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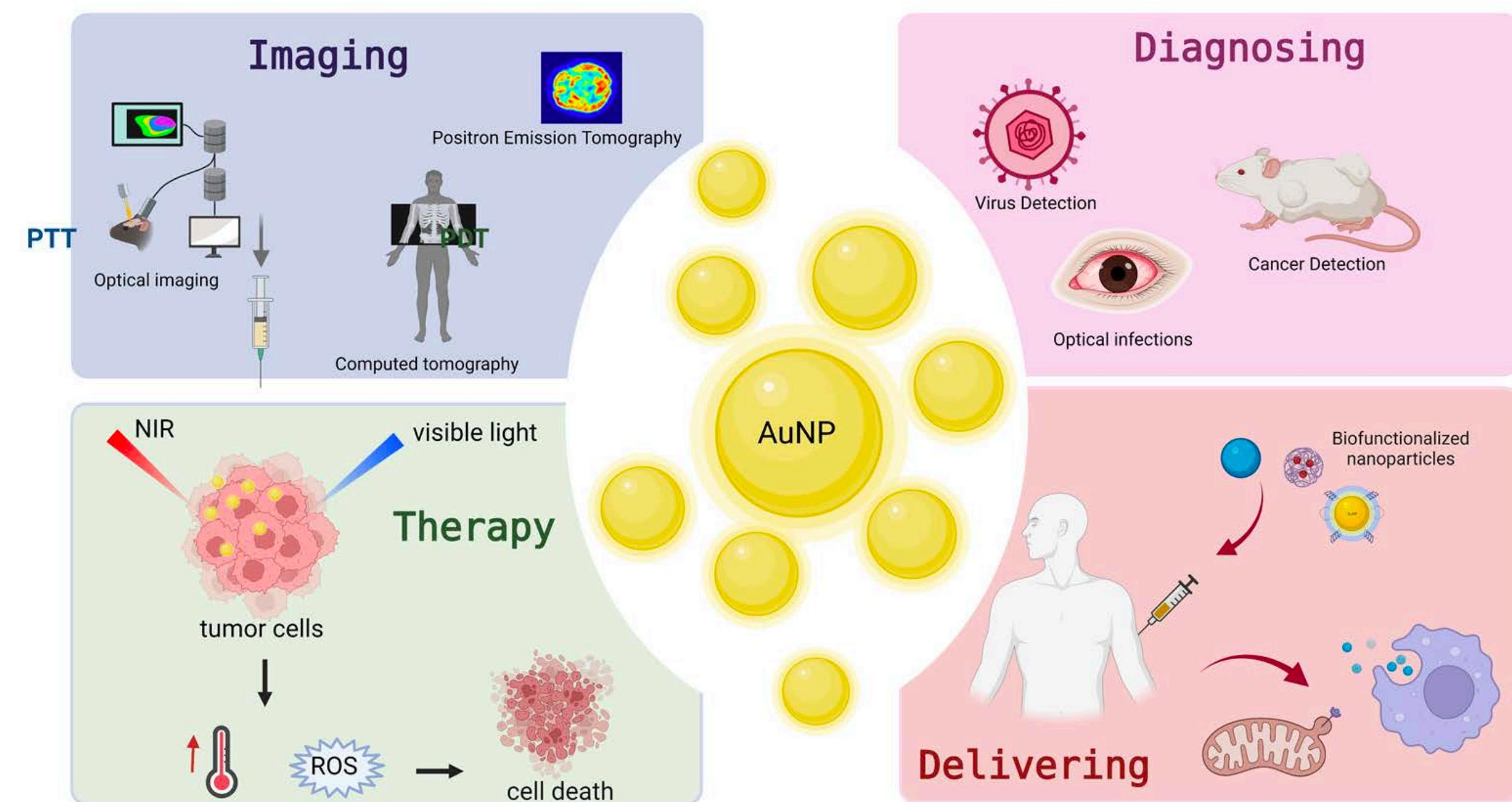
Deforming Membranes for Fun & Profit: untangling the mechanism of gold nanoparticle aggregation in lipid bilayers

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Integrative Biology
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Rutgers University - Camden

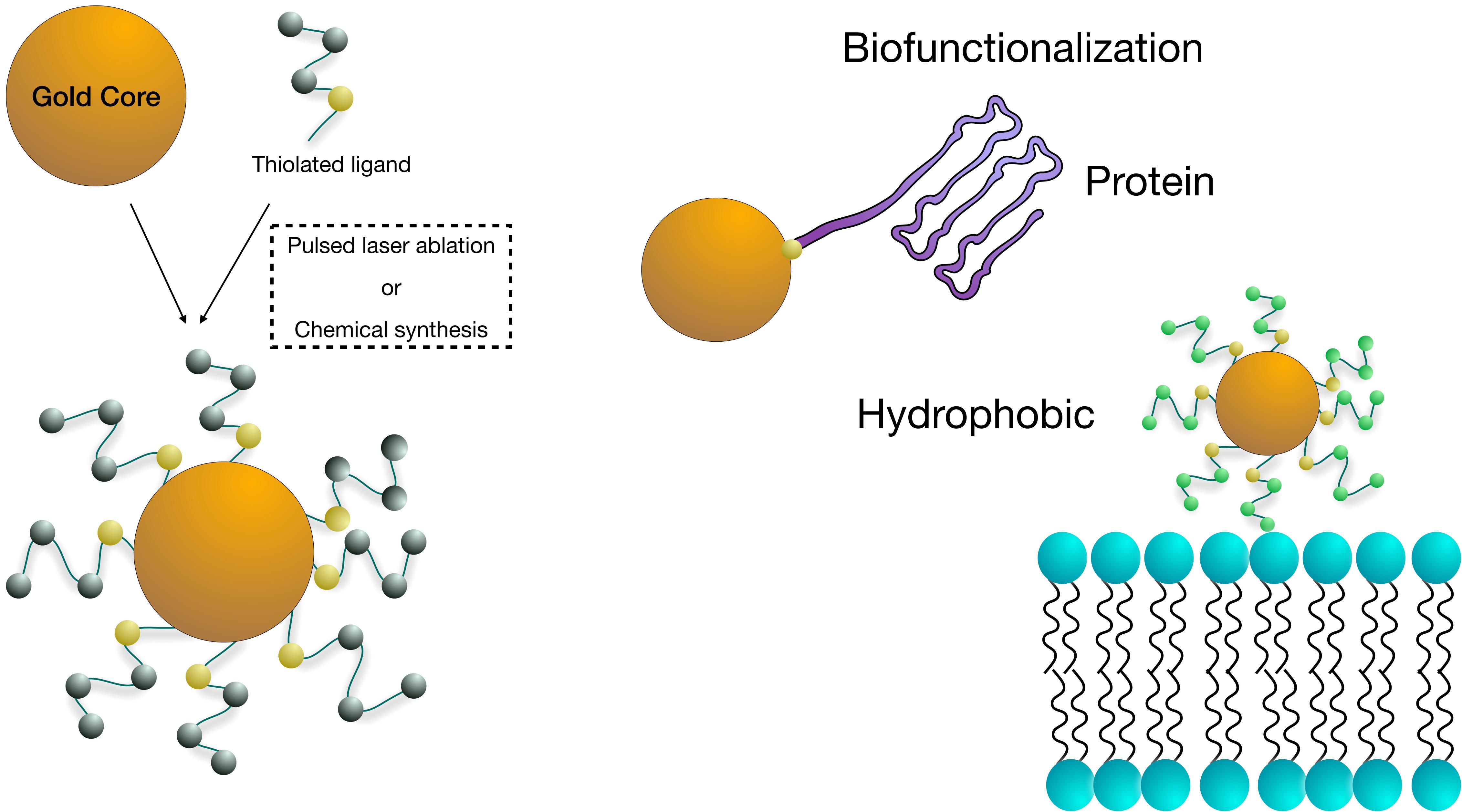


Applications of Gold Nanoparticles Often Require Interactions with Biological Systems, Including Lipid Membranes

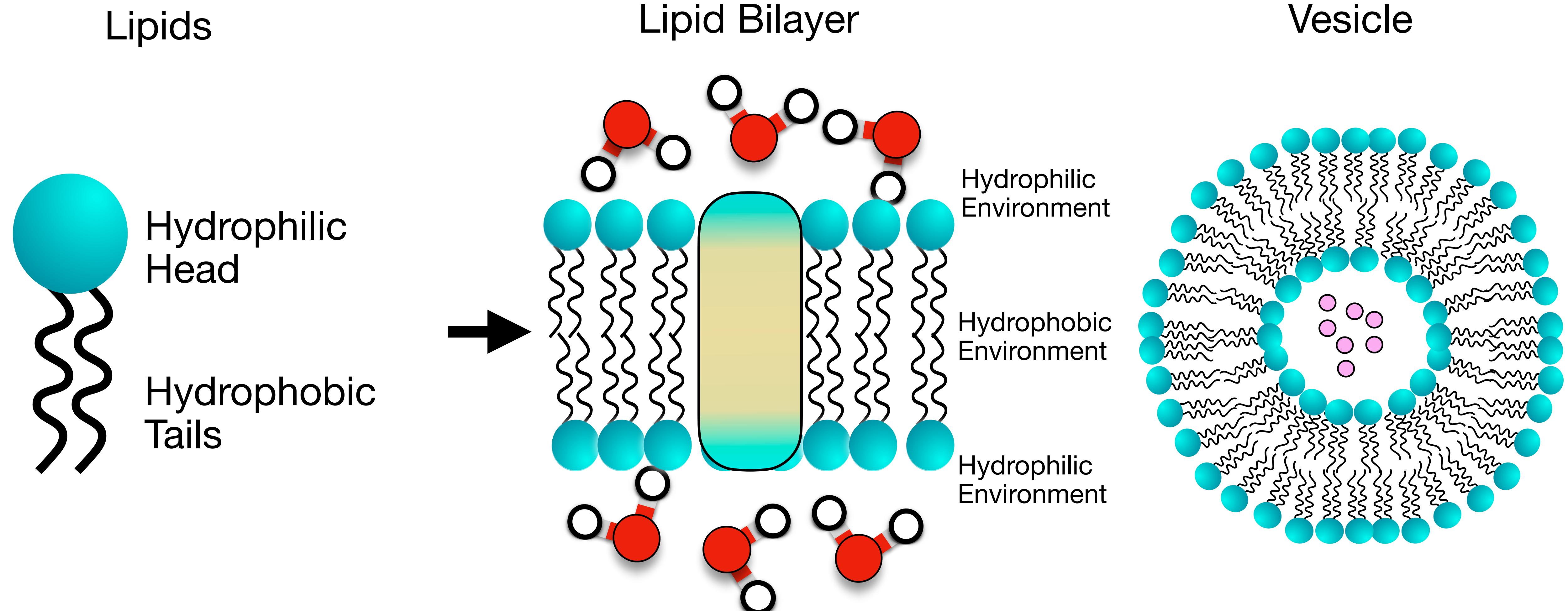
- Photodynamic Imaging
- Diagnostic Tool
- Targeted Drug Delivery Systems



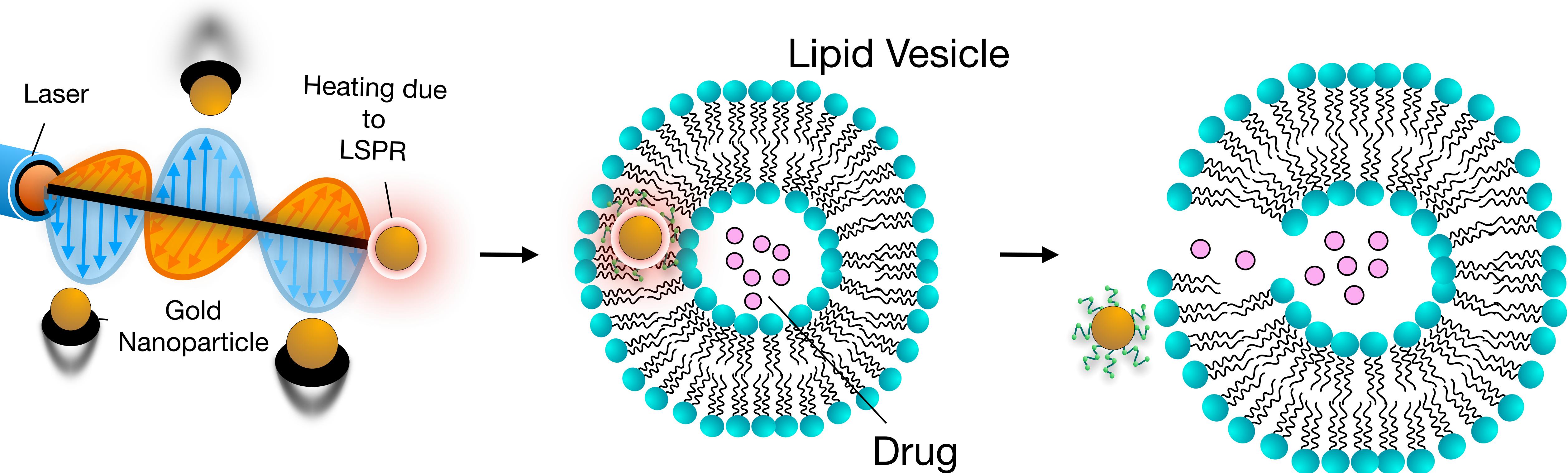
Functionalized Gold, a Non-Biological Material For Biological Applications



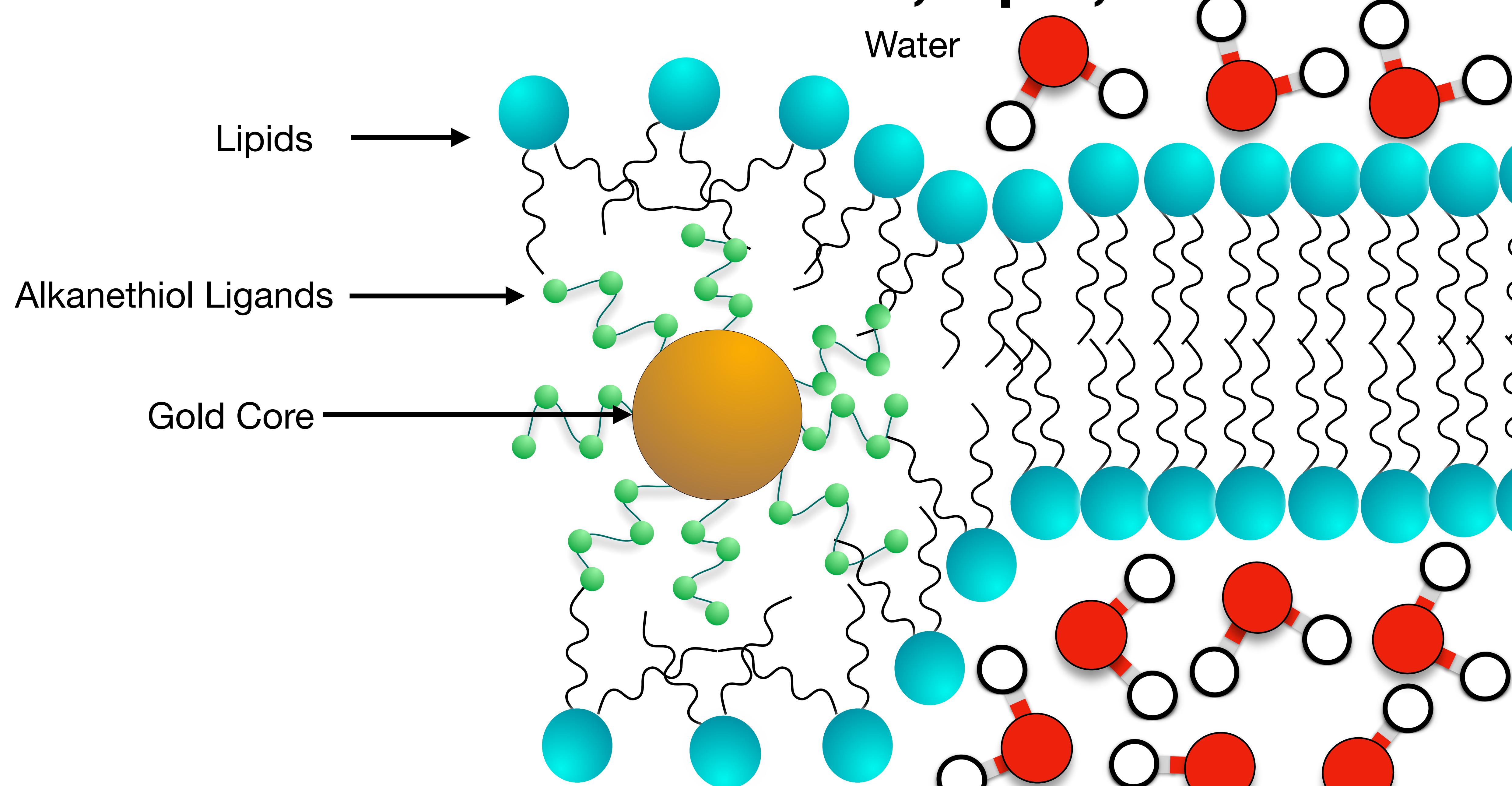
The Key Features of Lipids and Membranes



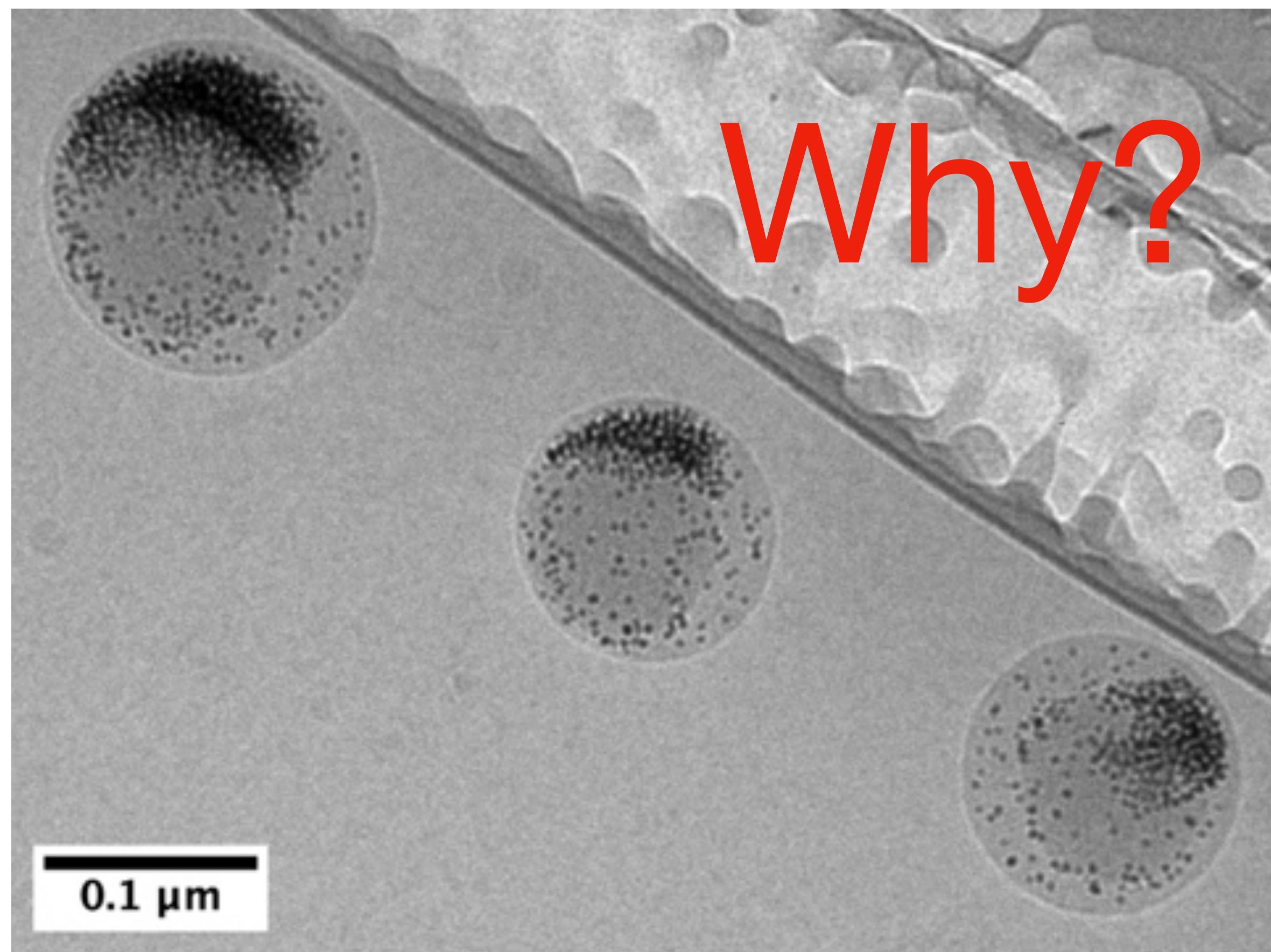
Lipid-Nanoparticles Hybrid Vesicles, A Tool For Non-Invasive Drug Delivery



The Interfaces Between Gold, Lipid, and Water

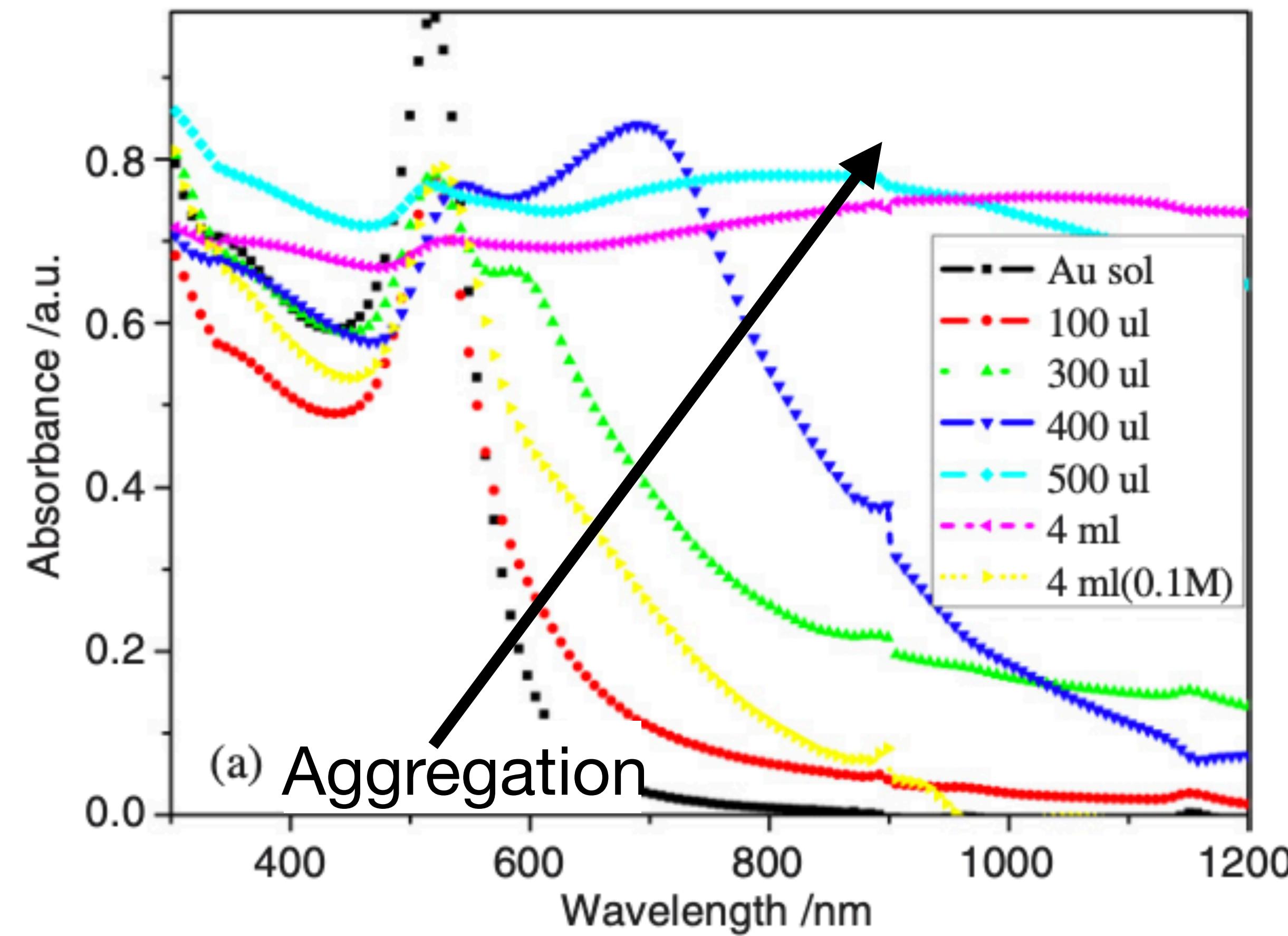


Aggregation Changes the Optical Properties of Gold



Why?

Increasing GNP aggregation changes optical response



Upcoming Questions

What mechanism drives the aggregation of ligand coated gold nanoparticles in lipid membranes?

What are some hypothetical mechanisms?

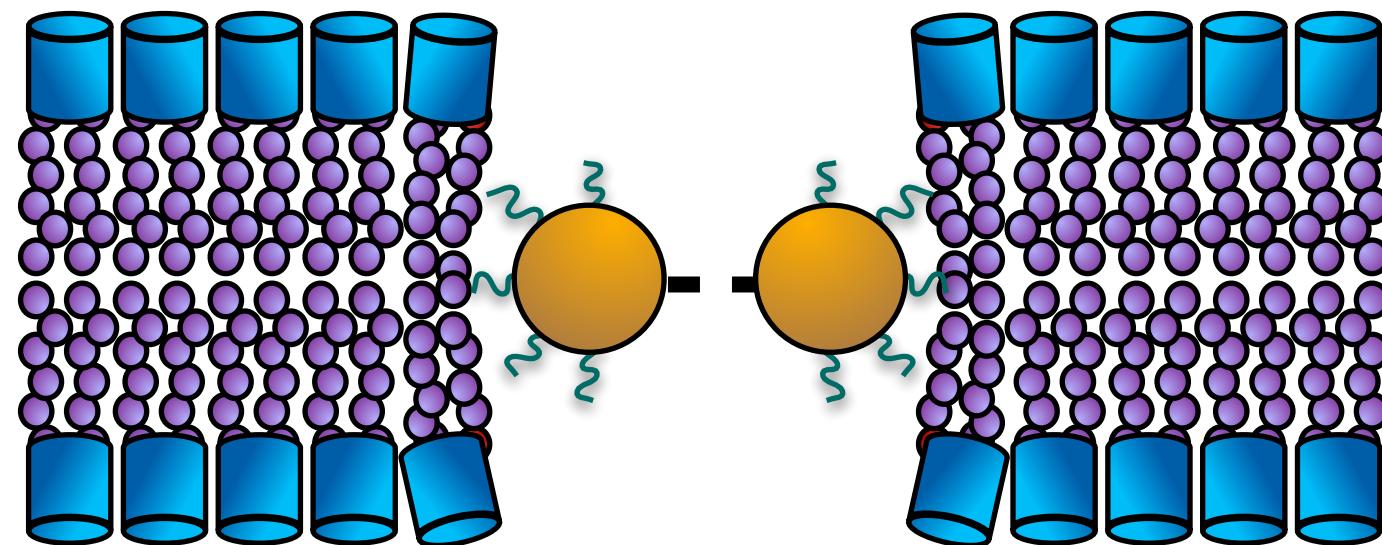
How can we test them computationally?

How can we model gold in a way that is consistent with biomolecular forcefields?

Hypothetical Mechanisms

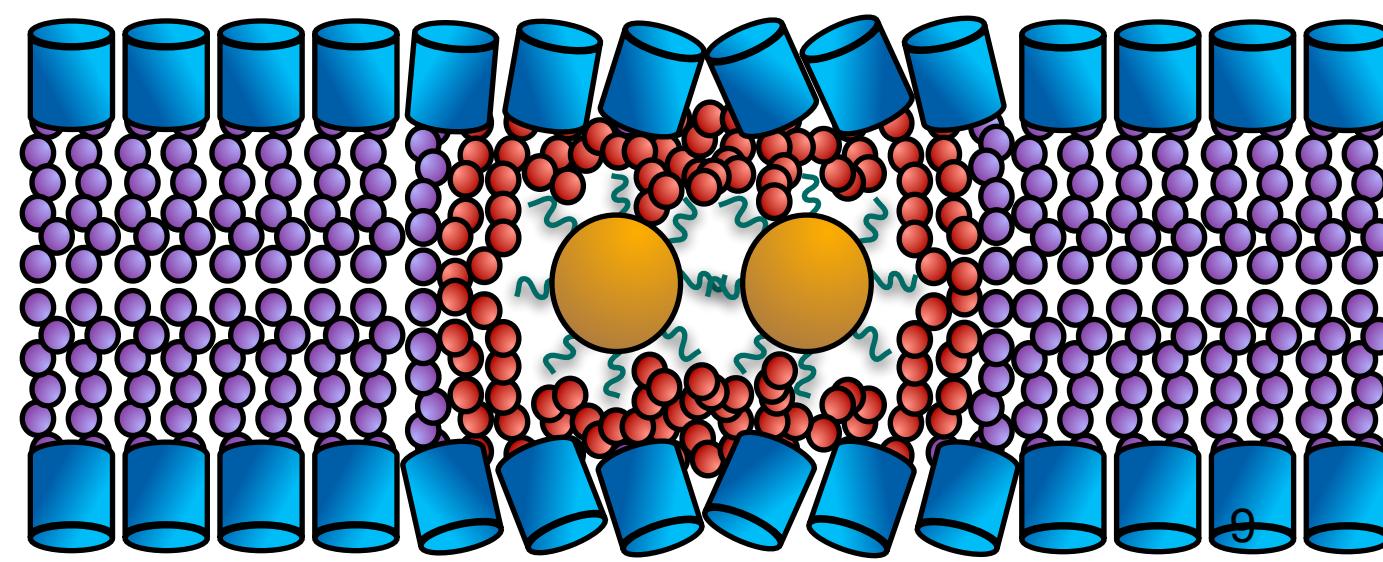
Should be highly sensitive to...

Direct



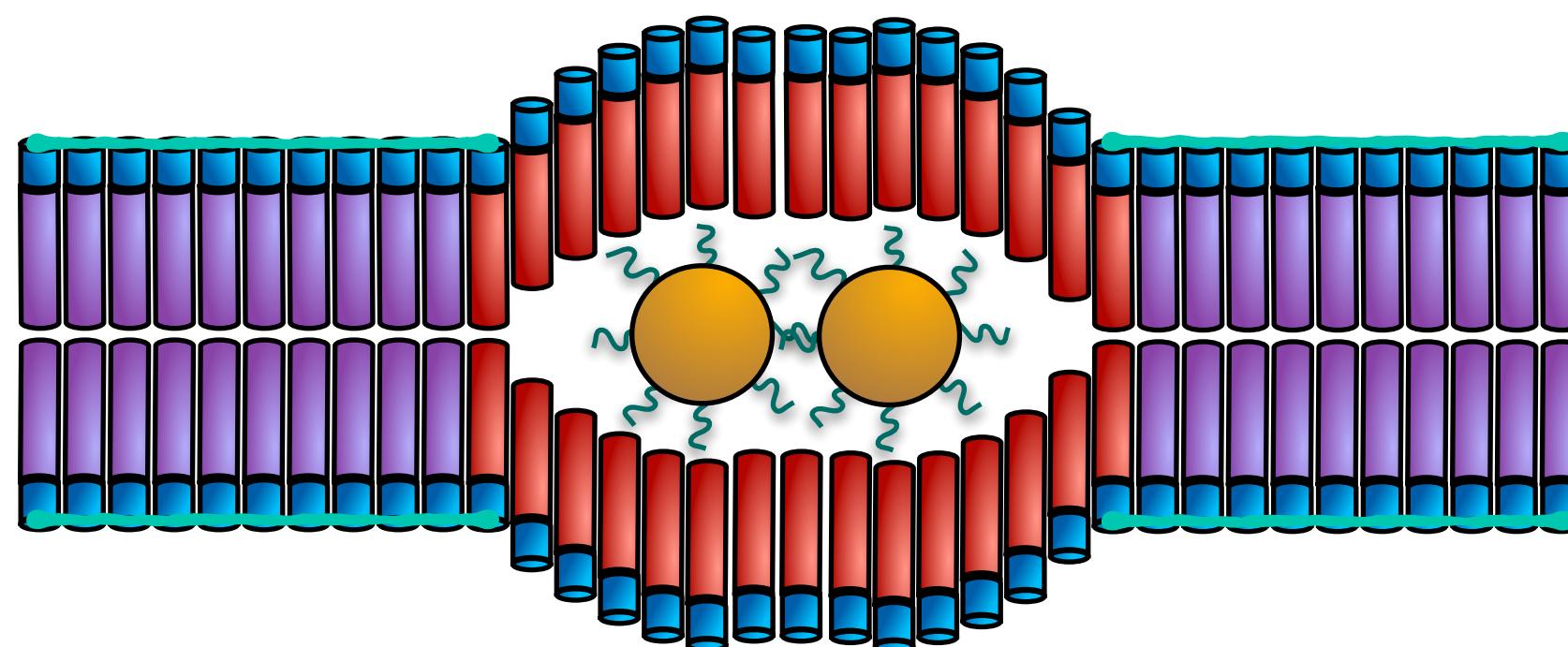
Chemical details
of the core

Packing-mediated



Nanoparticle size
and ligand length

Bending-mediated

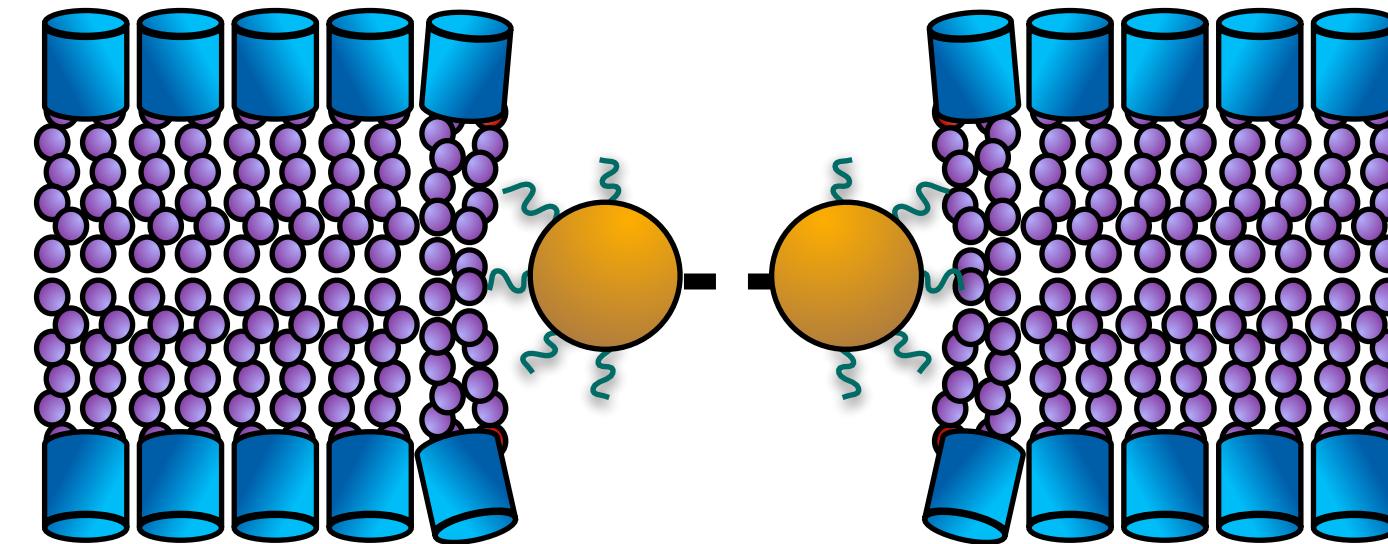


Nanoparticle
size

Testing for a Direct Mechanism

Should be highly sensitive to...

Direct

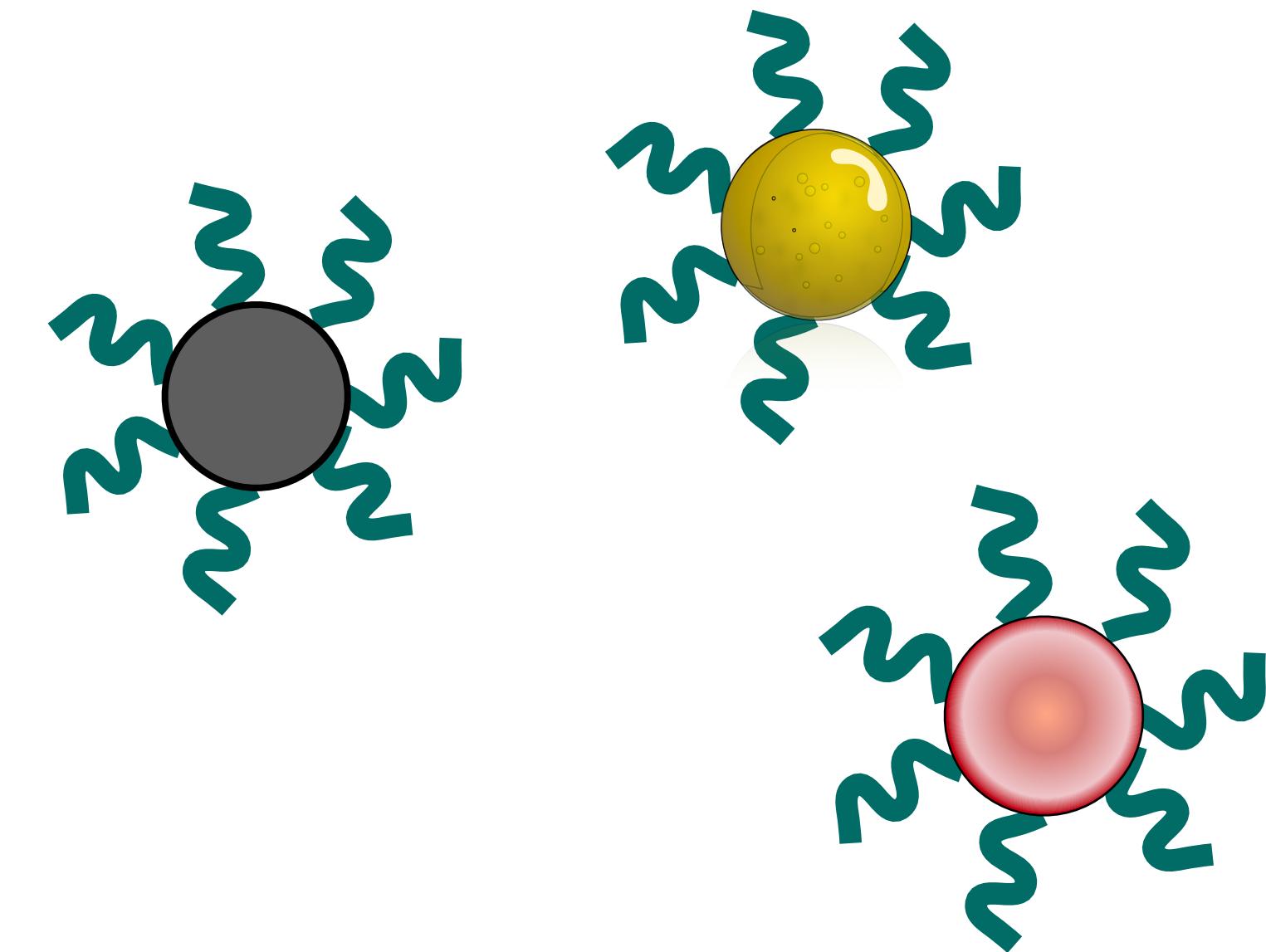


Chemical details
of the core

Approach:

Vary Core Model

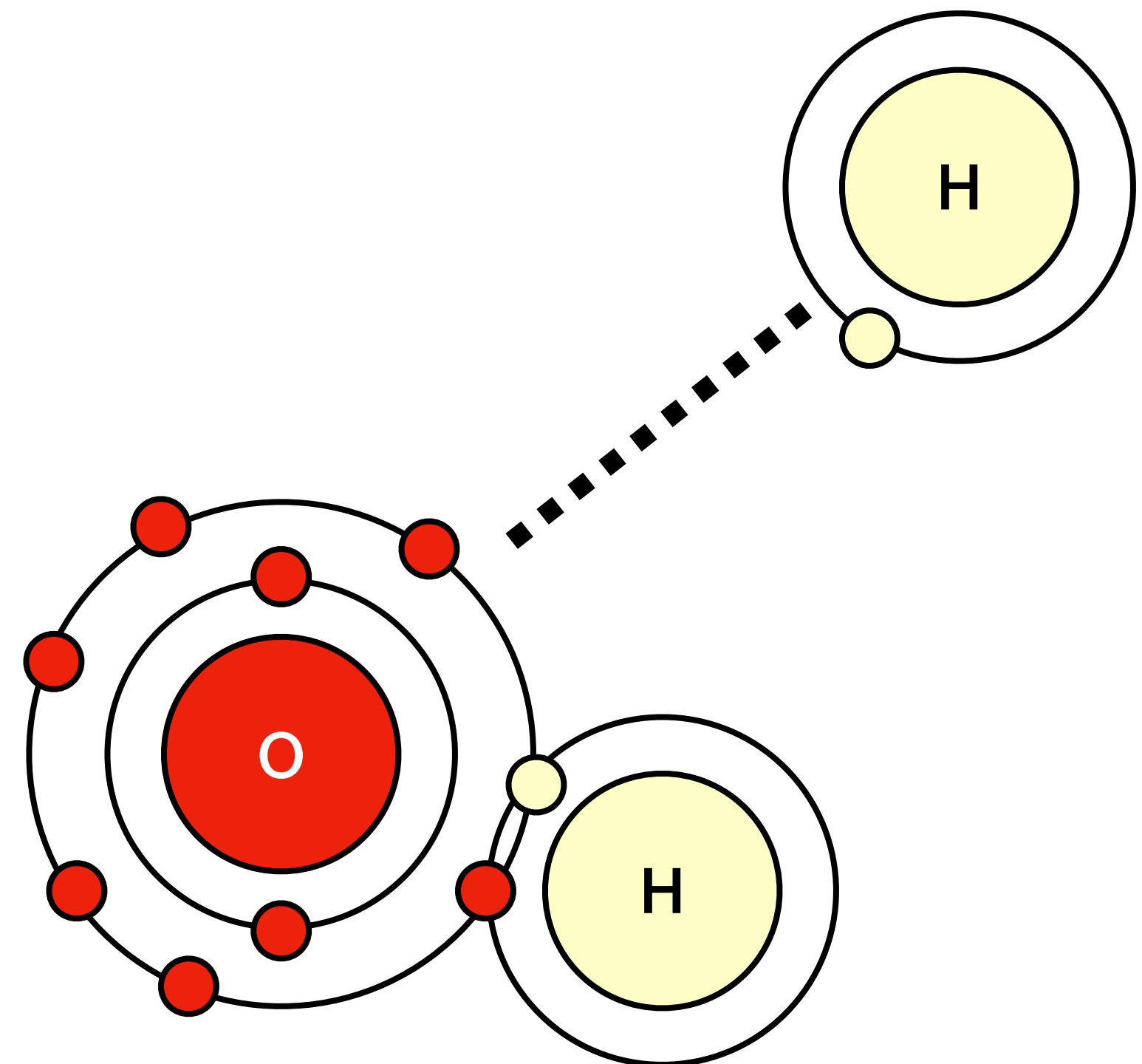
Detect effect on
aggregation?



Aside on MD Simulation



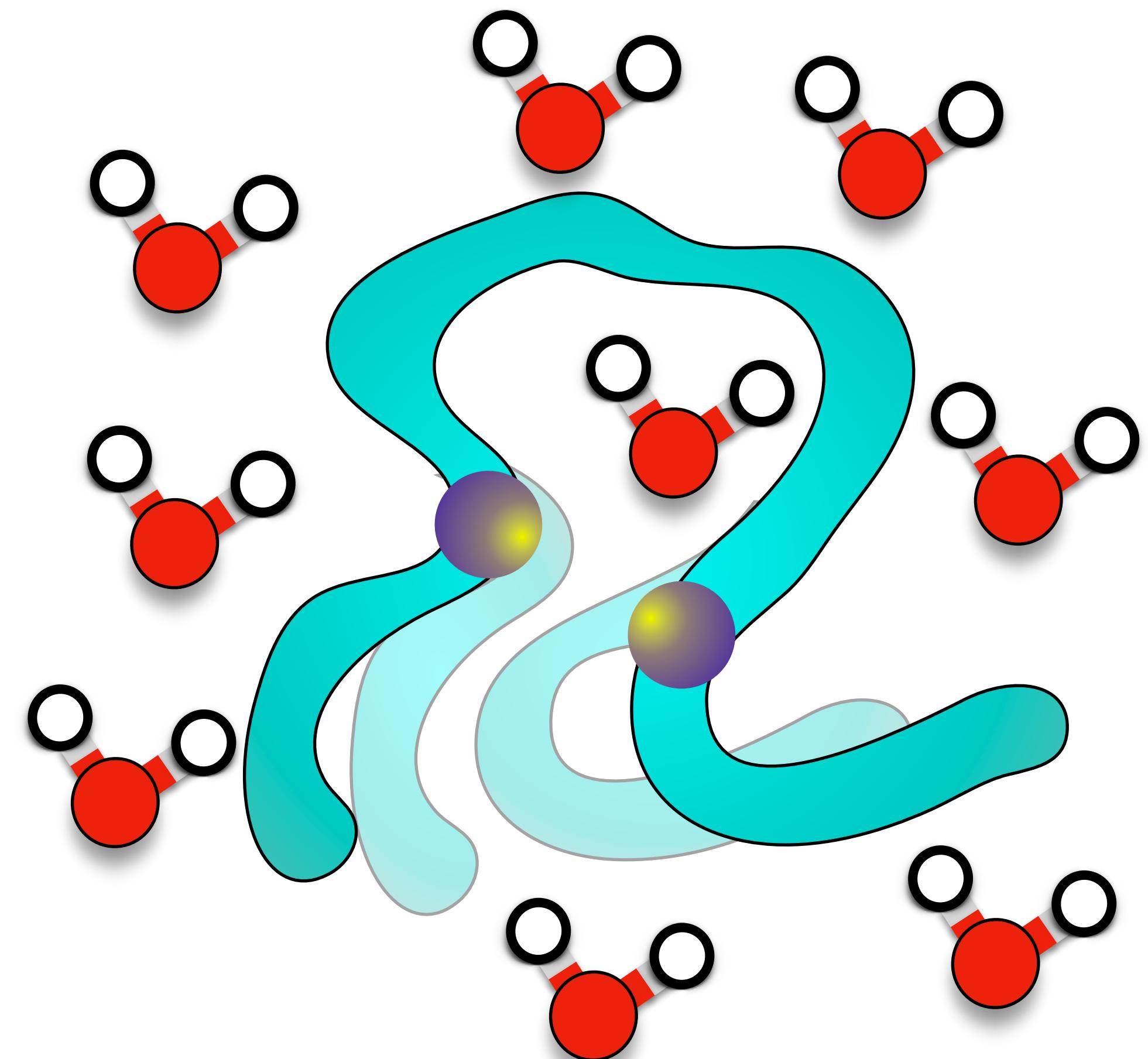
Interaction Scales



Covalent bonding

Electronic Structure

Quantum Mechanics

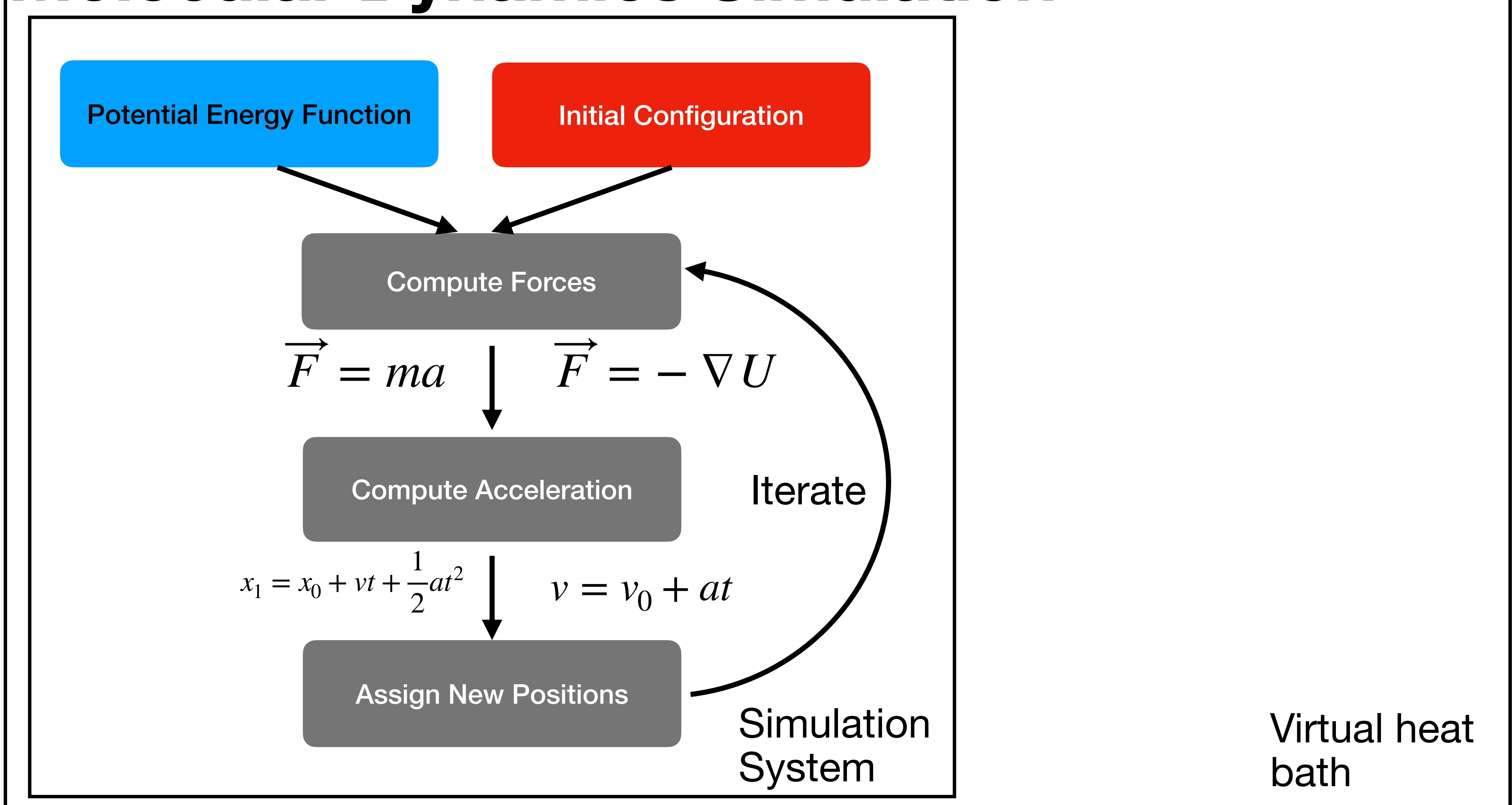


non-covalent interactions

Macromolecules

Classical & Statistical mechanics

Molecular Dynamics Simulation

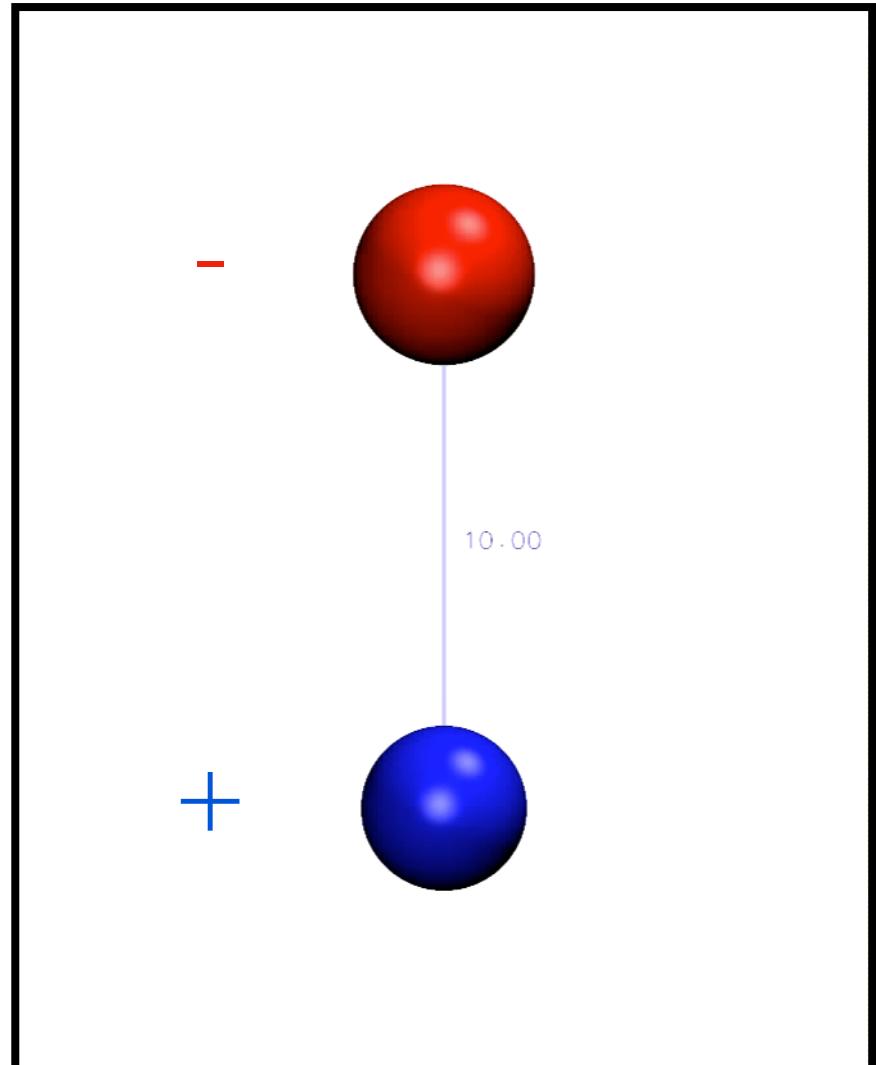


Classical MD : typical interactions

Lennard Jones
& Electrostatic

$$U_{LJ_{ij}} = \epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$

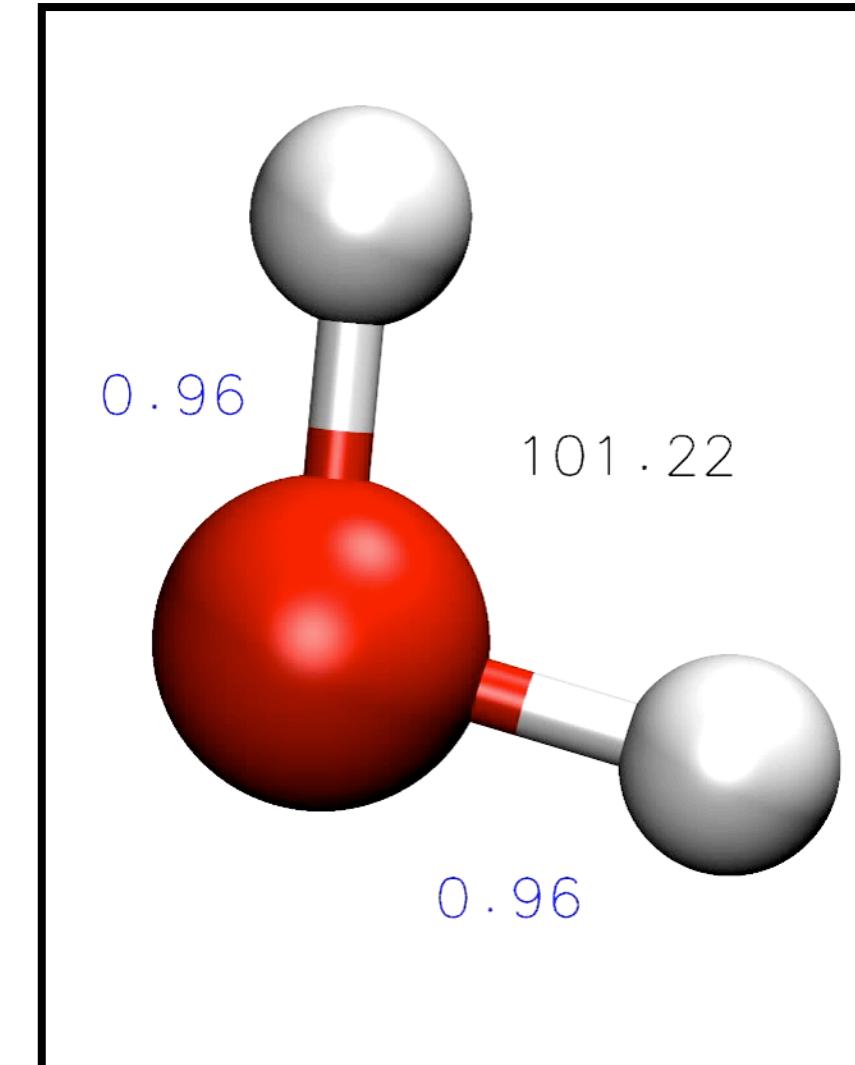
$$U_{elec} = \frac{q_i q_j}{4\pi\epsilon r_{ij}}$$



Bonds & Angles

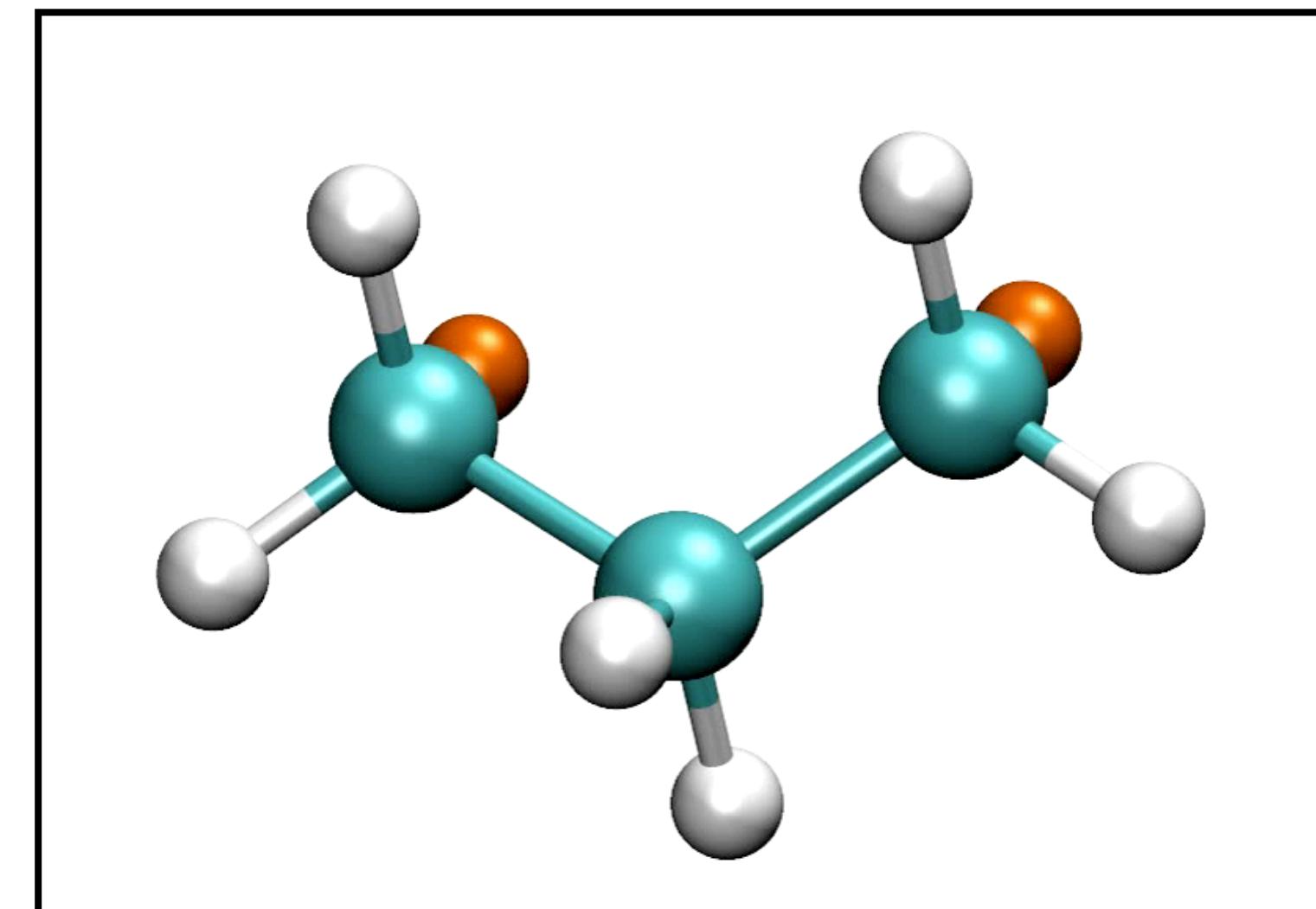
$$U_{bond_{ij}} = \frac{k_b(r_{ij} - r_0)^2}{2}$$

$$U_{angle_{ijk}} = \frac{k_\theta(\theta_{ijk} - \theta_0)^2}{2}$$

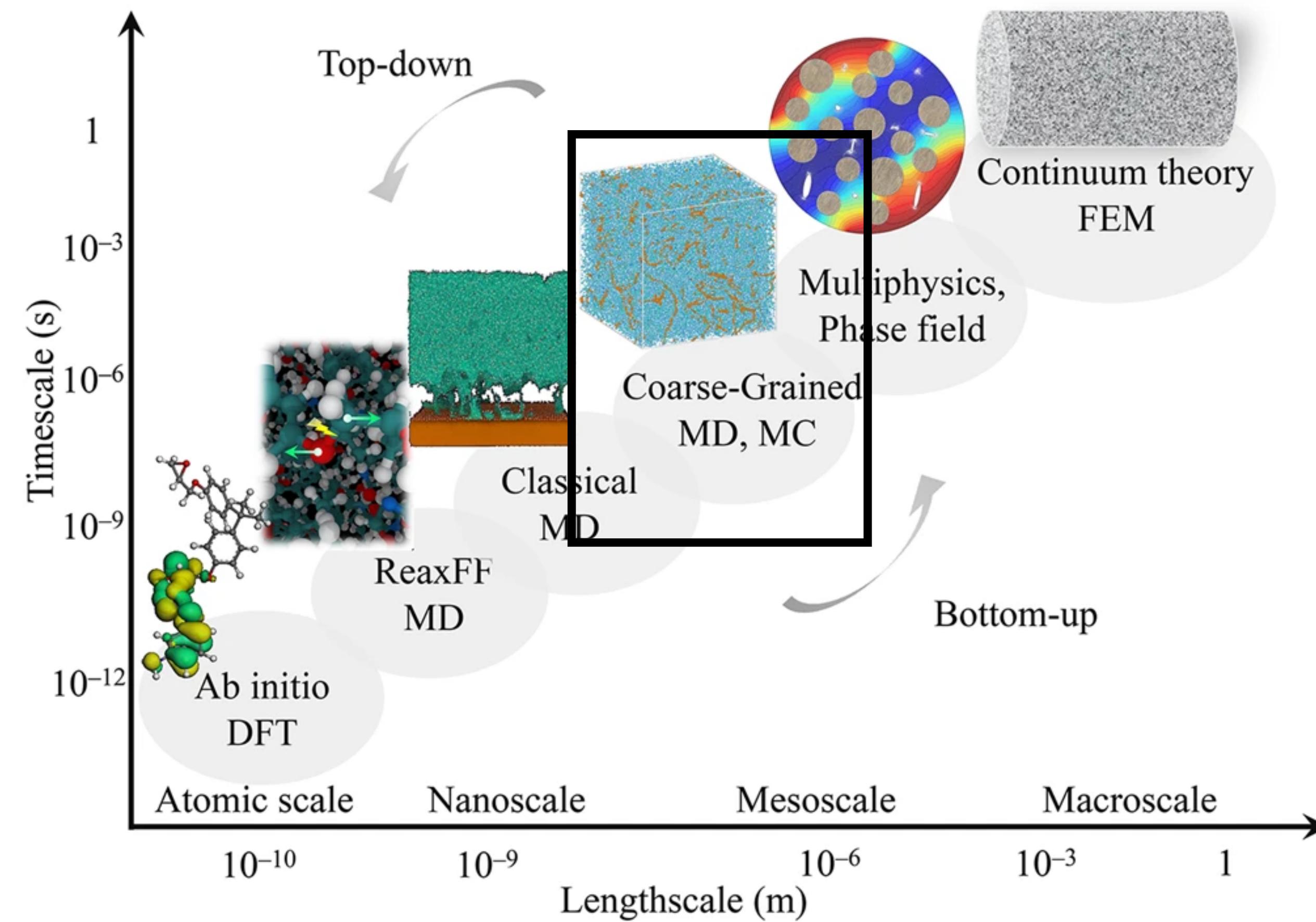


Dihedral angles/
torsions

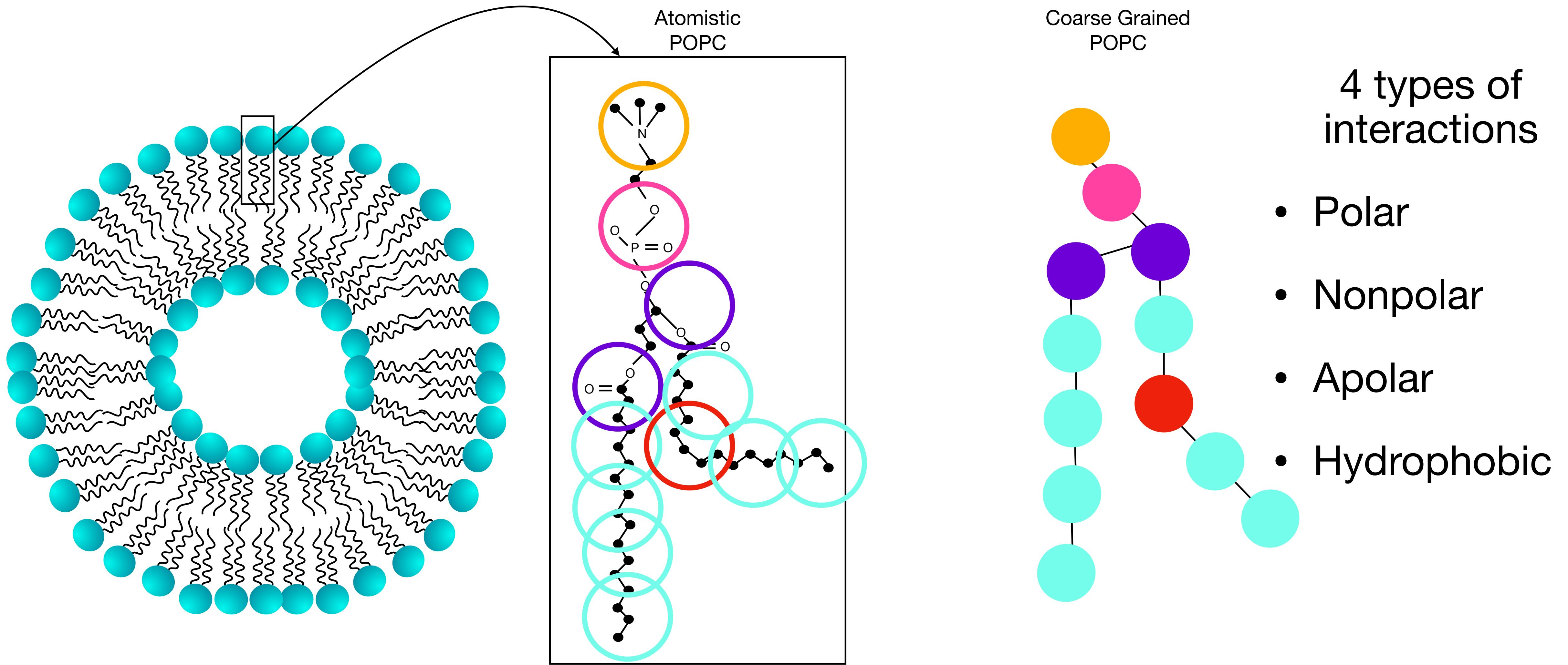
$$U_{\phi_{ijkl}} = k_\phi [1 + \cos(n\phi_{ijkl} - \delta)]$$



The Length and Time Scales we Can Simulate Over Depend on Our Compute Resource

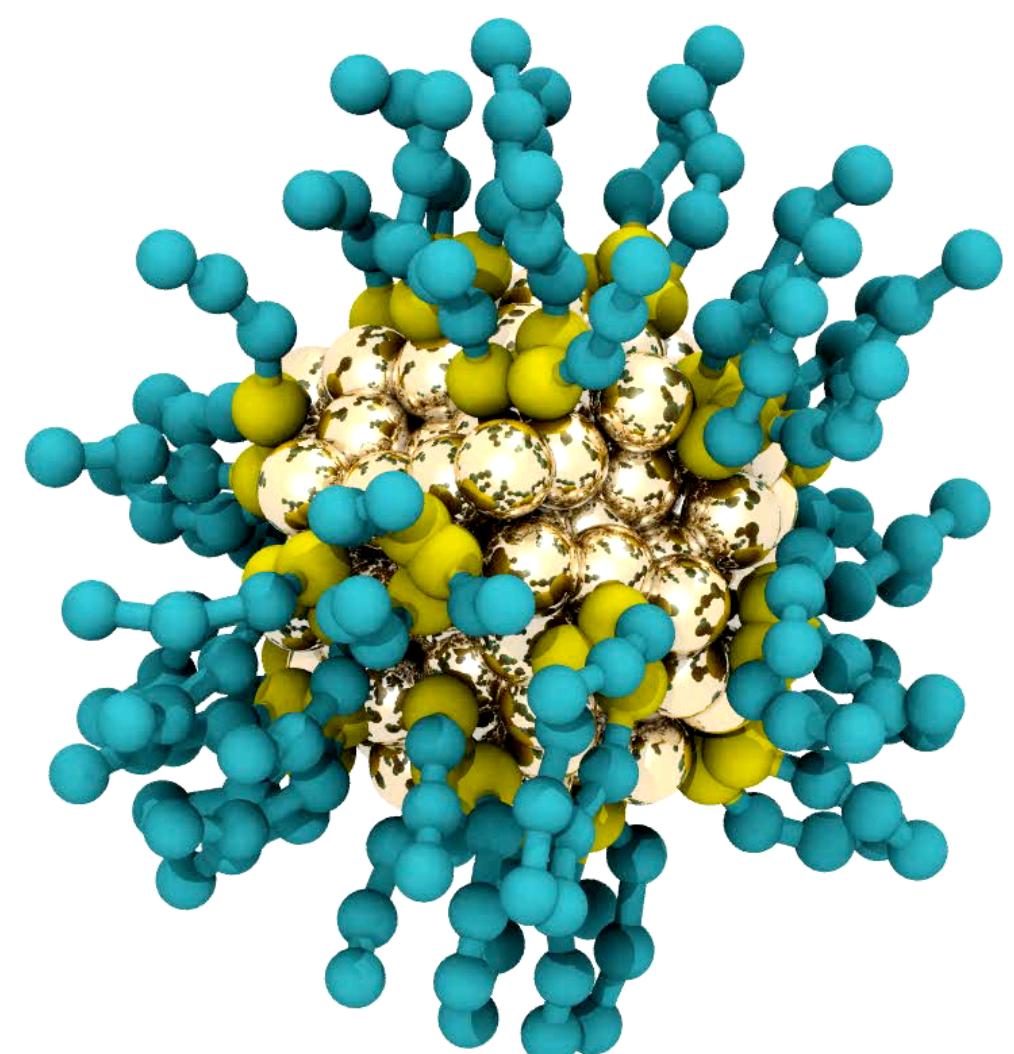


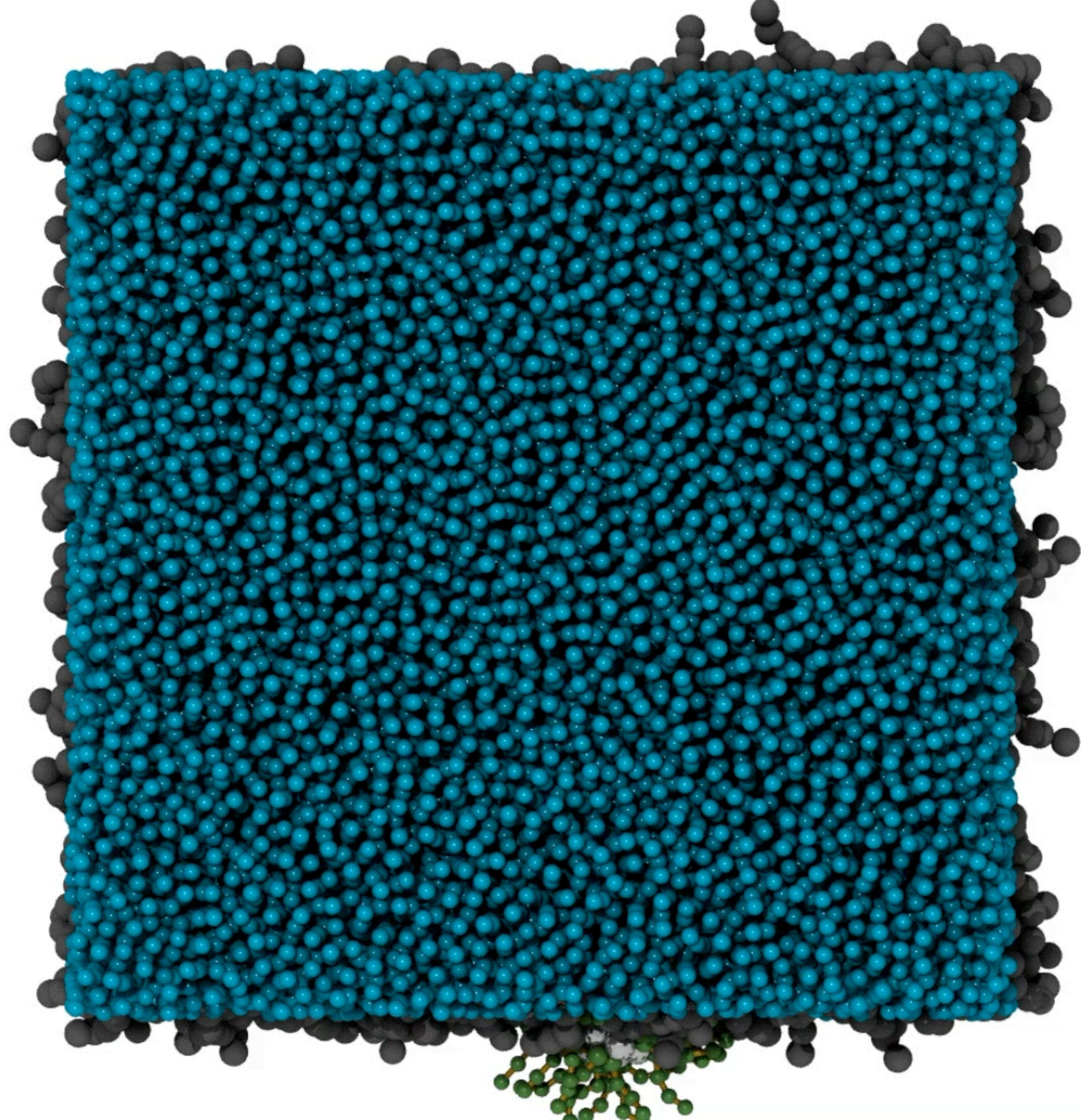
Coarse-Grained Molecular Dynamics: Same interactions types, lower resolution models, faster simulations



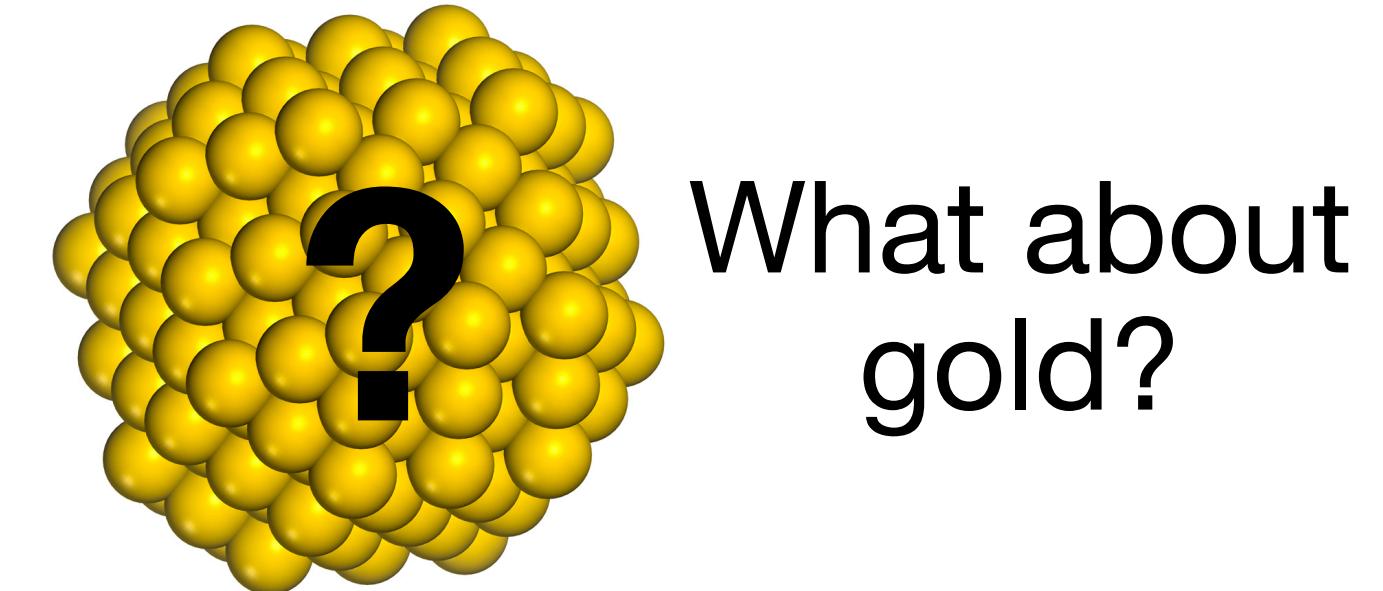
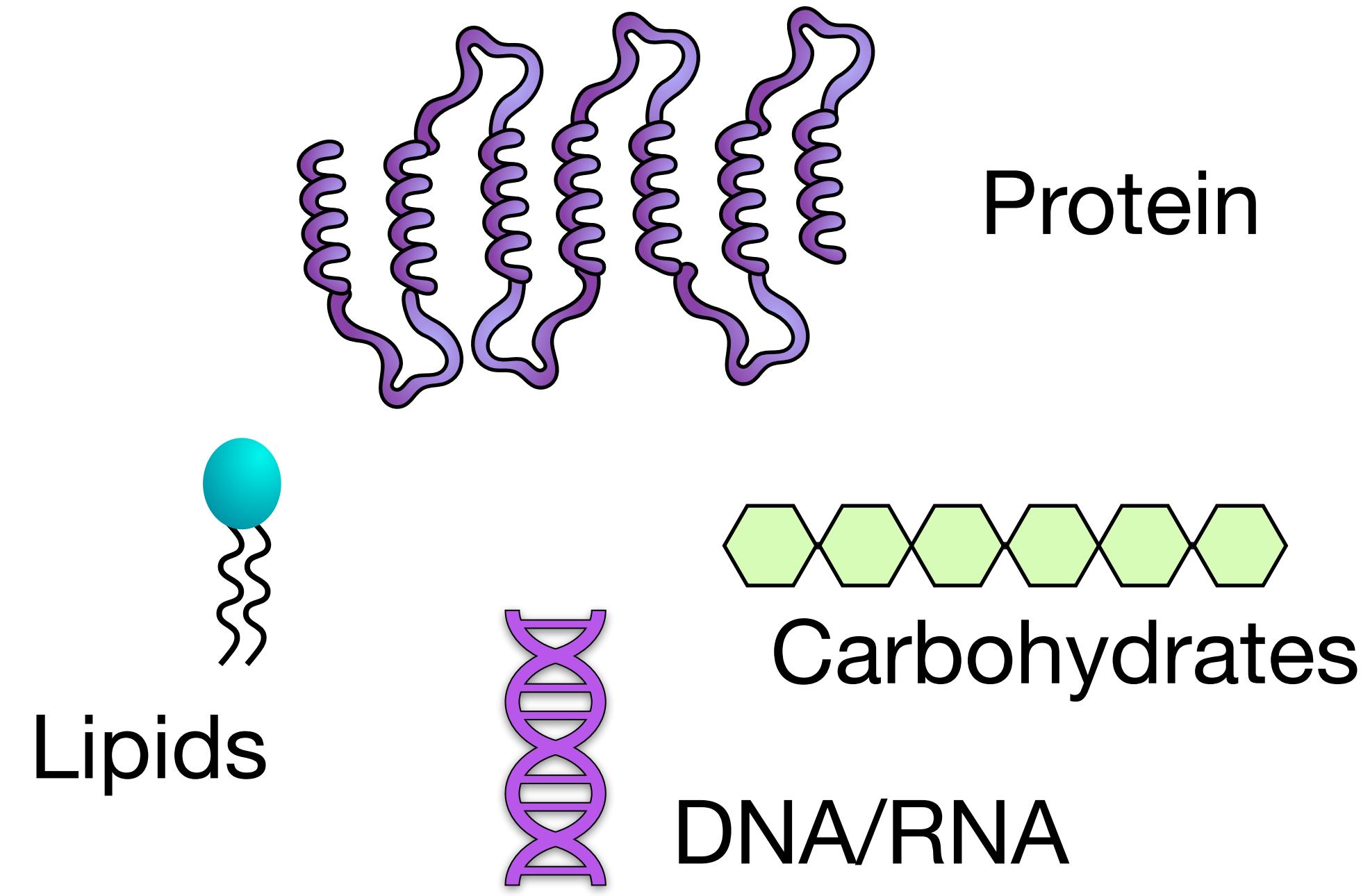
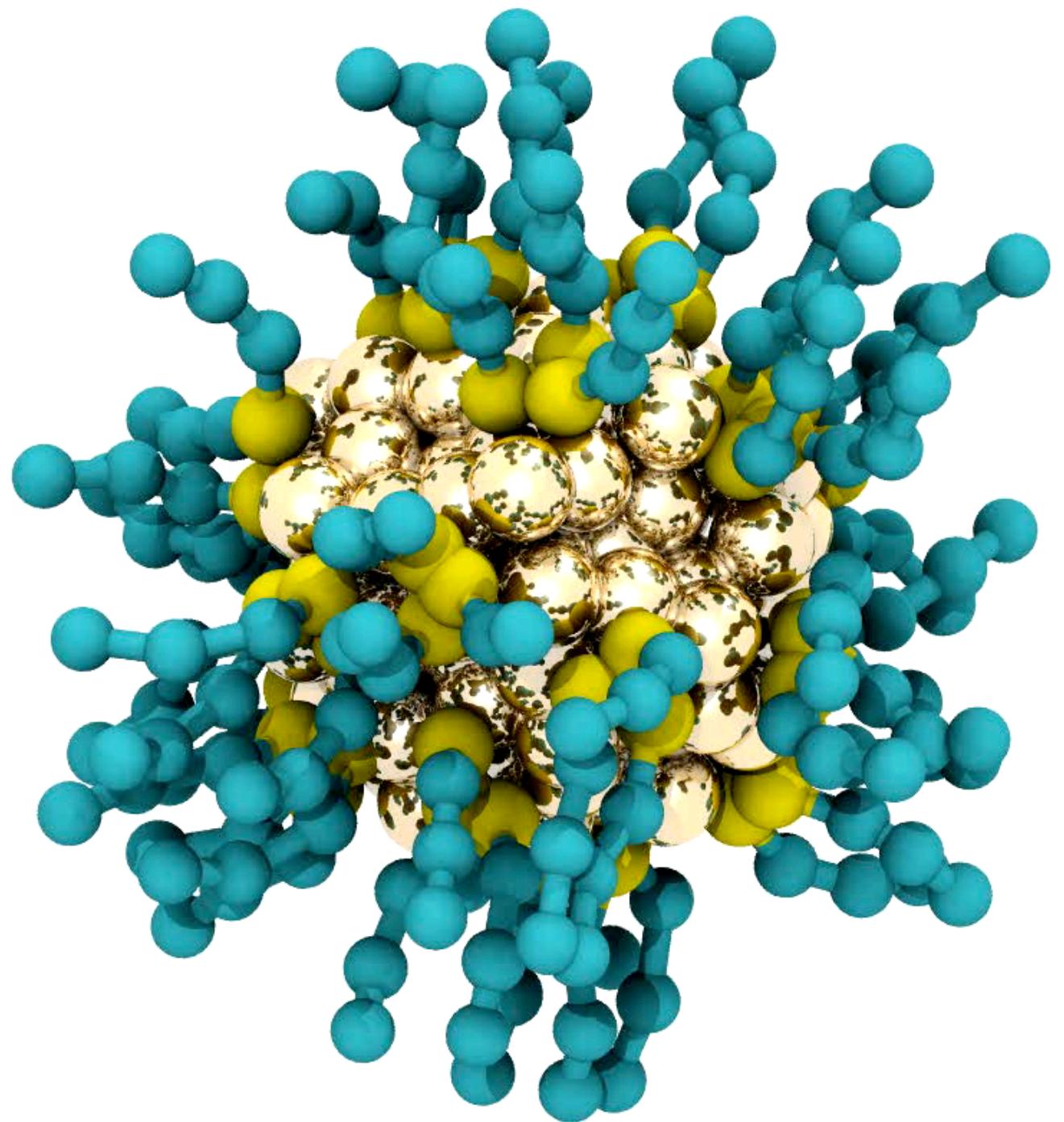
Combine interactions for complex molecular systems

$$U_{total} = \sum_{nonbonded} U_{LJ} + U_{elec} + \sum_{bonds} U_{bond} + \sum_{angles} U_{angle} \\ + \sum_{dihedrals} U_{dihedral} + \sum_{impropers} U_{improper} + \text{corrections}$$

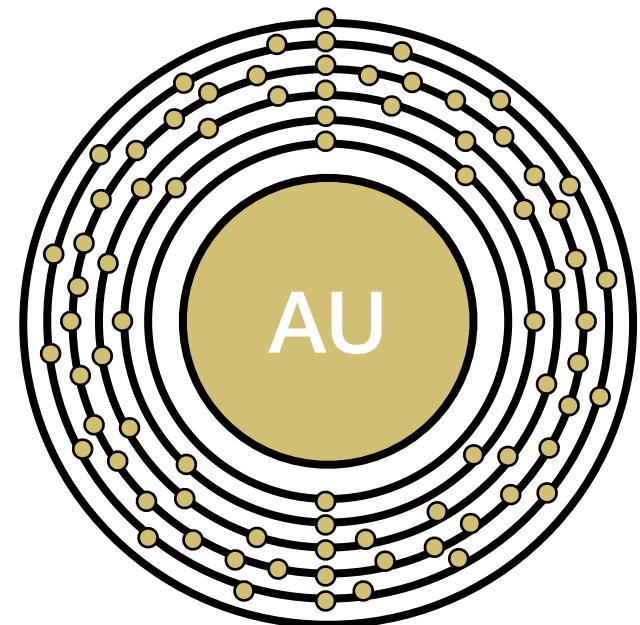




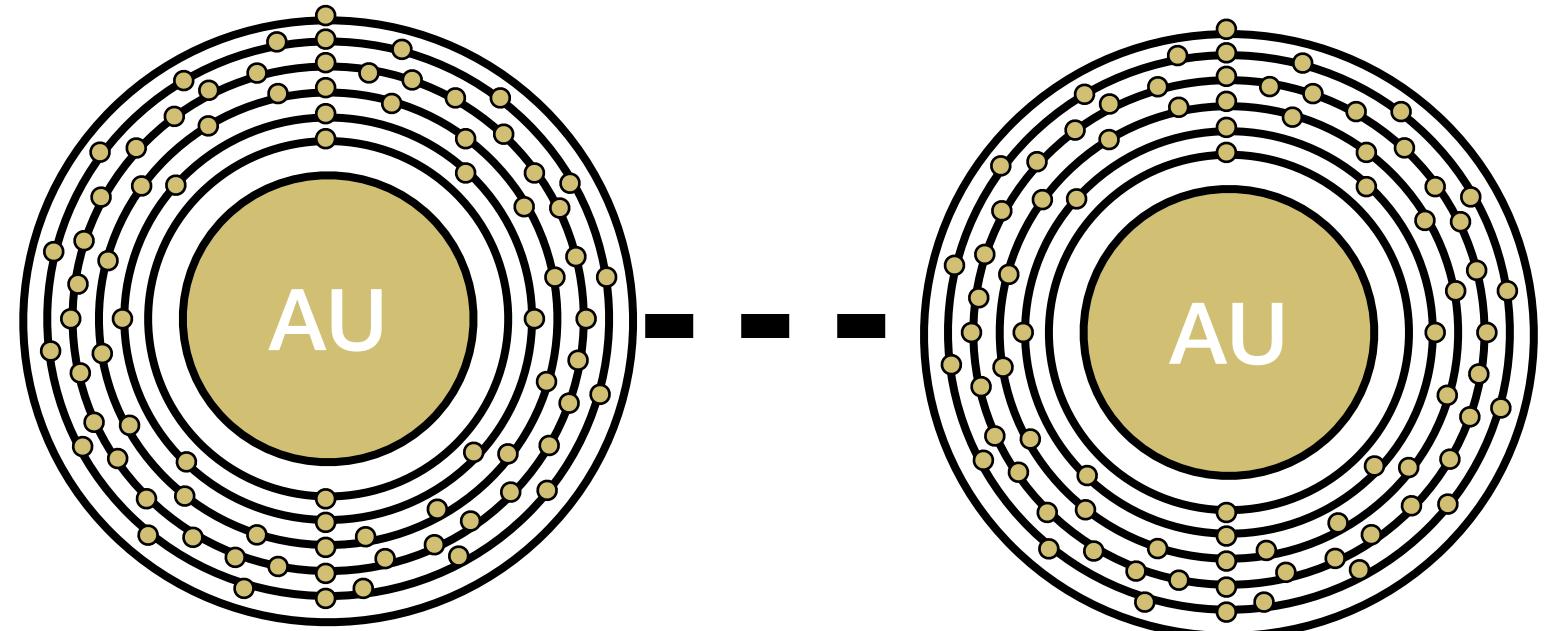
But there's a problem...



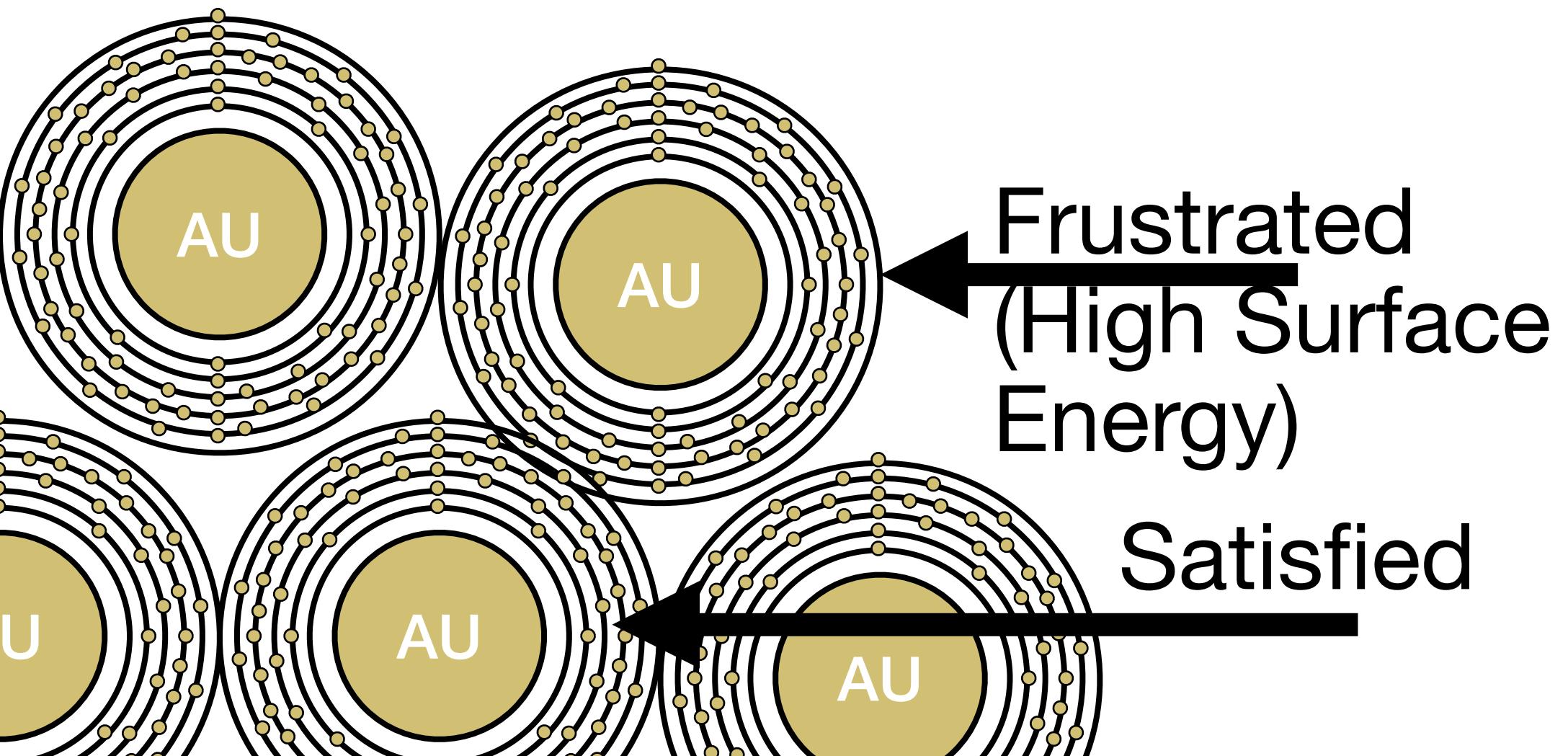
Properties of Nanoscale Gold



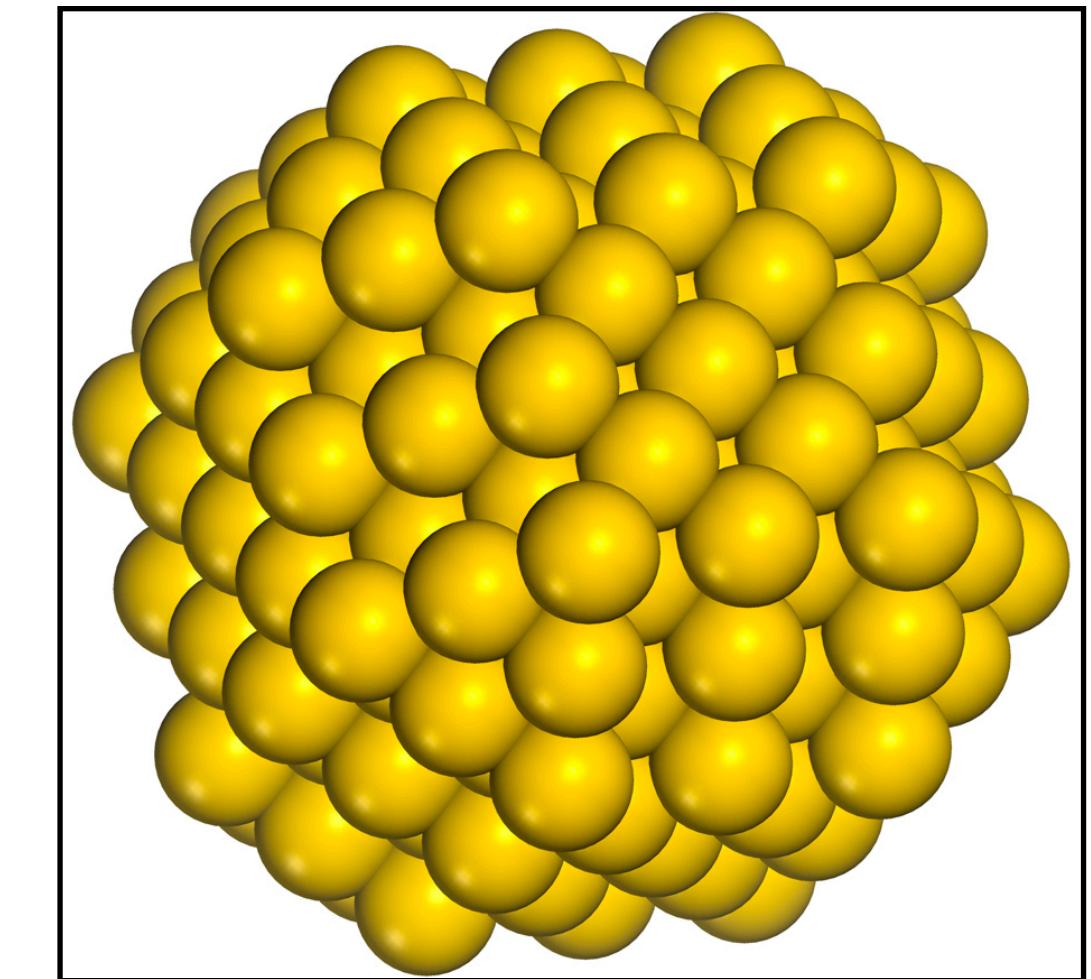
Large atoms with weak hold on their electrons



Form crystal lattices due to metal bonding

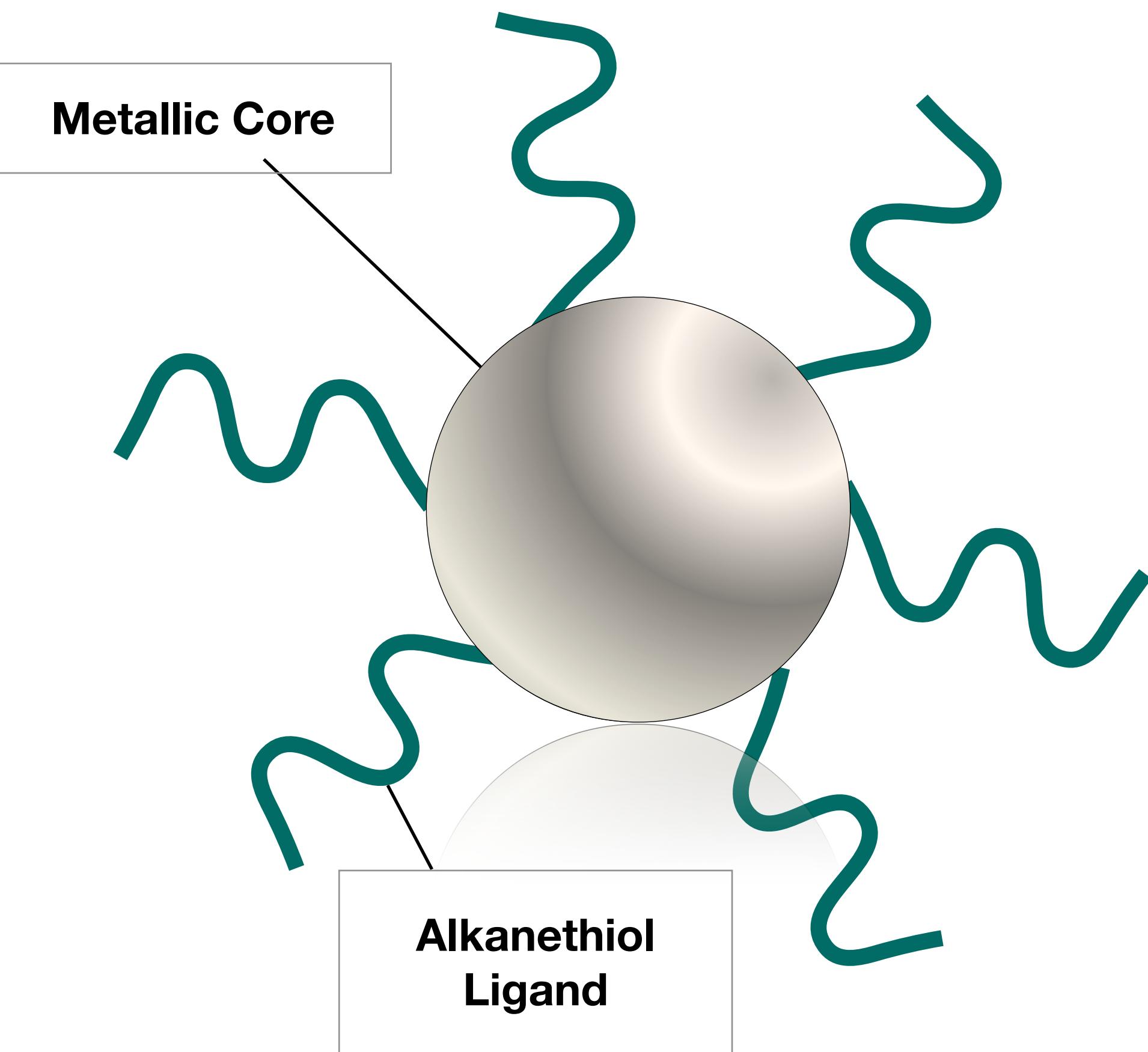


Increases epitaxial growth



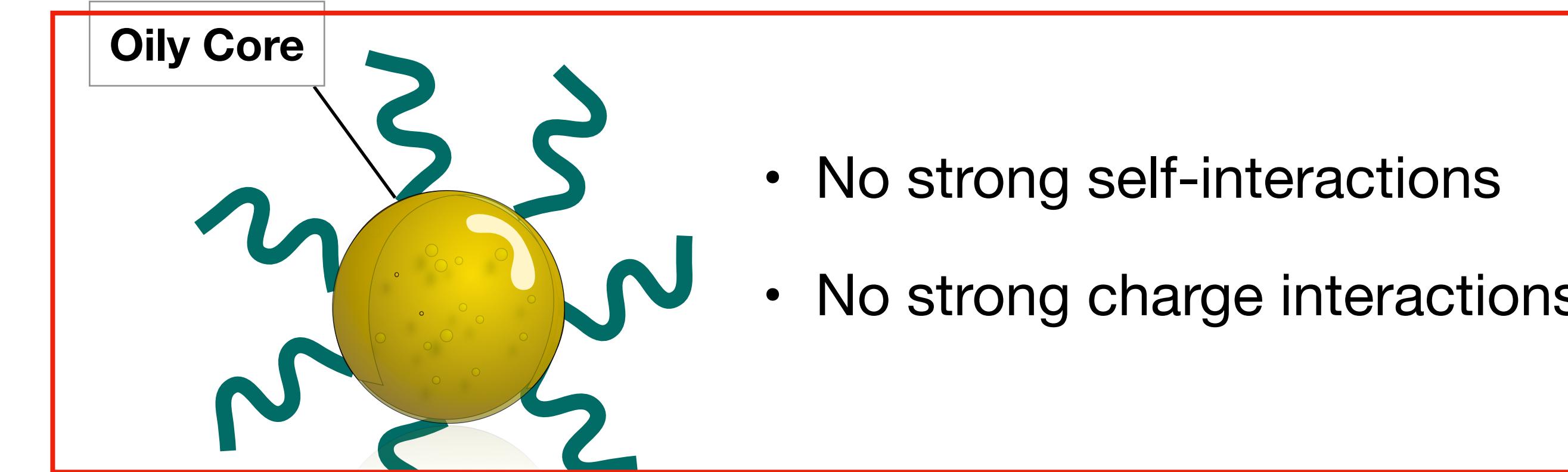
- 1 to 100nm
- Reactive
- Light sensitivity

What we Want in a Model



- Strong metal-metal interactions
- Strong interactions with charges

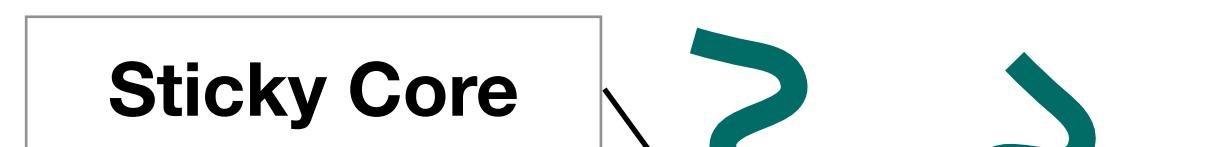
Available Model Choices



- No strong self-interactions
- No strong charge interactions



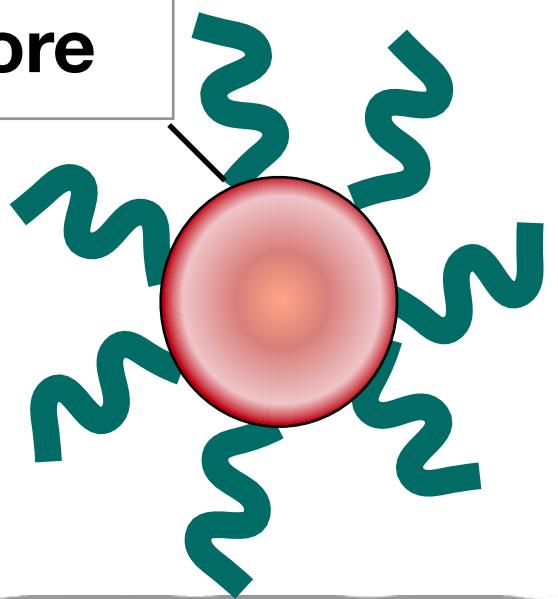
- No interactions



- Strong self-interactions
- Strong charge interactions

**Testing Direct Interaction Mechanism:
Does varying gold core parameters affect
aggregation?**

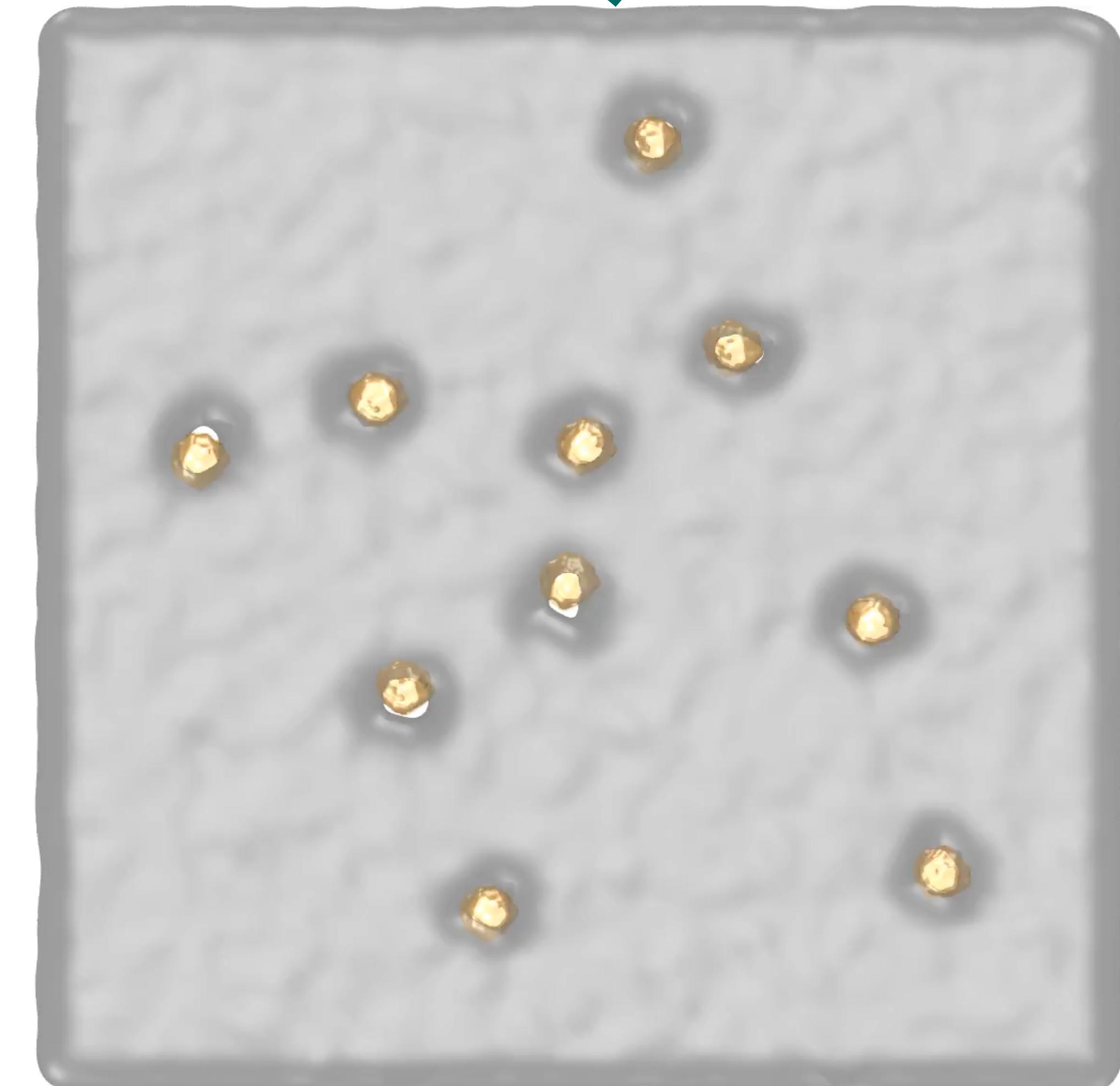
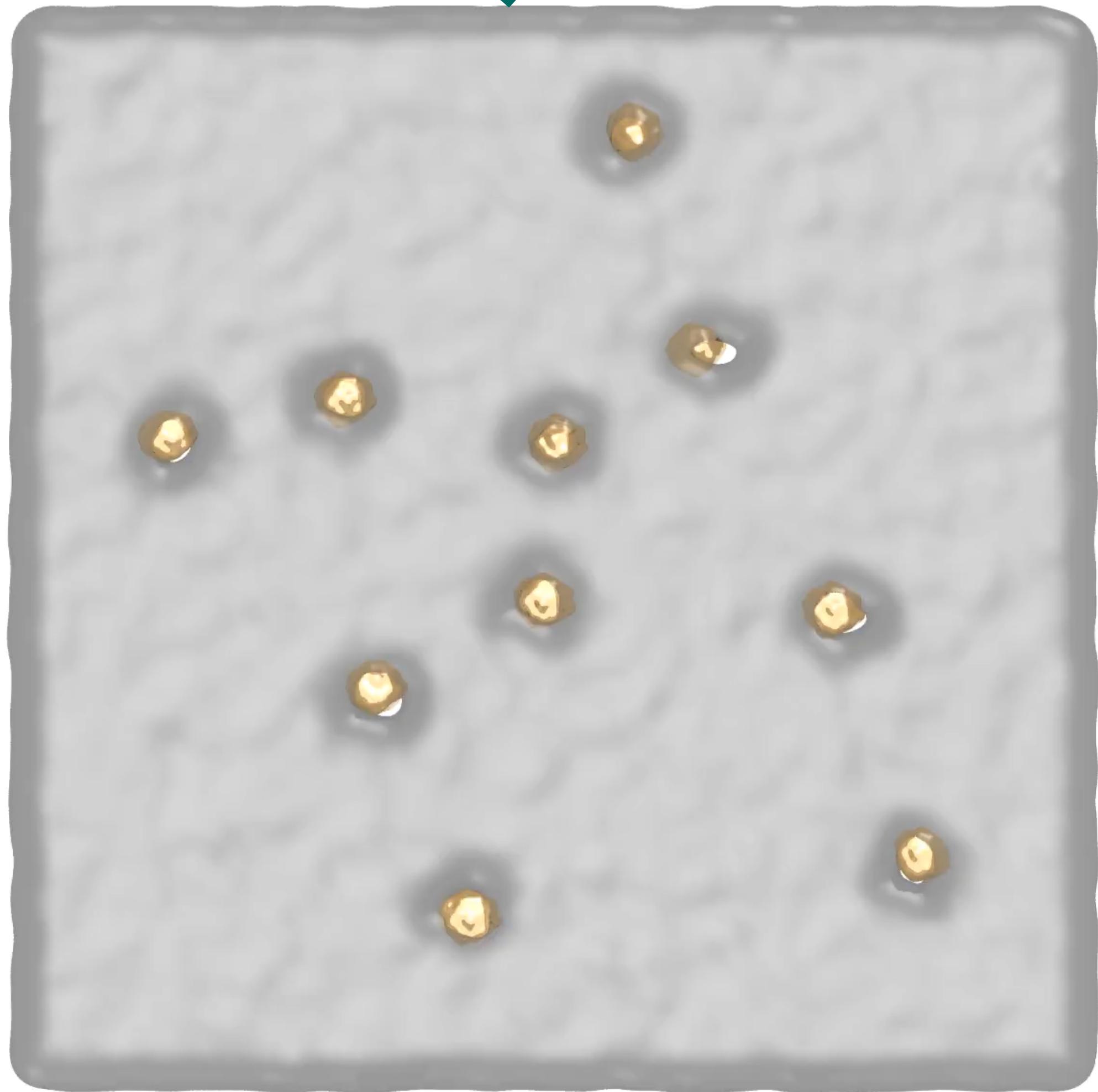
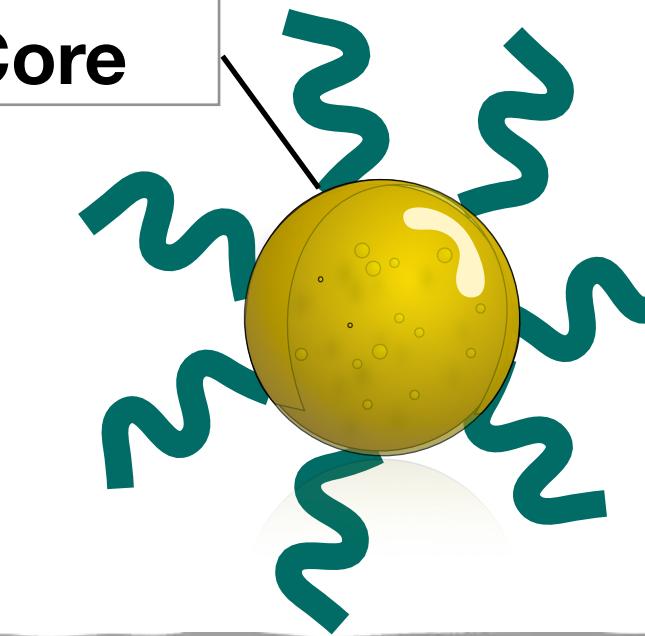
Sticky Core



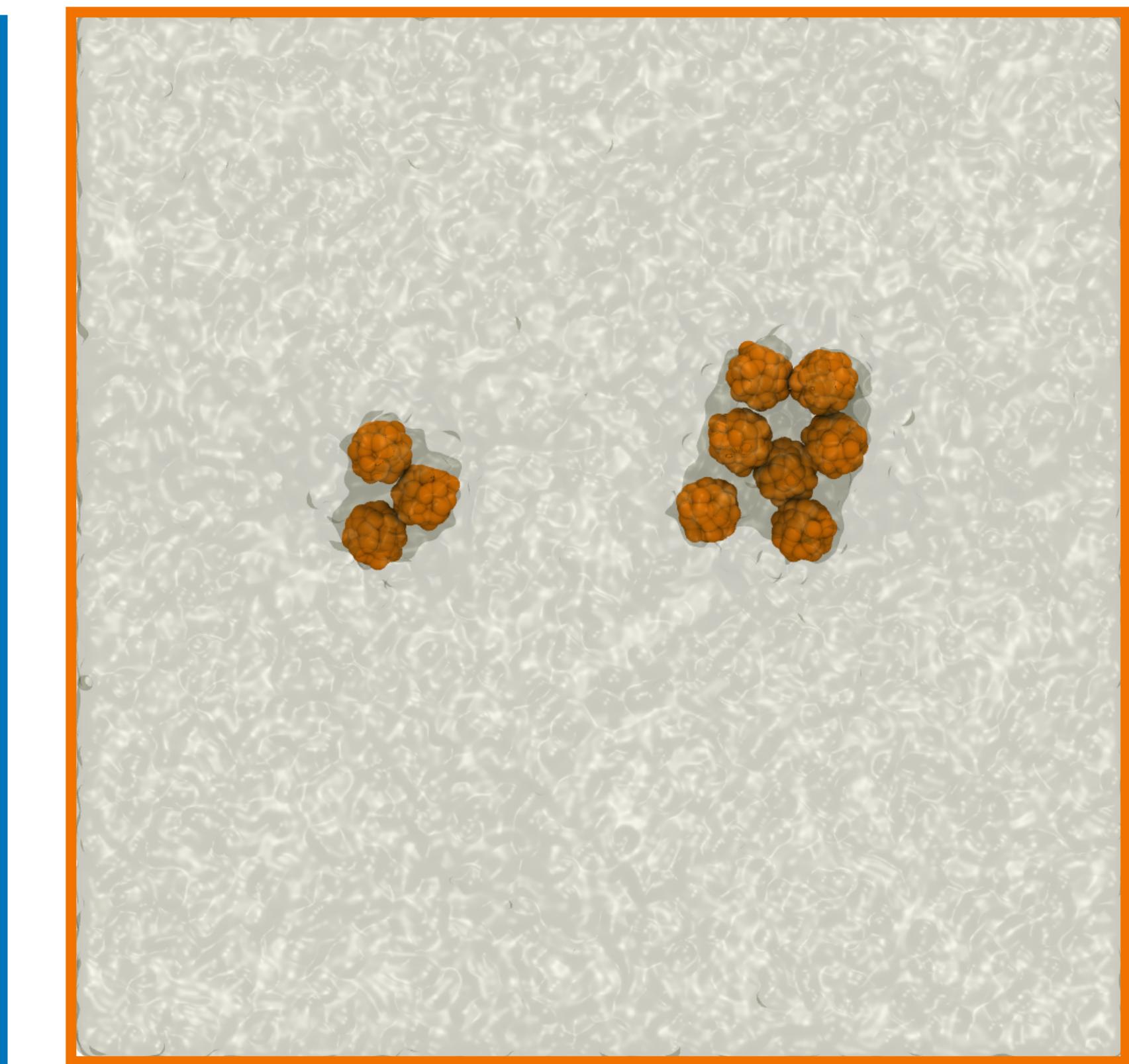
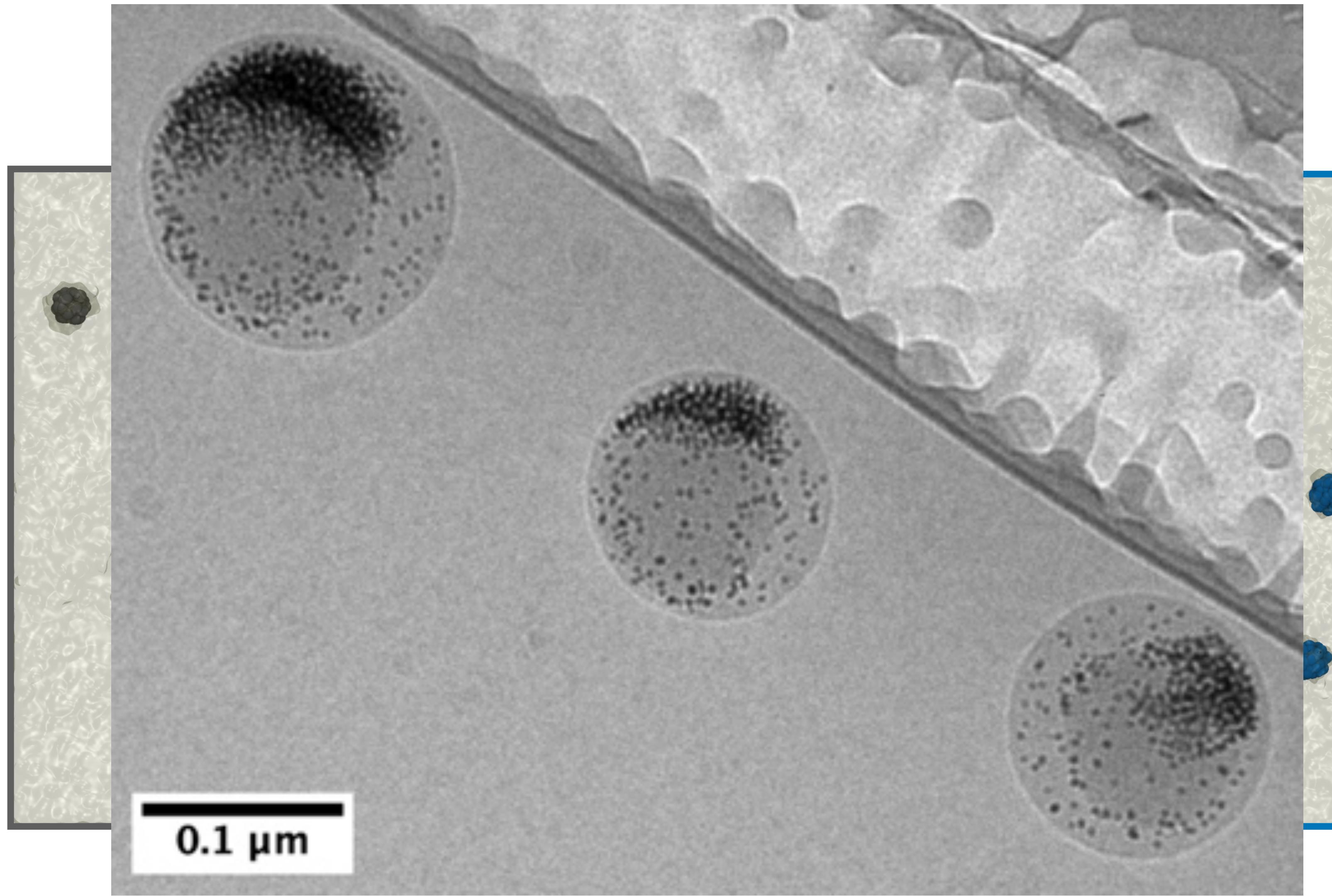
Lipids

Gold Nanoparticle

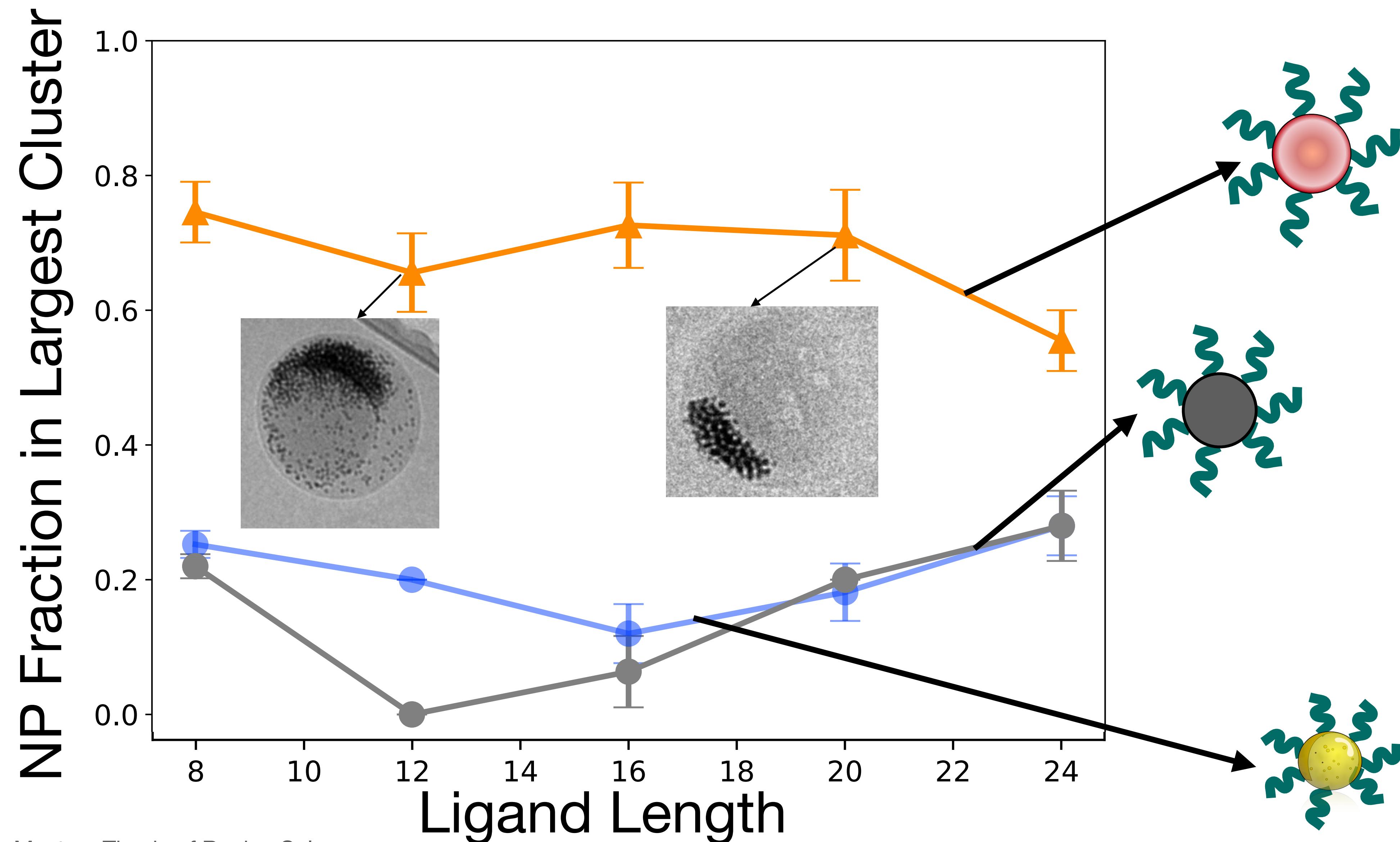
Oily Core



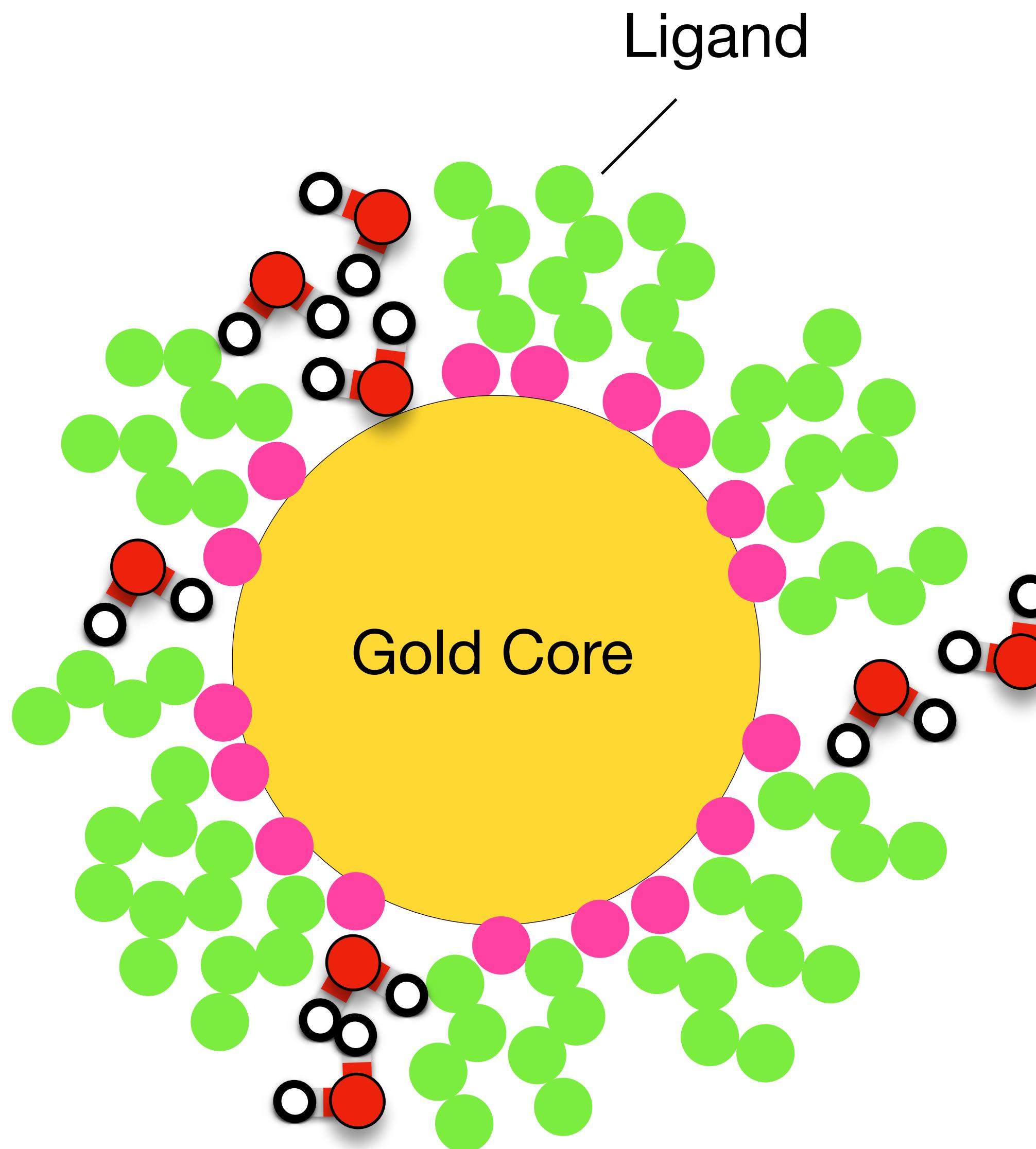
Different Gold Core Models Have Different Aggregation Behavior



Aggregation Behavior is Sensitive to Ligand Length and Core Parameter

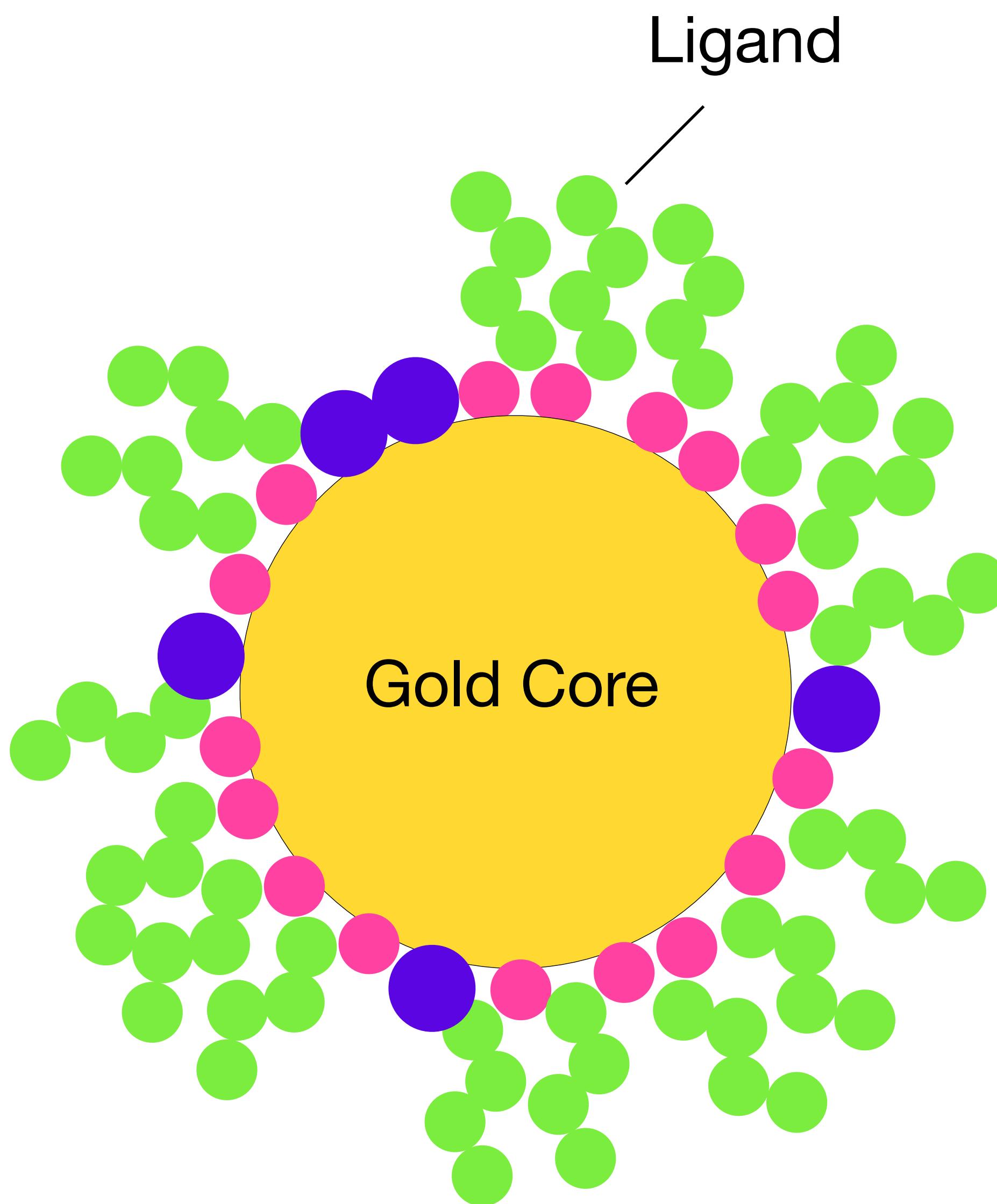


Direct Interaction (probably) Requires an Exposed Surface



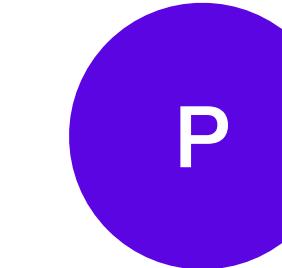
- Solvent Accessible Surface Area (SASA)
- May indicate regions of exposed surface which can interact

Quantifying the Exposed Surface Area

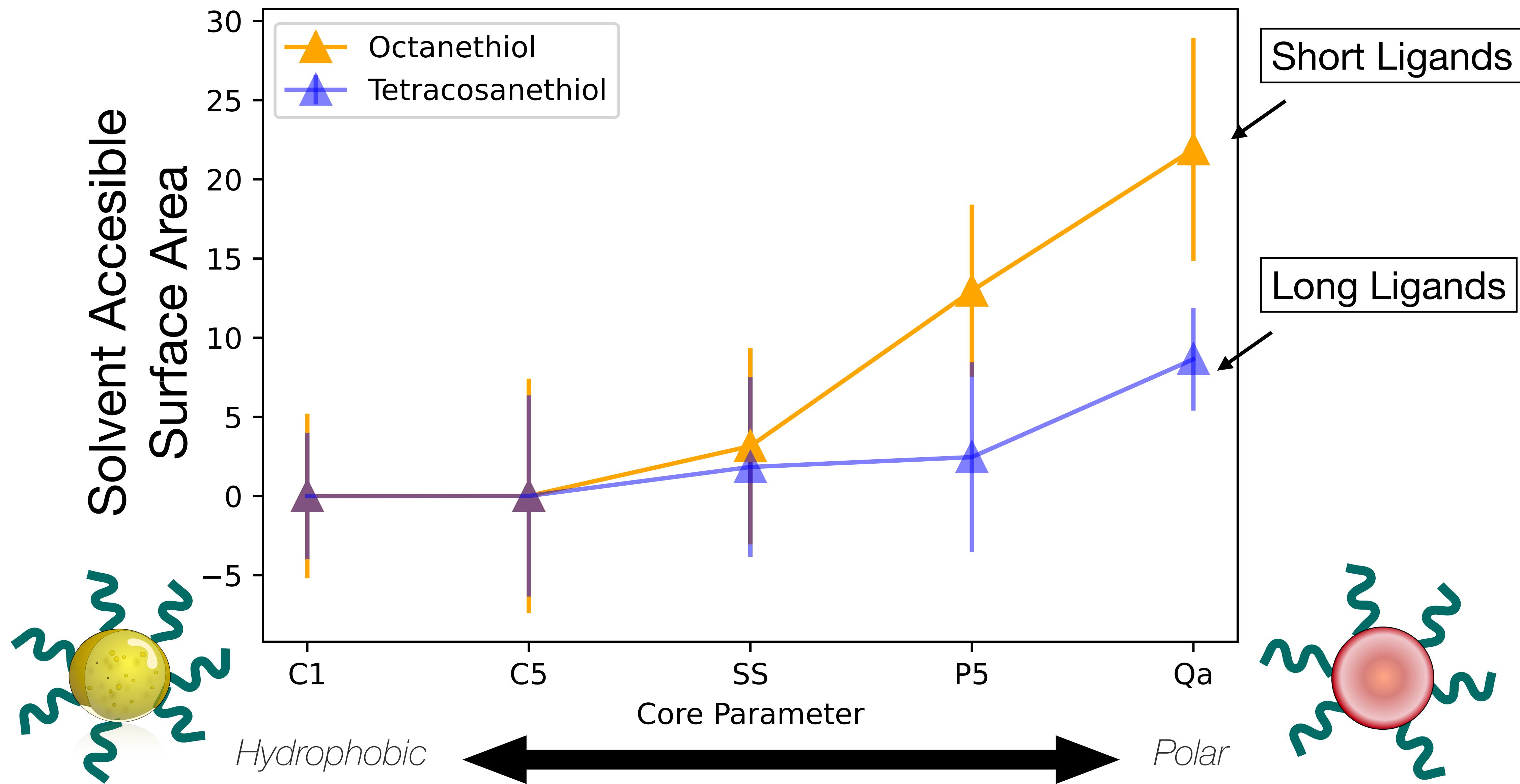


$$sasa = 4\pi r^2 p$$

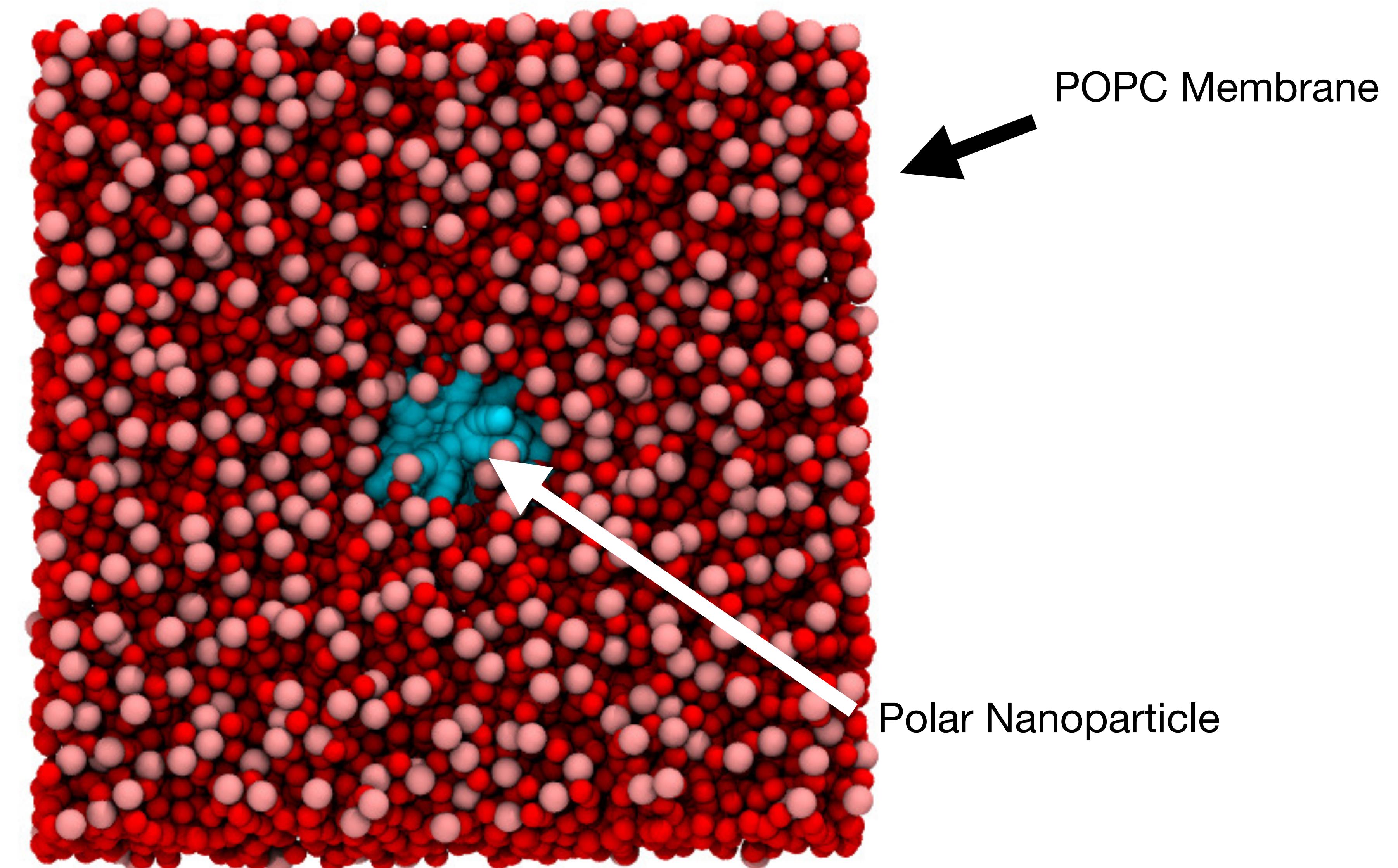
p = # of probes



Core polarity increases surface accessibility of nanoparticles embedded in the membrane

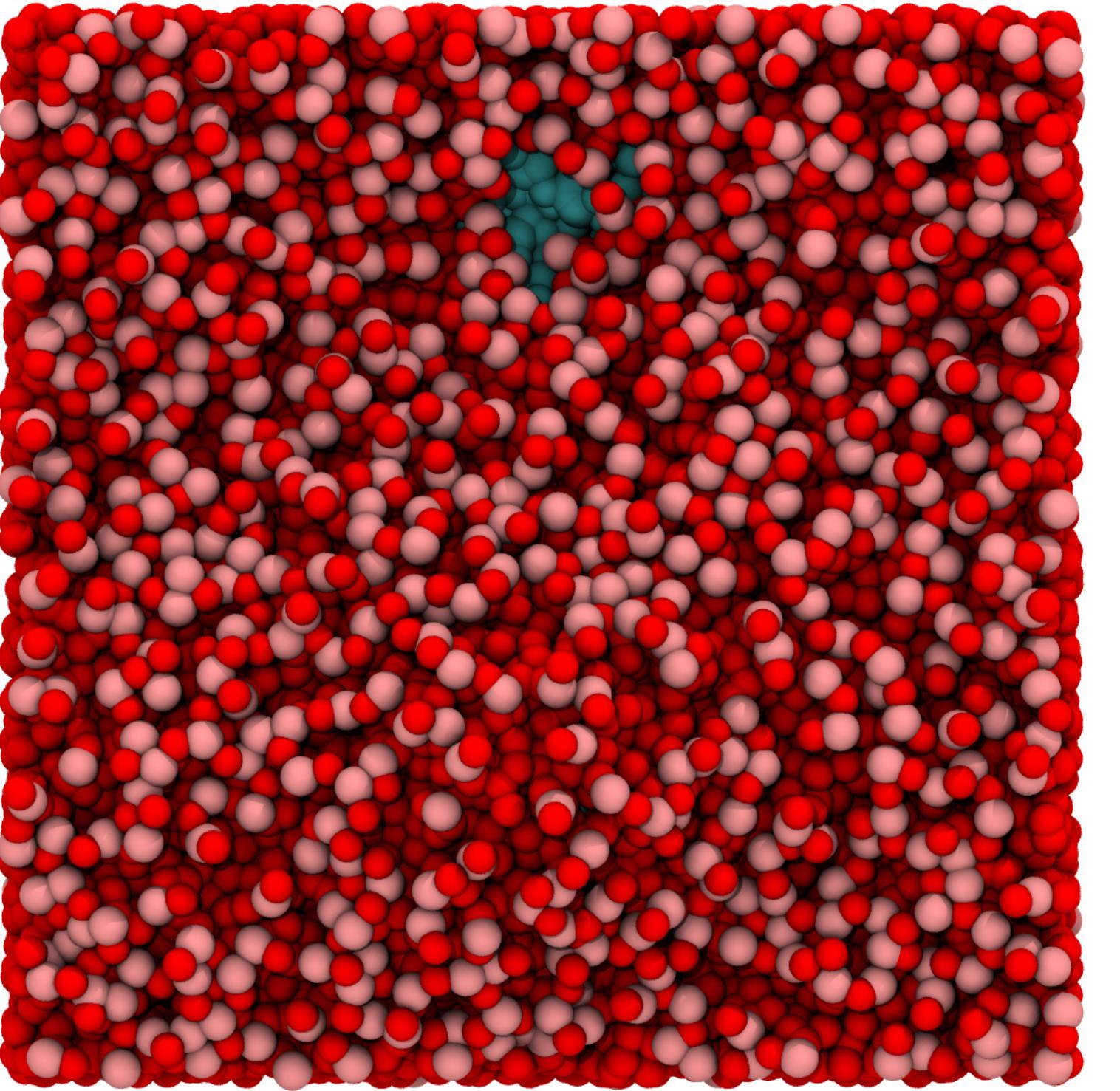


Increasing Nanoparticle Polarity Leads to Pore Formation In Single Nanoparticle Systems

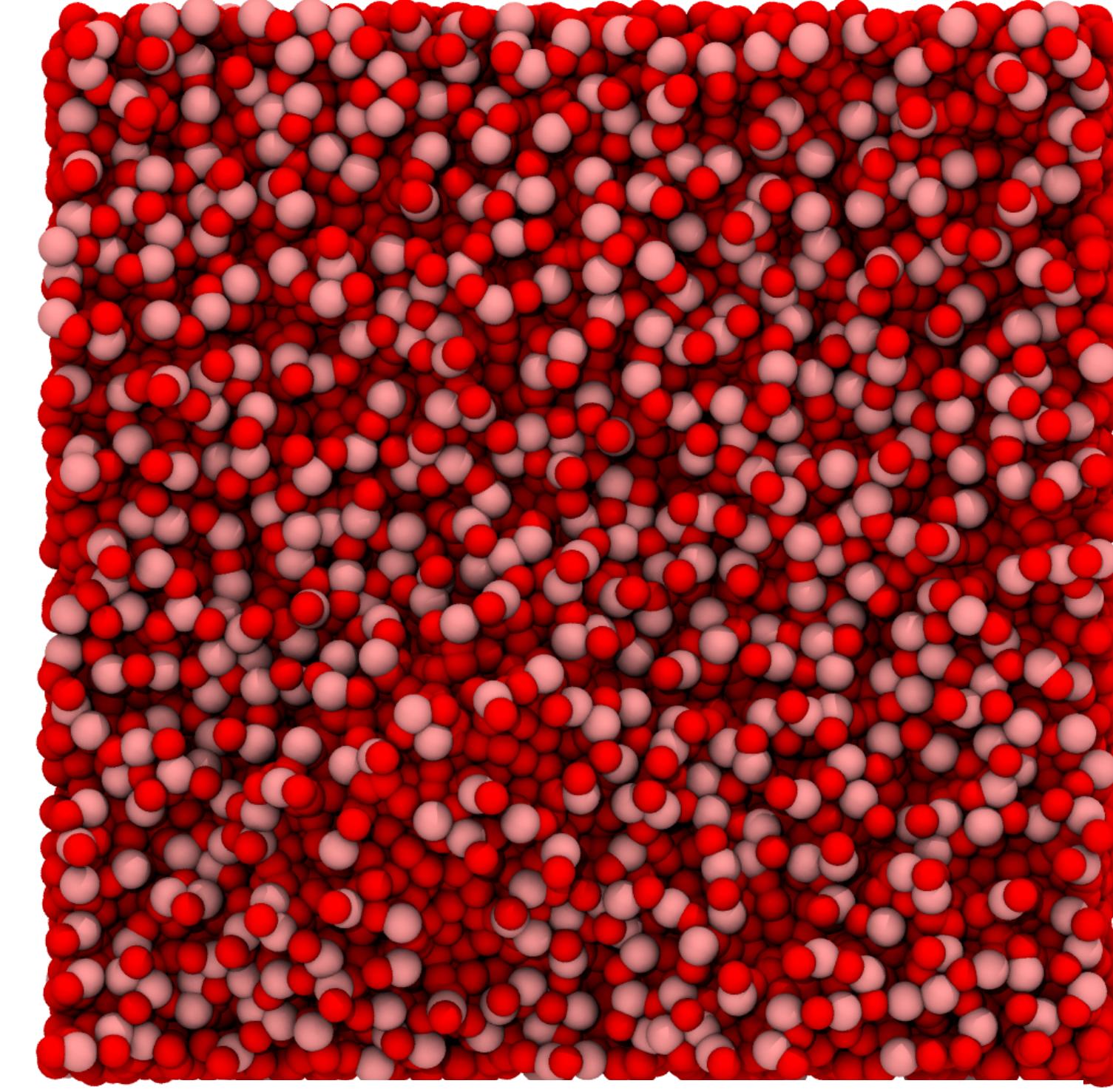


Aggregation Minimizes Pore Formation and Shifts Polar Interactions From Solvent to Gold Cores

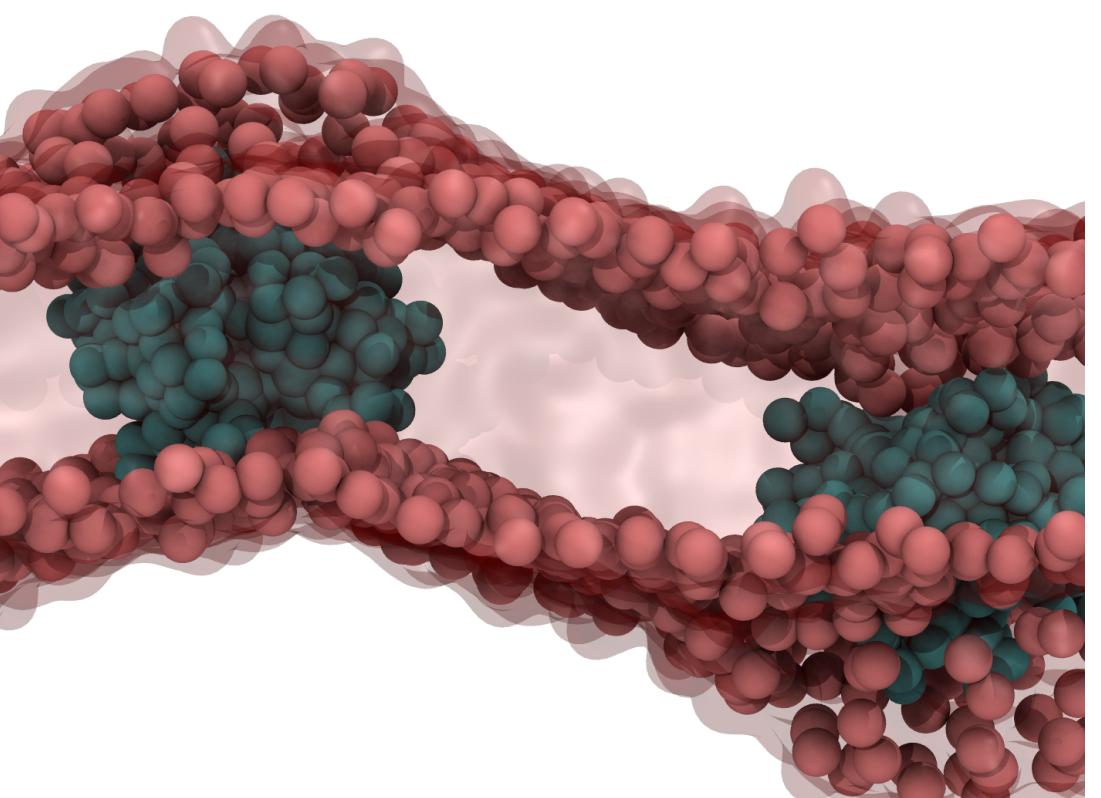
Non-Aggregated($1\mu s$)



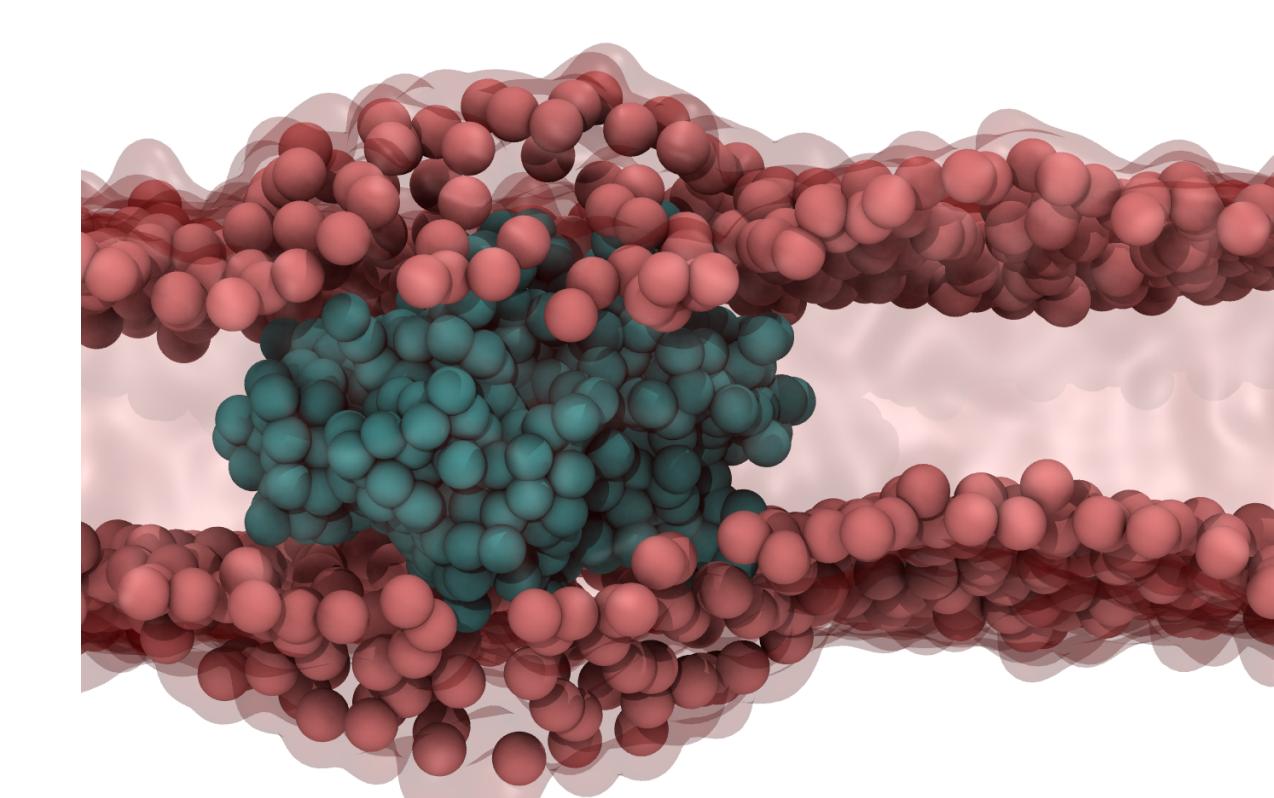
Aggregated($5\mu s$)



Top View

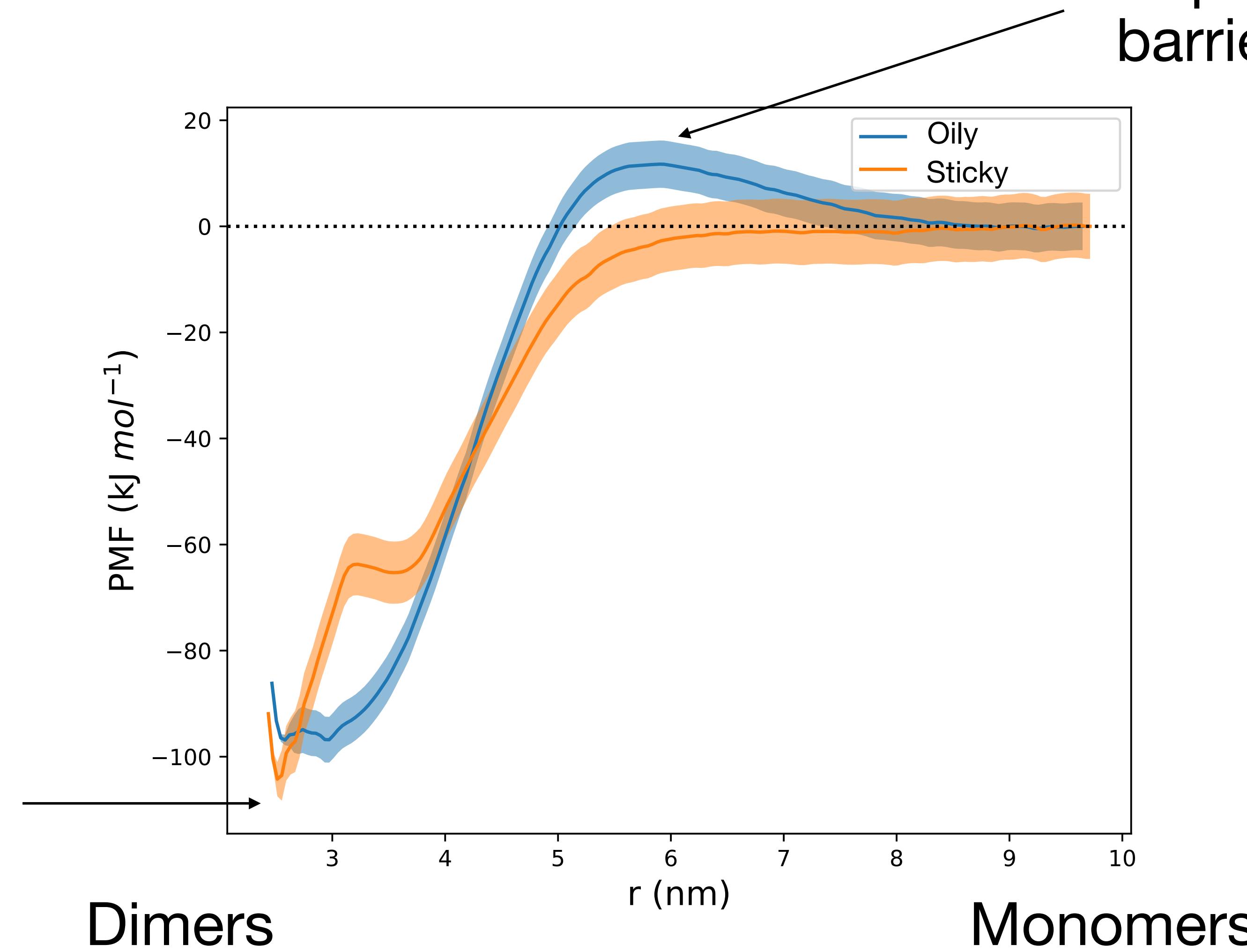


Side View



Free Energy of Dimerization

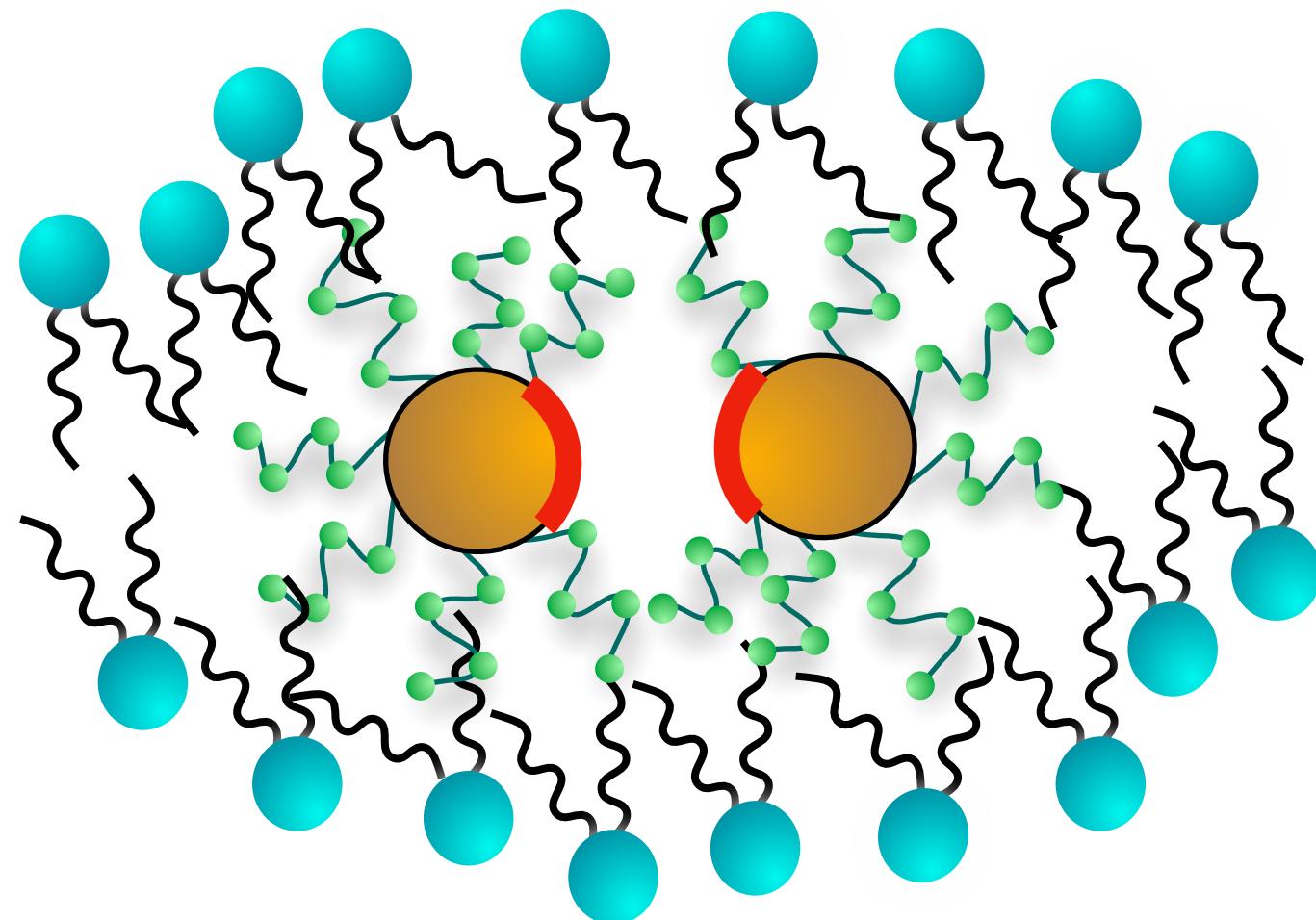
Dimerization is slightly more favorable for sticky cores



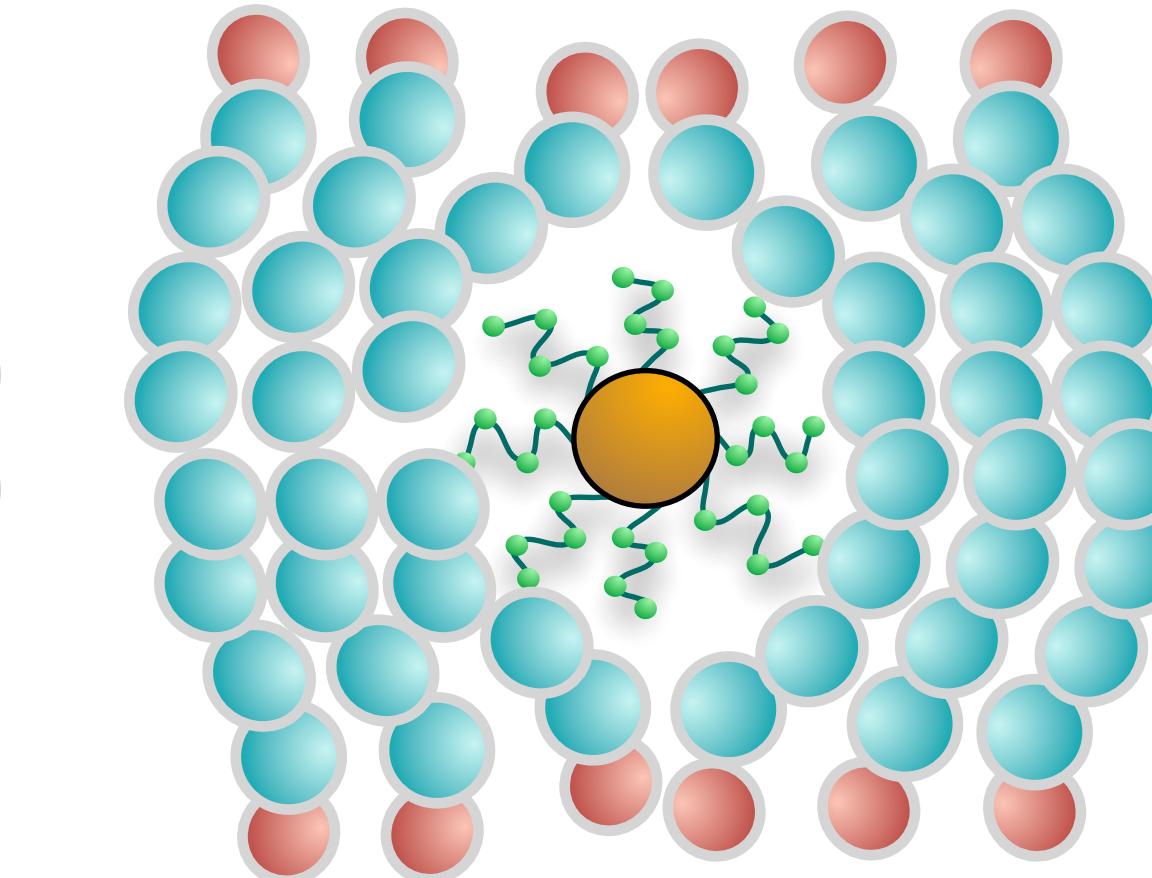
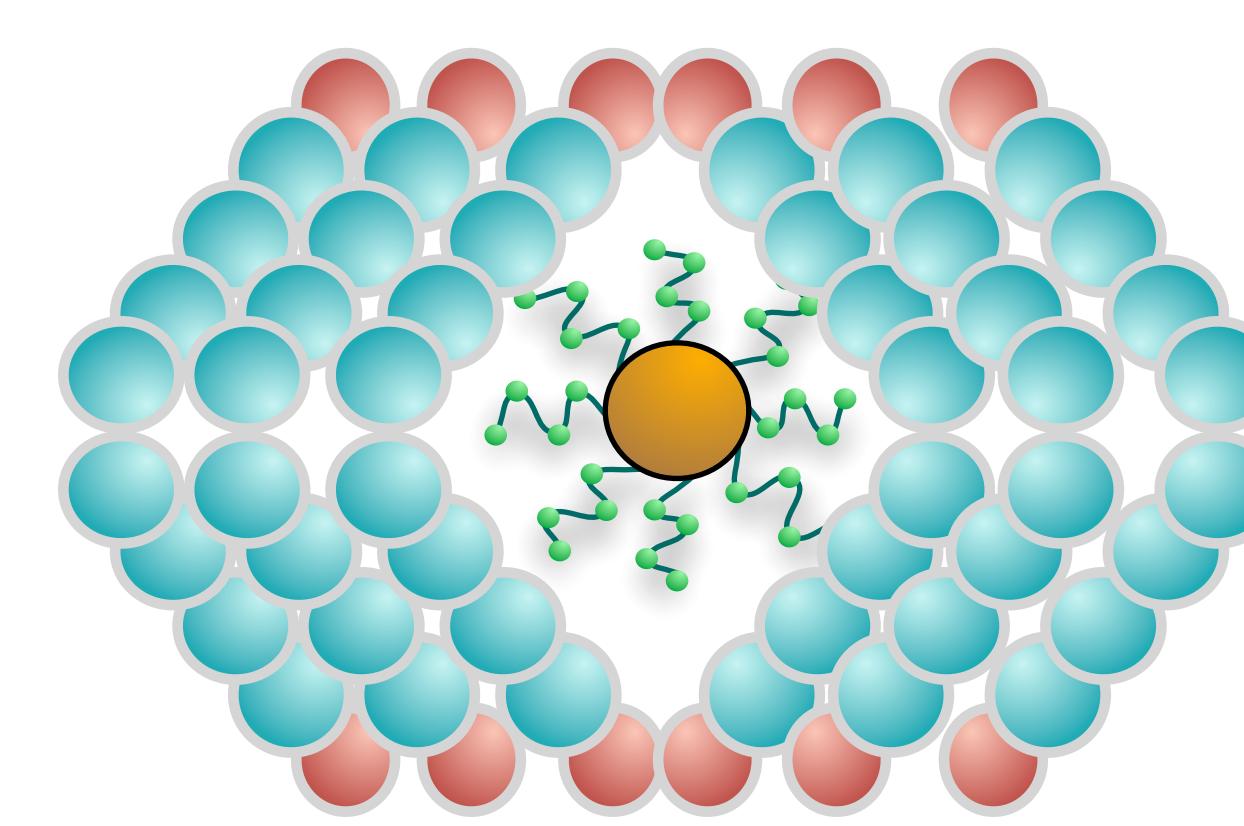
Bending or
Depletion-based
barrier?

Testing Local Packing Mechanism: How does increasing ligand length affect lipid order?

Gold-Gold interactions

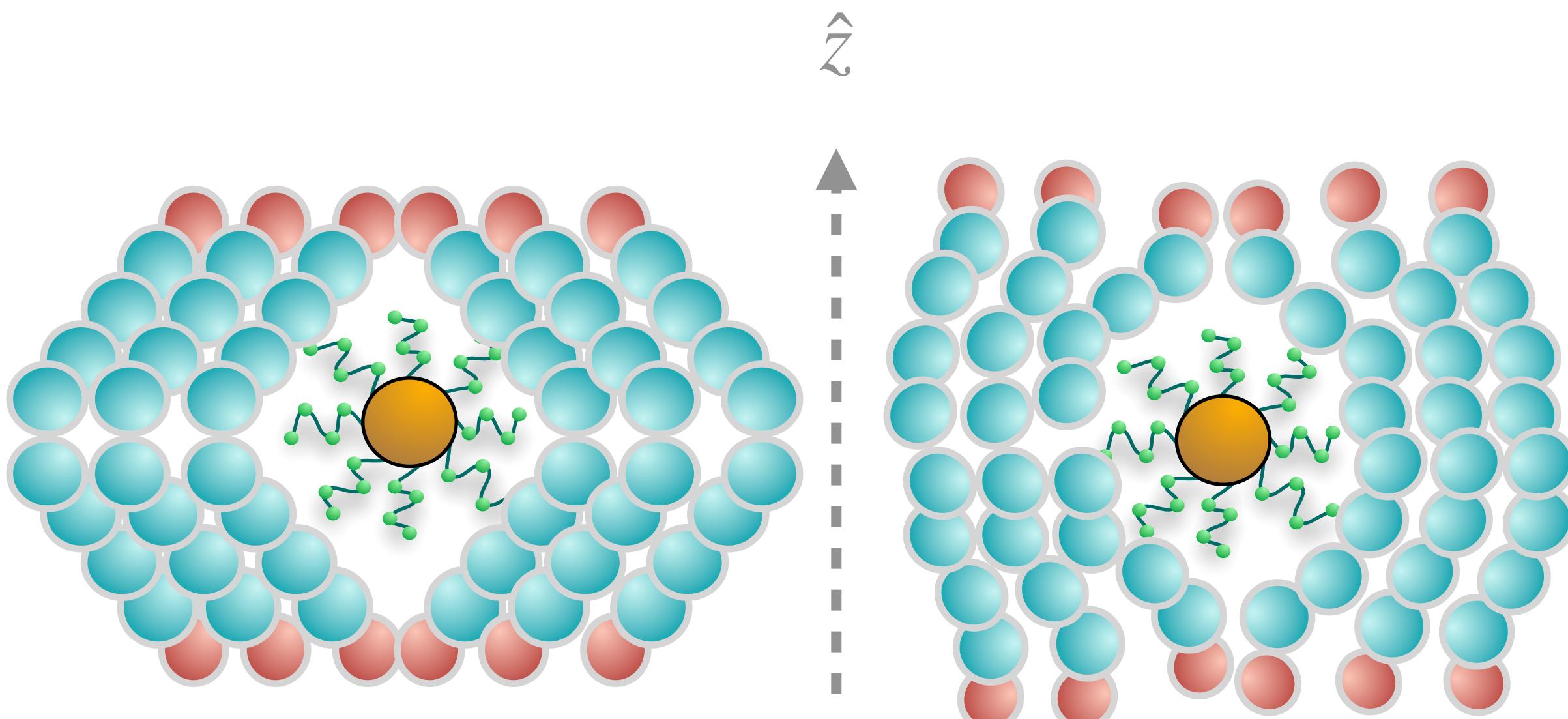


Ligand induced lipid deformation

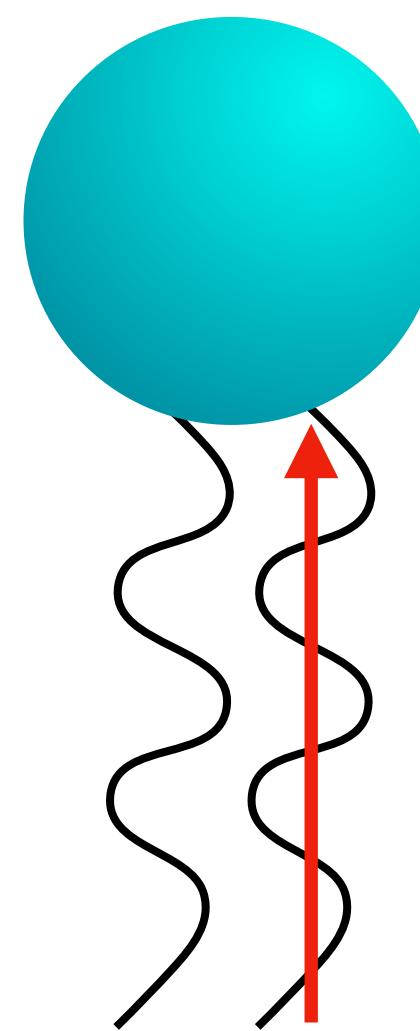


Quantifying Lipid Order

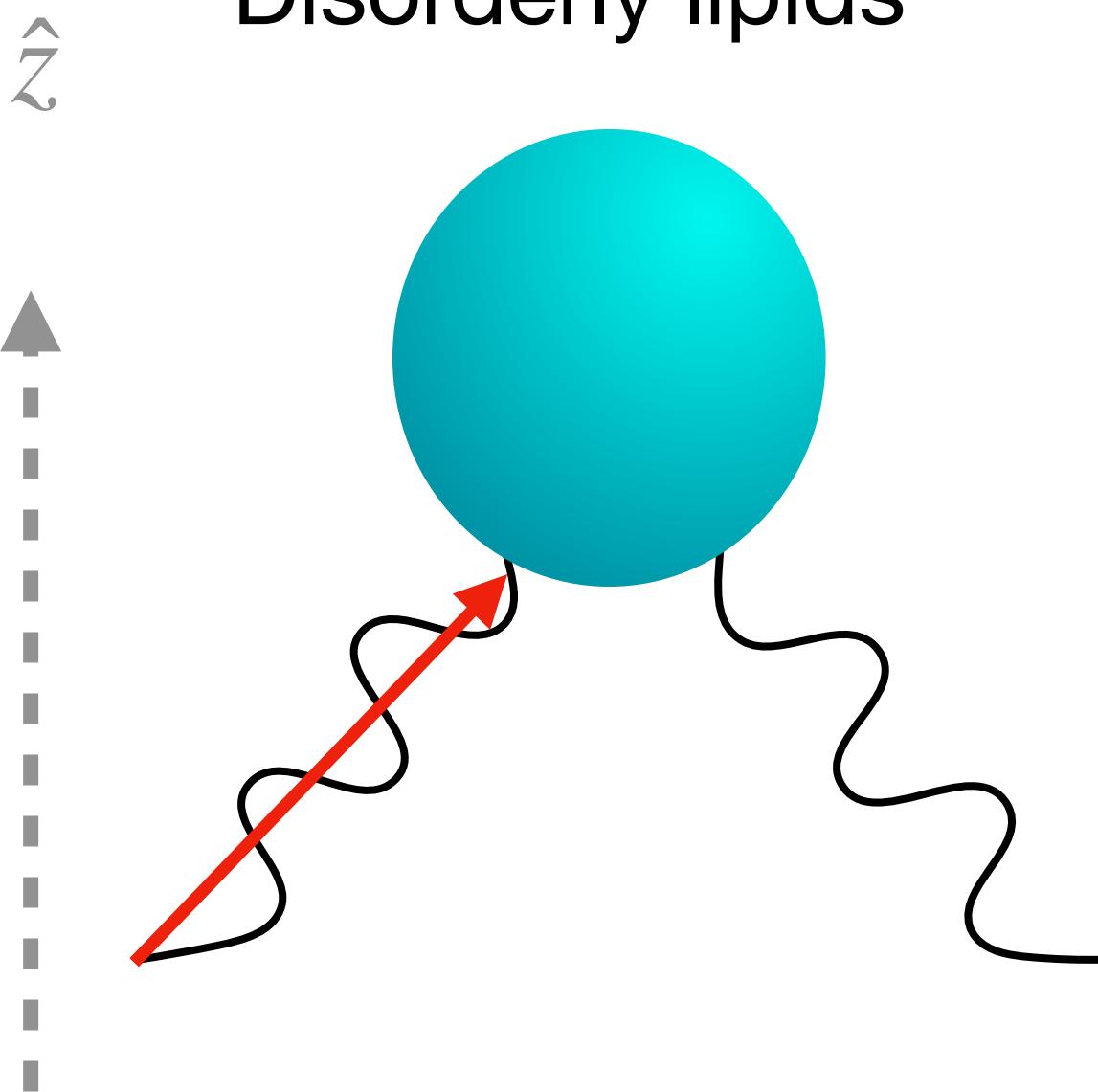
Ligand induced lipid deformation



Orderly lipids



Disorderly lipids

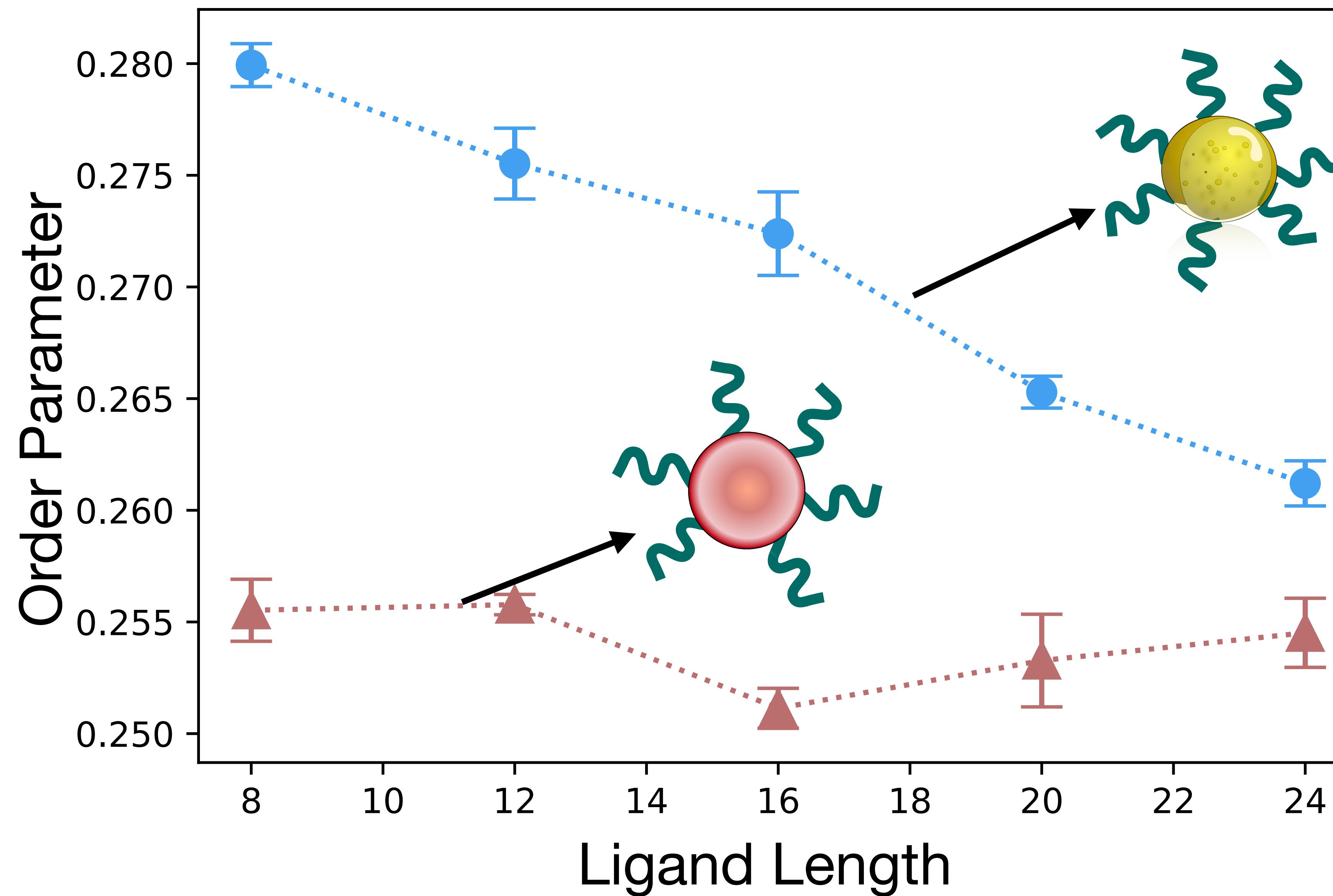


1: Completely Ordered

-0.5 : Completely Disordered

$$S_C = \frac{1}{2} \langle 3 \cos^2 \theta \rangle - 1$$

Do longer ligands decrease lipid order?



Possible Aggregation Mechanisms

- Question: What is the mechanism of ligand coated gold nanoparticle aggregation in lipid membranes?

Ligand induced lipid deformation

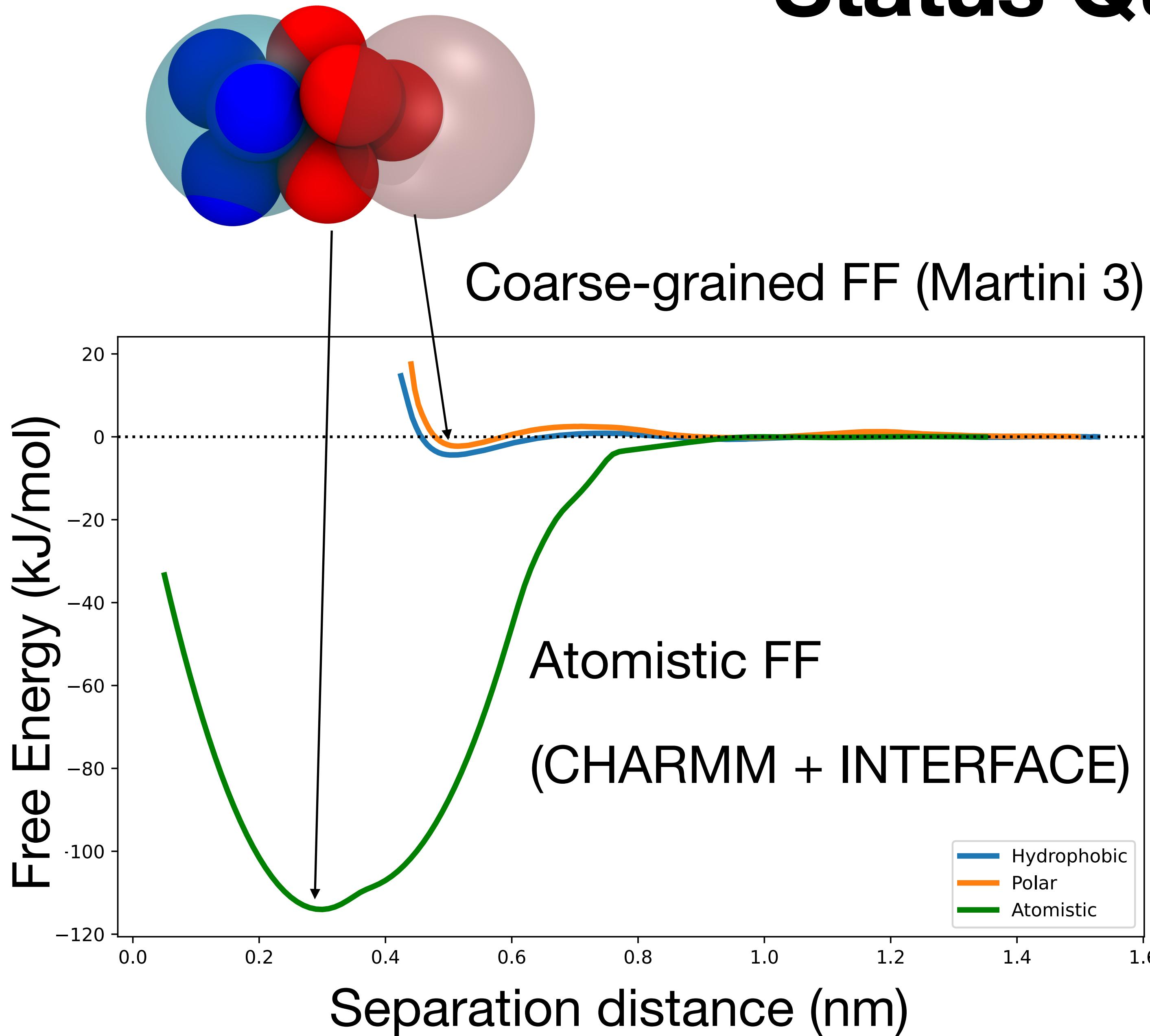
Probably Not for
Sticky Cores

Gold-Gold interactions

Some Evidence
For Direct Gold-
Gold Interaction

Can we do a better job modeling
gold?

Status Quo



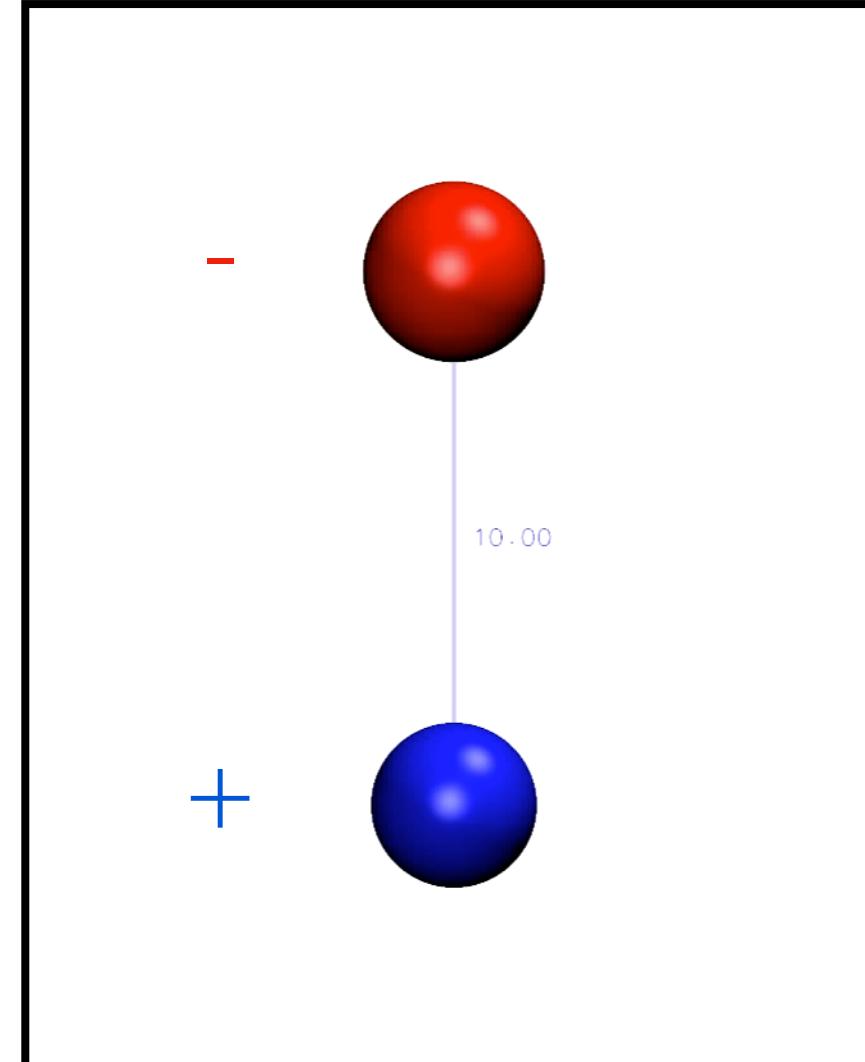
We are dramatically underestimating gold-gold interactions!!!

Can we do a better job modeling gold?

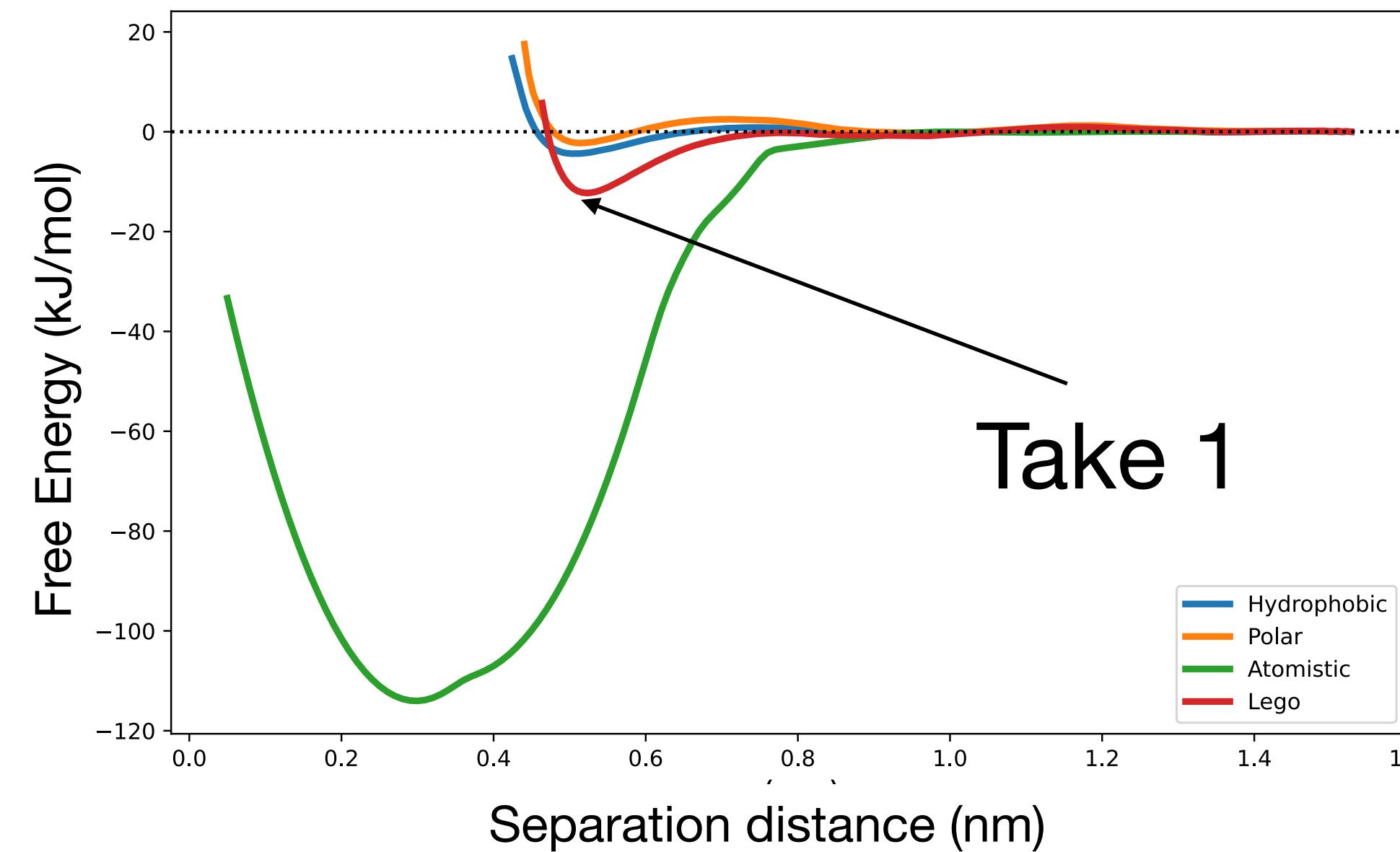
Lennard Jones
& Electrostatic

$$U_{LJ_{ij}} = \epsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right]$$

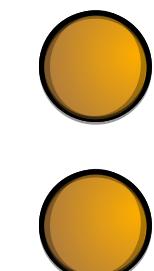
$$U_{elec} = \frac{q_i q_j}{4\pi\epsilon r_{ij}}$$



Maybe we can modify the CG parameters to better capture the fully atomistic forcefield?

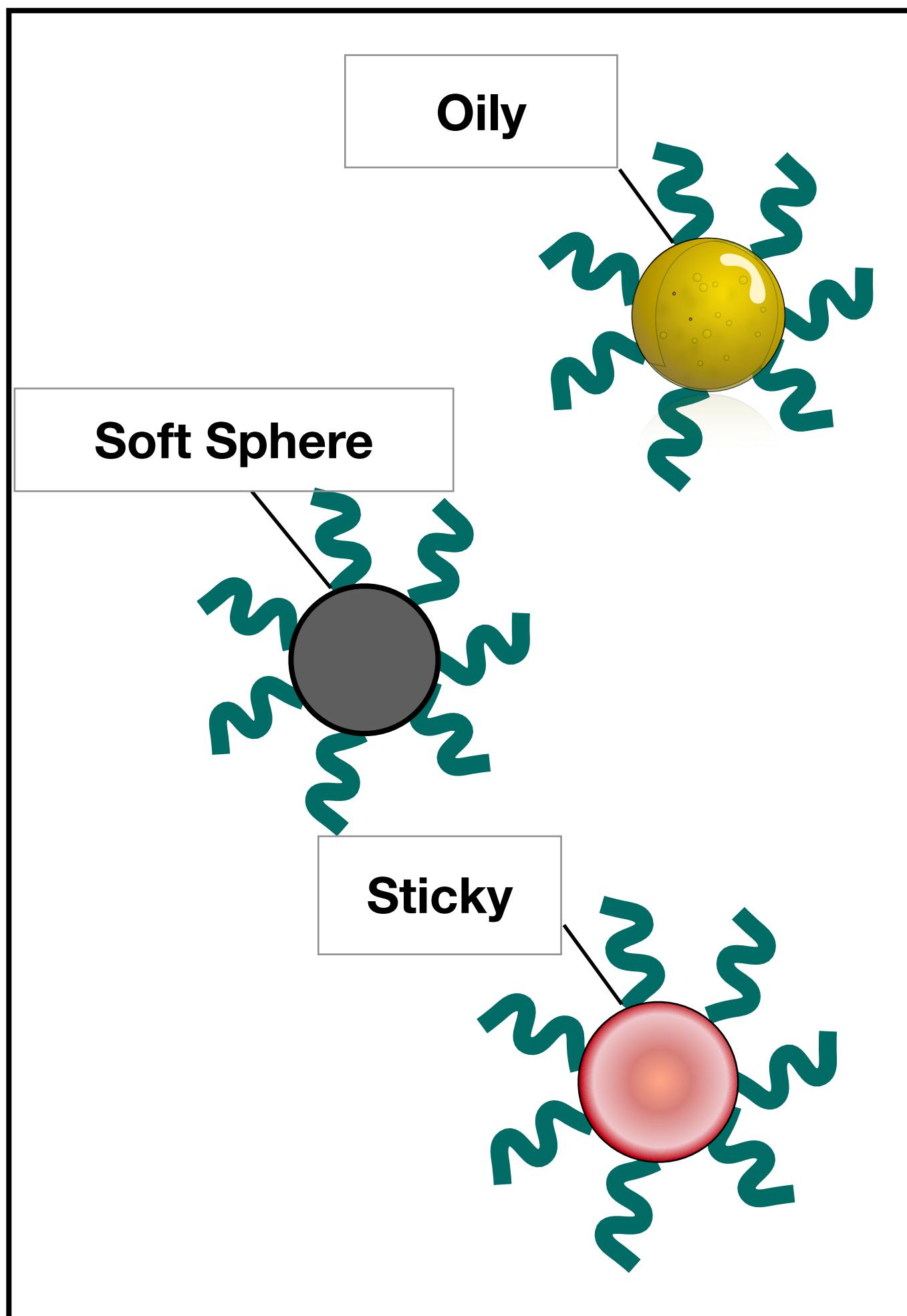


Plan: switch to Martini “tiny beads” and layer them

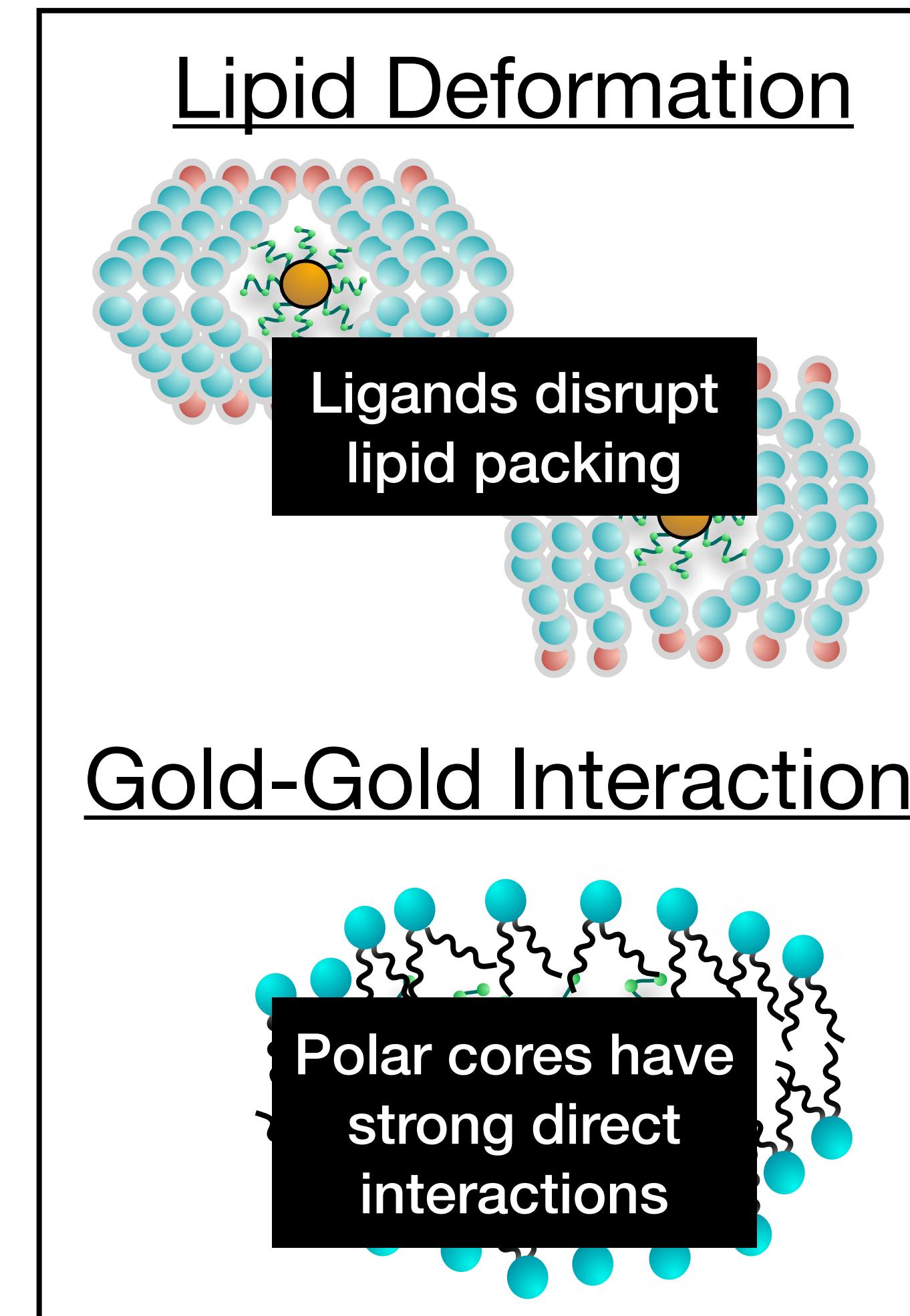


Summary

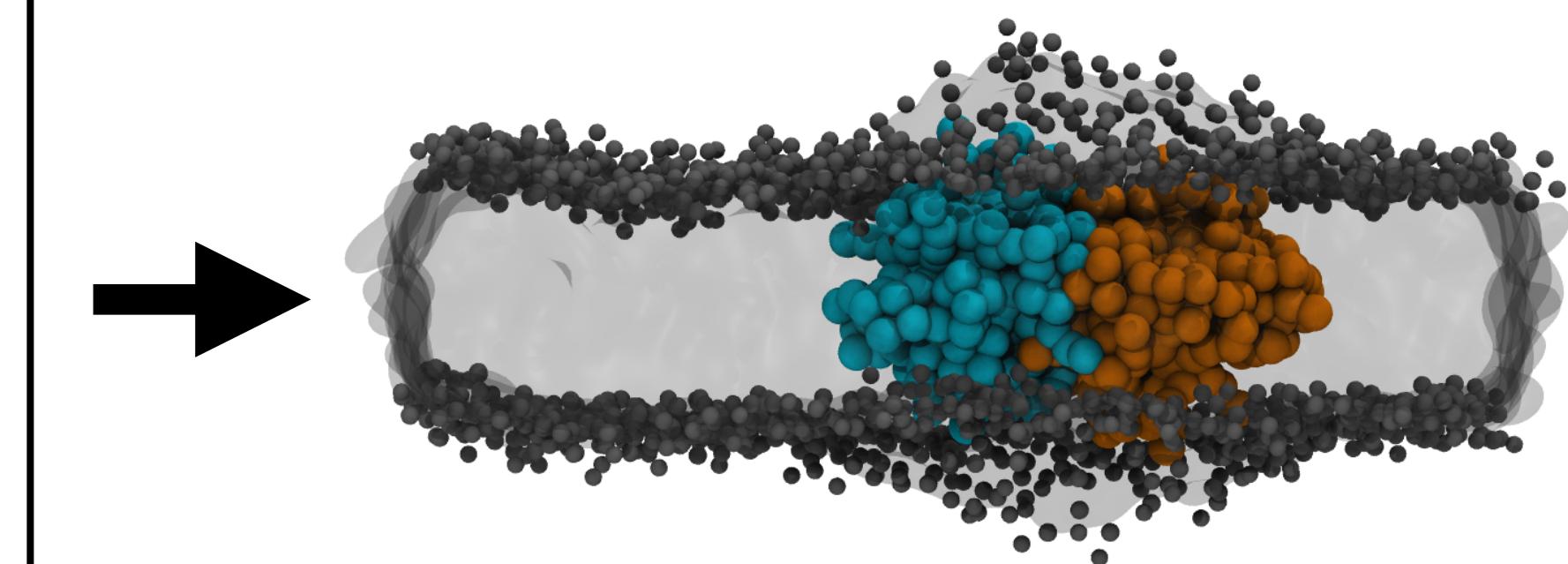
Tested 3 different gold models and compared to experimental data



Tested two possible mechanisms



Gold-Gold Interaction is the main driving mechanism for sticky “gold”



But...real gold is much stickier! We're working on it!

Acknowledgements



Jahmal Ennis Dr. Julie Griepenburg



Dr. Siewart-Jan Marrink

Dr. Paolo de Souza



RUTGERS

Office of Advanced Research
Computing

