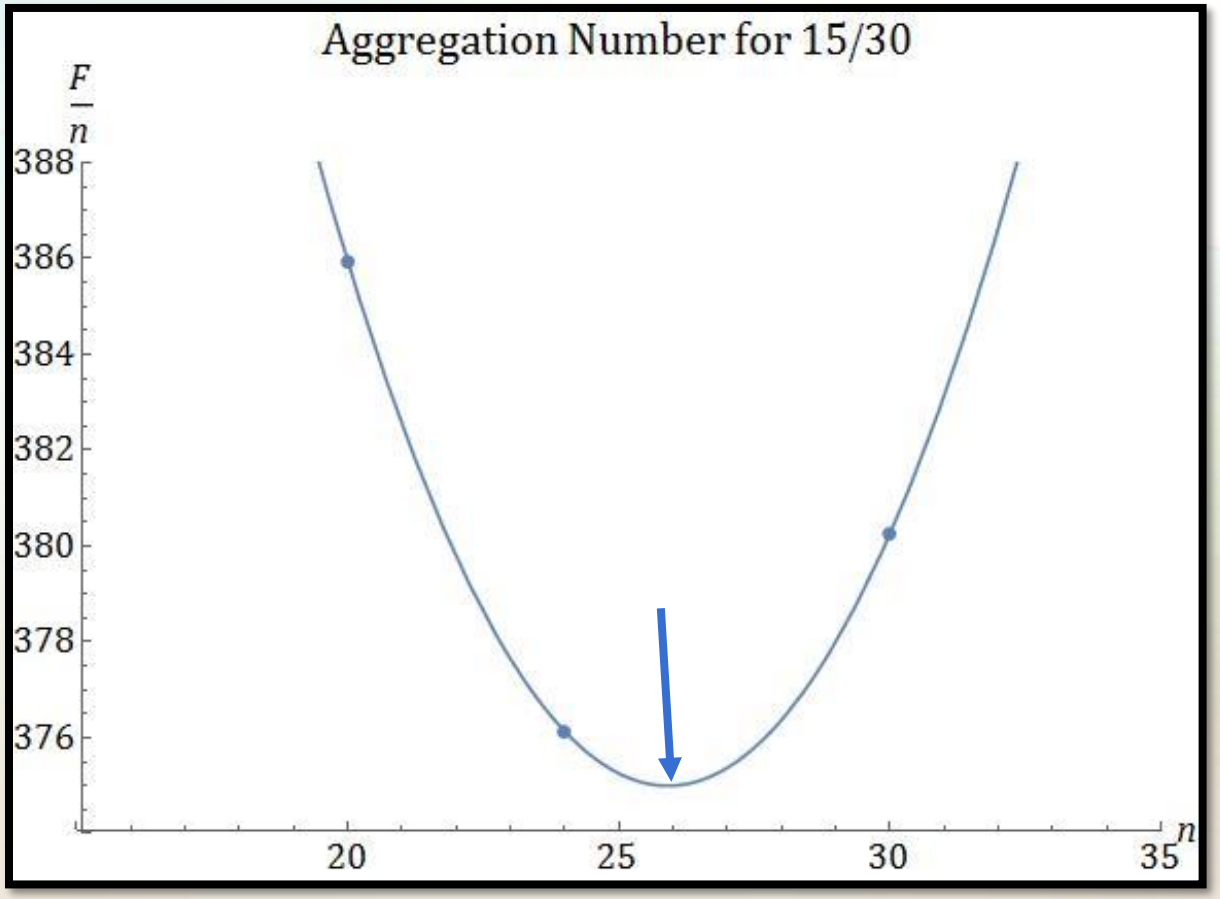




n Results

- Polymer with 15 charged beads and 30 neutral beads
- n ≅ 26
- Additional points needed to improve accuracy





Structural Results & Relations

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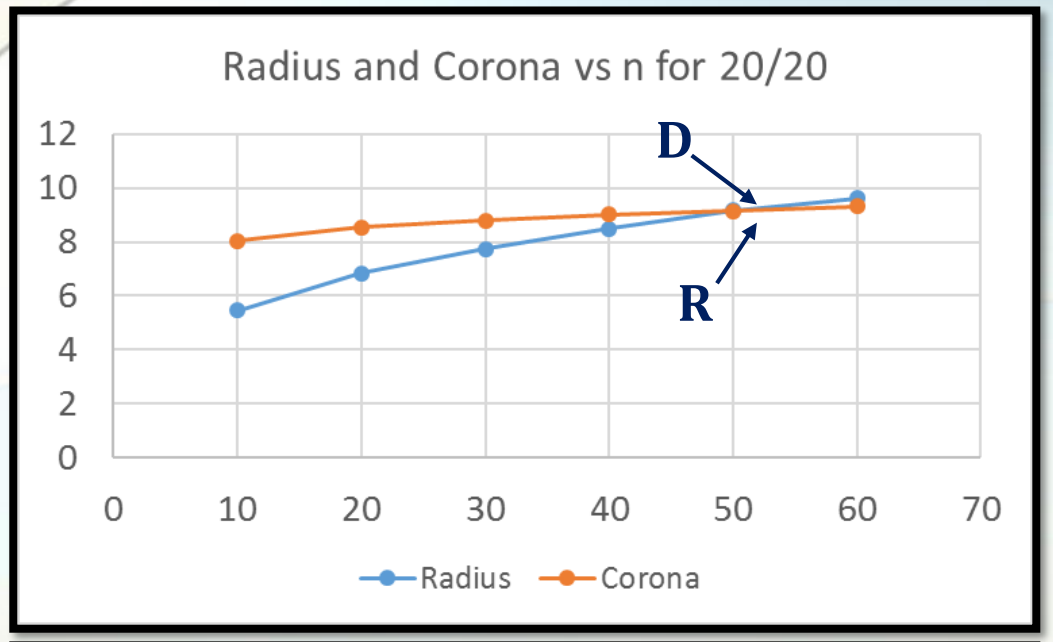

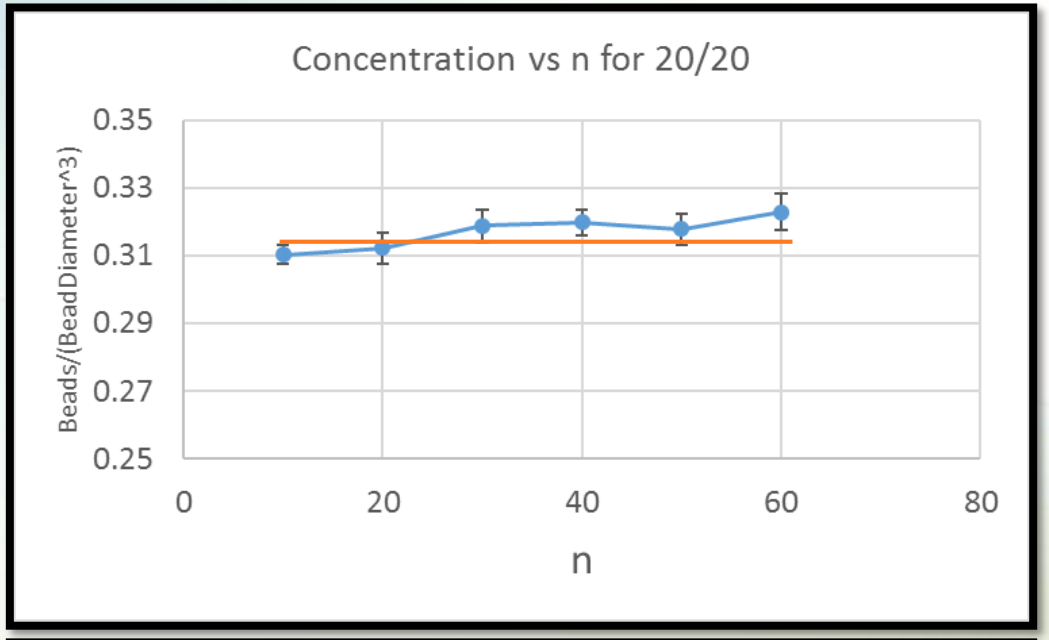

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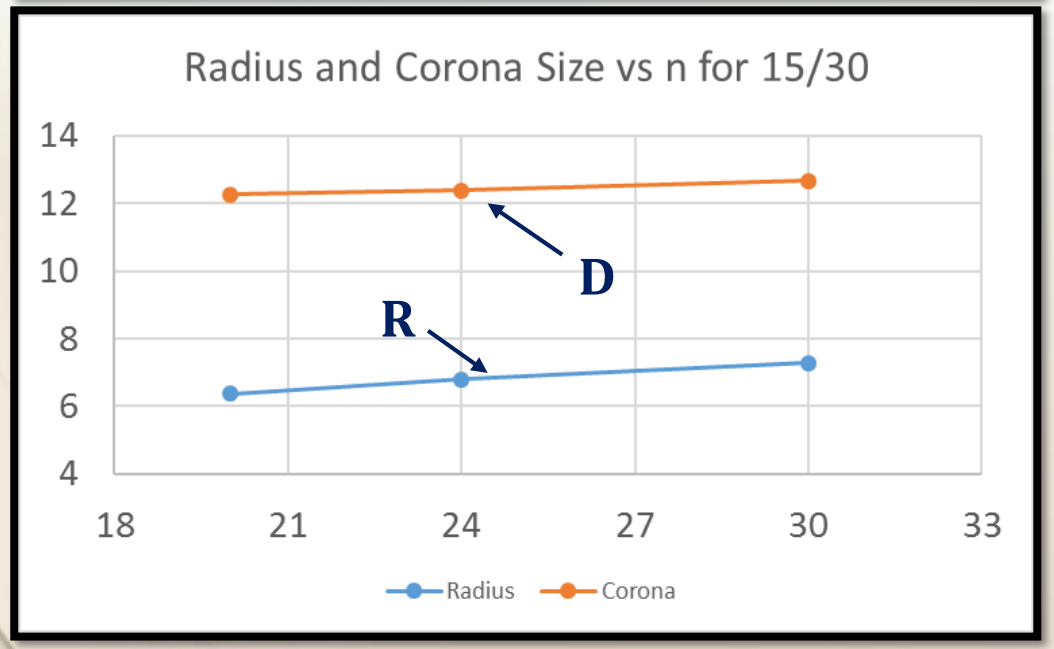

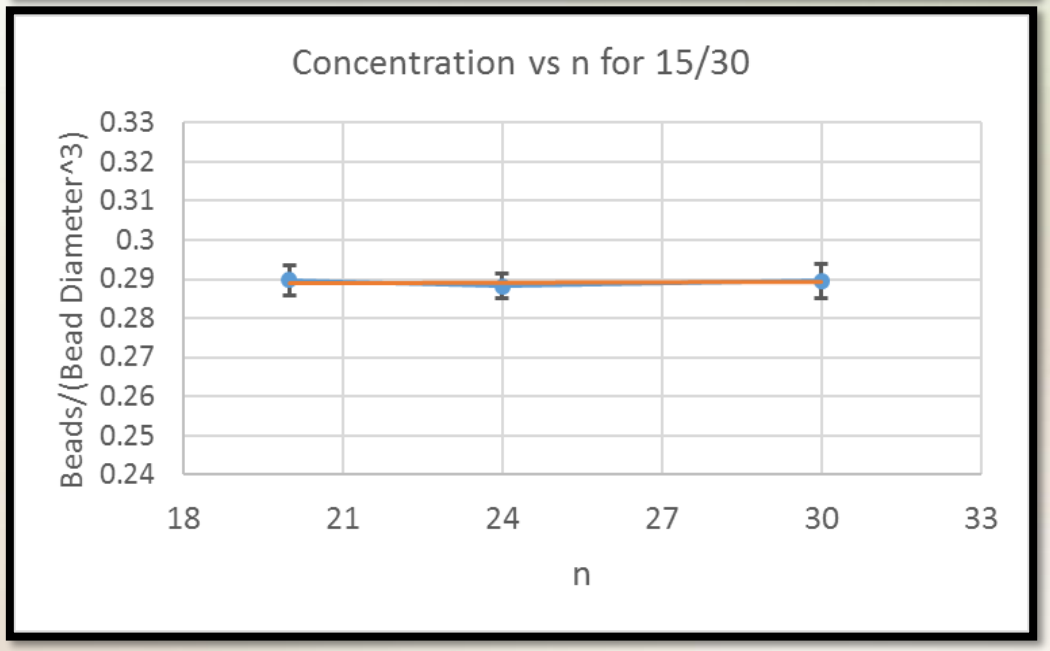

Comparison

	20/20	20/30	15/30
n	52	40	26
C	0.318	0.318	0.279
R	9.17	8.52	7.03
D	9.14	12.81	12.40
Accuracy expressed in significant figures			

- n is more dependent on N_c
- C only depends on N_c
- R scales with n
- D is more dependent on N_n

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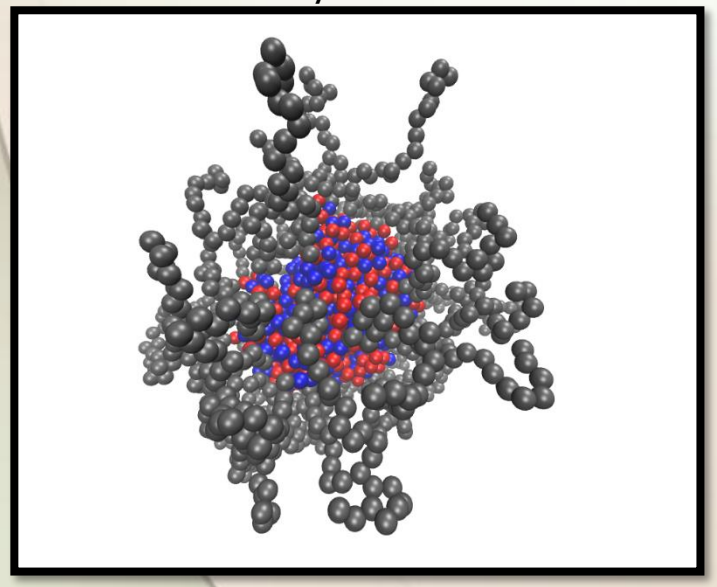

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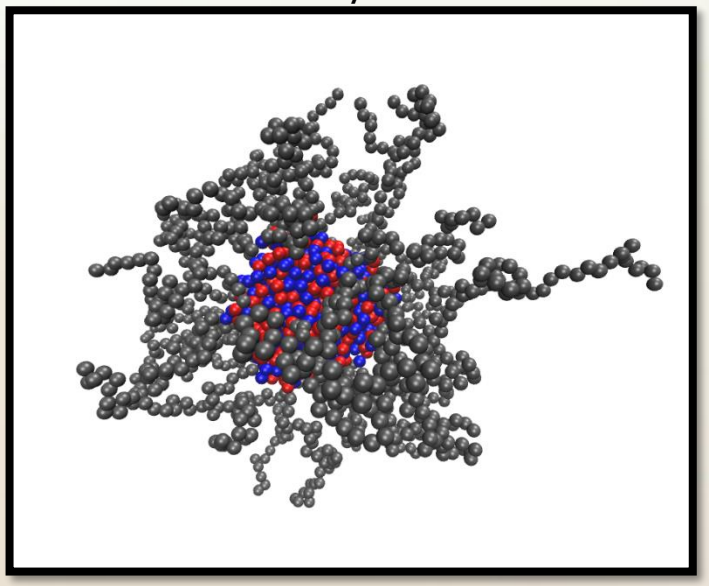

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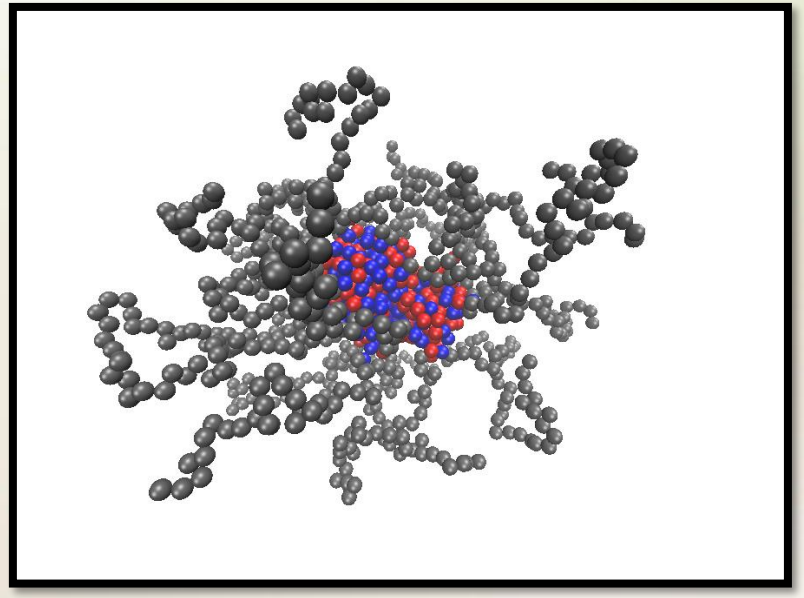

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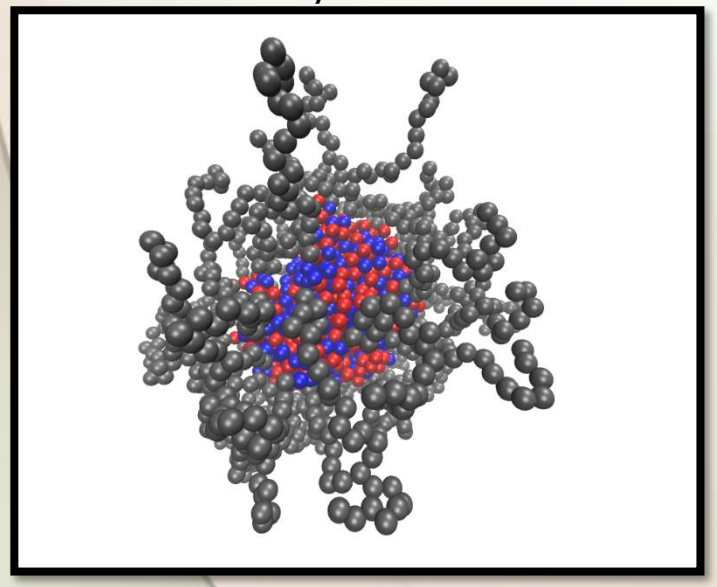

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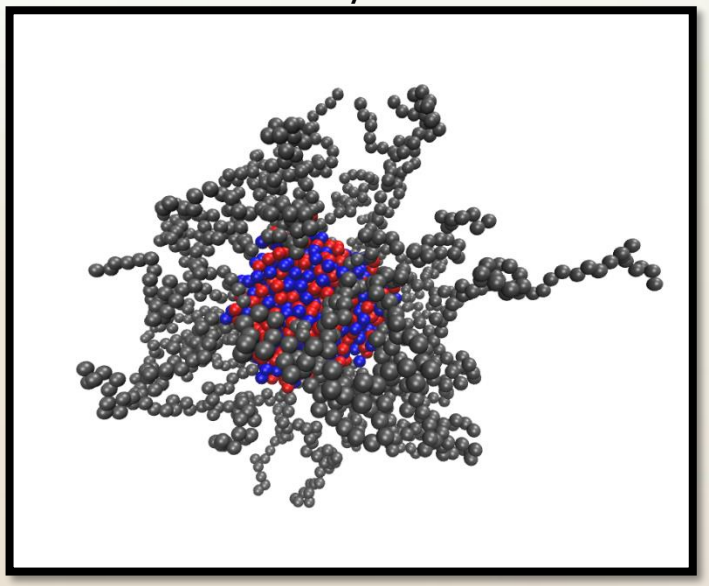

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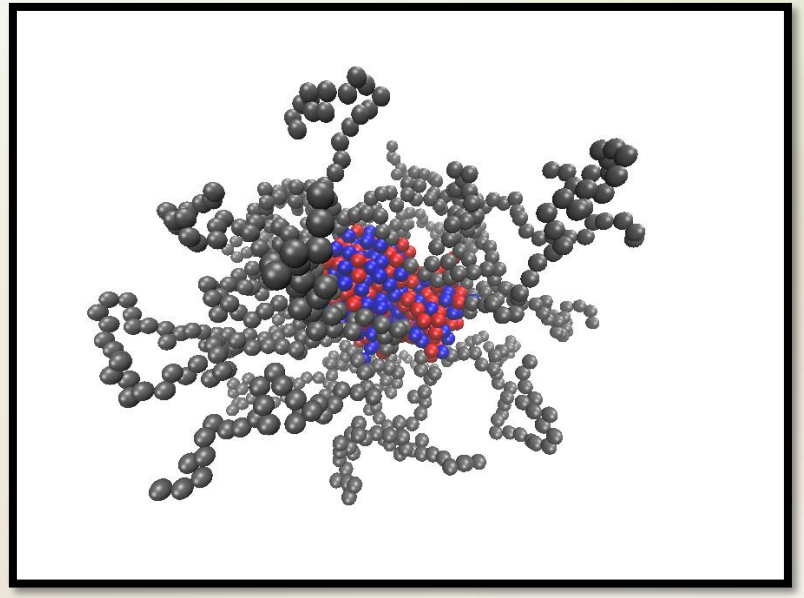

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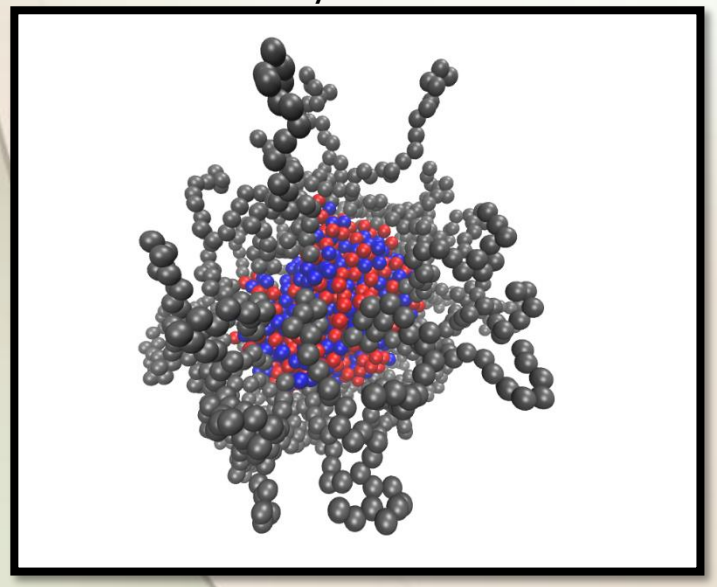

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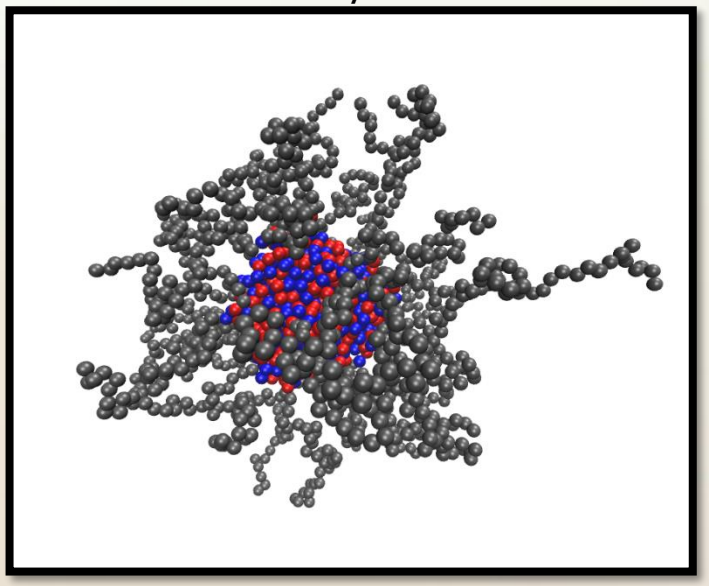

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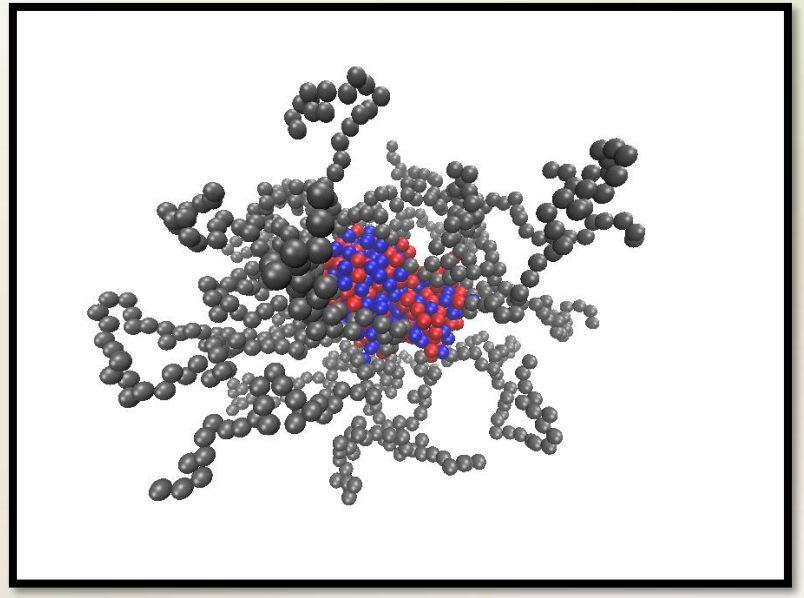

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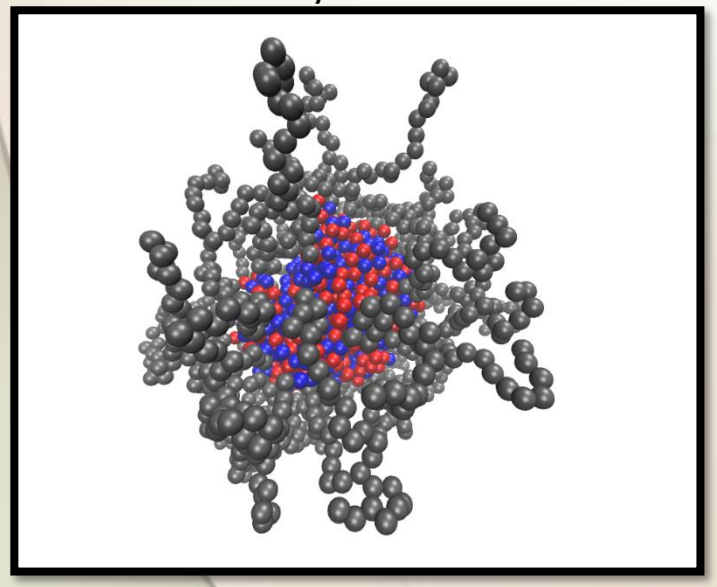

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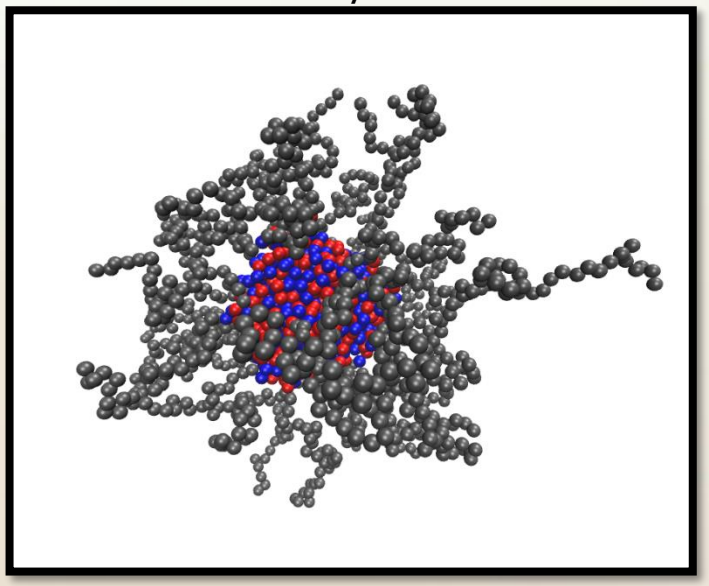

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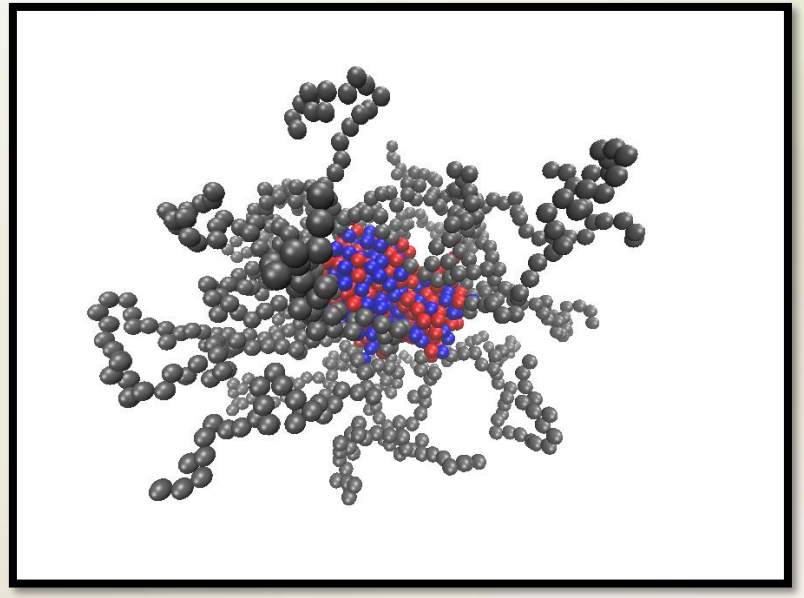

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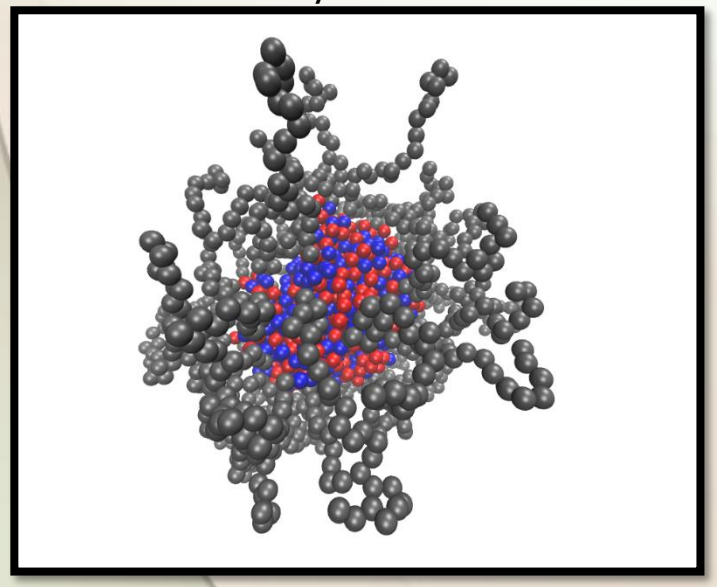

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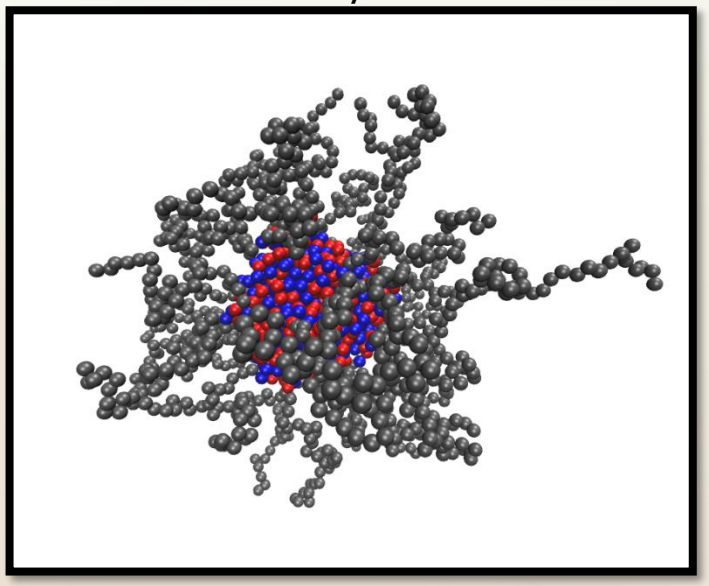

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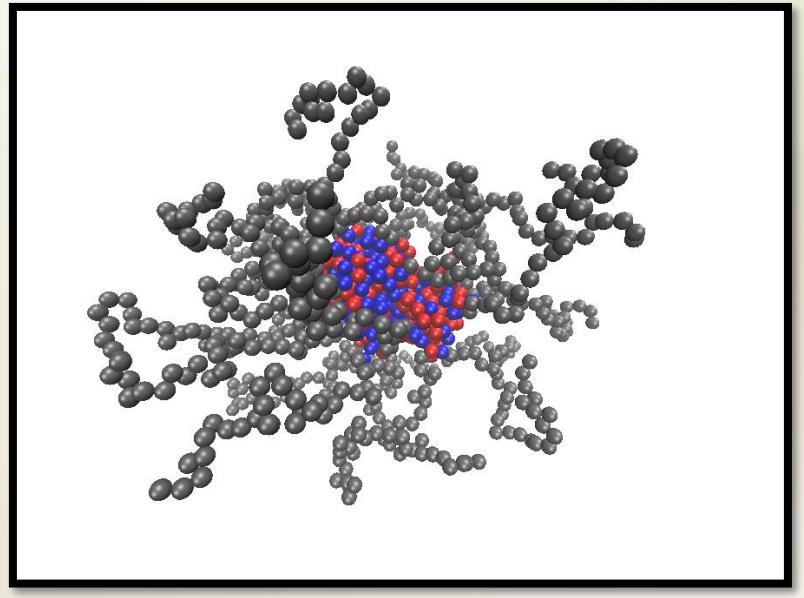

Conclusion

- Coacervation
- Use Molecular Dynamics and Thermodynamic Integration
- Established sizes and explored stability of polymer micelles
- Questions?