Membrane Simulations

Wonpil Im
MMTSB/CTBP
2006 Summer Workshop

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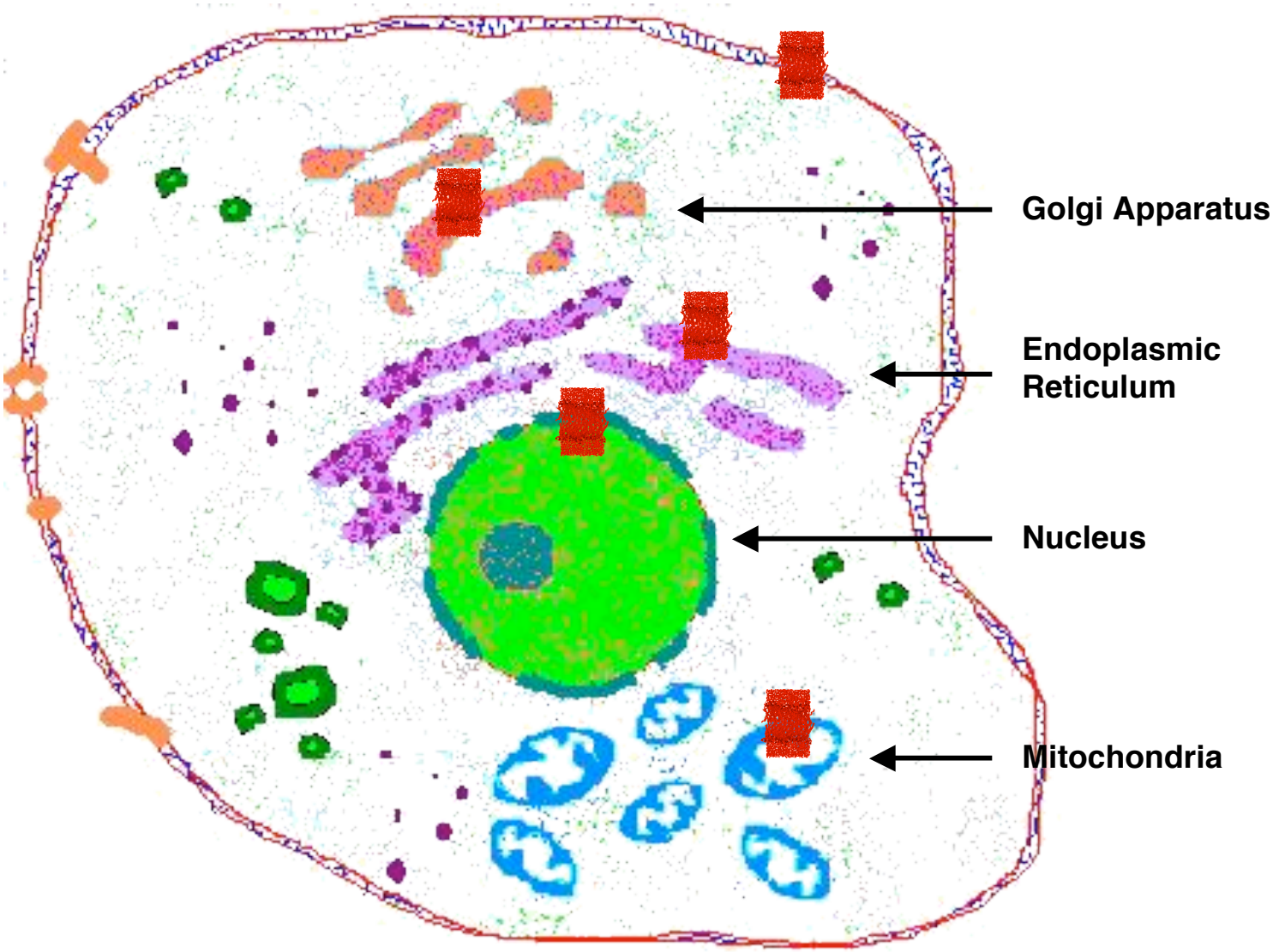
Why Membrane Proteins?



http://www.usd.edu/~bgoodman/ReviewFrames.htm

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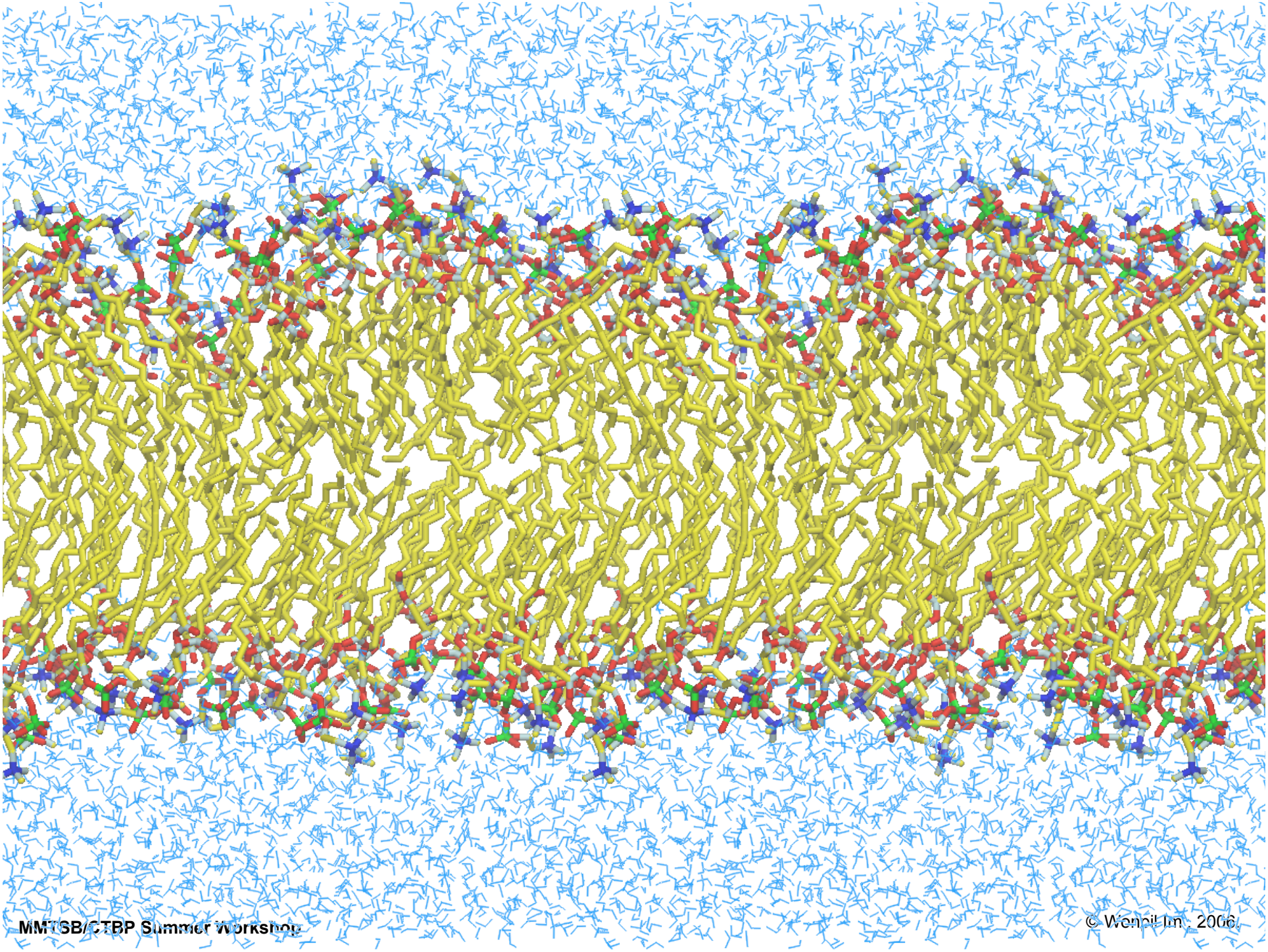
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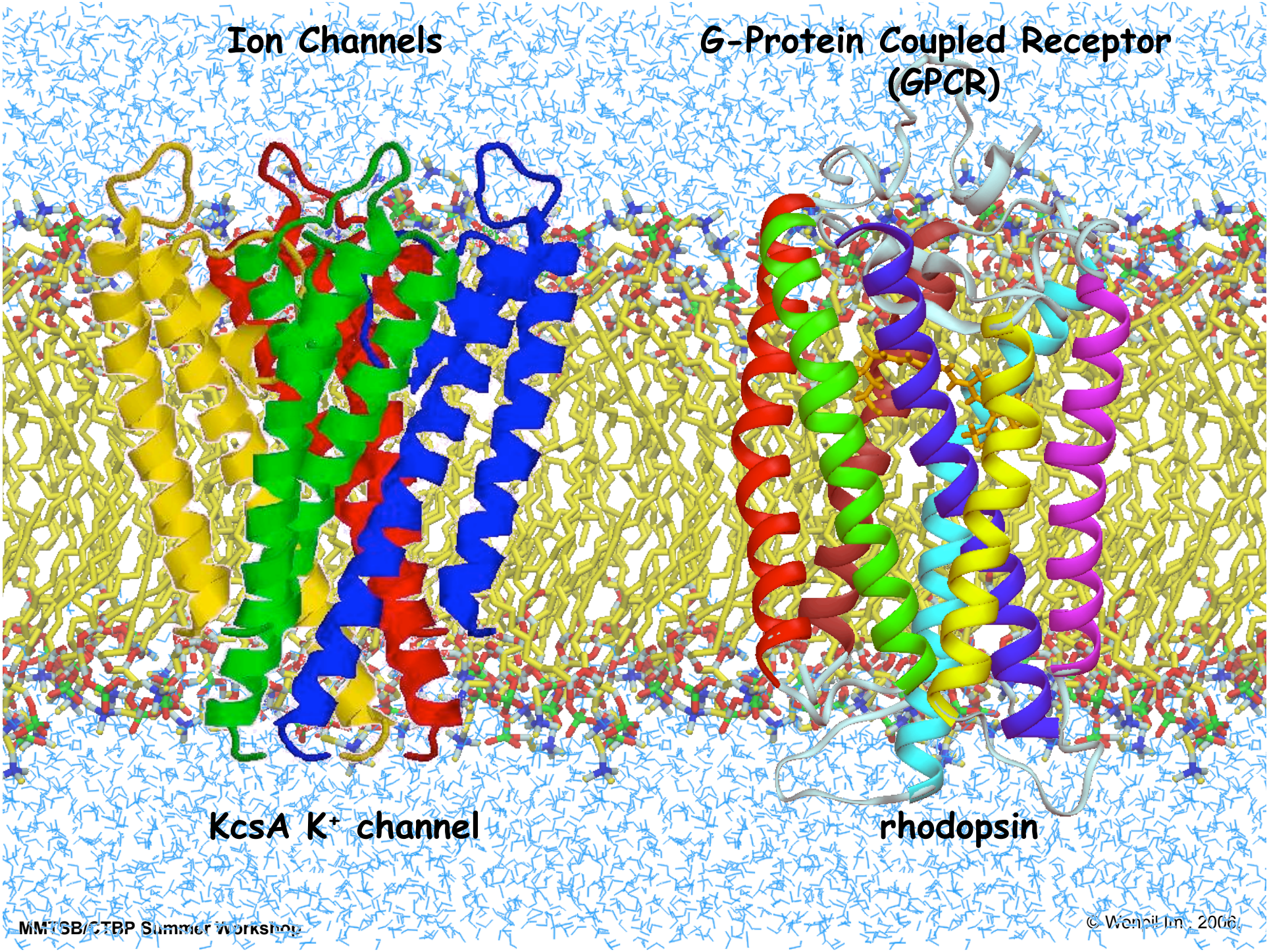
Ion Channels
G-Protein Coupled Receptor (GPCR)
KcsA K+ channel
rhodopsin
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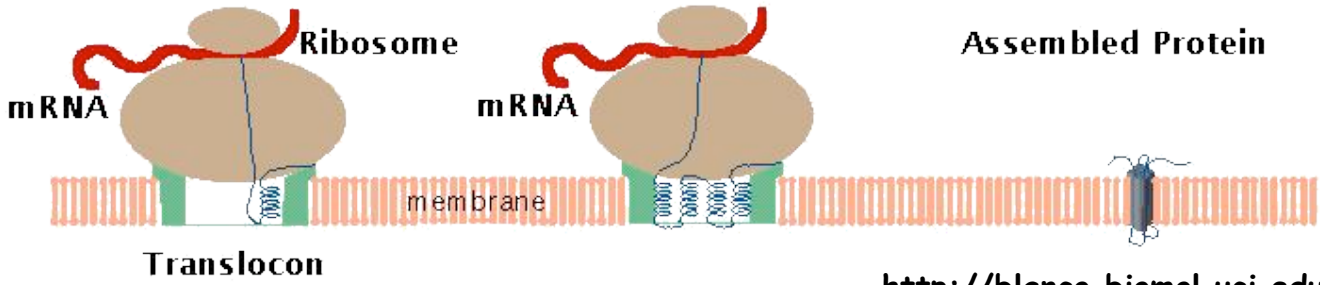
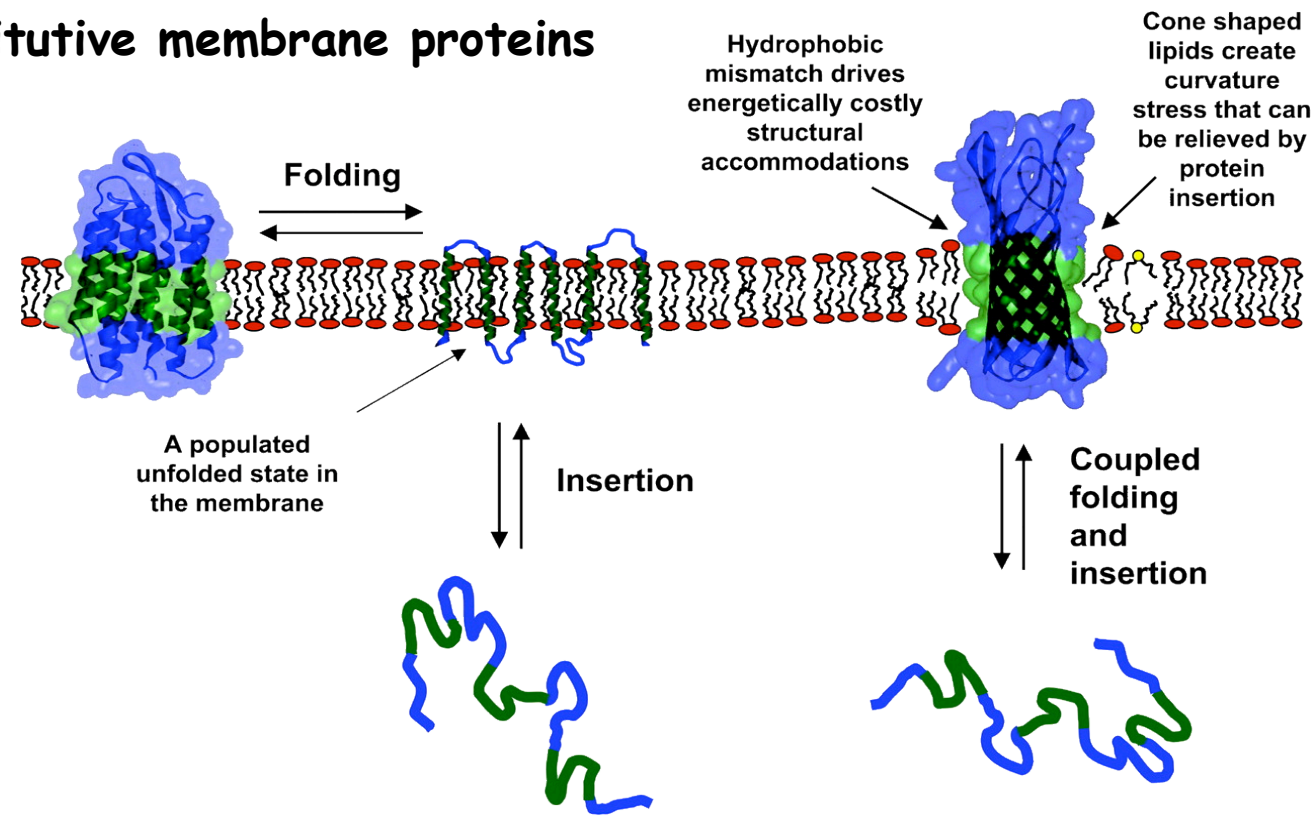
constitutive membrane proteins



http://blanco.biomol.uci.edu/mp_assembly.html

non-constitutive membrane proteins



Bowie (2004) Proc. Natl. Acad. Sci. USA

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Why Membrane Proteins?

- Biologically very important roles such as signal transduction.
- About 30% of all proteins encoded in known genome.
- Its folding and stability are governed by unique hydrophobic and hydrophilic membrane environment.
- Membrane environment is essential, but it makes experimental studies very difficult.

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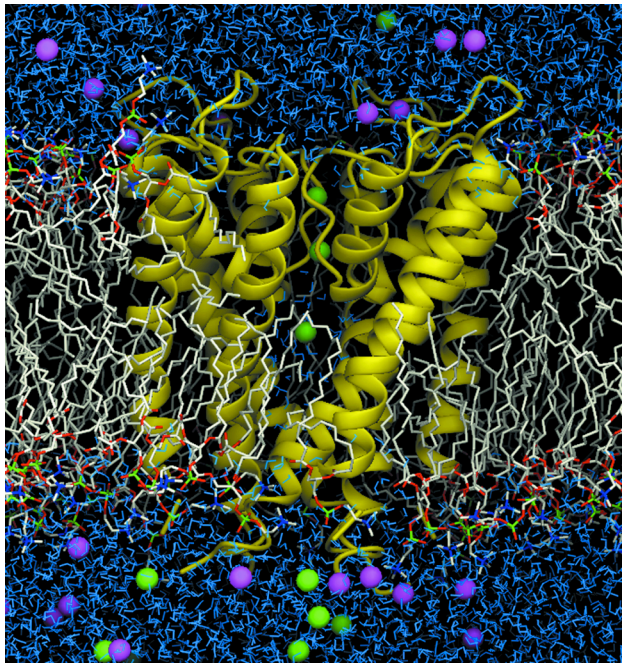

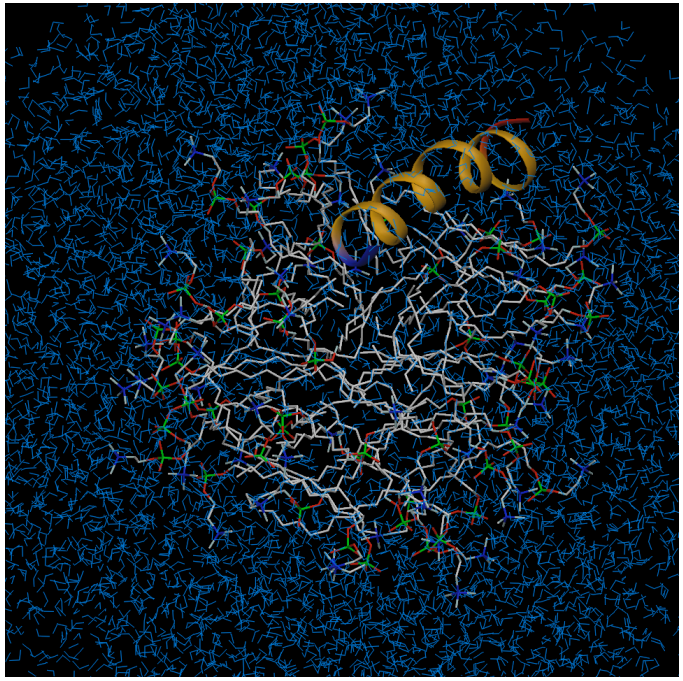

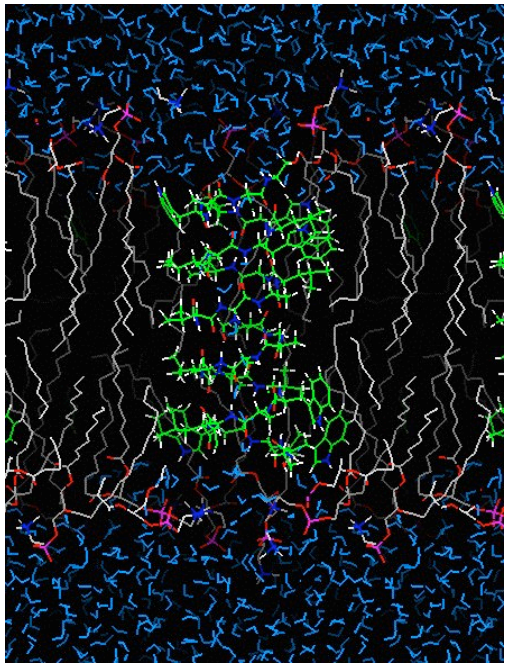

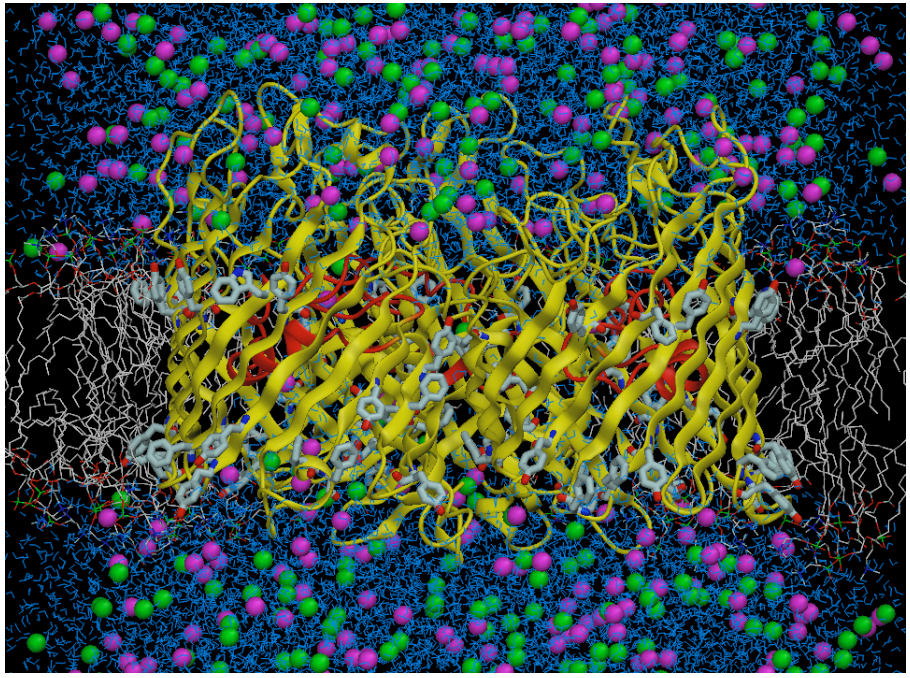

CHARMM Membrane Force Fields

Topology Files:

top_all27_lipid.rtf,
top_all27_prot_lipid.rtf,
top_all27_na_lipid.rtf

toppar_all27_lipid_cholesterol.str

Parameter Files:

par_all27_lipid.prm,
par_all27_prot_lipid.prm,
par_all27_na_lipid.prm

```
LPPC     0.00 ! deoxylysophosphatidylcholine
DLPE     0.00 ! 1,2 dilauroyl-DL-Phosphatidylethanolamine
DMPC     0.00 ! 1,2 dimiristoyl-SN-glycero-3-Phosphorylcholine
POPC     0.00 ! 1-palmytoil-2-oleoyl-sn-glycero-3-Phosphatidylcholine
POPE     0.00 ! 1-palmytoil-2-oleoyl-sn-glycero-3-Phosphatidylethanolamine
PCGL     0.00 ! glycerolphosphorylcholine
PALM    -1.00 ! palmitate
OLEO    -1.00 ! oleic acid
DHA     -1.00 ! docosahexaenoic acid
STEA    -1.00 ! stearoyl acid chain
SDS     -1.00 ! dodecylsulphate
```


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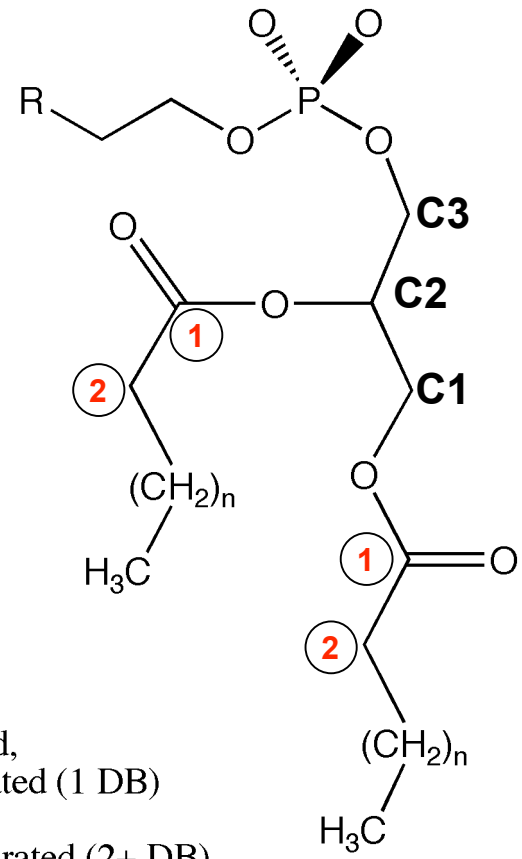
CHARMM Membrane Force Fields

LPPC	0.00 !	deoxylysophosphatidylcholine
DMPC	0.00 !	1,2 dimiristoyl-SN-glycero-3-Phosphorylcholine
POPC	0.00 !	1-palmytoil-2-oleoyl-sn-glycero-3 Phosphatidylcholine
PCGL	0.00 !	glycerolphosphorylcholine
POPE	0.00 !	1-palmytoil-2-oleoyl-sn-glycero-3-Phosphatidylethanolamine
DLPE	0.00 !	1,2 dilauroyl-DL-Phosphatidylethanolamine
PALM	-1.00 !	palmitate
OLEO	-1.00 !	oleic acid
DHA	-1.00 !	docosahexaenoic acid
STEA	-1.00 !	stearoyl acid chain
SDS	-1.00 !	dodecylsulphate

R = choline, serine ethanolamine



saturated, unsaturated (1 DB) and polysaturated (2+ DB) hydrocarbon chains

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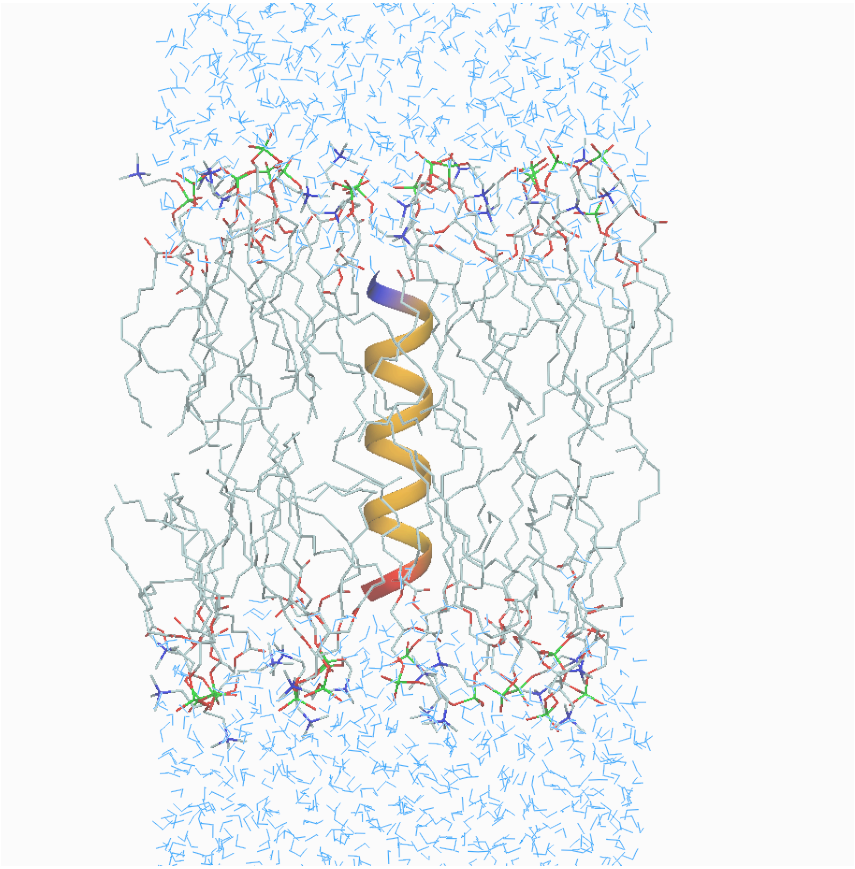
How to Assemble and Simulate?



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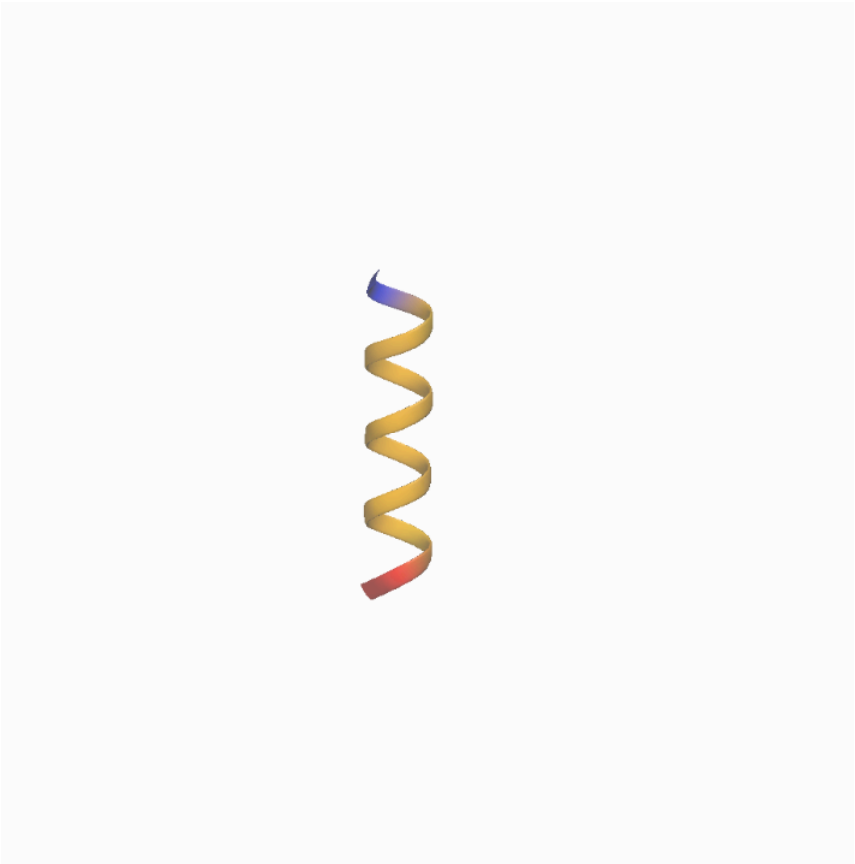
How to Assemble and Simulate?



Assembly of uncorrelated pieces!

↓

Equlibration, Equilibration, and Equilbration

Two Ensembles of Interest

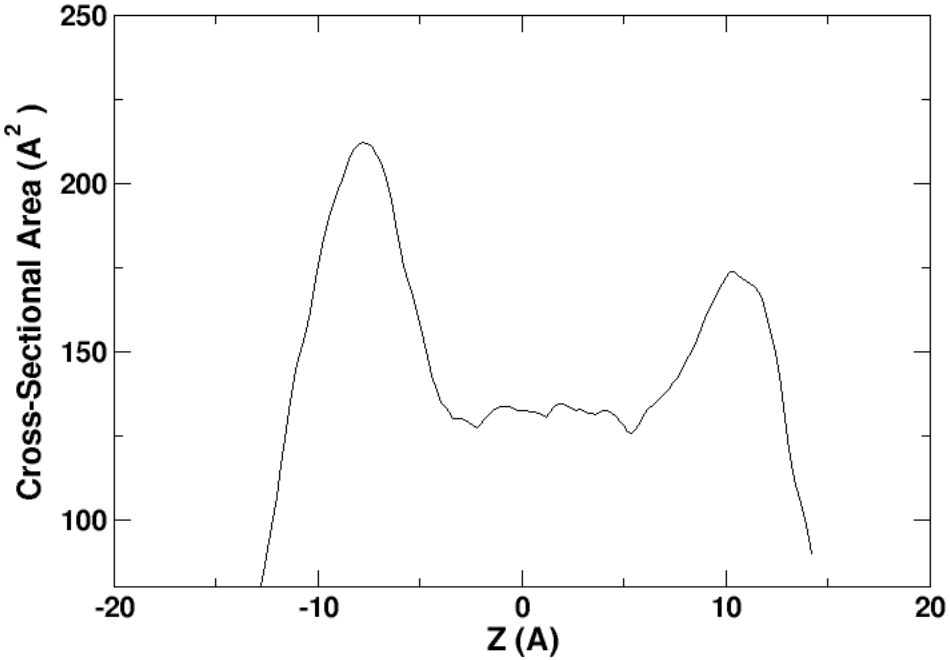
NPAT : constant pressure
surface area (along *XY*)
temperature

NPγT : constant pressure
surface tension
temperature

Zhang et. (1995) JCP 103:10252

©Wolynes, 2008.

Membrane Builder: Step 1



System Size along *XY*

Lipid Surface Area

60.7 Å^2 / DMPC @ 303 K
64.0 Å^2 / DPPC @ 323 K
68.3 Å^2 / POPC @ 303 K

Protein Surface Area

193 Å^2 =(173.7 Å^2 +212.2 Å^2) / 2

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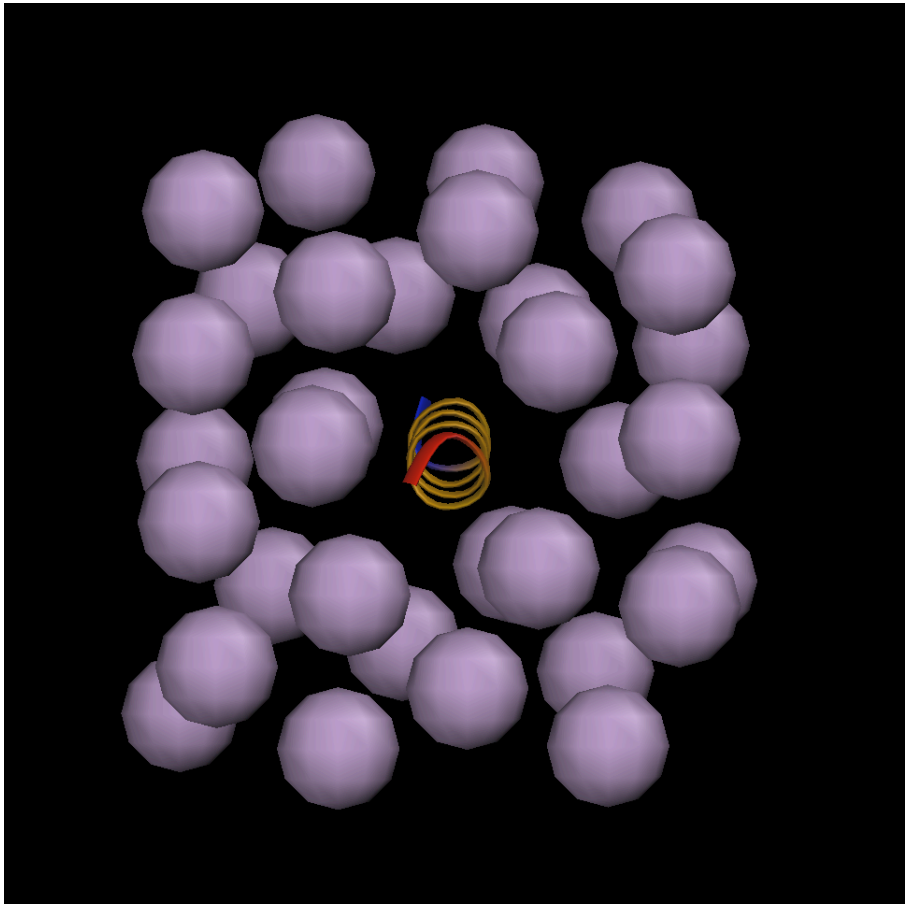
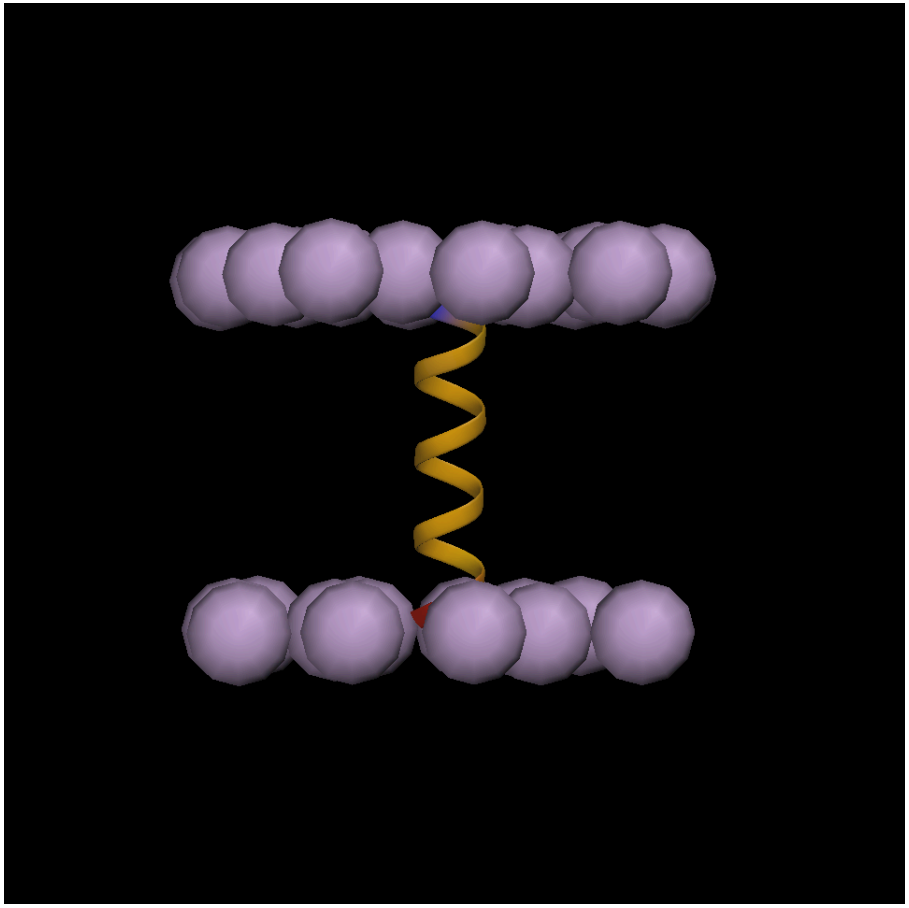
Membrane Builder: Step 2





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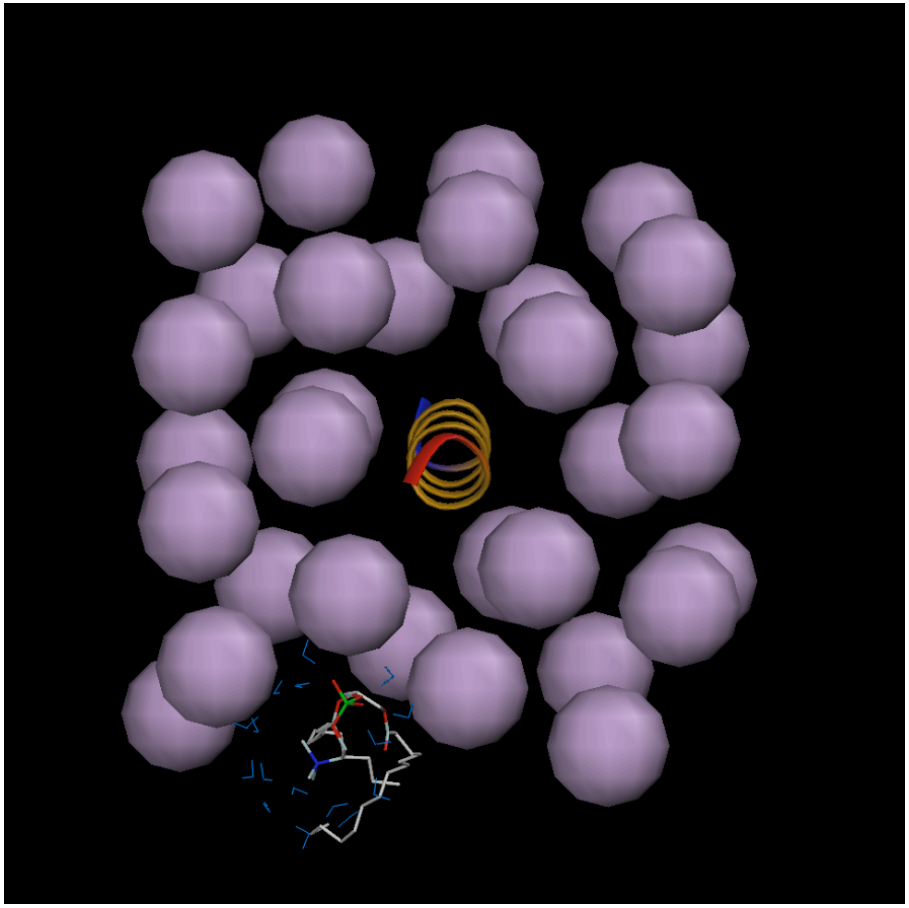
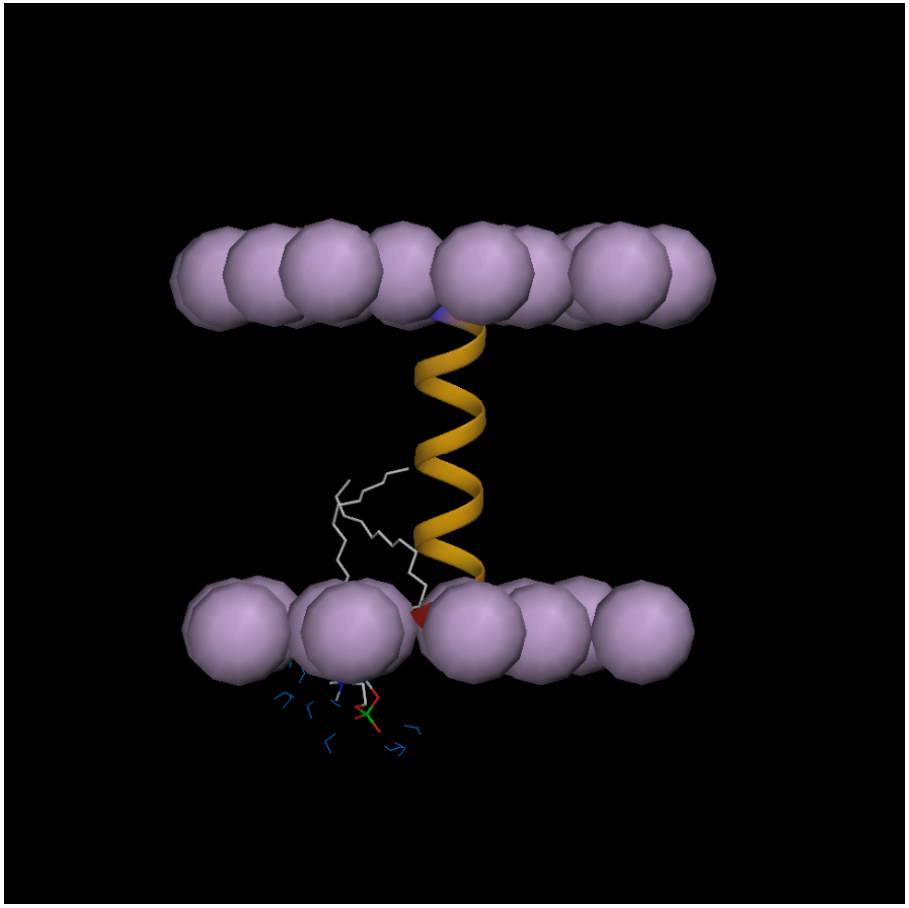
Membrane Builder: Step 3





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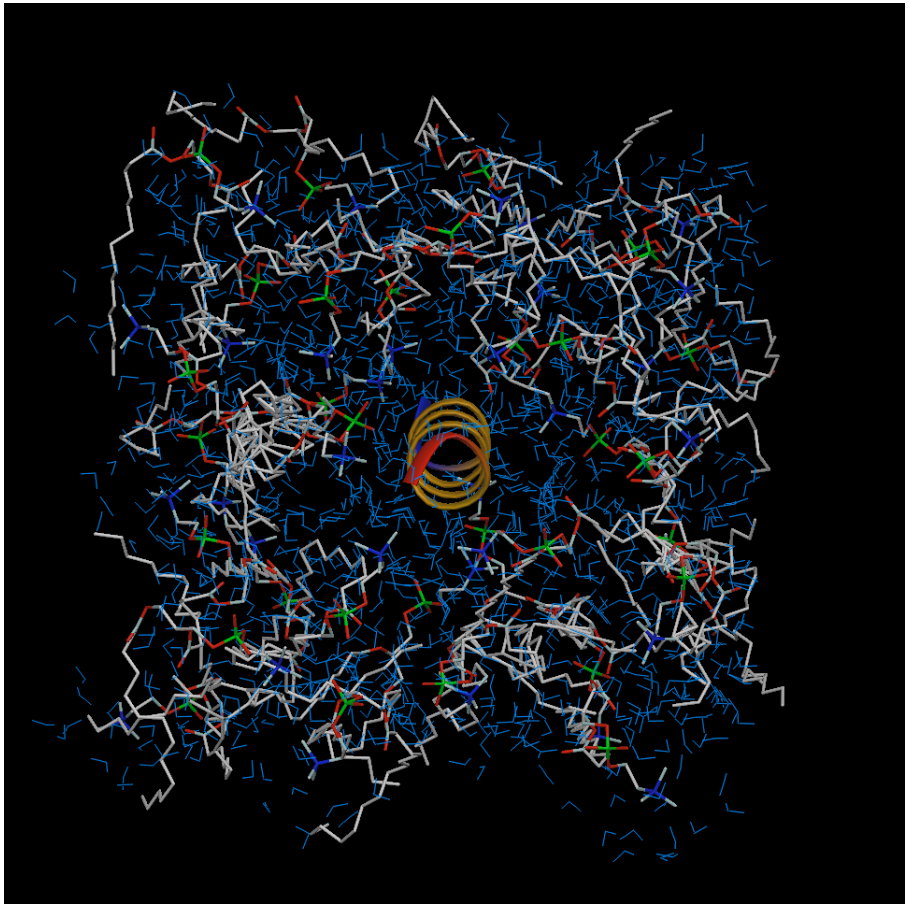
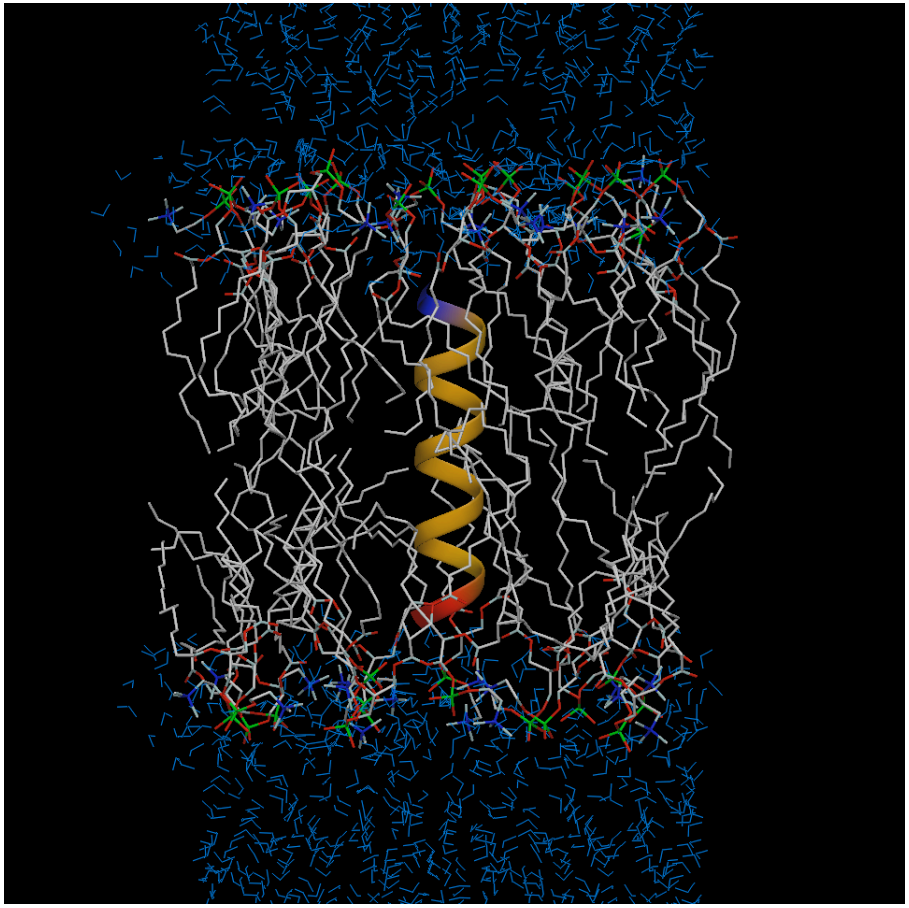
Membrane Builder: Step 4





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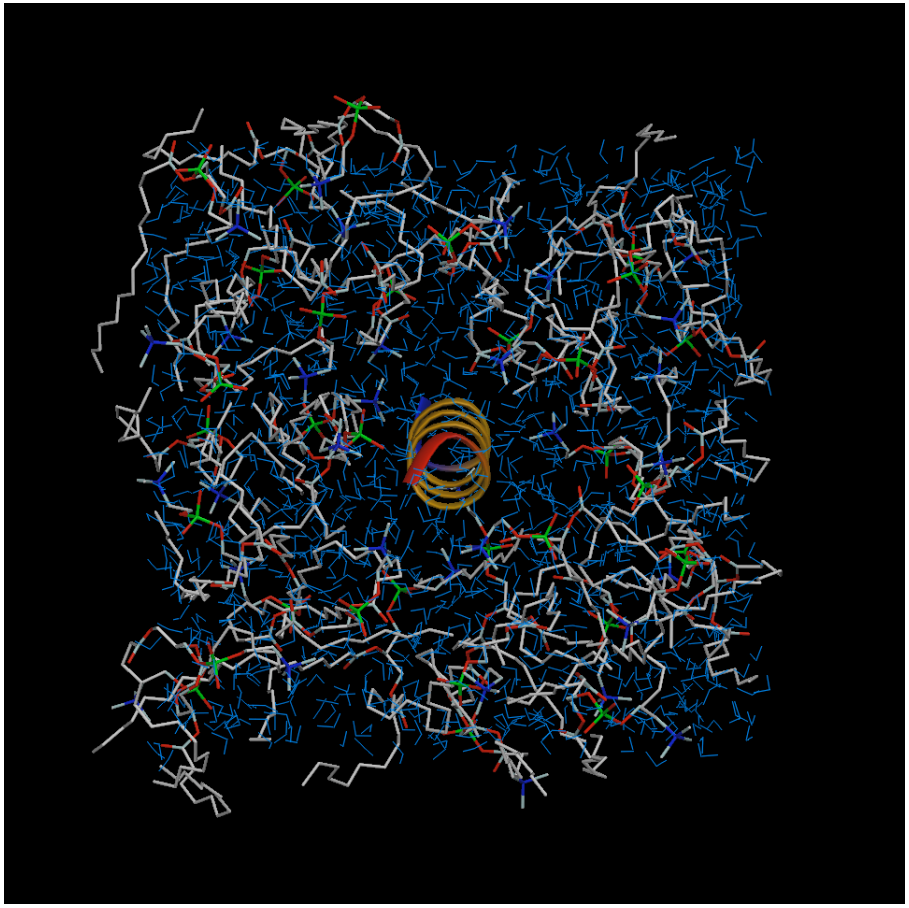
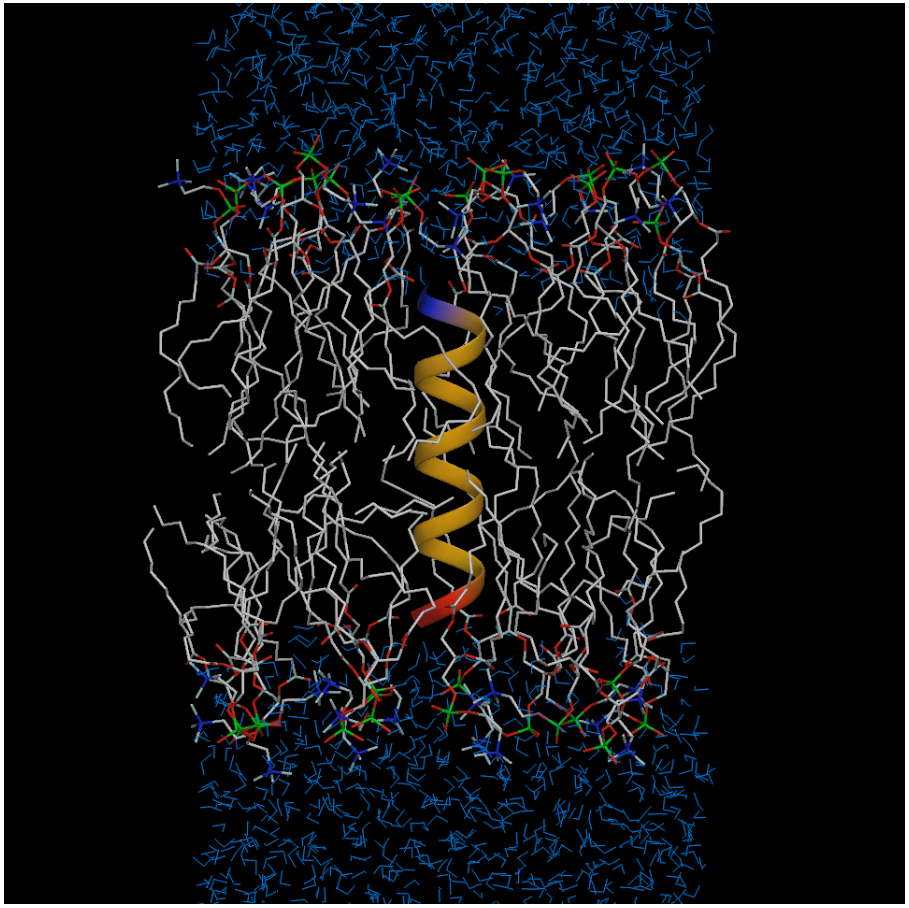
Membrane Builder: Step 5





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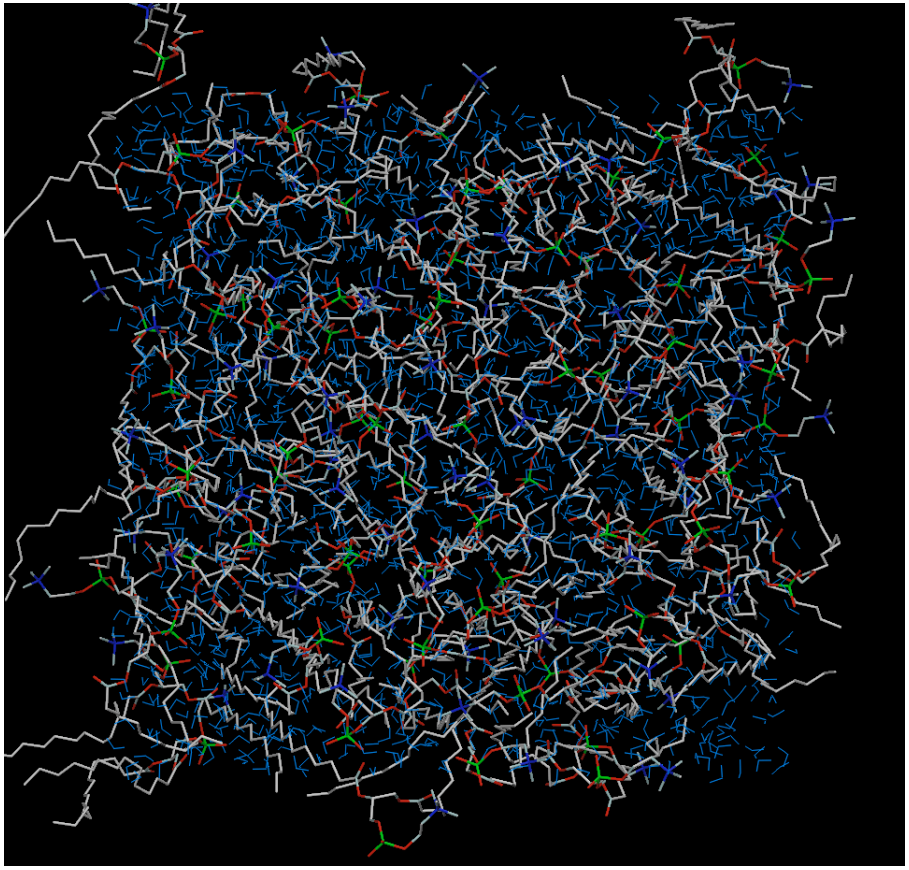
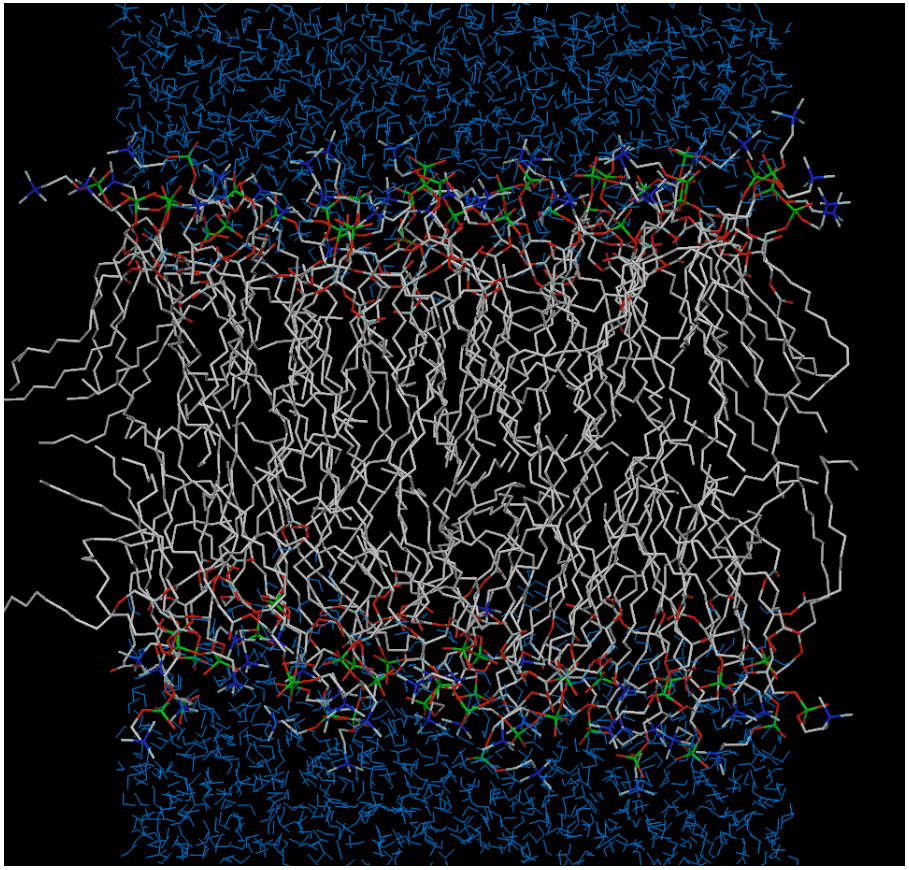
Insertion Method: Step 1





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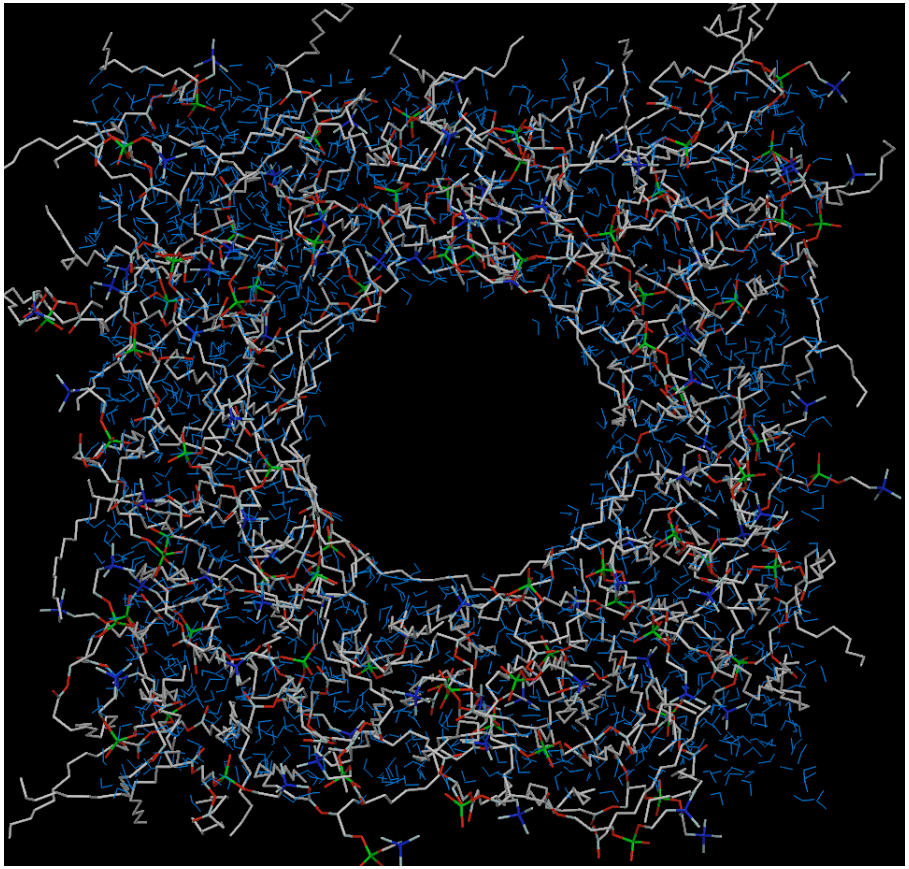
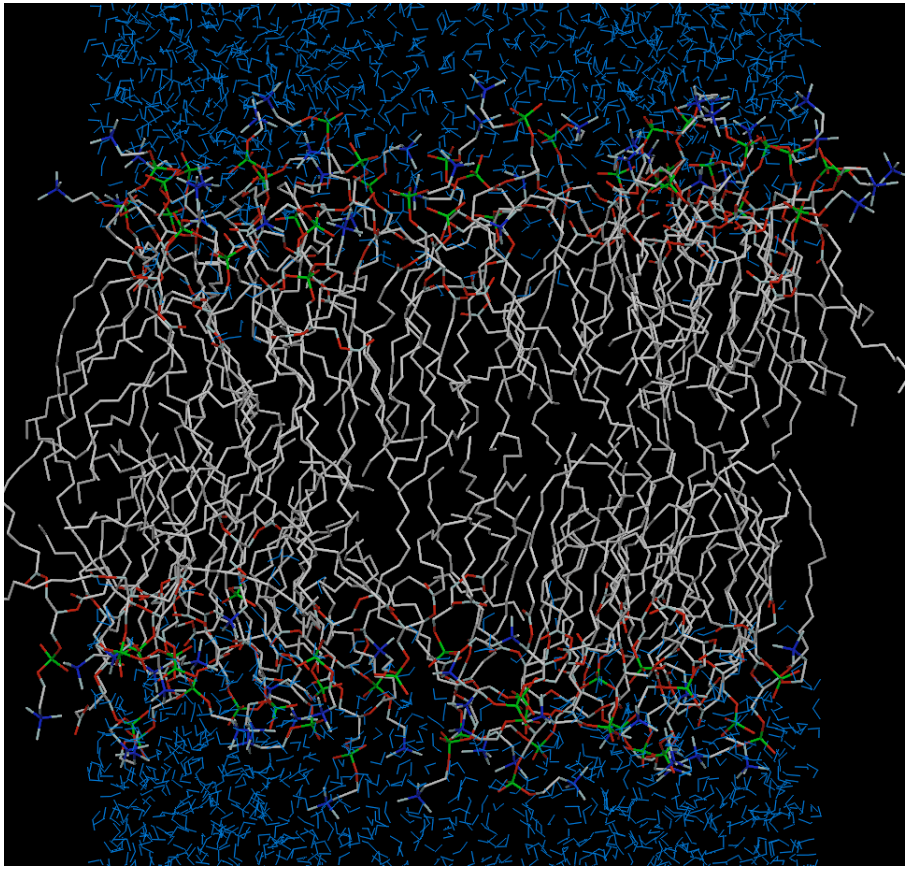
Insertion Method: Step 2





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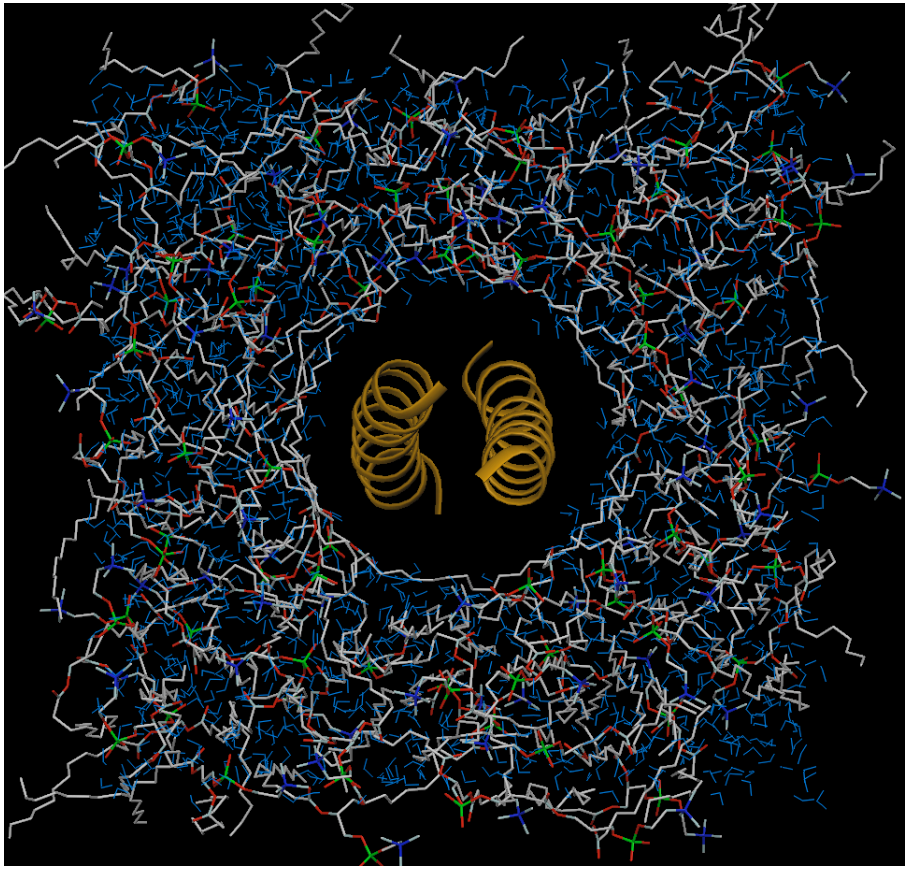
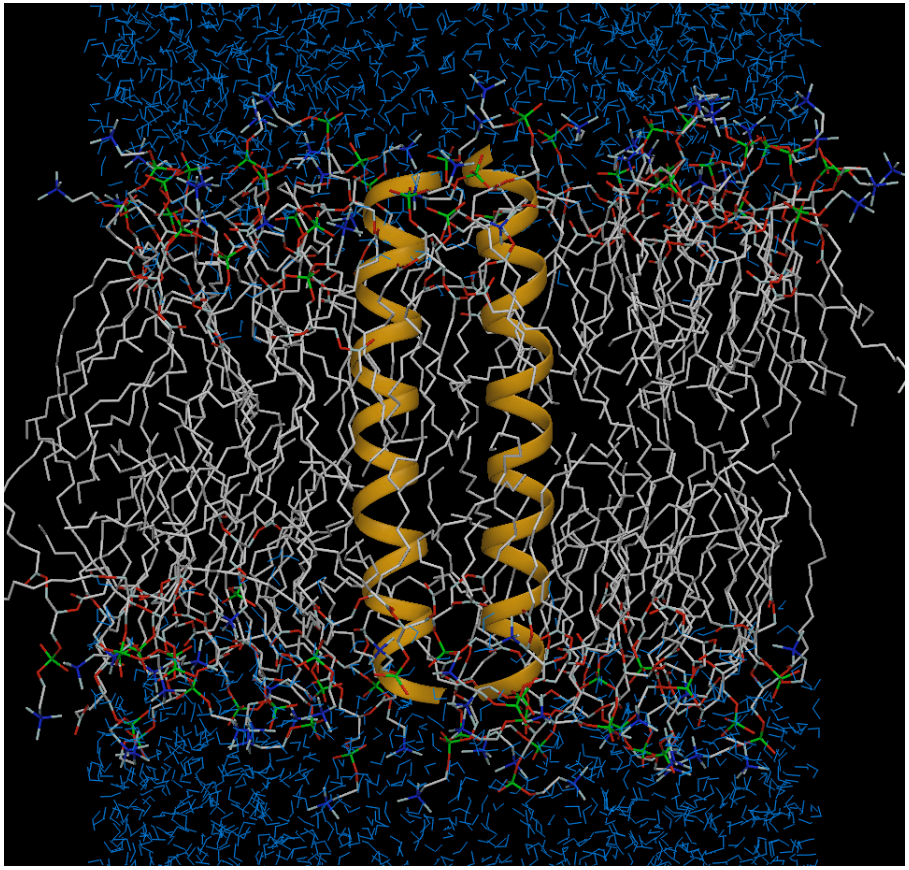
Insertion Method: Step 3





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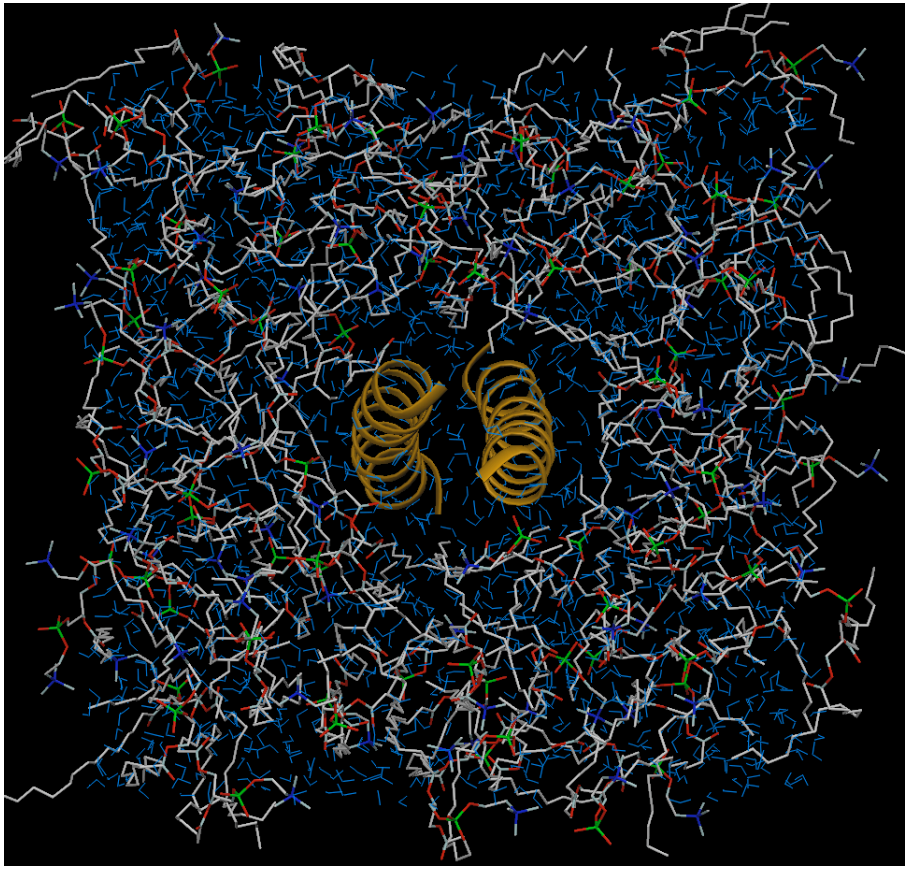
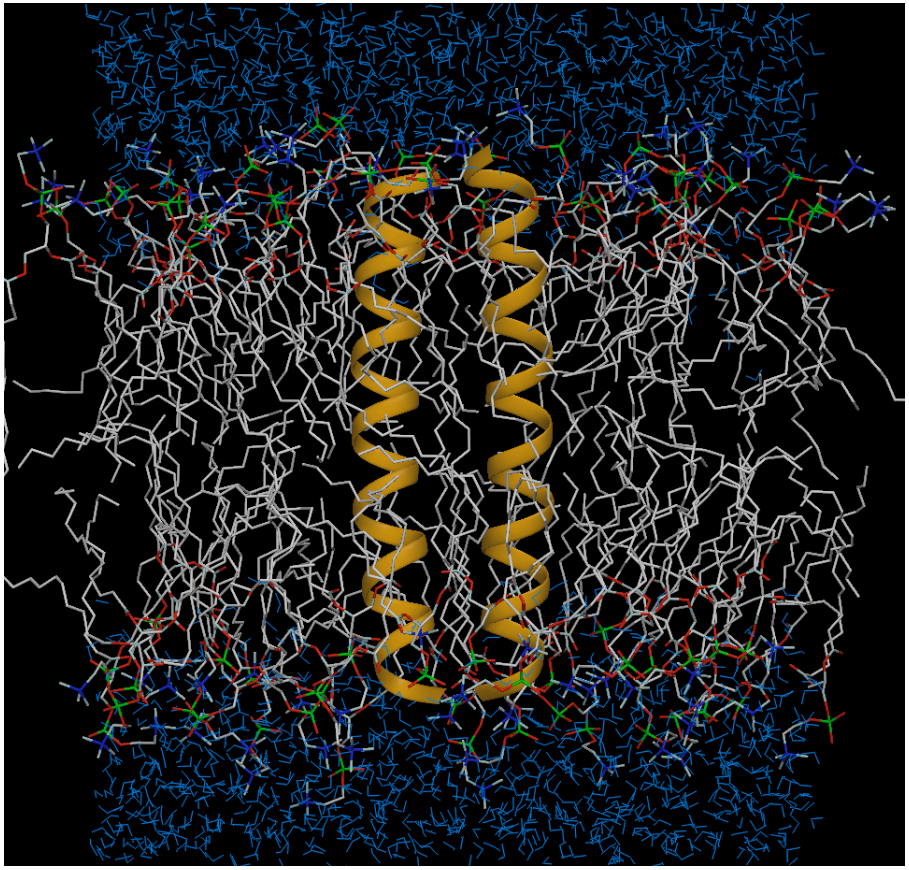
Insertion Method: Step 4





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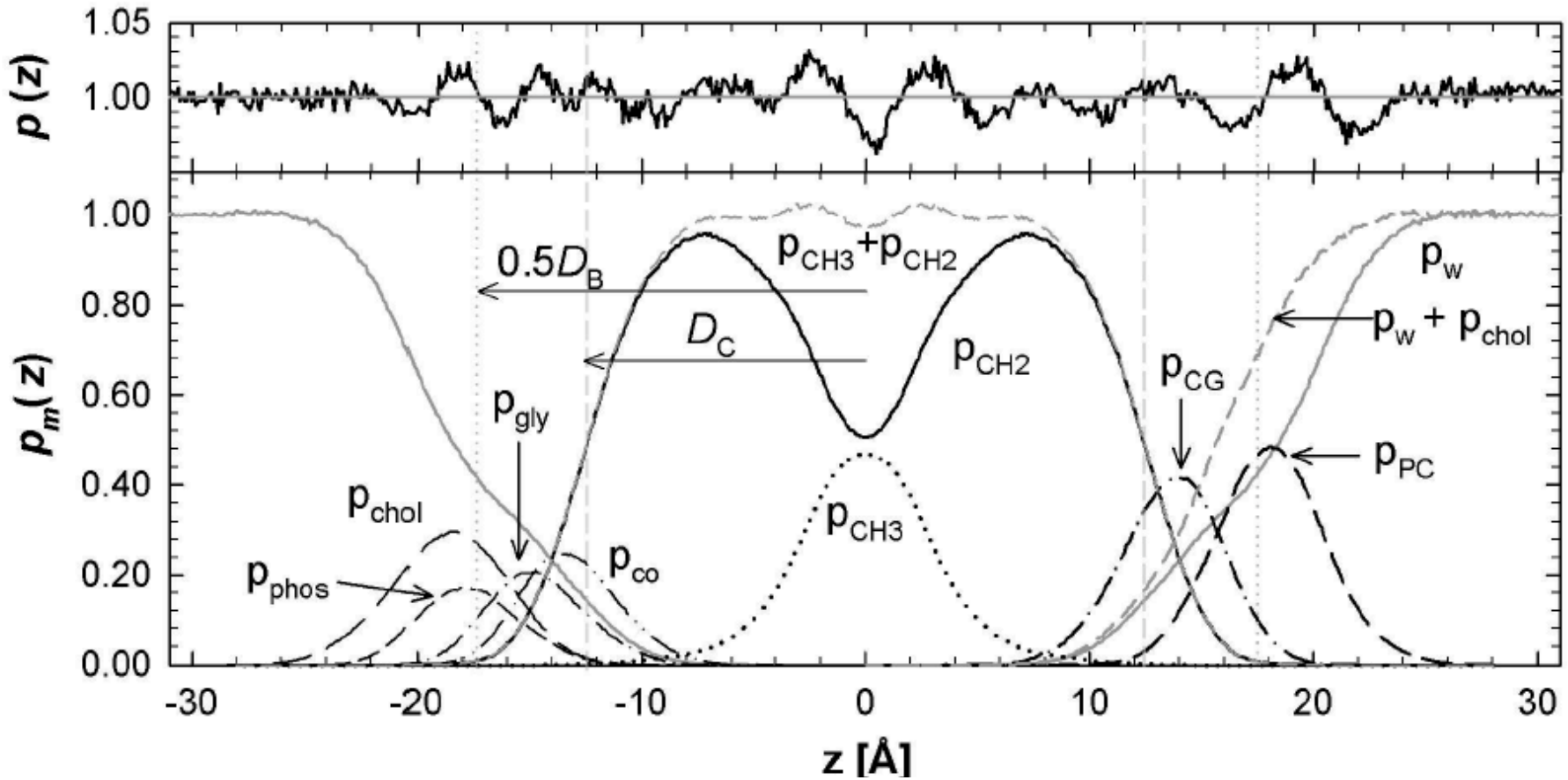
Observables: Density Distribution



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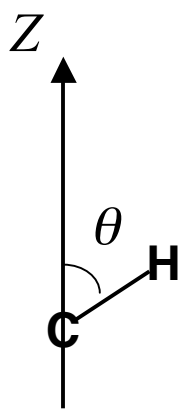
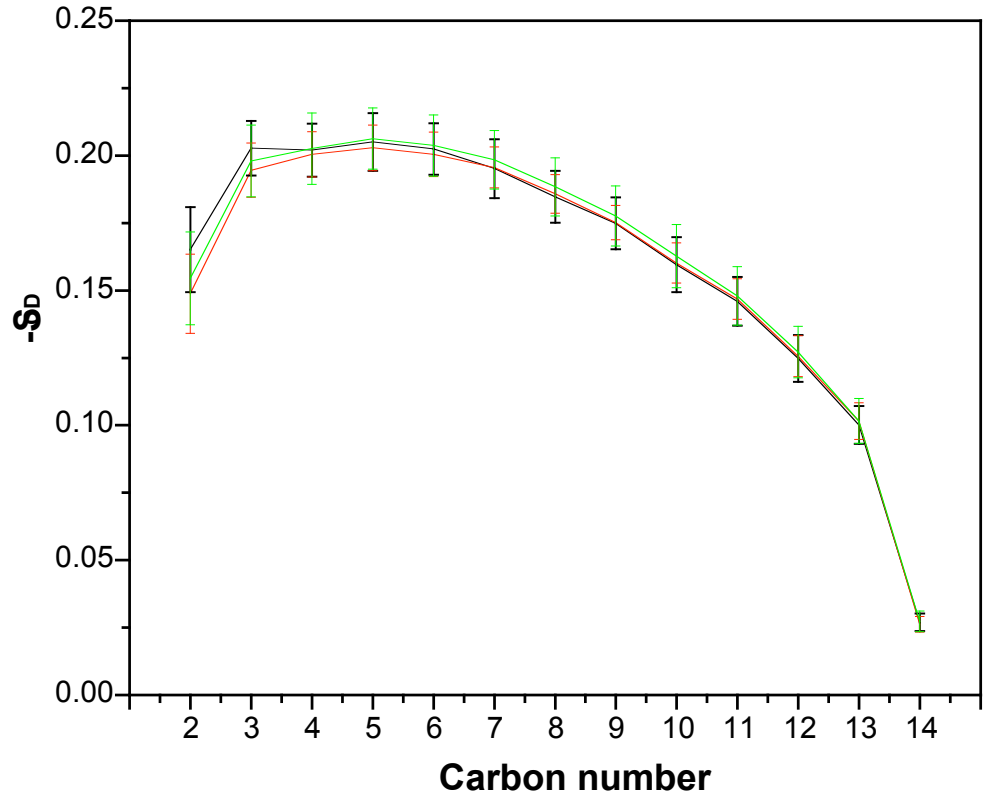
Observables: Lipid Order Parameters

$$\left|S_{CD}\right| = \left|\frac{3}{2}\left\langle \cos^2\theta - 1 \right\rangle\right|$$





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Observables: Lipid Length

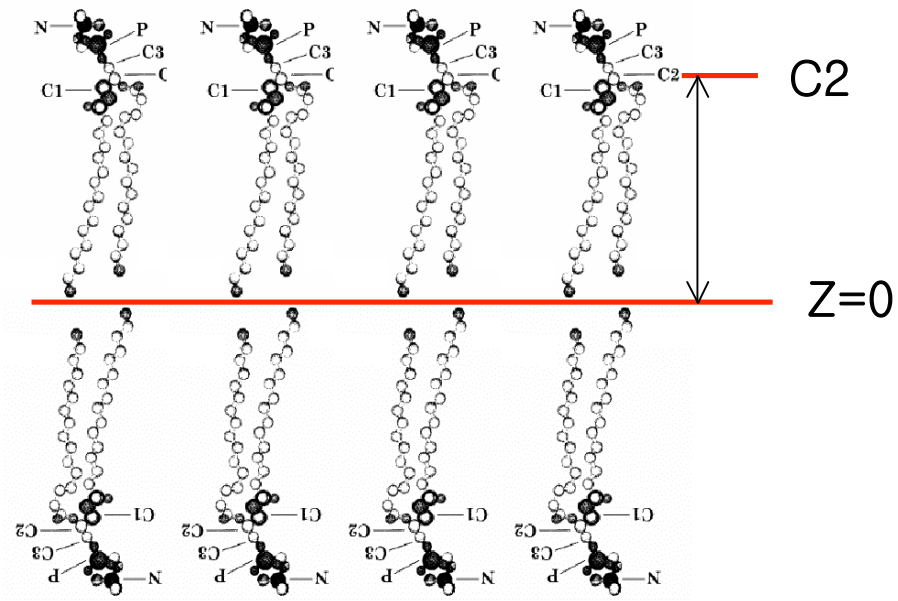

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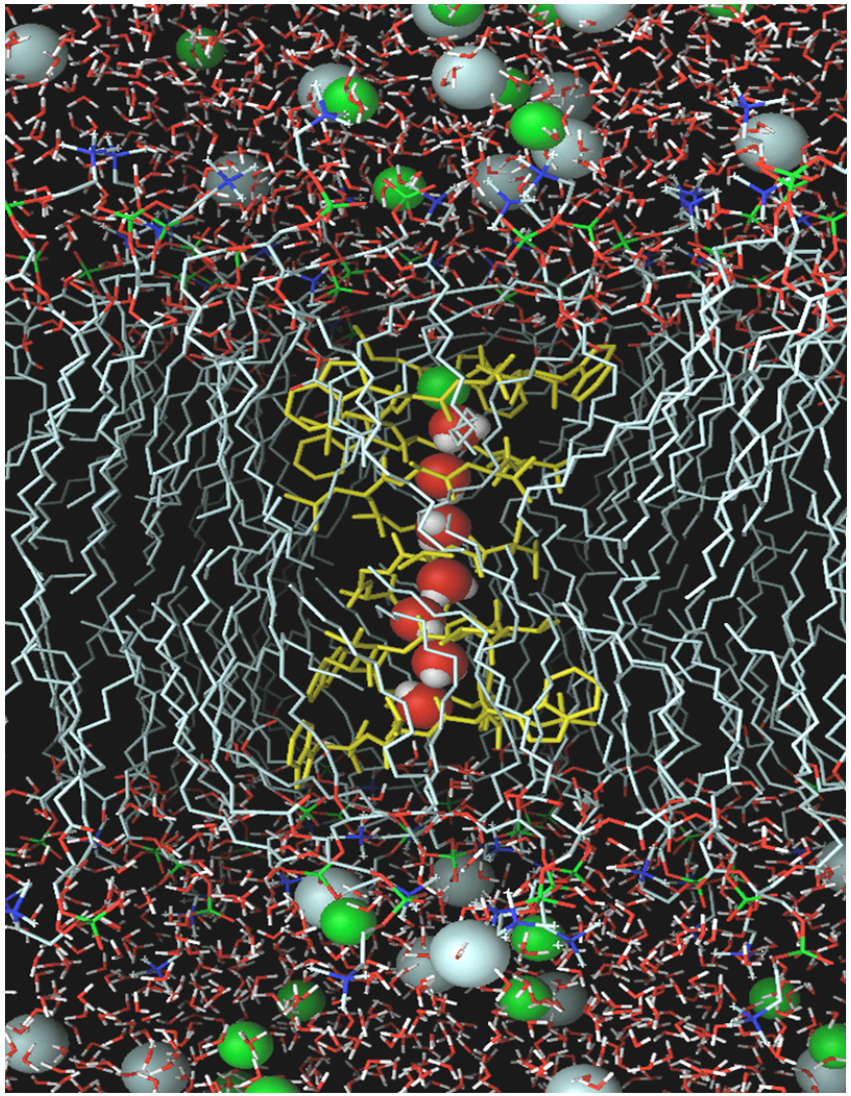
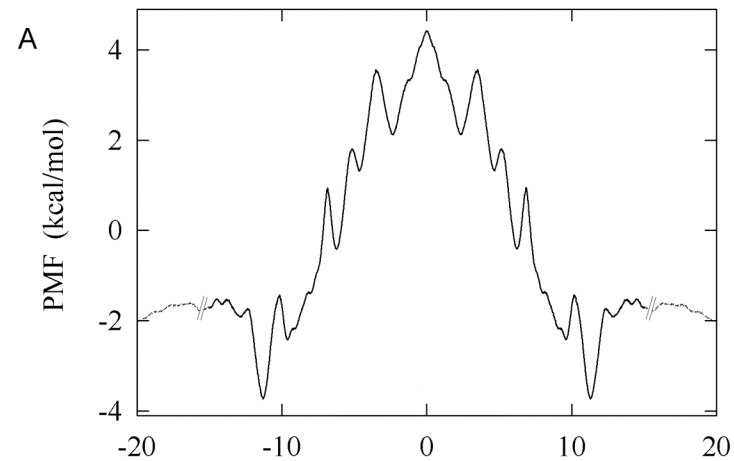
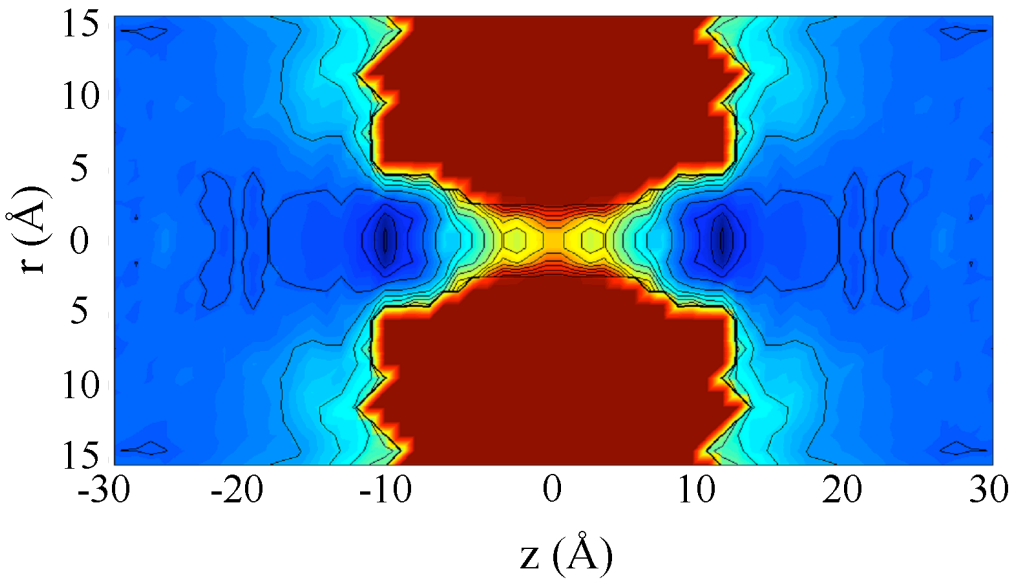
Illustration : gramicidin A







Allen, Andersen, and Roux (2003) PNAS 100:117

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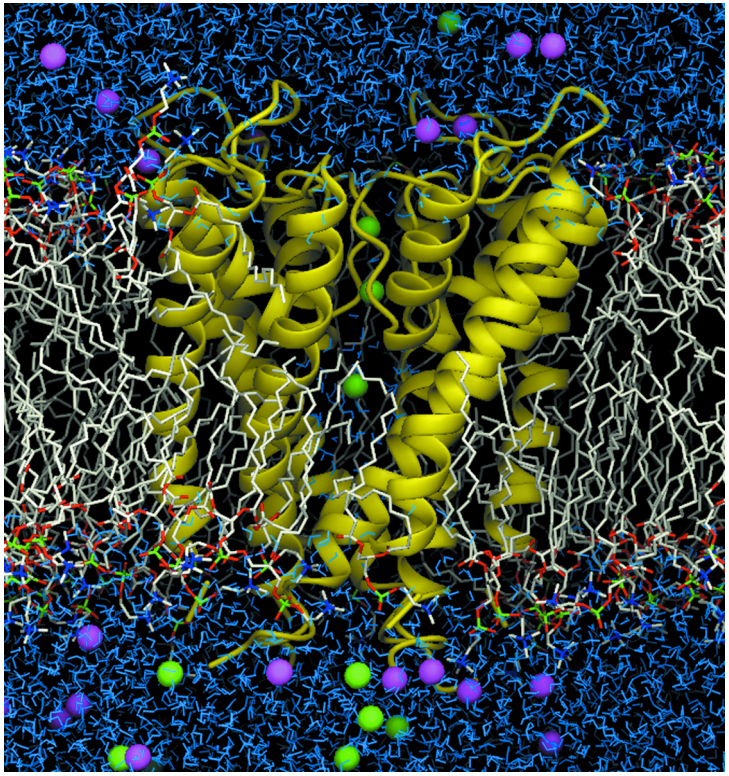
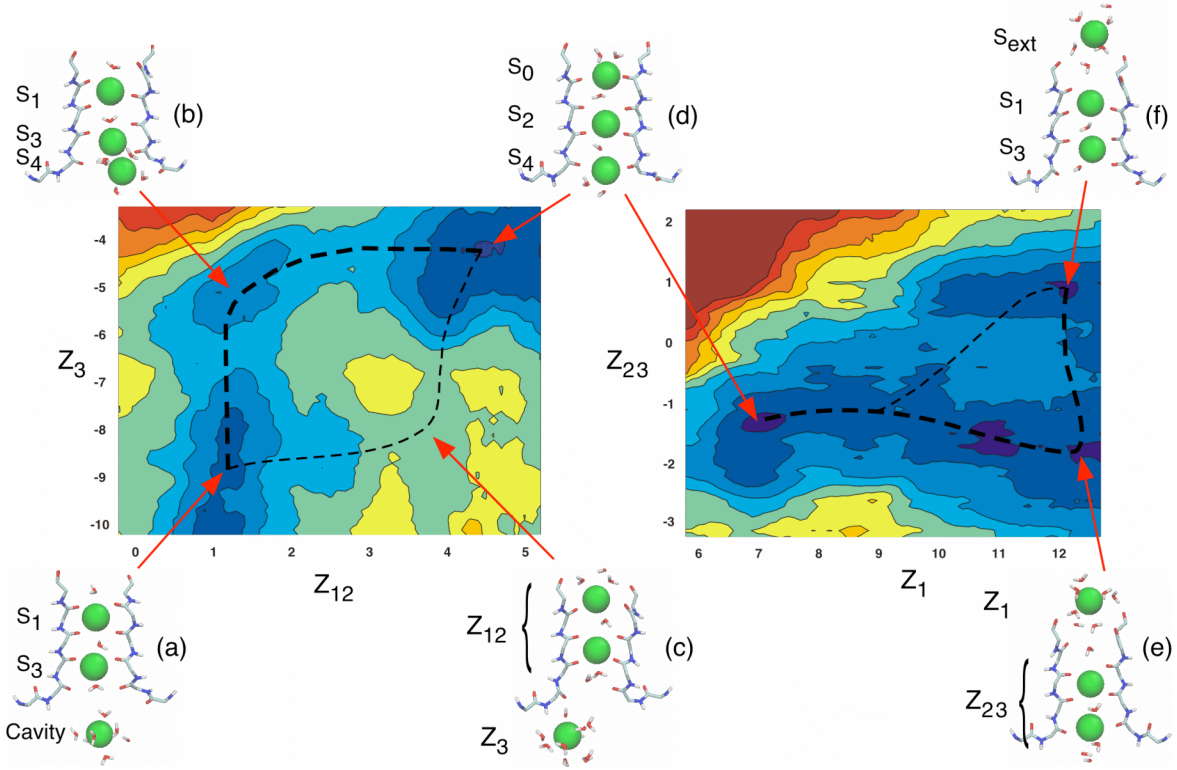
Illustration : KcsA K^+ Channel





Berneche & Roux (2001) Nature 414:73

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