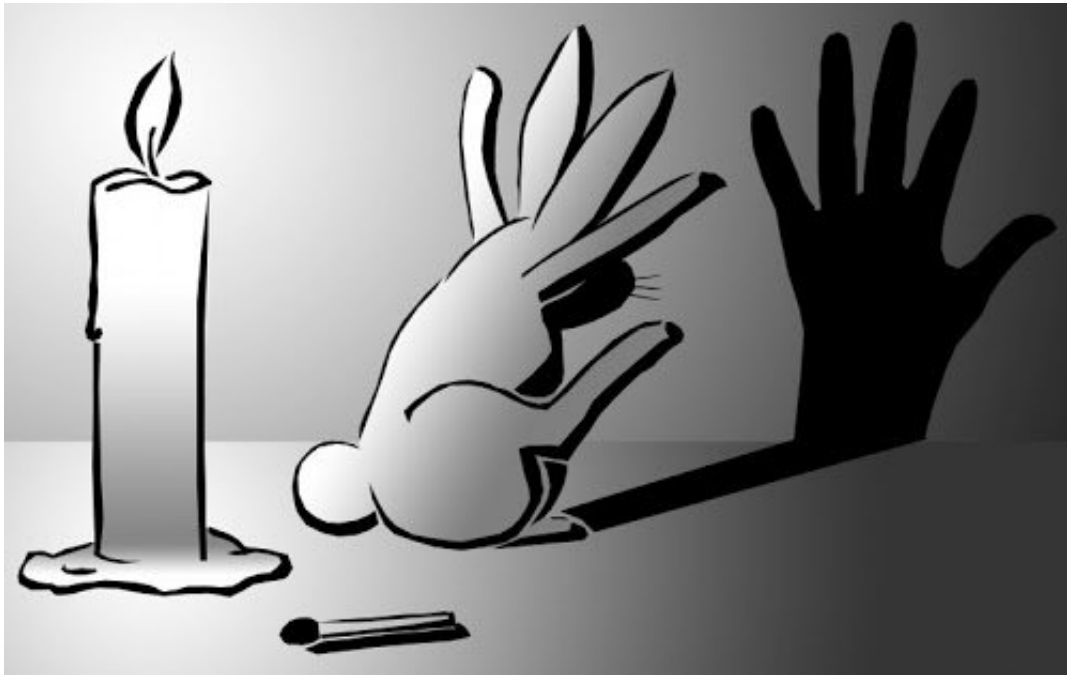


Ion binding at curved bilayers

ÚOCHB AV ČR
IOCB PRAGUE

Daniel Holý

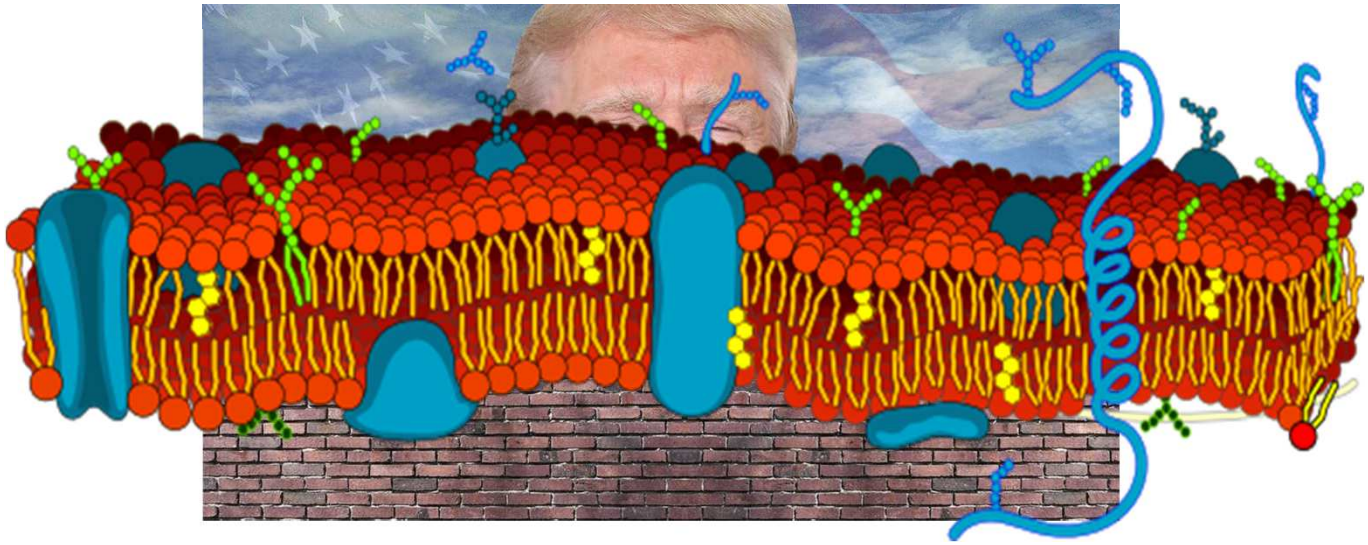
We care about membranes

Membranes are like walls, but better!

Sources: http://medcell.med.yale.edu/lectures/images/membrane_proteins.jpg

We care about membranes

Membranes are like walls, but better!



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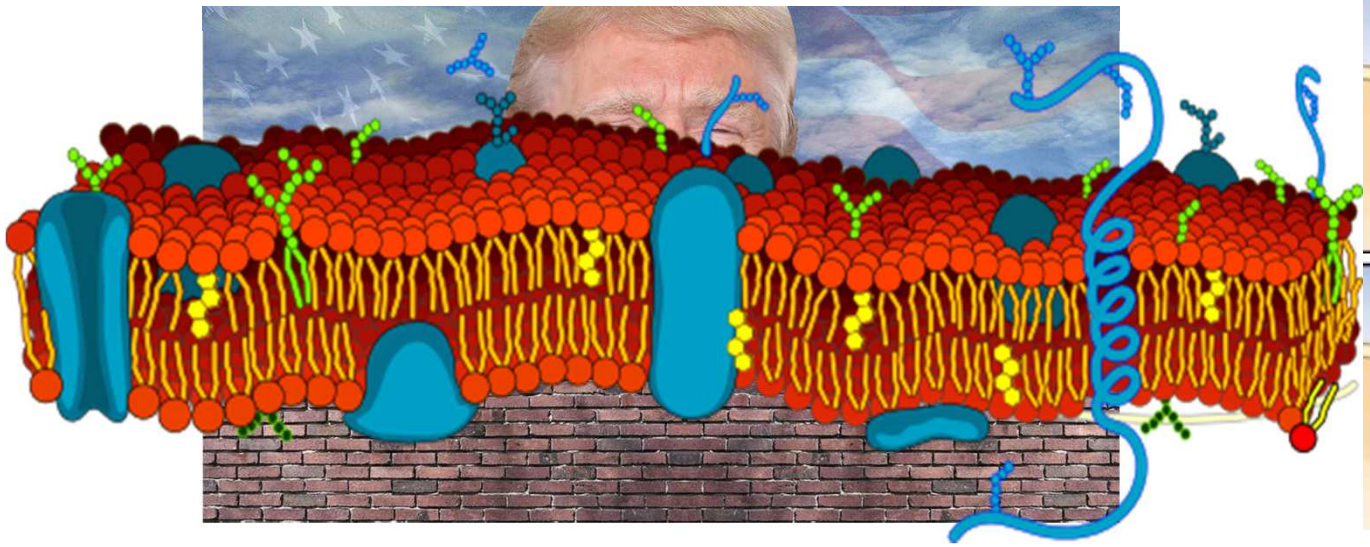
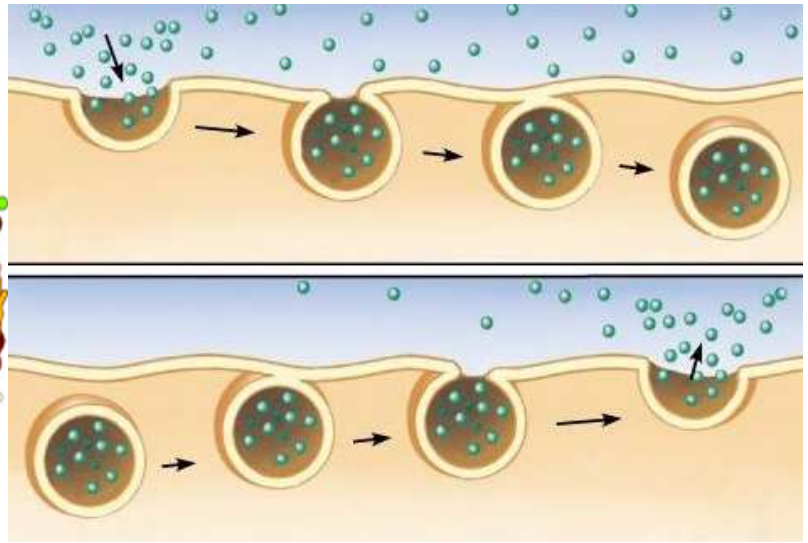


Membranes can fuse



Sources: http://medcell.med.yale.edu/lectures/images/membrane_proteins.jpg

We care about ions

IONS

- change lipid bilayer properties (some of them)
- are involved in signaling (some of them)
- bind to the membranes (some of them)

We care about ions

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CALCIUM!

We care about ions

IONS

- change lipid bilayer properties (some of them)
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CALCIUM!

CALCIUM!

We care about ions

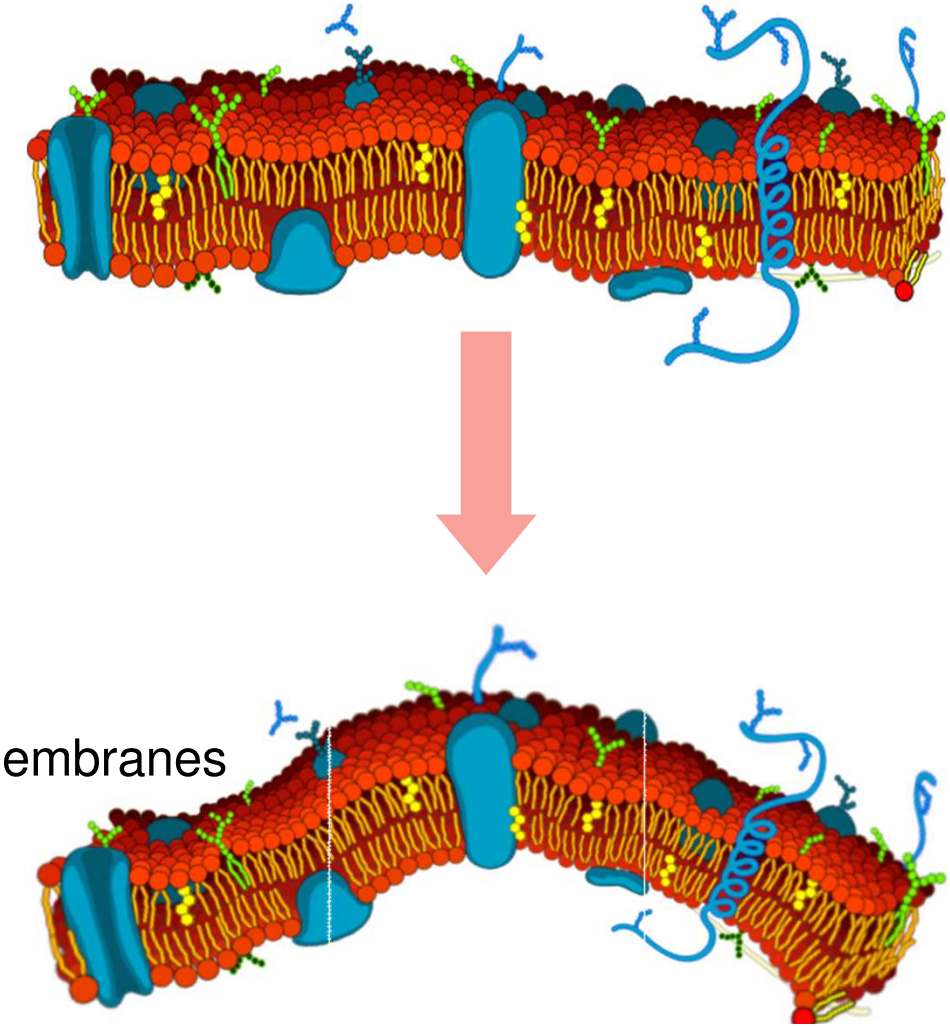
IONS

- change lipid bilayer properties (some of them) CALCIUM!
- are involved in signaling (some of them) CALCIUM!
- bind to the membranes (some of them) CALCIUM!

We care about curvature

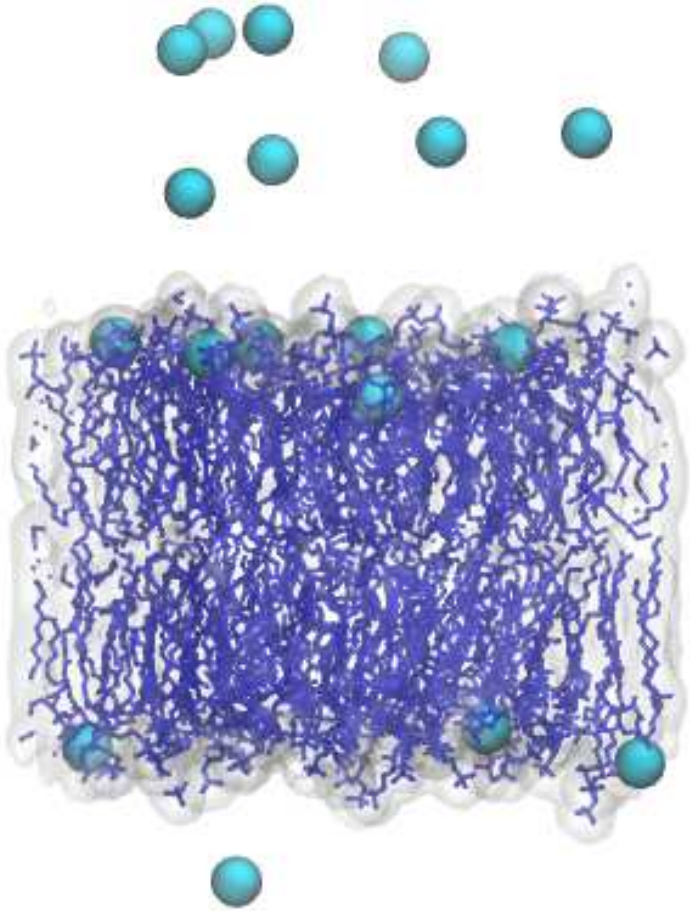
CURVATURE

- helps recruit proteins
- facilitates membrane fusion
- changes binding of calcium to membranes



Simulation details I

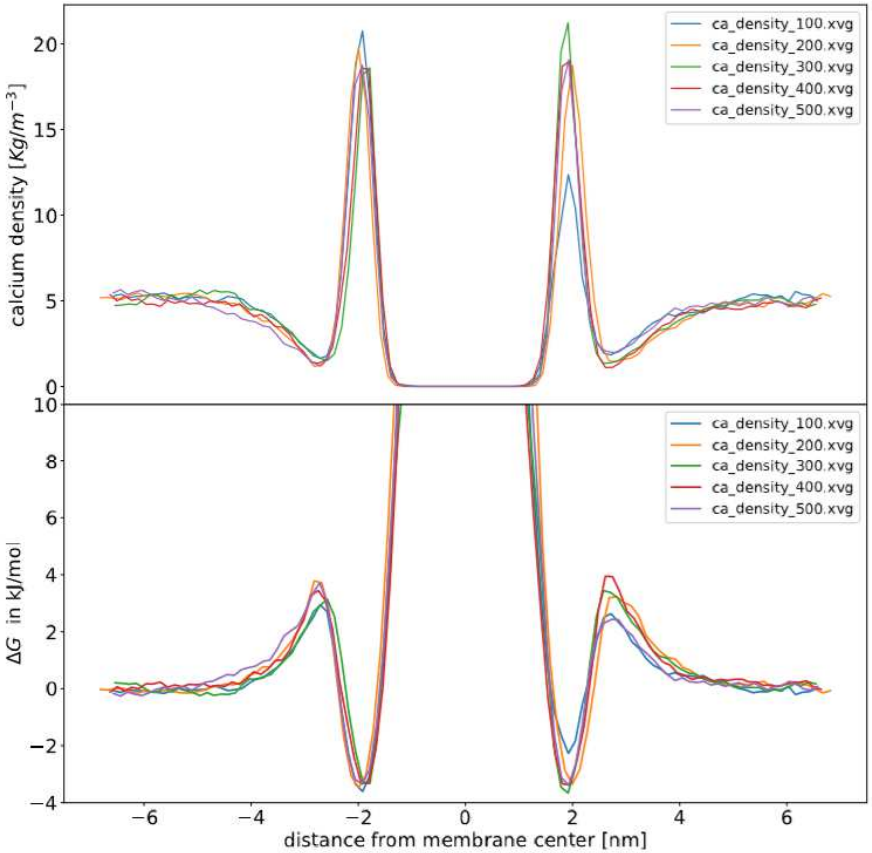
- 128 POPC moleculs
- 6 x 6 x 10 nm box
- NPT ensemble
- 150 mM $CaCl_2$ (~ 18 Ca^{2+} ions)
- GROMACS simulation package
- Scaled calcium ions (charge 1.5+)
- ECC-POPC forcefield

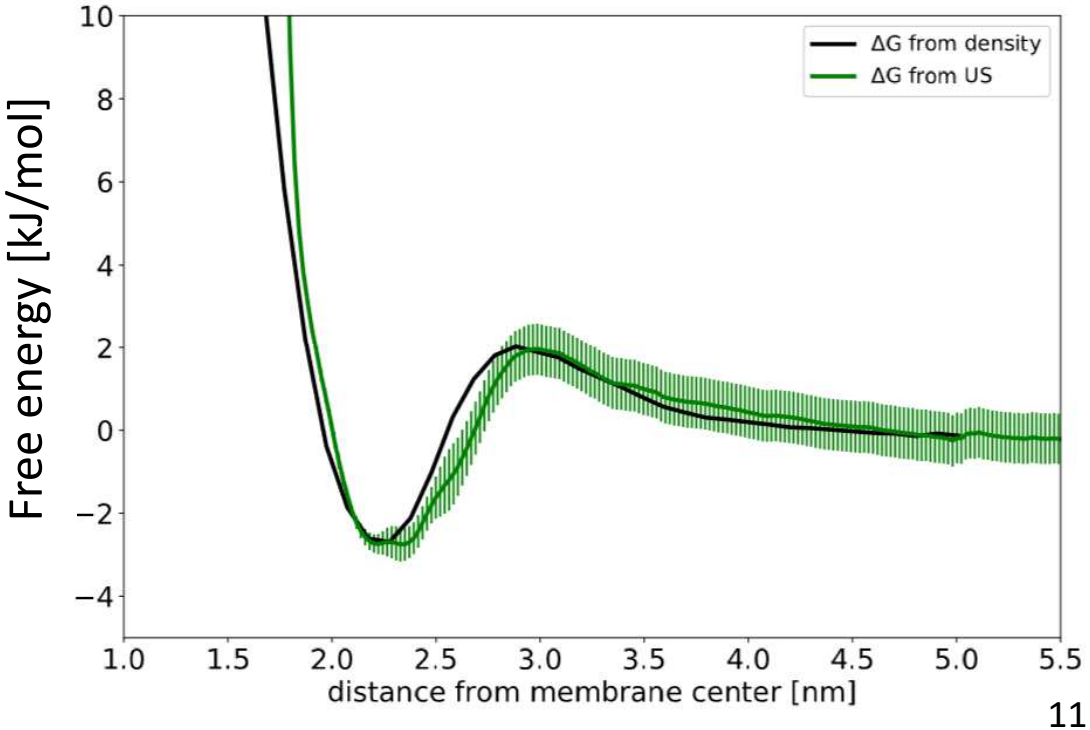


Note: ions not to scale

A flat POPC membrane…

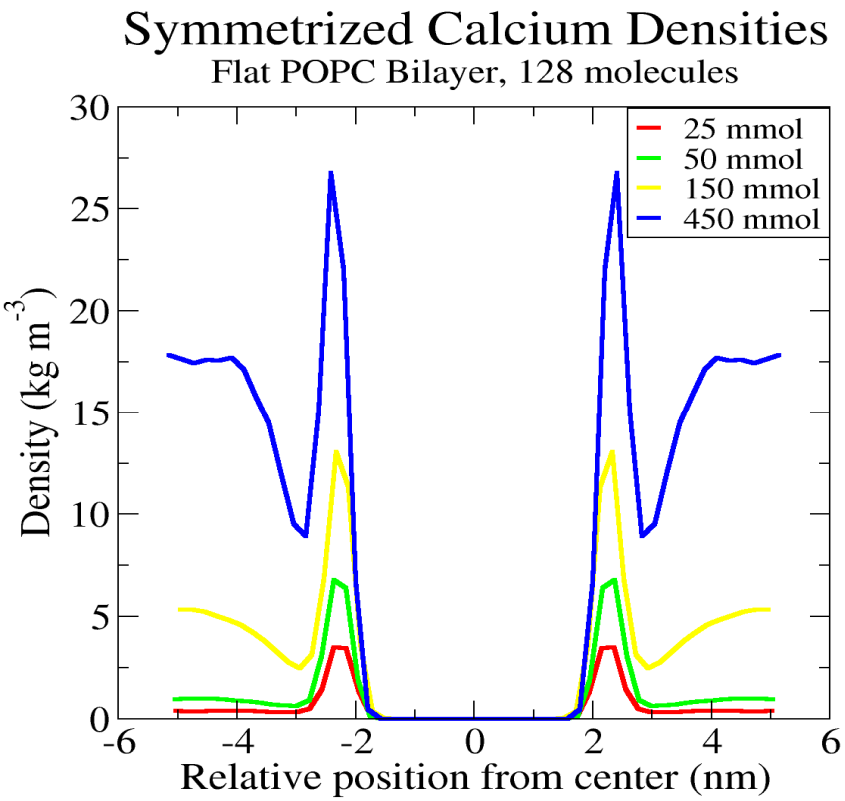
Convergence





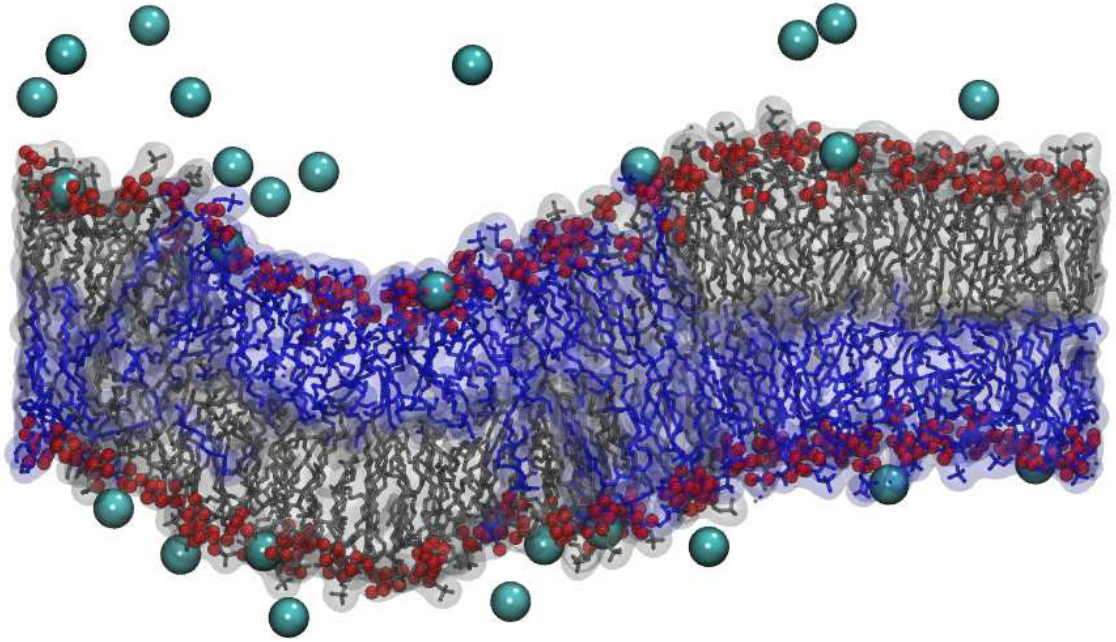
A flat POPC membrane

Concentration dependence



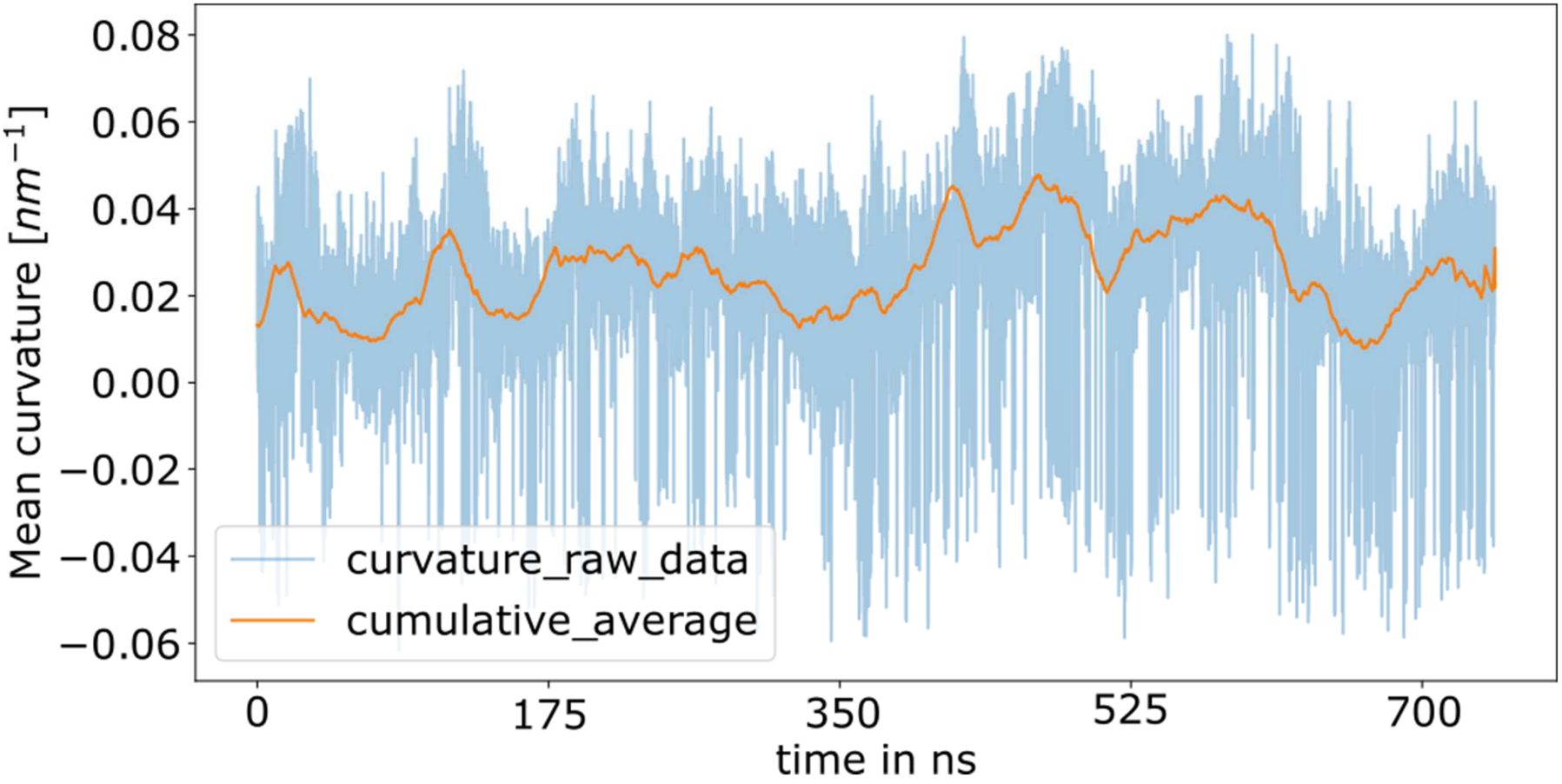
[Ca2+] mmol/ l	25	50	150	450
ΔG [kJ/mol]	-8.1	-4.9	-2.2	-2.0

Simulation details II

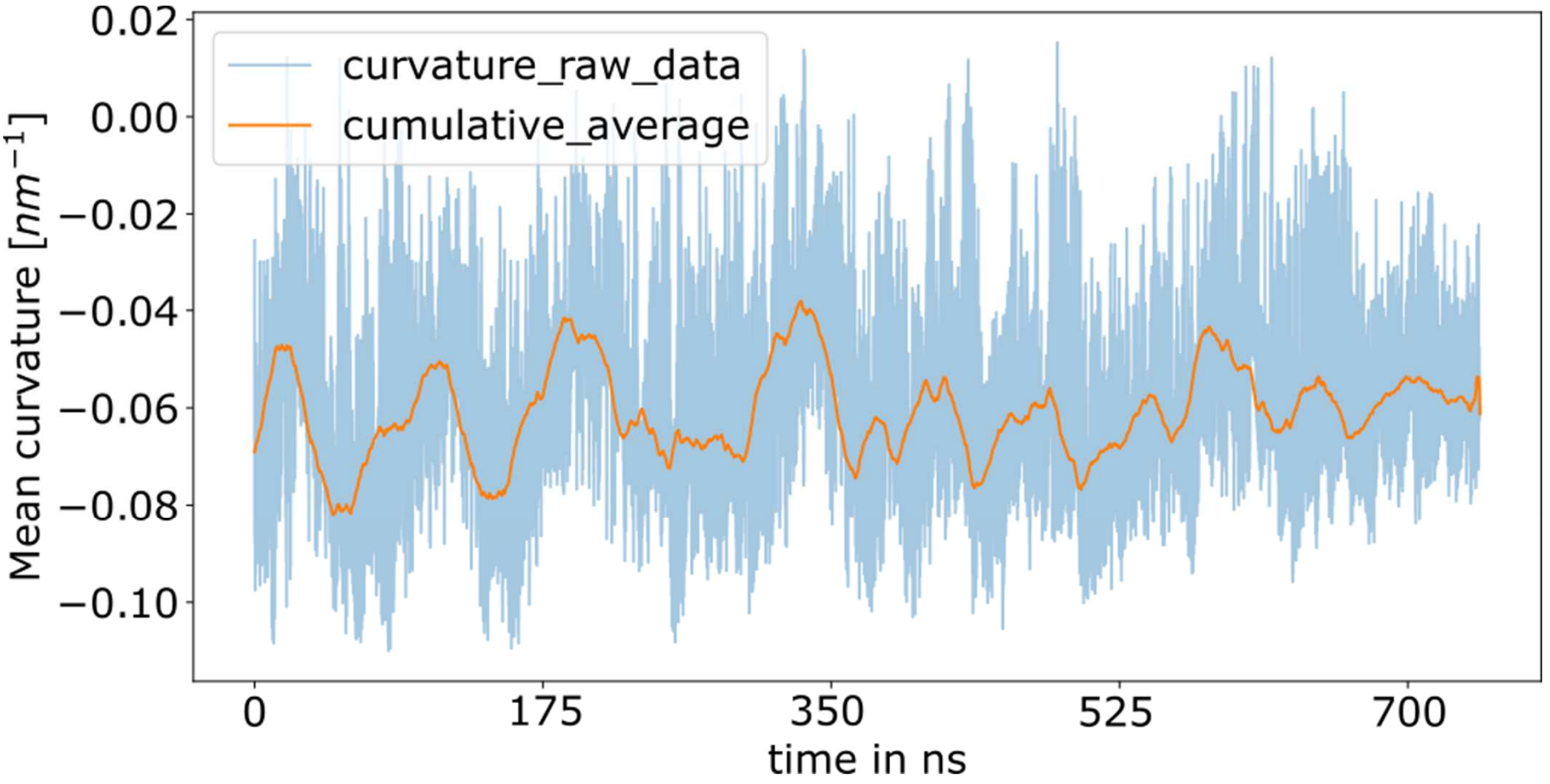


- 880 POPC molecules
- 15 x 15 x 15 nm box
- NPT ensemble
- 150 mM $CaCl_2$ (~ 246 Ca^{2+} ions)
- GROMACS simulation package
- Scaled calcium ions (charge 1.5+)
- ECC-POPC forcefield
- Harmonic restraints in z-direction

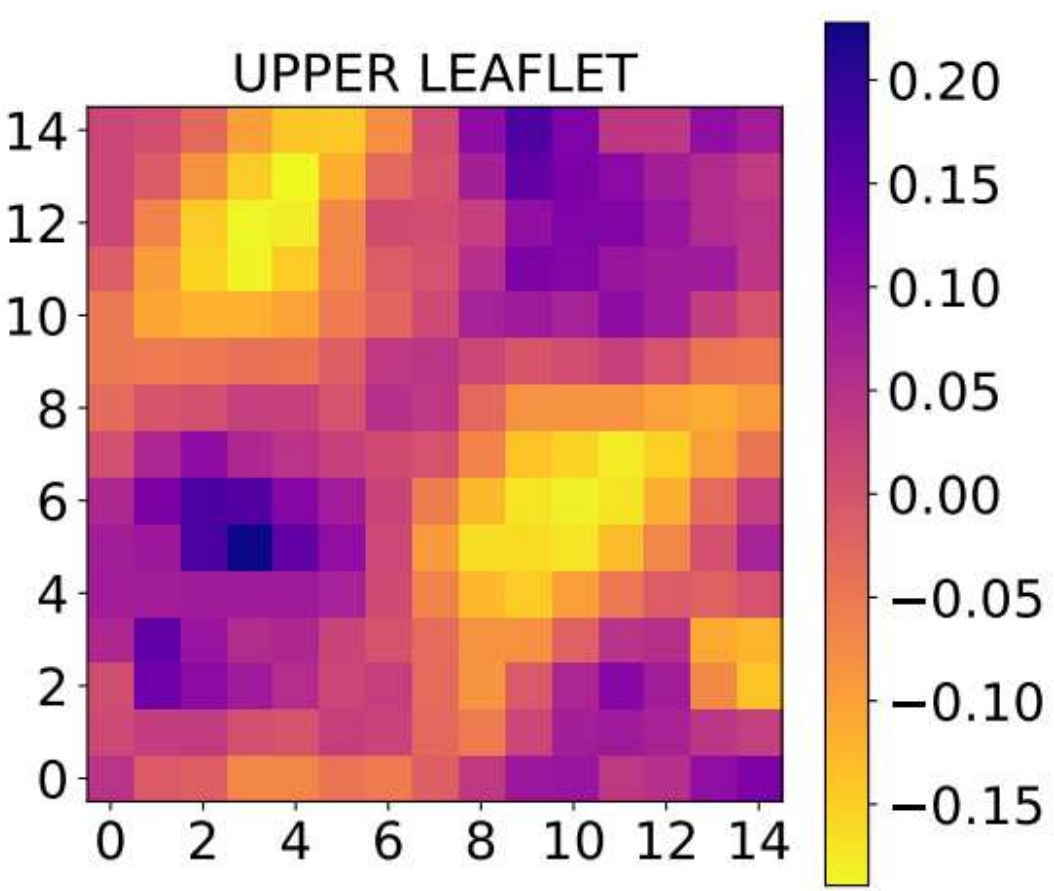
Curvature stability - positive

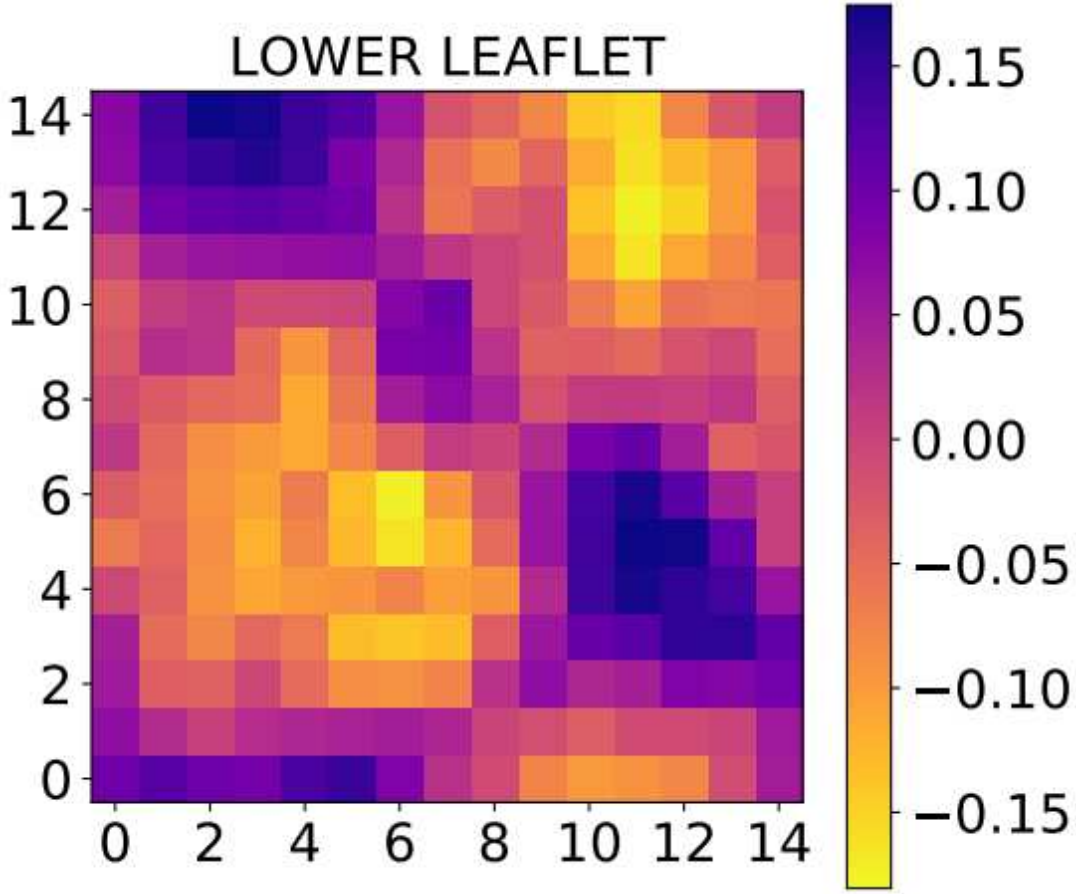


Curvature stability - negative

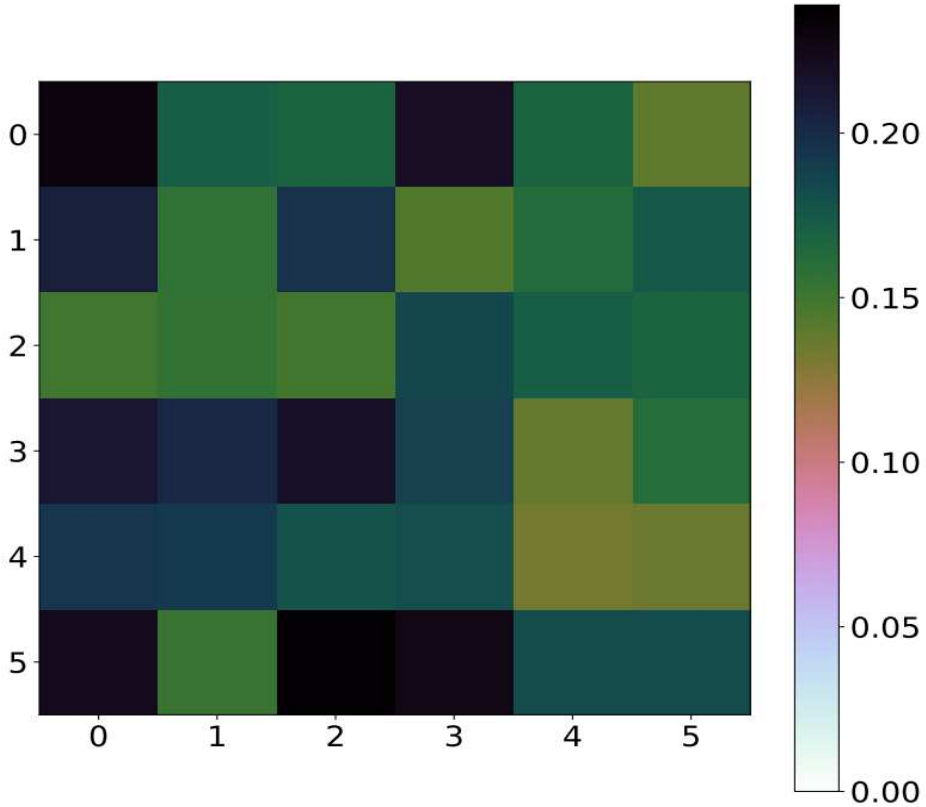


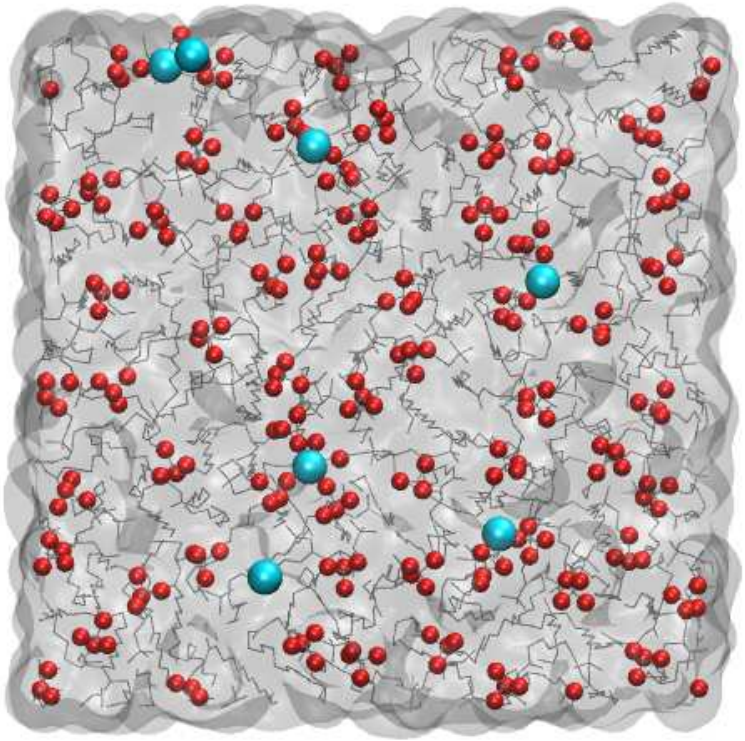
Time-averaged curvature values





Calcium concentration across the membrane





Summary

- Quantitative correlation of curvature and [Ca^{2+}] *in progress*
- Resolution dependent on convergence
- Stability of the harmonically restrained bilayer
- Testing multiple approaches

ACKNOWLEDGMENTS

Aniket Magarkar
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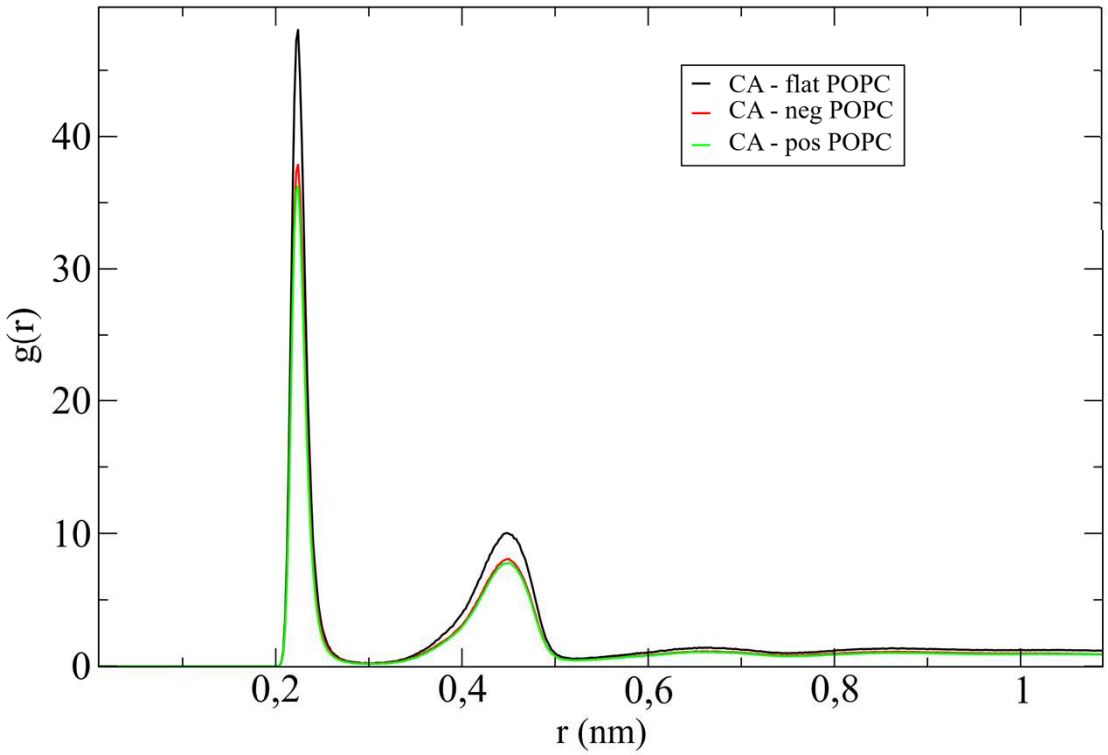
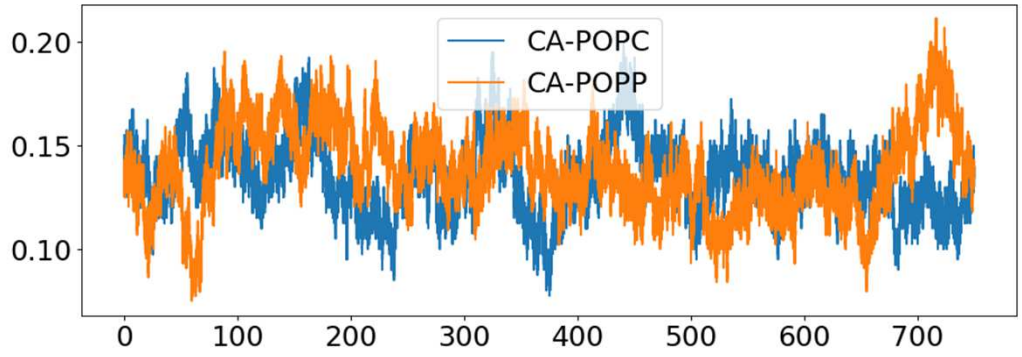
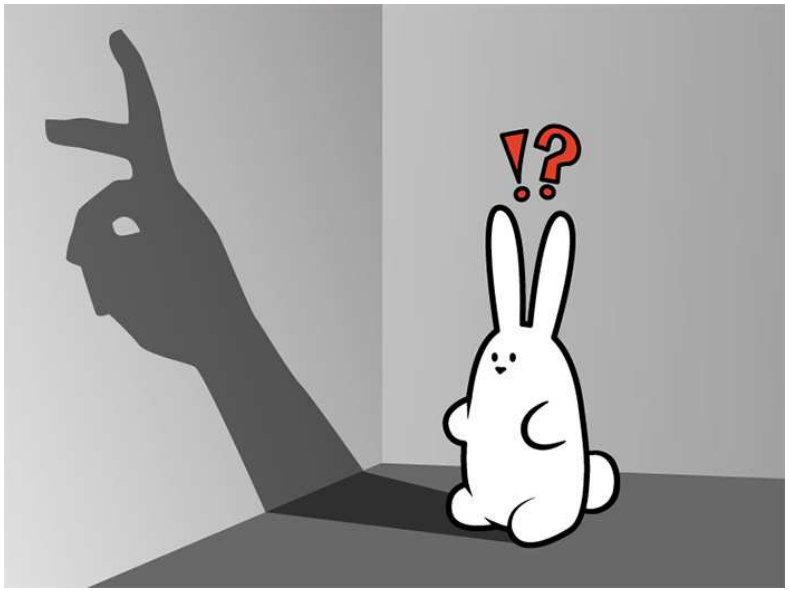
IT4Innovations national supercomputing center

This work was supported by The Ministry of Education, Youth and Sports from the Large Infrastructures for Research, Experimental Development and Innovations project „IT4Innovations National Supercomputing Center – LM2015070“.

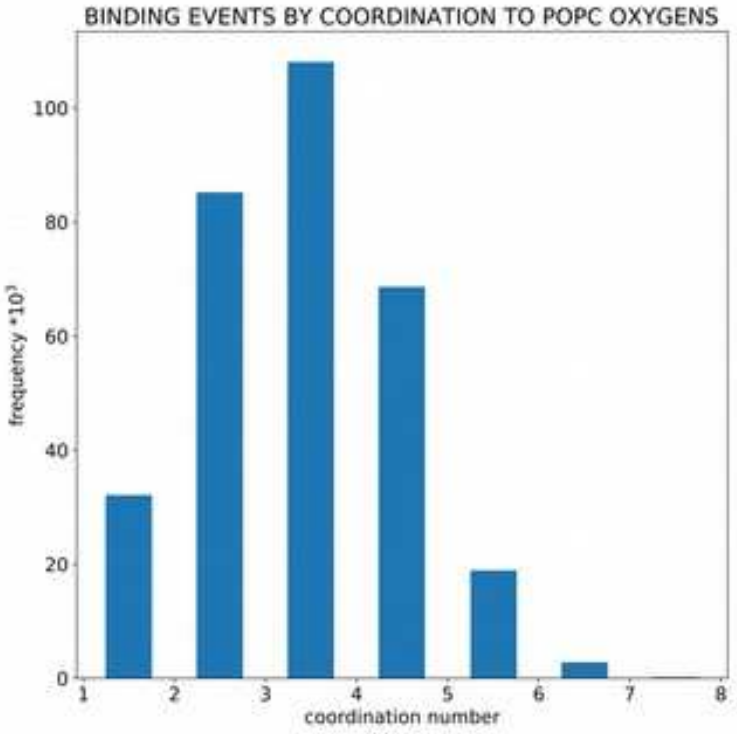
Some results are inconclusive

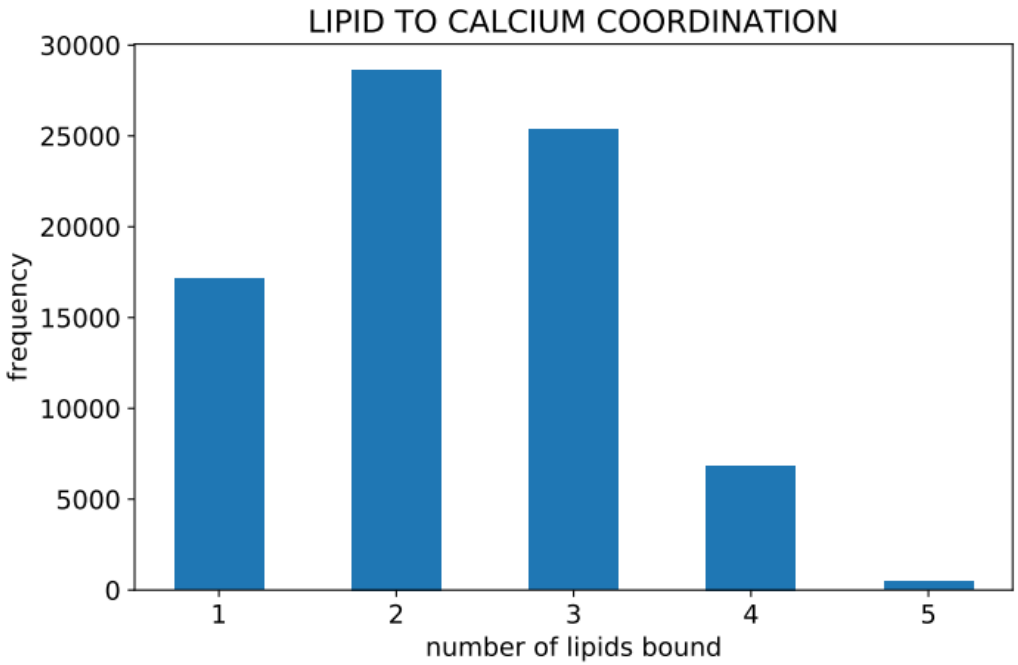




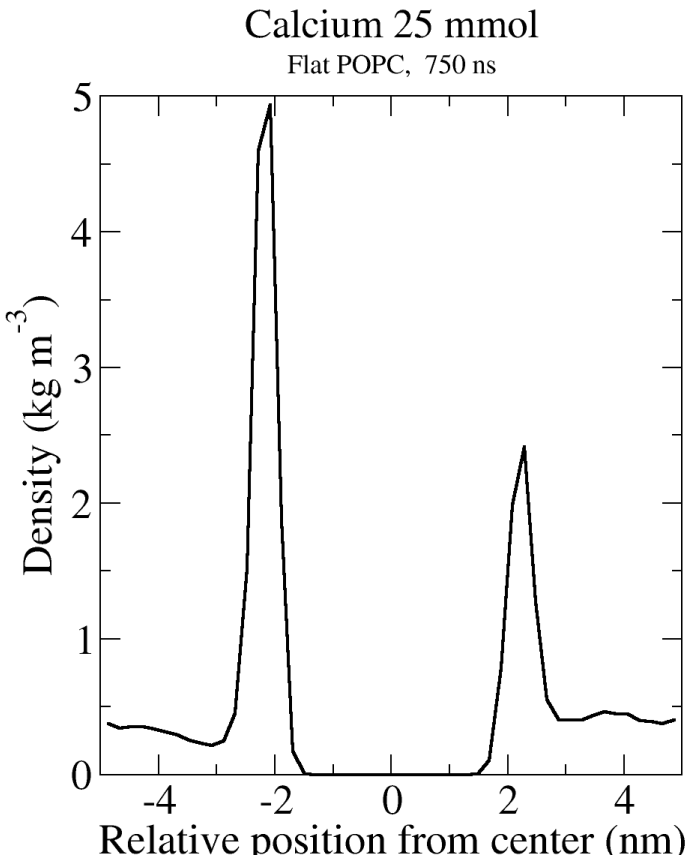


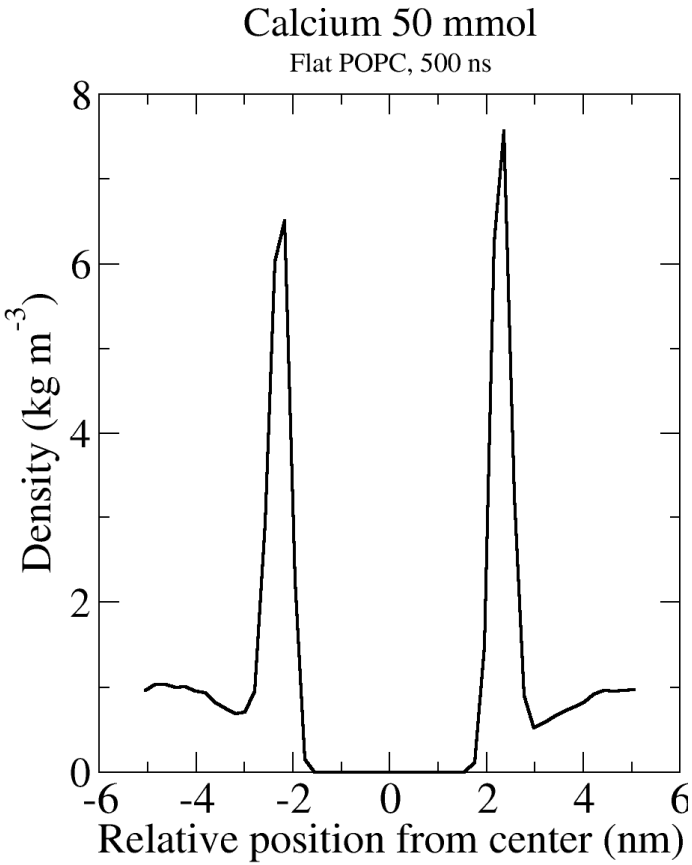
lipids to calcium coordination

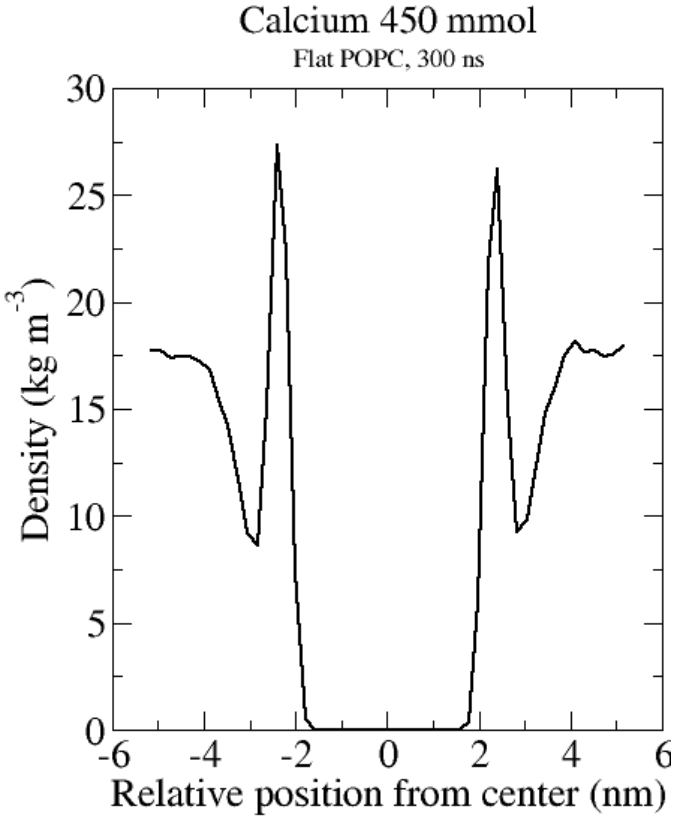




Unsymmetrized calcium density profiles







Calcium density across layers