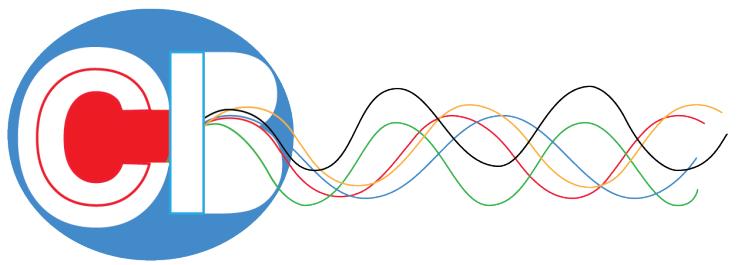
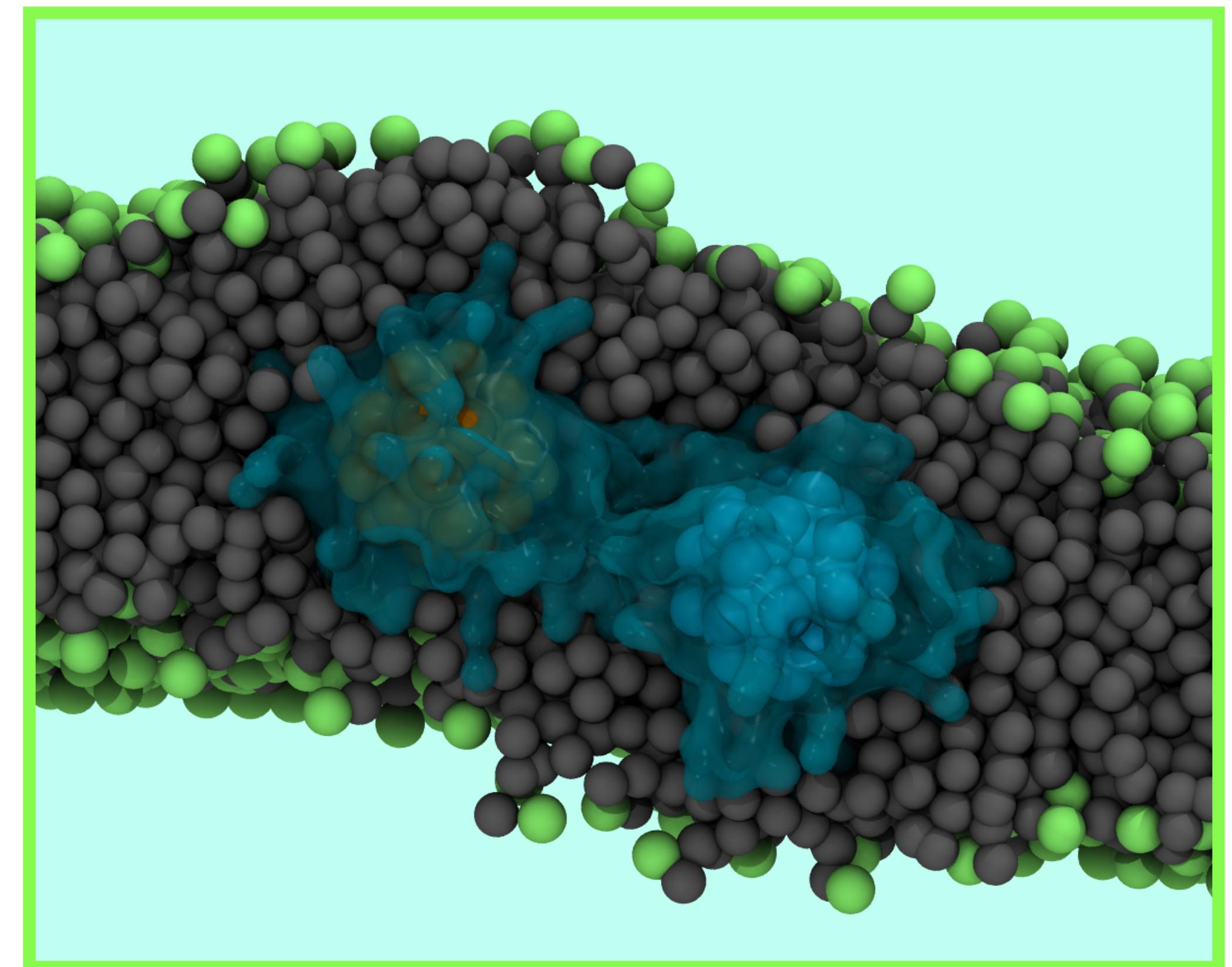


Understanding the Mechanisms of Gold Nanoparticle Aggregation in Lipid Membranes

Jahmal Ennis



Advisors: Dr. Grace Brannigan & Dr. Julie Griepenburg



Outline

- Background & Motivation
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- Result
 - Single Nanoparticle Inclusion
 - Observing and measuring aggregation
 - Membrane Bending Effect on Aggregation
 - Microscopic Deformations, Disordering the Lipid Membrane
- Summary

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Lycurgus Cup: an accidental use of dispersed gold nanoparticles

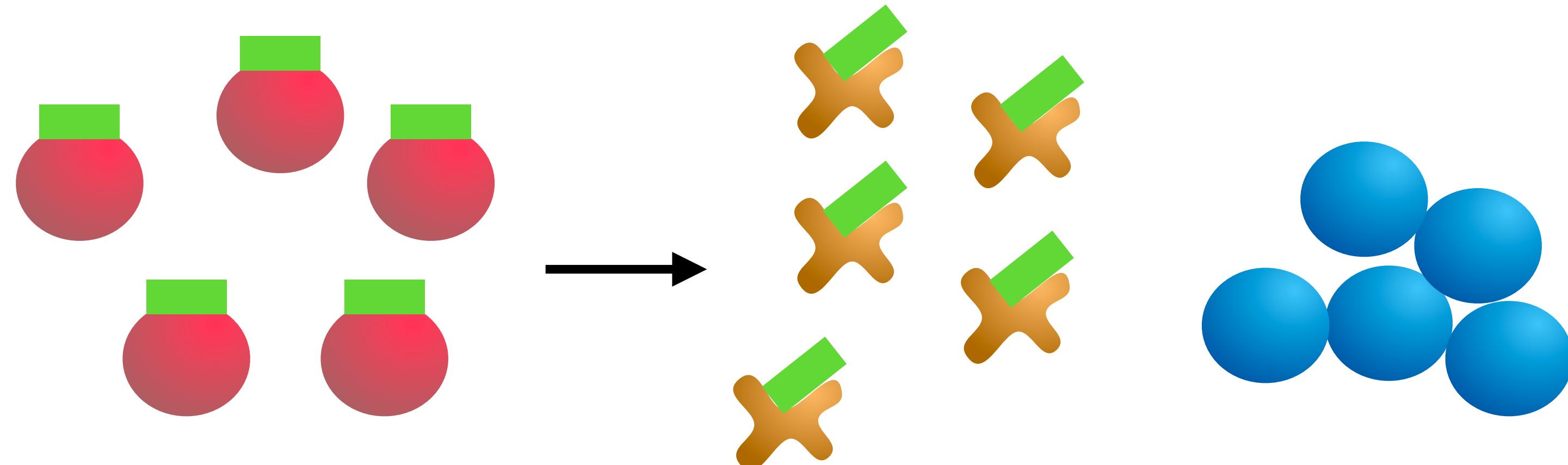


Gold nanoparticle aggregation is ubiquitous in modern applications

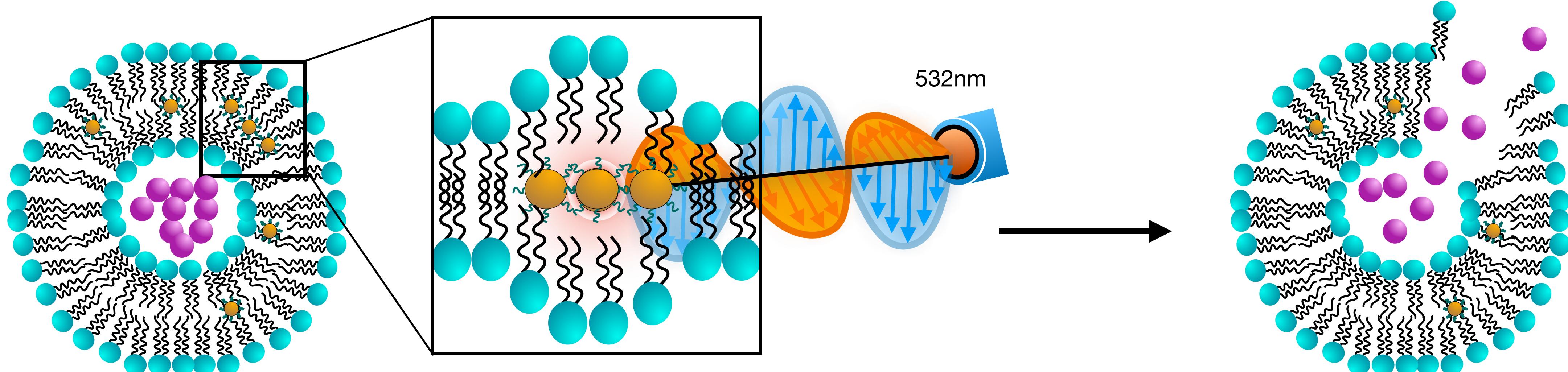
Imaging

- Dark Field Microscopy
- Differential Interference Contrast Microscopy
- Photothermal Imaging

Colormetric Detection

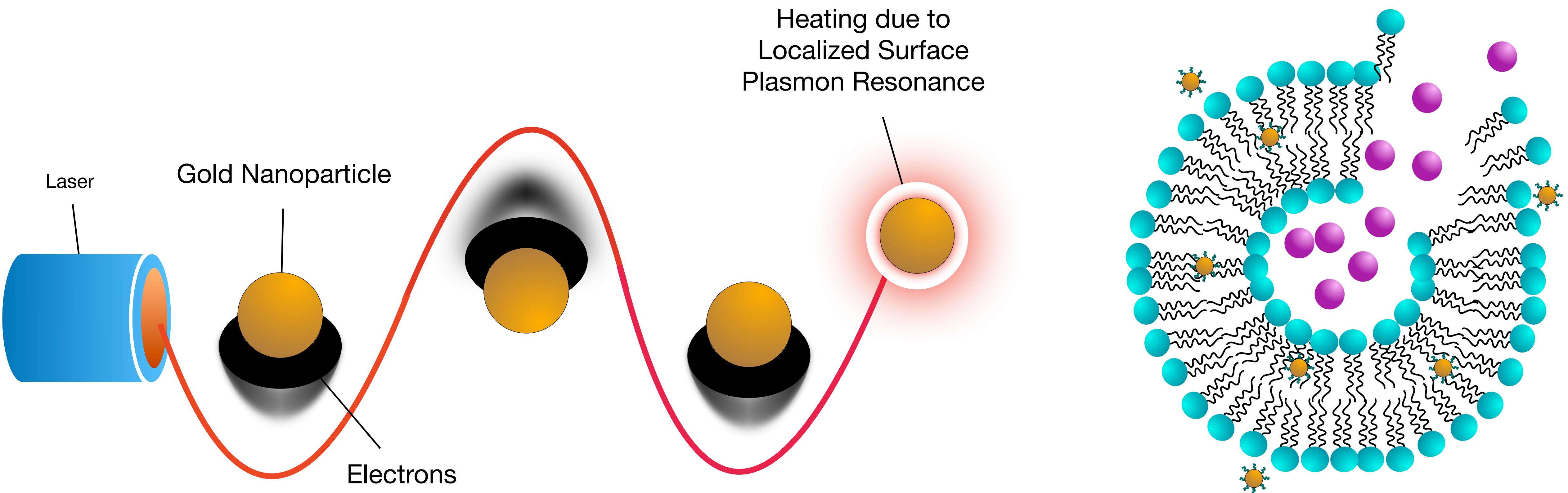


Targeted Drug Delivery

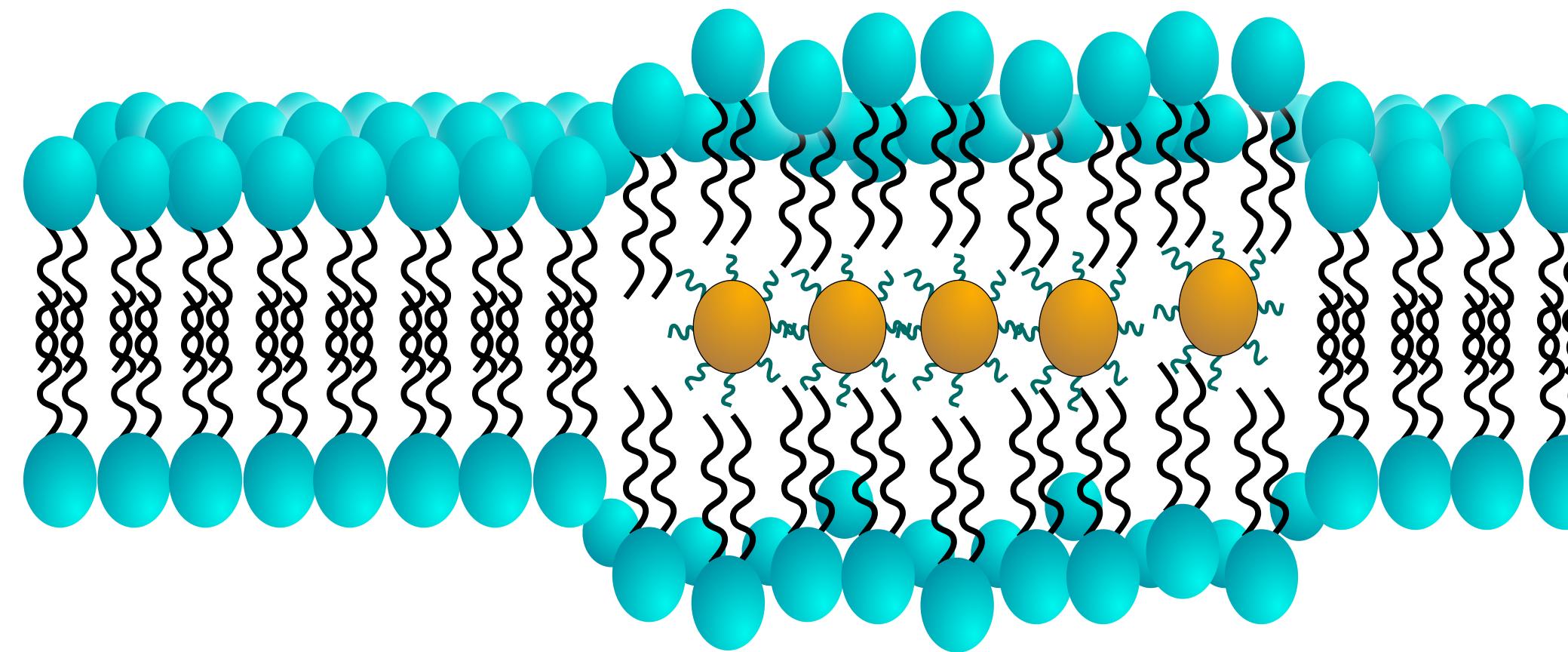


Irradiated gold nanoparticles in lipid membranes cause rupture and poration

- Control of Spacial Drug Release
- Control of Time Drug Release
- Goal of TDD is full control of vesicle
- Understand GNP Aggregation to better understand rupture

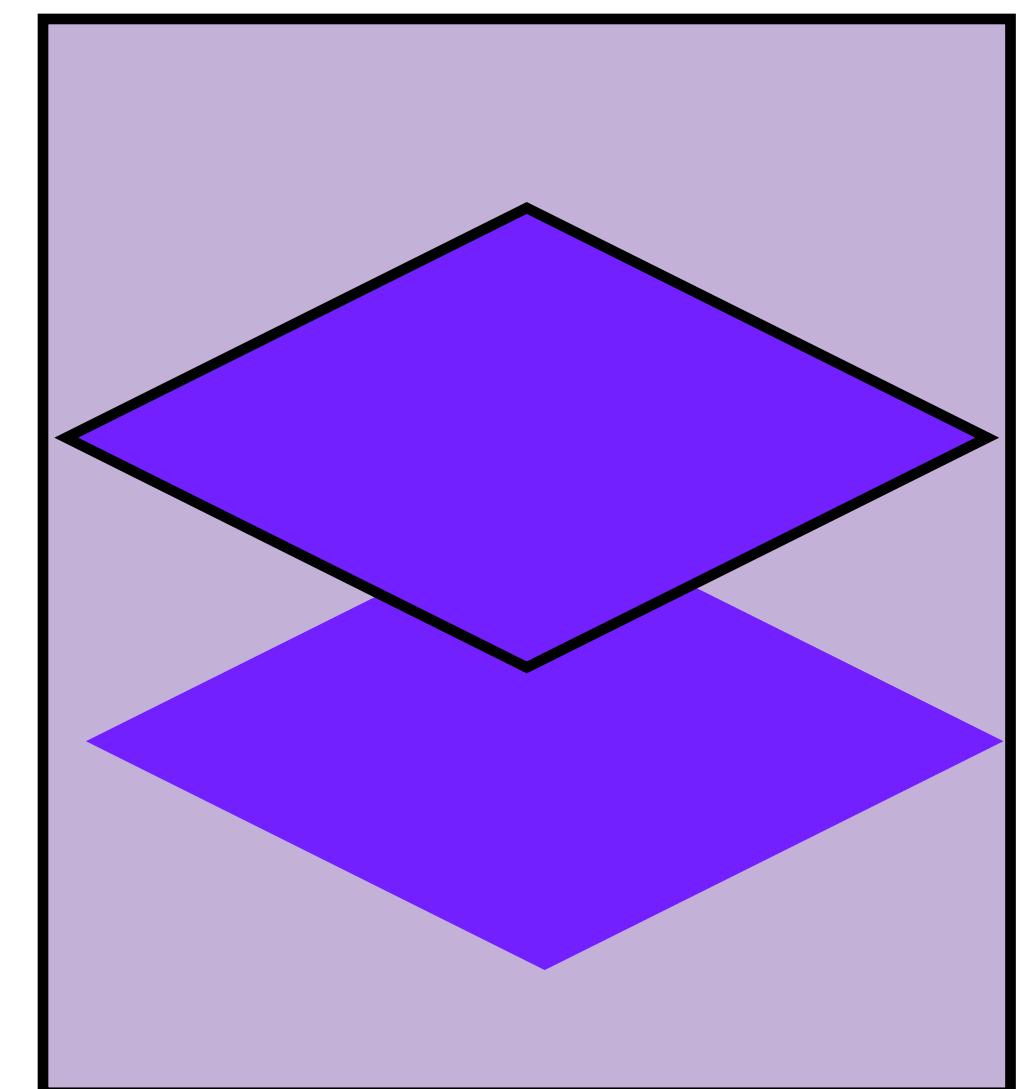


Research Question: What Is The Mechanism of Gold Nanoparticle Aggregation In Lipid Membranes?

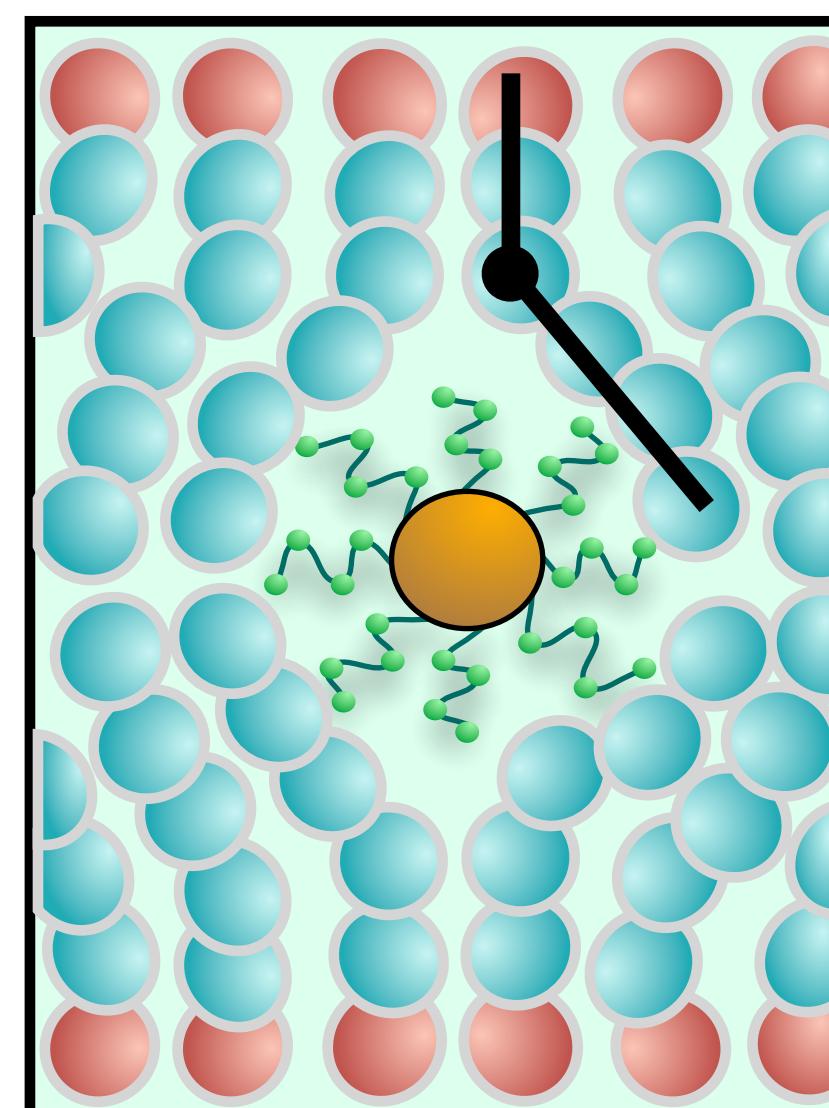
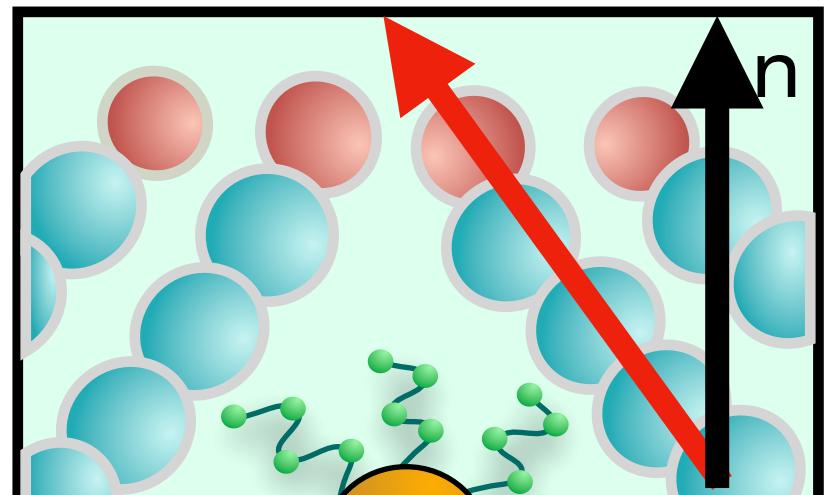
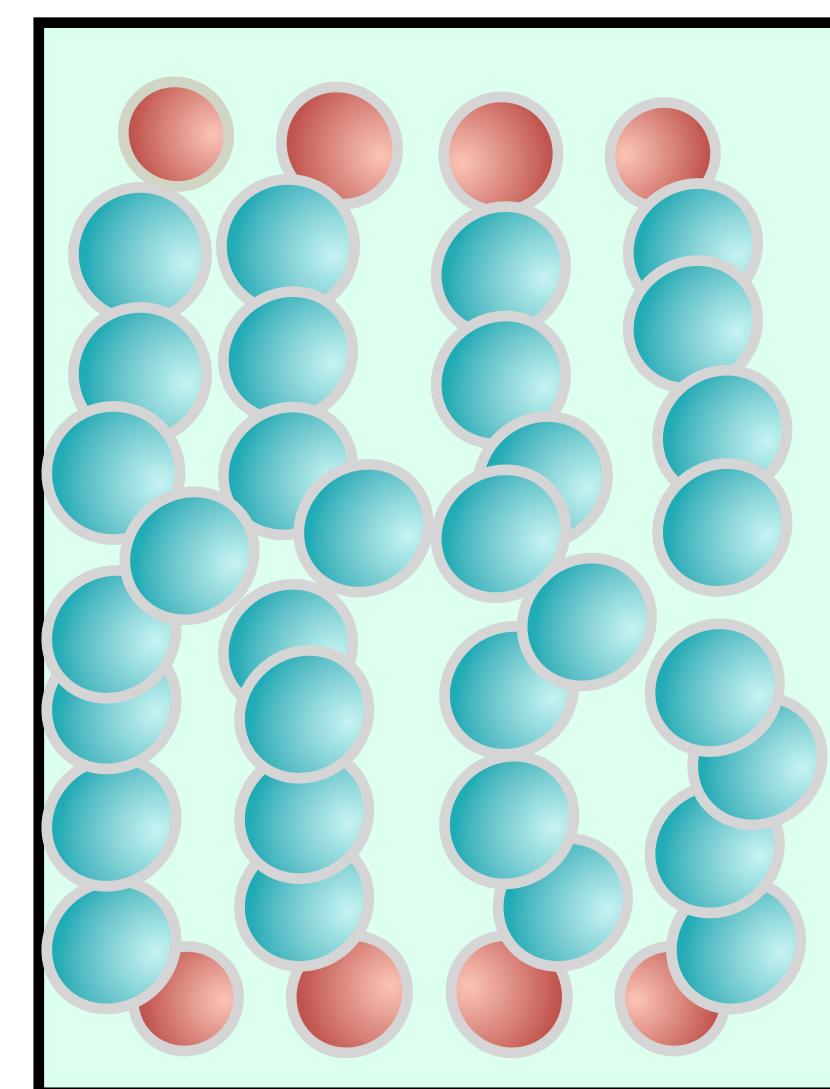


Single nanoparticles perturb membranes

Membrane Deformation



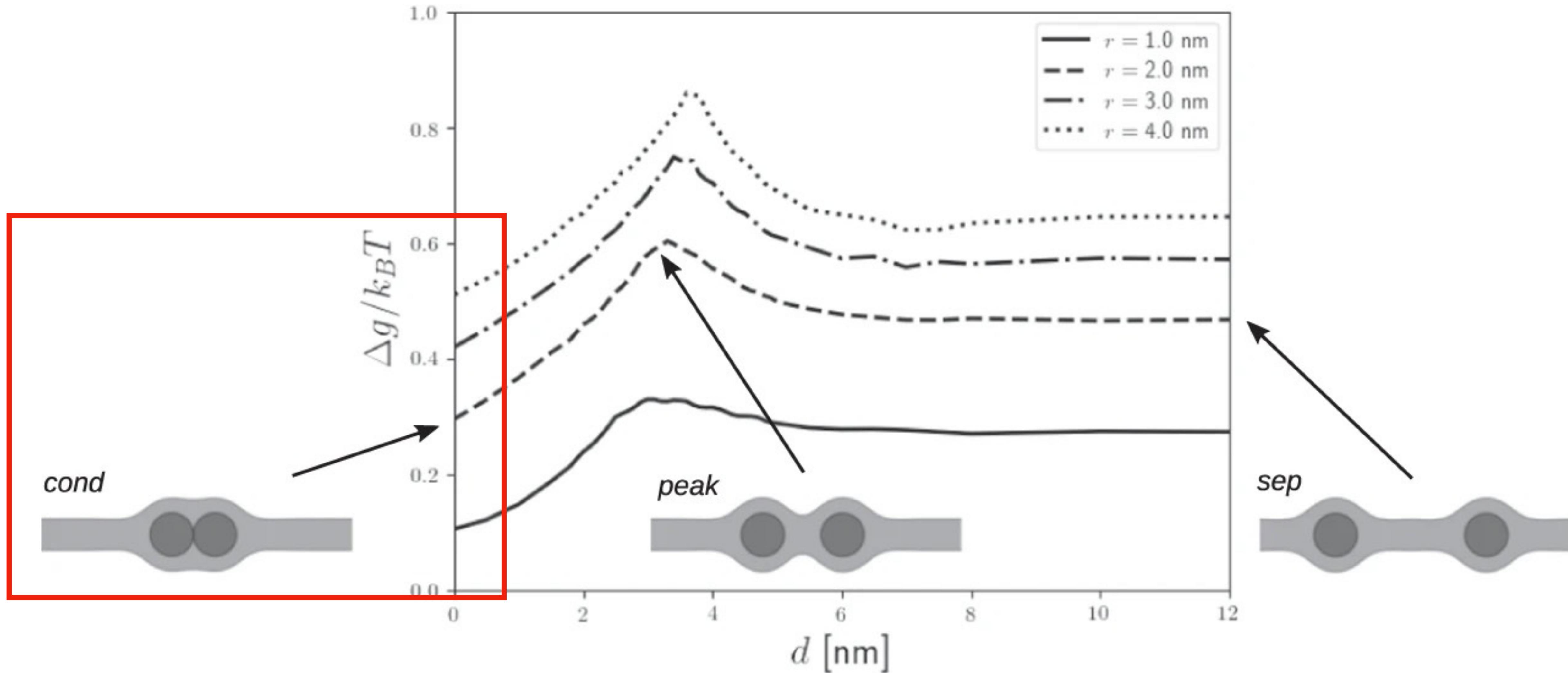
Lipid Deformation



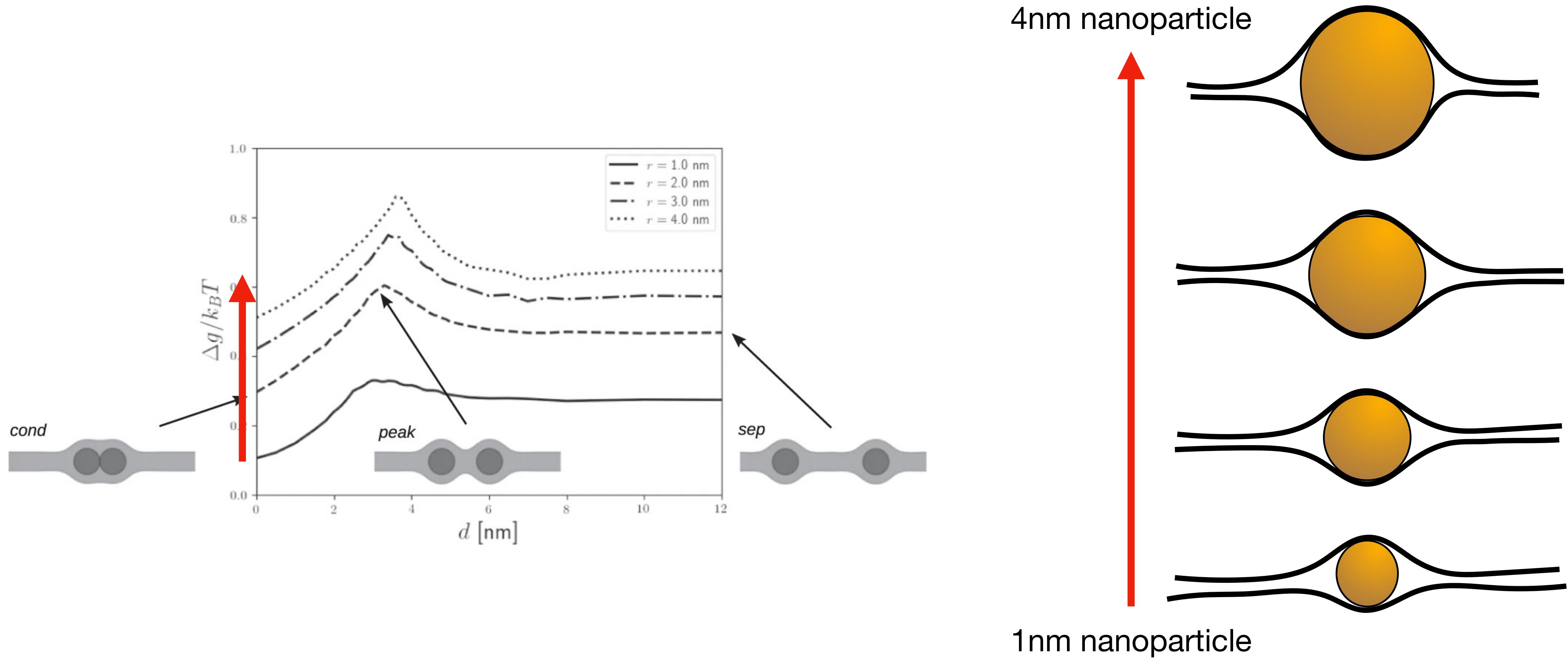
Multi-nanoparticle systems aggregate due to lipid membrane deformations

- Single nanoparticles deform membrane
- Aggregation is a way to resolve energetic cost of deformations
 - Membrane Bending
 - Microscopic Lipid Deformation

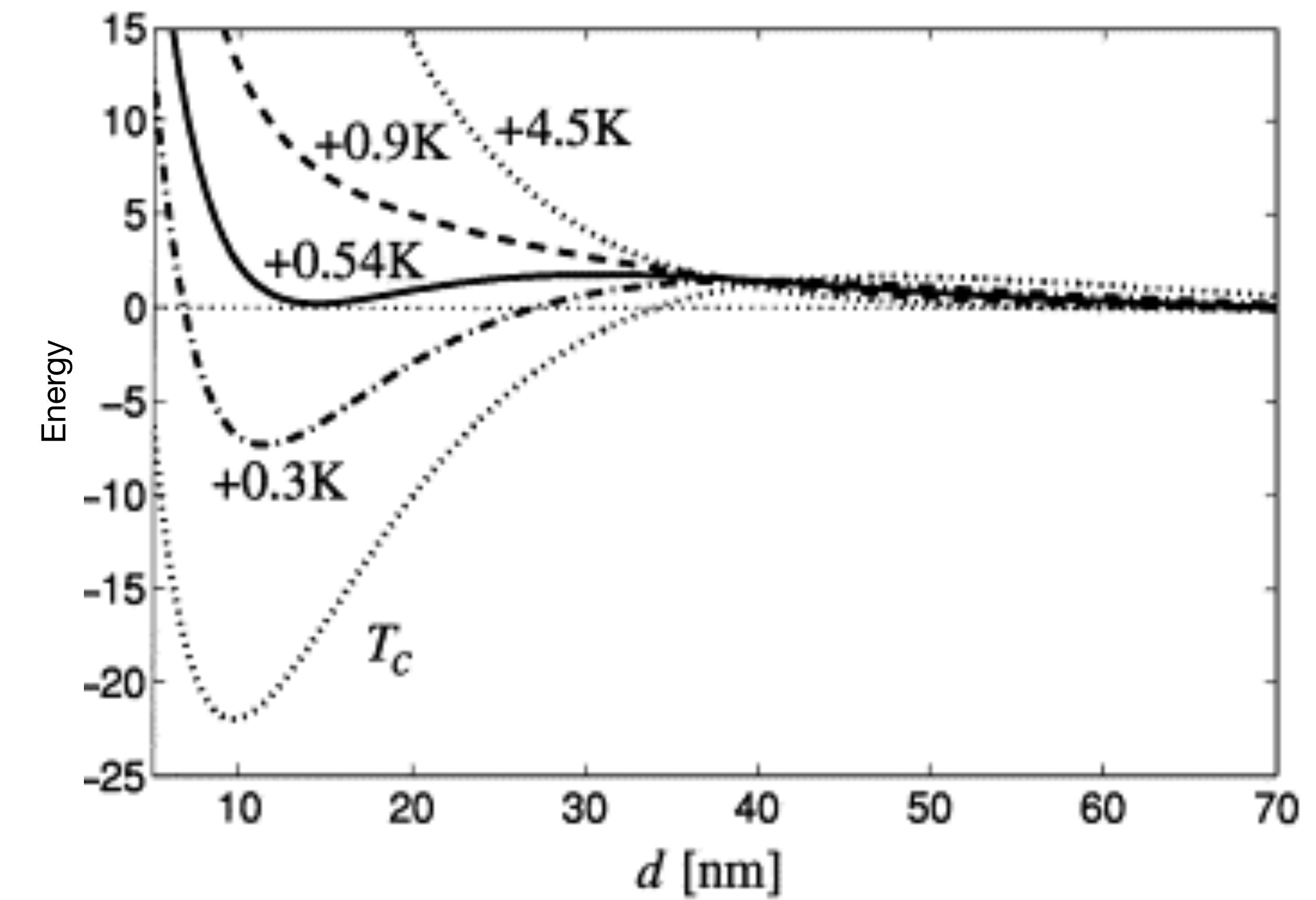
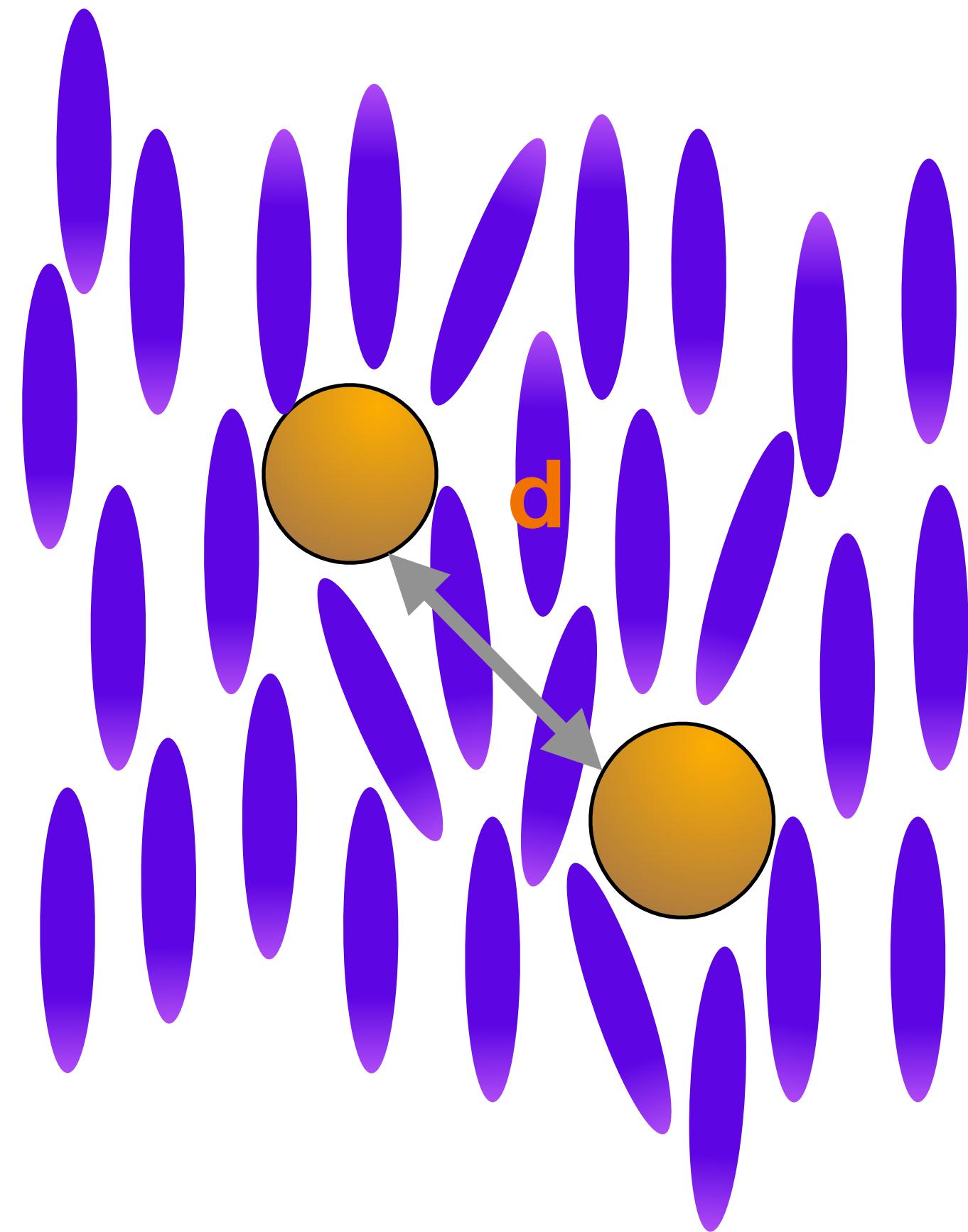
Aggregated gold nanoparticles are the lowest energy configuration for deformations caused by membrane bending



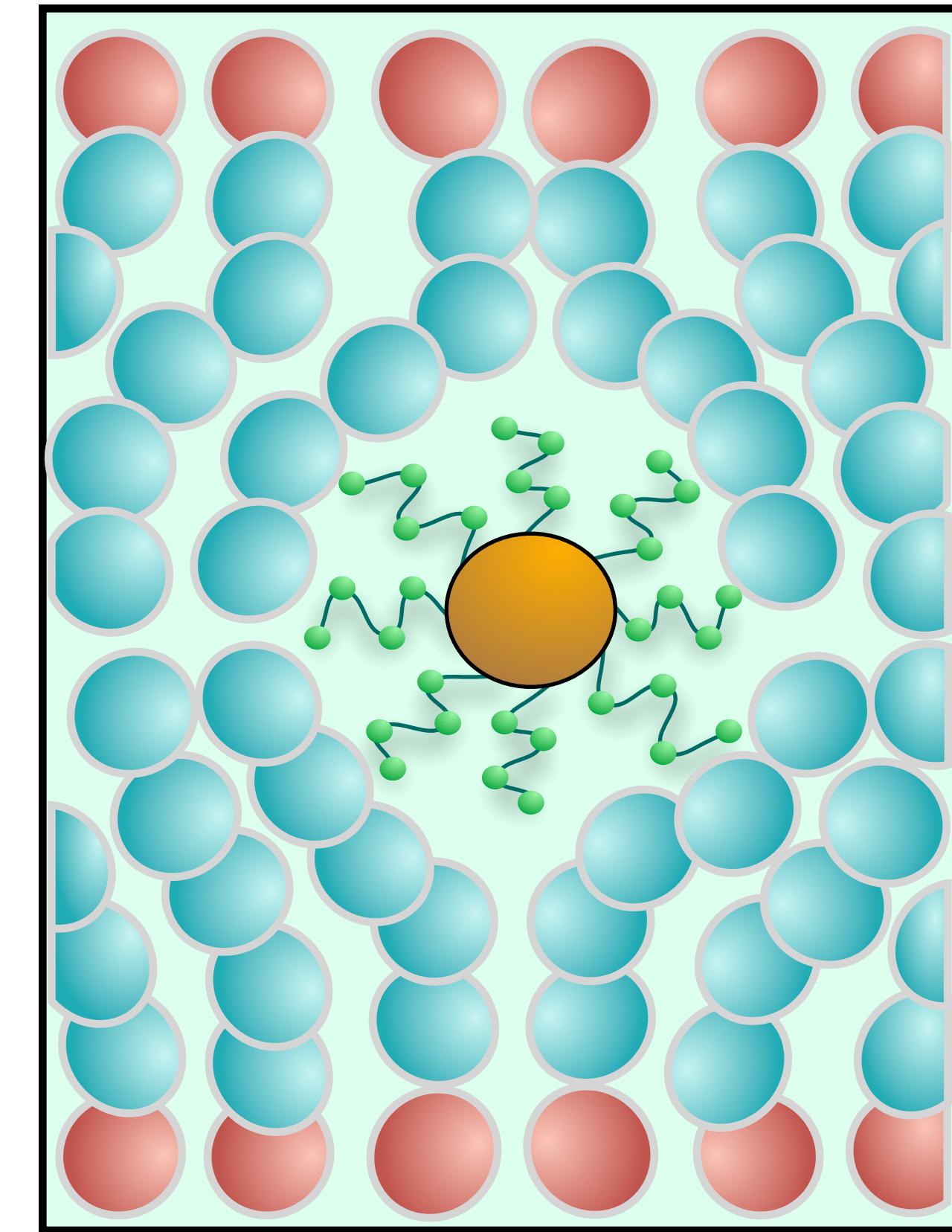
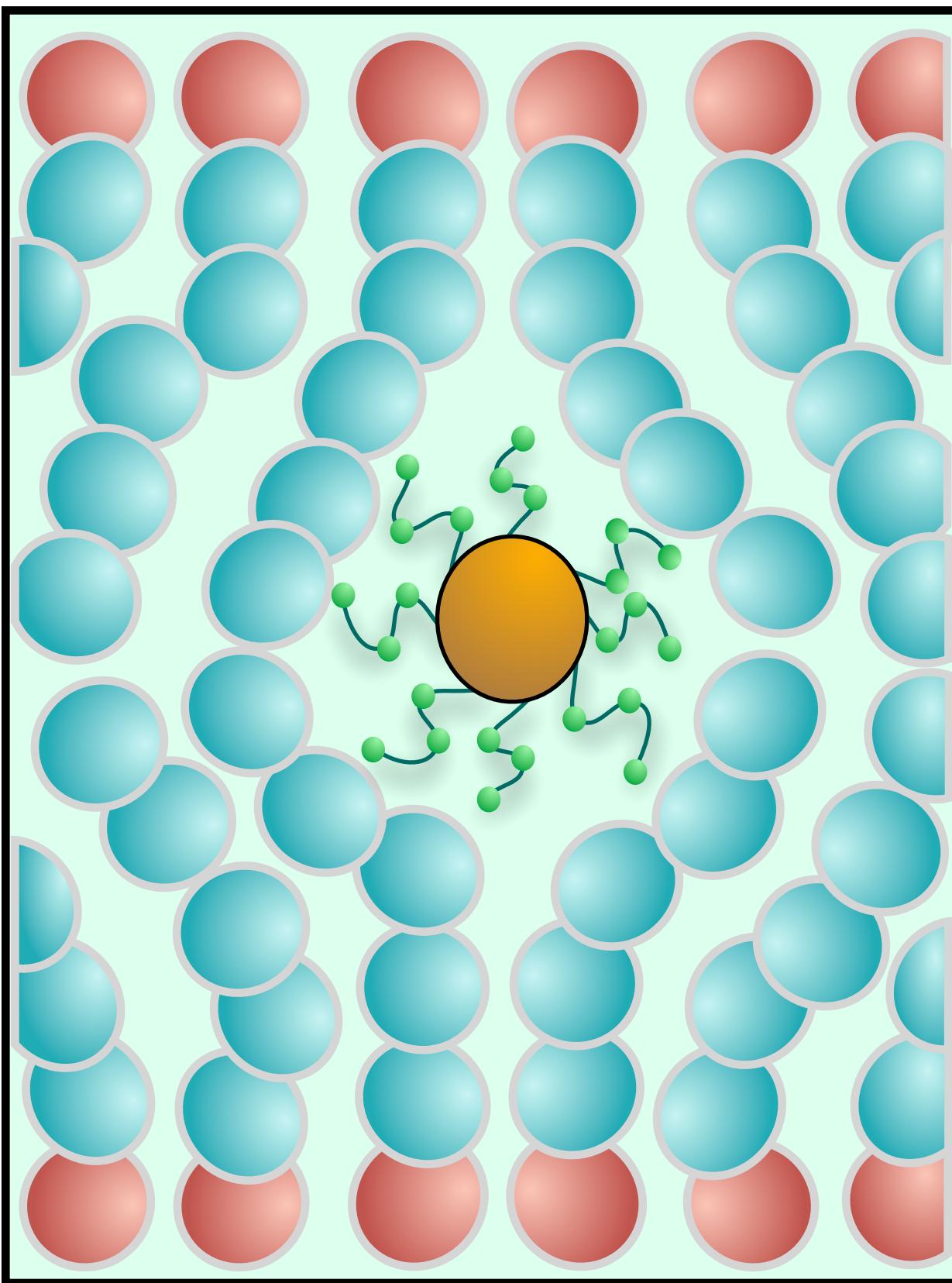
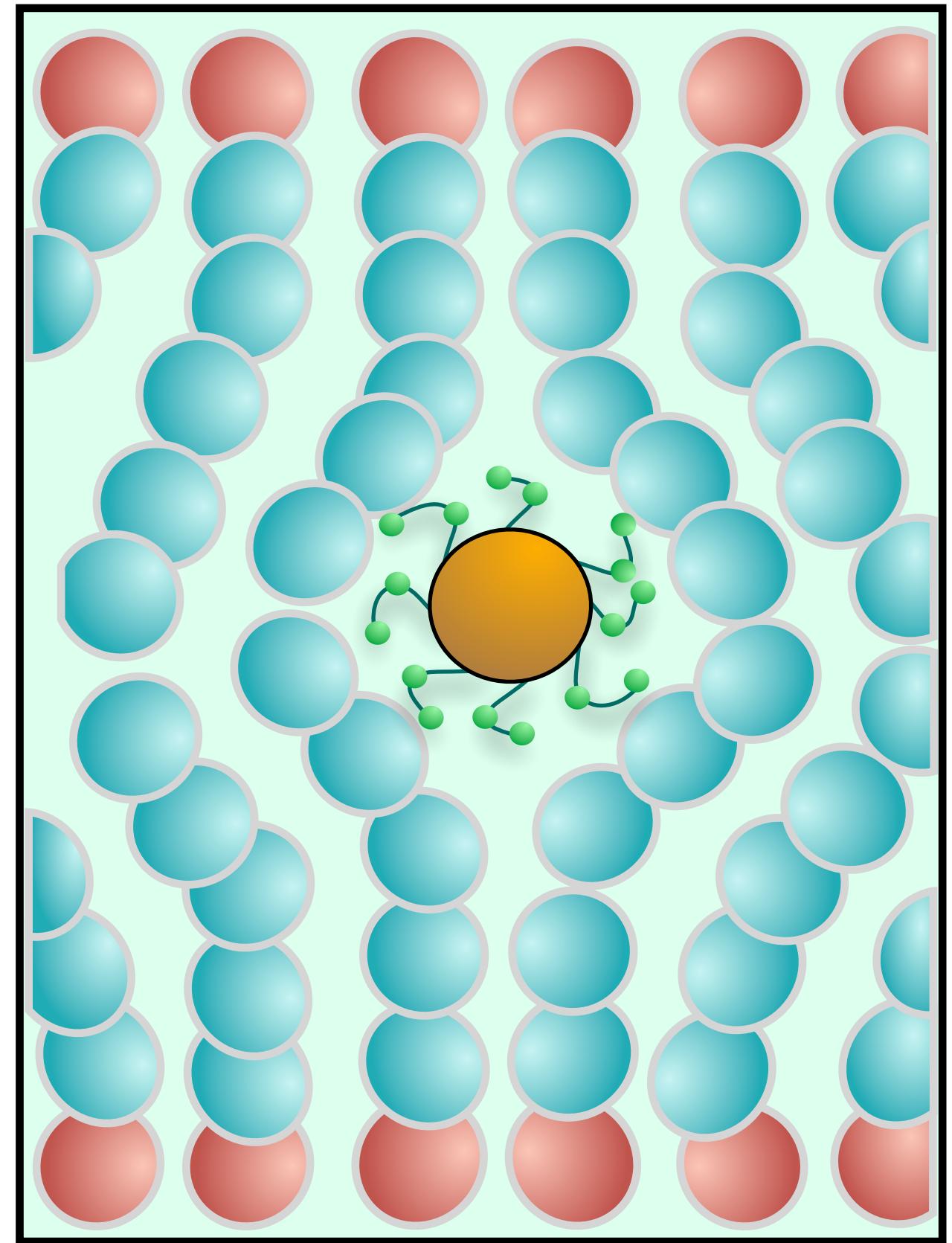
Bending deformations increase with nanoparticle size



Aggregation can be driven by molecular defects



Lipid mediated aggregation expected to increase with ligand length

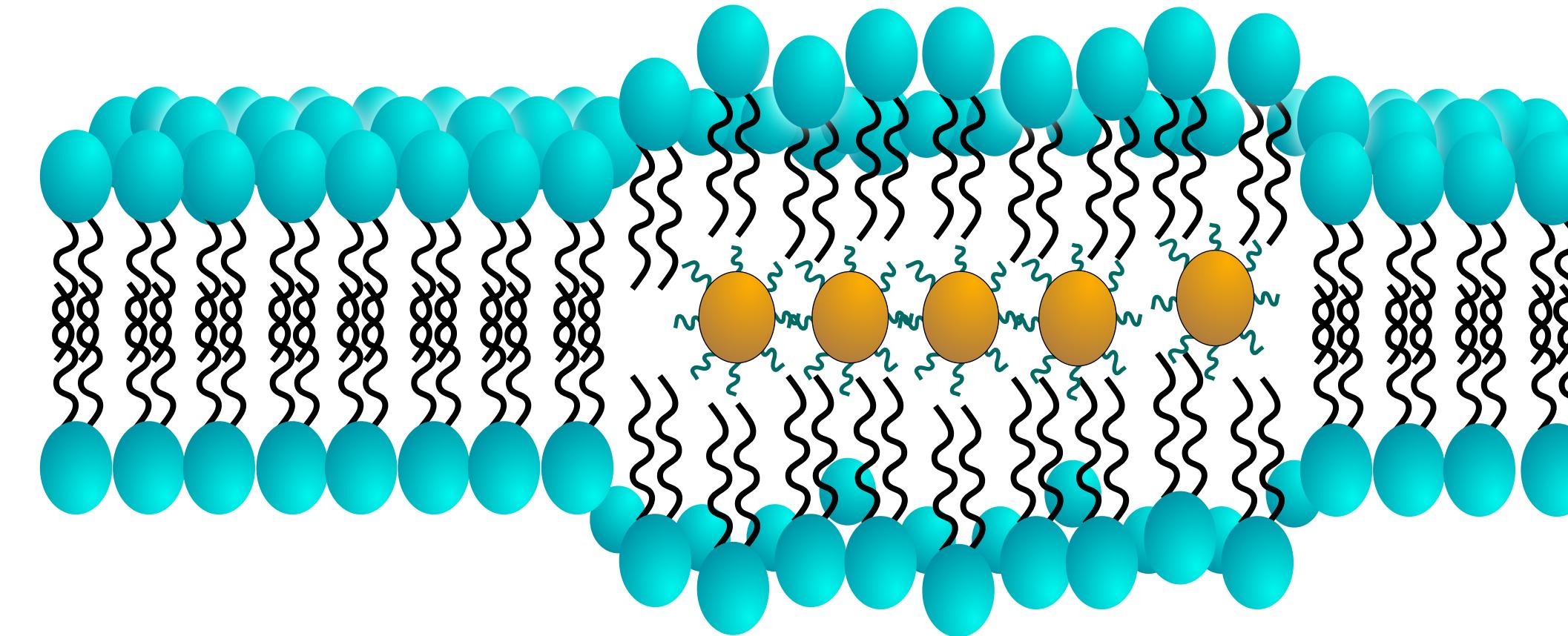


Octanethiol



Hexadecanethiol

Research Question: What Is The Mechanism of Gold Nanoparticle Aggregation In Lipid Membranes?



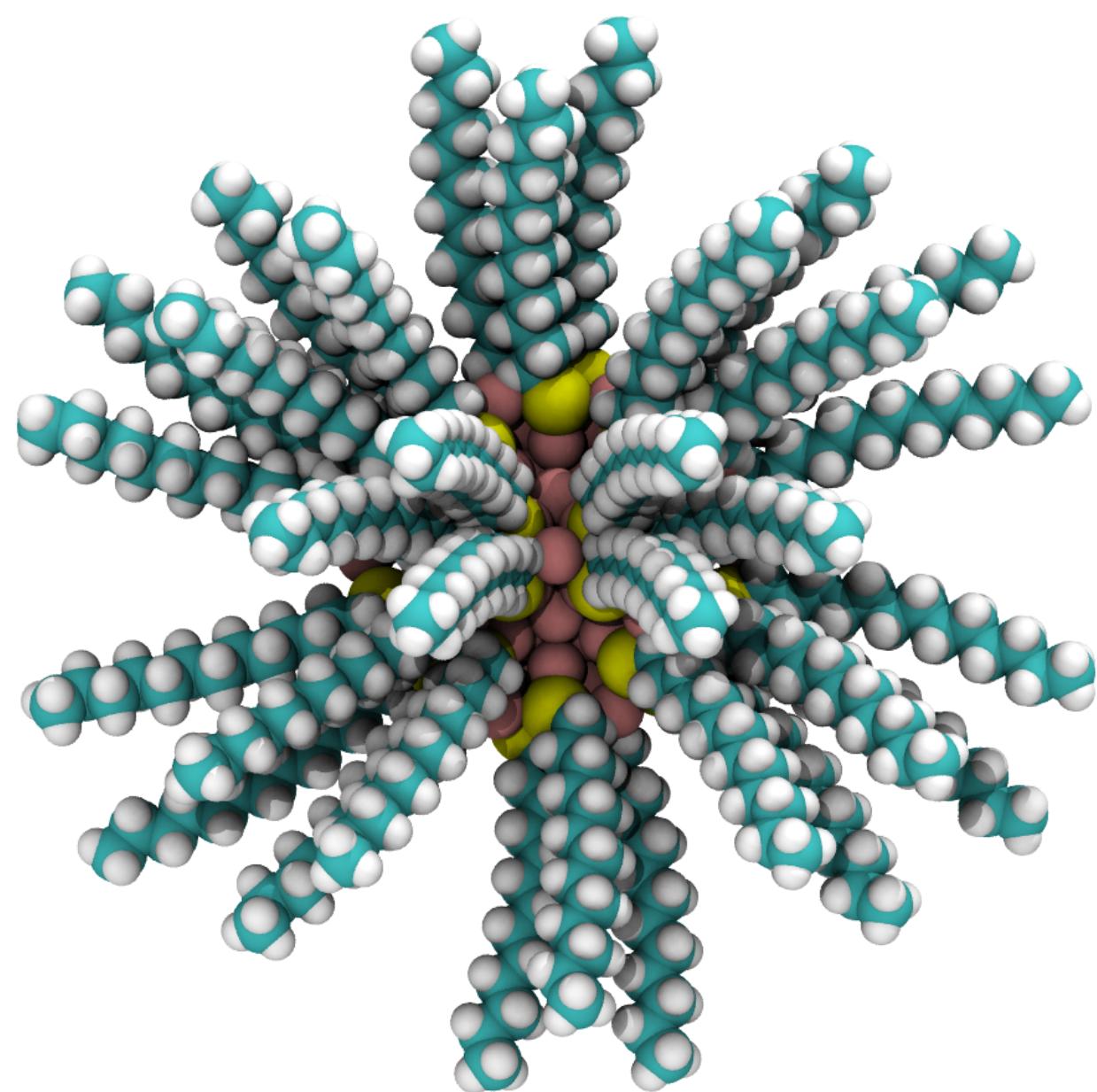
**Which Mechanism Causes Aggregation,
Membrane Bending or Lipid Chain Order?**

Outline

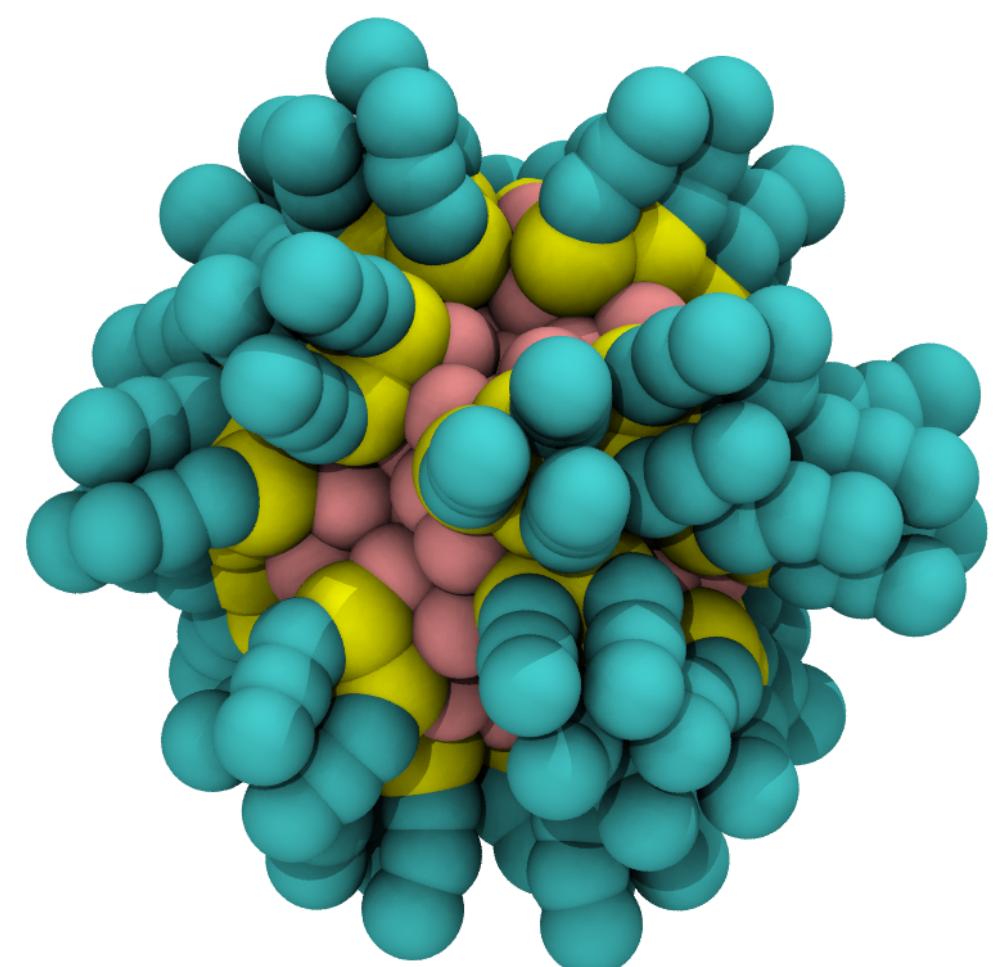
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Coarse grained molecular dynamics model of gold nanoparticle

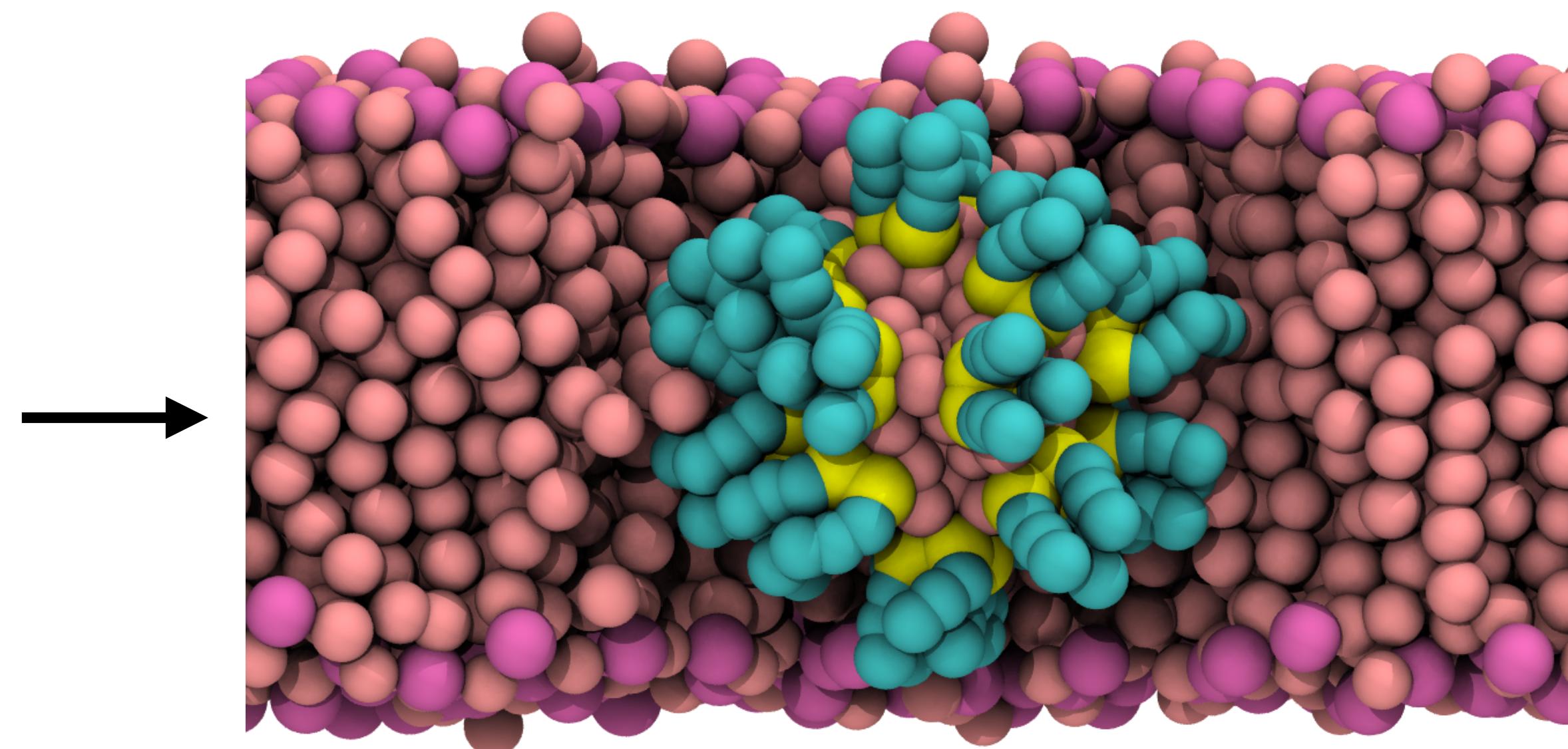
Atomistic GNP



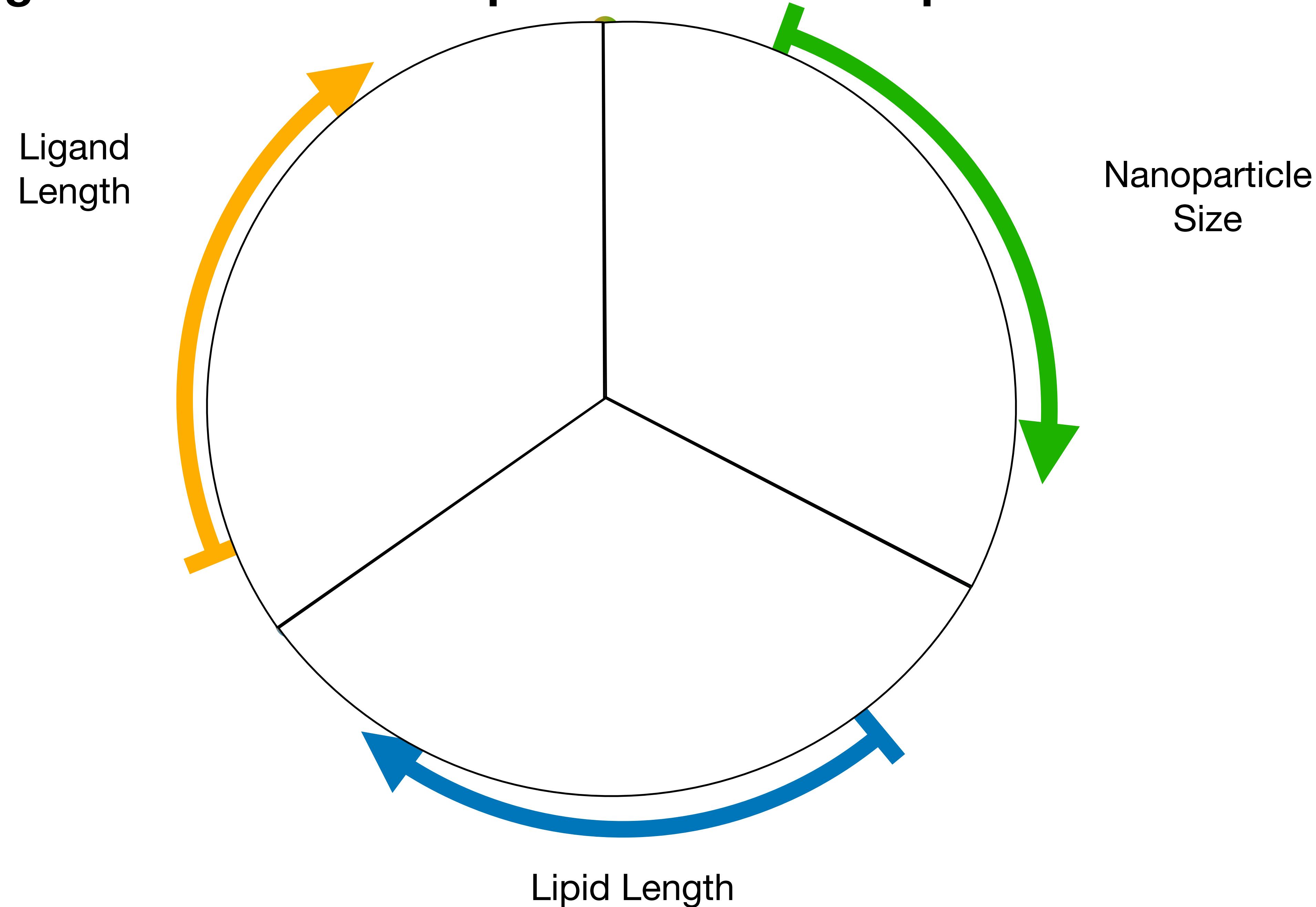
Coarse Grained GNP



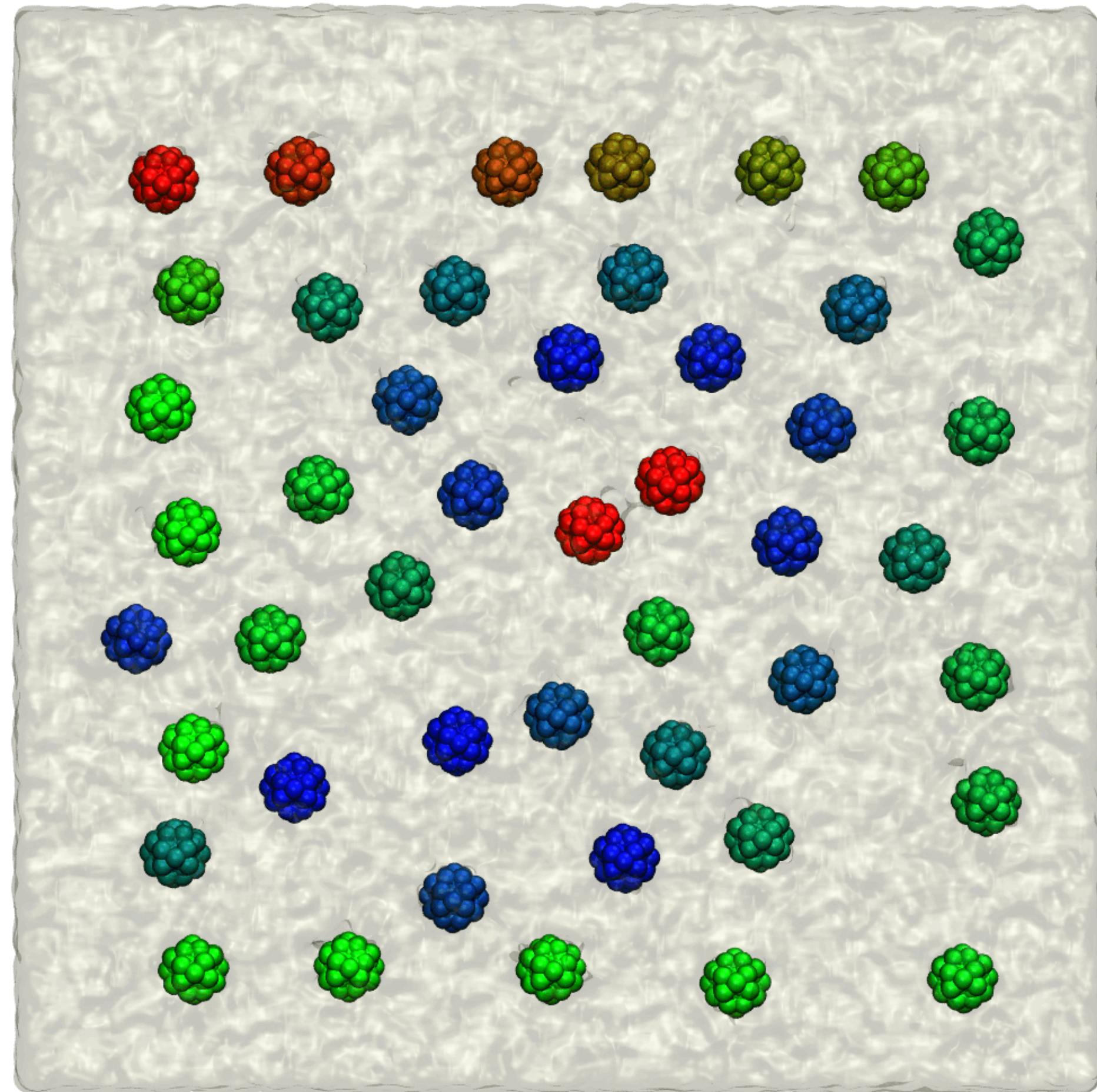
Coarse Grained GNP in Lipid Membrane



Adjusting the membrane composition to test the possible mechanism



Quantifying aggregation and lipid chain order

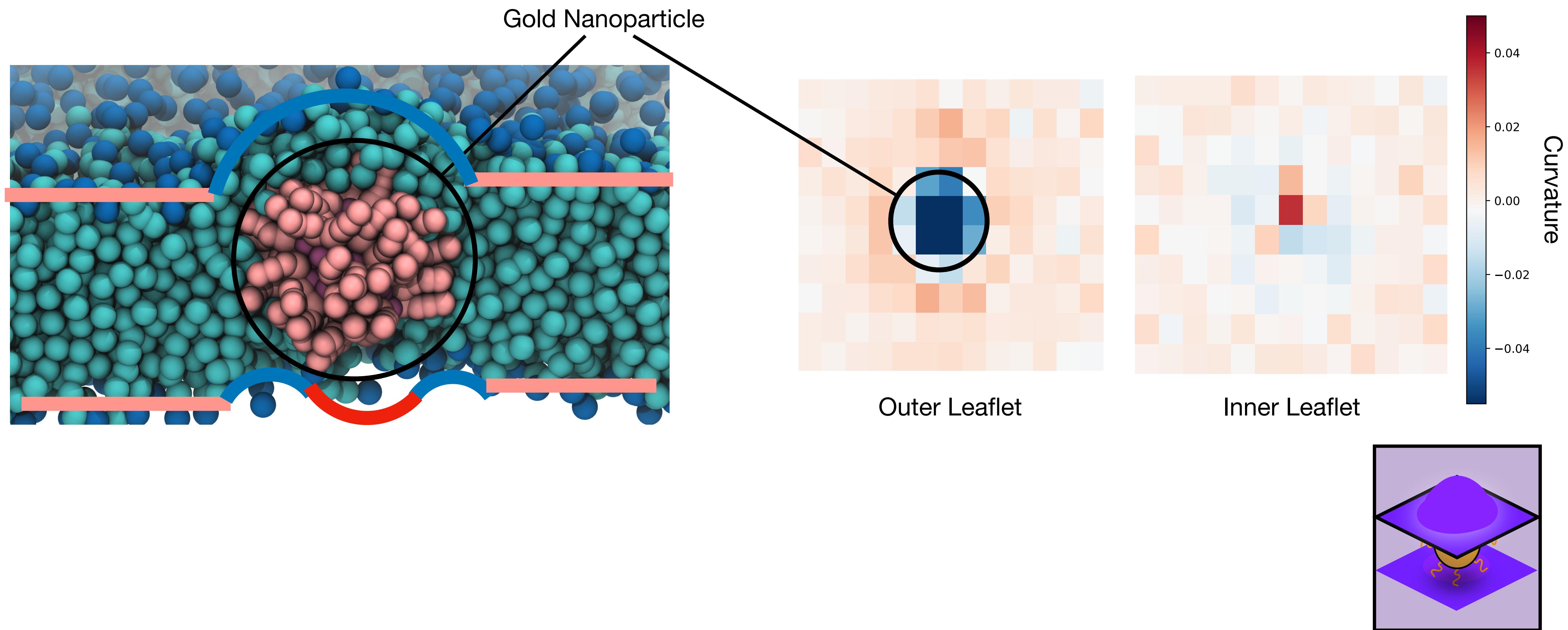


- Aggregation Fraction
- $f_{agg} = \text{Total Nanoparticles in largest aggregate} / \text{Total Nanoparticles in System}$
- Measuring lipid chain order using order parameter

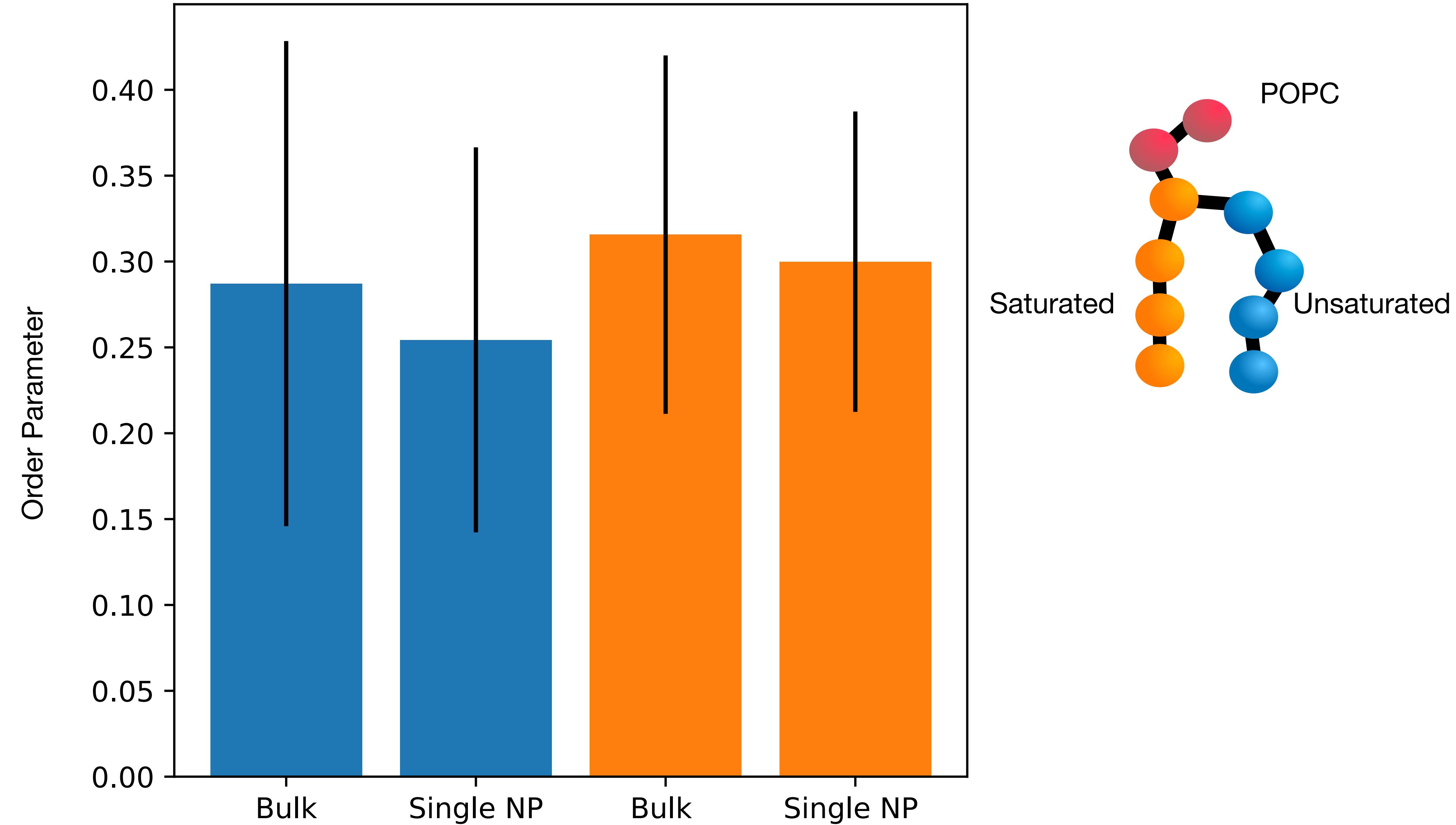
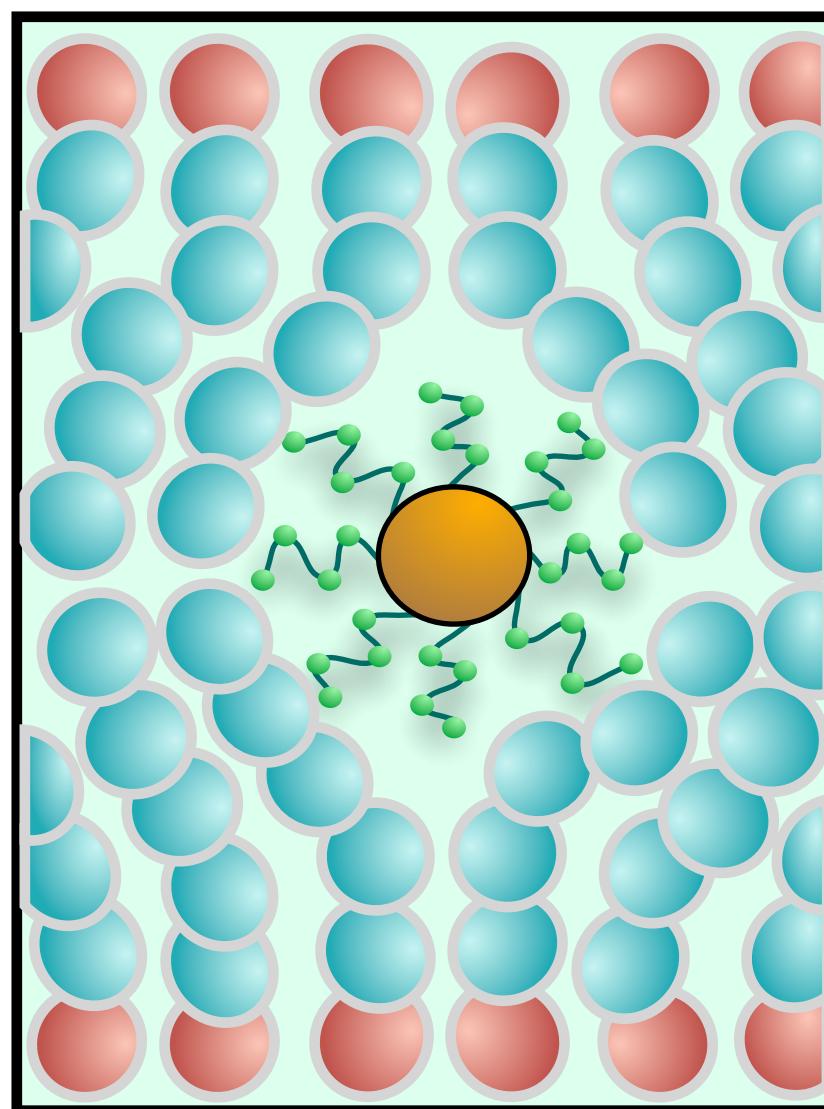
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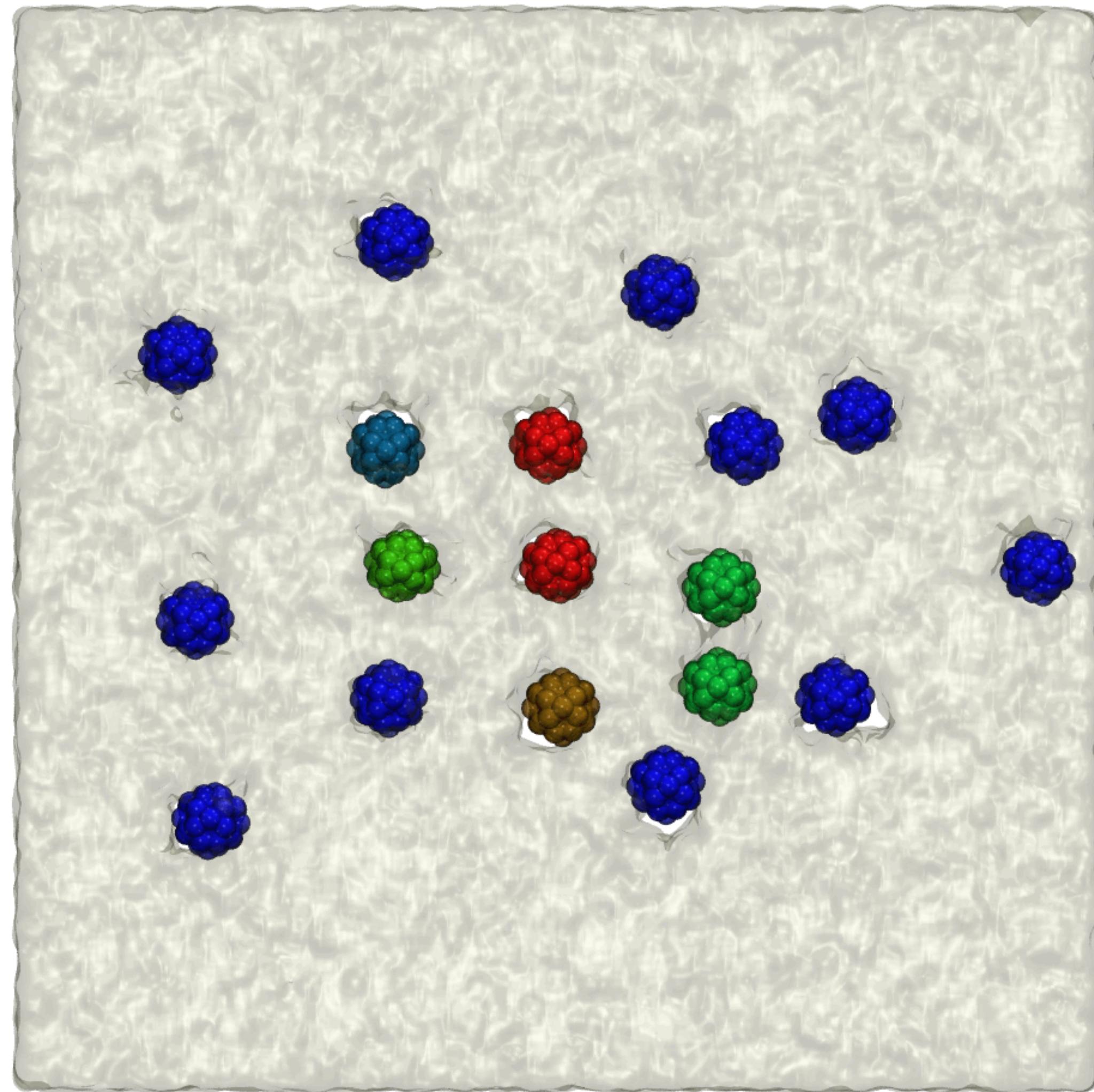
Single gold nanoparticles cause membrane bending



Disorder In Lipid Chains Around Single Nanoparticle Inclusion



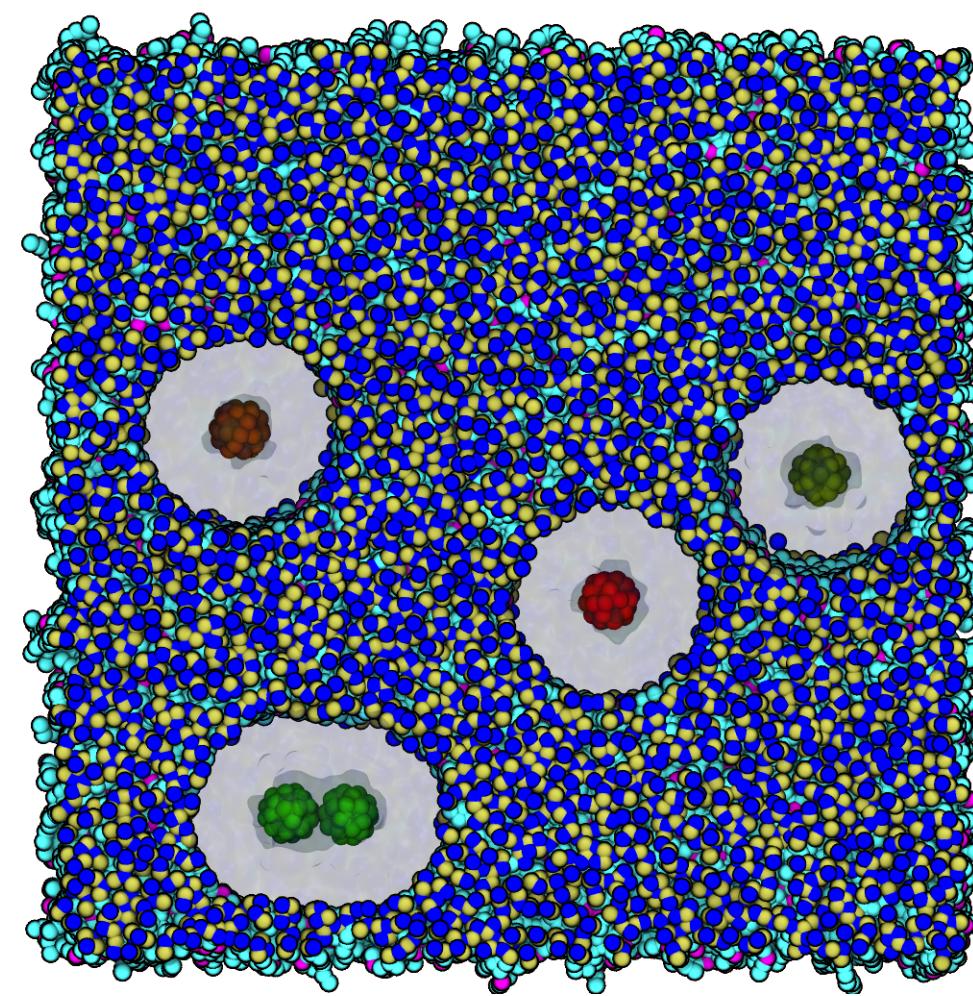
From a single nanoparticle to multiple nanoparticle



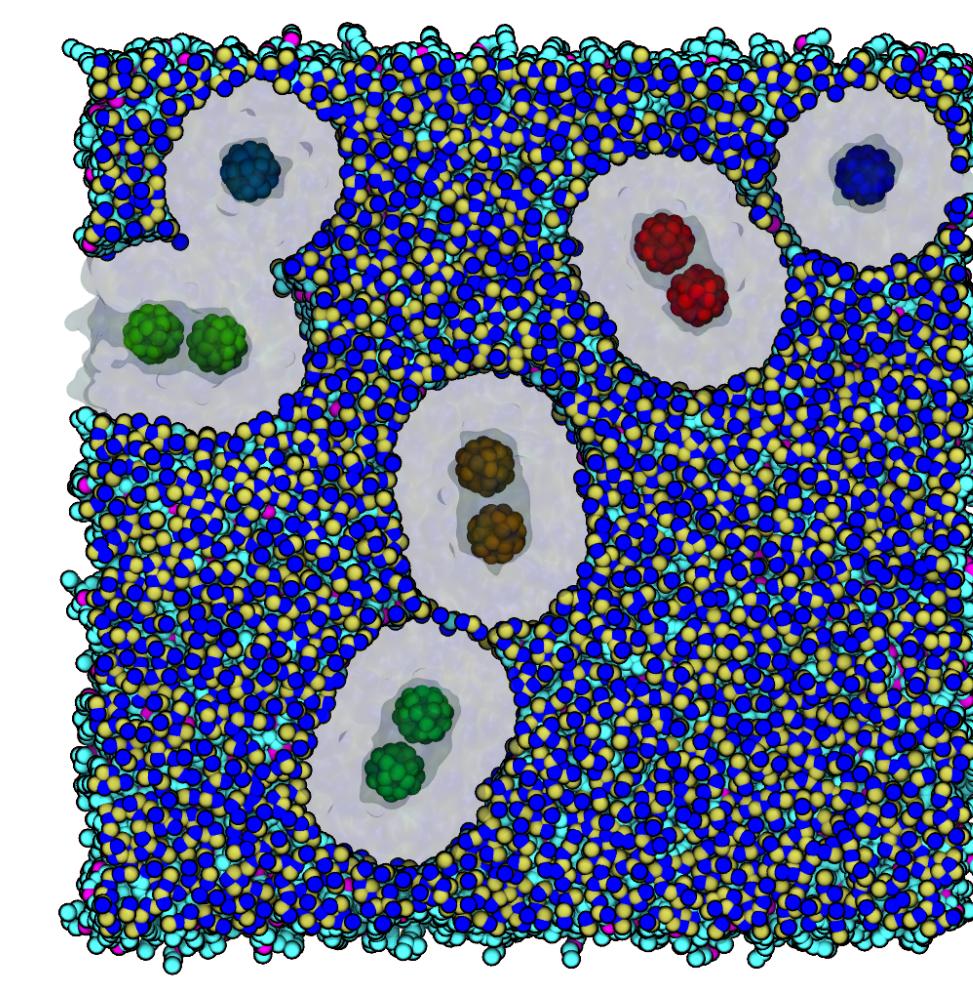
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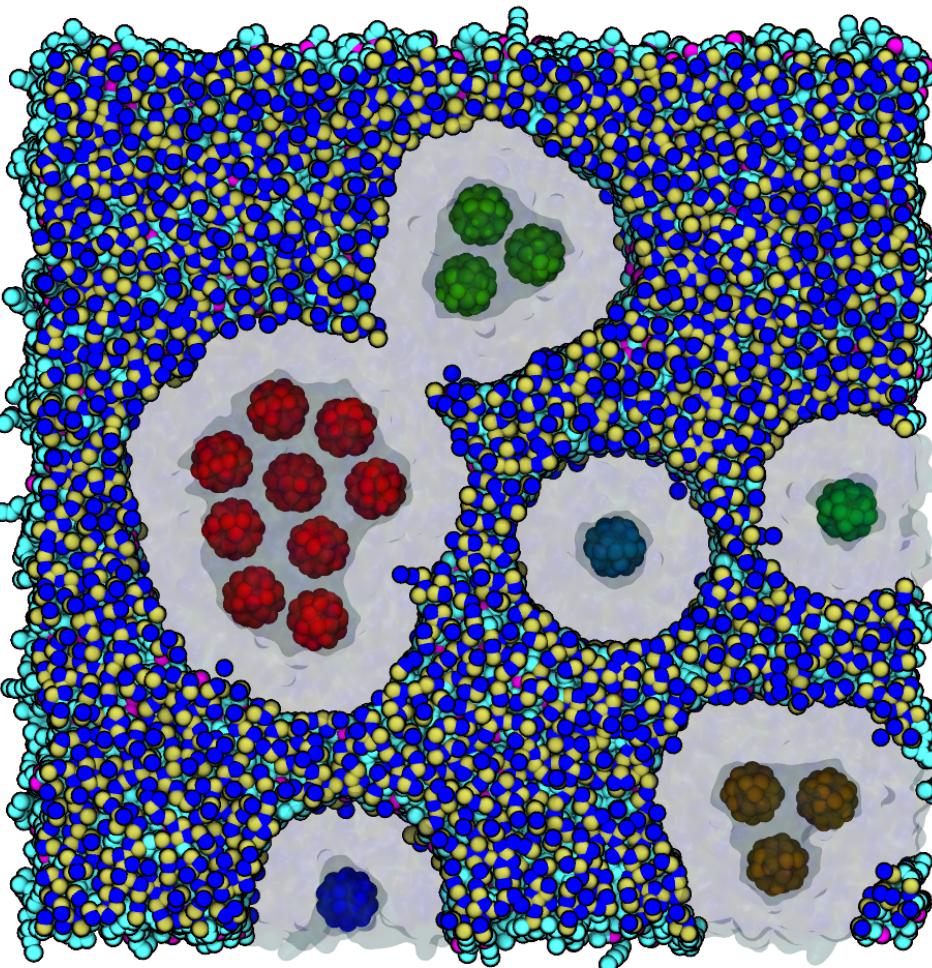
Observing aggregation in POPC lipid membranes



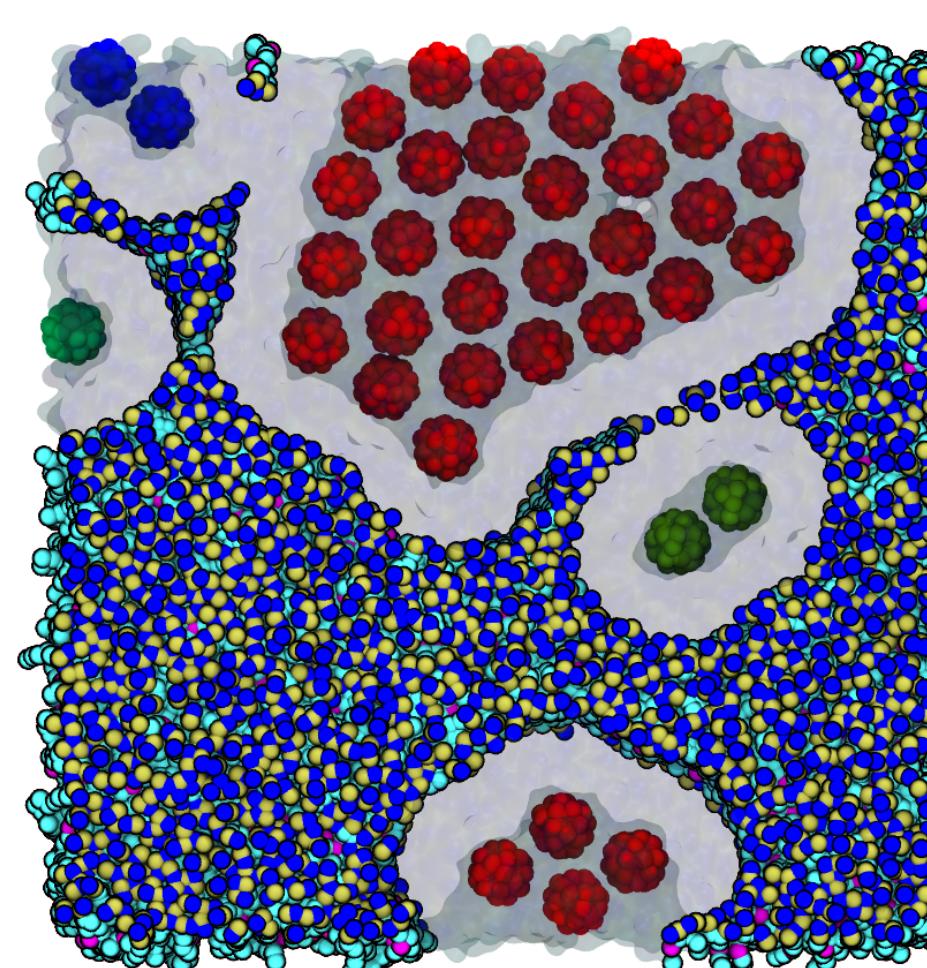
.00095 NP/Molecule



.0020 NP/Molecule

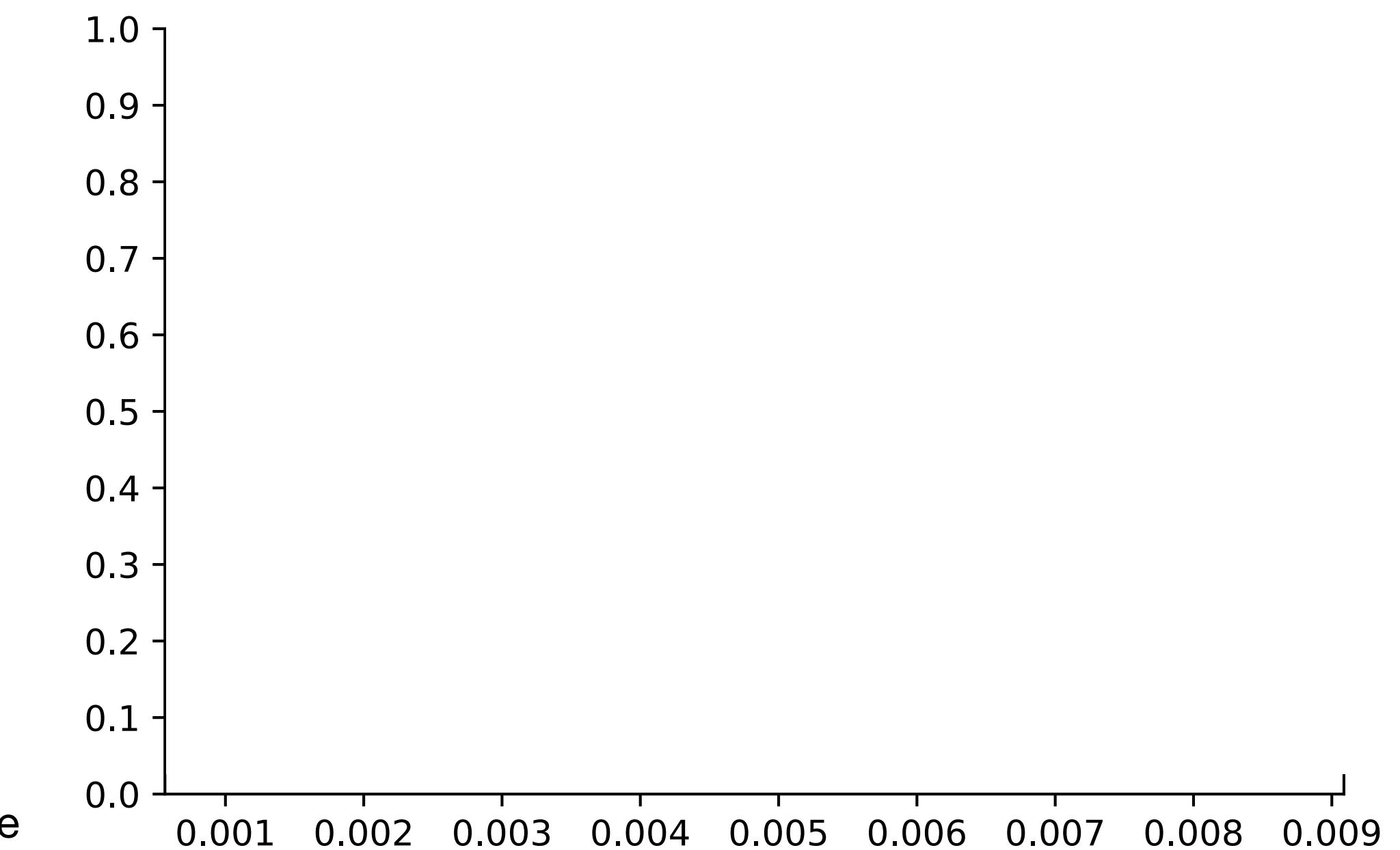


.0037NP/Molecule



.0087 NP/Molecule

F_{agg}

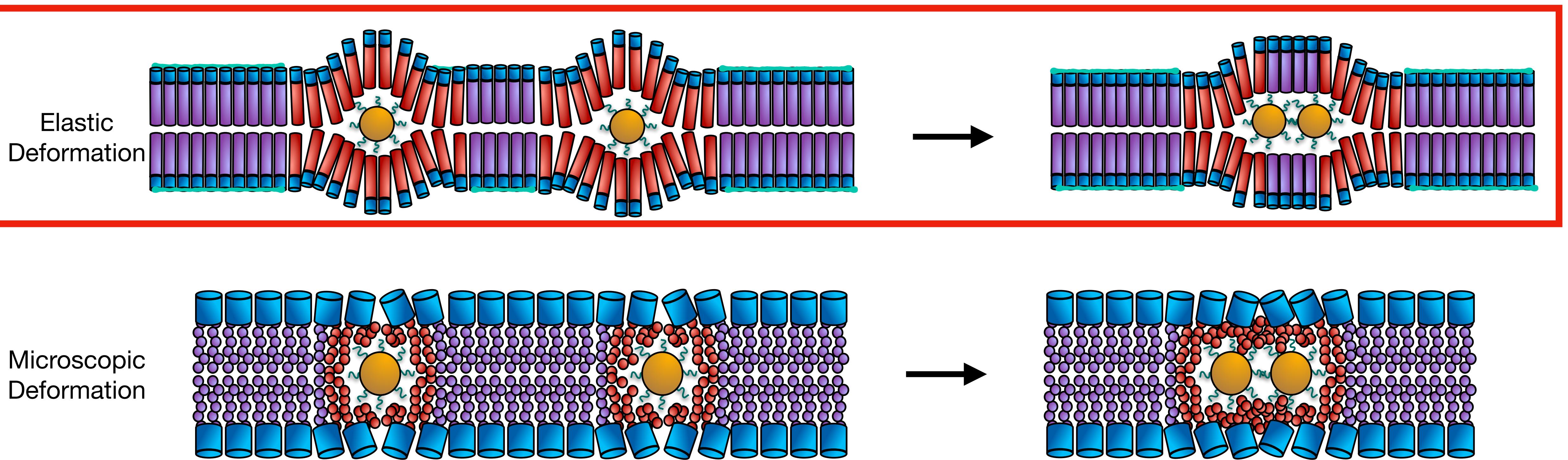


Concentration

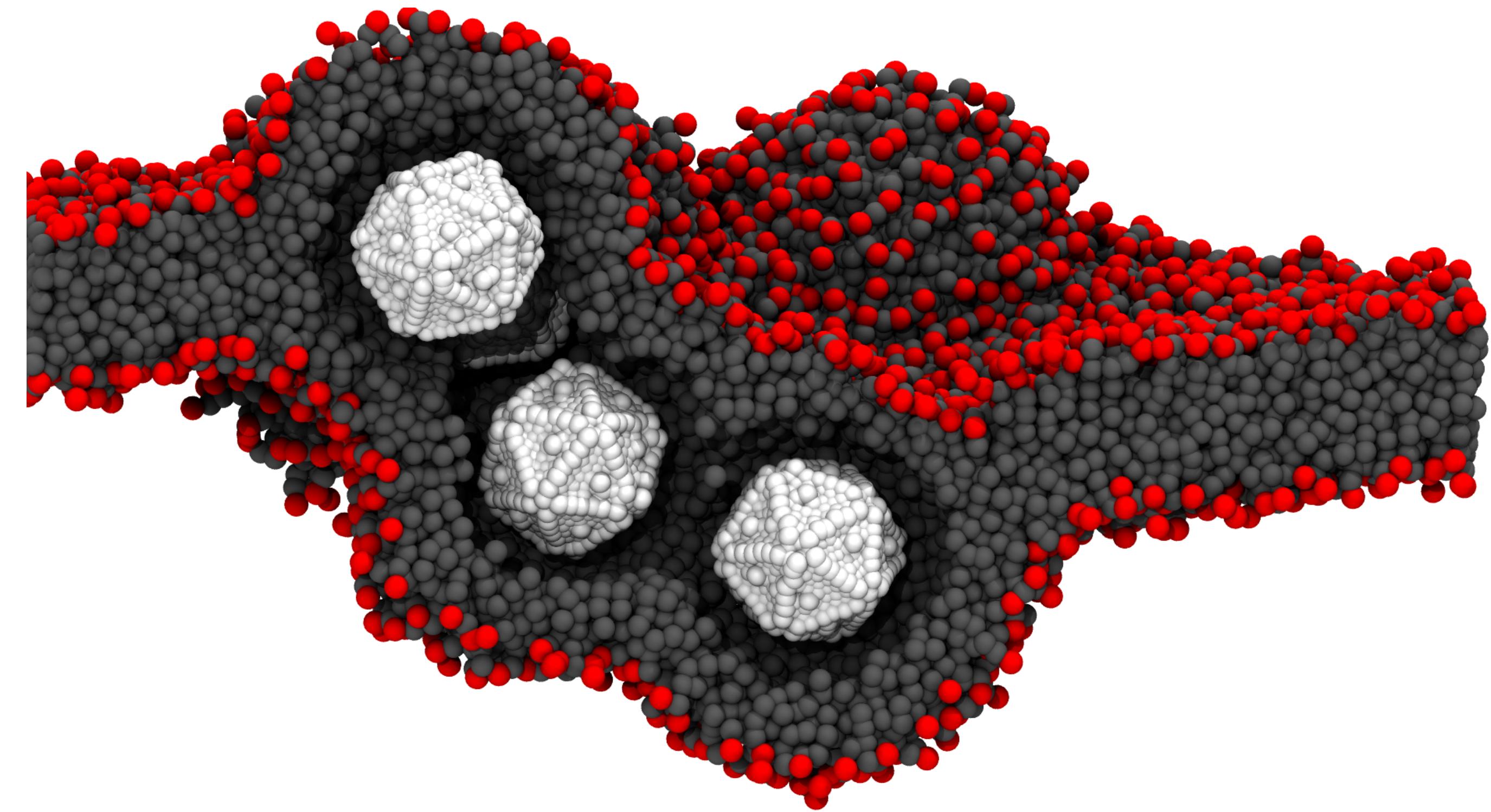
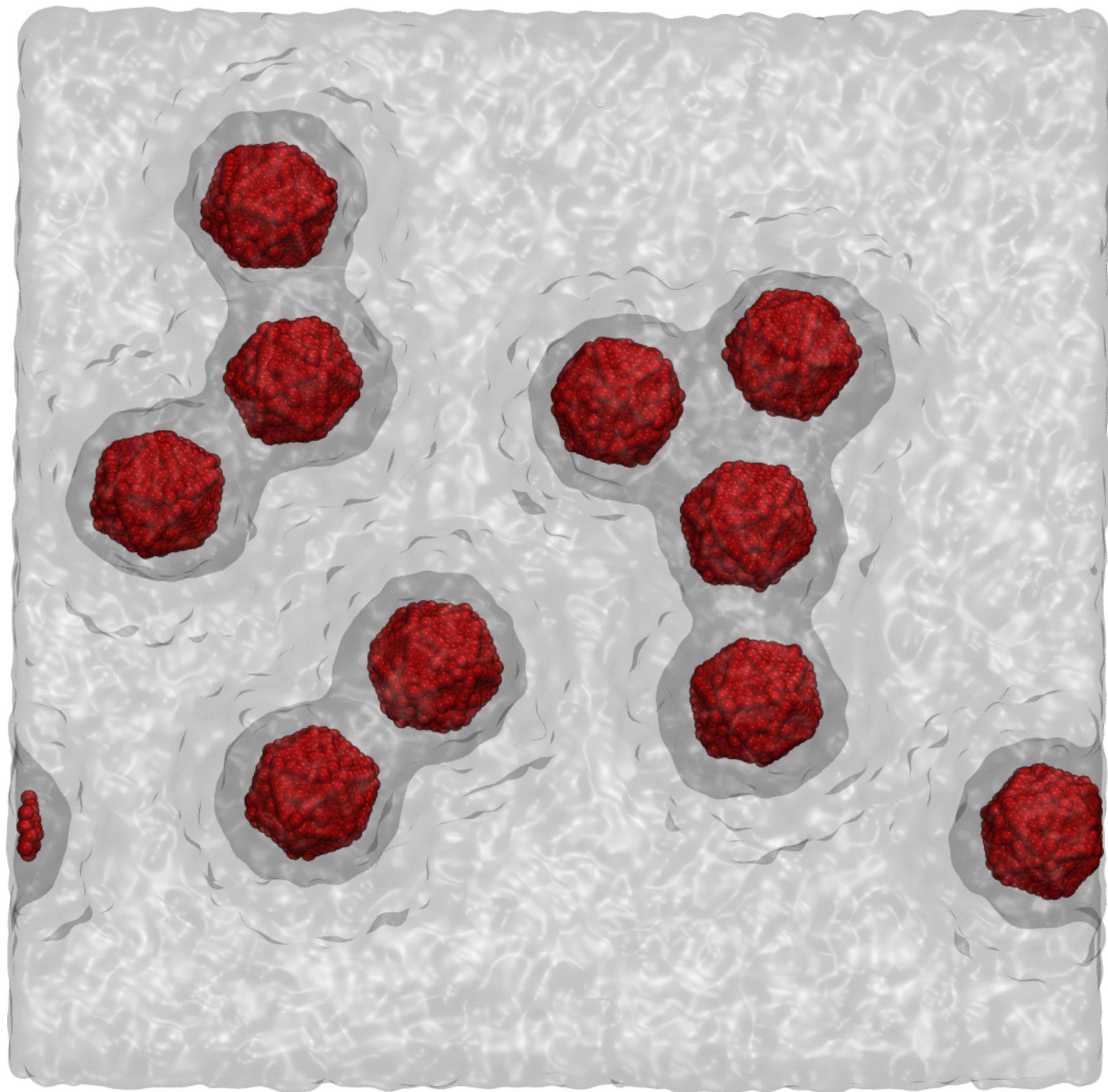
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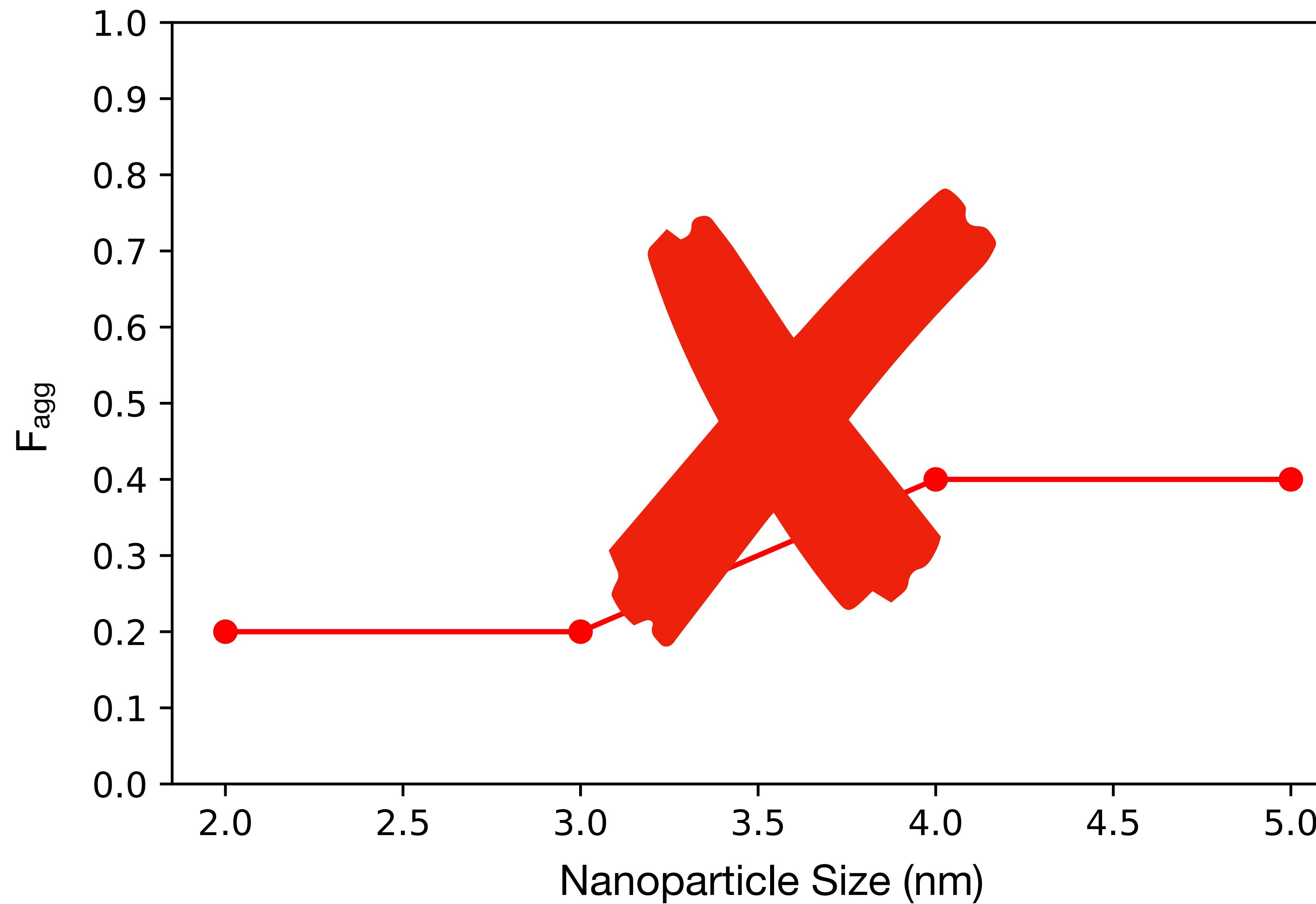
Which Mechanism Causes Aggregation?



Membrane bending is a likely mechanism for causing aggregation



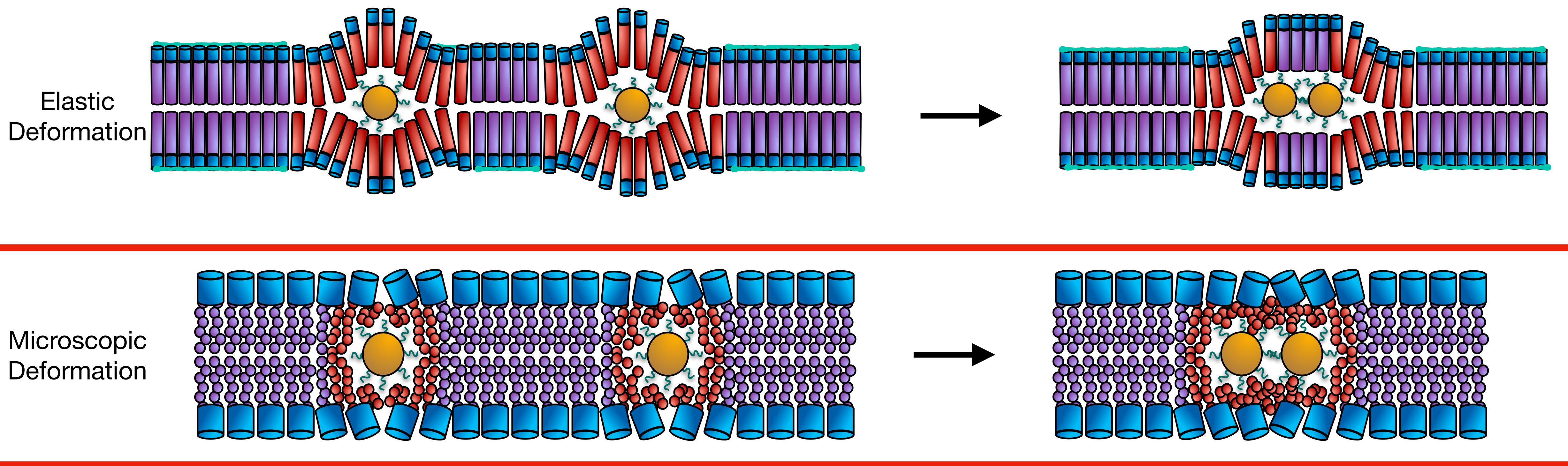
Aggregation increases slightly with increased deformations



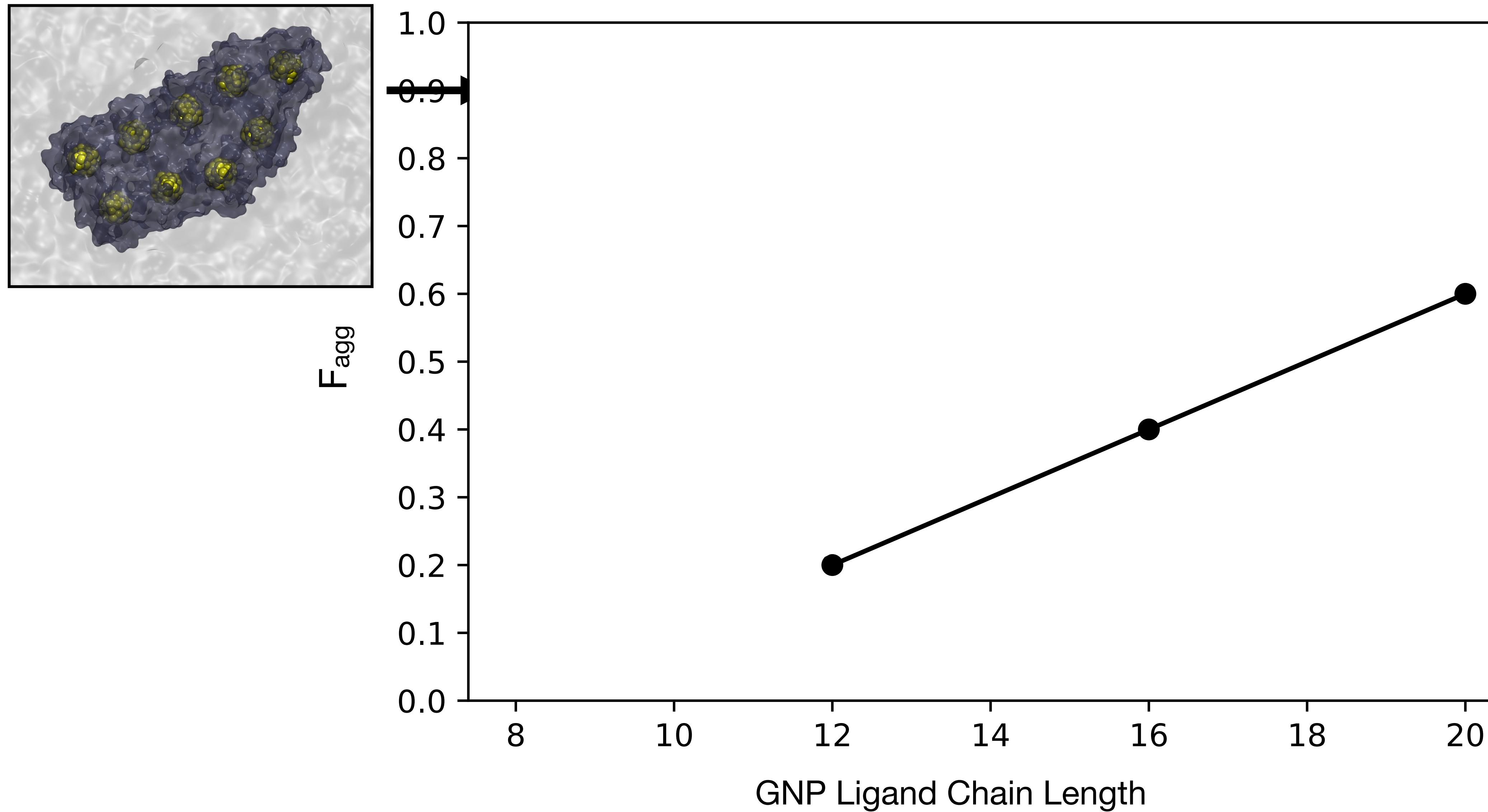
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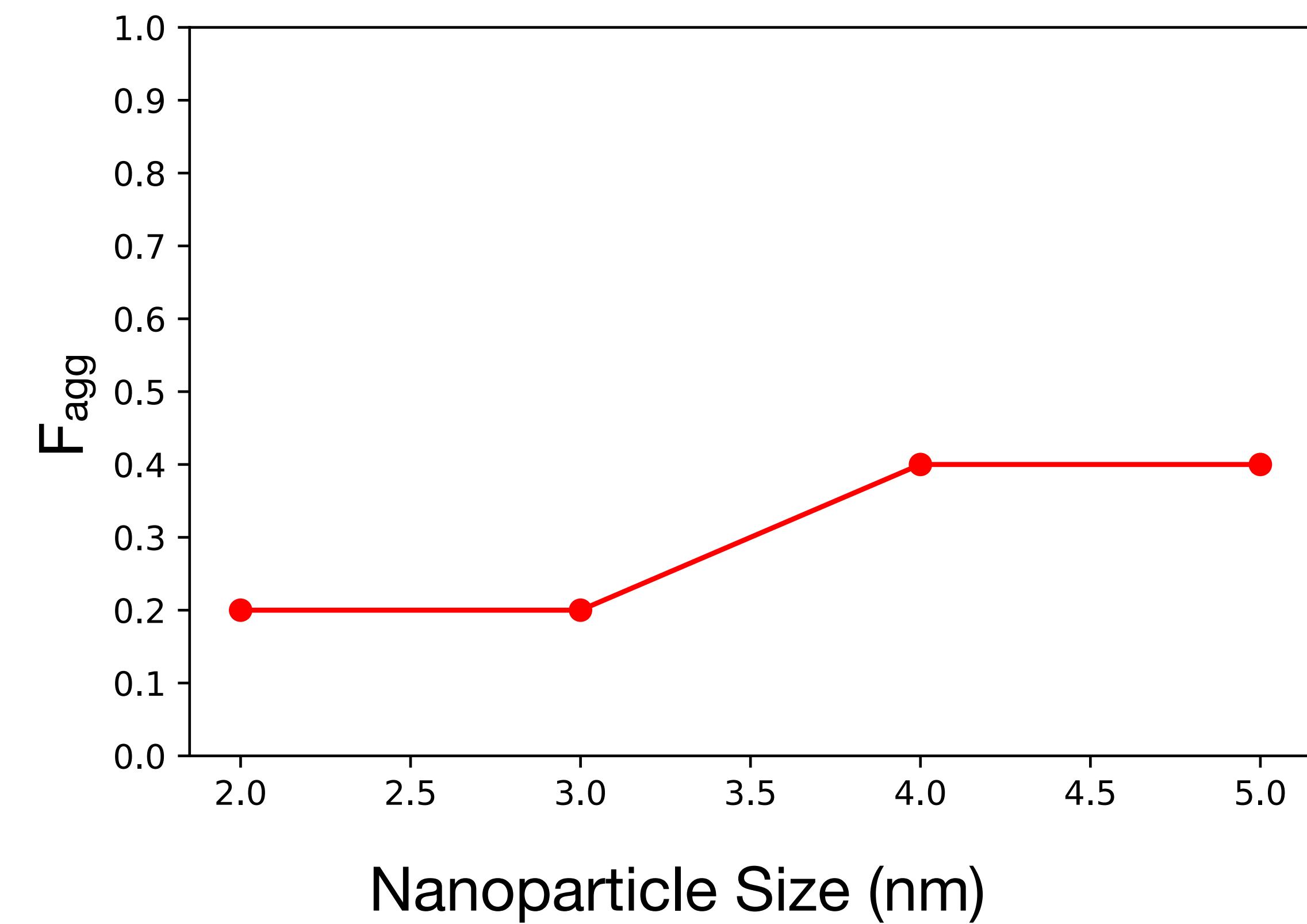


Aggregation Increases with Increasing Ligand Chain Length

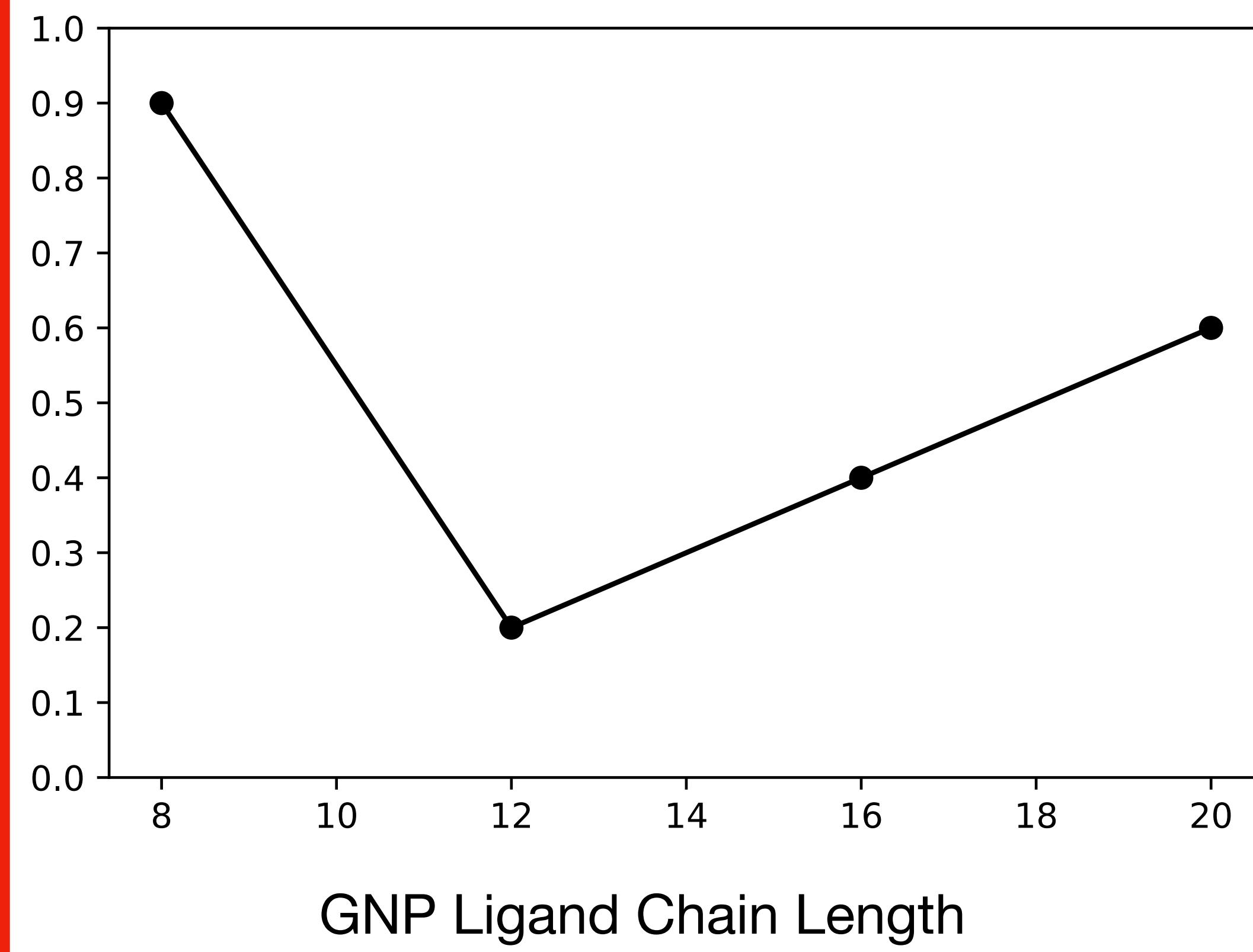


Ligand Chain Order Affects Aggregation More Than Membrane bending

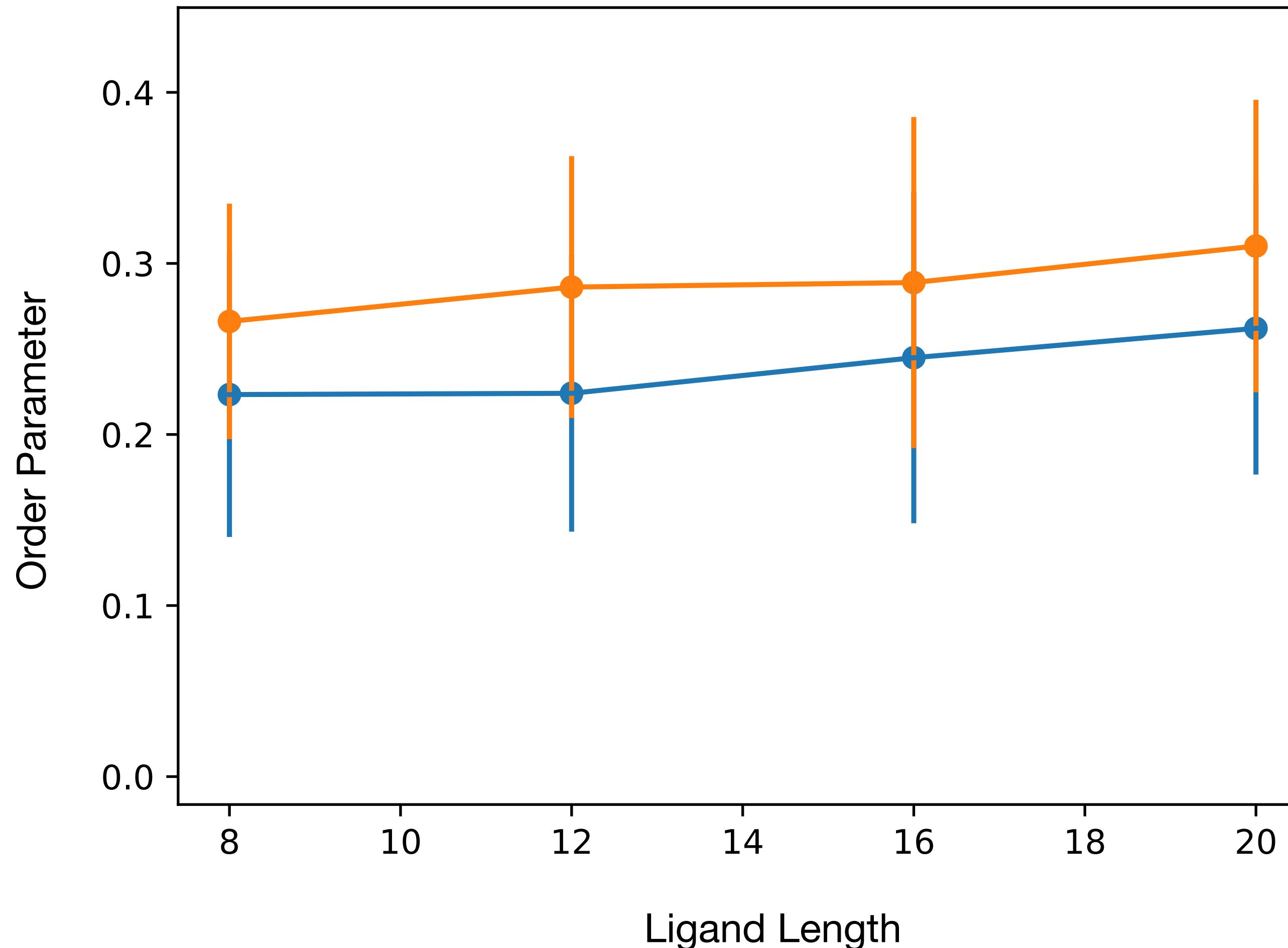
Membrane Bending Has Minimal Effect



Ligand Chains Have Greater Effect



Order Increases with Ligand Length Around Gold Nanoparticles



- Simulations are not long enough
- Ligands confine lipids increasing their order

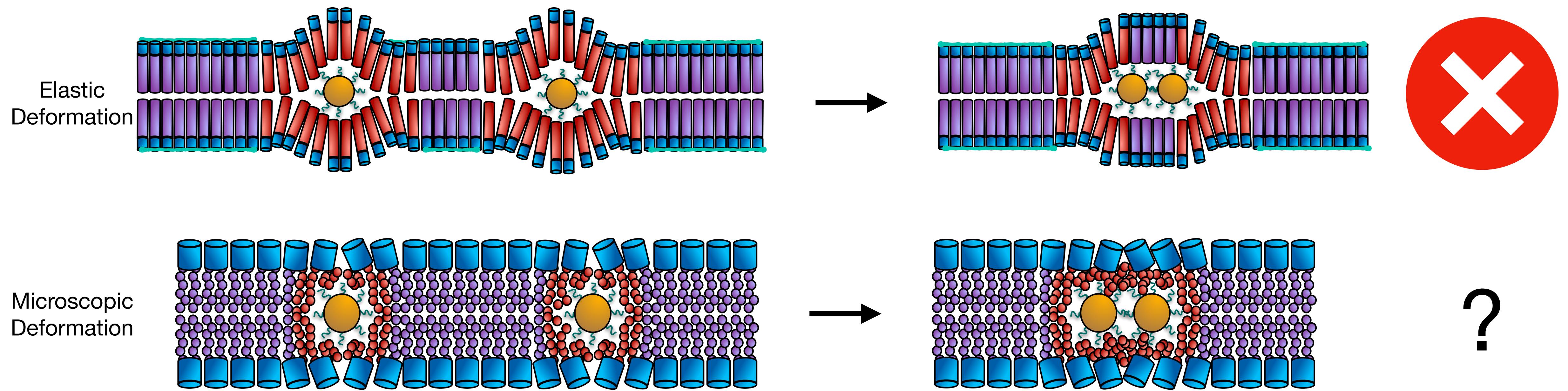
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Summary

- Observed and quantified aggregation in simulation
- Quantified membrane order and membrane bending around nanoparticles
- Ligand chain length affects large aggregates more than nanoparticle size
 - Suggest lipid deformations (rather than membrane deformations) drive formation of large aggregates

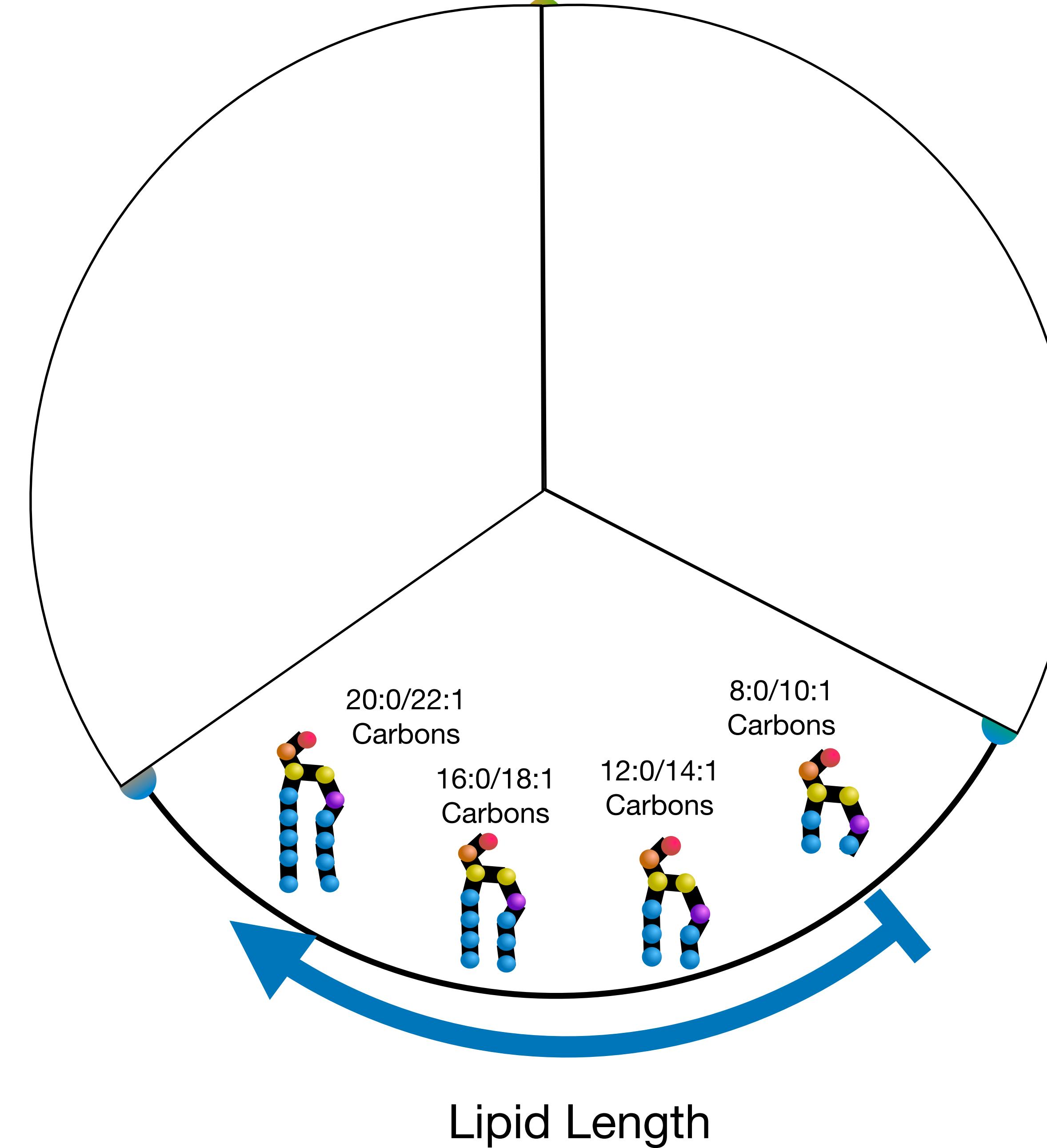
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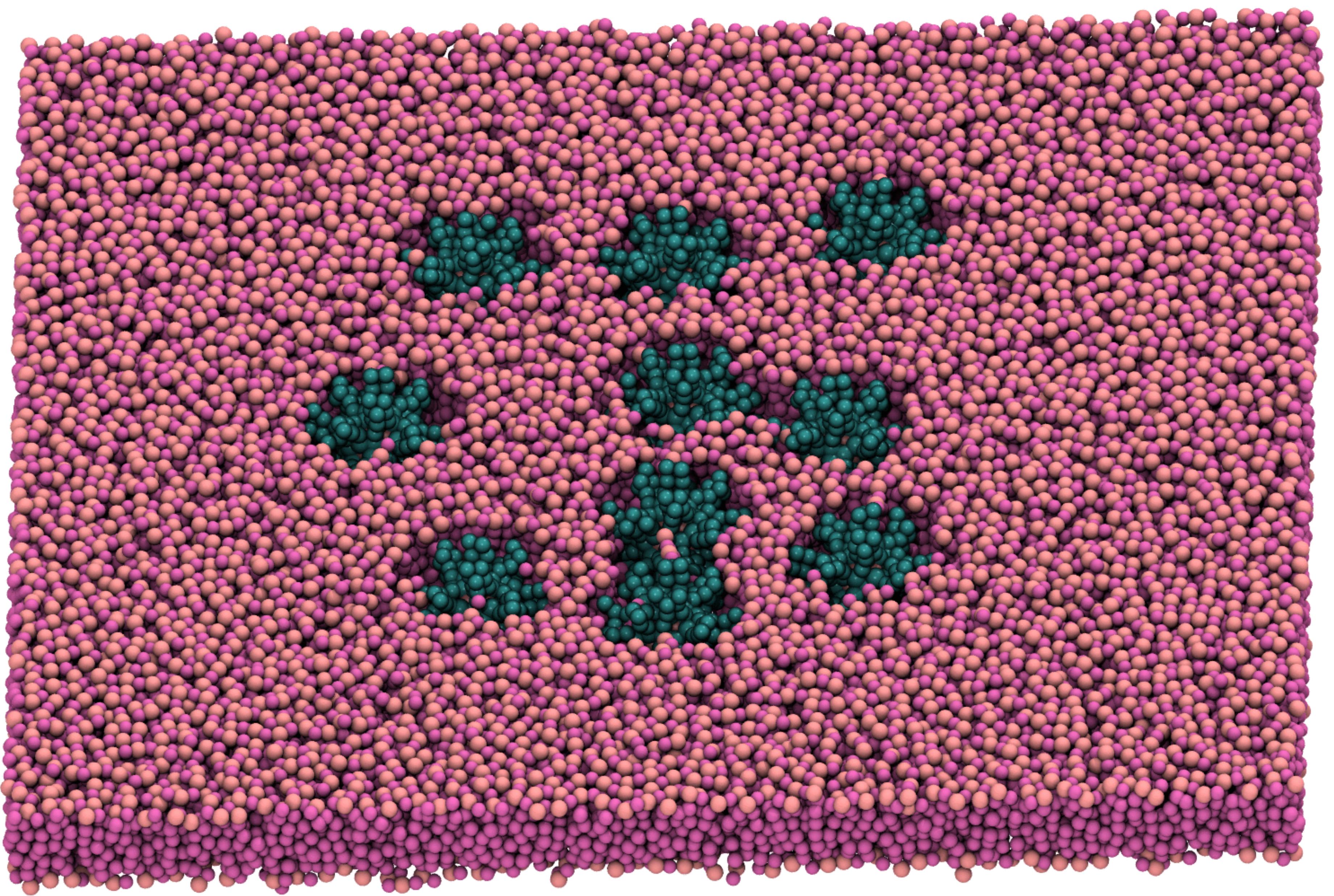


Next Steps

- Analyze replicas
- Extend Simulations to 20 microseconds
- Simulate restricted single nanoparticles at various ligand lengths
- Analyze ligand-ligand interaction between nanoparticles

Lipid chain length was also studied





Acknowledgments



Brannigan Lab Members

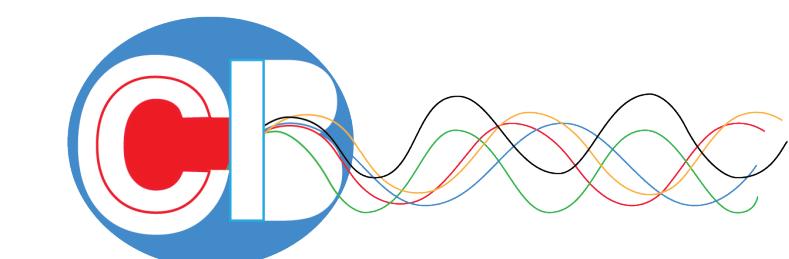
Dr. Grace Brannigan
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Jesse Sandberg
Ezry Santiago-McRae
Connor Pitman
Mariadelia Acuña
Noureen Abdelrahman

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Tom Skipper

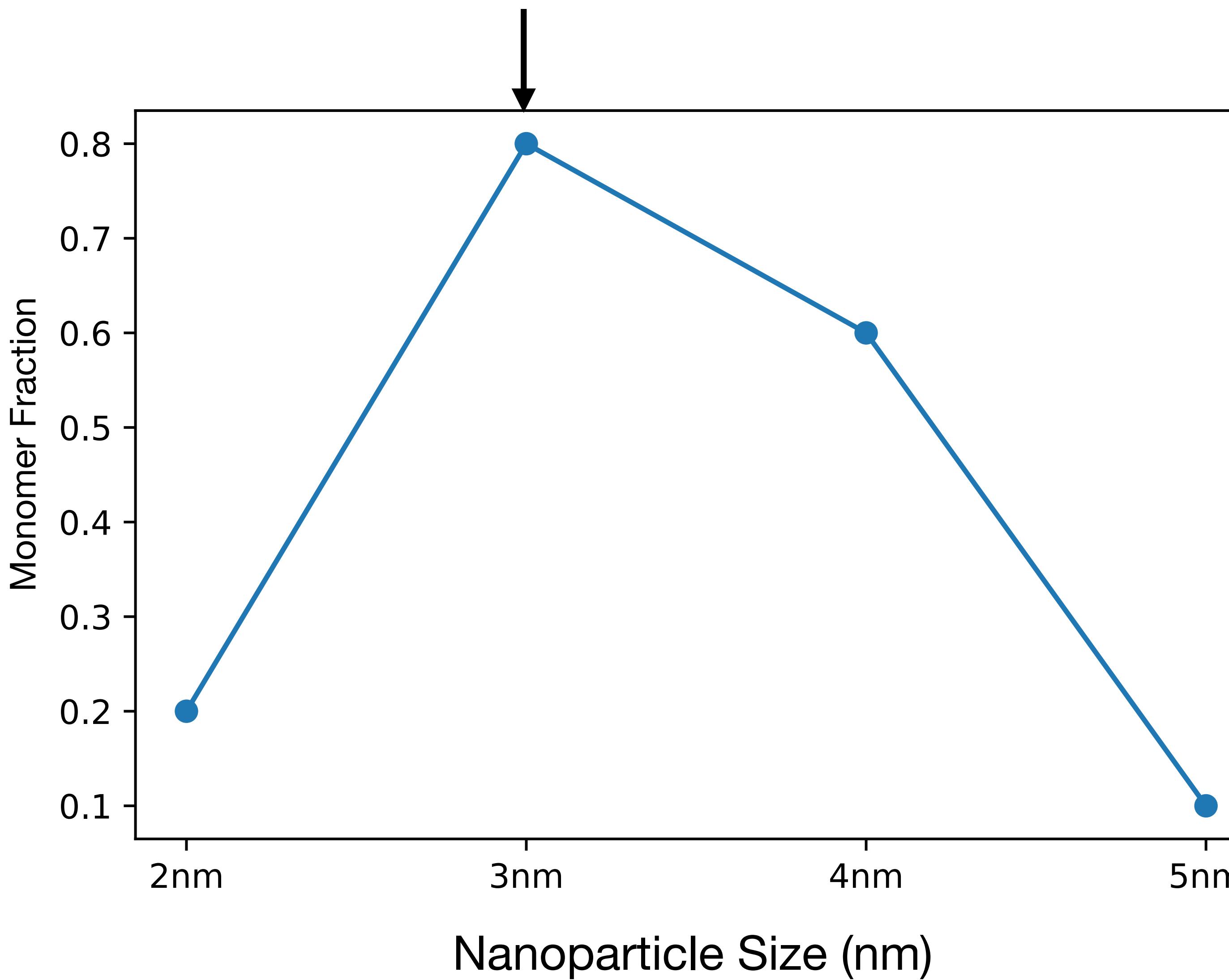
Griepenburg Lab Members

Dr. Julie Griepenburg
Regina Salzer



Questions?

Monomer Fraction Does not Decrease with Nanoparticle Size



Lipid Order Is Reduced at The Interface of an Aggregate

