Simulating Nanodisc Behavior using LAMMPS

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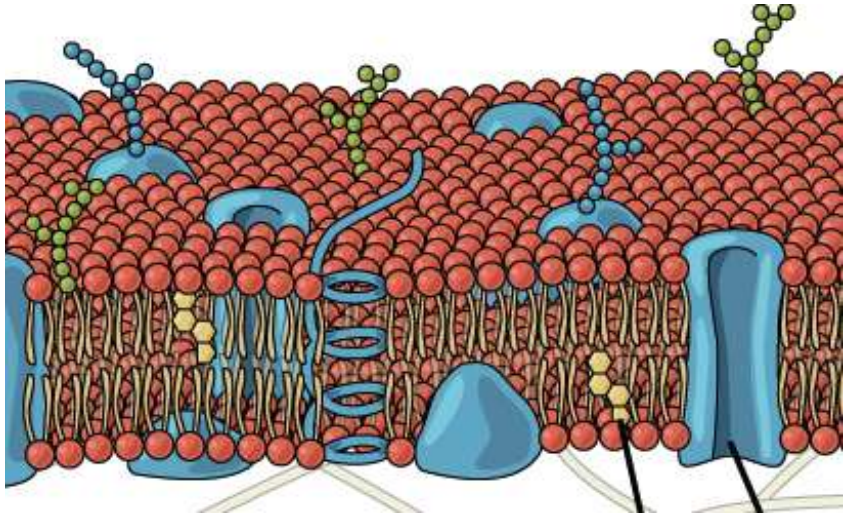
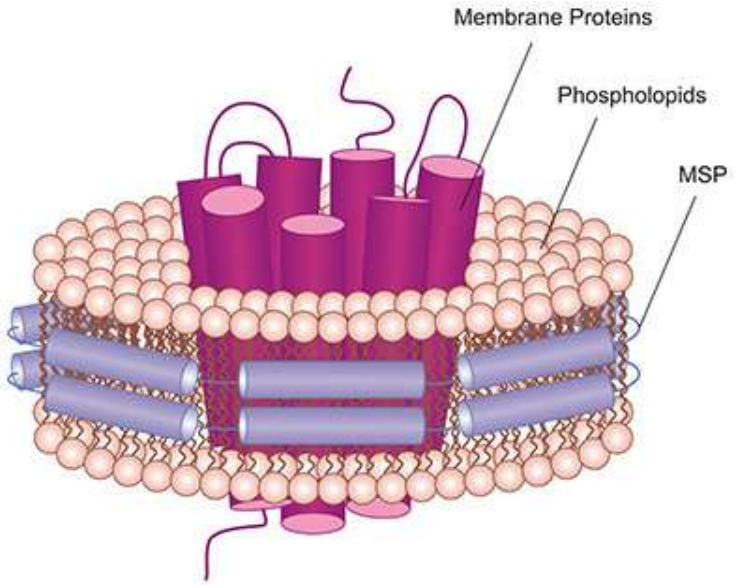
Alex Hernandez

Studying membrane proteins requires mimetic systems

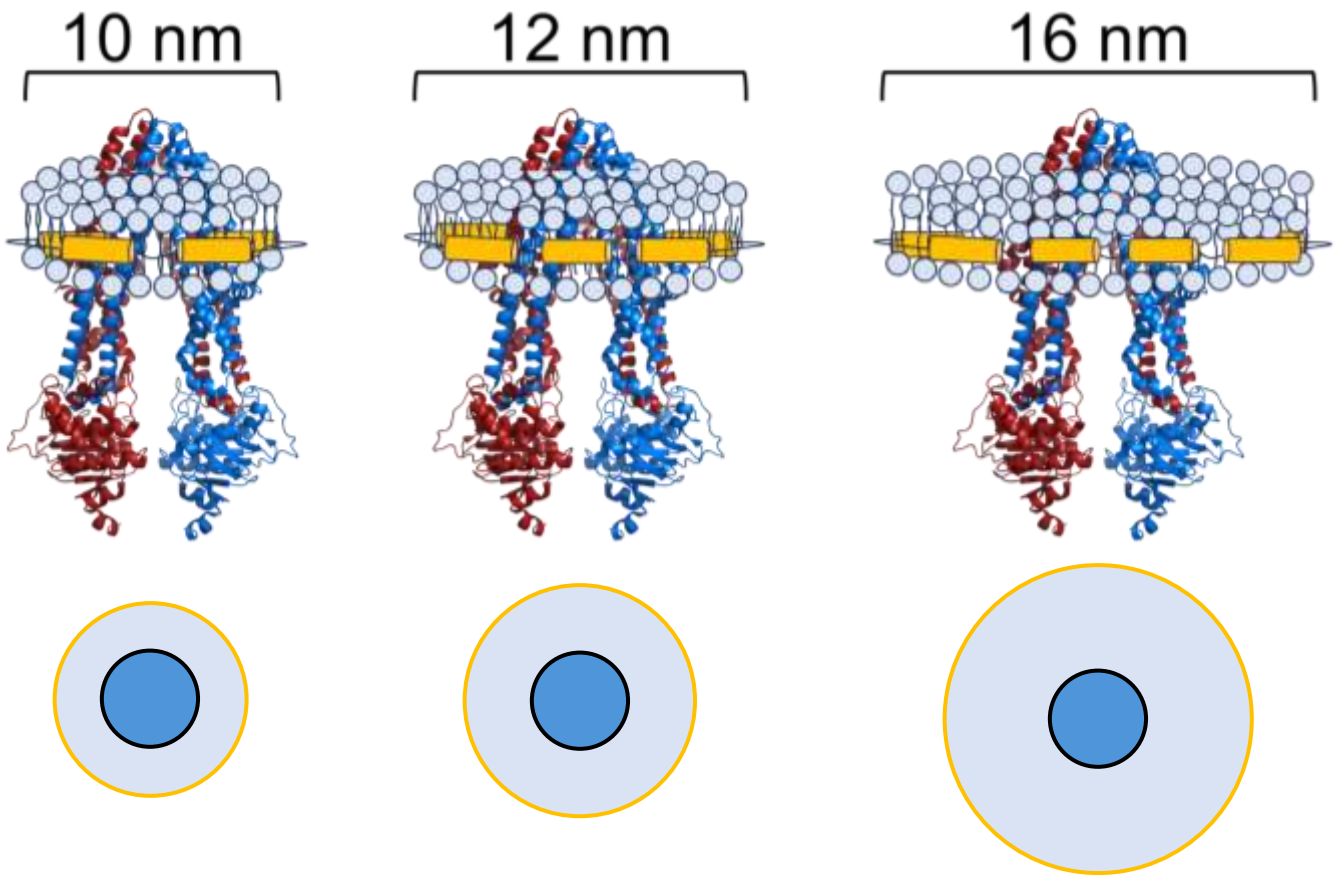


Native lipid-bilayer



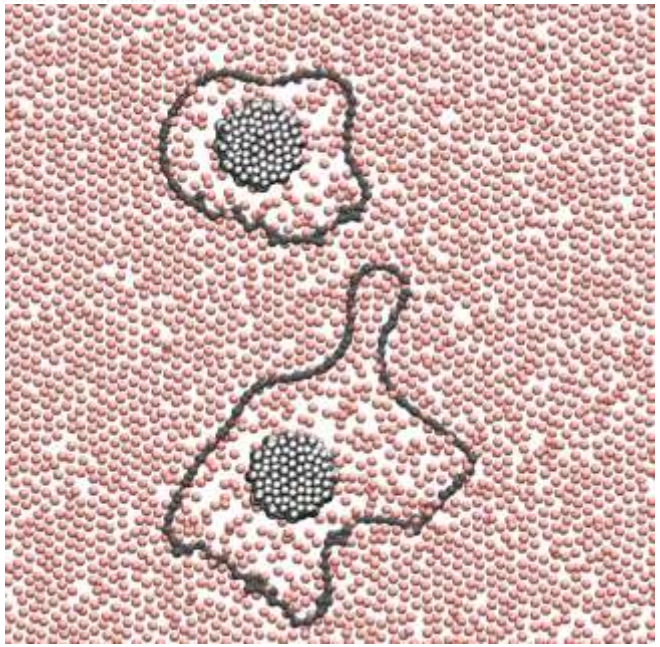
Mimetic lipid-bilayer
(Nanodisc)

Nanodisc size has been shown to affect protein behavior



Pre-transition effects mediate forces of assembly between transmembrane proteins

Shachi Katira[1†], Kranthi K Mandadapu[2,3†], Suriyanarayanan Vaikuntanathan[4†], Berend Smit[1,3,5], David Chandler[1*]



Can the Orderphobic Effect explain protein behavior in nanodisc?

Figure provided by Annabella Nouel Barreto.

Nouel Barreto, A., Cuello, L. G., & Zoghbi, M. E. (2025). https://doi.org/10.1002/1873-3468.15096

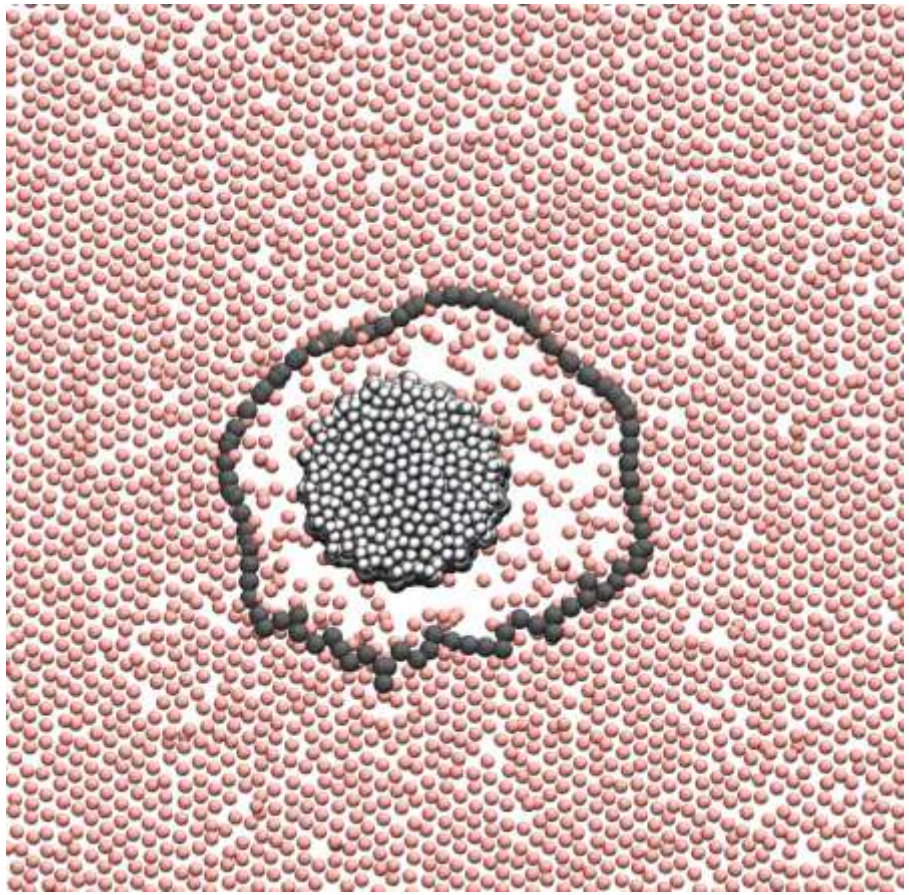
Project Outline

- Aim 1: Write a LAMMPS input script which will simulate the previously published "Orderphobic Effect"

- Aim 2: Introduce fixed "Orderphobic" boundaries which will simulate nanodiscs of variable sizes

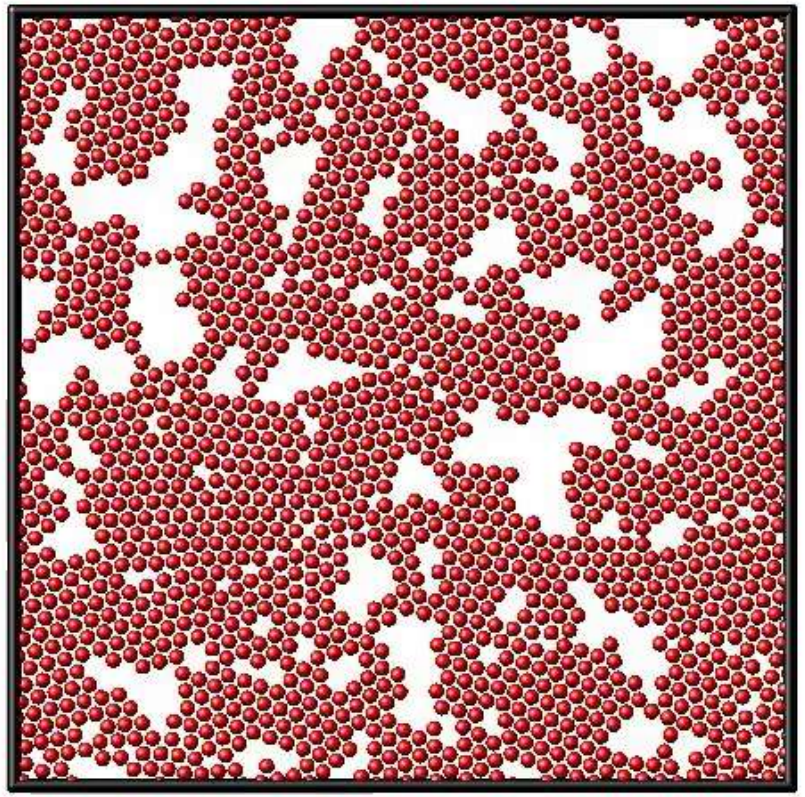
- Aim 3: Expand complexity to increase the accuracy of the simulated results

Aim 1 – The Orderphobic Effect



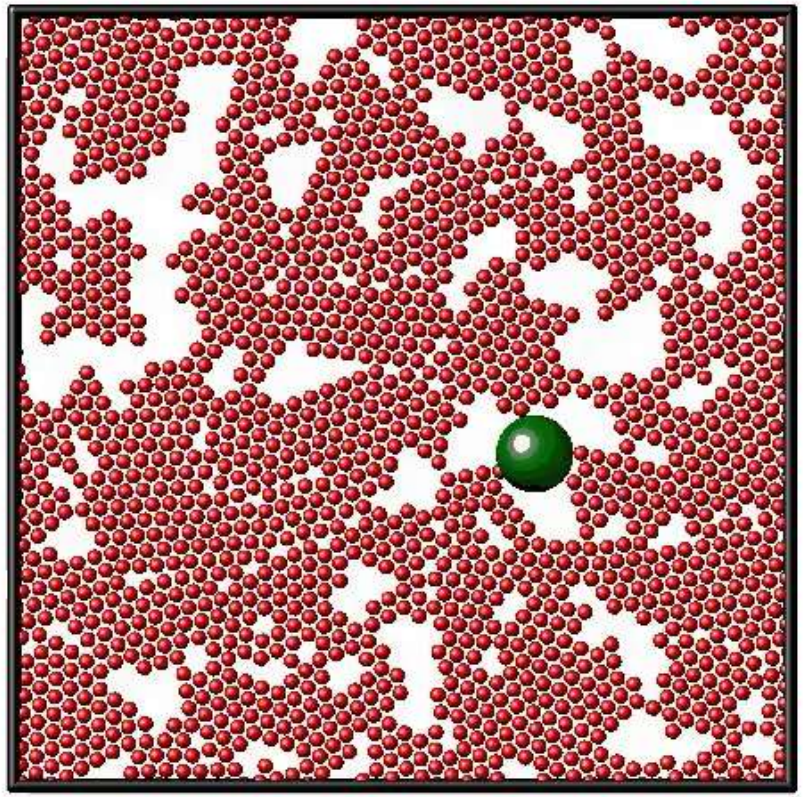
Aim 1 – The Orderphobic Effect

```
#Number of lipid particles.
variable npart  equal 1000
units           lj
dimension 2
atom_style      atomic
boundary        p p p

#Neighbor particles within a range of 6.
neighbor        6   bin
neigh_modify    every 1 delay 0 check yes

#Create 2D box region.
region box block -20 20 -20 20 -0.1 0.1

#Create simulation with two particles.
create_box 2 box

#Enforce 2D.
fix 2d  all enforce2d

#Create lipid particles at random positions.
create_atoms 1 random ${npart} 324523 safe

#Lipid particles have mass 1.
mass    1       1

#lj/cut interaction between lipids.
pair_style hybrid lj/cut 2.5
pair_coeff 1 1 lj/cut 1.0 1.0 2.5

#Velocity distribution of 1.0.
velocity all create 1.0  34234123 dist gaussian

#Energy minimization to remove overlapping particles.
minimize 1e-4 1e-4 1000 1000
reset_timestep 0

#Time step of integrator.
timestep        0.0005

#Number of steps to run.
run             5000000
```



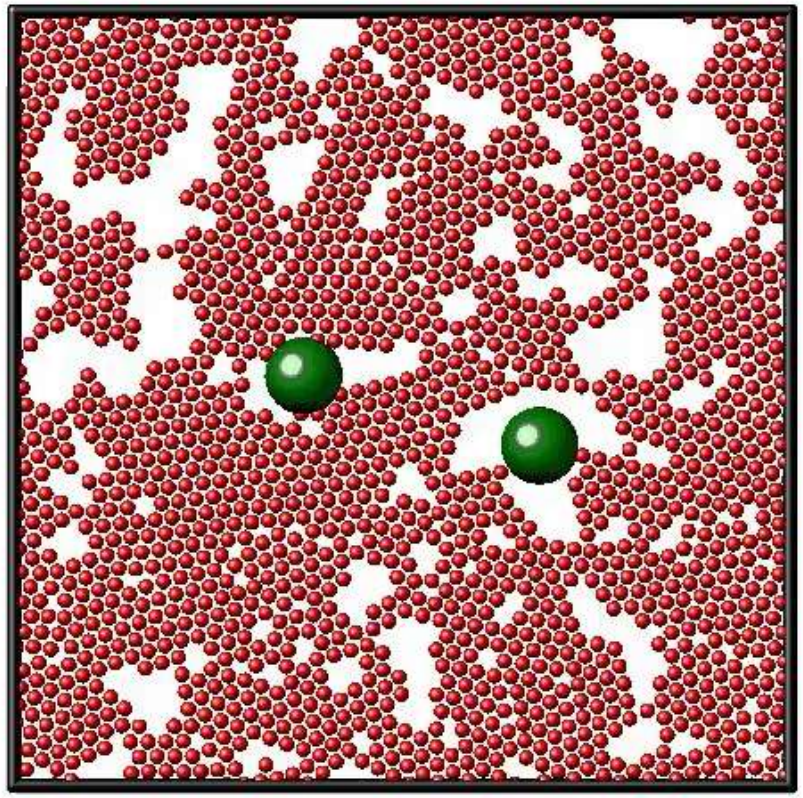
Aim 1 – The Orderphobic Effect

```
#Create lipid particles at random positions.
create_atoms 1 random ${npart} 324523 safe

#Create protein particle.
create_atoms 2 single 0 0 0

#Lipid particles have mass 1.  Protein particle has mass 40.
mass    1         1
mass    2         40

#Hybrid lj/cut and soft interactions between particles.
#Soft interactions used to create disorder in lipids.
pair_style hybrid lj/cut 2.5 soft 15.0
pair_coeff 1 1 lj/cut 1.0 1.0 2.5
pair_coeff 1 2 soft 1.0 8.0
pair_coeff 2 2 lj/cut 2.0 5.0 3.0
```



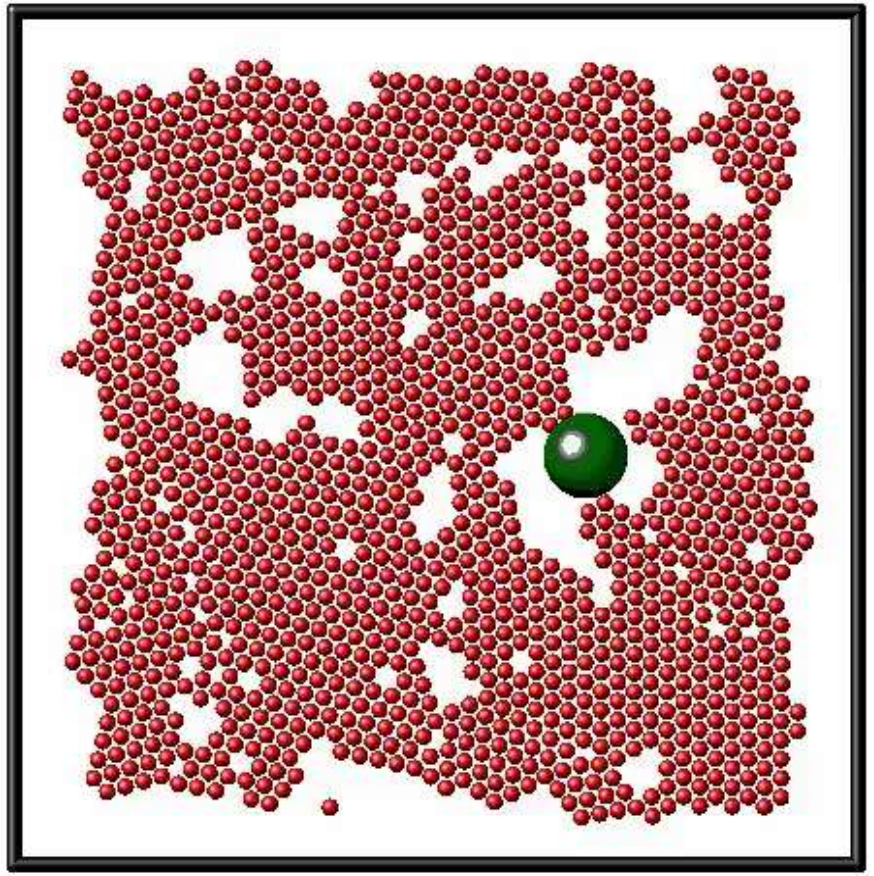
Aim 1 – The Orderphobic Effect

```
#Create lipid particles at random positions.
create_atoms 1 random ${npart} 324523 safe

#Create protein particle.
create_atoms 2 single 0 0 0

#Lipid particles have mass 1.  Protein particle has mass 40.
mass    1         1
mass    2         40

#Hybrid lj/cut and soft interactions between particles.
#Soft interactions used to create disorder in lipids.
pair_style hybrid lj/cut 2.5 soft 15.0
pair_coeff 1 1 lj/cut 1.0 1.0 2.5
pair_coeff 1 2 soft 1.0 8.0
pair_coeff 2 2 lj/cut 2.0 5.0 3.0
```

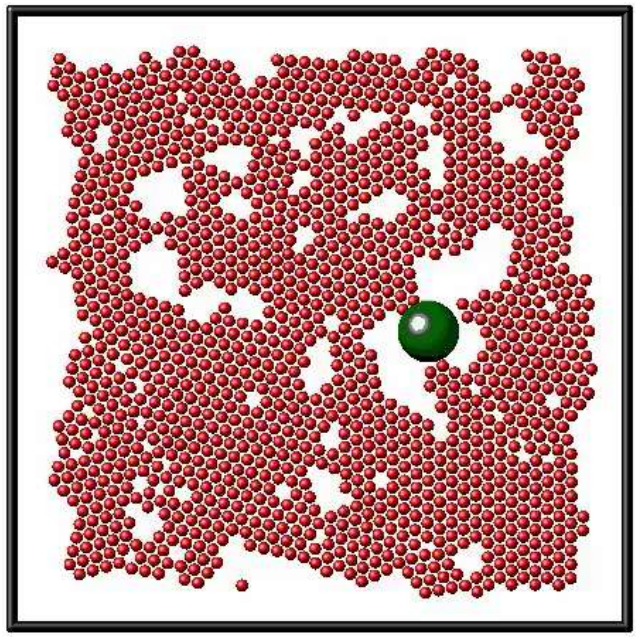


Aim 2 – Introducing the Nanodisc

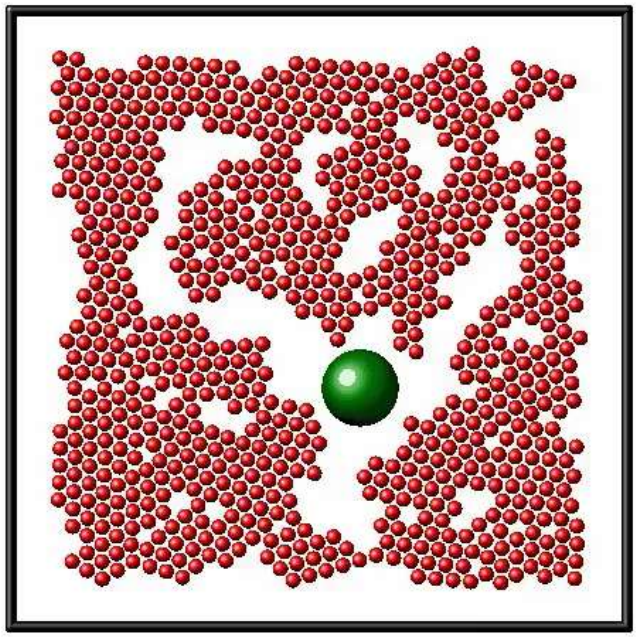
```
#Number of lipid particles.
variable npart  equal 1000
units           lj
dimension 2
atom_style      atomic
boundary        f f p

#Create 2D box region for simulation.
#Creates 2D safe region to place particles.
region box block -20 20 -20 20 -0.1 0.1
region safe block -18 18 -18 18 -0.1 0.1

#Create fixed boundaries with soft repulsion.
fix wallx  all wall/lj126 xlo EDGE 0.05 3.0 5.5
fix wallx2 all wall/lj126 xhi EDGE 0.05 3.0 5.5
fix wally  all wall/lj126 ylo EDGE 0.05 3.0 5.5
fix wally2 all wall/lj126 yhi EDGE 0.05 3.0 5.5
```



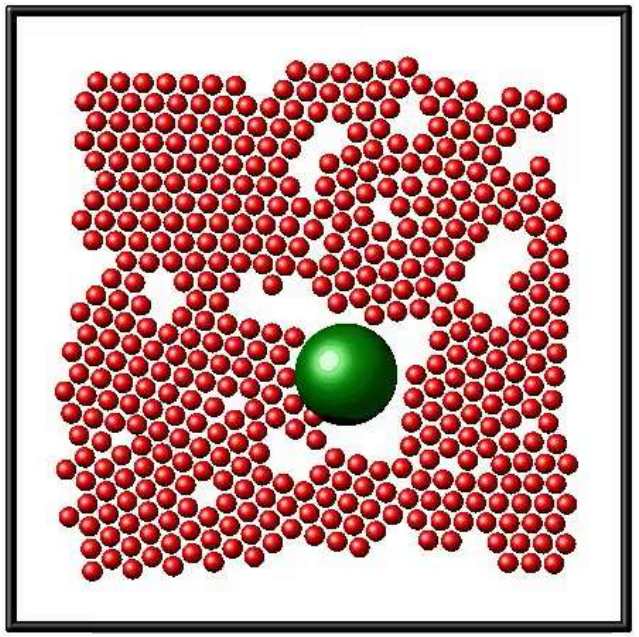
Aim 2 – Introducing the Nanodisc



25x25

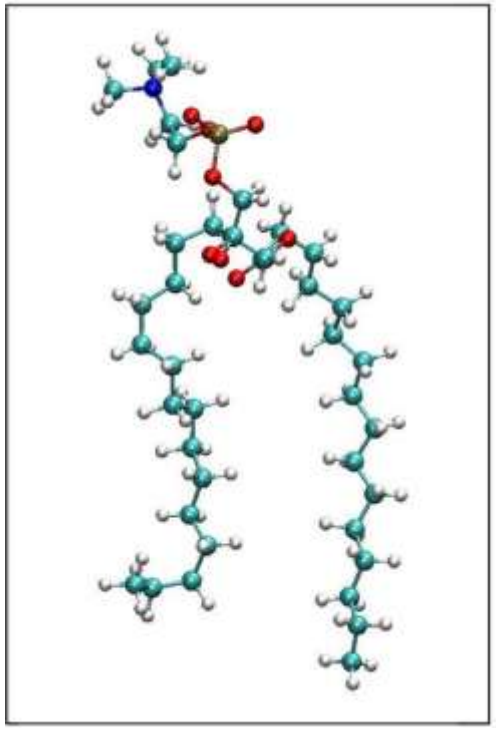


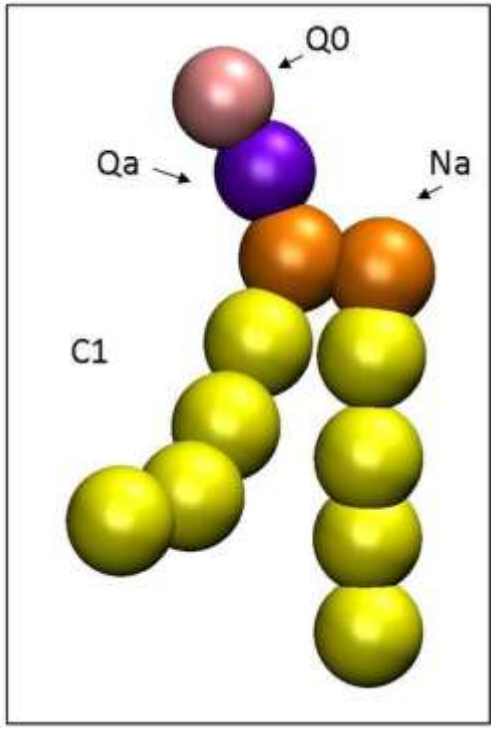
20x20

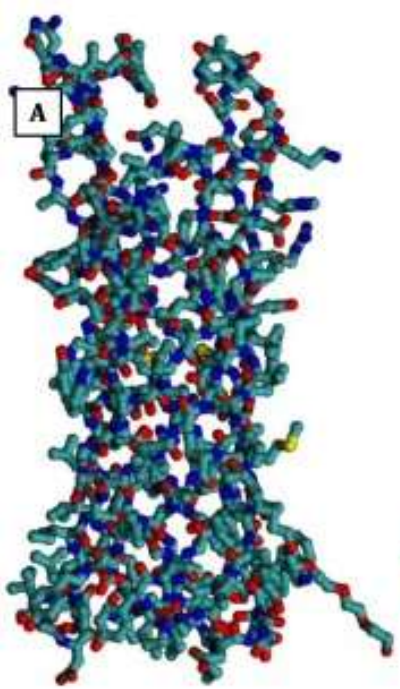


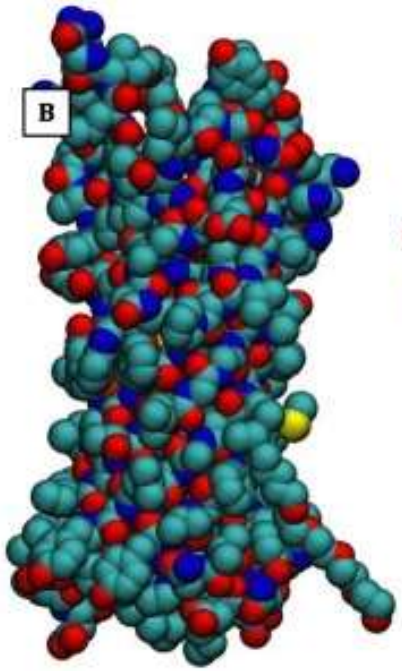
15x15

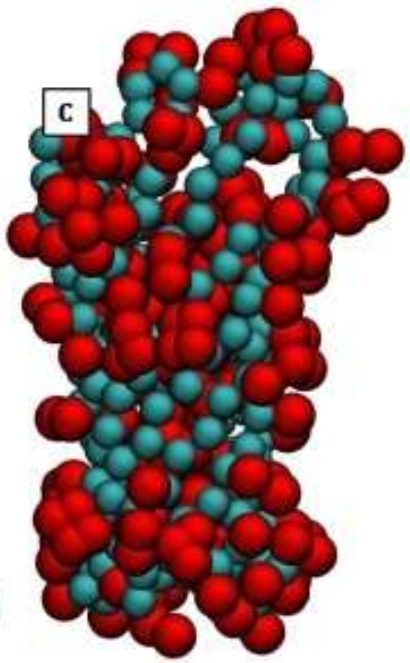
Aim 3 – Increasing Complexity



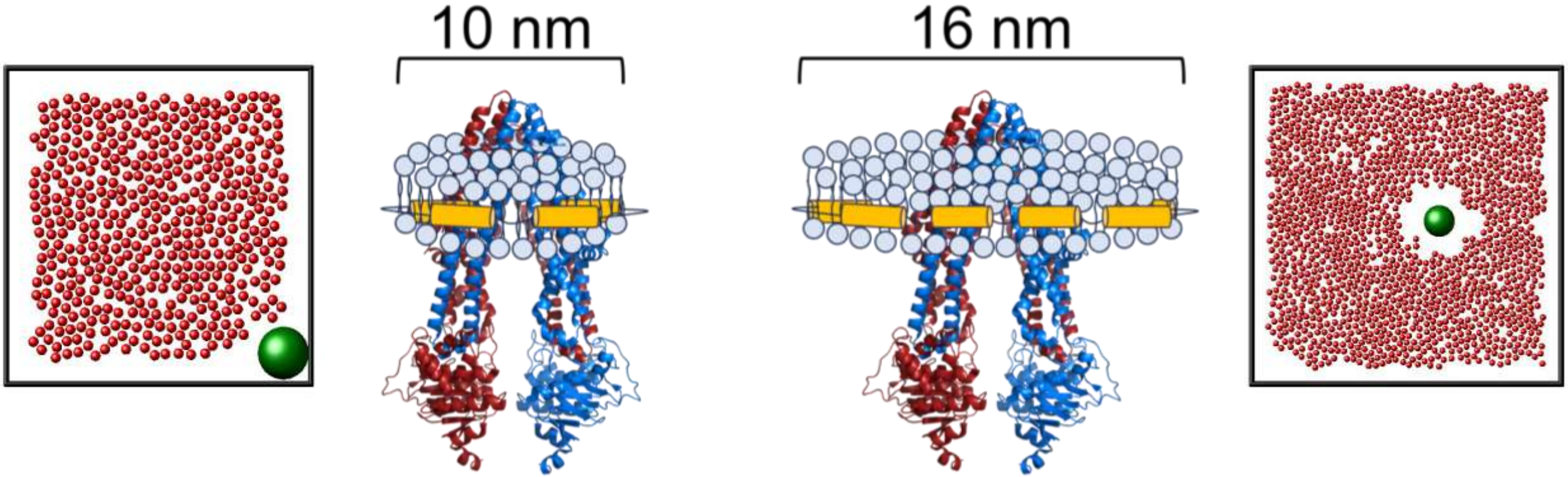








Conclusion



The Orderphobic Effect may result in undesirable protein aggregation in small nanodiscs

Future Directions

- Switch to GROMACS
- Increase complexity of membrane composition
- Write Python script to quantify simulation results