

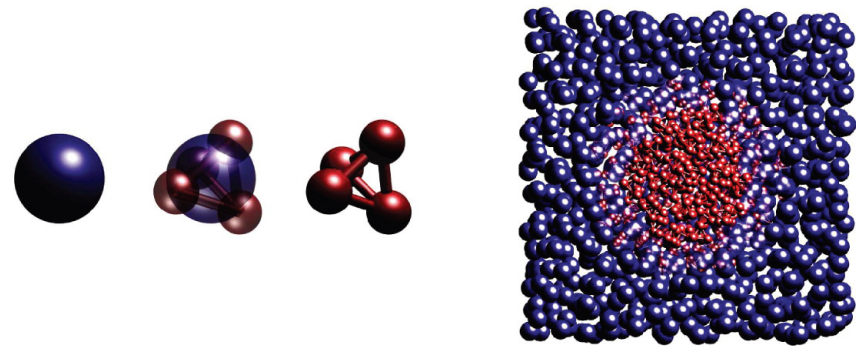
Blending Martini

Manuel Melo (m.n.melo@itqb.unl.pt)



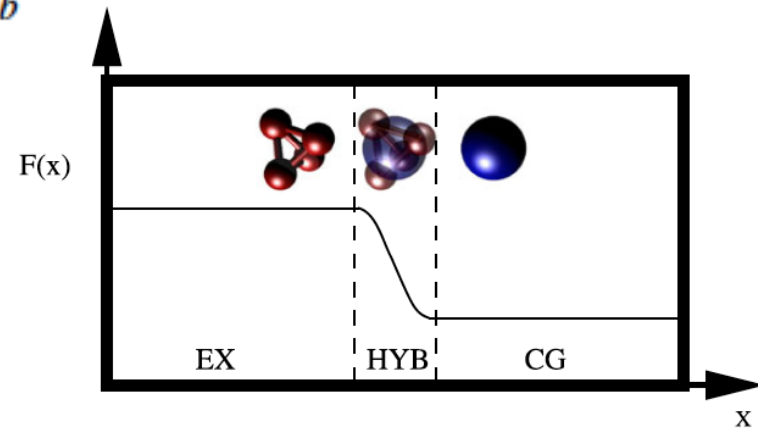
The AdResS Scheme

Adaptive Resolution Scheme



$$\mathbf{F}_{ab} = w(x_a)w(x_b)\mathbf{F}_{ab}^{ex} + [1 - w(x_a)w(x_b)]\mathbf{F}_{ab}^{cg}$$

$$w(r) = \begin{cases} 1, & r_0 > r \geq 0 \\ 0, & r \geq r_0 + d \\ \cos^2[\pi/2d(r - r_0)], & r_0 + d > r \geq r_0, \end{cases}$$



Original scheme: random molecule insertion

Density

Differences in chemical potential will create inhomogeneities in the density



A correcting thermodynamic force must be introduced

$$\mathbf{F}_a = \sum_{b \neq a} (w(x_a)w(x_b)\mathbf{F}_{ab}^{ex} + [1 - w(x_a)w(x_b)]\mathbf{F}_{ab}^{cg}) - \mathbf{F}^{TD}(x_a)$$

Implementation and Limitations

Available since GROMACS 4.6

But...

What you read may not be what you get:

Only stochastic temperature coupling

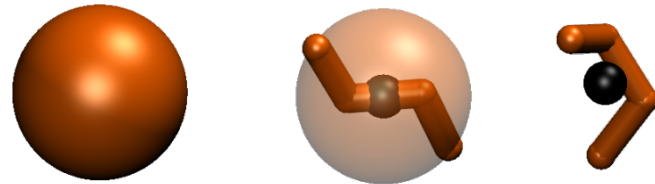
Random structure insertion not implemented (AA atoms and bonds are kept)

Other issues

Tables must be used if CG and AA potentials differ

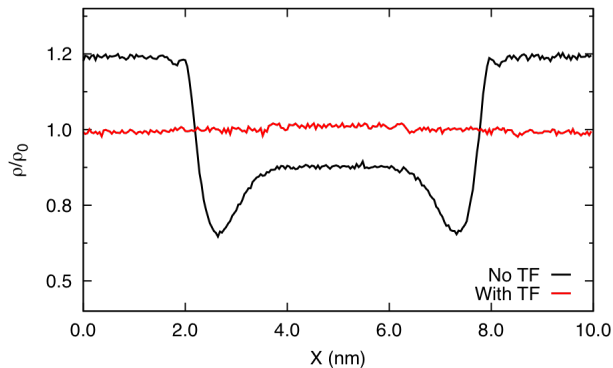
Butane System

Compressed butane
(gromos 53a6/Martini)

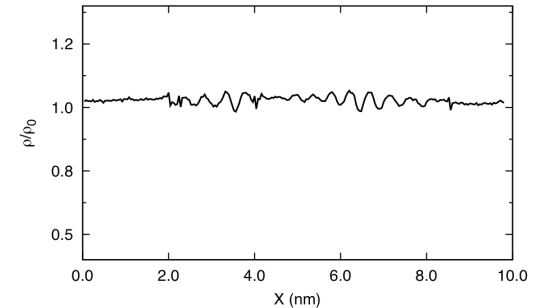
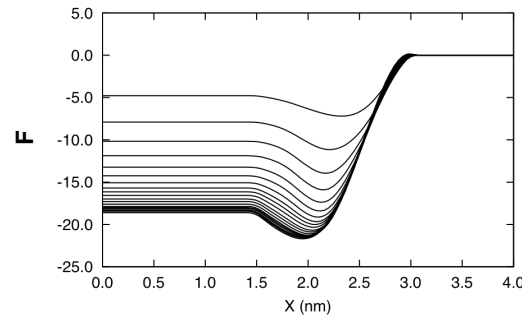


Thermodynamic Force

Density



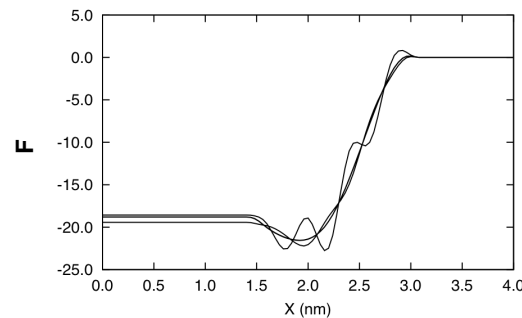
Take I



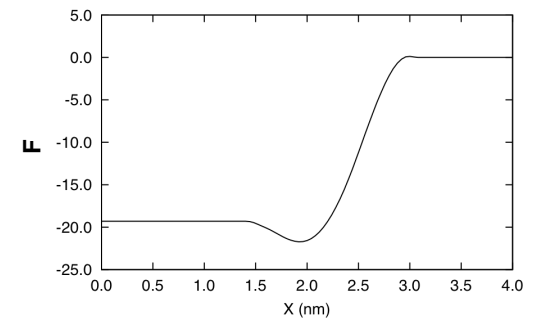
$$\mathbf{f}_{\text{th}}^{i+1}(\mathbf{r}) = \mathbf{f}_{\text{th}}^i(\mathbf{r}) - \frac{1}{\rho_0^2 \kappa_T^{\text{at}}} \nabla \rho_i(\mathbf{r})$$

Implemented in the latest
VOTCA releases

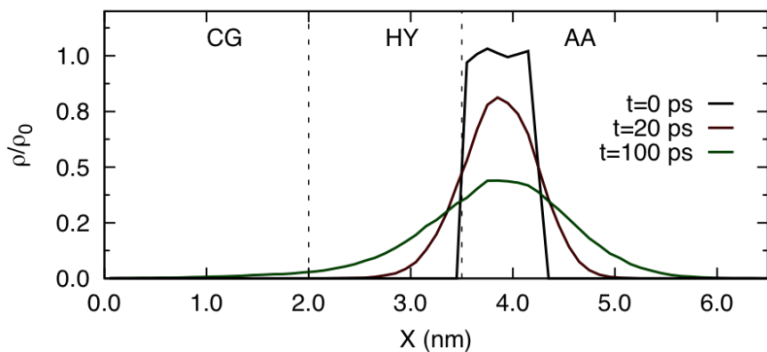
Take II



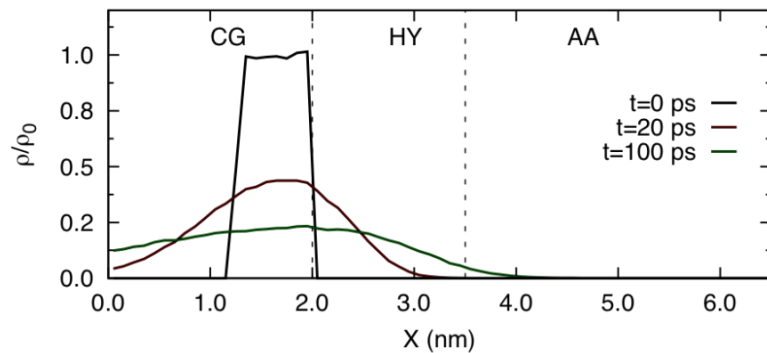
Take III



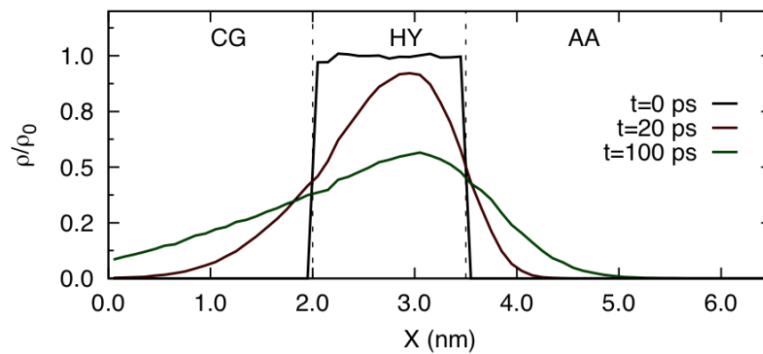
Solvent Diffusion



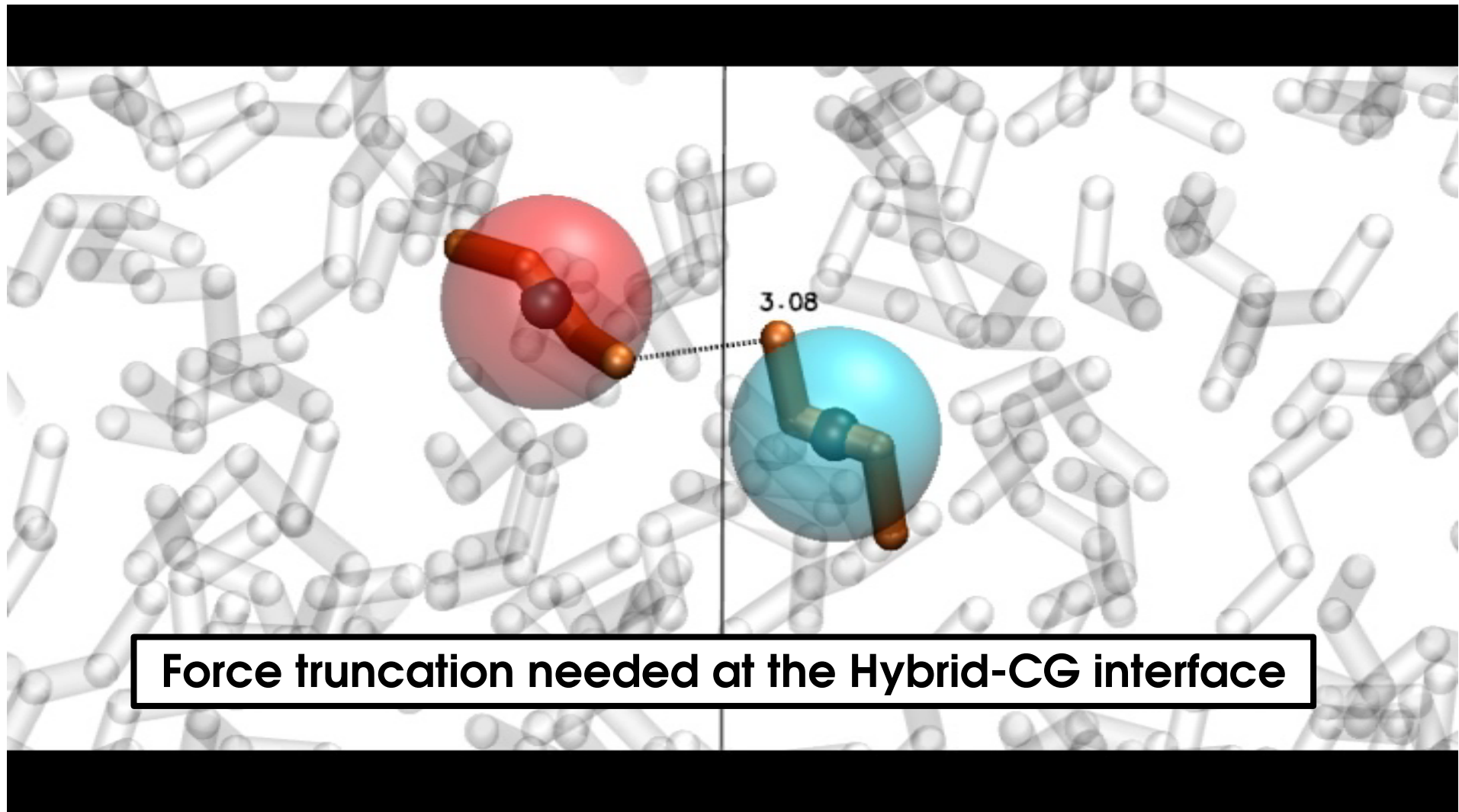
No obvious barriers to diffusion



Asymmetric diffusion (expected)



System **Instability**



Hybrid

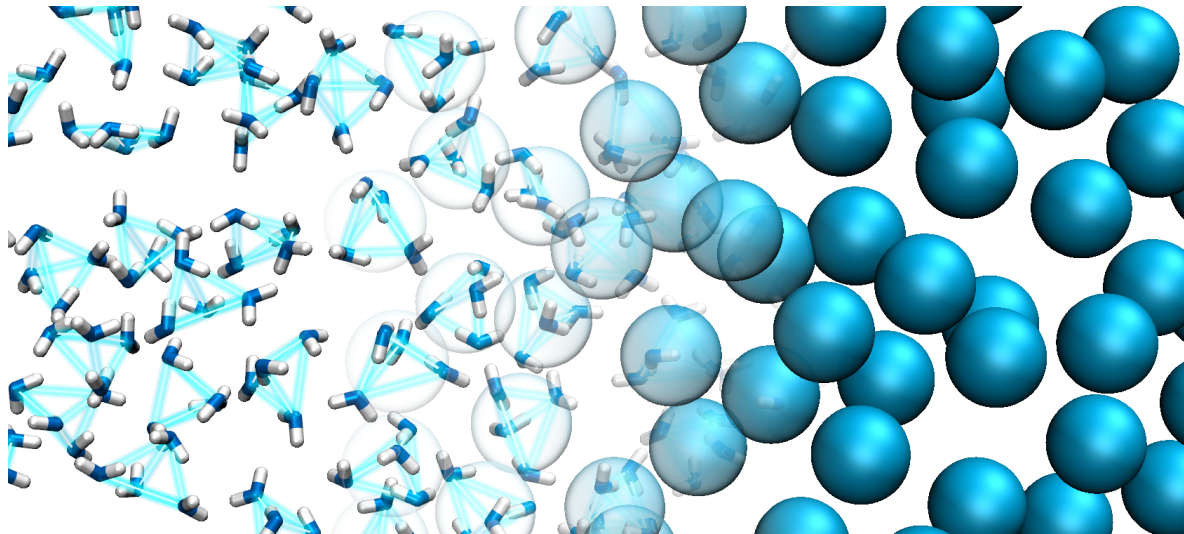
CG

Water System

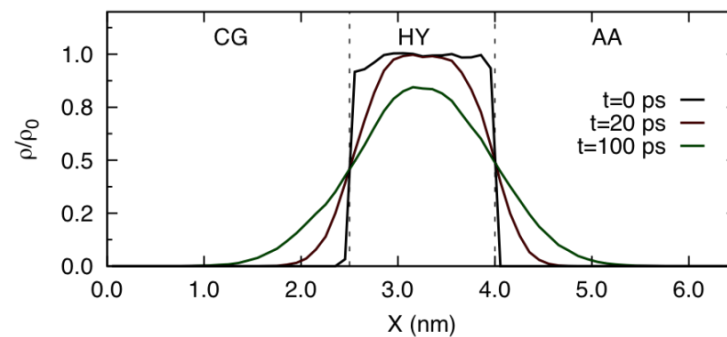
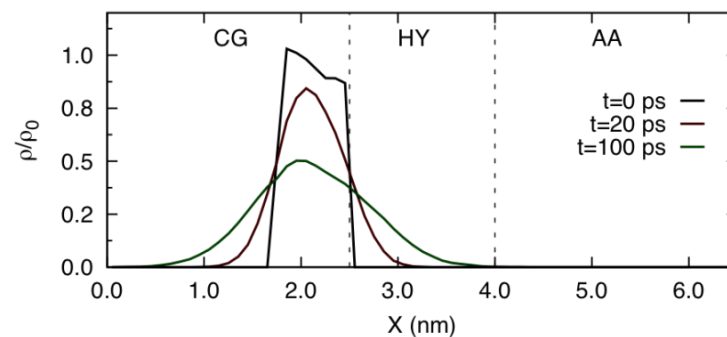
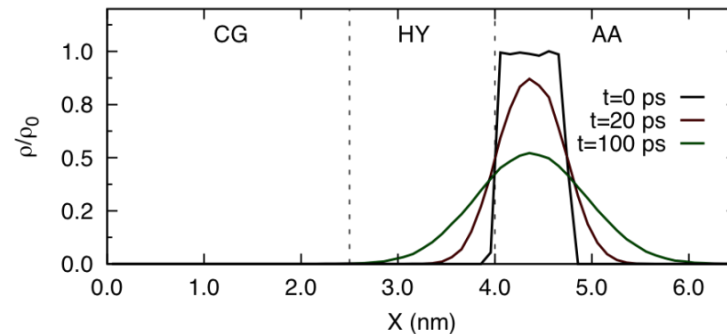
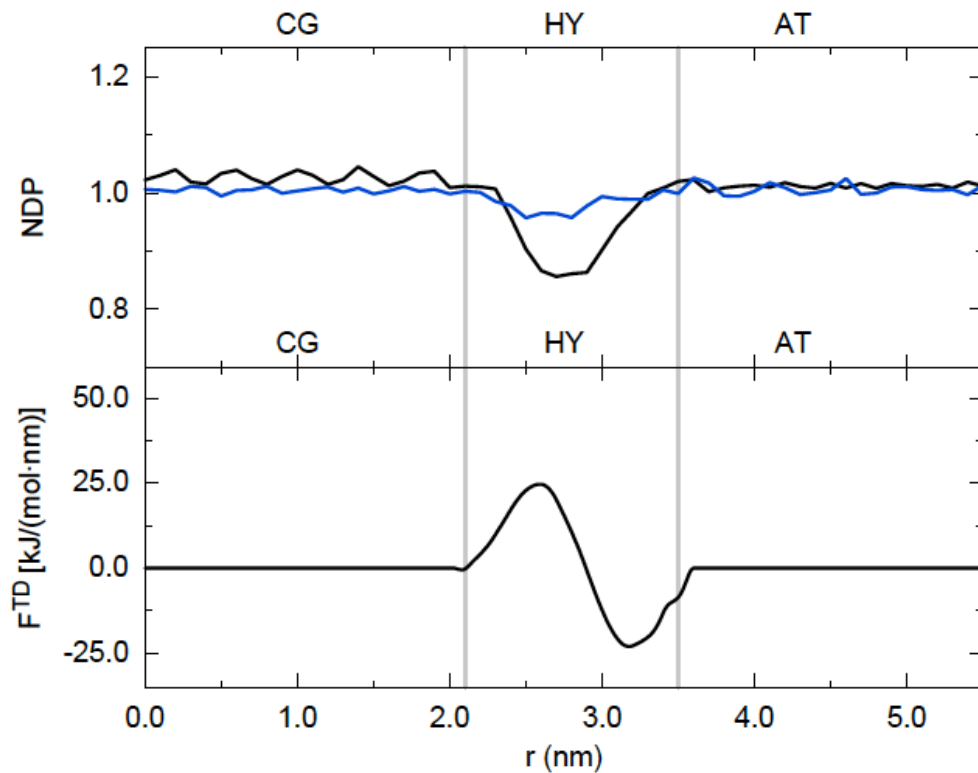
Bundled SPC water

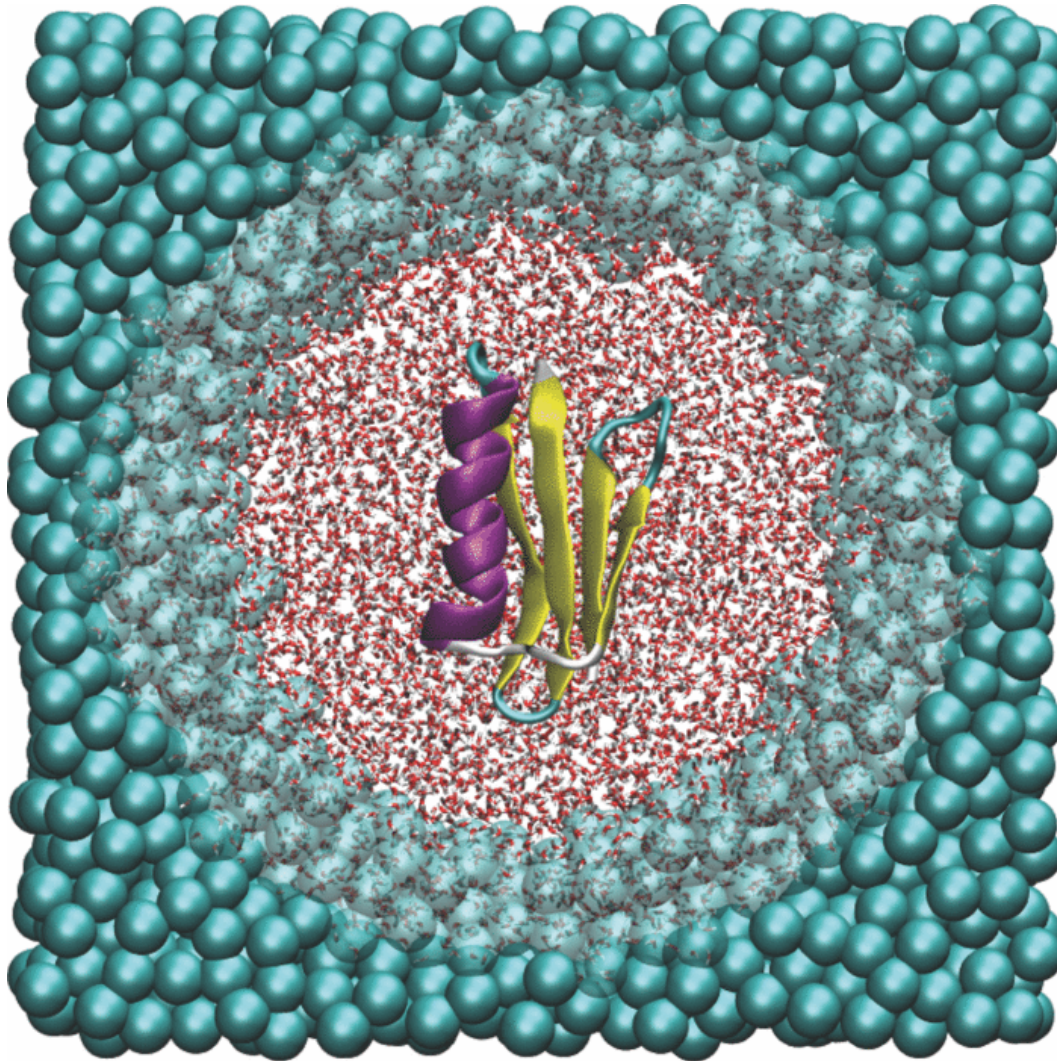
Oxygens of four waters connected by semi-harmonic attractive bonds

O-O Lennard-Jones repulsion increased by 30%



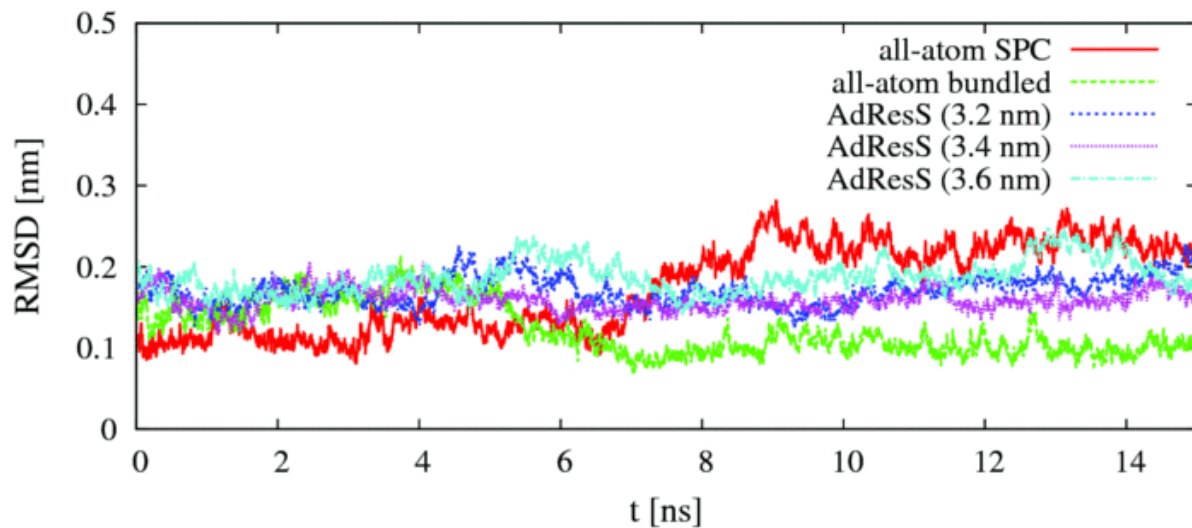
Solvent Properties



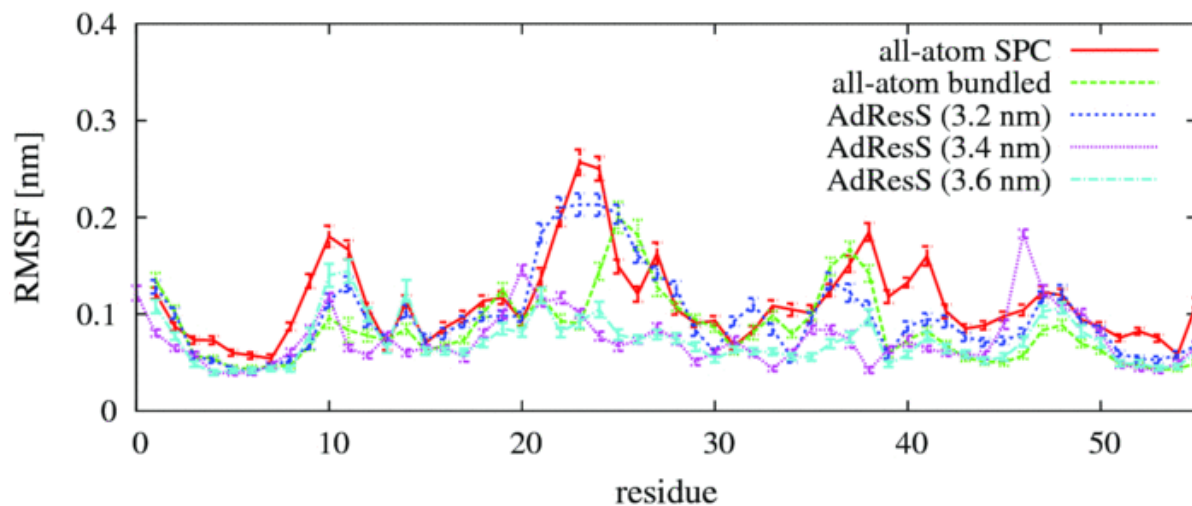


56-residue Protein G

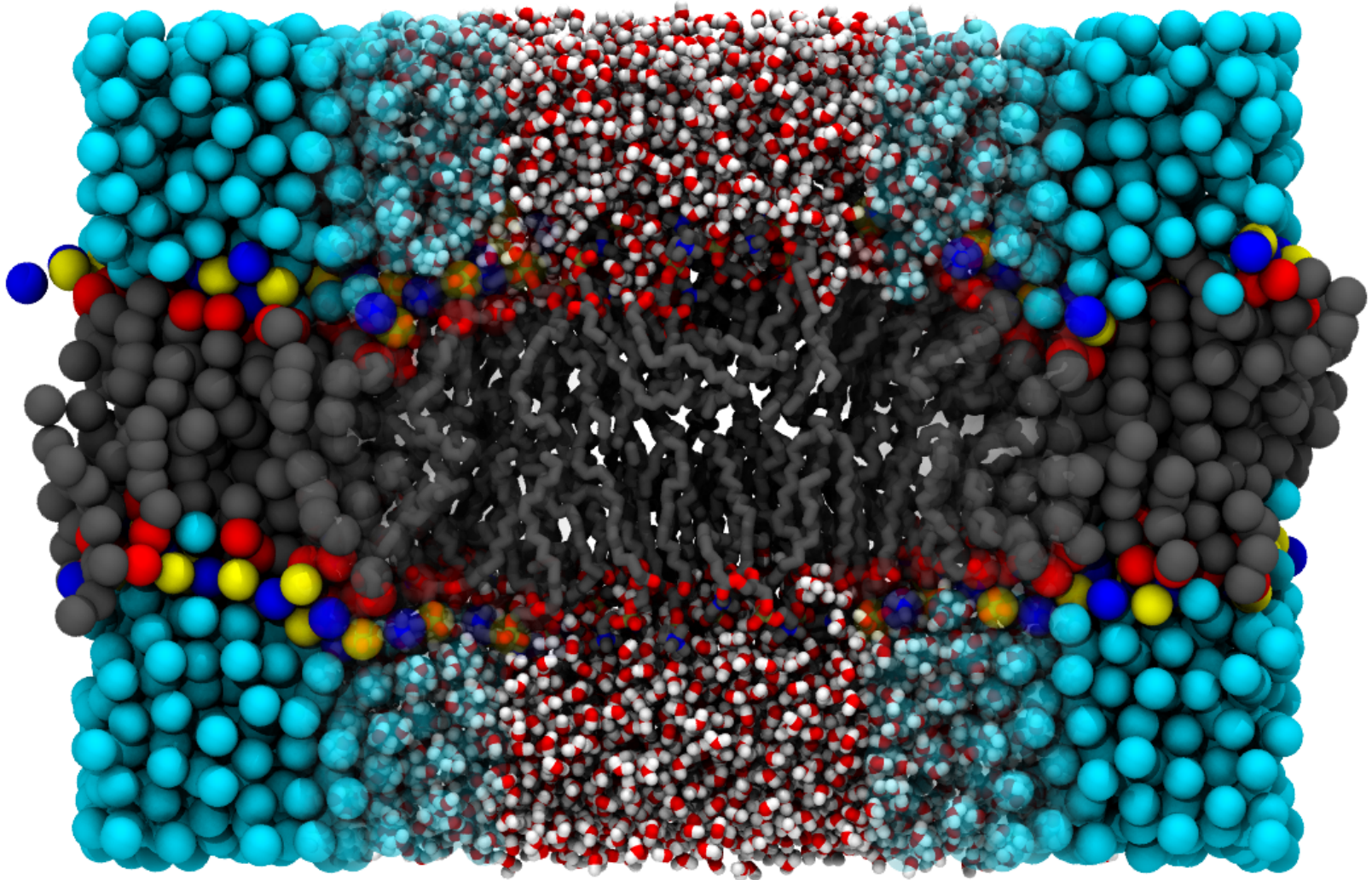
Bundled SPC water



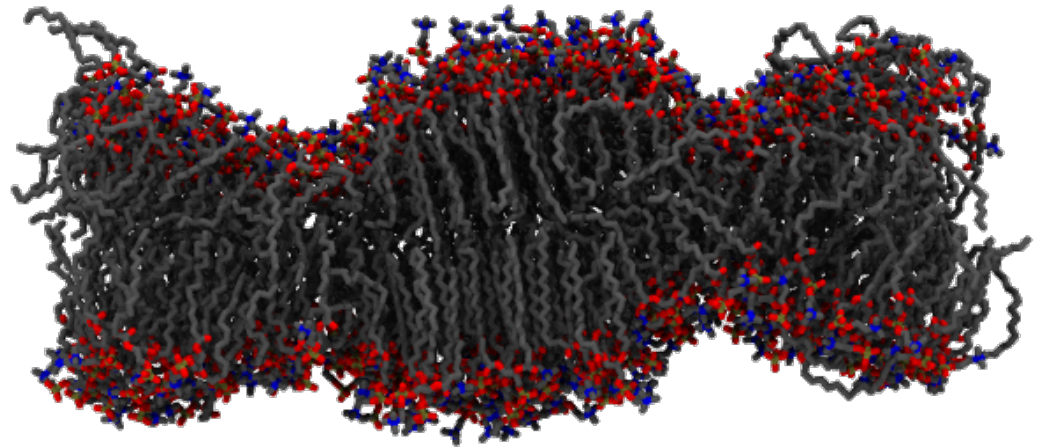
Structure and Dynamics are kept



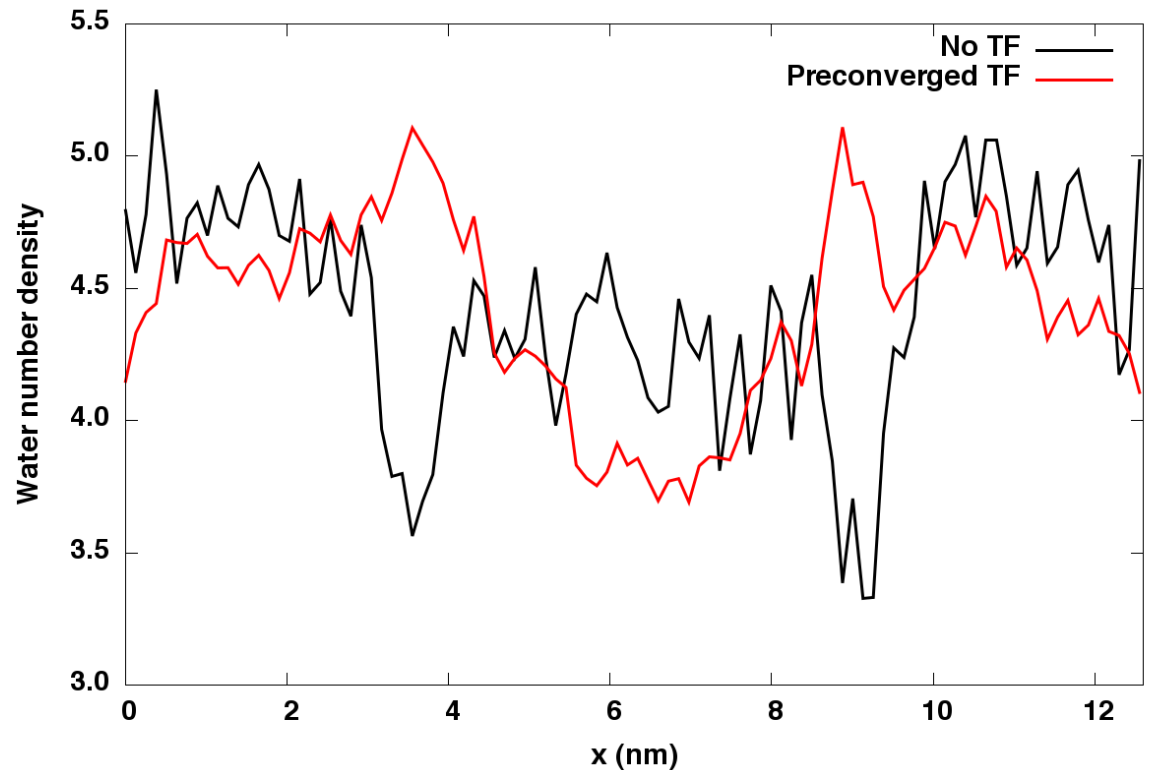
The goal



Global apl: 59.6 Å²
AA apl: 58.3 Å²
CG apl: 69.0 Å²



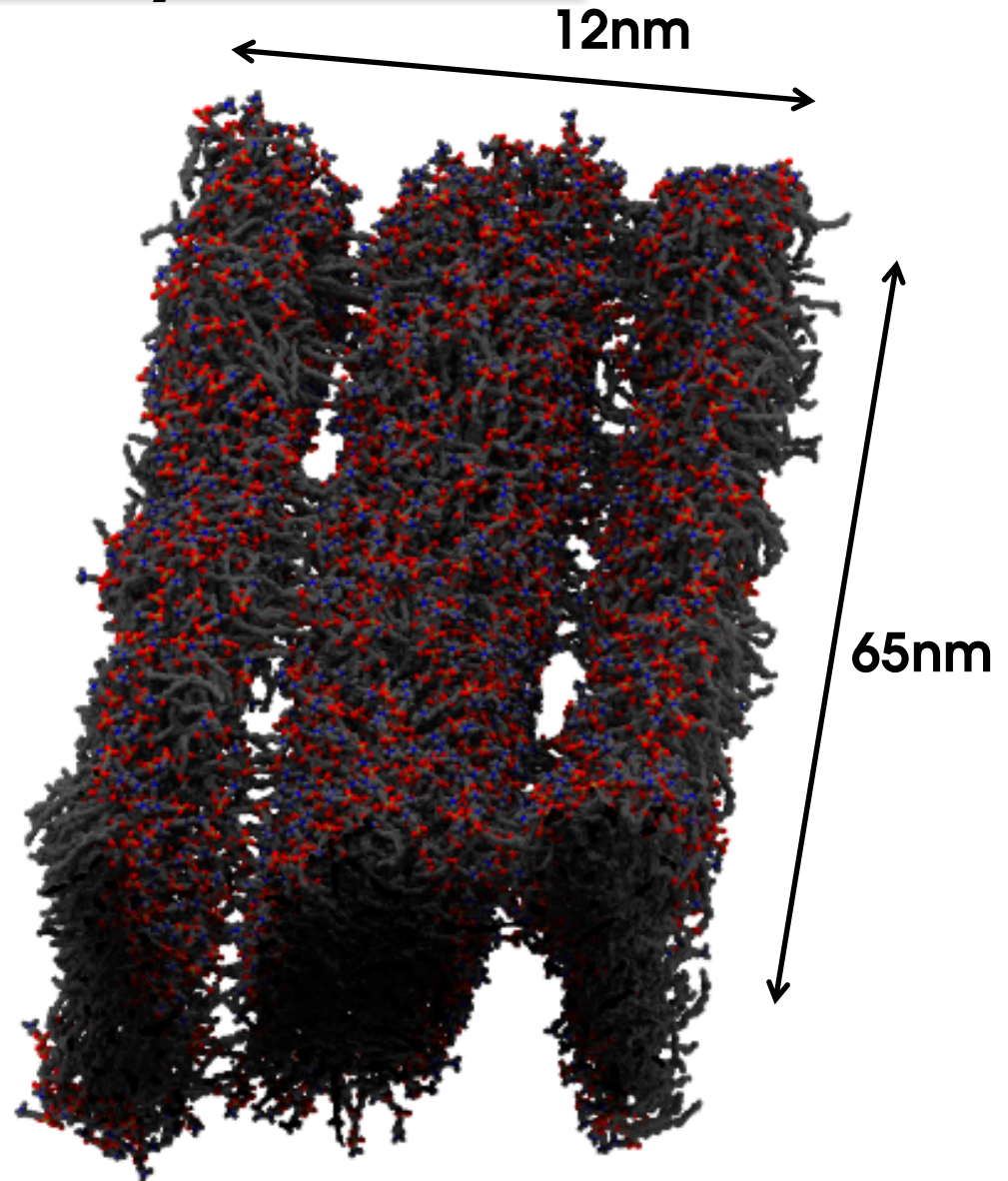
Fixing the water first?



Bilayers

More data?

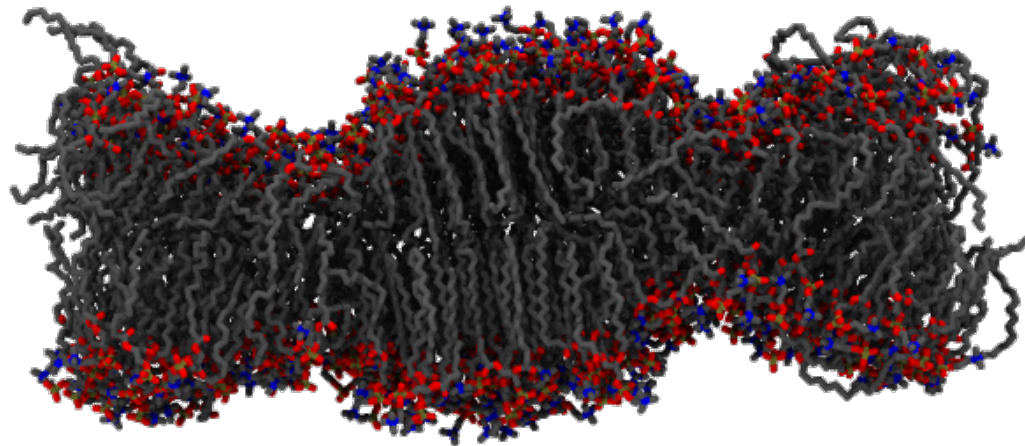
Can we get an estimate of the correction magnitude?



Is the goal even feasible?

Forces normal to the membrane might originate from the phase's anisotropic character

Cross-interactions with the water phase require a thermodynamic force converged simultaneous for both. Shear may be introduced.



The (late) GROMACS implementation keeps AA degrees of freedom in the CG region

CG secondary structure must be enforced

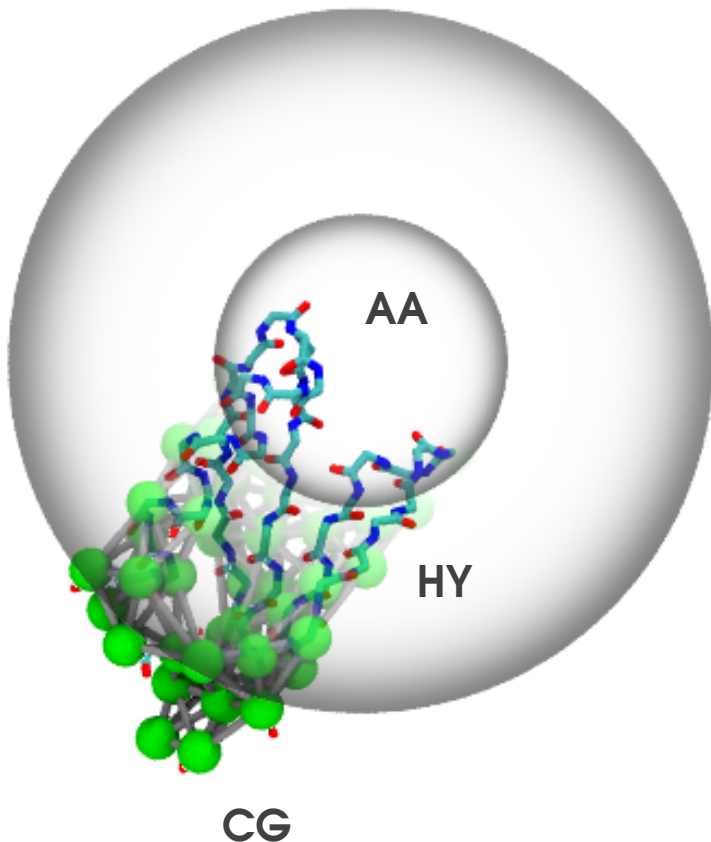
Elastic networks must be used

CG bonds must be switched on/off

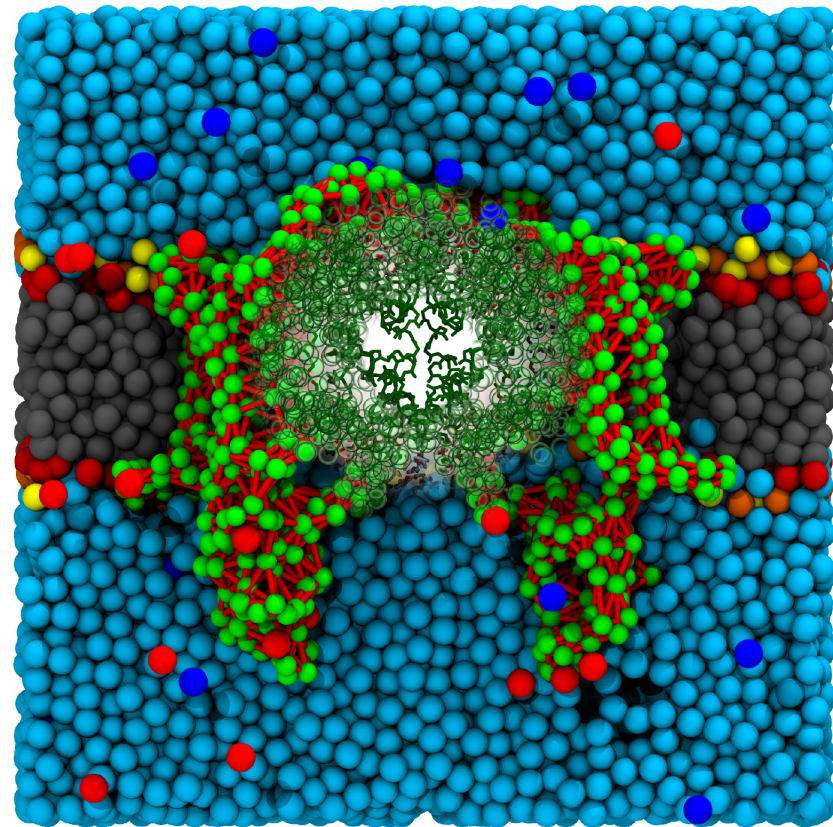
Bond forces scaled according to λ

Angles and dihedral torsions scaled according to λ at midpoint of each side

No CG constraints



TPC1



Martini-GROMOS (54A7) AdResS

AdResS region centered on the pore

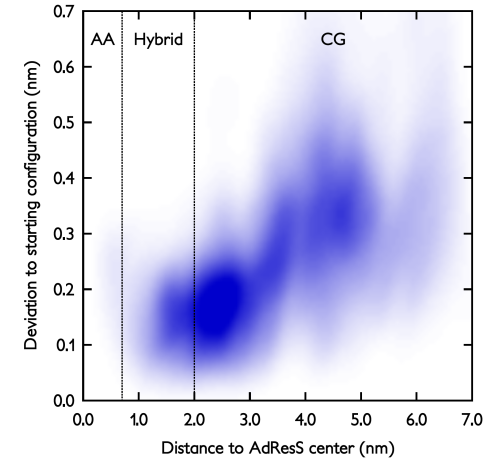
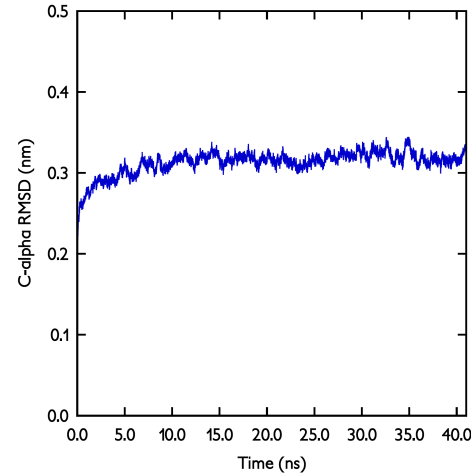
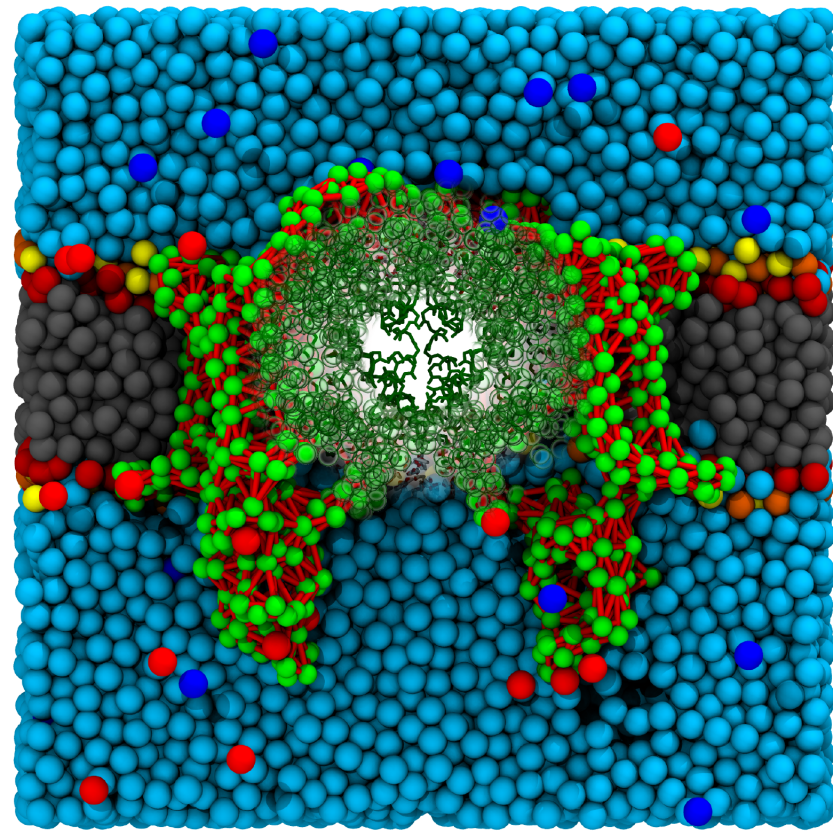
Soft restraints prevent protein diffusion.

Thin hybrid region (1.3 nm) doesn't reach the lipids.

Relative resolution

A Chaimovich, C Peter, K Kremer – J Chem Phys 2015

TPC1



Structure well-kept in the atomistic and hybrid regions

No bilayer deformation

To Do:

~~Cylindrically shaped region~~

Water/ion density correction

Updating AdResS center

Actually interesting stuff

Performance

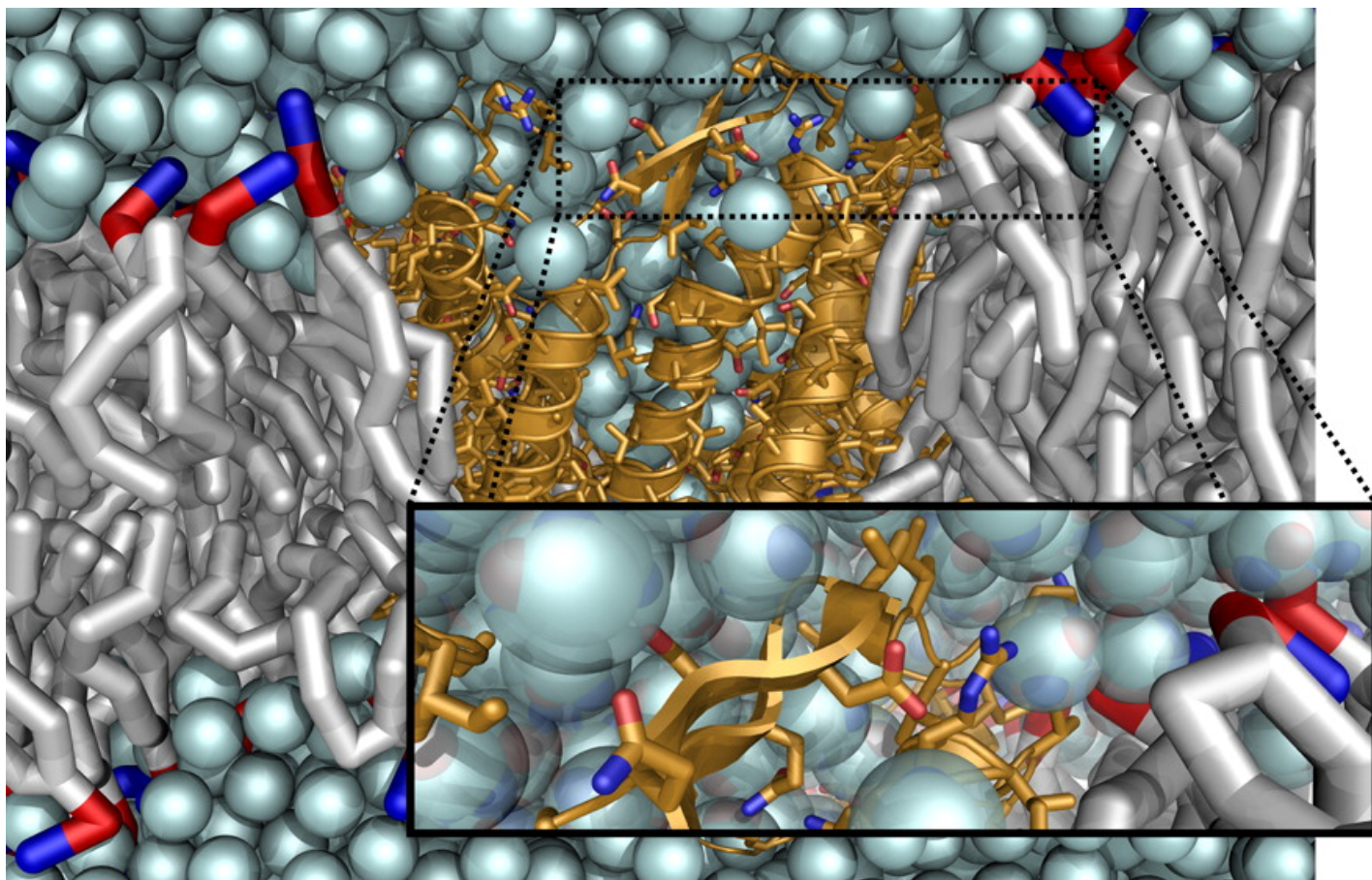
Comparison with a full AA system

	AdResS	Full AA
single CPU	0.8 ns/day	0.4 ns/day
12 CPUs	3.5 ns/day	2.3 ns/day
12 CPUs + GPU	—	5.0 ns/day

Already a real-life speedup

Must implement other optimizations

The Hybrid Scheme



The Hybrid Scheme

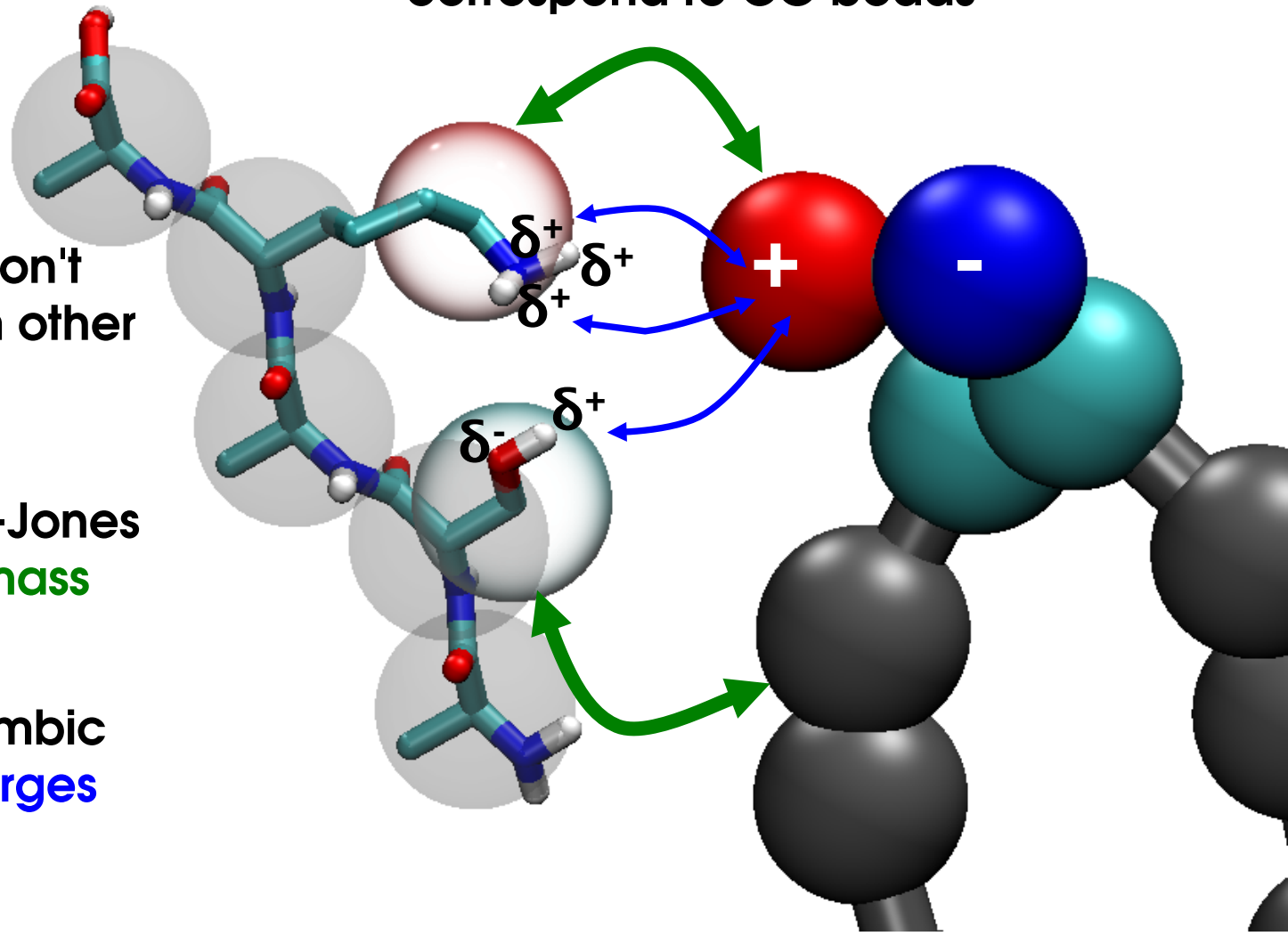
AA—AA interactions
CG—CG interactions
Normal

Centers of mass don't
interact with each other

CG—AA Lennard-Jones
Via centers of mass

CG—AA Coulombic
Via partial-charges

AA configuration has extra particles
at the center of mass of groups that
correspond to CG beads



Pros and Cons

Pros

No need for specific AA-CG potentials;
Directly implementable into GROMACS.

Cons

The AA molecules see a very simplified electrostatic world;
There's practically no friction for small protruding AA groups;
Speedup is limited by the need of a small time step.

Technical Details (with GROMACS in mind)

To have the highest possible time step (5 fs)

All AA bonds are constrained;

Hydrogens and planar rings are built as virtual sites.

To stabilize the AA structure

Angles and rotations of outer groups are frozen.

To combine potentials

Tabulated potentials must be created for each specific interaction.

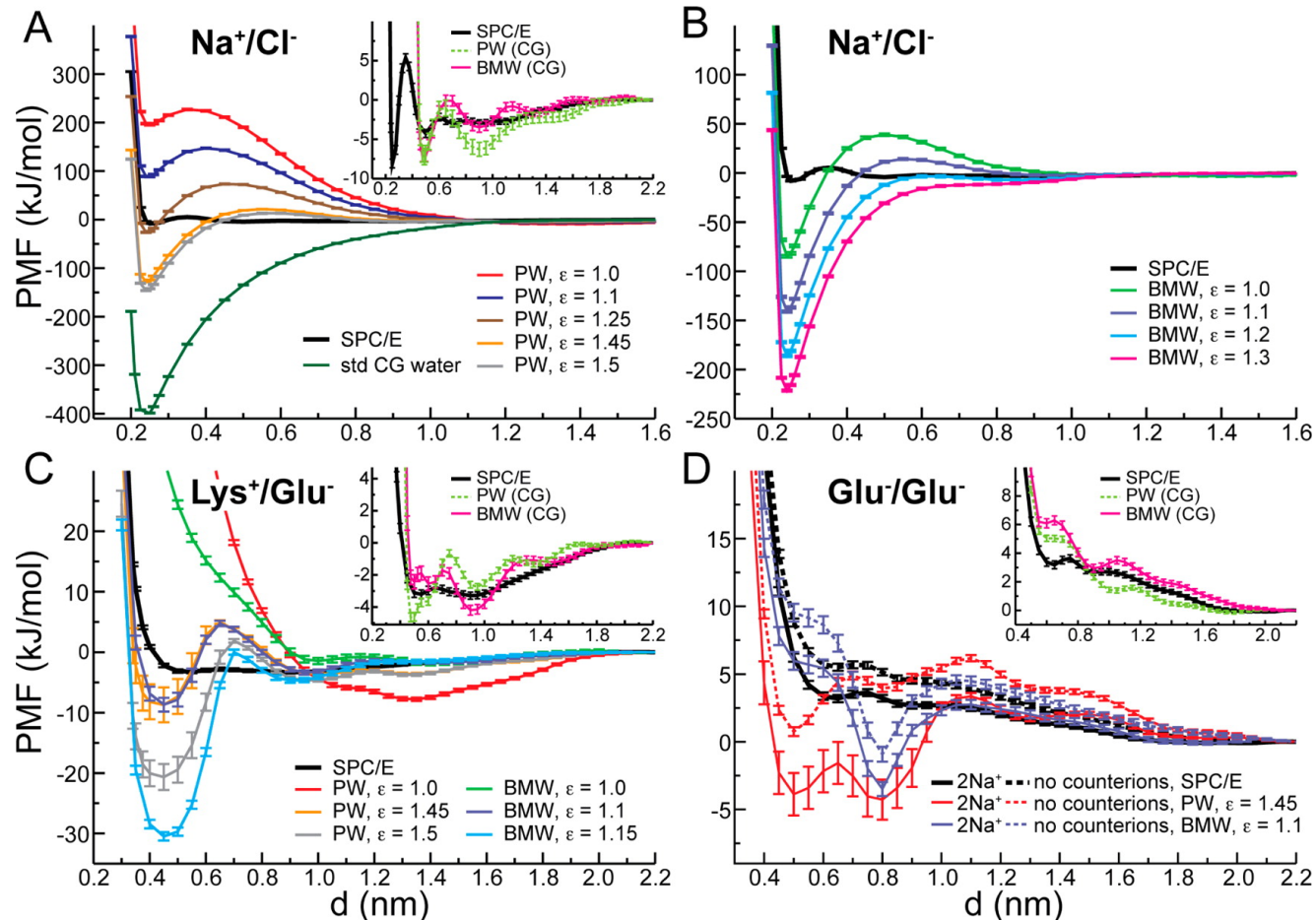
To improve performance

Specifically tell GROMACS to ignore center—center and center—AA interactions.

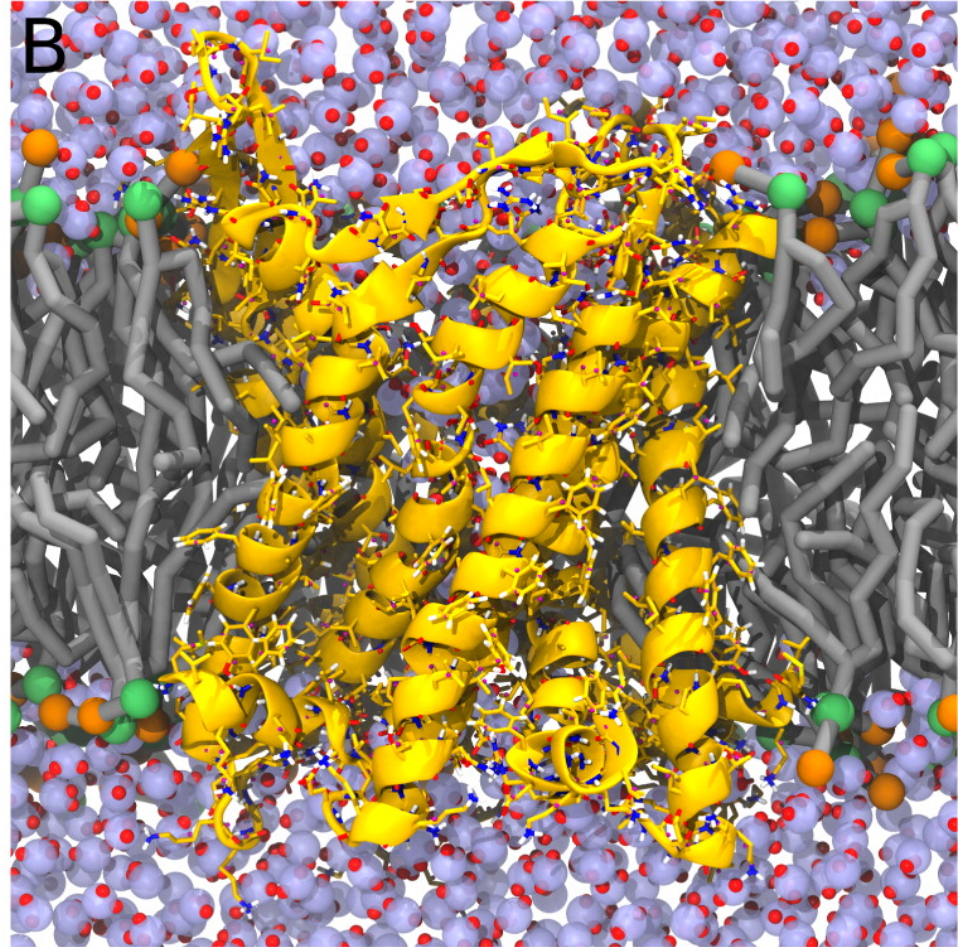
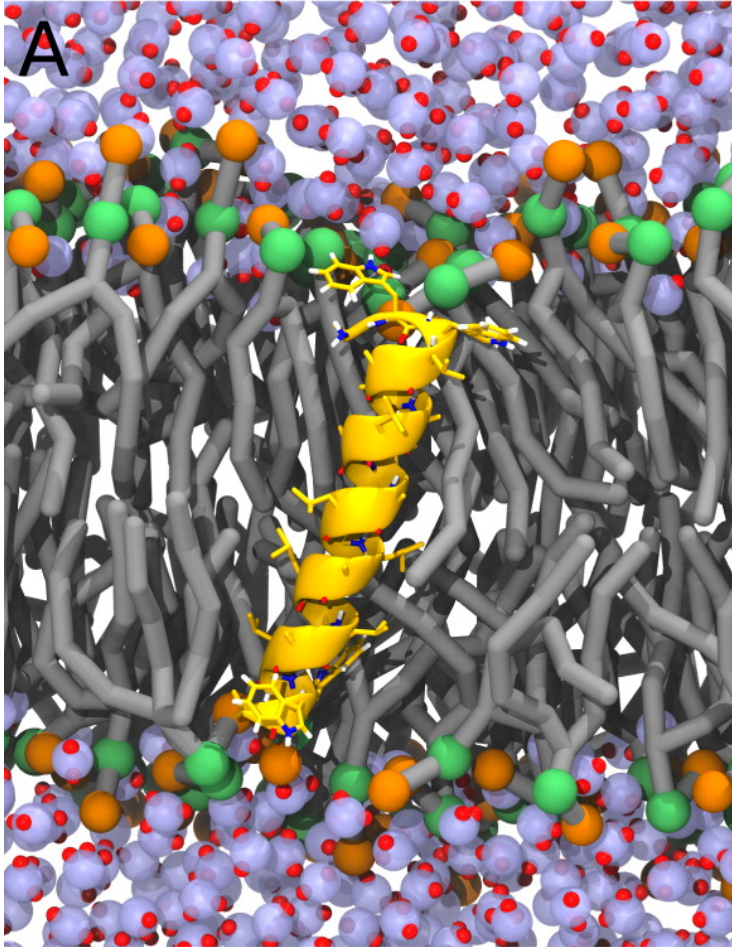
A bit more truth about electrostatics

Most atomistic models expect a degree of explicit screening;

Using polarizable water helps, but behavior is still far from optimal.



Hopeless?



Work is in progress to try and address the current limitations.