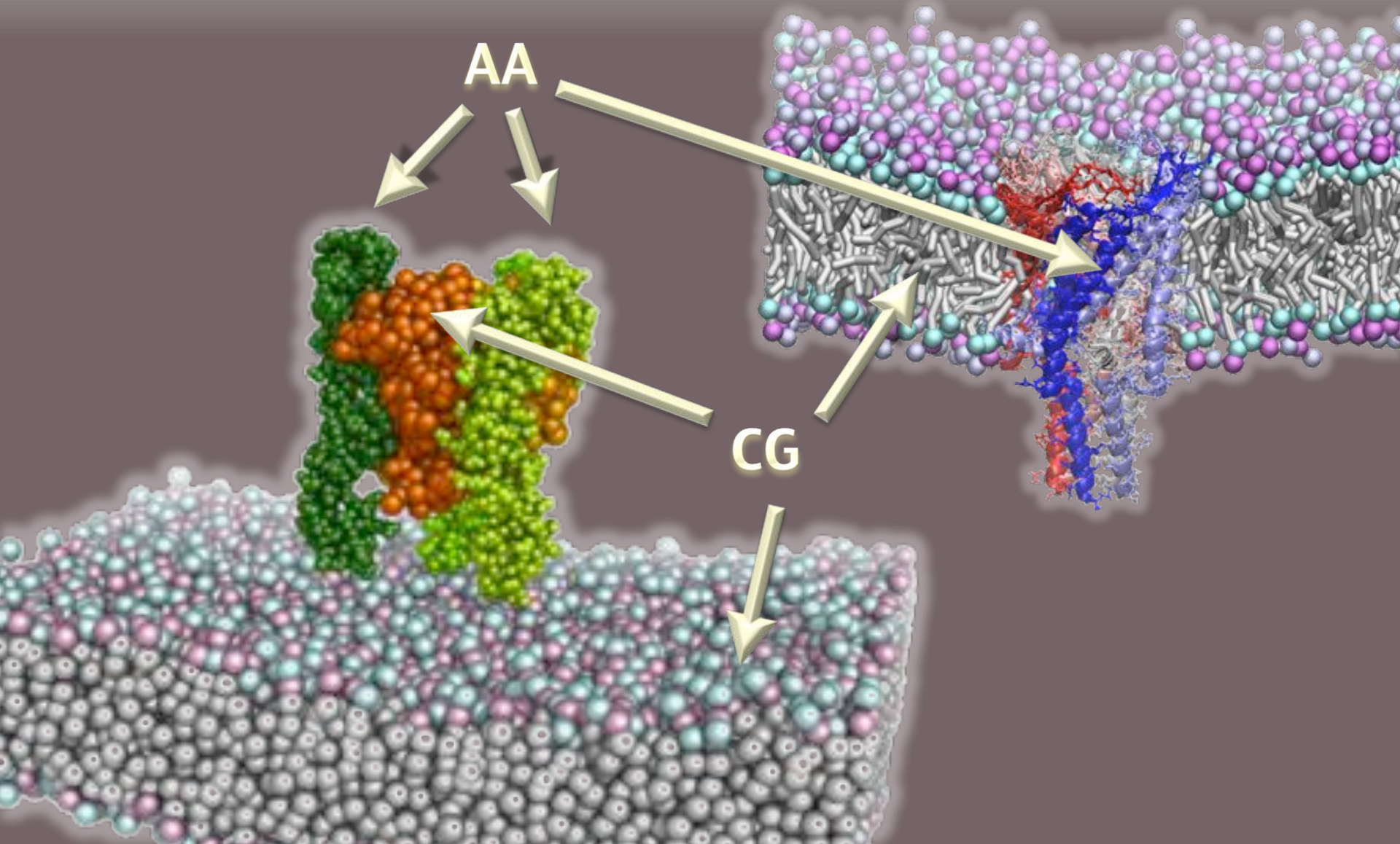
Hybrid simulations

The advantage of multiple levels of resolution



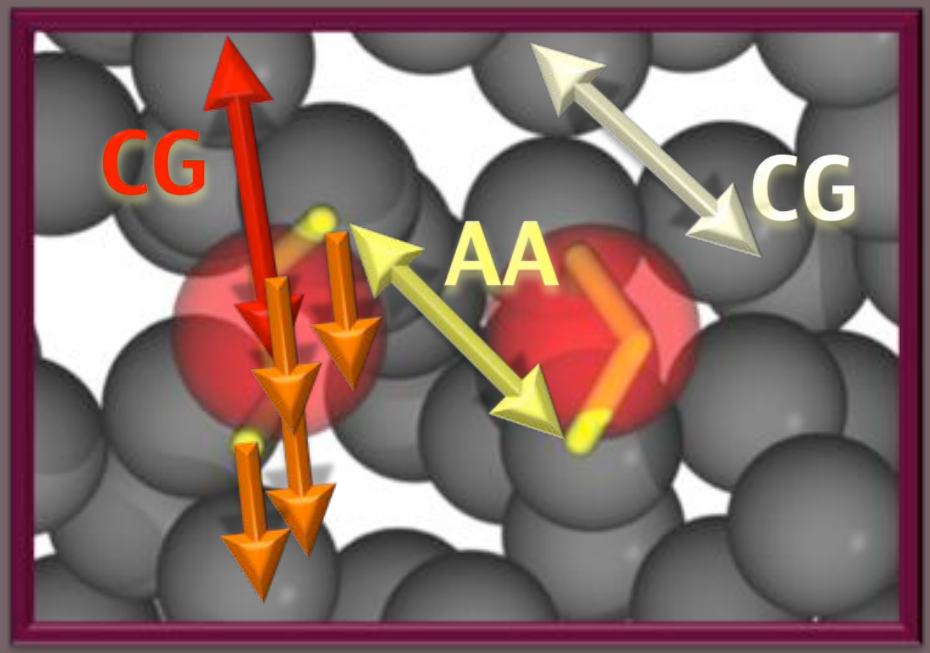
Hybrid simulations

Key challenges

- How to avoid extensive cross-parameterization ?
- How to treat electrostatic interactions ?
- How to avoid artefacts due to size mismatch ?

Hybrid simulations

Combining atomistic and CG interactions using virtual sites



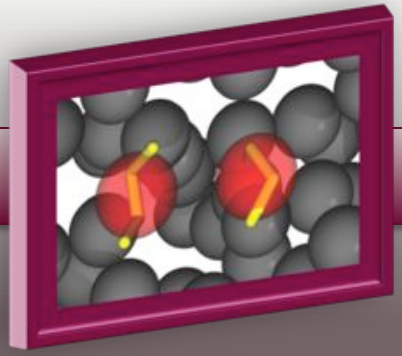
$$f_{AA} = m_{AA}/m_{CG}\, f_{CG}$$

- No need for new parameters
- Combines any two forcefields

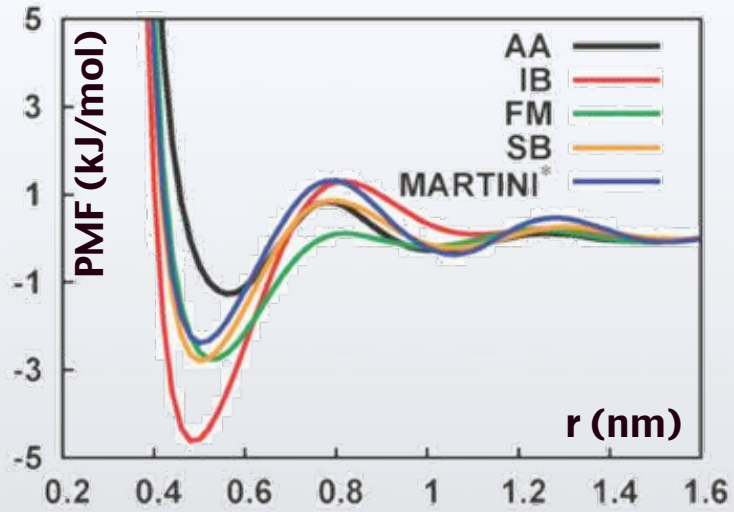
Rzepiela, Louhivuori, Peter, Marrink
Phys. Chem. Chem. Phys., 2011

Hybrid simulations

PMF between two AA butanes in CG solvent



butane-butane PMF



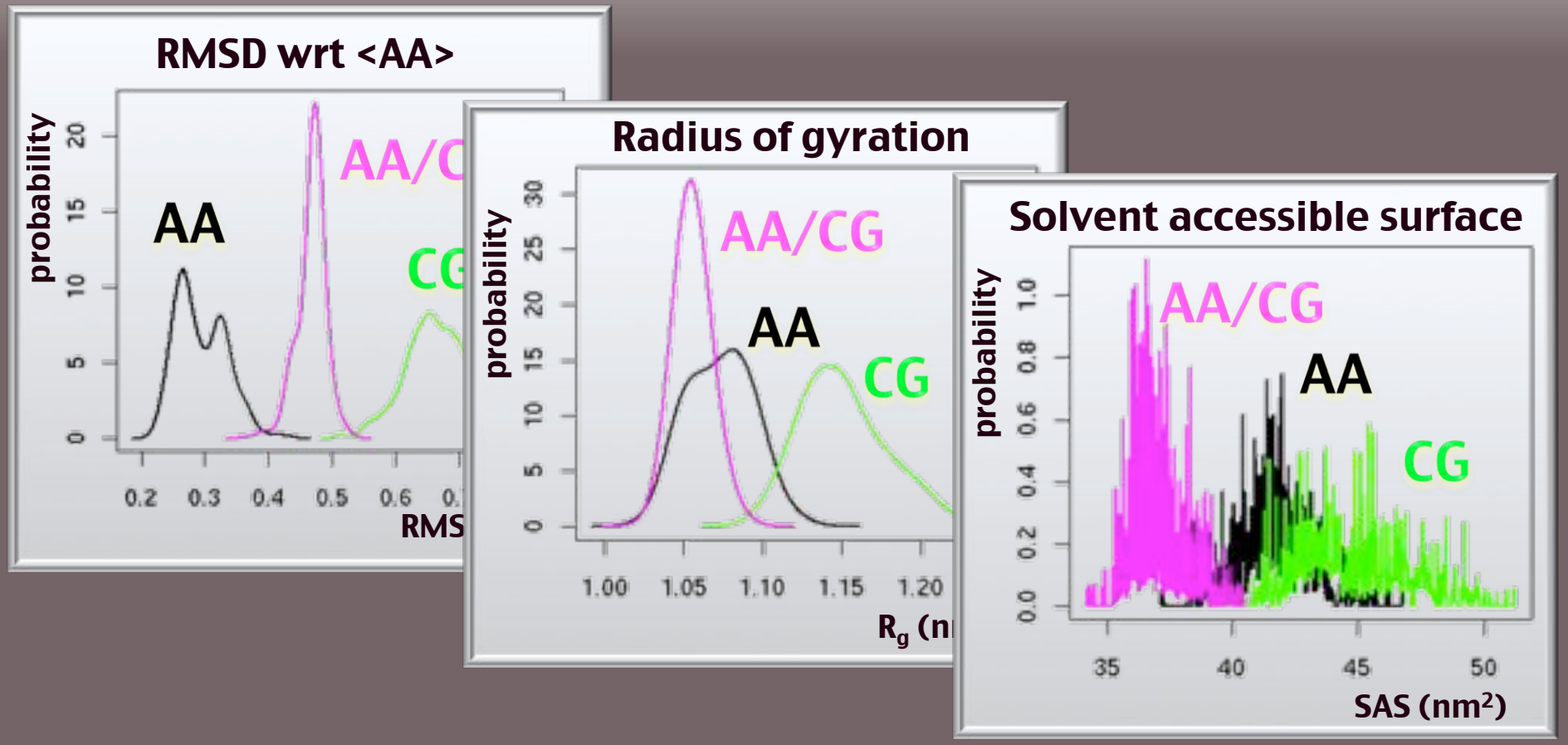
preferential solvation

CG potential	δ_{AA}	δ_{CG}
IB	-118	-111
FM	902	684
SB	61	8
MARTINI	-17	-32

- MARTINI reproduces PMF in hybrid system quite well
- Structure-based methods appear less suited for hybrid simulations
- Matching of thermodynamic rather than structural properties important

Hybrid simulations

Test-set of 50 atomistic proteins in CG water

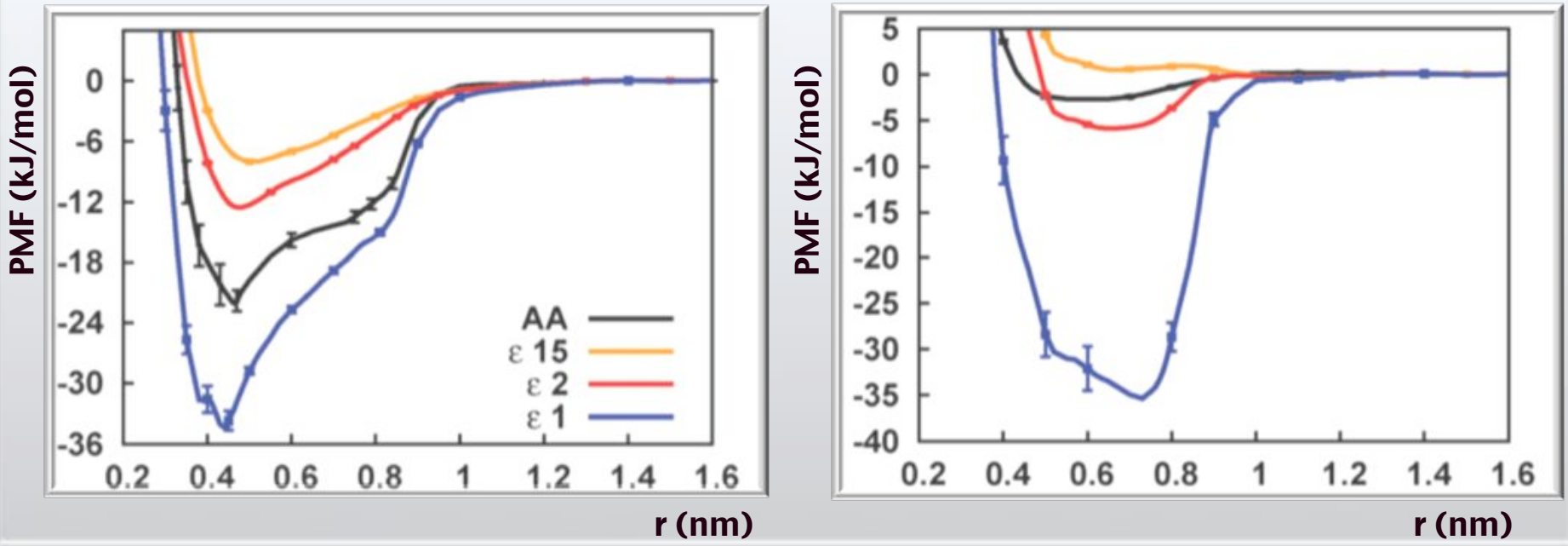


- Hybrid model improves protein behavior wrt pure CG system
- Hybrid proteins too solid and compacted
- Absence of screening of electrostatic interactions

Hybrid simulations

Atomistic dialanine in CG solvent

dialanine-dialanine PMF



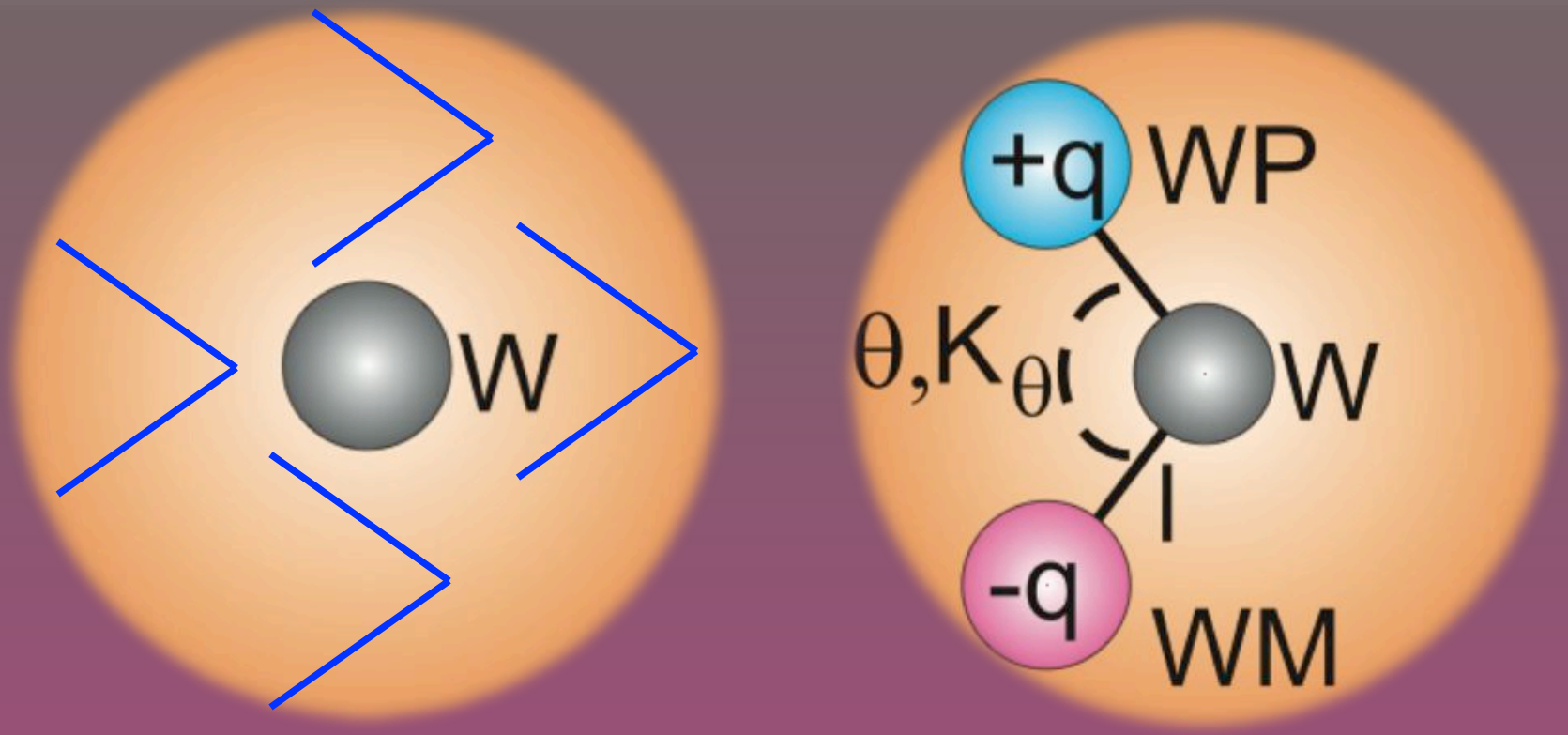
Best results with ε = 1.5

Best results with ε = 5

◆ Implicit screening state dependent

Hybrid simulations

Explicit screening by a polarizable water model



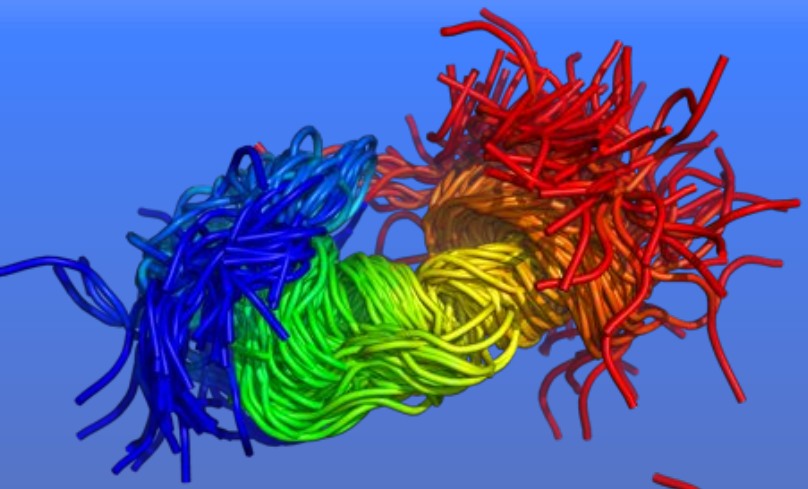
Standard Martini water

Polarizable Martini water

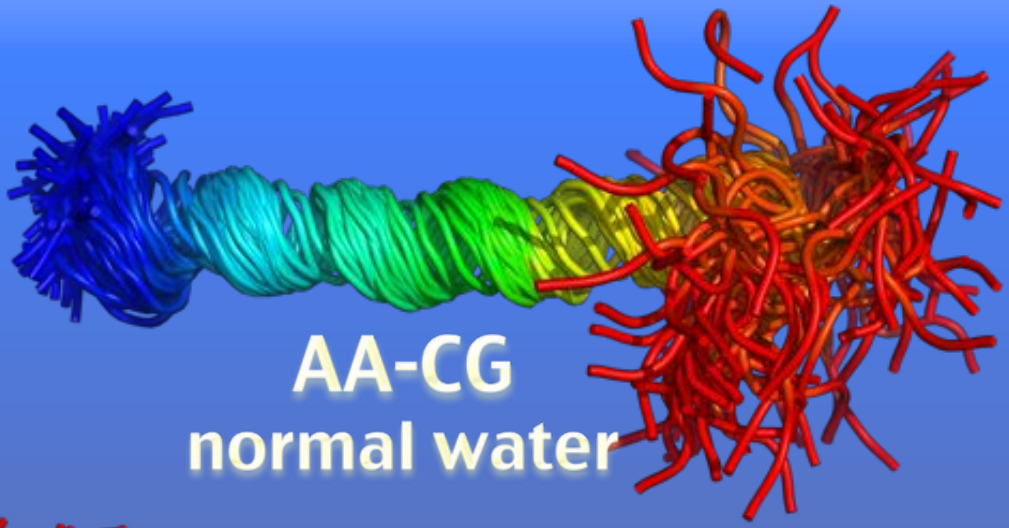
Yesylevskyy, Schäfer, Sengupta, Marrink
PLoS Comp. Biol., 2010

Hybrid simulations

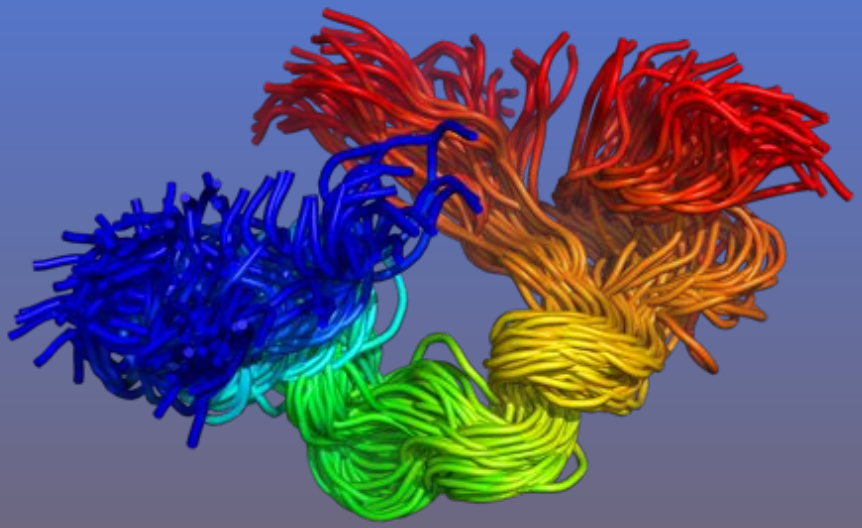
Atomistic proteins in polarizable CG water



AA-CG
normal water



AA



AA-CG
polarizable water

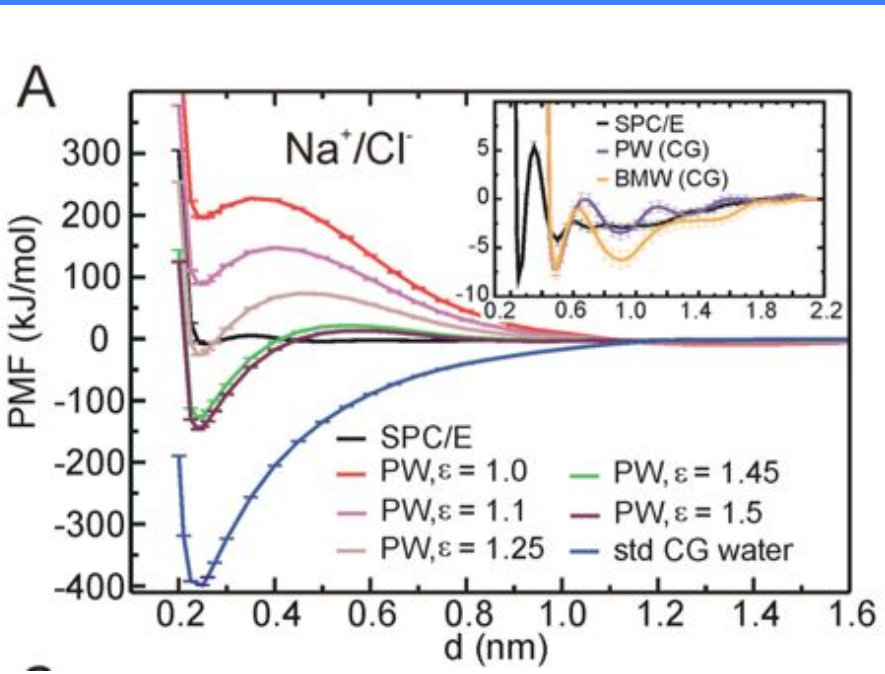
direct interaction

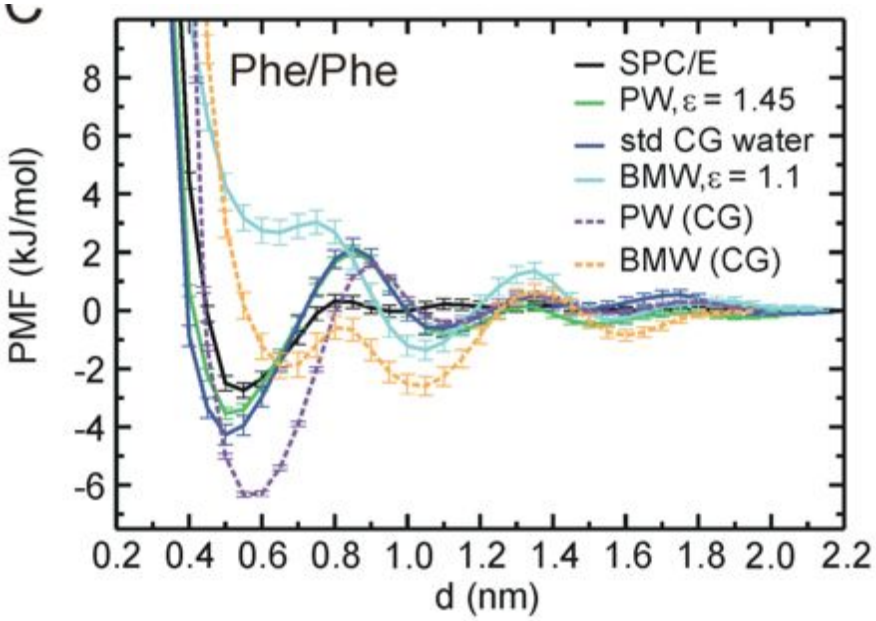
$\varepsilon_{AA\text{-}CG} = 1$

Synthetic peptide, 30 amino acids

Hybrid simulations

PMFs of Na/CL, Phe/Phe with various electrostatic coupling schemes





- Strong sensitivity to level of electrostatic cross-coupling
- Size mismatch leads to artefacts

Hybrid simulations

Conclusions

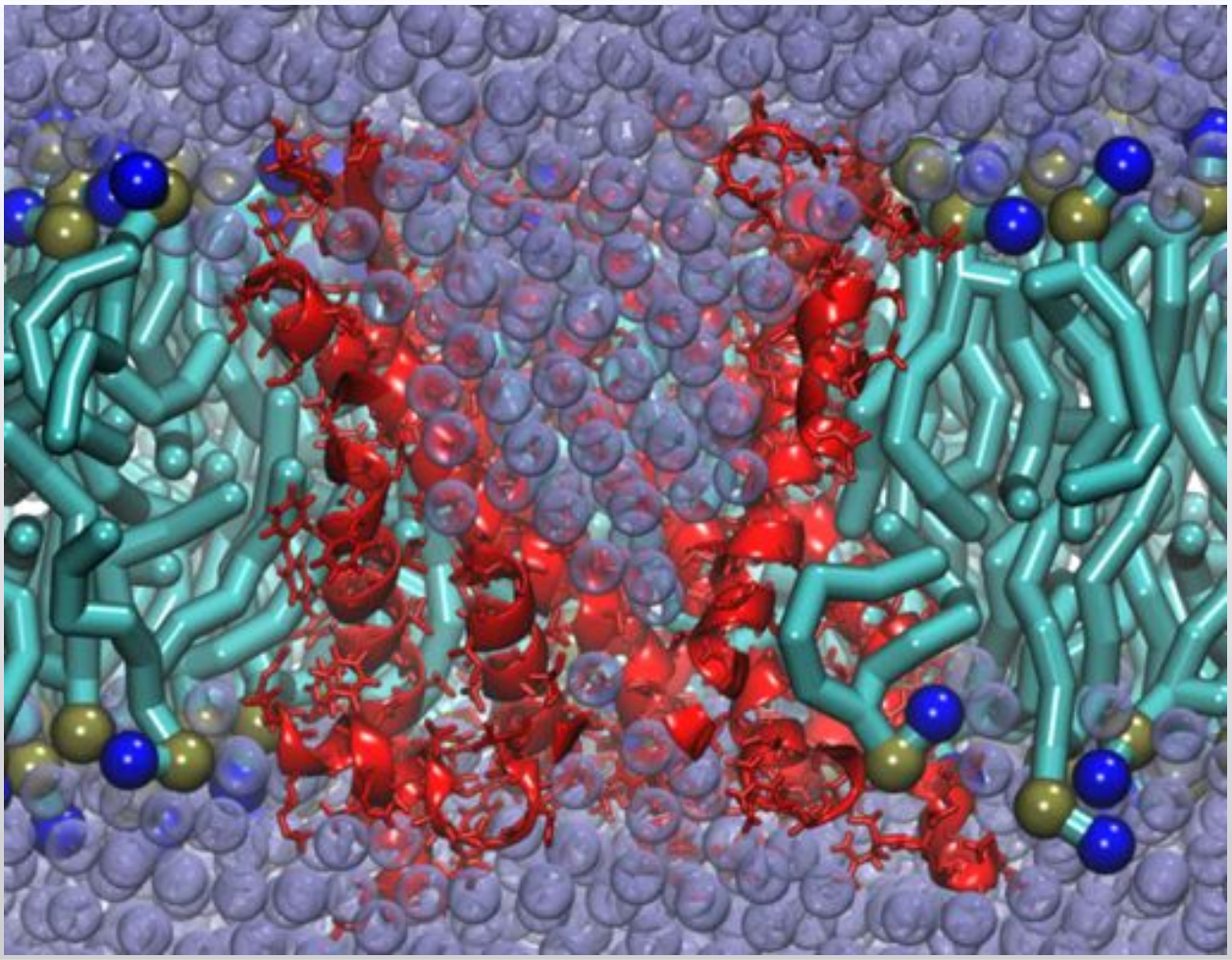
- Mixing requires an energetically compatible CG model
- Treatment of electrostatics is state-dependent
- Polarizable water model required for improvement
- Size mismatch is still problematic
- In apolar medium hybrid model already works well

Hybrid simulations

AA mechanosensitive channel in CG bilayer

Martini:
- POPC lipids
- Polarizable water

Gromos:
- Mechanosensitive channel



Schäfer, Wassenaar, Marrink, in preparation, *2012*

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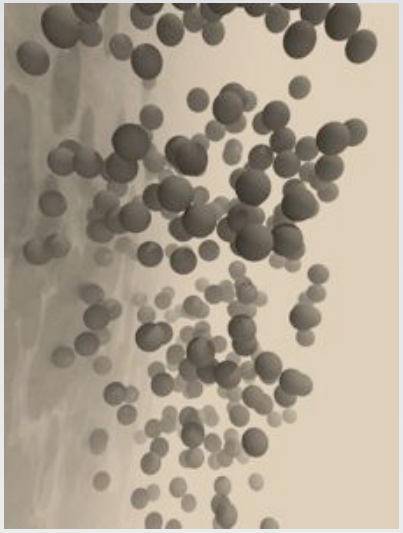

Thanks !