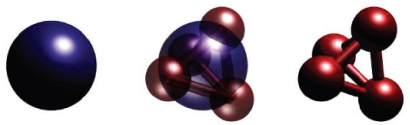
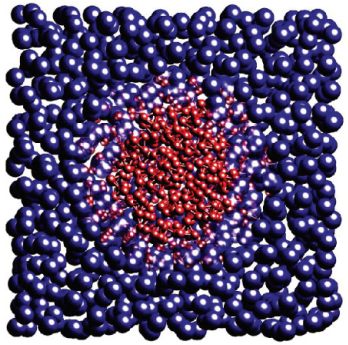
Blending Martini

The AdResS Scheme

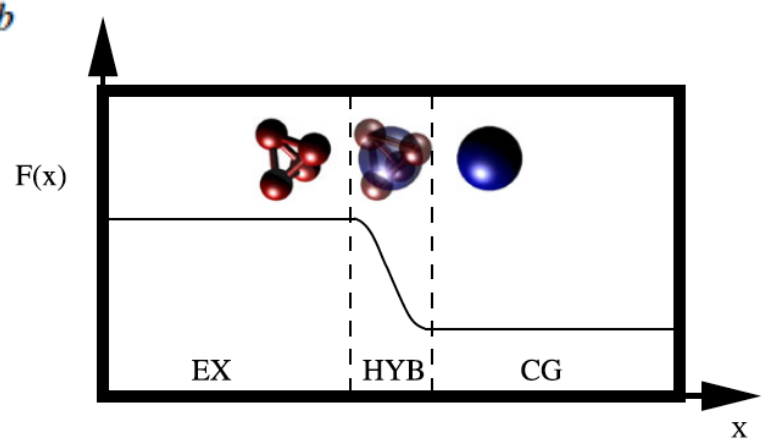
Adaptive Resolution Scheme





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

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



Original scheme: random molecule insertion

M Praprotnik, LD Site, K Kremer - Annu. Rev. Phys. Chem., 2008

M Praprotnik, L Delle Site, K Kremer – J. Chem. Phys., 2007

Density

Differences in chemical potential **will** create inhomogeneities in the density

A correcting thermodynamic force must be introduced

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

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)

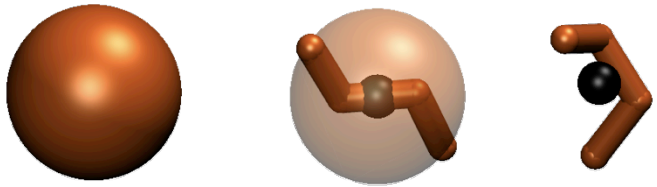
Other issues

Tables must be used if CG and AA potentials differ

S Fritsch, C Junghans and K Kremer – J. Chem. Theory Comput., 2012

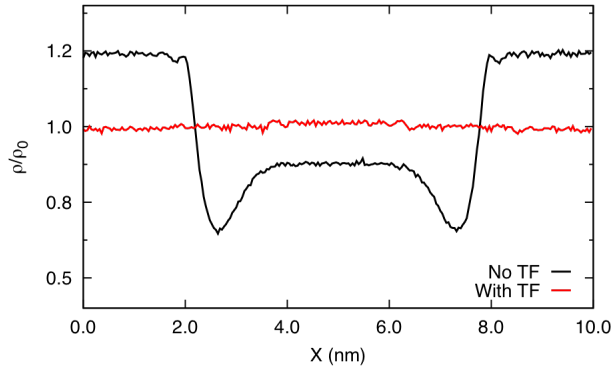
Butane System

Compressed butane
(gromos 53a6/Martini)

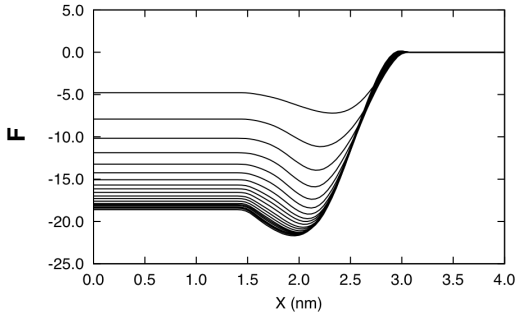


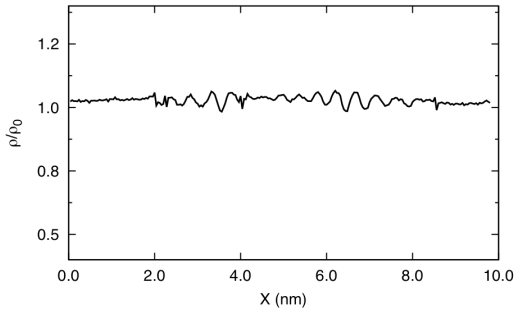
Thermodynamic Force

Density



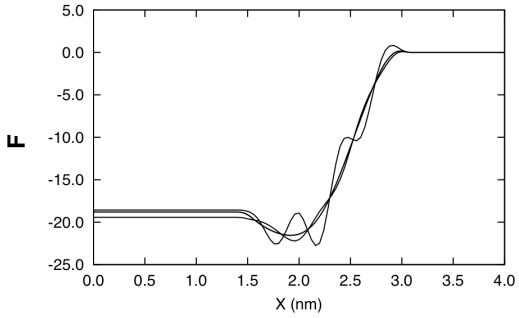
Take I



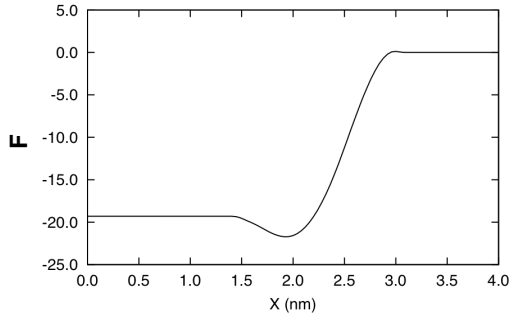


$$\mathbf{f}_{\mathbf{th}}^{i+1}(\mathbf{r}) = \mathbf{f}_{\mathbf{th}}^{i}(\mathbf{r}) - \frac{1}{\rho_0^2 \kappa_T^{\mathbf{at}}} \nabla \rho_i(\mathbf{r})$$

Take II

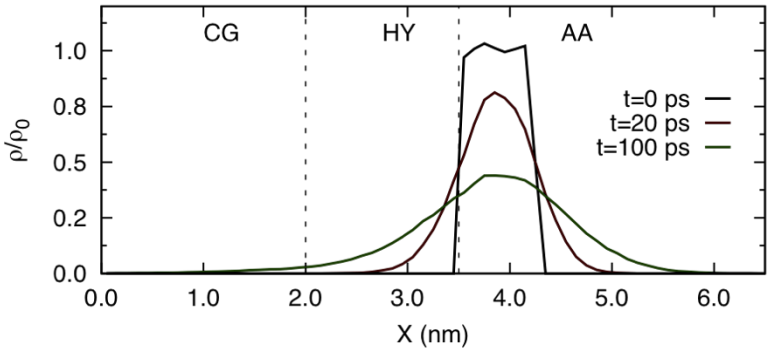


Take III

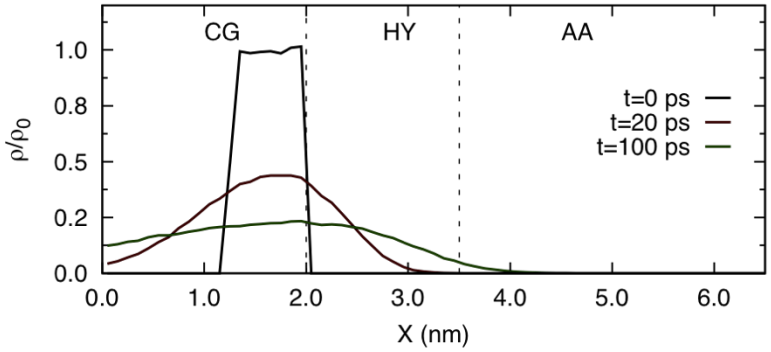


Implemented in the latest VOTCA releases

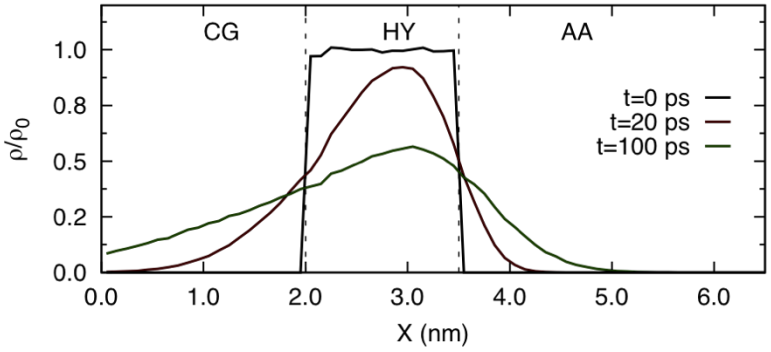
Solvent Diffusion



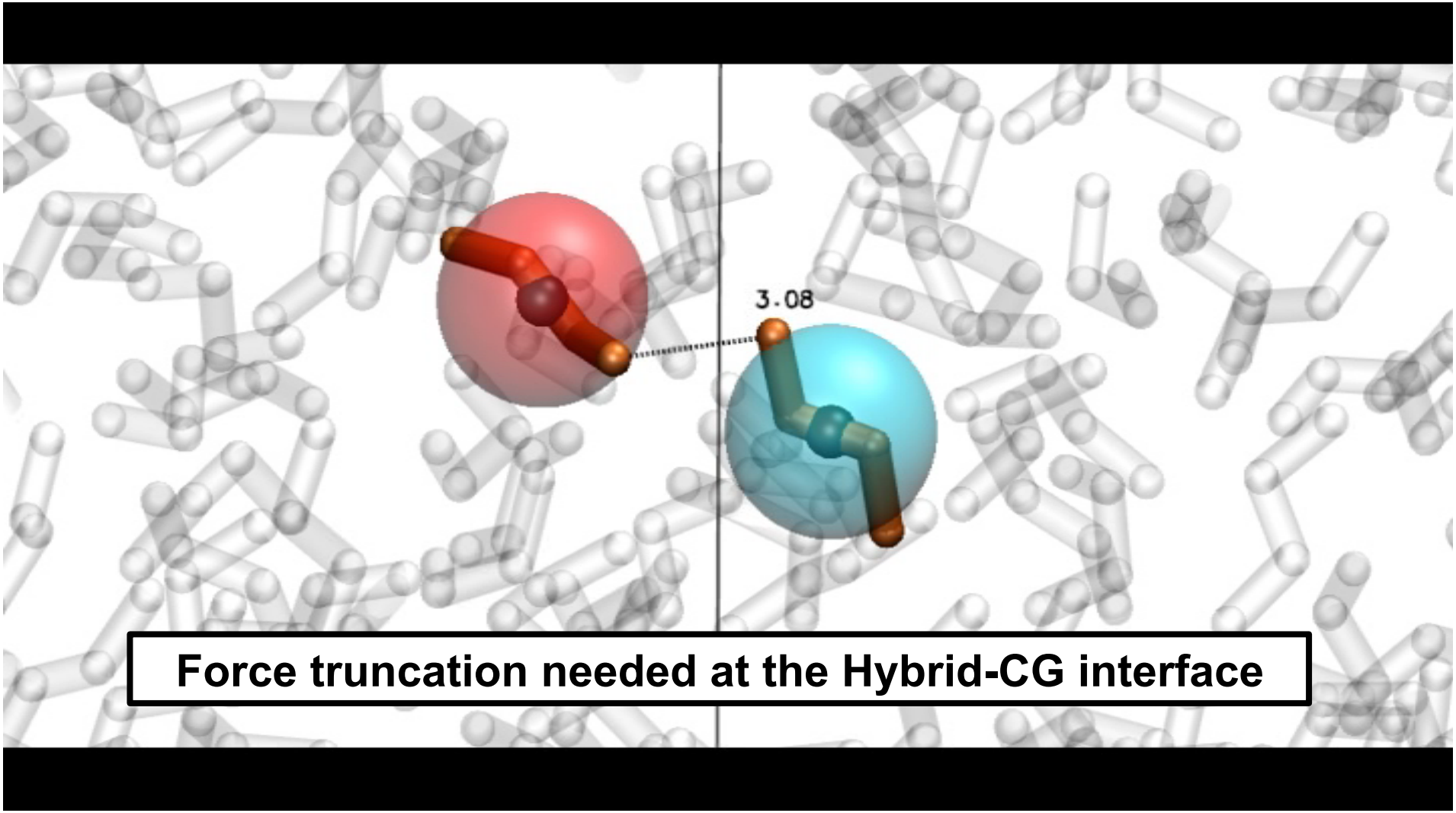
No obvious barriers to diffusion



Asymmetric diffusion (expected)



System Instability

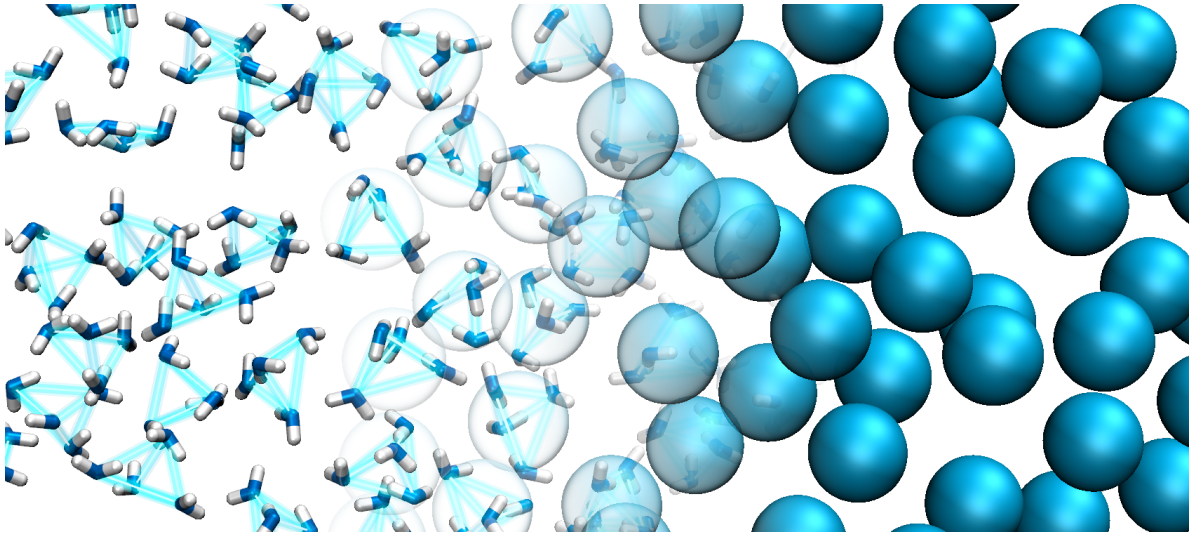


Water System

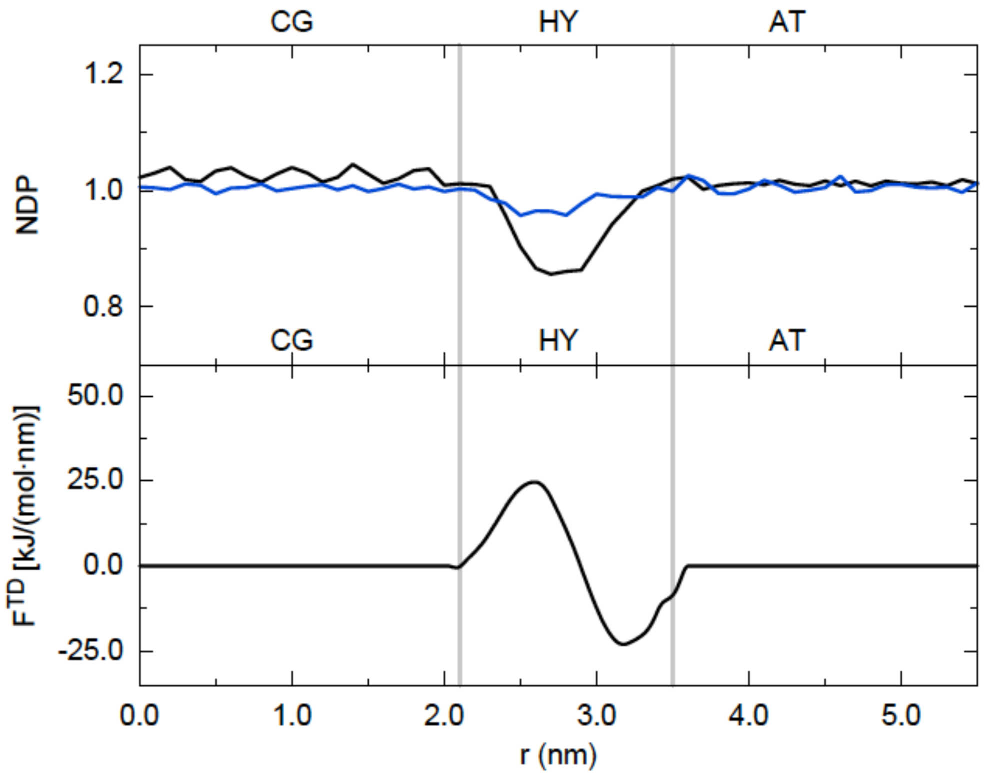
Bundled SPC water

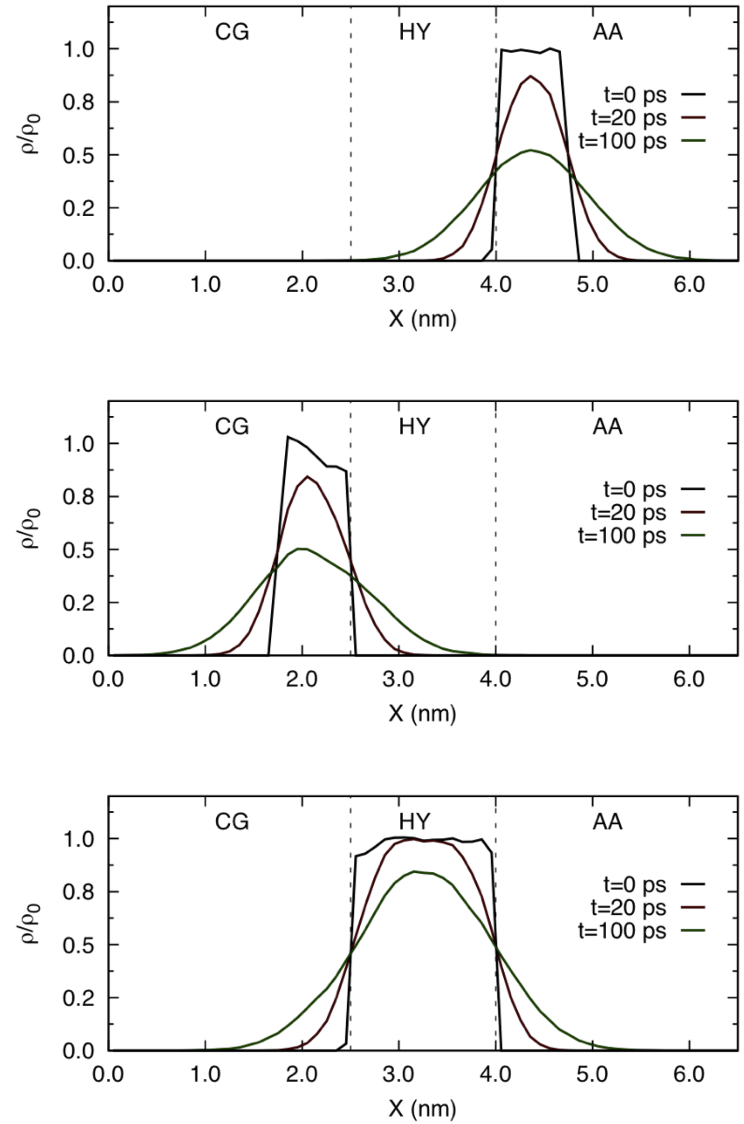
Oxygens of four waters connected by semi-harmonic attractive bonds

O-O Lennard-Jones repulsion increased by 30%



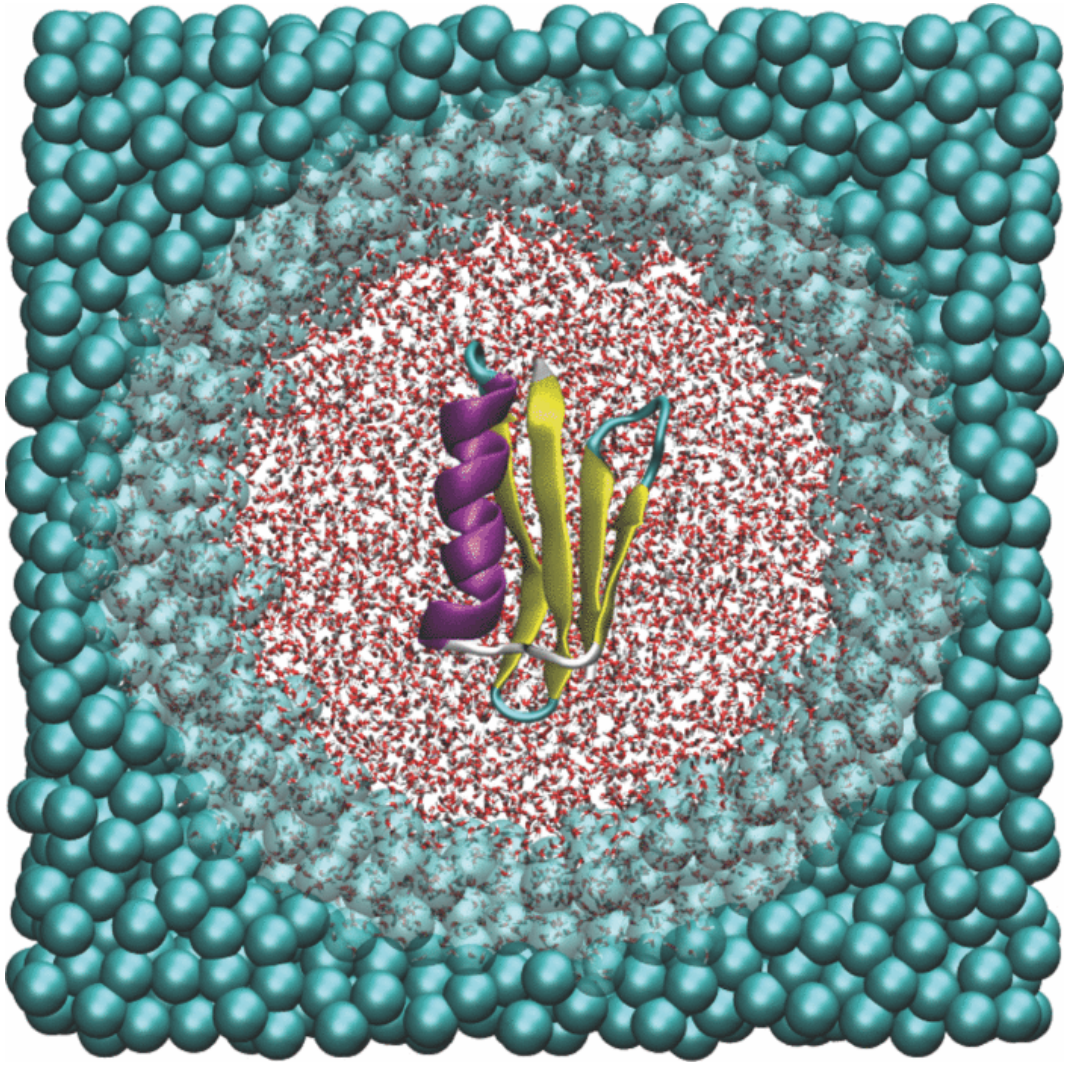
Solvent **Properties**





Greater Challenges

Proteins

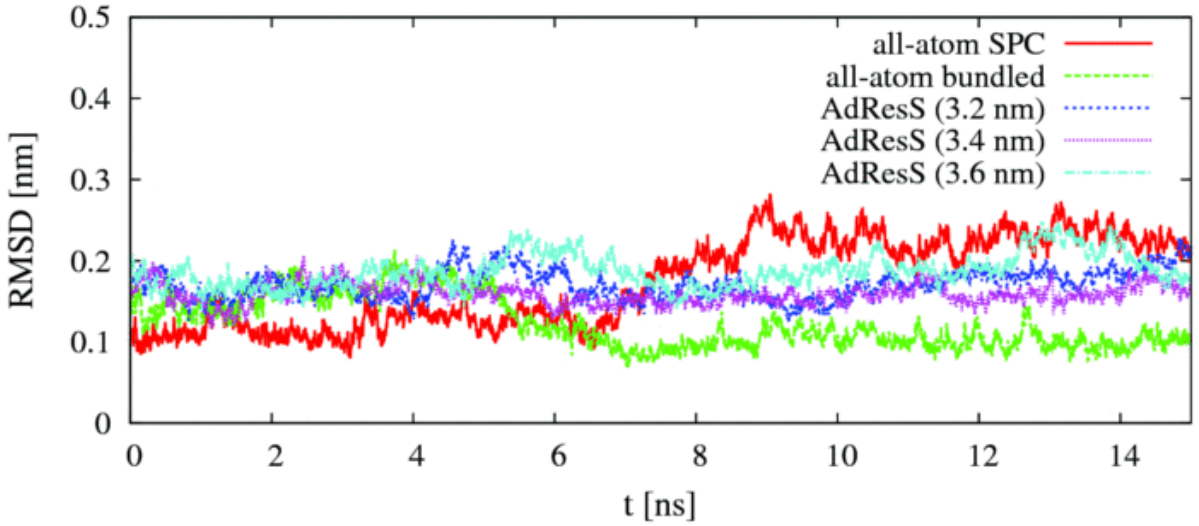


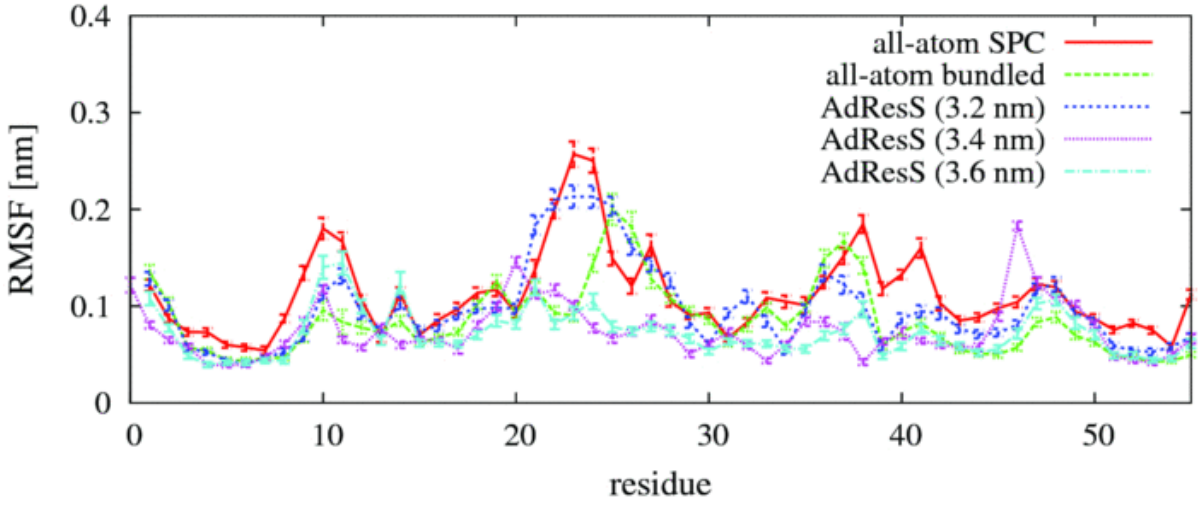
56-residue Protein G

Bundled SPC water

Greater Challenges

Proteins

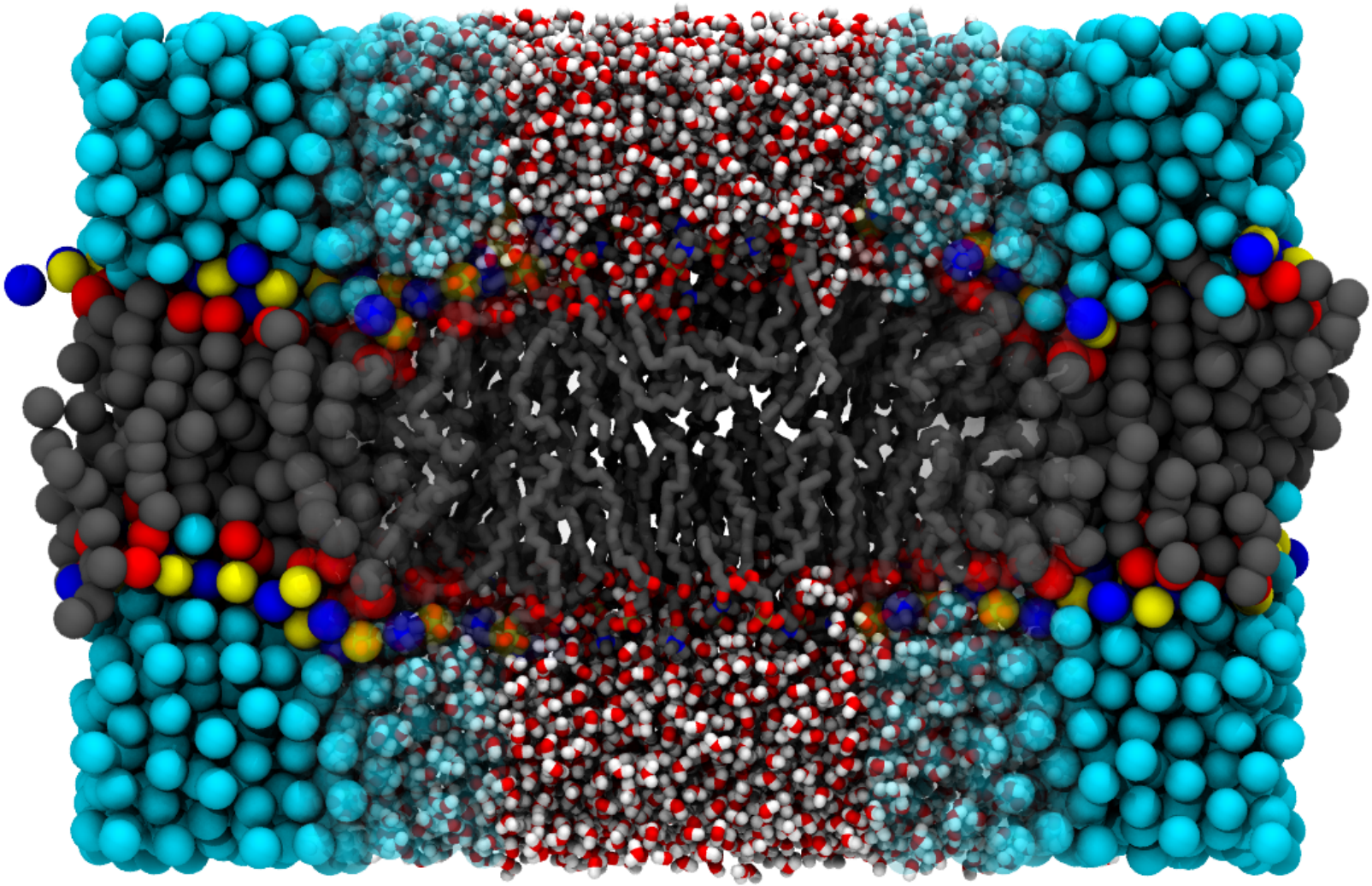




Structure and Dynamics are kept

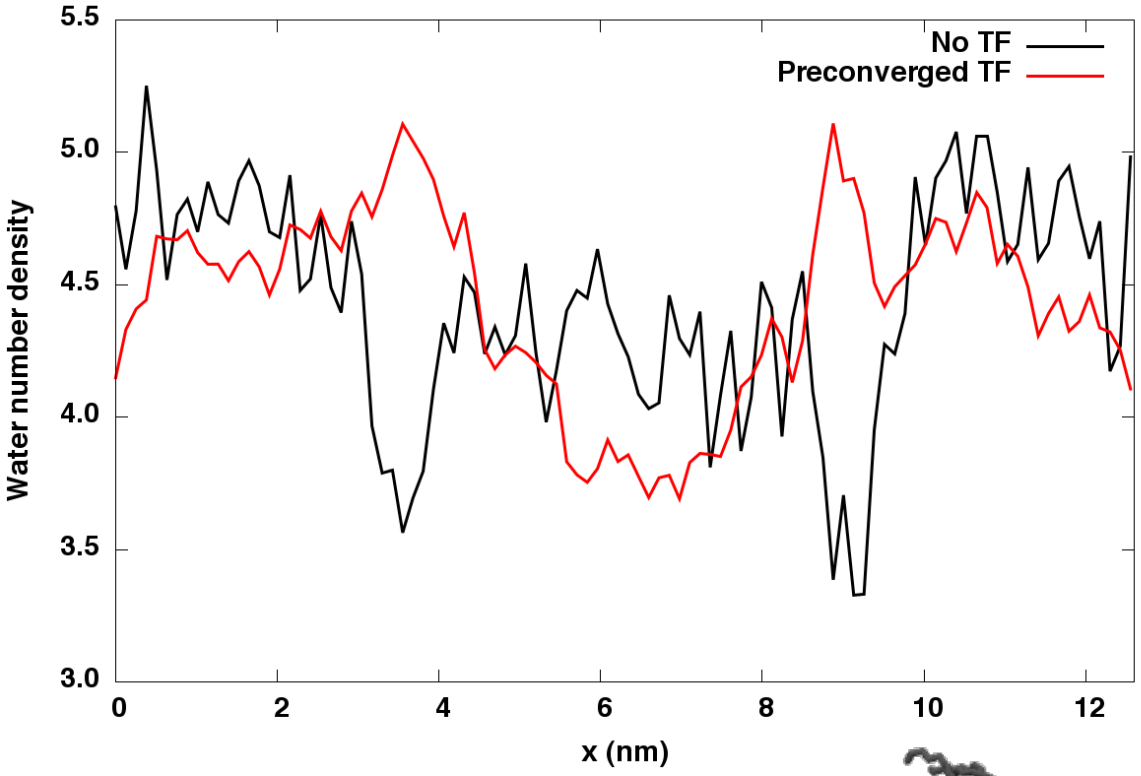
Bilayers

The goal

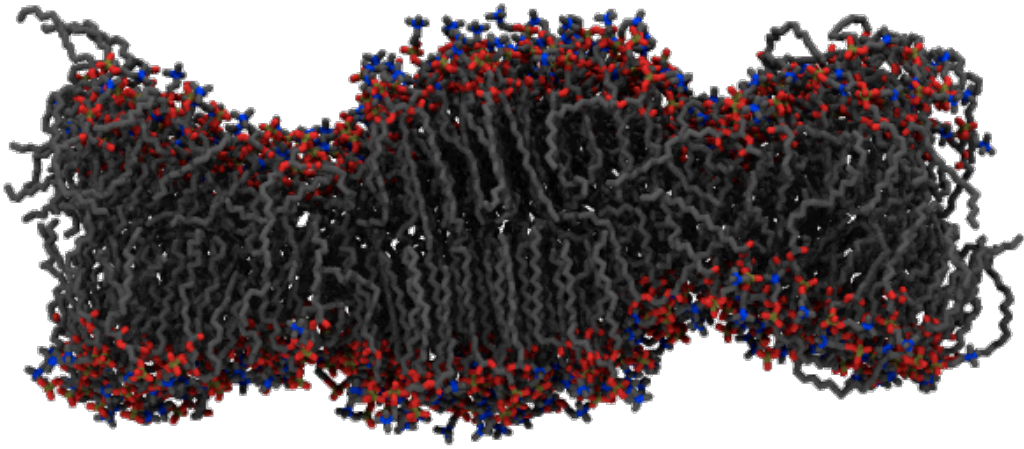


Greater Challenges II

Bilayers



Global Area/Lipid: 59.6 Å²
AA apl: 58.3 Å²
CG apl: 69.0 Å²



Performance

Comparison with a full AA system

Tabulated potentials used in both cases

GROMACS 4.6, on 12 CPUs

AdResS	AA-optimized	AA
5.3 ns/day	11.1 ns/day	2.4 ns/day

Outlook

The good

AdResS works on GROMACS 4.6

It is relatively straightforward to use with Martini/GROMOS

The bad

Is it worth the hassle and the potential artifacts?

The ugly

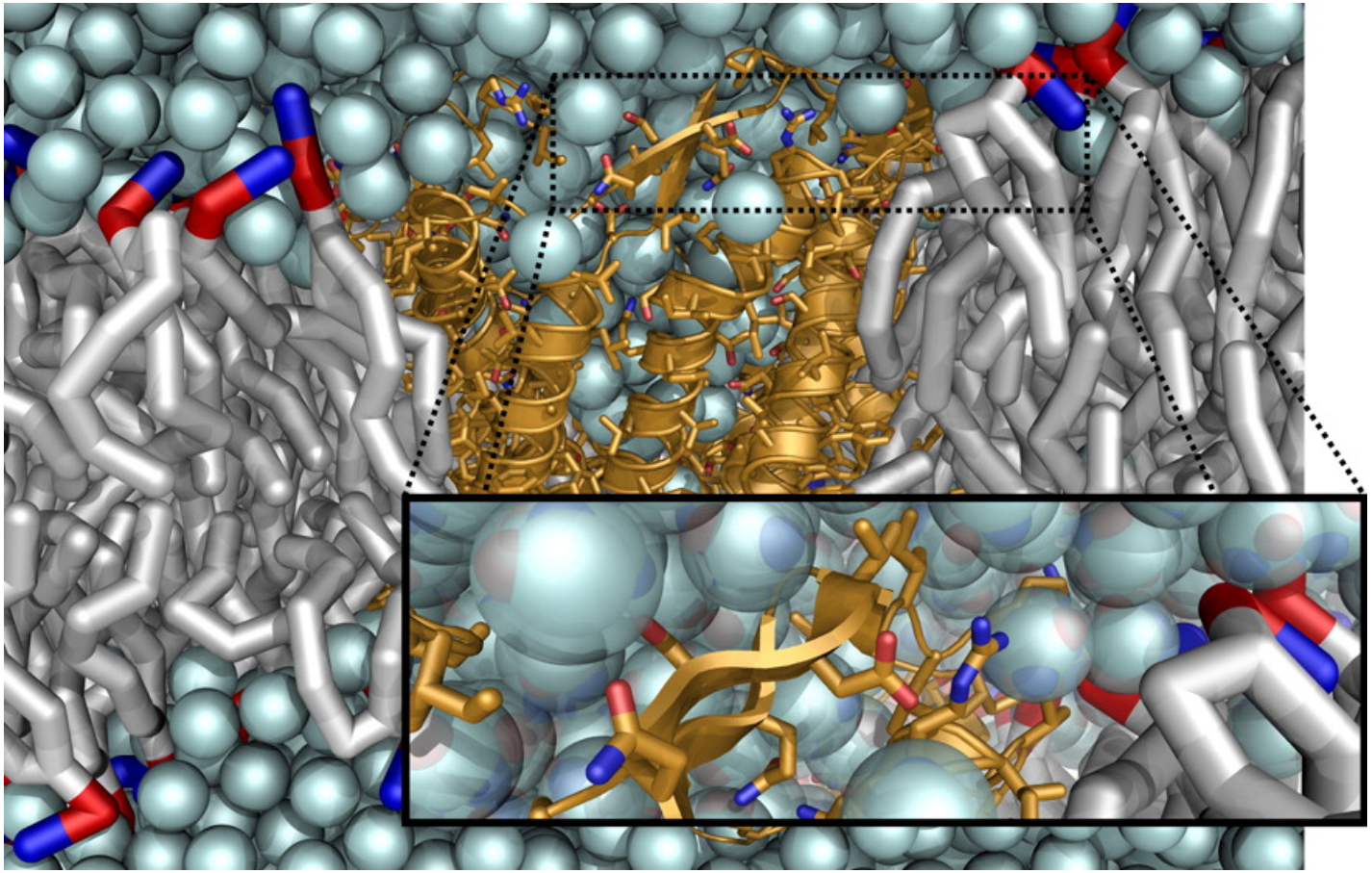
Some important stuff still ‘to-be-implemented’

The future

Convergence of Thermodynamic force for bilayers

Parts of proteins?

The Hybrid Scheme



J. Phys. Chem. B, 2013, 117 (13), pp 3516–3530

The Hybrid Scheme

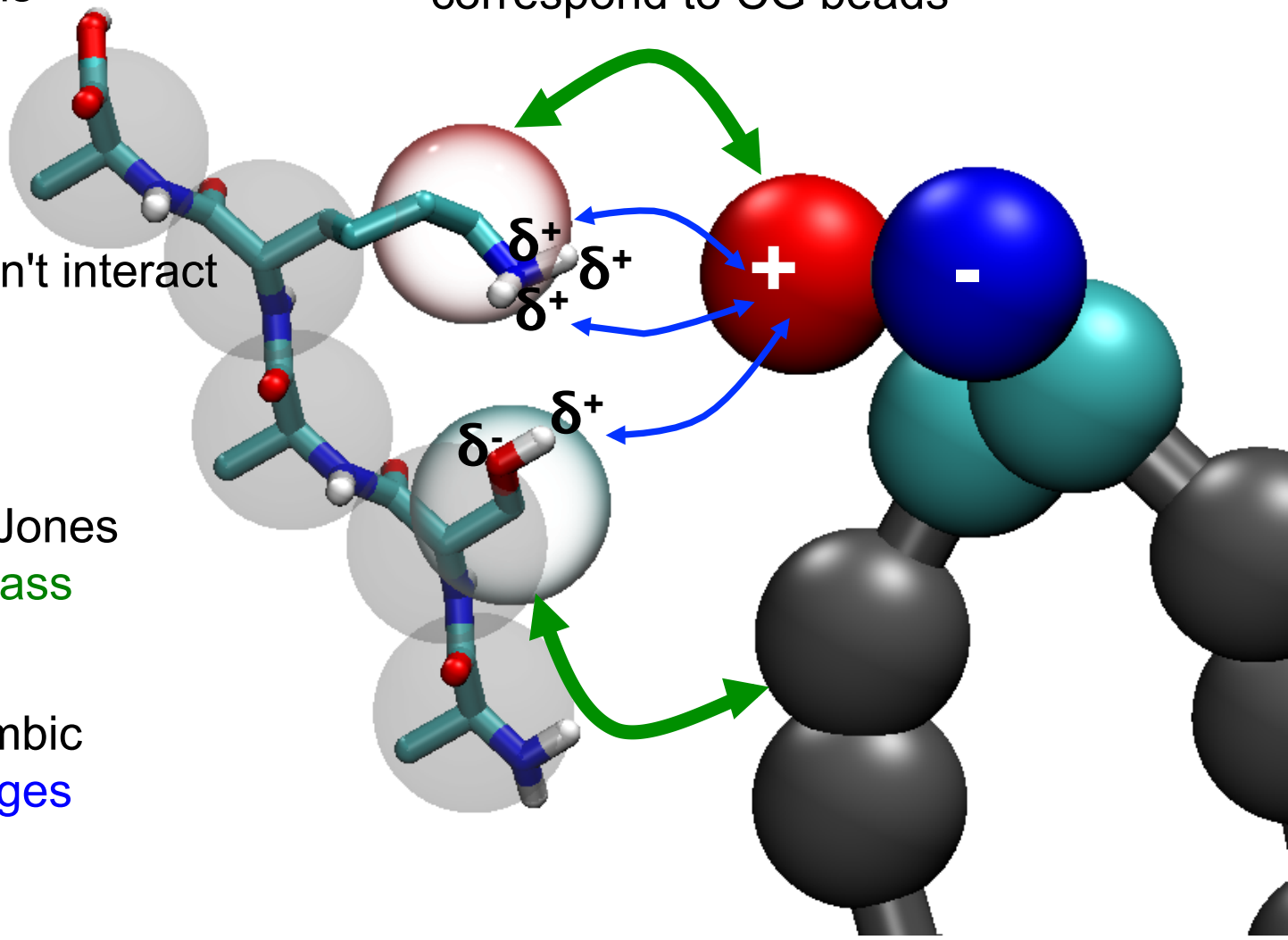
AA—AA interactions
CG—CG interactions
Normal

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

Centers of mass don't interact with each other

CG—AA Lennard-Jones
Via centers of mass

CG—AA Coulombic
Via partial-charges



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.

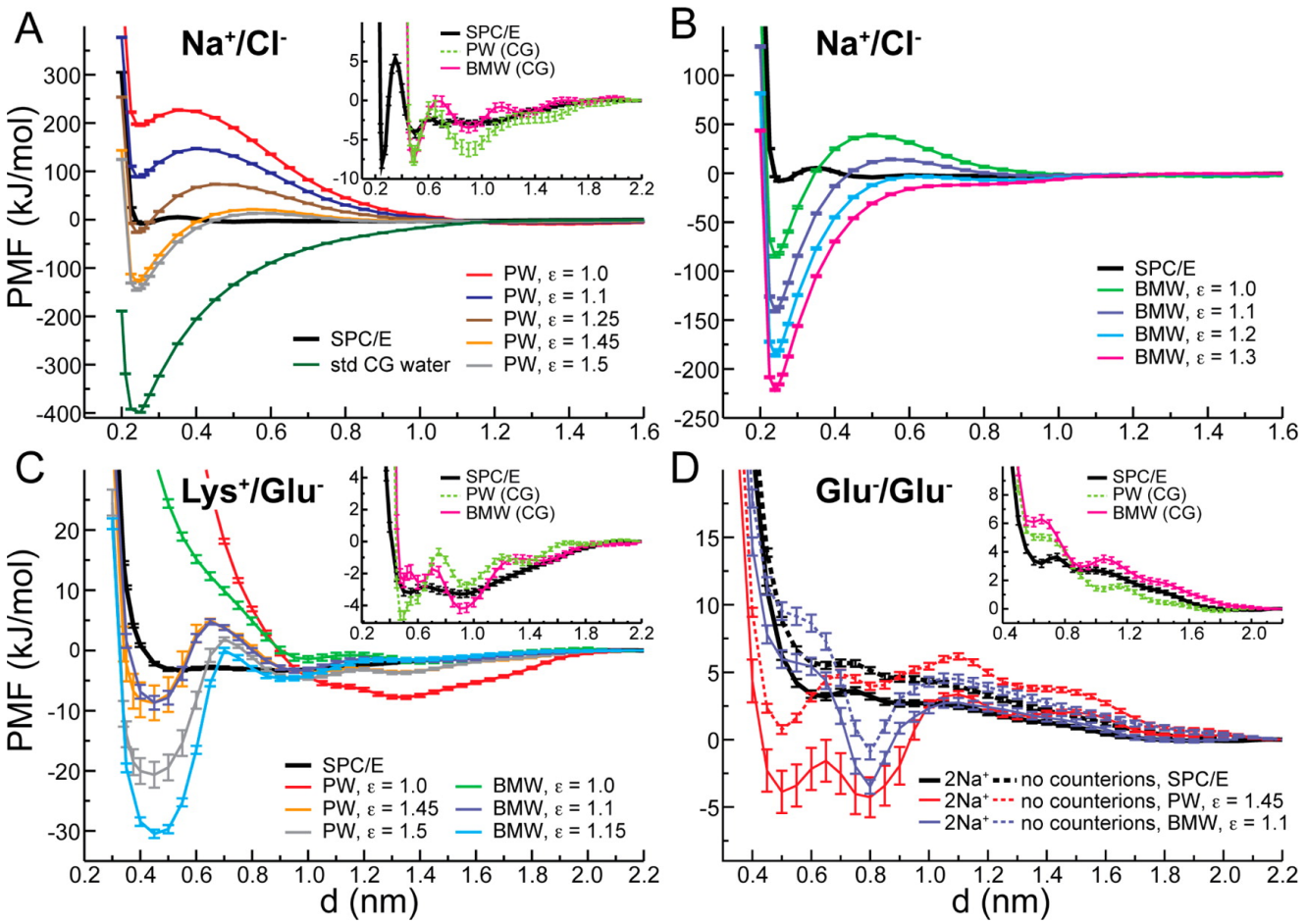
To improve performance

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

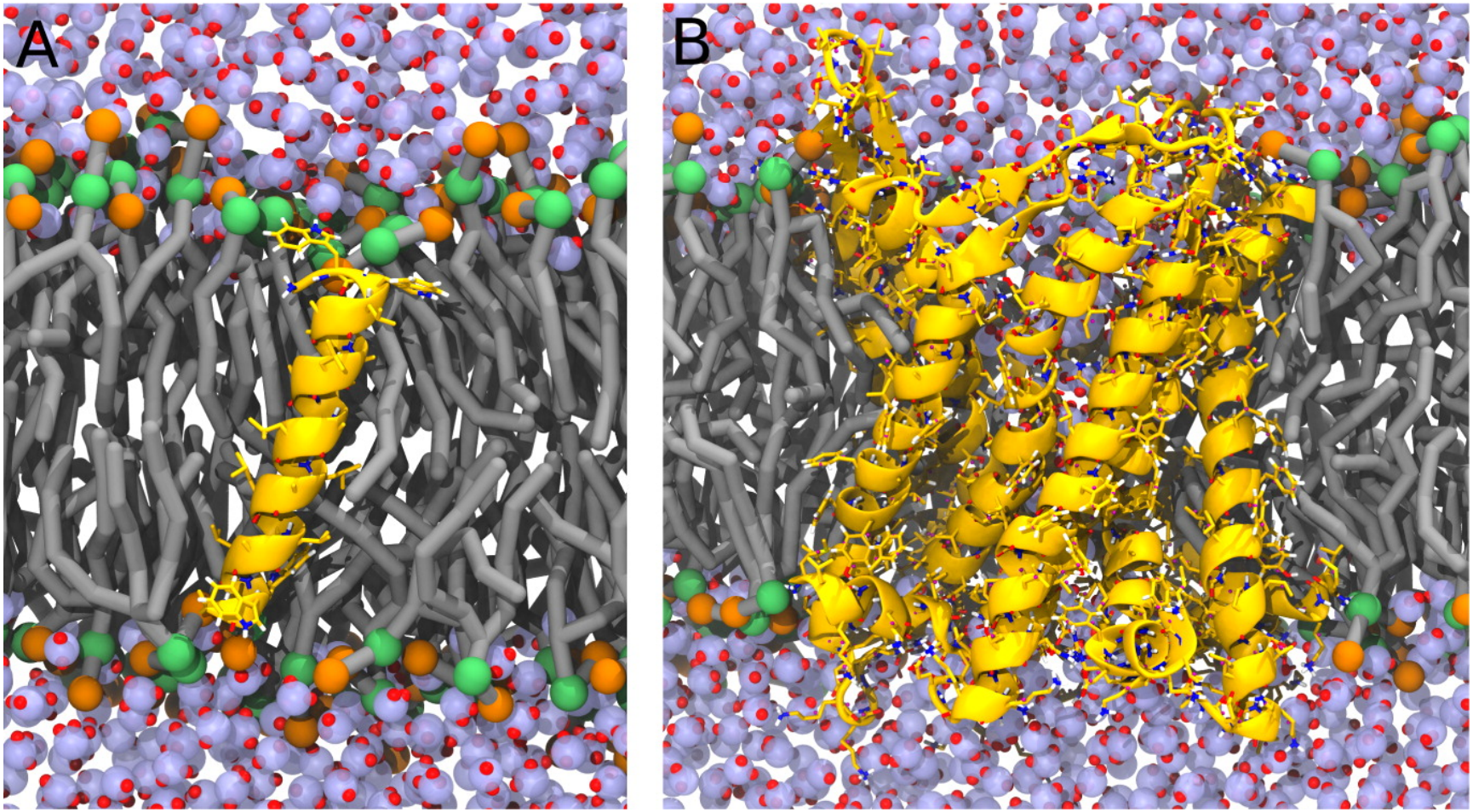
A bit more truth about electrostatics

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.