Adaptive Resolution Simulations for Soft Matter

Applications and New Developments

K. Kremer
Max Planck Institute for Polymer Research, Mainz

September - 12 - 2013

COWORKERS:

Luigi Delle Site, FU Berlin
Matej Praprotnik , Ljubljana

Christoph Junghans , Los Alamaos
Simon Poblete , FZ Jülich
Han Wang, Beijing, now FU Berlin
Adolfo Poma , La Sapienza Rome,
Sebastian Fritsch, MPIP

Debashish Mukherji, MPIP
Nico van der Vegt, TU Darmstadt

Raffaelo Potestio, MPIP
Davide Donadio, MPIP

Ralf Everaers, ENS Lyon
Pep Espanol, Madrid
Rafa Delgado Buscalioni, Madrid

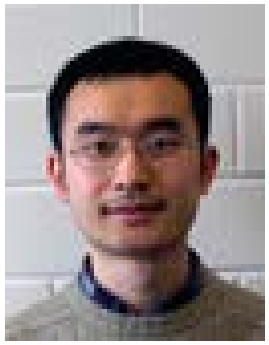
C. Clementi and her group (Rice),
G. Ciccotti (Rome), …

Support: **MMM Initiative of the MPG, Volkswagen Foundation, DAAD, KITP(NSF) …**













Outline

- **Motivation: Soft and Nanostructured Matter**
- AdResS: **Ad**aptive **Res**olution MD **S**imulation
  - **Method, first Applications**
  - **Recent developments**
- Particle-Continuum: AdResS + Hybrid MD
- **Conclusions/Outlook**

Soft Matter

“Soft” means:

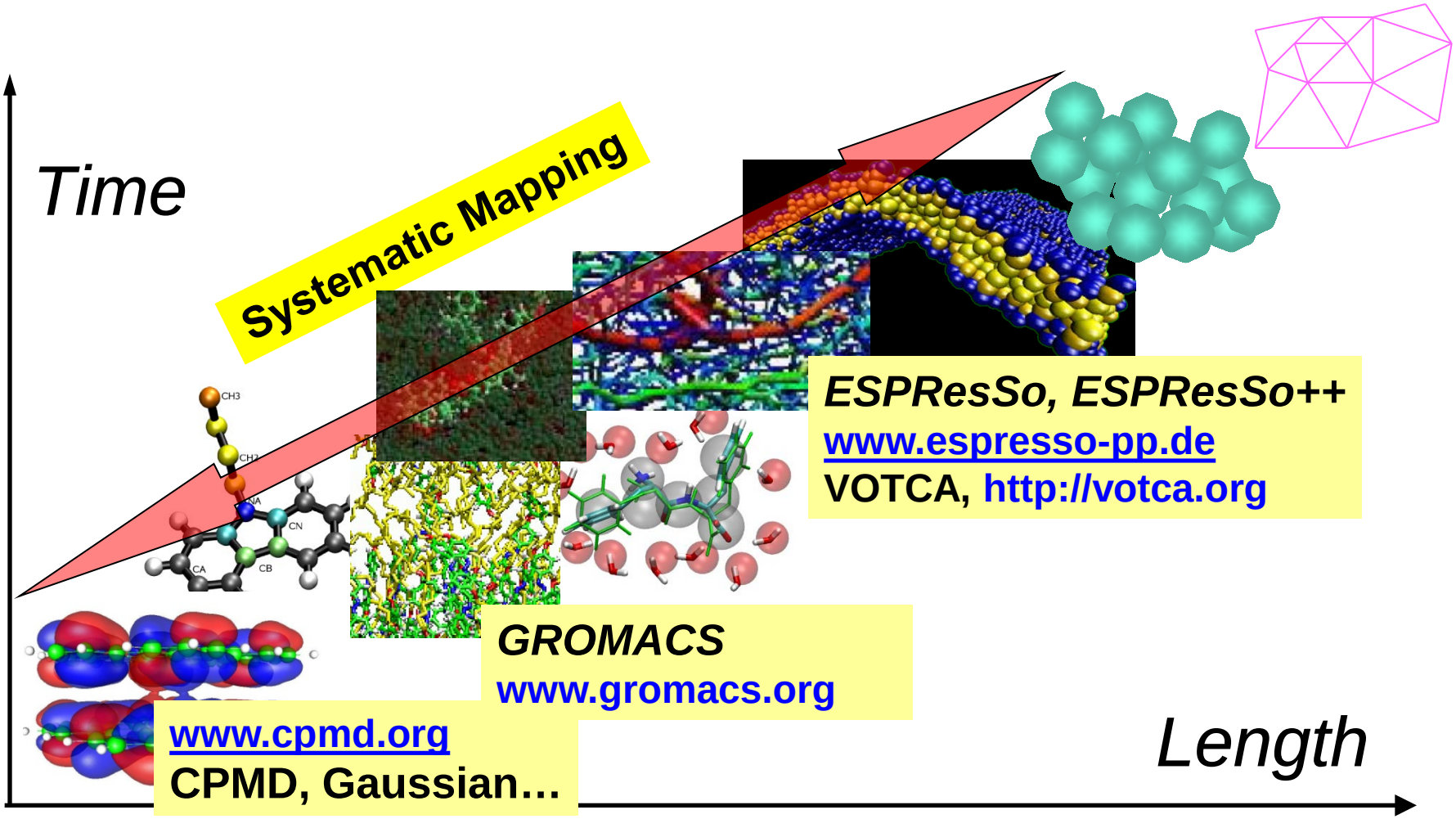
- low energy density

- nanoscopic length scales
(10Å …1000Å)

- large (conformational) fluctuations
large *intra* molecular entropy

- thermal energy k_BT
relevant energy scale

Characteristic Time and Length Scales



Local Chemical Properties --- Scaling Behavior of Nanostructures
Energy Dominance --- Entropy Dominance of Properties

Energy Scale $k_B T$ forT=300K

$$E = 1.38 \cdot 10^{-23} J/K \cdot 300K$$

$$kT \approx 4.1 \cdot 10^{-21} J$$

$$kT \approx 2.5 \cdot 10^{-2} eV$$

$$kT \approx 9.5 \cdot 10^{-4} E_H$$

$$kT \approx 4.1 pNnm$$

$$kT \Rightarrow 200 cm^{-1}$$

$$kT \Rightarrow 0.6 kcal/mol$$

$$kT \Rightarrow 2.5 kJ/mol$$

Electronic structure, CPMD

Quantum Chemistry

Biophysics Membranes, AFM

Spectroscopy

$$E \approx 3 \cdot 10^{-19} J \approx 80kT$$

$$E \approx 4kT - 10kT$$

Chemical Bond
Hydrogen Bond

Energy Scale k_BT forT=300K

$$E = 1.38 \cdot 10^{-23} J/K \cdot 300K$$

$$kT \approx 4.1 \cdot 10^{-21} J$$

$$kT \approx 2.5 \cdot 10^{-2} eV$$

$$kT \approx 9.5 \cdot 10^{-4} E_H$$

$$kT \approx 4.1 pNnm$$

$$kT \Rightarrow 2$$

$$kT \; .6kcal/mol$$

$$kT \Rightarrow 2.5kJ/mol$$

Electronic st MD

Qu istry

ophysics Membranes, AFM

Spectroscopy

Green light photon ≈ 2-2.5 eV ≈ 100 kT

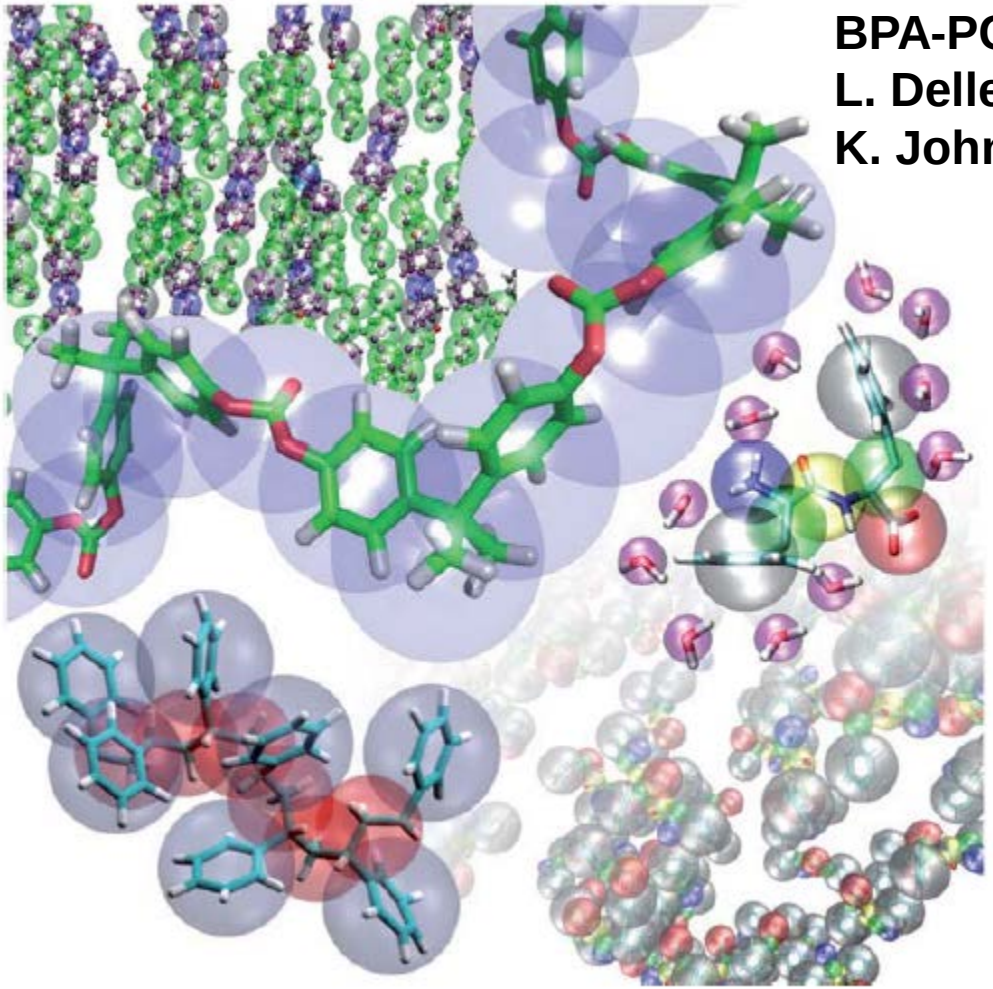
$$E \approx 3 \cdot 10^{-19} J \approx 80kT$$

$$E \approx 4kT - 10kT$$

Chemical Bond
Hydrogen Bond

Coarse Graining of Macromolecules: Examples

Azo Benzene LCs
C. Peter, L. Delle Site,
D. Marx



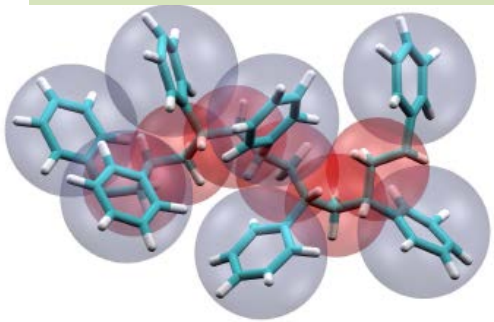
BPA-PC
L. Delle Site, C. Abrams
K. Johnston (1998ff**)**

Polystyrene,
(w/wo additives)
V. Harmandaris,
D. Fritz
N. Van der Vegt

Peptides
C. Peter

Application: Diffusion Constant of PS

(two step approach AA->UA->CG)

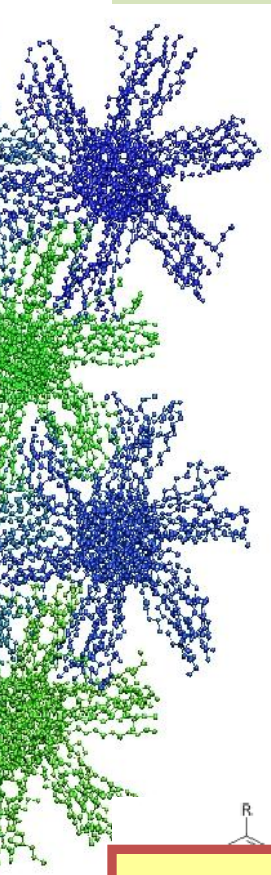


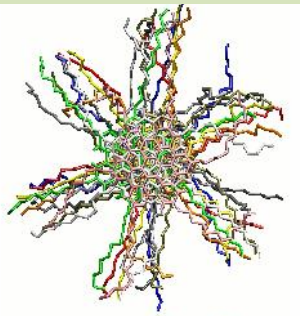
Simulation:
NO adjustable parameter
M_W ≈ 50kD

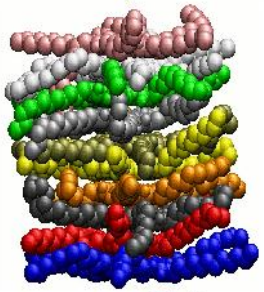
Experiment:
Raw FRS data, Sillescu

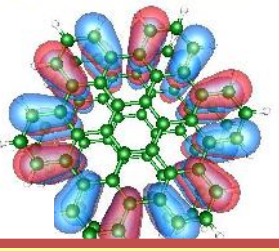
V. Harmandaris, KK, Soft Matt. 2009

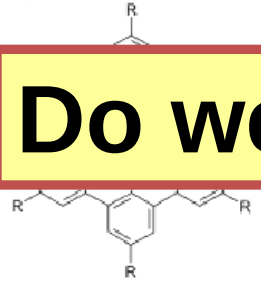
Standard Approach:
Run whole system on one level of resolution.



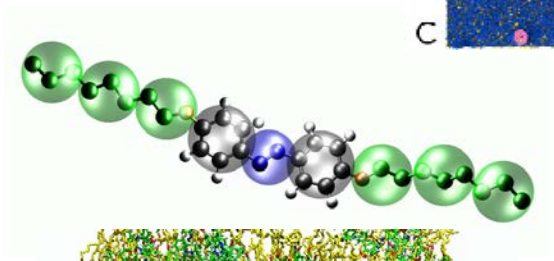


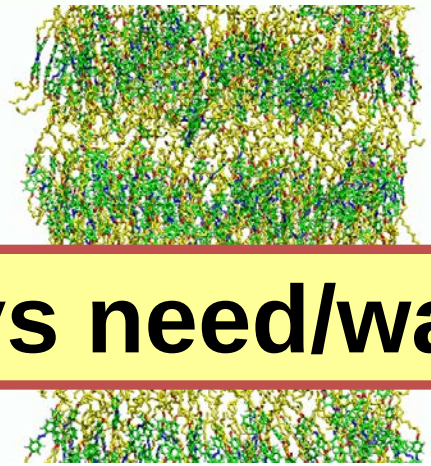




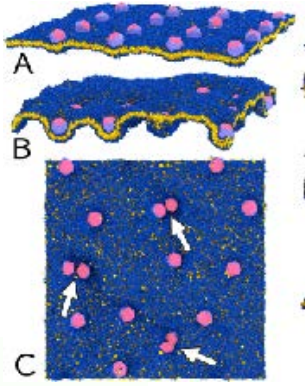


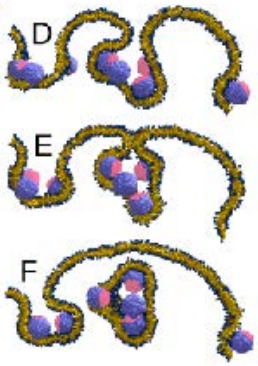
Andrienko et al,
PRL 98, 227402 (2007)

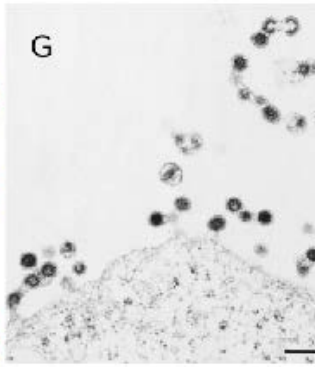




C. Peter et al, 2008ff







M. Deserno et al.,
Nature, 2007

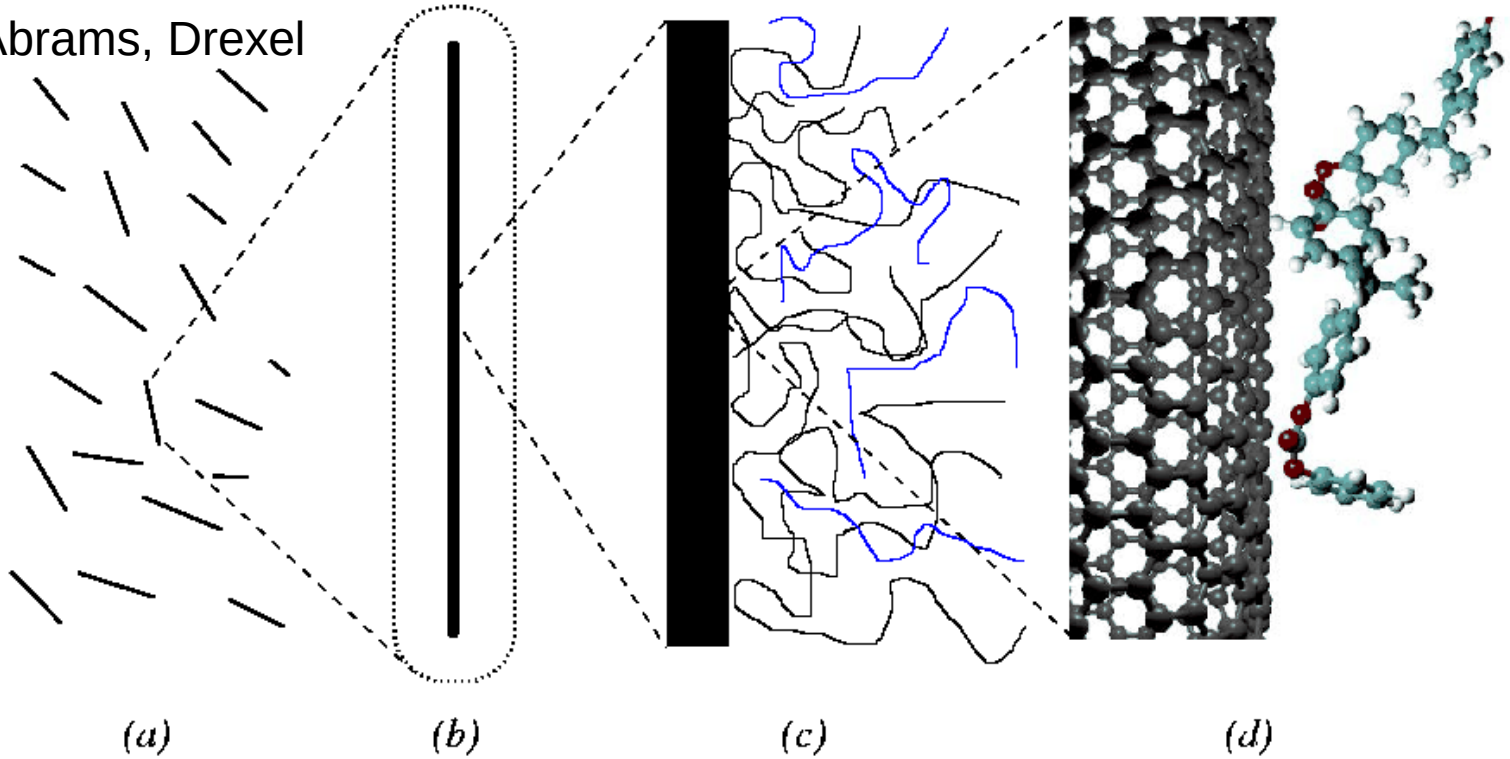
Do we always need/want to do that?

Outline

- **Motivation: Soft and Nanostructured Matter**
- AdResS: **Ad**aptive **Res**olution MD **S**imulation
  - **Method, first Applications**
  - **Recent developments**
- Particle-Continuum: AdResS + Hybrid MD
- **Conclusions/Outlook**

Relevant Levels of Resolution
Example:Polymer/Nanotube Composites

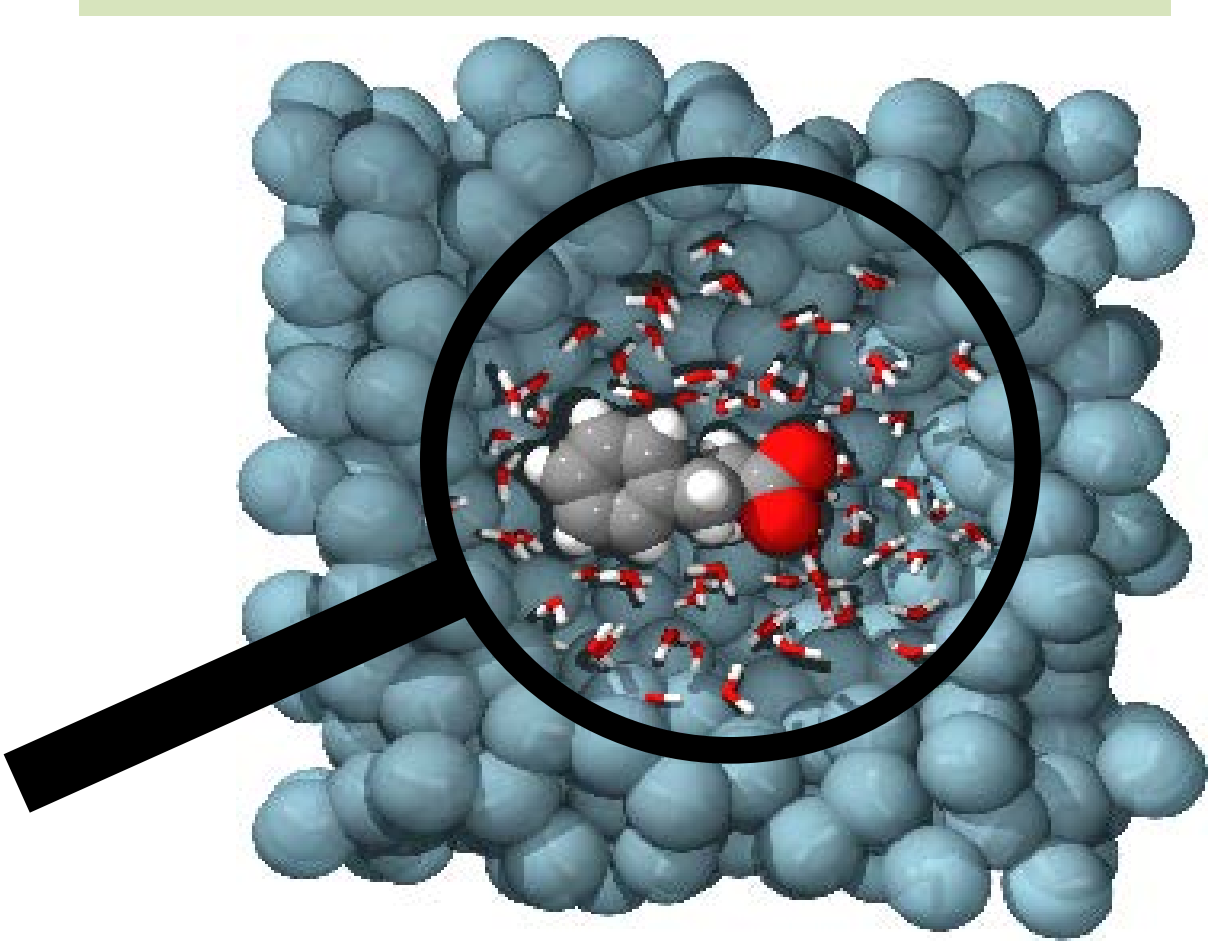
C. F. Abrams, Drexel

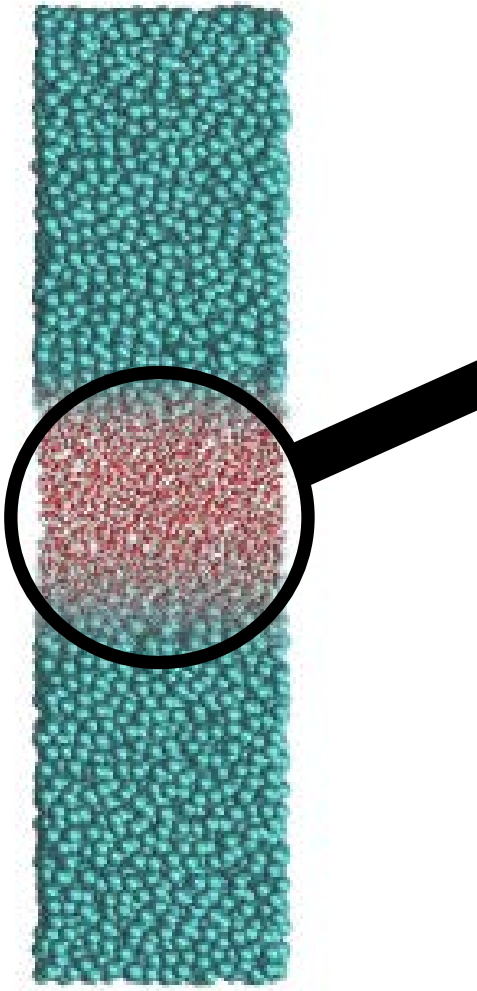


Aim at: **Adsorption – Desorption, Flux of Chains, Additives, Structure Formation, grand canonical MD**

AdResS

Adaptive Resolution MD Simulation



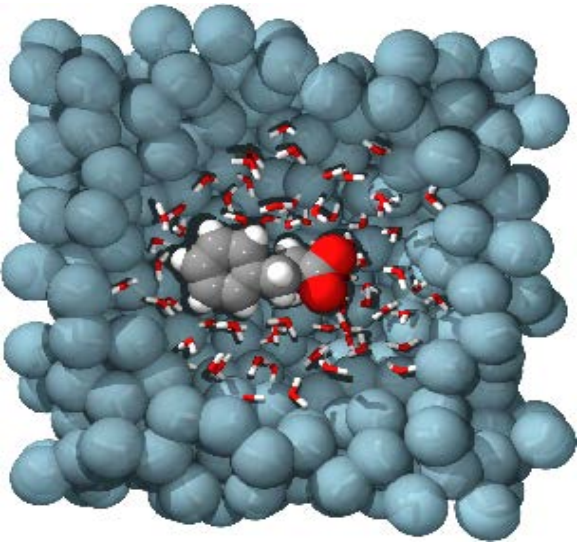


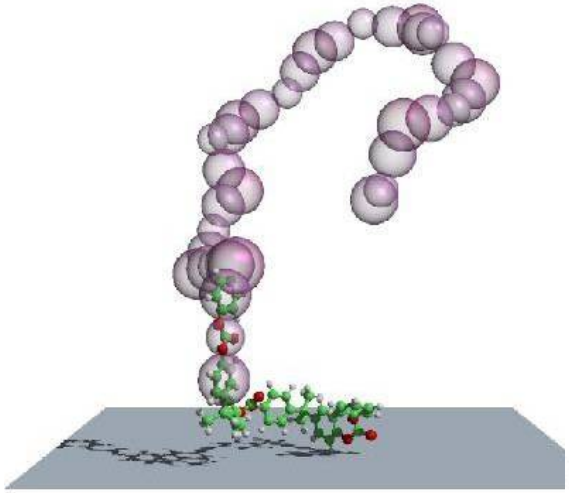
Praprotnik, Delle Site, KK, JCP., 123, 224106 (2005).

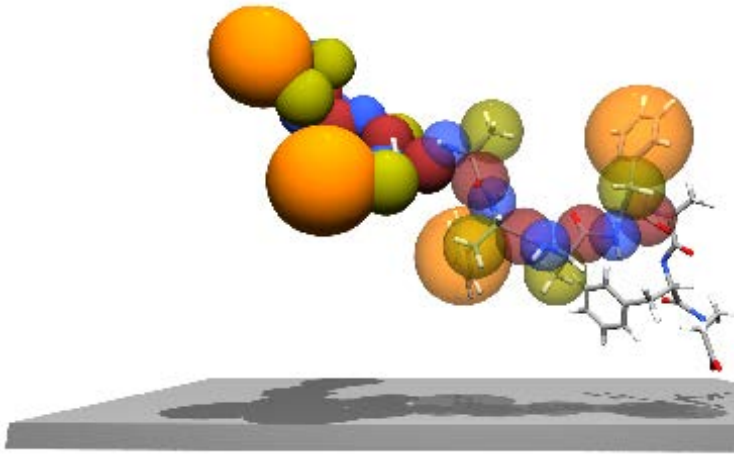
AdResS: Adaptive Resolution Simulations

***Free exchange** of molecules/particles between regimes with different levels of resolution:*

equilibrium between both regimes, no kinetic barrier







M. Praprotnik, L. Delle Site, KK, JCP 2005, Ann. Rev. Phys. Chem. 2008, 59: 545-71

Adaptive Methods:
Changing degrees of freedom (DOFs) on the fly

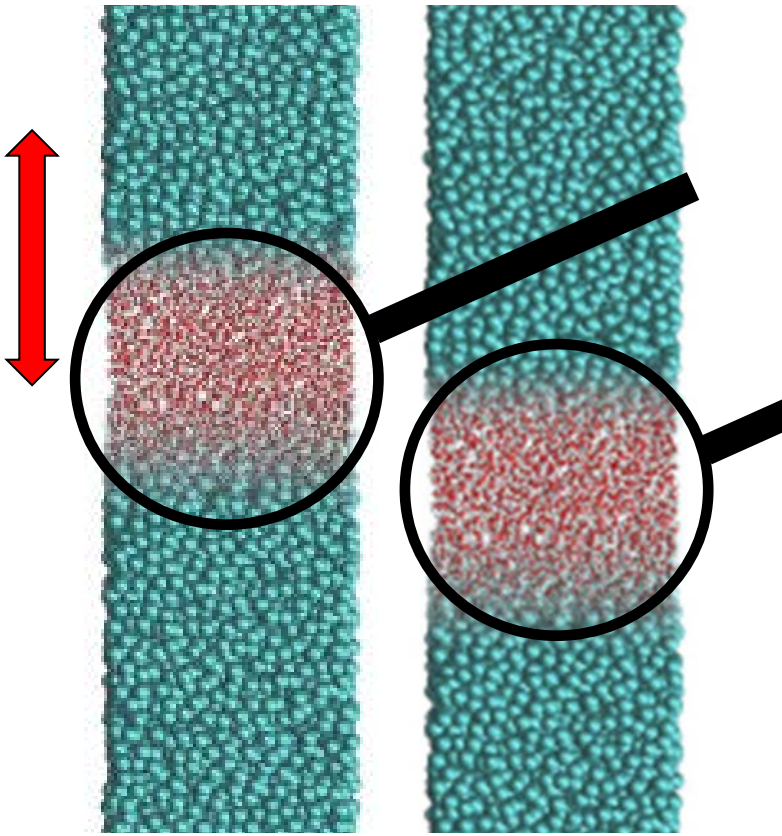
Requirements

- Same mass density
- Same Pressure (=>Eq. of state, ?)
- Same temperature

- **Free exchange between regimes**
- Same center-center g(r) (?)

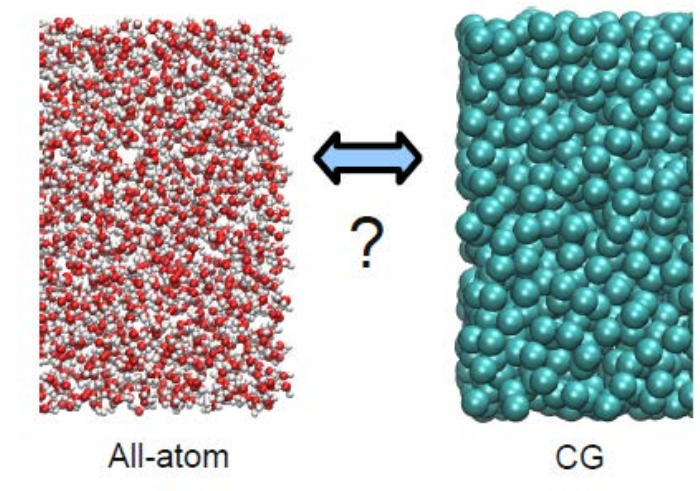
- (Simple two body potential)

⇒ "Some similarities" to 1st order phase transition
⇒ "Phase equilibrium"
⇒ Thermostat has to provide/take out latent heat due to change in degrees of freedom

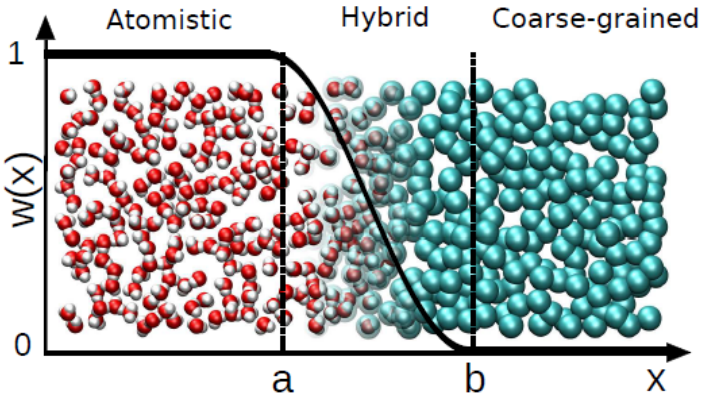


VW Foundation Project
M. Praprotnik, L. DelleSite, KK, JCP 2005, PRE (2006)

Adaptive Methods:
Changing degrees of freedom (DOFs) on the fly



$U^{AA}_{\alpha\beta}$ $U^{CG}_{\alpha\beta}$



$$w(x) = \begin{cases} 1 & : \text{atomistic/explicit region} \\ 0 < w < 1 & : \text{hybrid region} \\ 0 & : \text{coarse-grained region} \end{cases}$$

Requirements:

- Free exchange of molecules
- NO (free) energy barriers
- Smooth transition forces
- Structure and dynamics preserved
  - (at least in all atom region)

Newton's 3rd law:

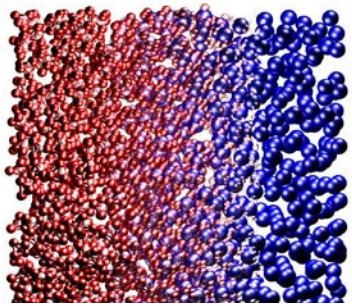
- Force should be antisymmetric on exchange of particles $\alpha \leftrightarrow \beta$
- Weight must depend on both particles

Transition Regime – Interpolation of Energy $U_{\alpha\beta}$?

$$U_{\alpha\beta} = w(X_\alpha)w(X_\beta)U_{\alpha\beta}^{atom} + [1 - w(X_\alpha)W(X_\beta)]U_{\alpha\beta}^{cg}$$

Full atomistic potential

Full coarse grained potential



$$\mathbf{F}_{\alpha\beta} = -\nabla_\alpha U = \mathbf{F}_{\text{Newton}} - [\nabla_\alpha w(\mathbf{X}_\alpha)]w(\mathbf{X}_\beta)(U_{\alpha\beta}^{AA} - U_{\alpha\beta}^{CG})$$

$$\mathbf{F}_{\beta\alpha} = -\nabla_\beta U = -\mathbf{F}_{\text{Newton}} - w(\mathbf{X}_\alpha)[\nabla_\alpha w(\mathbf{X}_\beta)](U_{\alpha\beta}^{AA} - U_{\alpha\beta}^{CG})$$

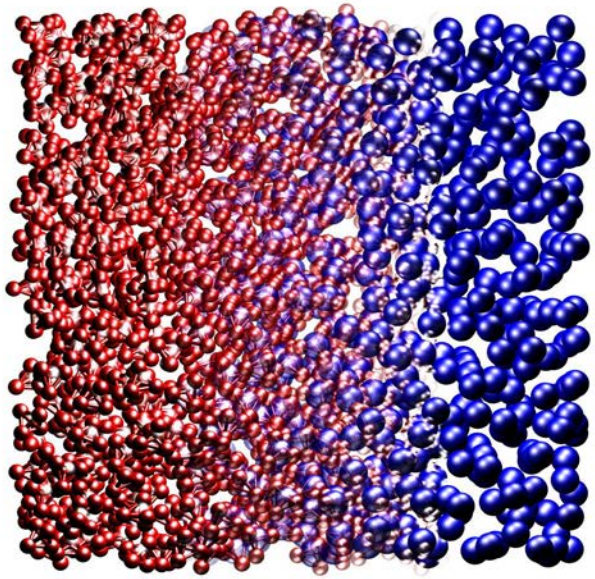
$\mathbf{F}_{\alpha\beta} \neq -\mathbf{F}_{\beta\alpha}$

Transition Regime – Interpolation of Energy $U_{\alpha\beta}$?

$$U_{\alpha\beta} = w(X_\alpha)w(X_\beta)U_{\alpha\beta}^{atom} + [1 - w(X_\alpha)W(X_\beta)]U_{\alpha\beta}^{cg}$$

Full atomistic potential

Full coarse grained potential



- **Drift terms from *W(x)***
- **Violation of Newton's 3rd law**
- **Mathematical inconsistencies at boundaries**

- **There exists no *W(x)*, such that forces become conservative**
  (L. Delle Site PRE 2007)

=> Force interpolation

AdResS:
Transition Regime - Force Interpolation

$$F_{\alpha\beta} = w(X_\alpha)w(X_\beta)F^{atom}_{\alpha\beta} + [1 - w(X_\alpha)W(X_\beta)]F^{cg}_{\alpha\beta}$$

Full atomistic force

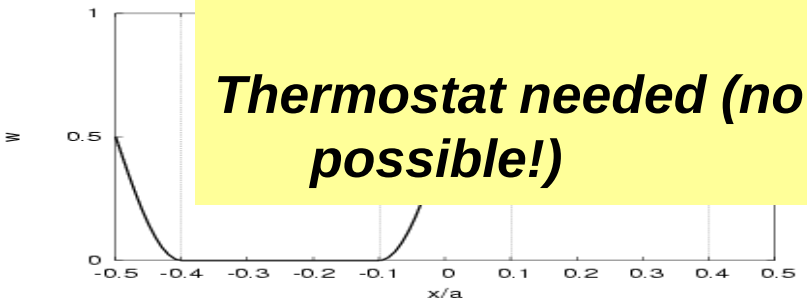
Full coarse grained force

Transition regime: Force interpolation
(Newtons 3rd law fulfilled, no drift forces)

No transition energy function defined!

Pressure, Temperature, Density everywhere well defined

Thermostat needed (no microcanonical simulation possible!)

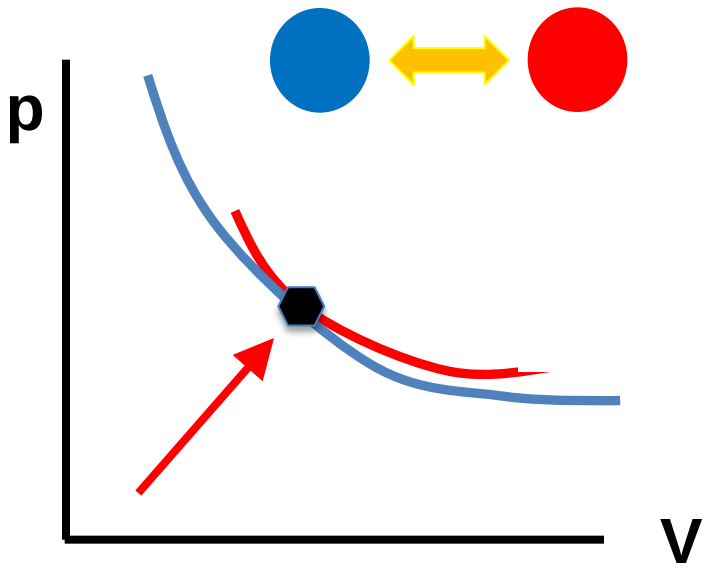


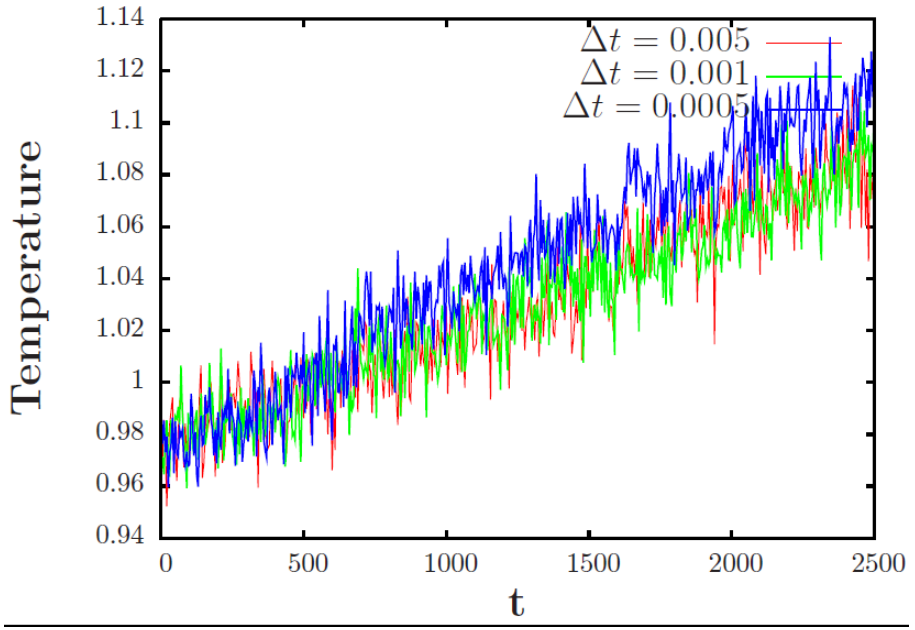
explicit hybrid: explicit explicit

* Similar problem already in H.C. Andersen, JCP **72,** 2384 (1979)

Theoretical Basis: Temperature…
Necessity of Thermostat

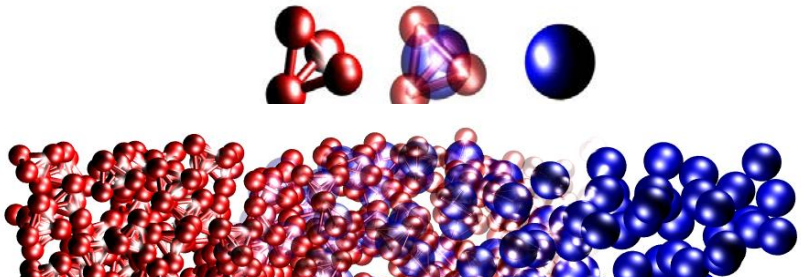
Example: Two spherical Particles, no new DOFs

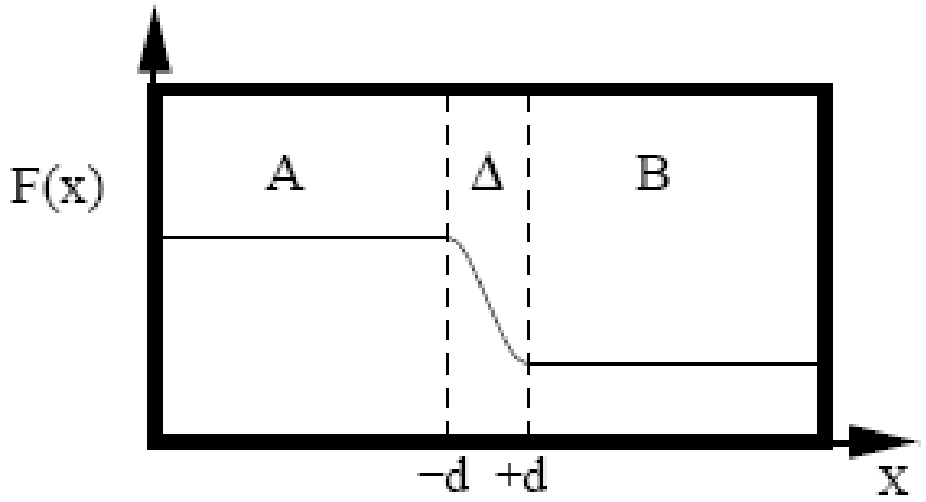




$$p_A(\mu_A, T)V = p_B(\mu_B, T)V; \qquad \kappa_A = \kappa_B$$

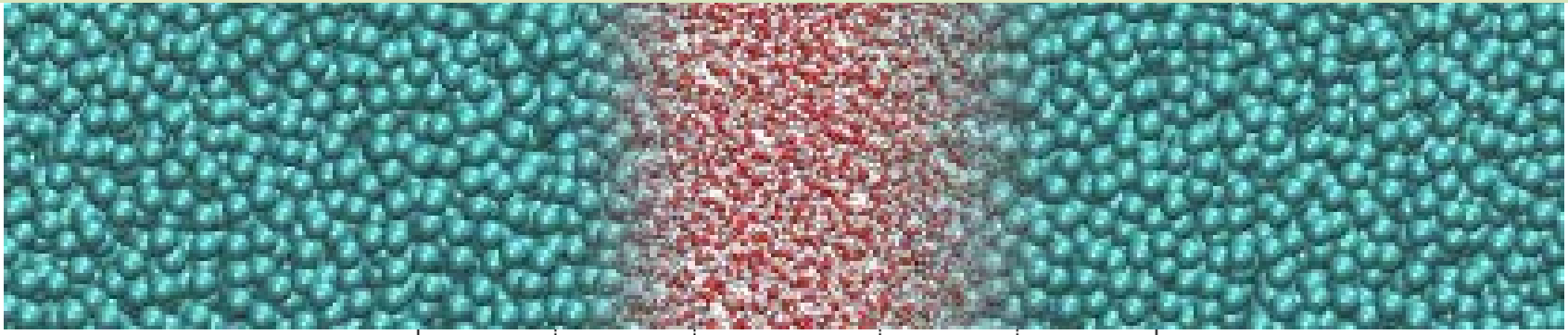
Transition between models/levels of description => change in Free Energy

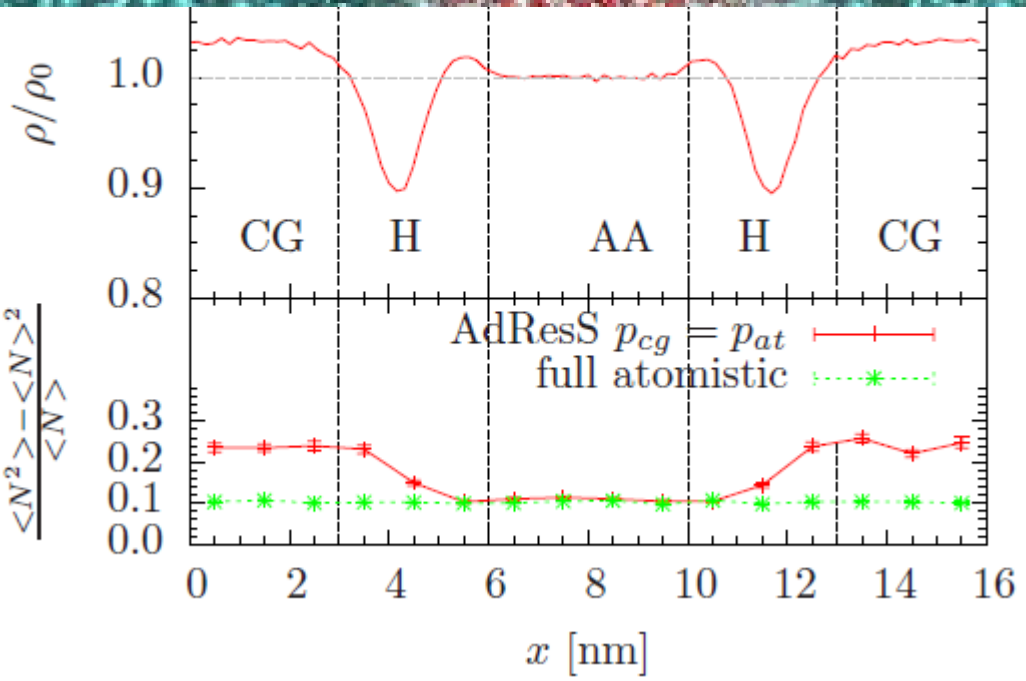




- **Temperature well defined in whole box, fixed by thermostat**
- **Densities well defined**
- **Forces well defined => virial pressure well defined**

Transition between models/levels of description => change in Free Energy

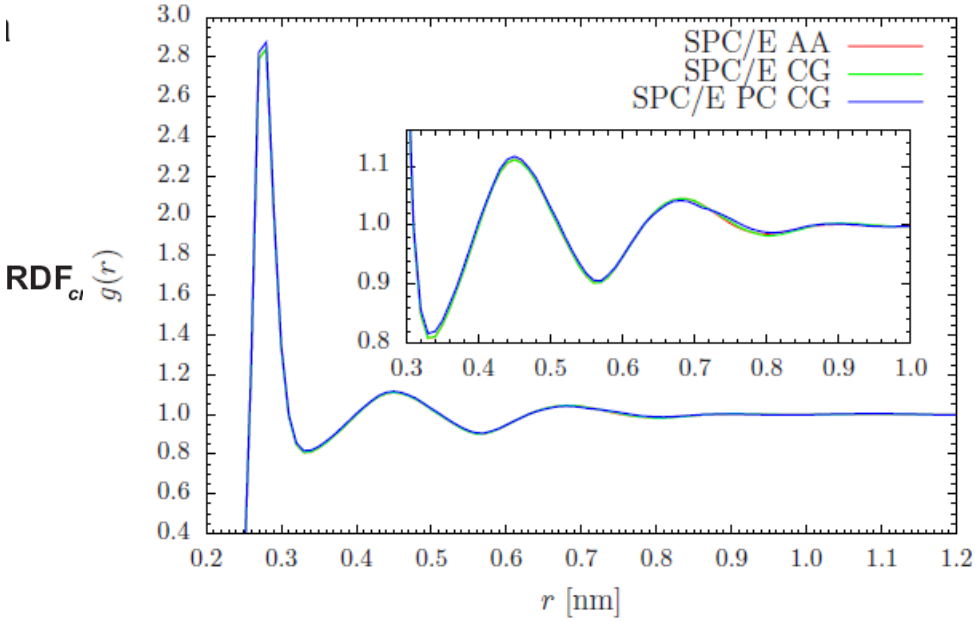




System will adjust to constant pressure everywhere.

How to keep all atom region unperturbed?

Structure based CG - Compressibility



SPC/E water,
cg based on matching g(r)

Pressure

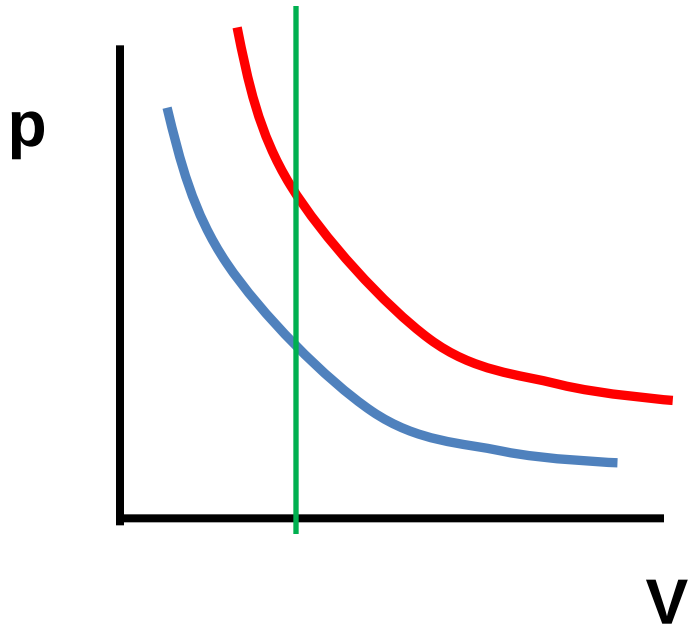
$$P = \rho k\,T\; - {}^{2}/_{3}\,\pi\rho^{2}\int_{0}^{\infty} U'(r)g(r)r^{3}dr$$

Compressibility

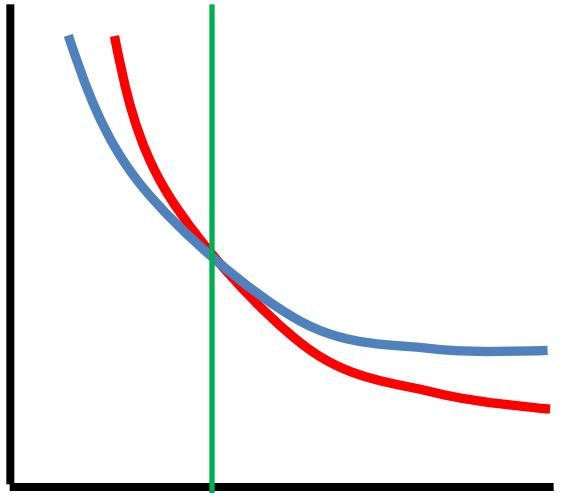
$$\kappa_T = \frac{1}{\rho k_B T}\left(1 + 4\pi\rho\int_0^\infty r^2[g(r)-1]dr\right) = \frac{1}{\rho k_B T}\frac{\langle N^2\rangle - \langle N\rangle^2}{\langle N\rangle}$$

Equation of State: Pressure Correction

Structure based CG, based on g(r) - pressure corrected

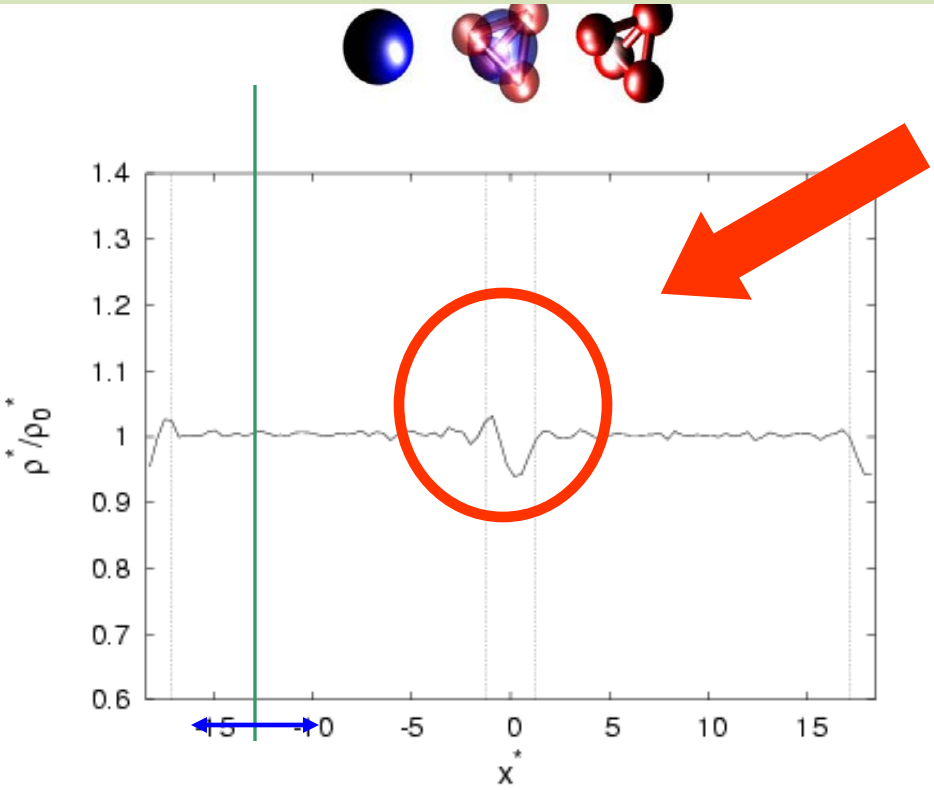


$$p_A(\mu_A, T) \neq p_B(_{\mu B}, T)$$
$$\kappa_A = \kappa_B$$



$$p_A(\mu_A, T) = p_B(_{\mu B}, T)$$
$$\kappa_A \neq \kappa_B$$

Pressure leverage causes density wiggles: special model with $p_{cg}=p_{AA}$



Equation of state in transition regime not the same!
(not surprising)

No energy function
but
well defined **forces** and thus
well defined **pressures**

Calculate pressure in a plane ⊥ x **(Todd, Evans, Davies)**

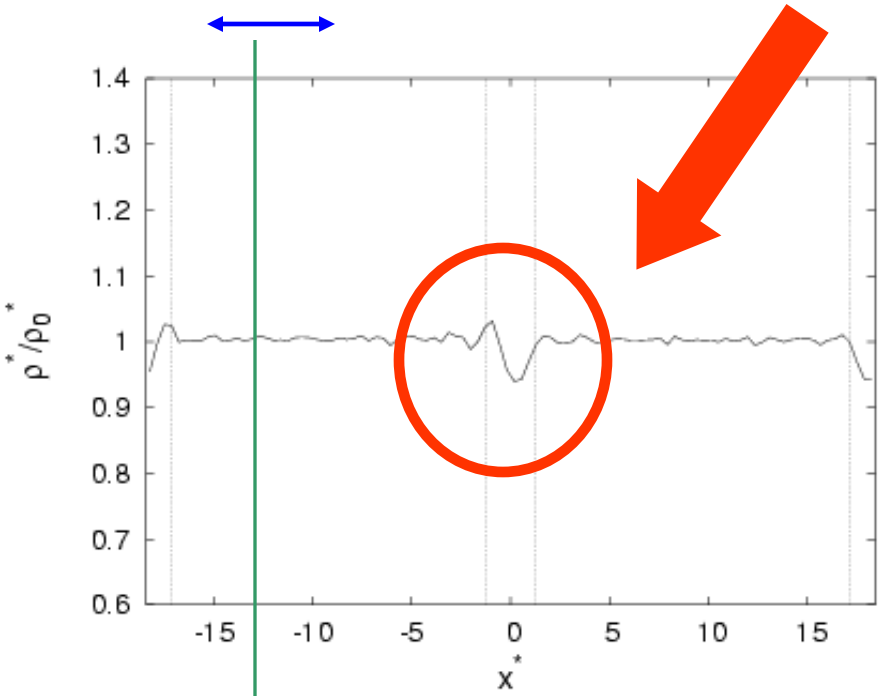
$$\bar{p}_{\beta\alpha}(\alpha) = \frac{1}{2A_\alpha \Delta\alpha}\Big\langle \sum_{\alpha-\Delta\alpha\le\alpha_i\le\alpha+\Delta\alpha} m_i v_{i\beta} v_{i\beta}\Big\rangle + \frac{1}{2A_\alpha}\Big\langle \sum_{i=1}^{N} F_{i\beta} sgn(\alpha_i-\alpha)\Big\rangle$$

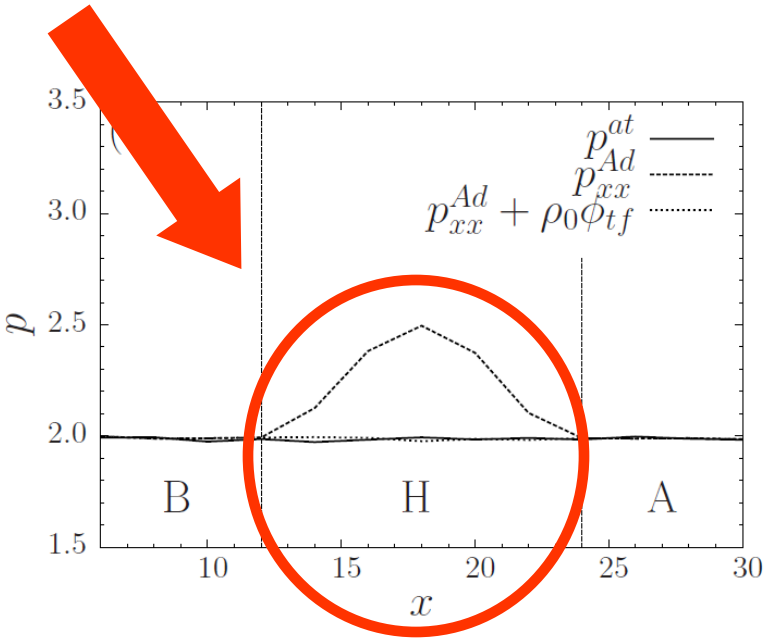
S. Poblete, S. Fritsch, G. Ciccotti, L. Delle Site, KK, PRL 2012

Pressure

If density fixed to constant value

⇒ Pressure bump in hybrid zone



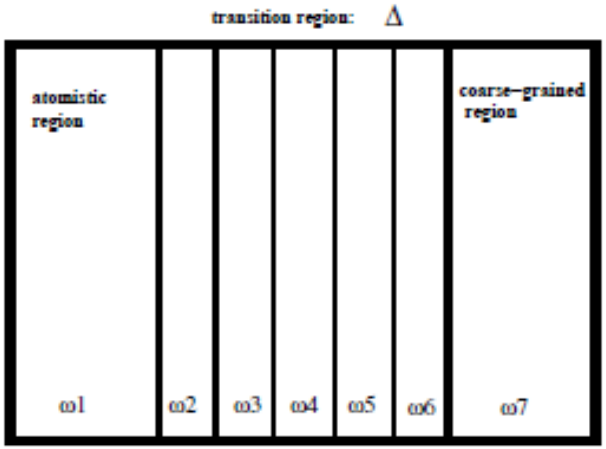


Calculate pressure in a plane ⊥ x **(Todd, Evans, Davies)**

$$\bar{p}_{\beta\alpha}(\alpha) = \frac{1}{2A_\alpha \Delta\alpha}\Big\langle \sum_{\alpha-\Delta\alpha\le\alpha_i\le\alpha+\Delta\alpha} m_i v_{i\beta} v_{i\beta}\Big\rangle + \frac{1}{2A_\alpha}\Big\langle \sum_{i=1}^{N} F_{i\beta}\, sgn(\alpha_i - \alpha)\Big\rangle$$

Effective Chemical Potential, at target density

- $\phi(x) = \mu_{atom} - \mu(w_i)$ (free energy per particle)



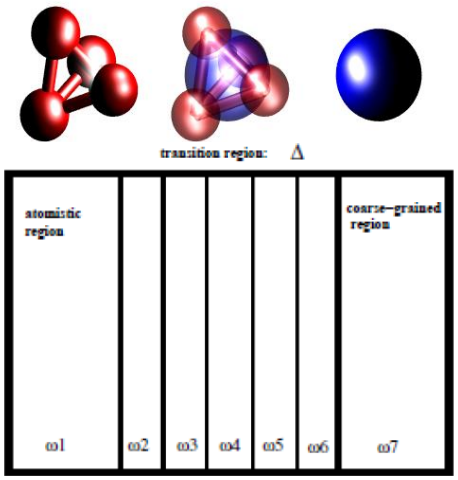
- Calculating $\mu(w_i)$ with $i = 2, 3, 4, 5, 6, 7$:
  (a): **insertion particle method (IPM)** for each $i \Longrightarrow$ Excess chemical potential $\mu^{exc}(w_i)$
  (b): **fractional formula** $\Longrightarrow$ kinetic (ideal gas) contributions $\mu^{kin}(w)$

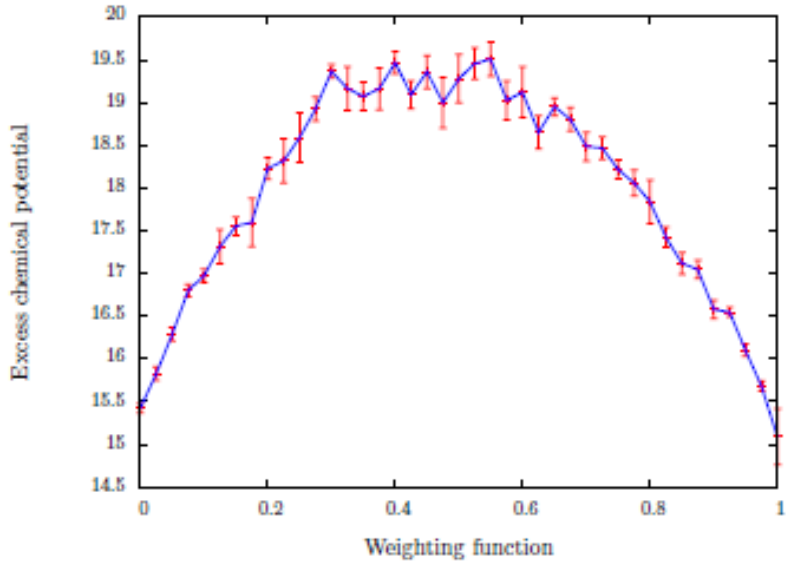
S. Poblete, M. Praprotnik, KK, L. Delle Site, JCP, 132, 114101 (2010)

Effective Chemical Potential

at target density

(a) Excess Chemical Potential μ^{exc}



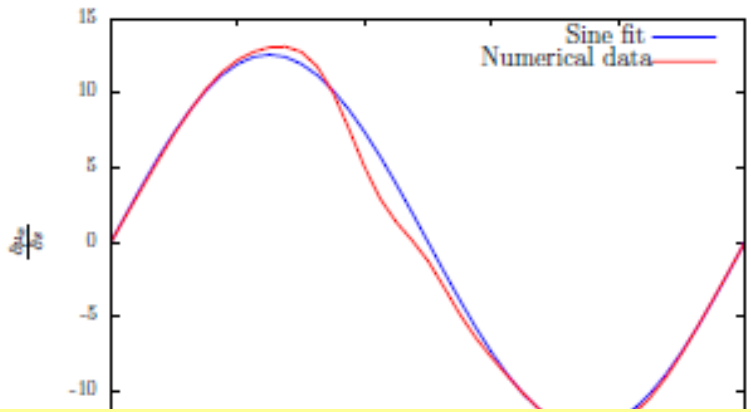


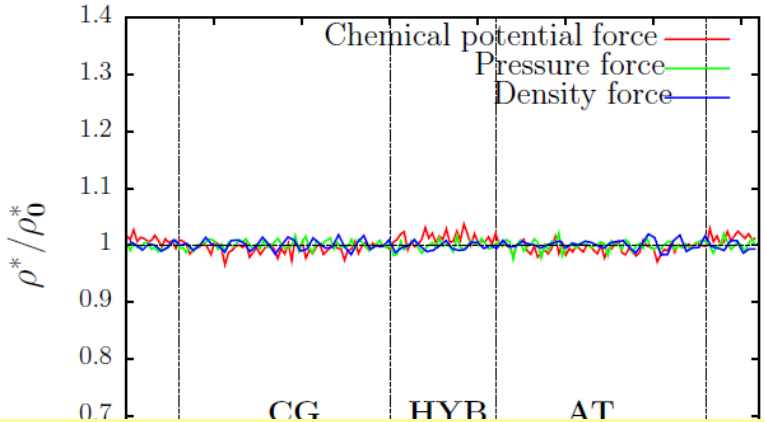
(b) Kinetic contribution : $\mu^{kin} \propto \left(\frac{w}{2}\right) lg(T) + lg\frac{\Gamma\left(\frac{w}{2}\right)}{\Gamma(w)}$

S. Poblete, M. Praprotnik, KK, L. Delle Site, JCP, 132, 114101 (2010)

Effective Chemical Potential: Thermodynamic Force F_{thm}

- "latent heat" leads to force: $F_{thm} = -\nabla_x \mu(x)$
- $-\nabla_x \mu^{exc}$ + *thermostat for kinetic part*
-



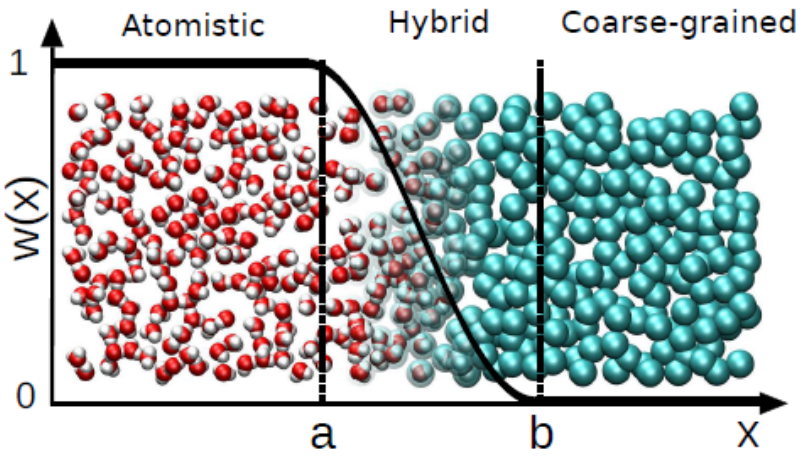


F_{thm} can perform work on the particles in transition regime

Allows to couple almost any system
No need to have same μ, same p in both regimes

S. Poblete, M. Praprotnik, KK, L. Delle Site, JCP, 132, 114101 (2010)

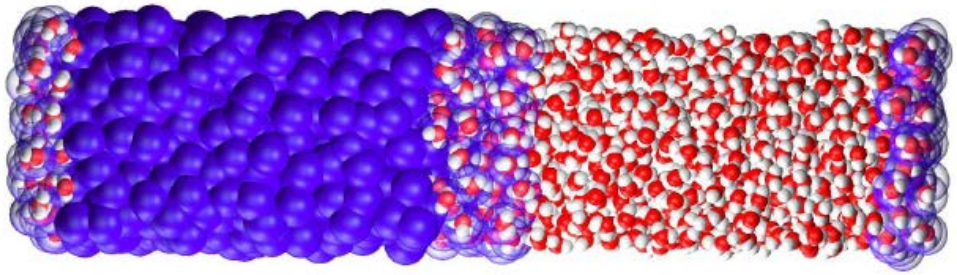
Variable pressure in *AA* and *CG* region: Thermodynamic Force F_{thm}

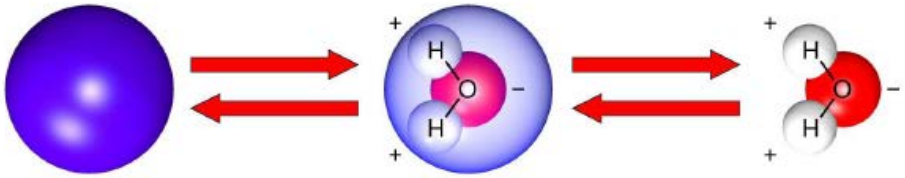


$$p_A(\mu_A, T)V \neq p_B(\mu_B, T)V; \qquad \kappa_A = \kappa_B$$

$$\left(p_A(\mu_A, T) + \frac{\rho_0}{M_\alpha}\int_a^b \mathbf{F}_{\mathrm{th}}(x)\mathrm{d}x\right)V = p_B(\mu_B, T)V$$

Test case: Coarse Grained Water: SPC/E





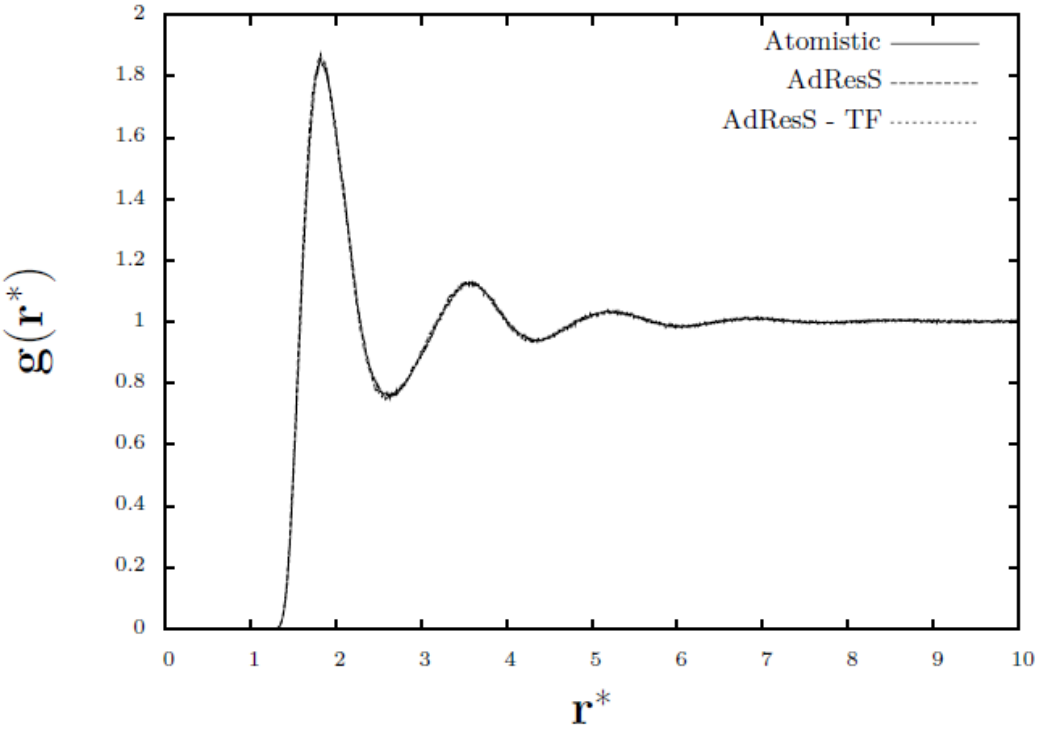
Structure based
Coarse Graining:

Perfect match of g(r)
all atom – coarse grained

$\kappa_{atomistic} = \kappa_{cg}$

BUT

$p_{cg} = 6200 p_{atomistic}$



Control of Thermodynamics in Explicit Region

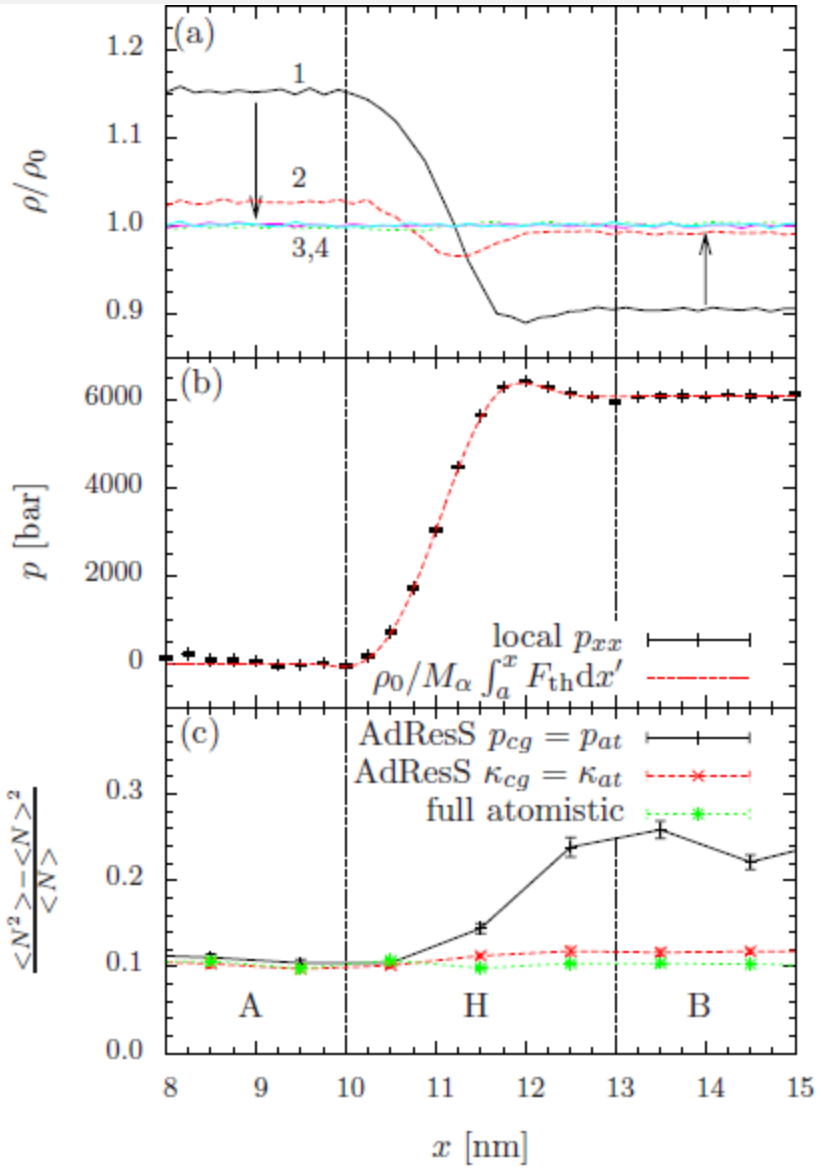
Coarse-grained potentials usually don't match the atomistic system's virial pressure

The difference can be balanced via an iteratively-refined thermodynamic force [1]

$$\mathbf{F}_{th}^{i+1}(x) = \mathbf{F}_{th}^{i}(x) - \frac{M}{\rho_0^2 \kappa_T} \nabla \rho^i(x)$$

Density and particle fluctuations are preserved

The explicit region behaves as an open system



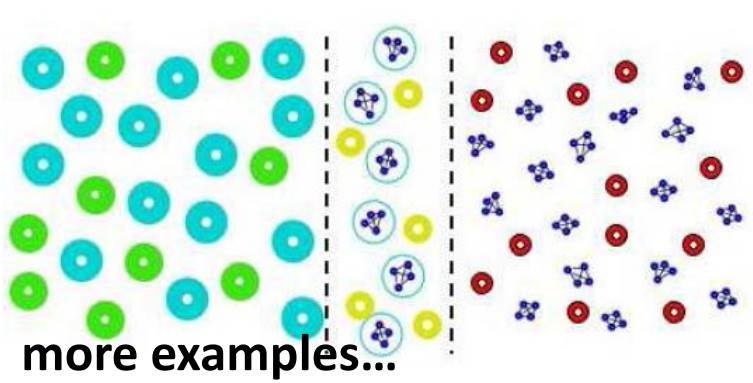
[1] S. Fritsch, S. Poblete, C. Junghans, G. Ciccotti, L. Delle Site, and K. Kremer, Phys Rev Lett 17, vol 108, 2012 [Figures from therein]

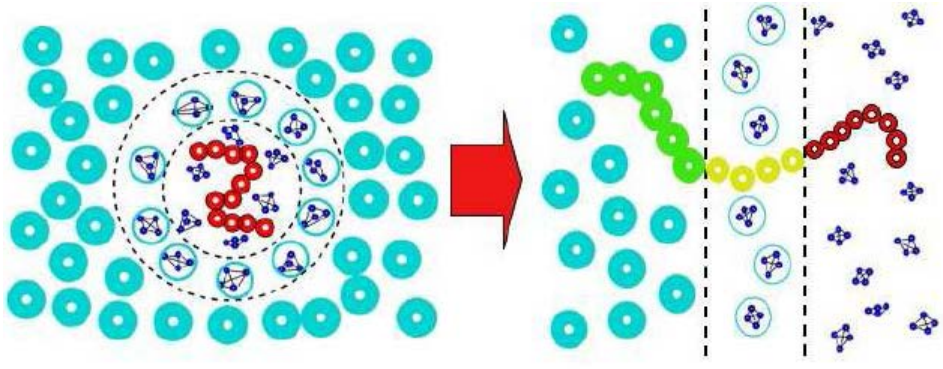
Some Applications

- Fullerene in Toluene
- Fullerenes in water

Kirkwood Buff integrals:

- Peptides in water urea mixtures
- PNIPAM in water alcohol mixtures





more examples…

C60 in Toluene

C. Junghans, S. Fritsch

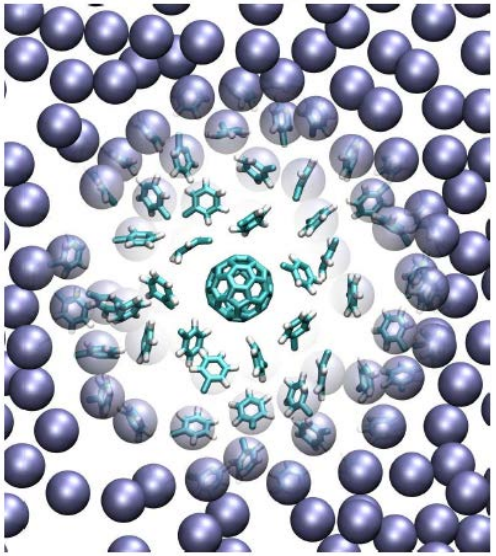
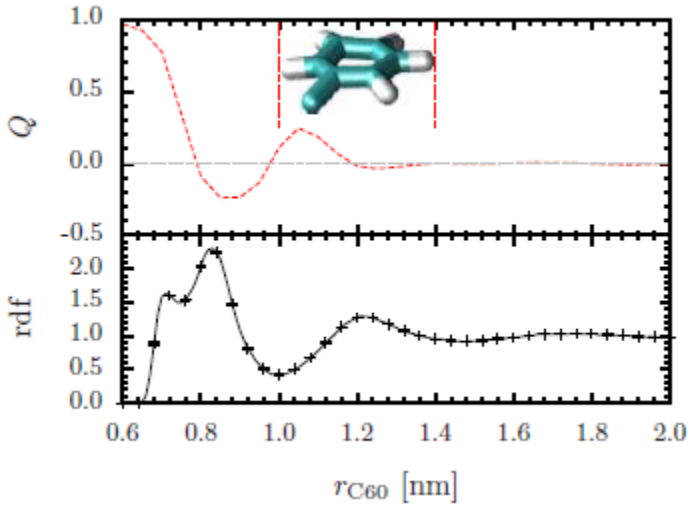
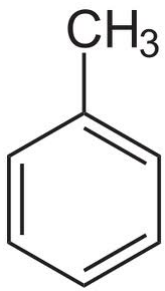


Table 1: Diffusion constants for the C60/toluene center of mass

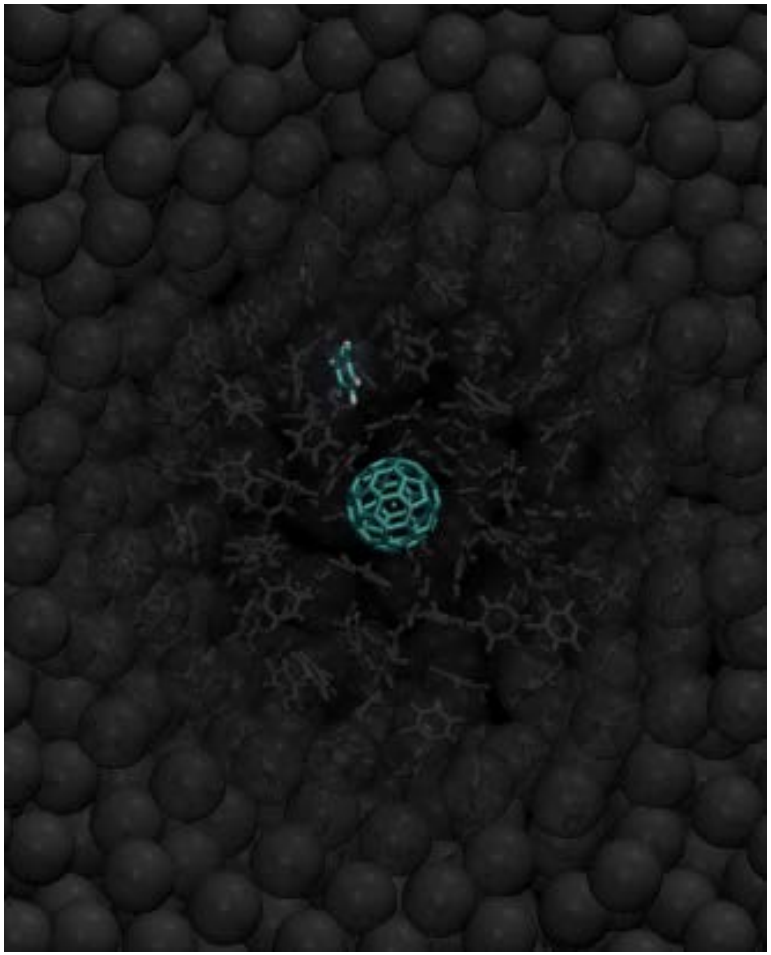
C_{60}	Diffusion constants $[nm^2/ps]$
All-atom	$D = 6.3 \times 10^{-4}$
AdResS	
$r_{at} = 0.75\,nm$	$D = 9.0 \times 10^{-4}$
$r_{at} = 1.0\,nm$	$D = 8.2 \times 10^{-4}$
$r_{at} = 1.5\,nm$	$D = 7.9 \times 10^{-4}$
AdResS with TF	
$r_{at} = 0.75\,nm$	$D = 7.2 \times 10^{-4}$
Pure toluene	
All-atom	$D = 2.2 \times 10^{-3}$
Coarse-grained	$D = 8.6 \times 10^{-3}$

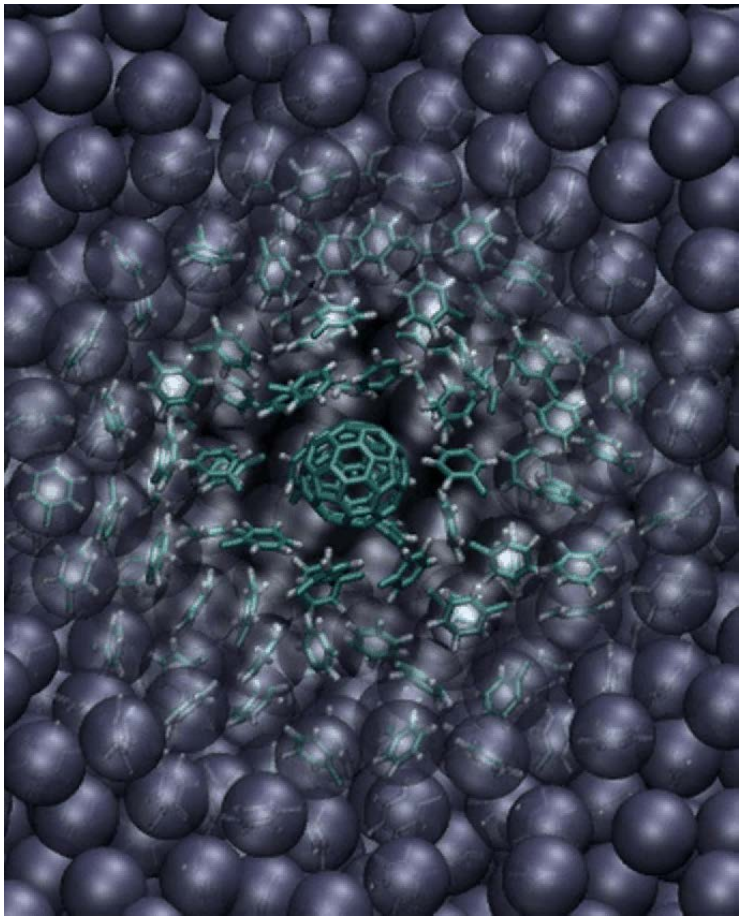




C60 in Toluene

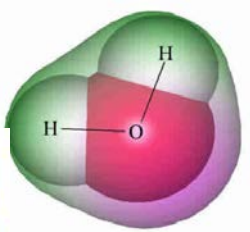
C. Junghans, S. Fritsch

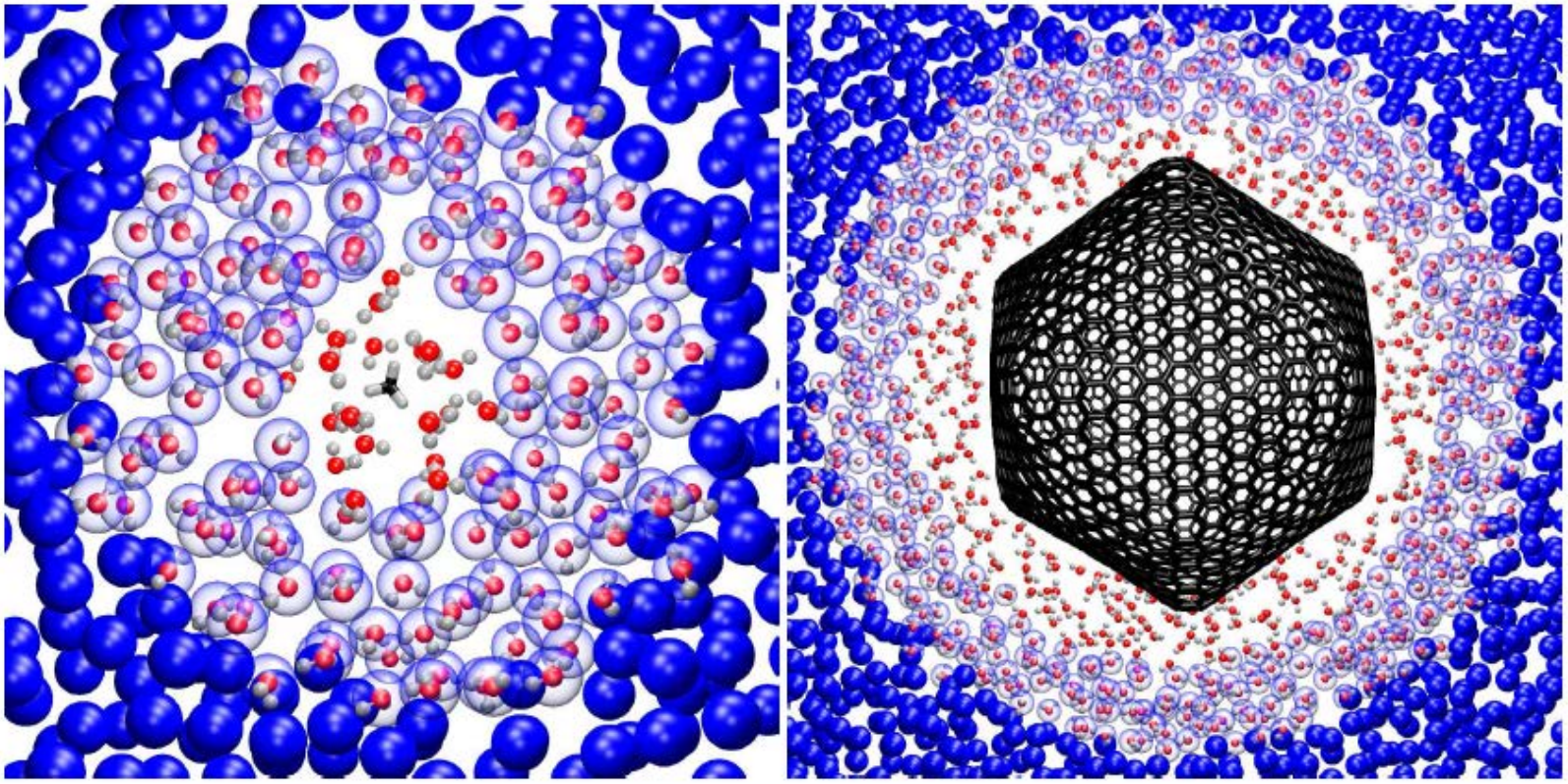




Example for
GROMACS implementation

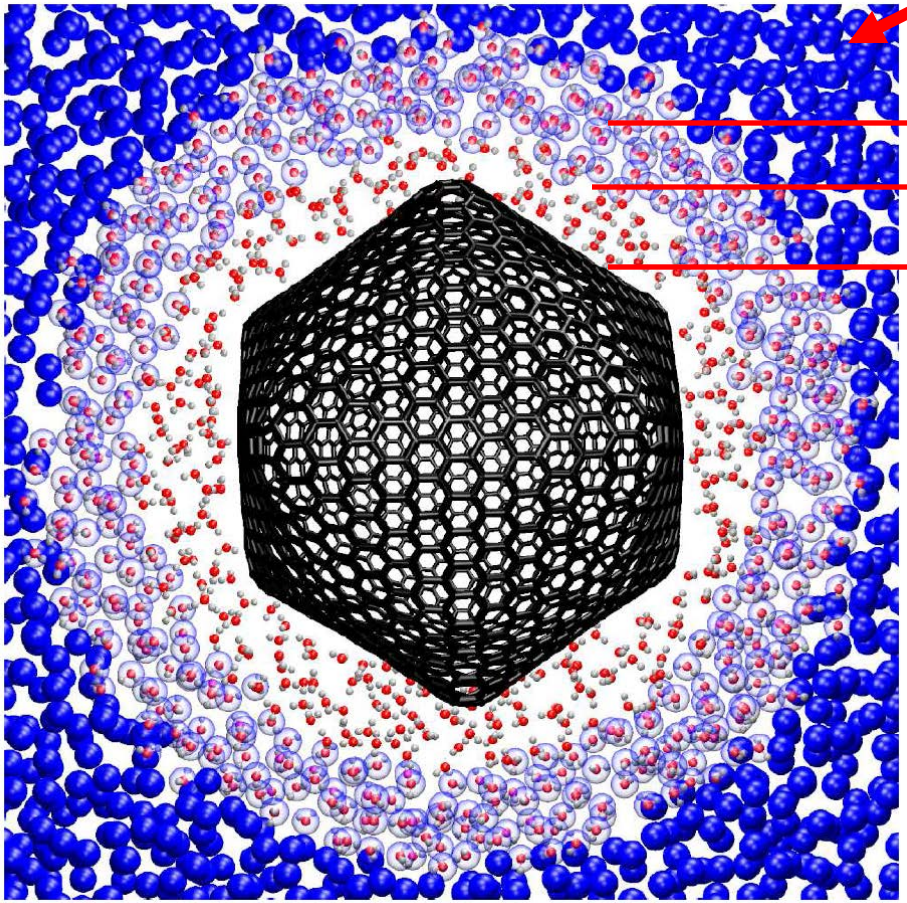
Hydrophobic Solutes





B. P. Lambeth, C. Junghans, KK, C. Clementi, L. Delle Site, JCP 2010

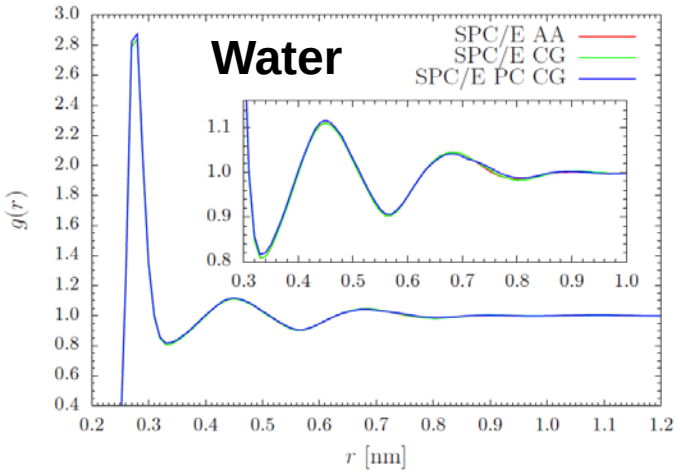
Hydrophobic Solutes: Surface vs Bulk



CG regime

Transition layer

All atom layer, d_{ex}



cg water reproduces g(r)
but NOT tetrahedral packing!

B. P. Lambeth, C. Junghans, KK, C. Clementi, L. Delle Site, JCP 2010

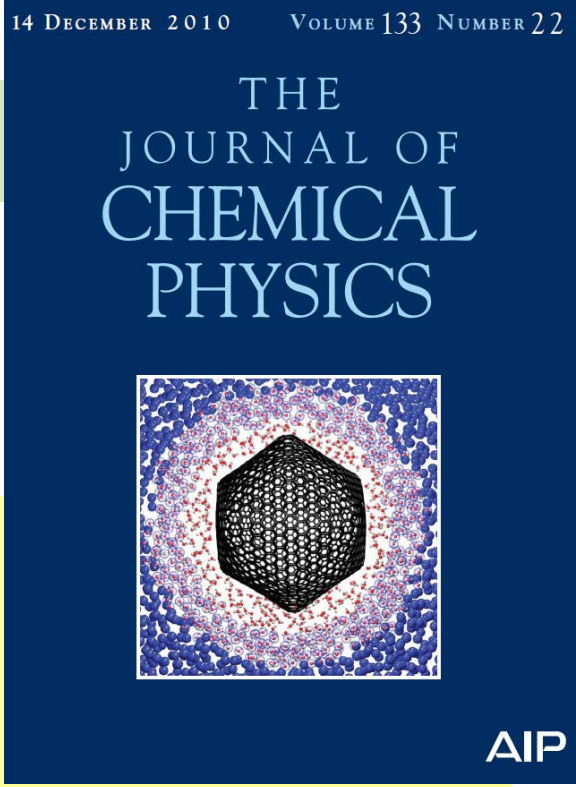
Hydrophobic Solutes

C_{60}

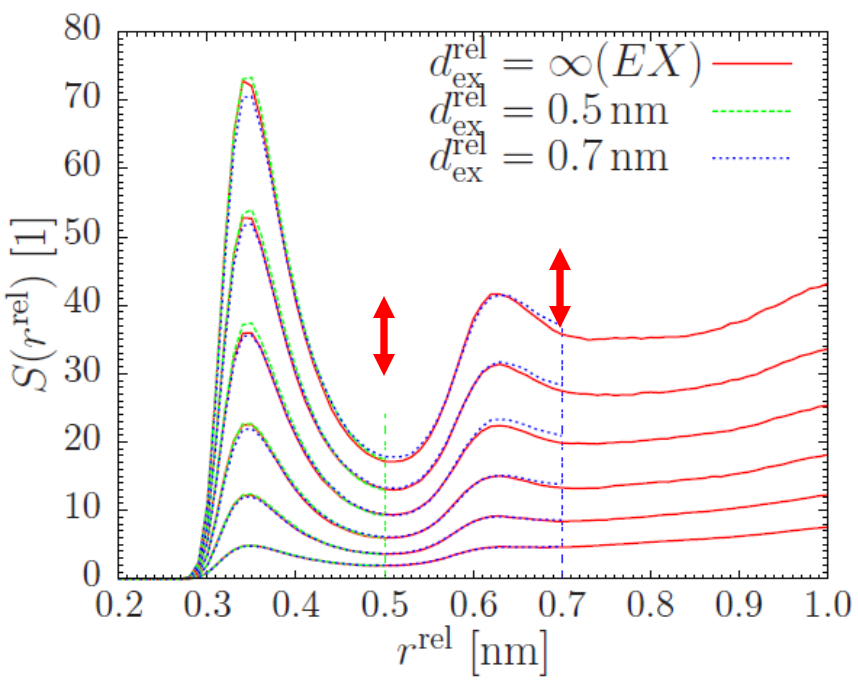
C_{2160}

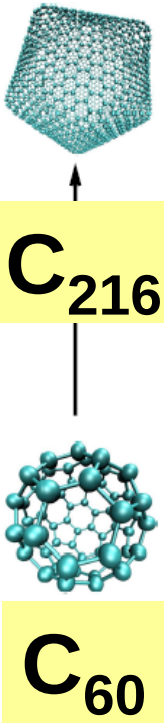
Influence of bulk H-bond structure on surface layer

 # two surface potentials
- standard (weak) Lennard Jones
($\varepsilon_{CO} \approx 0.2 k_B T$, $\sigma_{CO} \approx 0.34$nm)
- purely repulsive (r^{-12})
 # variable width of explicit layer



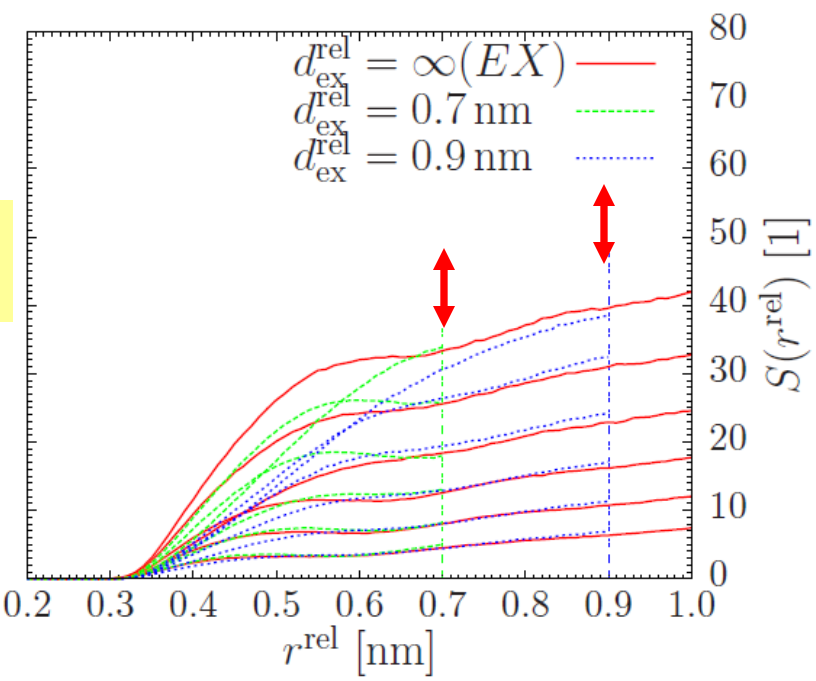
of Water Molecules around Solute, variable all atom water layer d_{ex} (1st, 2nd shell,)





C_{2160}

C_{60}

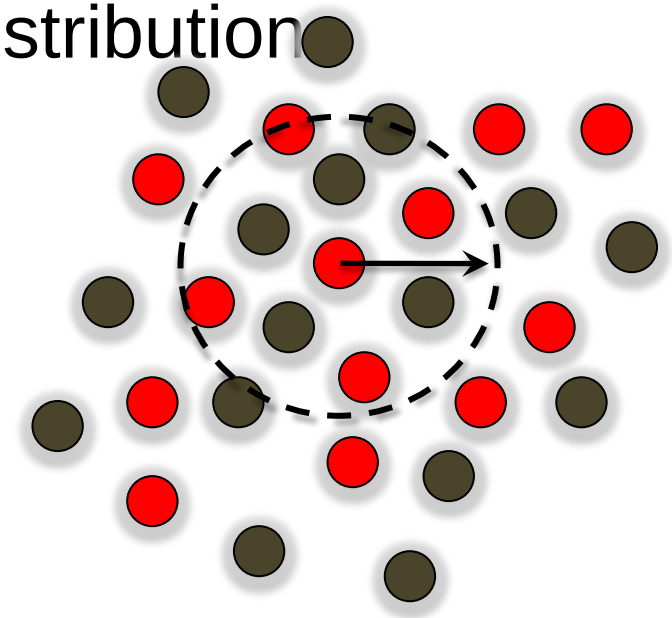


LJ interaction
dominated by surface Interaction

Repulsive
# of waters close to surface strongly depleted

Fluctuation theory of Kirkwood-Buff

Fluctuation theory: Global thermodynamic properties from microscopic (pair-wise) molecular distribution



$$G_{ij} = V\left[\frac{\langle N_i N_j\rangle - \langle N_i\rangle\langle N_j\rangle}{\langle N_i\rangle\langle N_j\rangle} - \frac{\delta_{ij}}{\langle N_j\rangle}\right]$$

$$= 4\pi\int_0^\infty \left[g_{ij}^{\mu VT}(r) - 1\right] r^2 dr,$$

Excess (depletion) coordination number

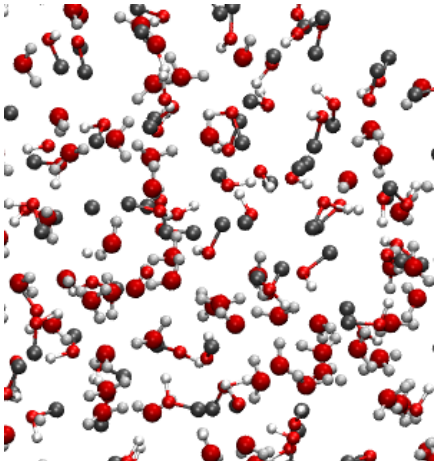
$$\Delta N_{ij} = \rho_j G_{ij}$$

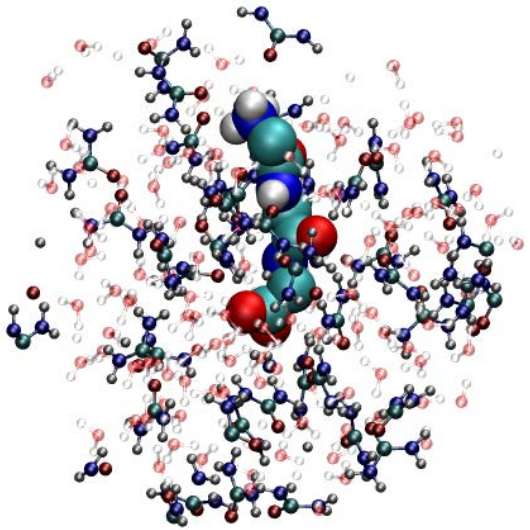
- Solvation energy
- Partial molar volume
- Activity coefficient
- Compressibility …….

Kirkwood and Buff, J. Chem. Phys. 19, 774 (1951).

Fluctuation theory of Kirkwood-Buff

Solvation Free Energies





Activity coefficient

$$\gamma_{cc} = 1 + \left(\frac{\partial \ln \gamma_c}{\partial \ln \rho_c}\right)_{p,T} = \frac{1}{1 + \rho_c \left(\mathrm{G}_{cc} - \mathrm{G}_{cw}\right)}$$

$$k_B T \ln \gamma_c$$

Solvation free energies

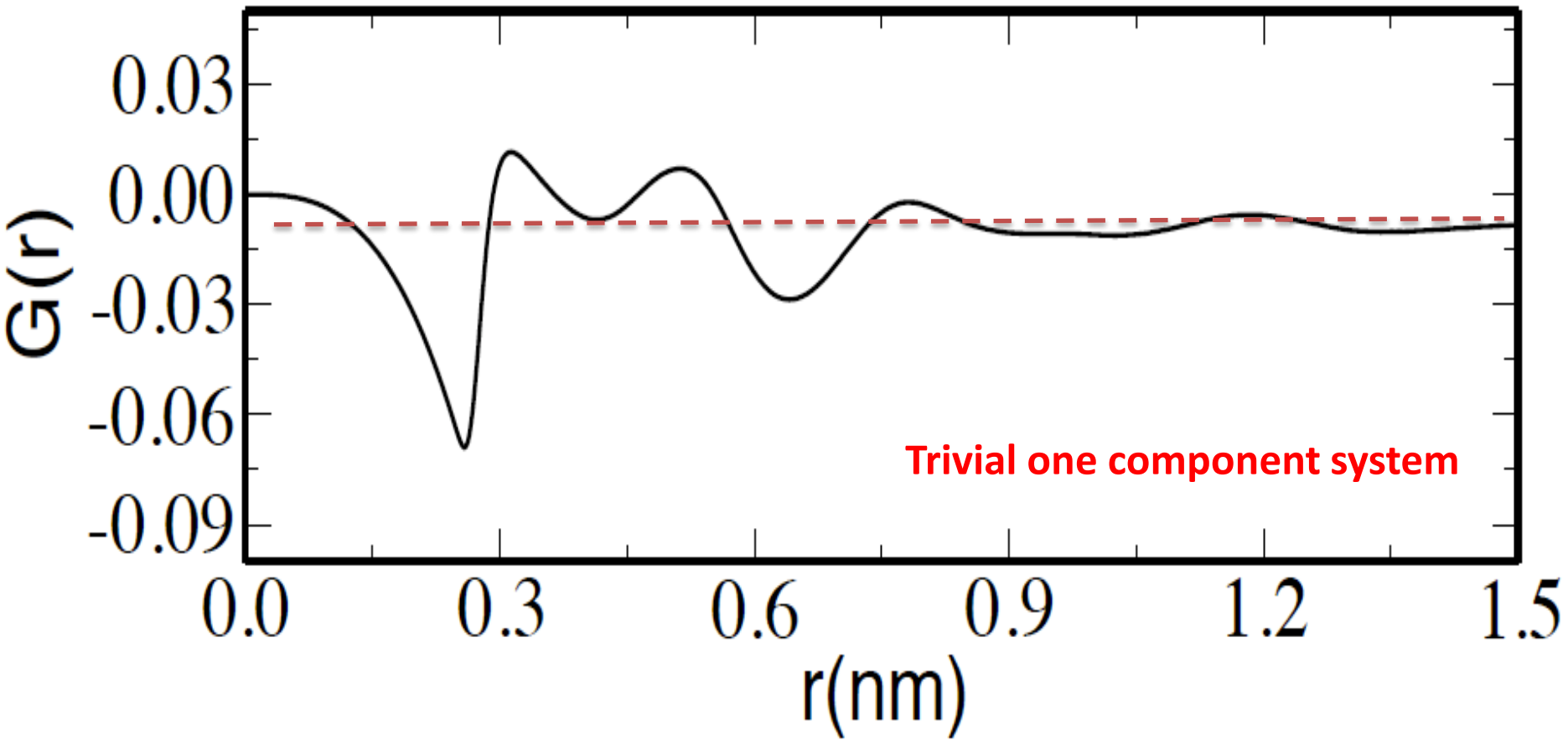
$$\lim_{\rho_s \to 0} \left(\frac{\partial \Delta \mathcal{G}_s}{\partial x_c}\right)_{p,T} = \frac{RT\left(\rho_w + \rho_c\right)^2}{\eta}\left(\mathrm{G}_{sw} - \mathrm{G}_{sc}\right)$$

$$\eta = \rho_w + \rho_c + \rho_w \rho_c \left(G_{ww} + G_{cc} - 2G_{cw}\right)$$

Kirkwood and Buff, J. Chem. Phys. 19, 774 (1951).

Kirkwood-Buff integrals

$$G_{ij}(r) = 4\pi \int_0^r \left[g_{ij}(r') - 1 \right] r'^2 \, dr'$$



Kirkwood and Buff, J. Chem. Phys. 19, 774 (1951).

Problems with closed boundary simulation

- Non-ideal mixture (water-cosolvent)

- Biophysical processes are intimately linked with large density fluctuations (conformational transition)

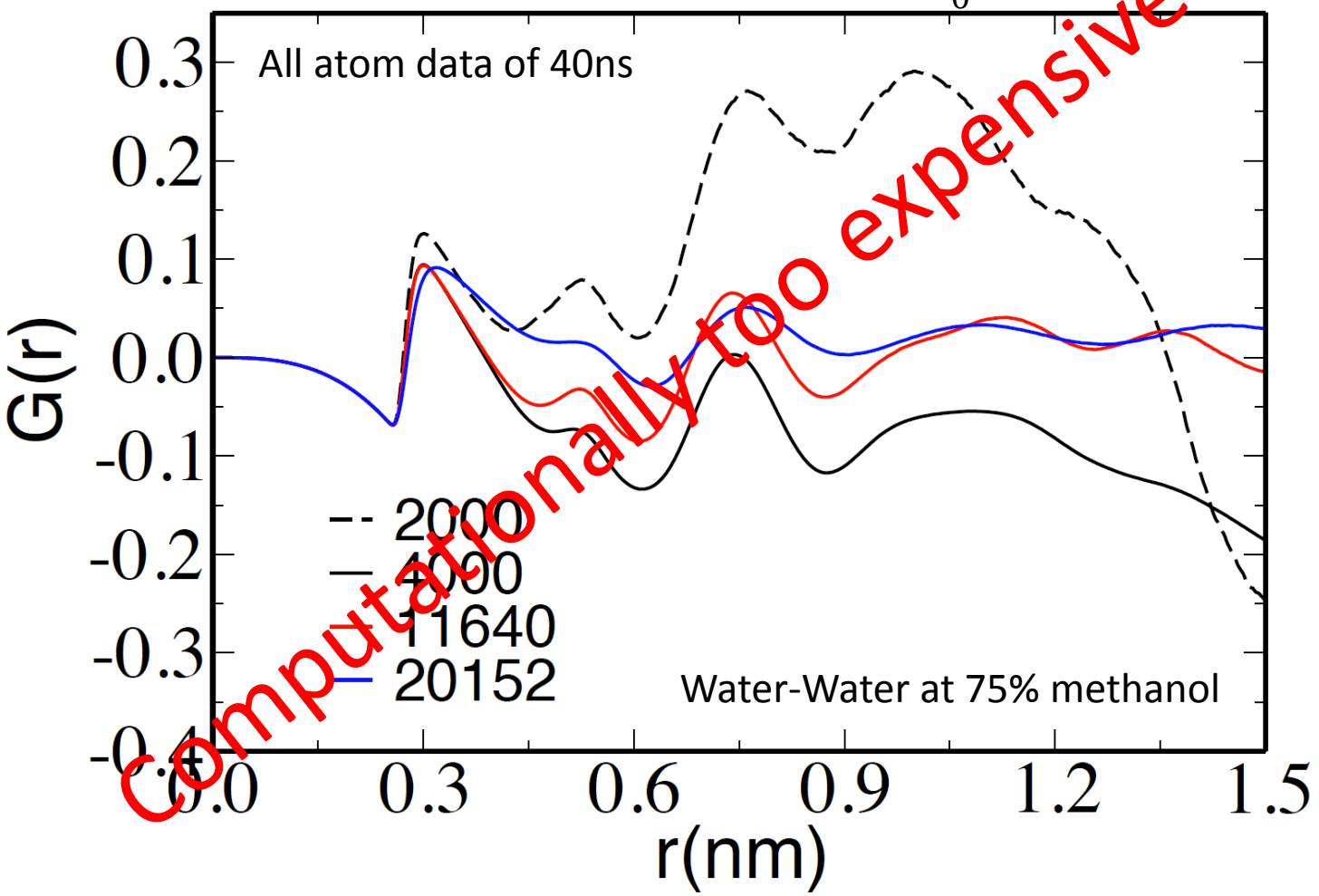
- Excess in one region leads to depletion elsewhere

- KBI does not converge

- Thermodynamics away from a protein structure is ill-defined

Test case: methanol water mixture

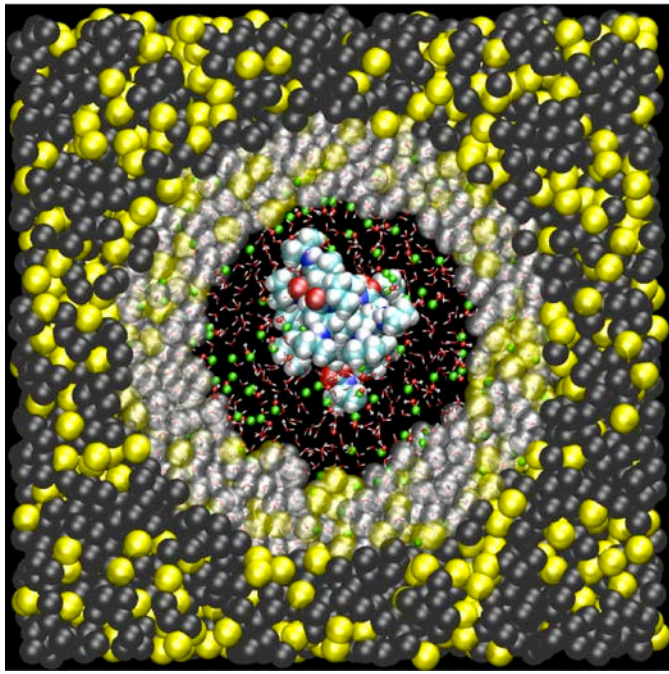
Where to take the value? $G_{ij}(r) = 4\pi \int_0^r \left[g_{ij}(r') - 1\right] r'^2 \, dr'$



Mukherji, van der Vegt, Kremer, and Delle Site, J. Chem. Theory Comp. (Letter) 8, 375 (2012).

Our Goal

- Study solvation of large (bio)macromolecules
- Device an efficient method
- Correct concentration fluctuations
- Solvent equilibrium

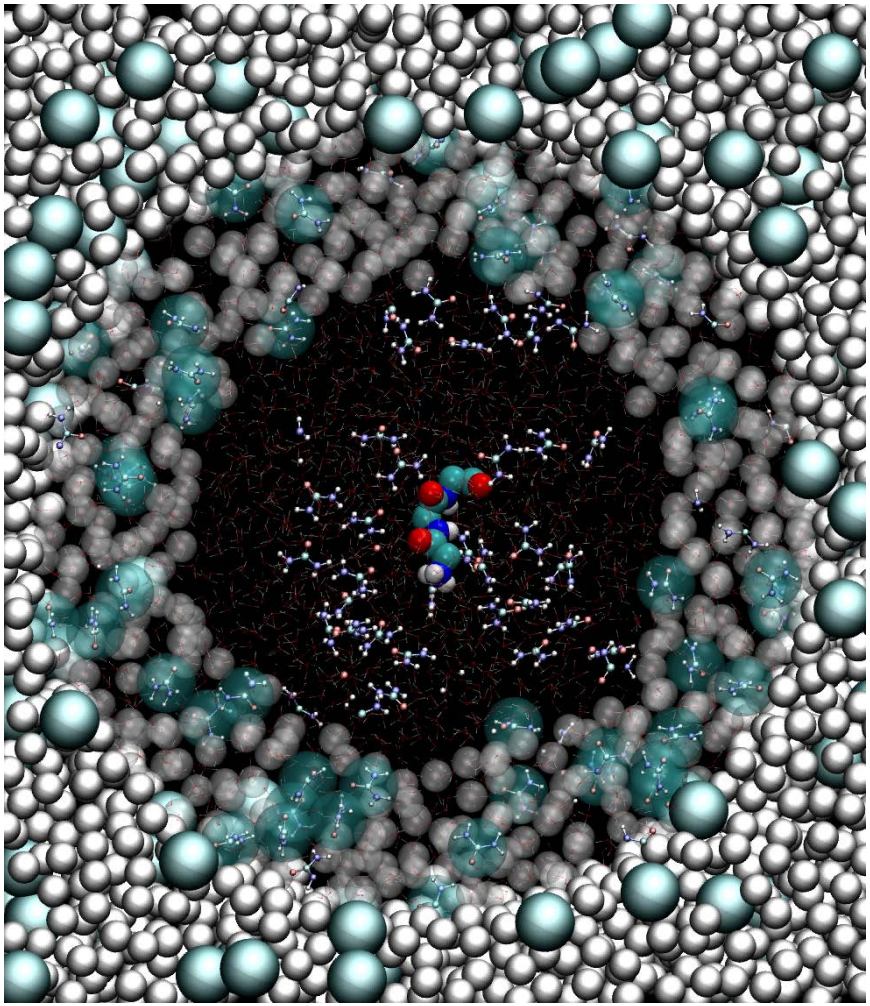


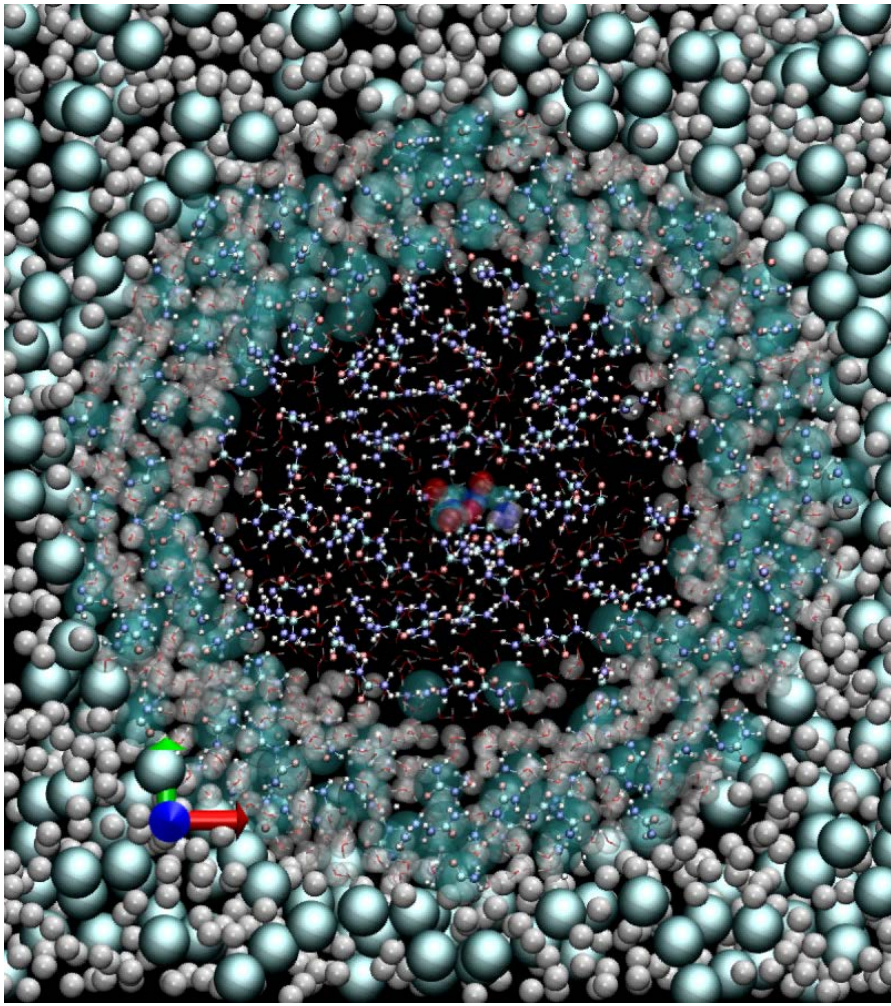
"Effective" open boundary

Why not go open boundary?

Make use of Kirkwood-Buff theory!

Tri-glycine in Urea-Water Mixture

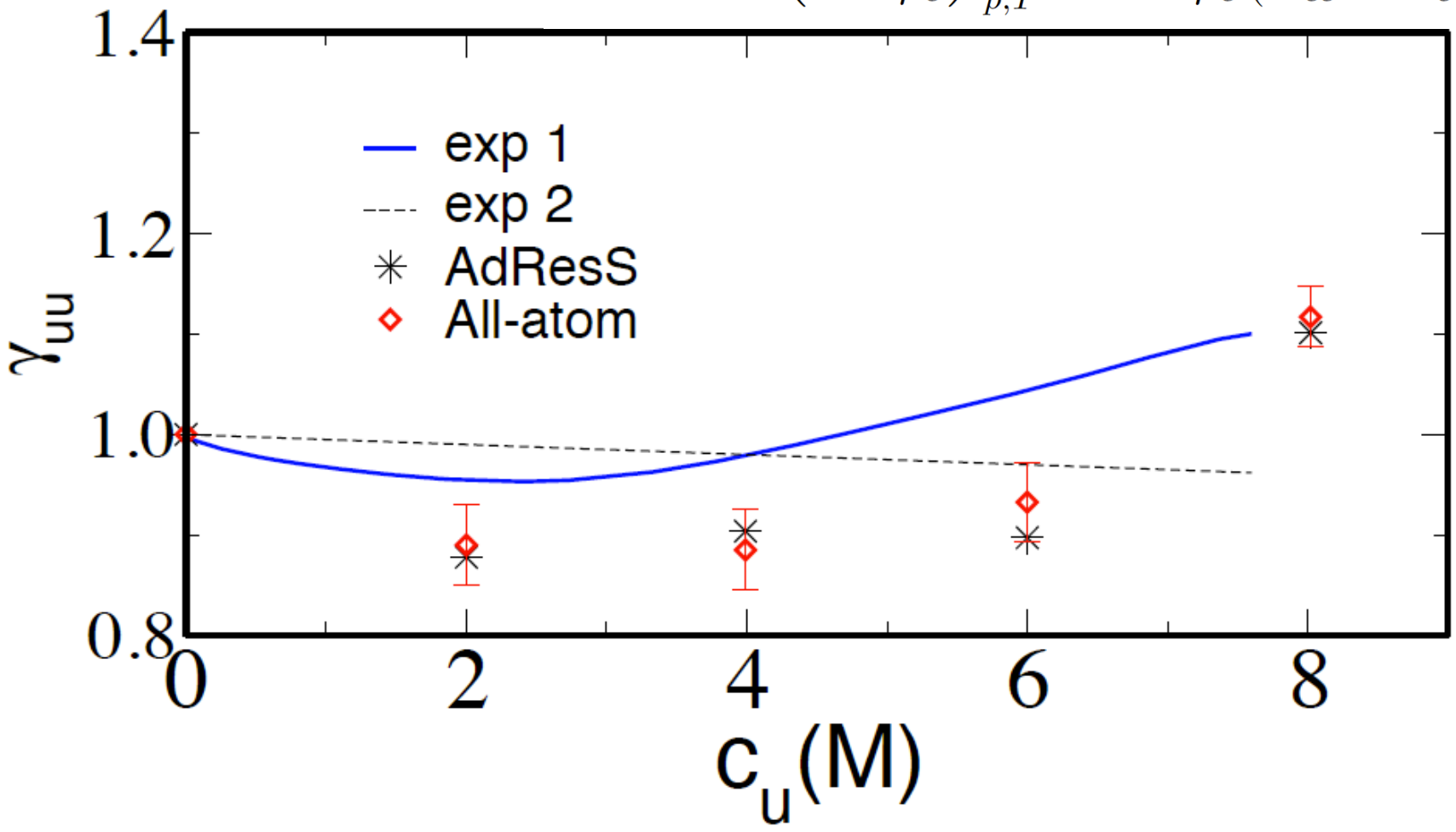




Mukherji, van der Vegt, and KK, JCTC 8, 3536 (2012).

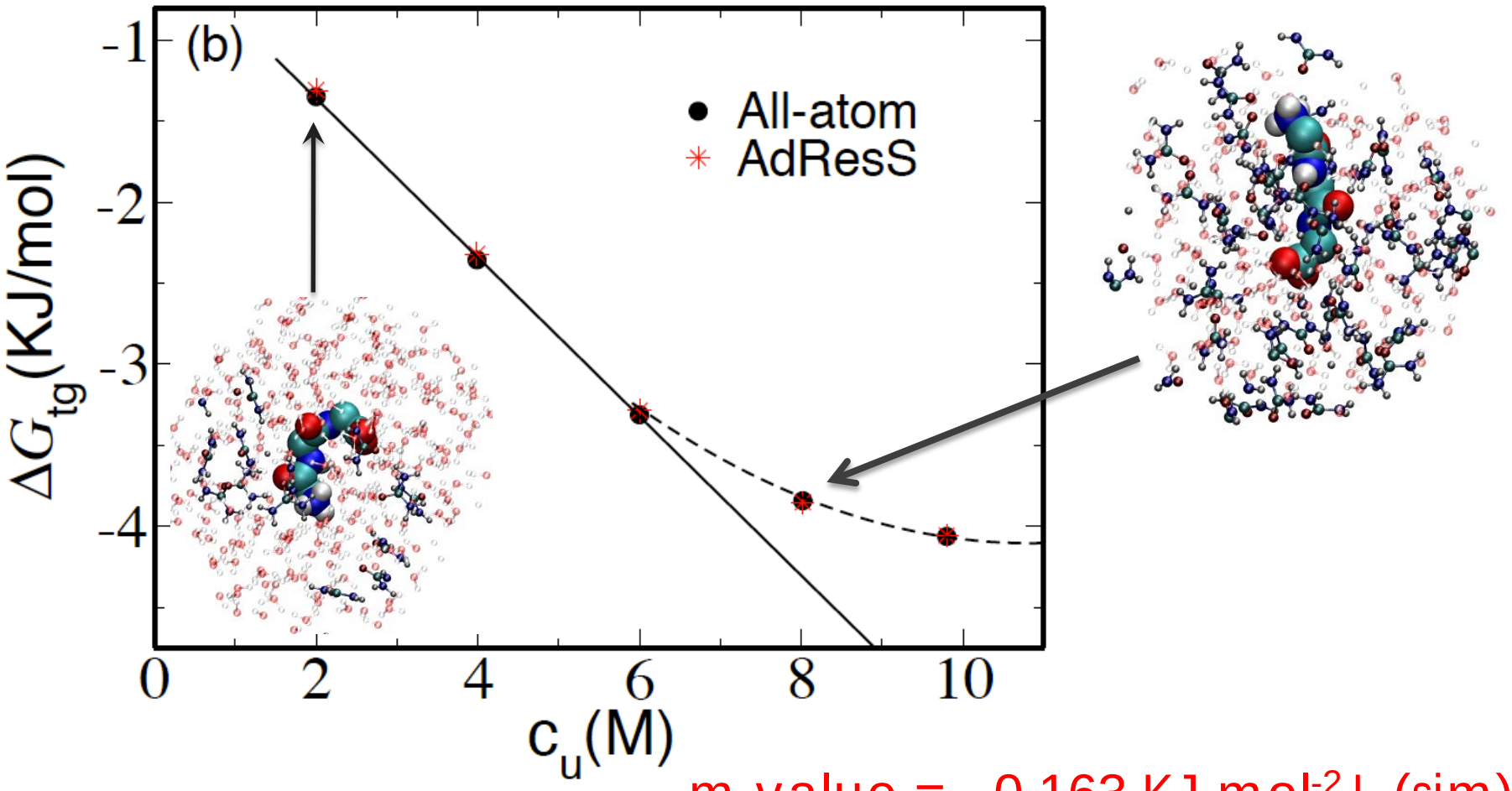
Urea-Water

$$\gamma_{cc} = 1 + \left(\frac{\partial \ln \gamma_c}{\partial \ln \rho_c}\right)_{p,T} = \frac{1}{1 + \rho_c \left(G_{cc} - G_{cw}\right)}$$



Mukherji, van der Vegt, and KK, JCTC 8, 3536 (2012).

Solvation free energy of tri-glycine



m-value = - 0.163 KJ mol^{-2} L (sim)

= - 0.164 KJ mol^{-2} L (exp)

Auton and Bolen, PNAS 102, 15065 (2005).

Mukherji, van der Vegt, and Kremer, J. Chem. Theory Comp. 8, 3635 (2012).

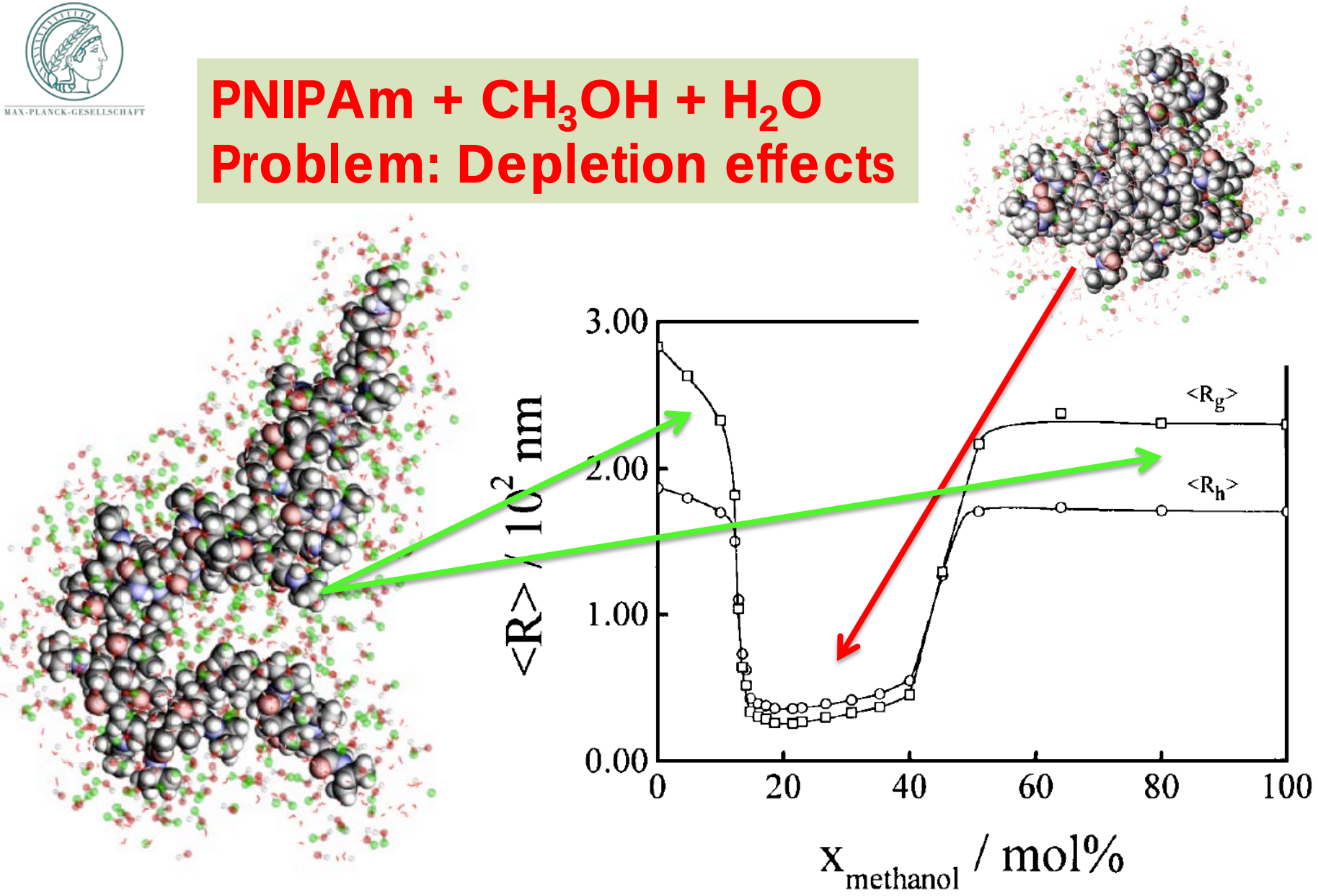
Some Applications

- Fullerene in Toluene
- Fullerenes in water

Kirkwood Buff integrals:

- Peptides in water urea mixtures
- PNIPAM in water alcohol mixtures: "Grand Canonical" AdResS

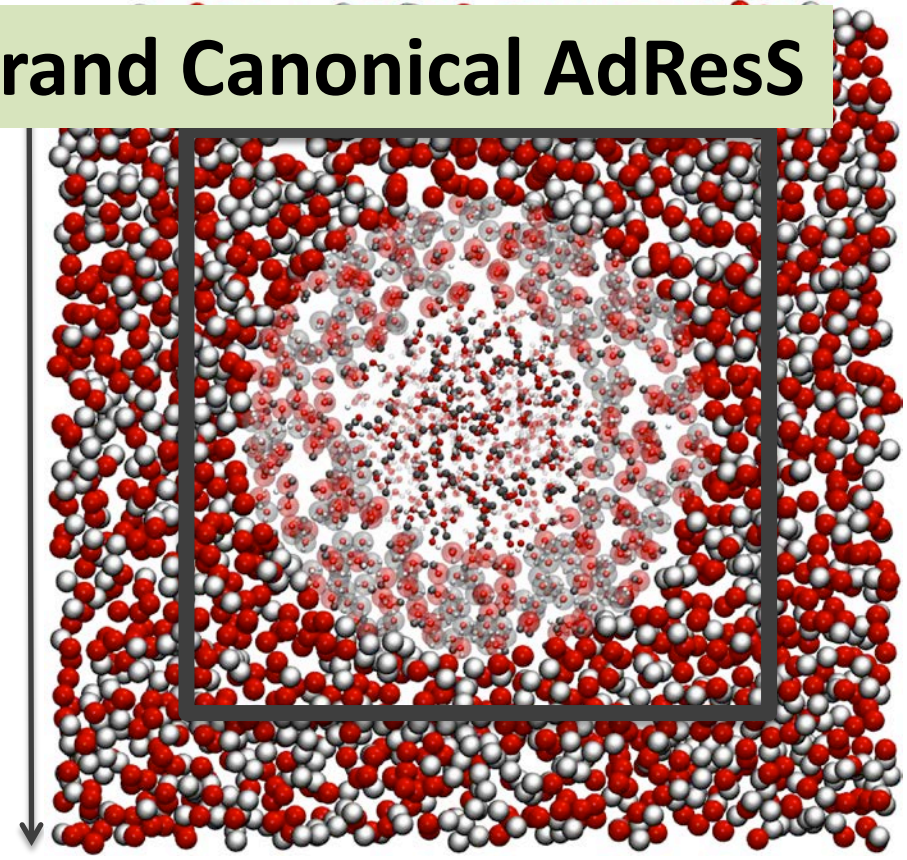
PNIPAm + CH_3OH + H_2O
Problem: Depletion effects



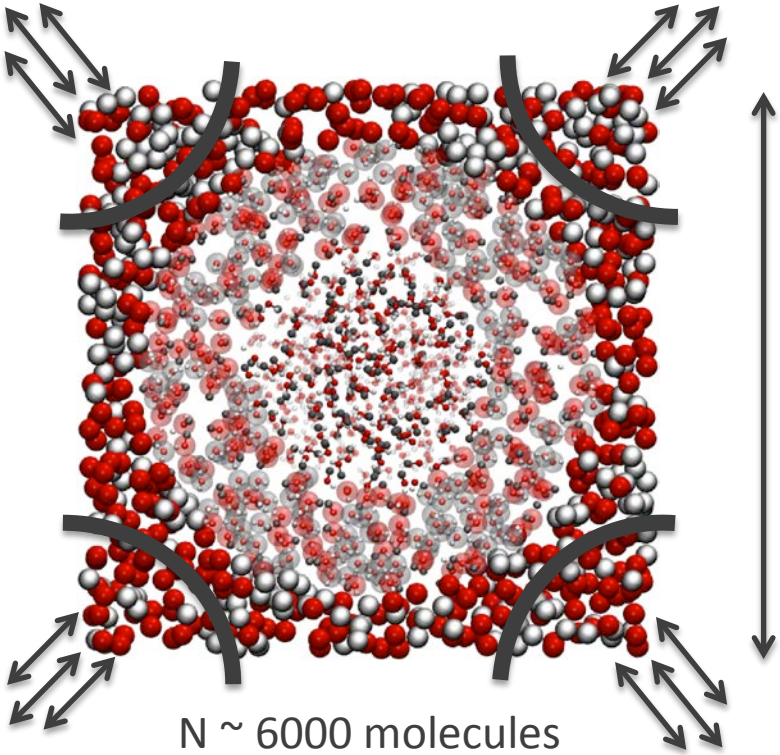
Zhang and Wu, Physical Review Letters 86, 822 (2001).

Mukherji and Kremer, submitted (2013).

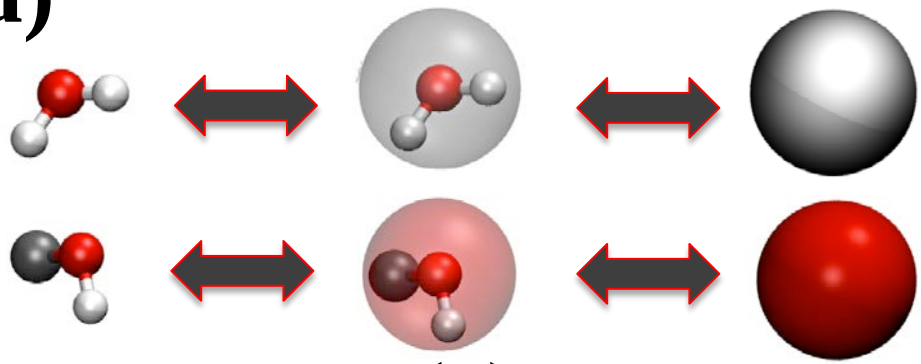
Grand Canonical AdResS



(a)



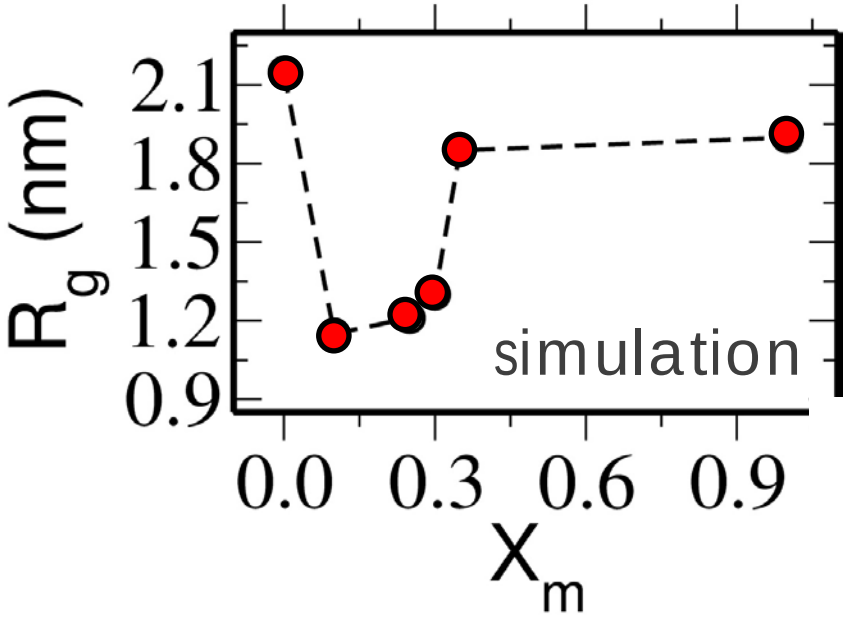
(b)

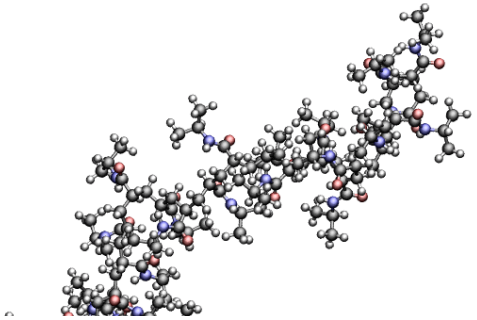


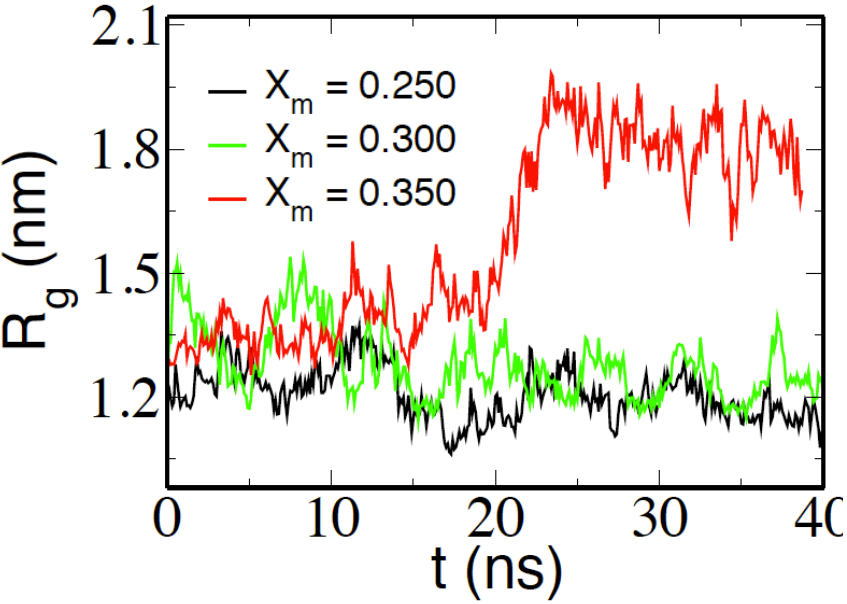
(c)

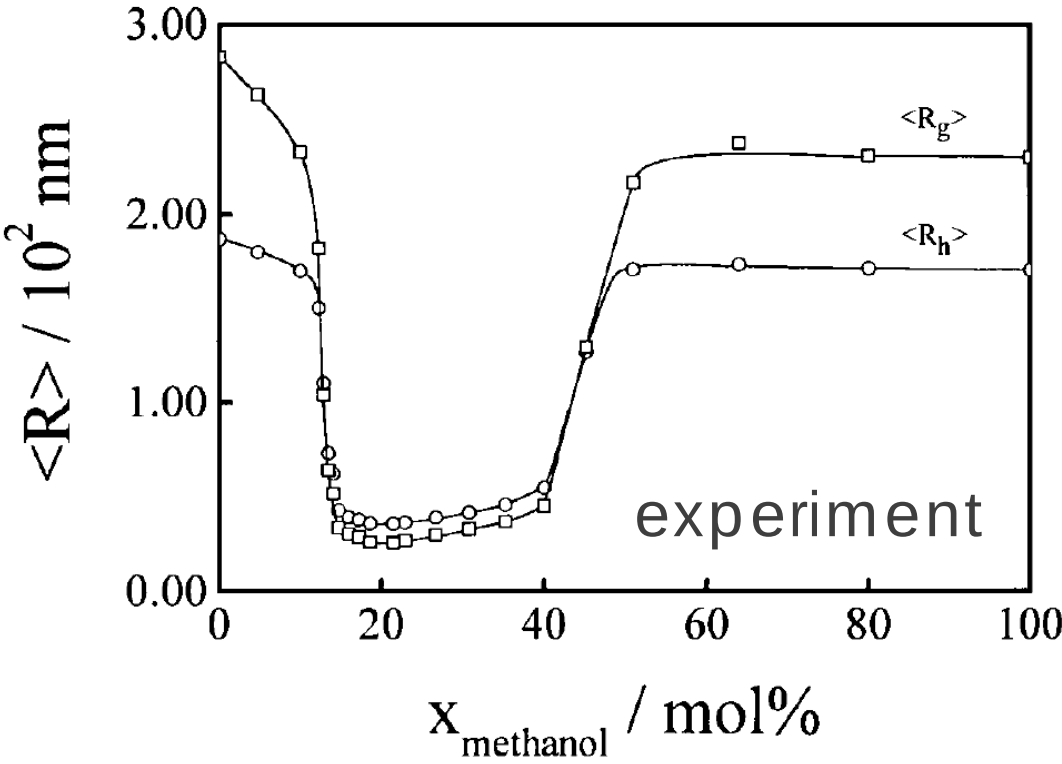
D. Mukherji, KK, 2013

Poly-NIPAm in aqueous methanol



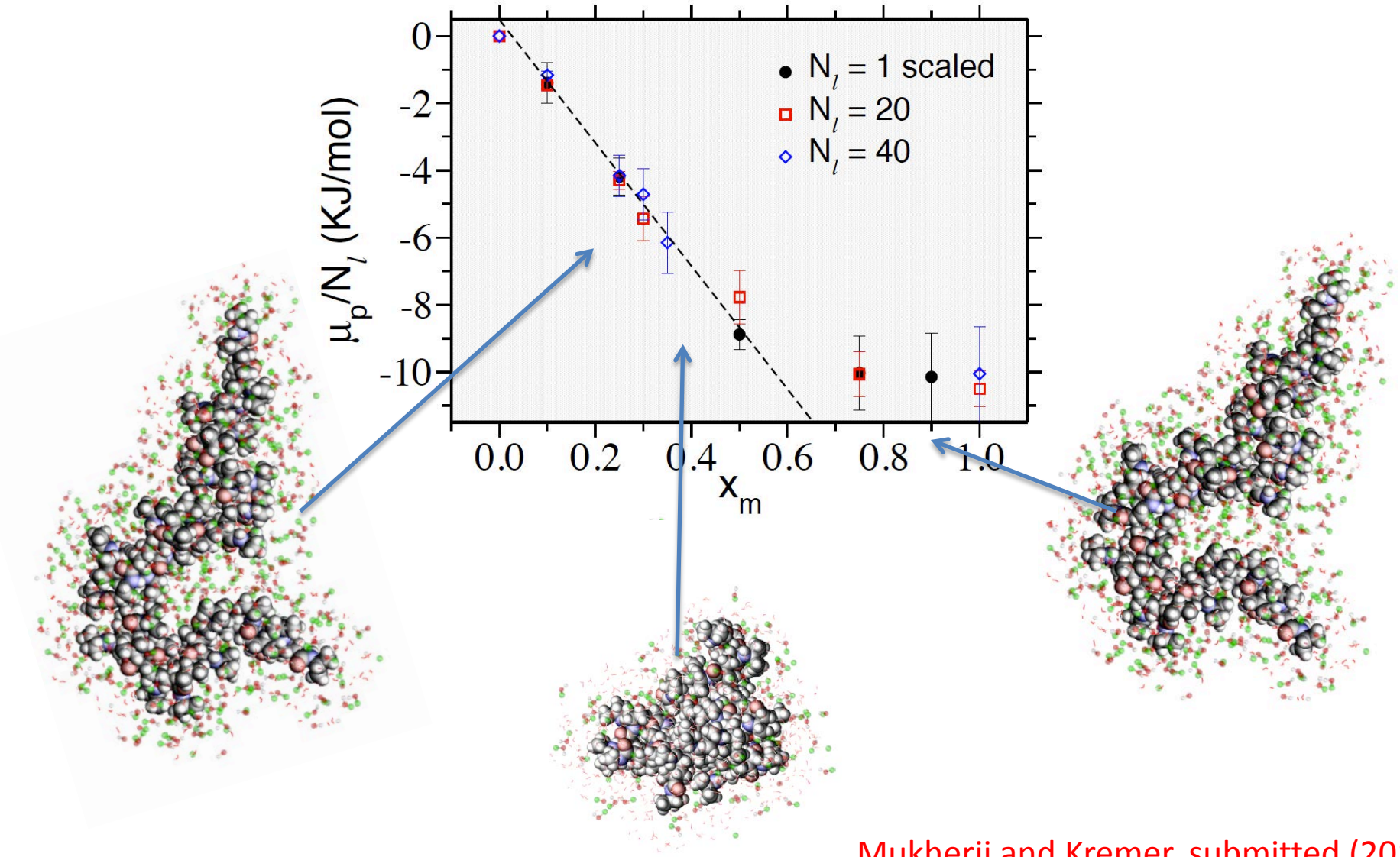






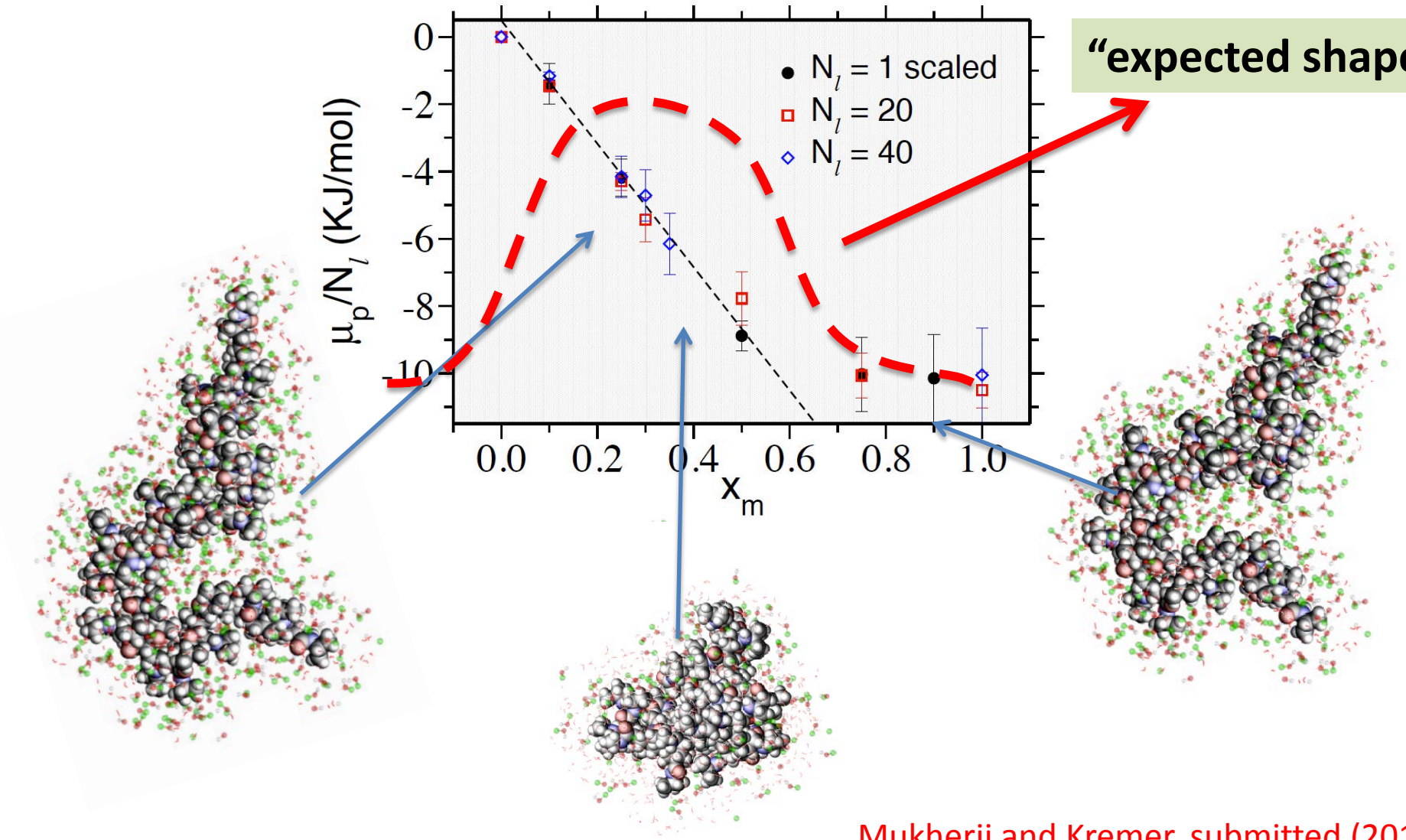
Mukherji and Kremer, submitted (2013).

Poly-NIPAm chemical potential



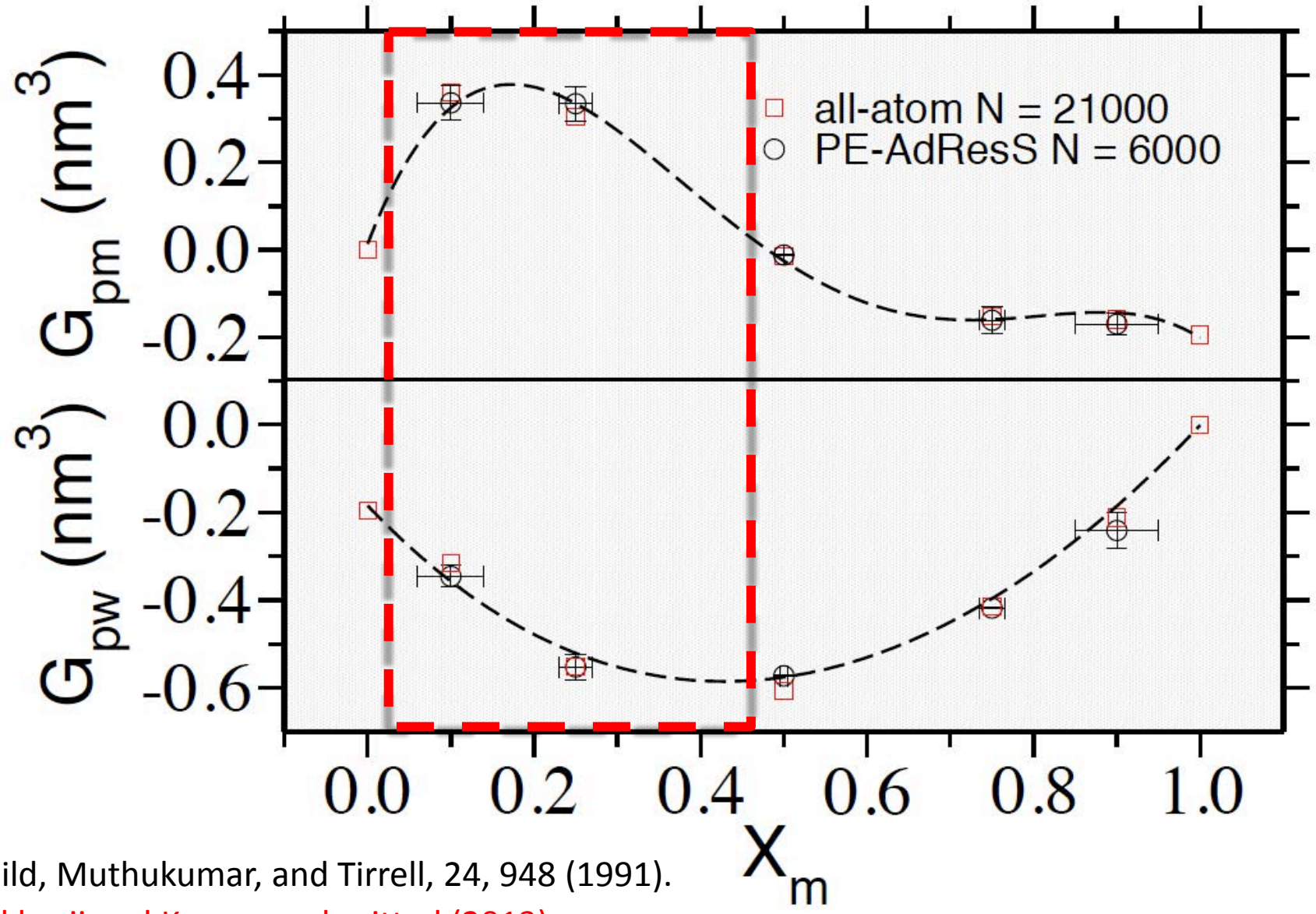
Mukherji and Kremer, submitted (2013).

Poly-NIPAm chemical potential



Mukherji and Kremer, submitted (2013).

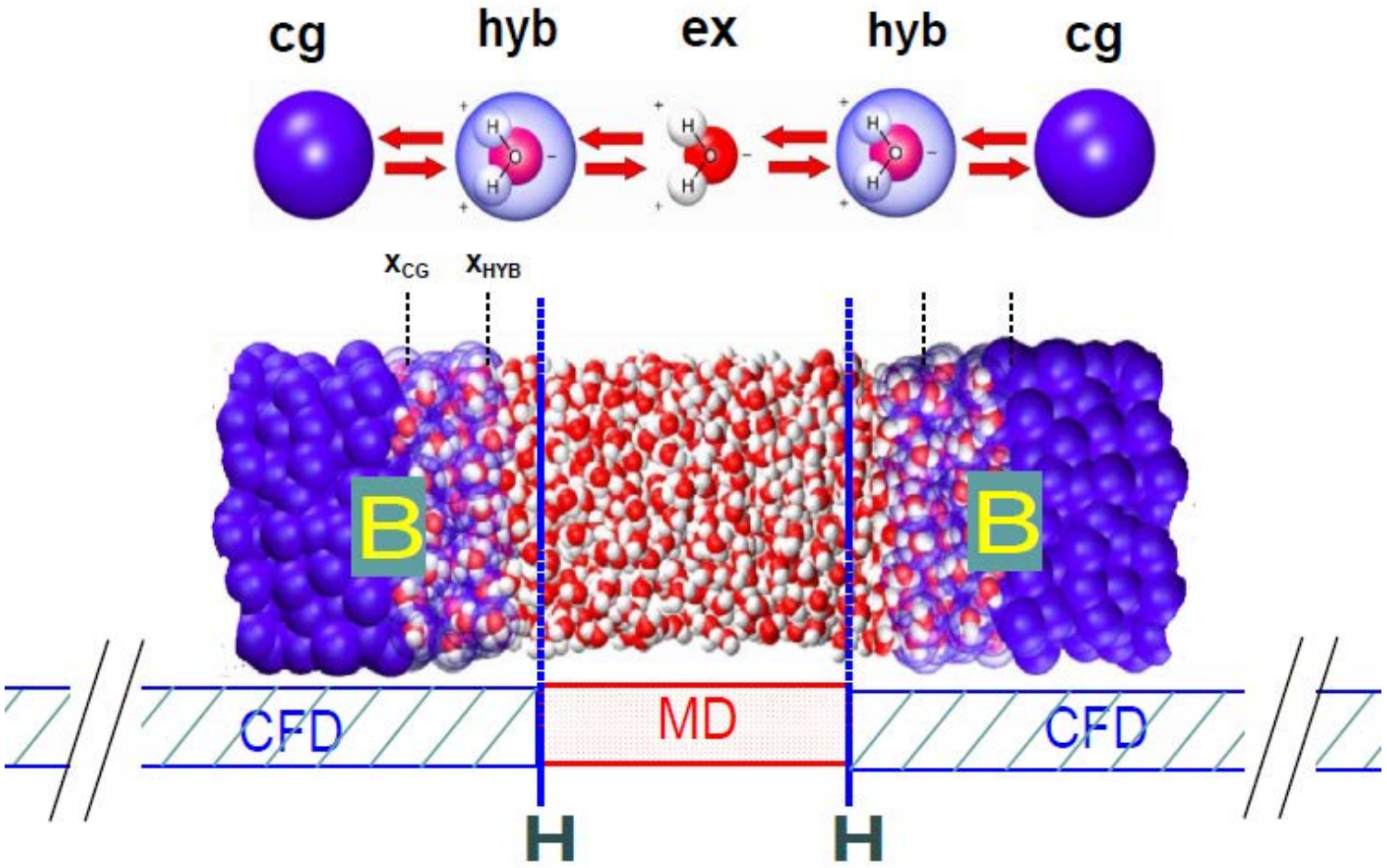
NIPAm in aqueous methanol



Schild, Muthukumar, and Tirrell, 24, 948 (1991).

Mukherji and Kremer, submitted (2013).

AdResS-HybridMD: Water



R. Delgado Buscalioni, KK, M. Praprotnik, JCP 131, 244107 (2009)

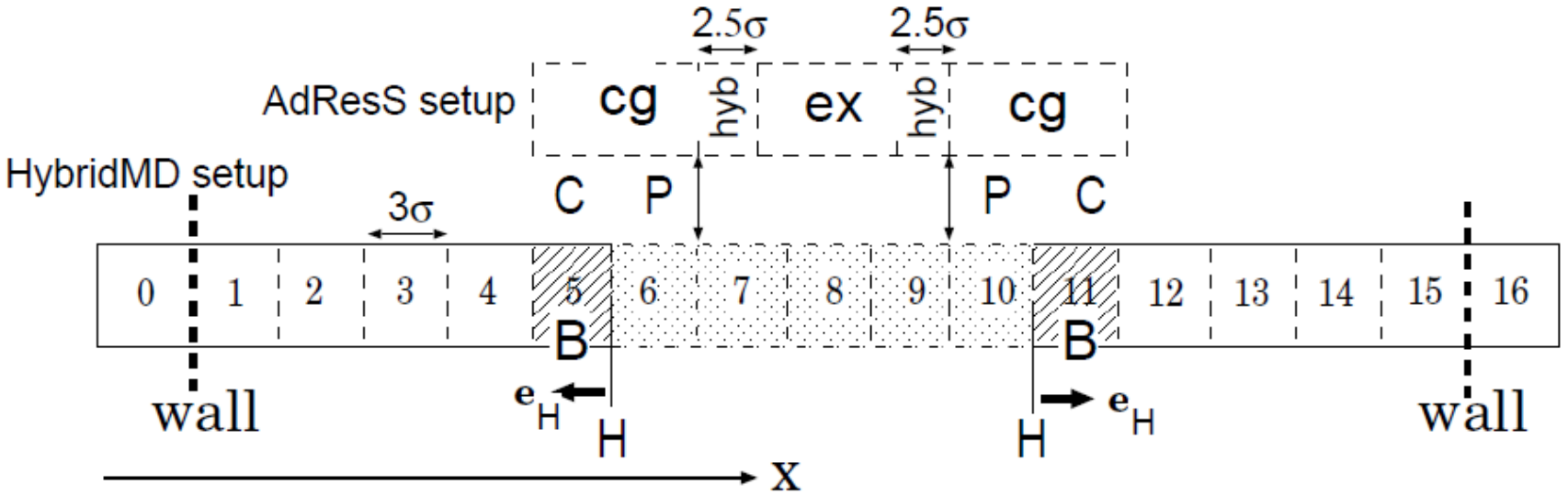
HybridMD: Coupling Particle-Based and Continuum Descriptions

- The hybrid particle-continuum scheme (HybridMD) is designed to connect the dynamics of a "**molecular domain**" with that obtained from a **continuum description** of the surrounding fluid flow.
- The method is based on **flux-exchange**.
- The system is divided in (at least) two domains, described via classical **molecular dynamics (MD)** and **continuum fluid dynamics (CFD)**, i.e., solving the **Navier-Stokes** equations.
- The MD and CFD domains share one unique "hybrid interface", H: Flux balance implies the **conservation of mass and momentum** across H.

PROBLEM: Particle Insertion into Buffer

G. De Fabritiis, R. Delgado Buscalioni, P. Coveney, Phys. Rev. Lett **97**, 134501 (2006).
R. Delgado Buscalioni, G. De Fabritiis, Phys. Rev. E **76**, 036709 (2007).

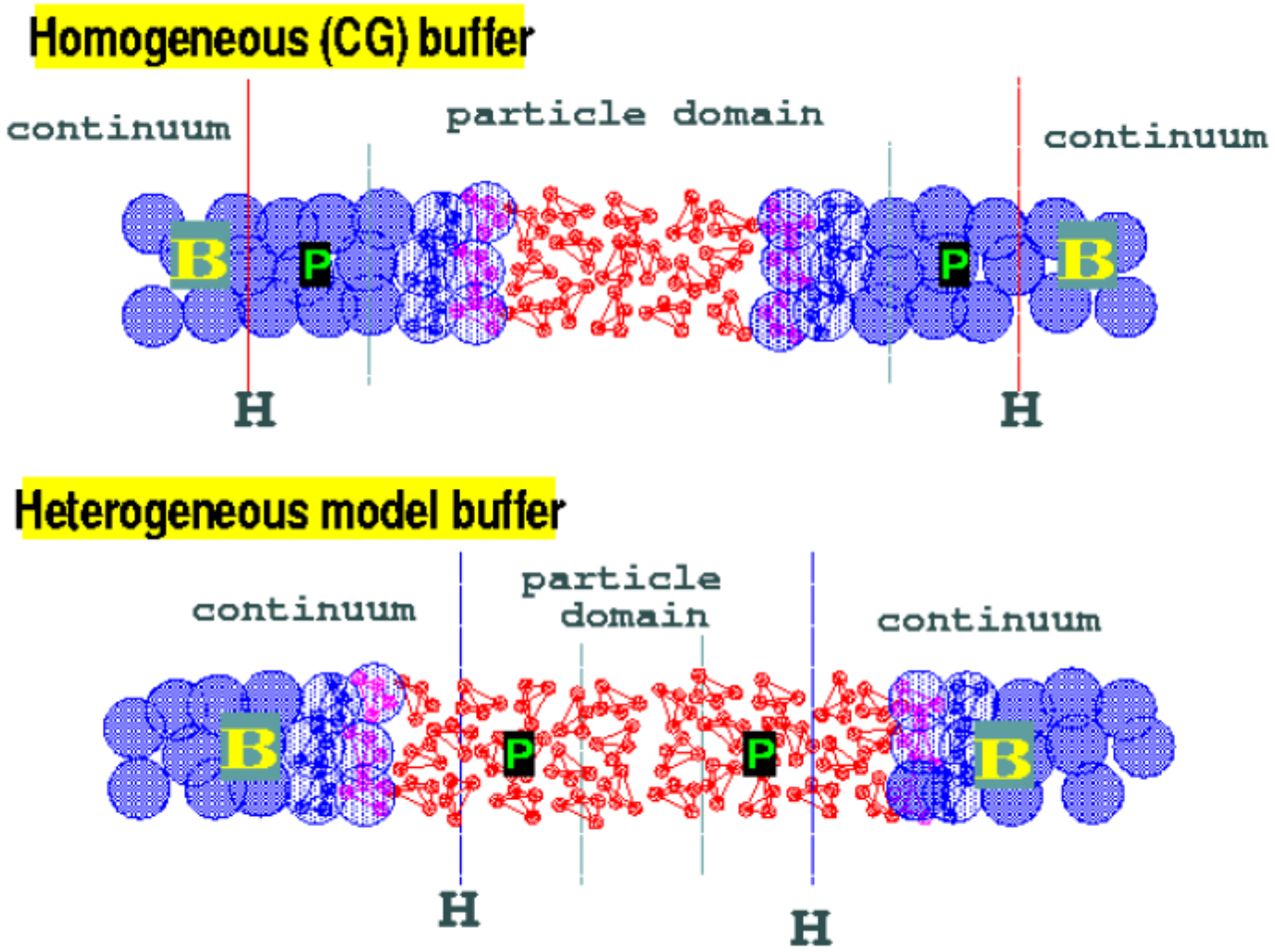
AdResS-HybridMD combined



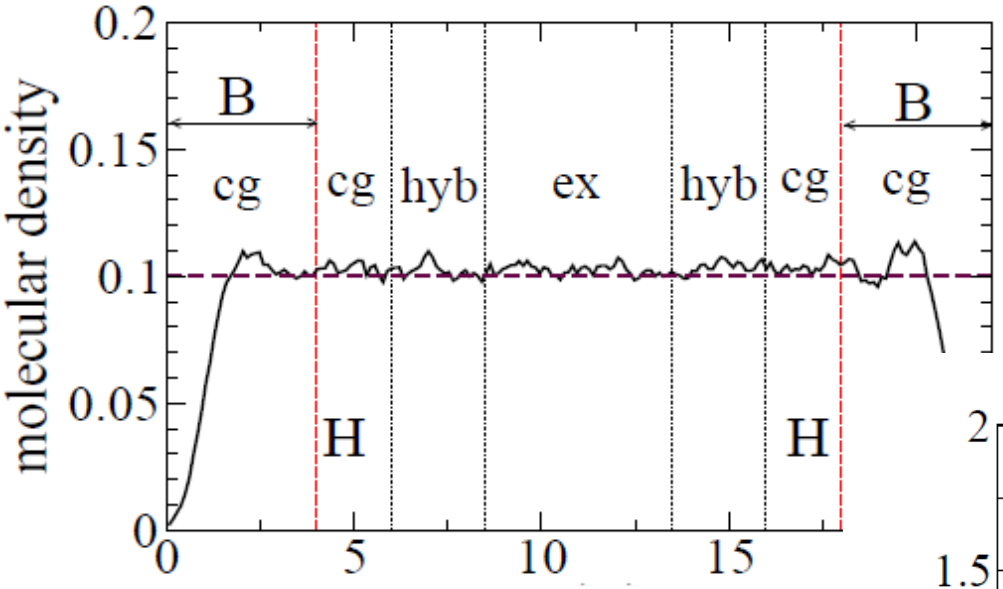
Domain decomposition of the combined scheme. The top part of the figure shows the location of the fluid model layers (cg, hyb and ex) within the HybridMD setup. The bottom part of the figure shows the set of control cells used in the HybridMD setup.

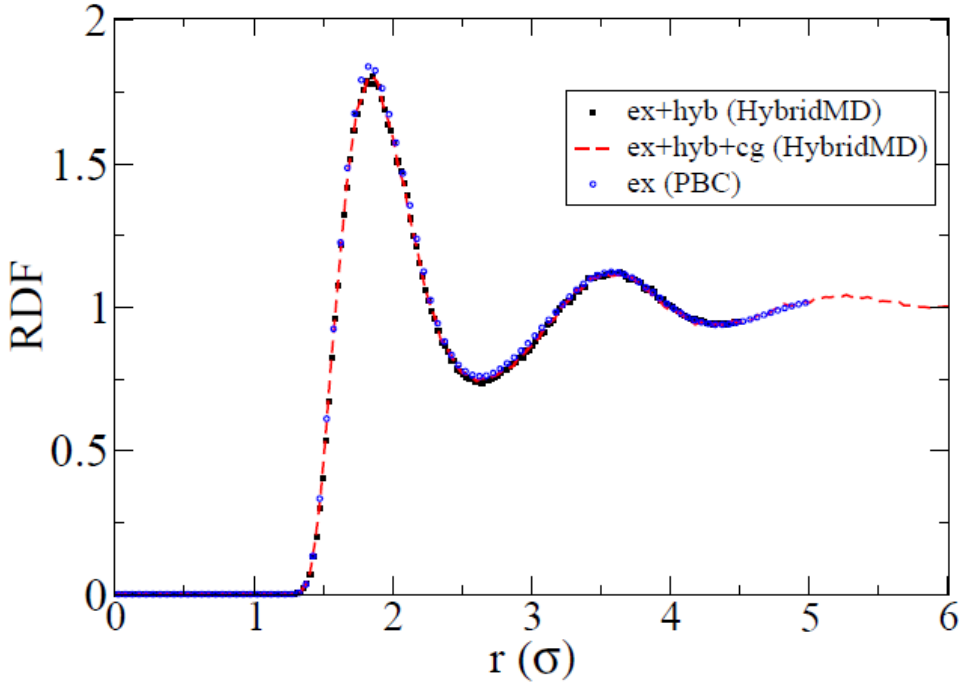
Particle Insertion into Buffer SIMPLE

AdResS-HybridMD: Setups

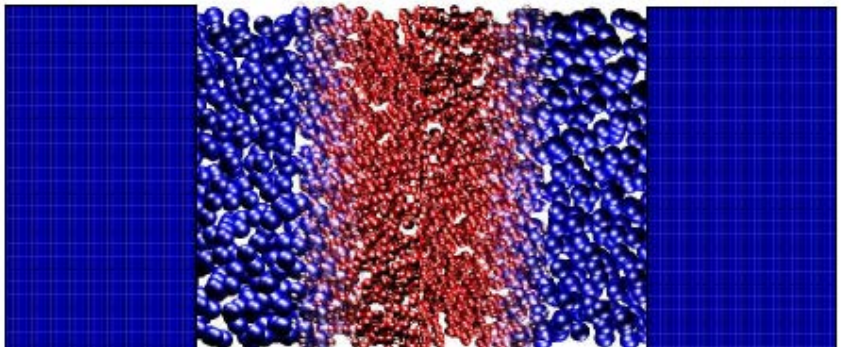


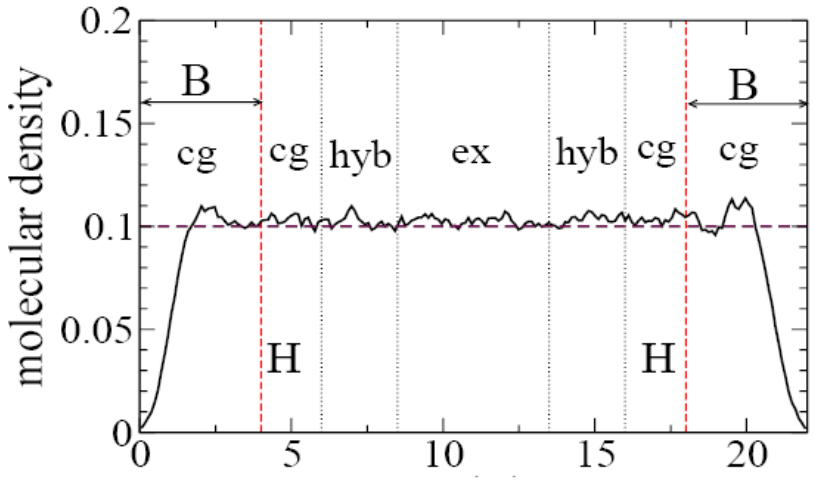
AdResS-HybridMD combined



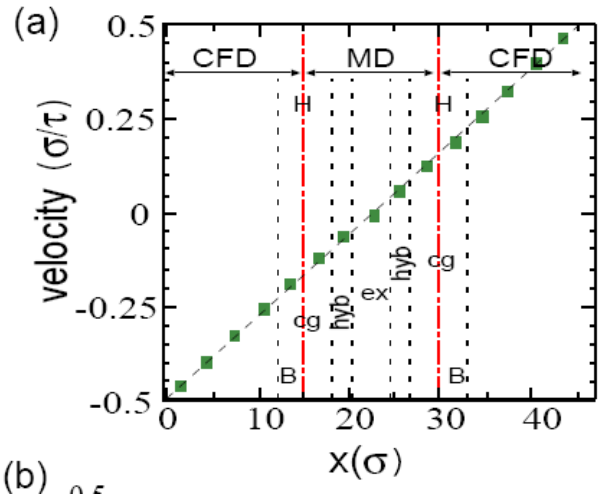


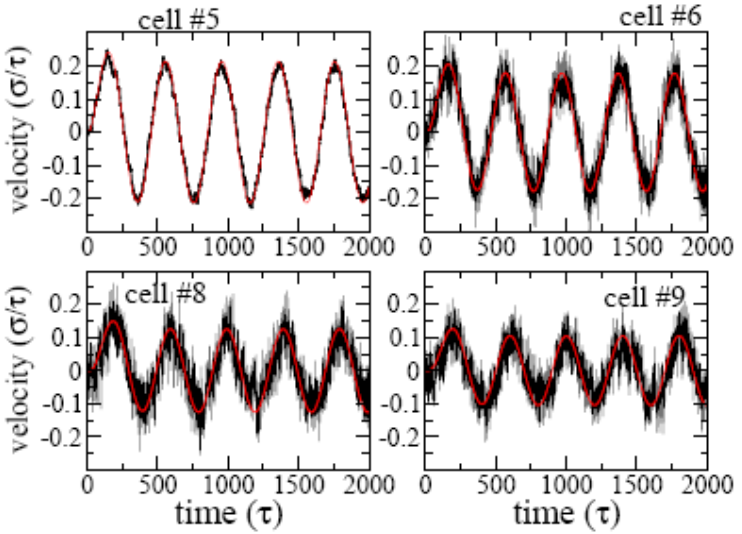
Concurrent Triple-Scale Simulation of Molecular Liquids





Simple shear





Oscillatory shear
(------ exact solution)

Conclusion / Challenges

- **Dual-Triple… Scale Simulations/Theory**
  - **Adaptive** quantum⇔force field⇔coarse grained …
  - **Grand Canonical** i.e. salt etc
  - **Thermodynamic Force/ compenstion scheme:** couple rather different systems
  - **H-AdResS:** adaptive Monte Carlo possible
- **Nonbonded Interactions: NEMD, Structure Formation, Morphology…**
- **Conformations ⇔ Electronic Properties**
- **Structure Formation, Aggregation**
- **Online Experiments:**
  - **Nanoscale Experiments, long Times**