Quantifying water density fluctuations

B. Shadrack Jabes

Motivation:

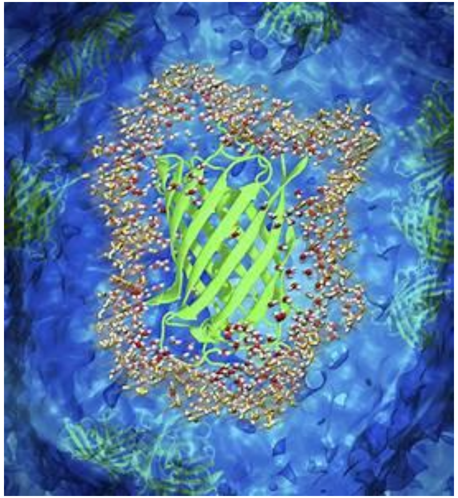
Local water density fluctuations different for surface-water's / bulk-water's

Binding processes involve disrupting the surface-water interaction

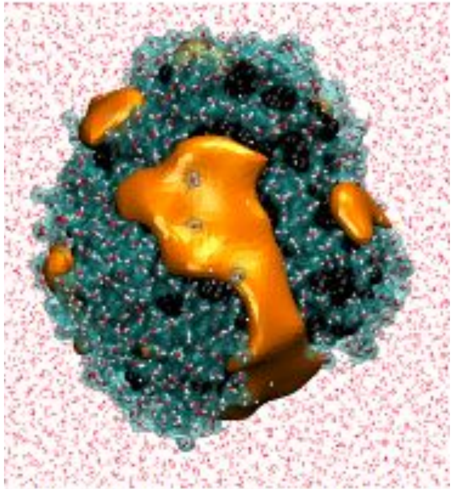
surface-water interactions influence thermodynamics, kinetics of surface interactions, stability and phase behavior of surfaces in water

Characterize - disrupting the surface-water interactions

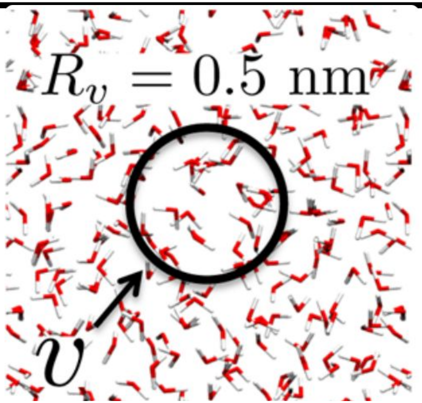
J. Am. Chem. Soc. **139**(3), 1098–1105 (2017).



Identifying interfacial water sites



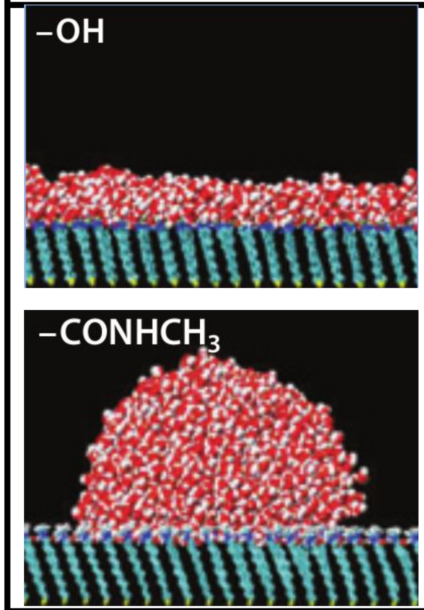
Bulk water



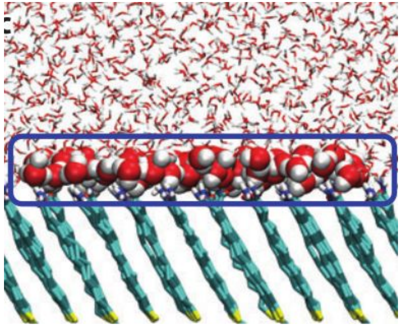
Using MD employed with unfavourable potential

$$H_\Phi = H_0 + \text{unfavorable potential}$$

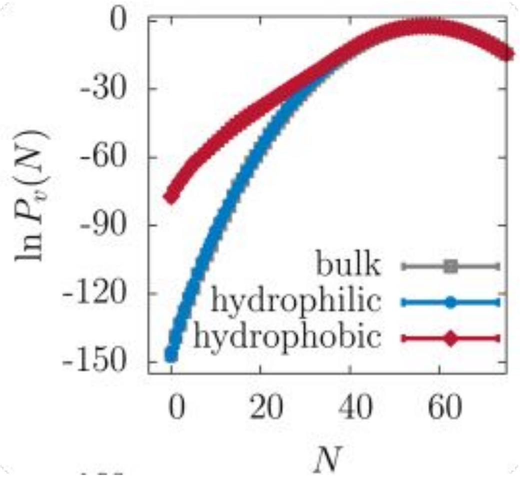
$$\beta F_v(\tilde{N}) \equiv -\ln P_v(\tilde{N})$$



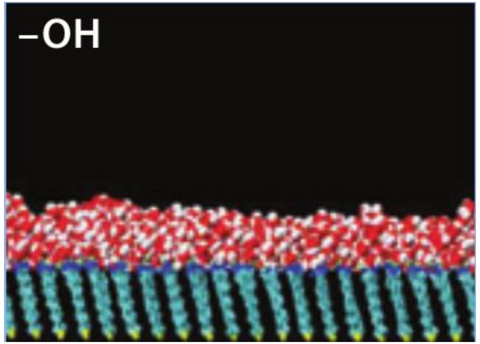
Interfacial water

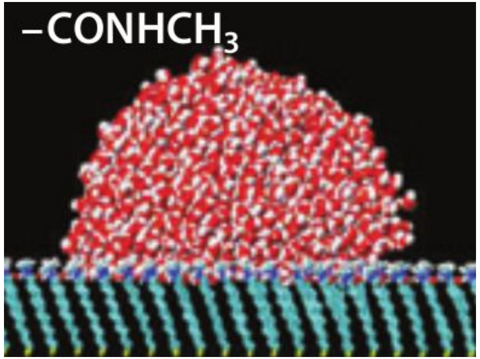


J. Phys. Chem. B 2010, 114, 1632–1637



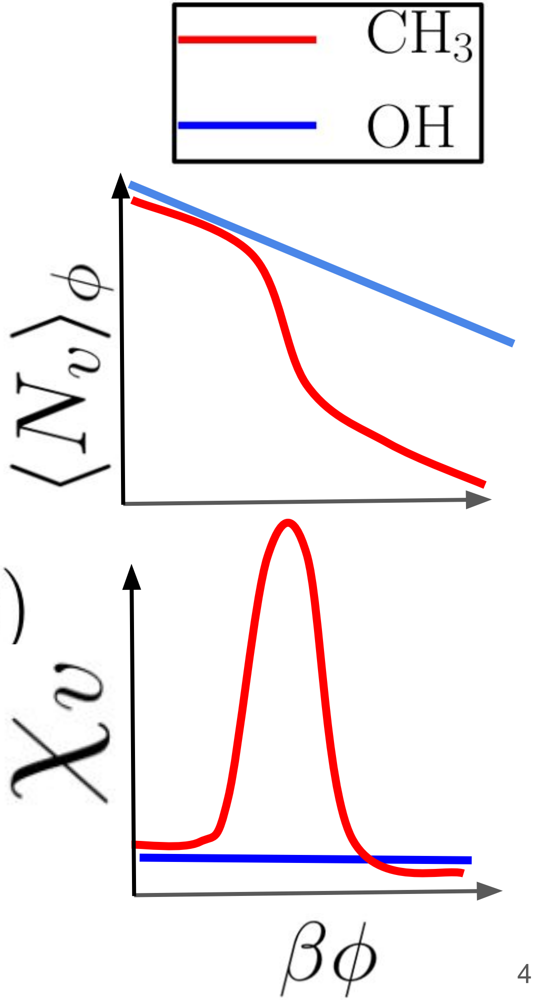
Disrupting the surface-water interactions





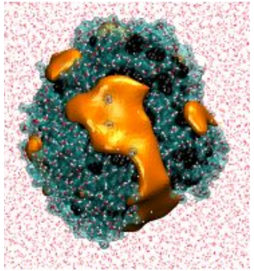
$$\mathcal{H}_\phi = \mathcal{H}_0 + \phi N_v$$

$$\chi_v \equiv -\partial \langle N_v \rangle_\phi / \partial(\beta\phi)$$



Annu. Rev. Chem. Biomol. Eng. 2011. 2:147–71

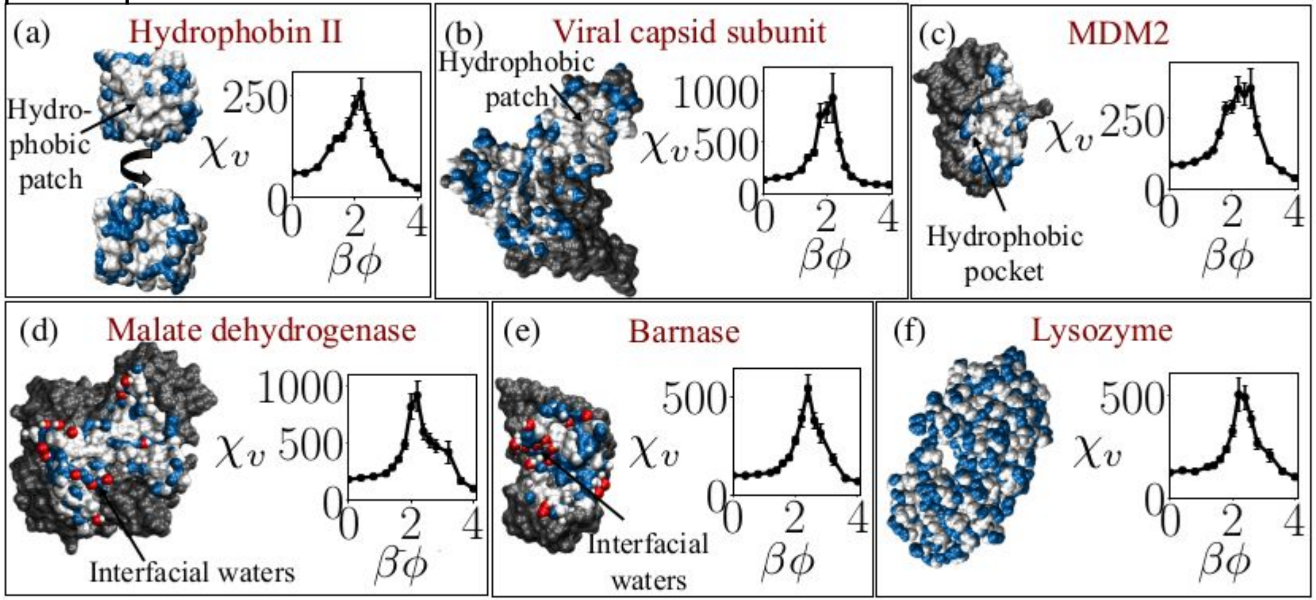
Protein Hydration Waters Are Susceptible to Unfavorable Perturbations



well-defined hydrophobic patches

amphiphilic

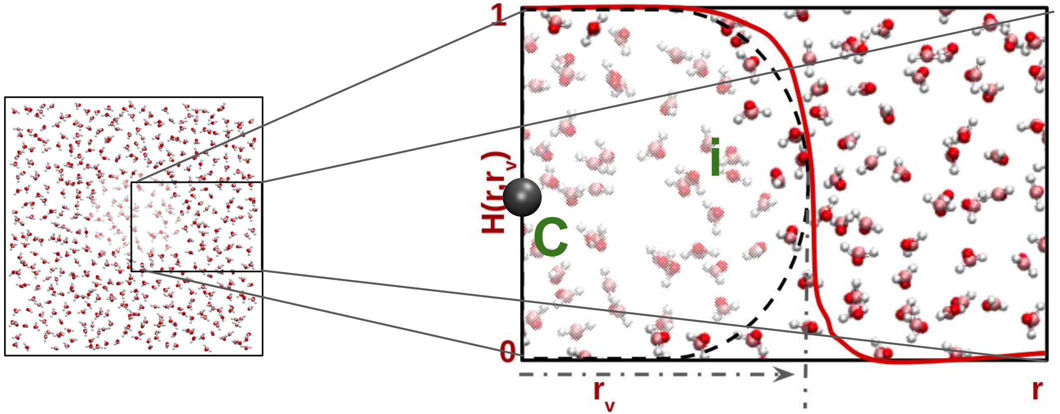
super-hydrophilic



J. Am. Chem. Soc., 2019 **DOI:** 10.1021/jacs.8b11448

INDUS: Static observation volume

$$\mathcal{H}(r, r_\nu) = \begin{cases} 1, & \text{if } r \le r_\nu \\ 0, & \text{otherwise} \end{cases}.$$



Mapping N_v to positions

$$\tilde{N}_\nu = \sum_{\mathrm{i}=1}^{N} h(|\vec{r}_{\mathrm{ic}}|, r_\nu),$$

$$\vec{r}_{\mathrm{ic}} = \vec{r}_{\mathrm{i}} - \vec{r}_{\mathrm{c}}.$$

Force

$$U_{\mathrm{linear}} = \phi \tilde{N}_\nu,$$

$$= -\frac{\partial h(|\vec{r}_{\mathrm{ic}}|, r_\nu)}{\partial |\vec{r}_{\mathrm{ic}}|} \frac{\partial |\vec{r}_{\mathrm{ic}}|}{\partial \vec{r}_{\mathrm{i}}} = -\frac{\partial h(|\vec{r}_{\mathrm{ic}}|, r_\nu)}{\partial |\vec{r}_{\mathrm{ic}}|} \hat{r}_{\mathrm{ic}},$$

Average particle fluctuations control the direction of force

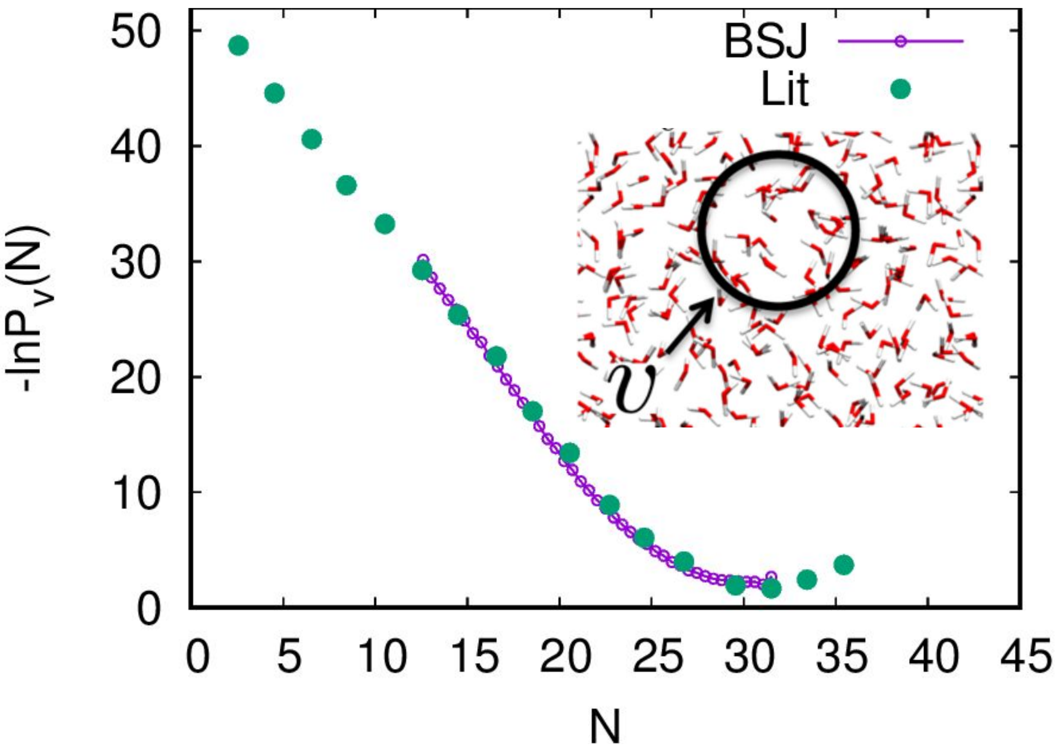
$$U_{\mathrm{Harmonic}} = k \left(\tilde{N}_\nu - \tilde{N}_{\nu,\mathrm{fix}} \right)^2,$$

$$= -k \left(\tilde{N}_\nu - \tilde{N}_{\nu,\mathrm{fix}} \right) \frac{\partial h(|\vec{r}_{\mathrm{ic}}|, r_\nu)}{\partial |\vec{r}_{\mathrm{ic}}|} \frac{\partial |\vec{r}_{\mathrm{ic}}|}{\partial \vec{r}_{\mathrm{i}}} = -k \left(\tilde{N}_\nu - \tilde{N}_{\nu,\mathrm{fix}} \right) \frac{\partial h(|\vec{r}_{\mathrm{ic}}|, r_\nu)}{\partial |\vec{r}_{\mathrm{ic}}|} \hat{r}_{\mathrm{ic}},$$

INDUS : indirect umbrella sampling

Test of the method

The free energy landscape for the coarse-grained number of waters, Ñ , in a small probe volume in bulk water at T = 300 K and P = 1 bar. The probe volume, v , is a sphere of radius r = 0.6 nm in a box of about 4, 000 SPC/E water molecules.



J. Phys. Chem. B 2010, 114, 1632–1637

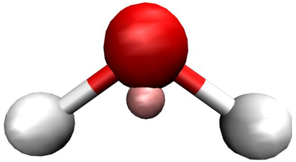
INDUS: Dynamic observation volume

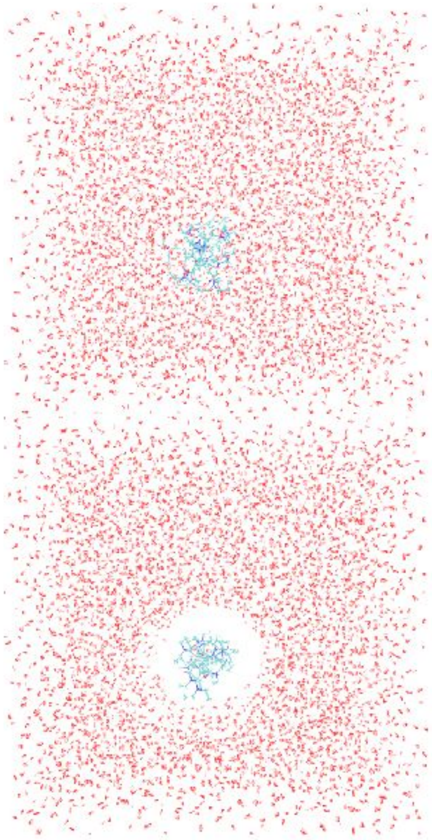
$$h(r, r_\nu) = \frac{1}{2}\left(\tanh\frac{r}{b} - \tanh\frac{r - r_\nu}{b}\right)$$

$$U_{\text{linear}} = \phi \tilde{N}_\nu,$$

Force $$= -\frac{\partial h(|\vec{r}_{\text{ic}}|, r_\nu)}{\partial |\vec{r}_{\text{ic}}|}\frac{\partial |\vec{r}_{\text{ic}}|}{\partial \vec{r}_{\text{i}}} = -\frac{\partial h(|\vec{r}_{\text{ic}}|, r_\nu)}{\partial |\vec{r}_{\text{ic}}|}\hat{r}_{\text{ic}},$$

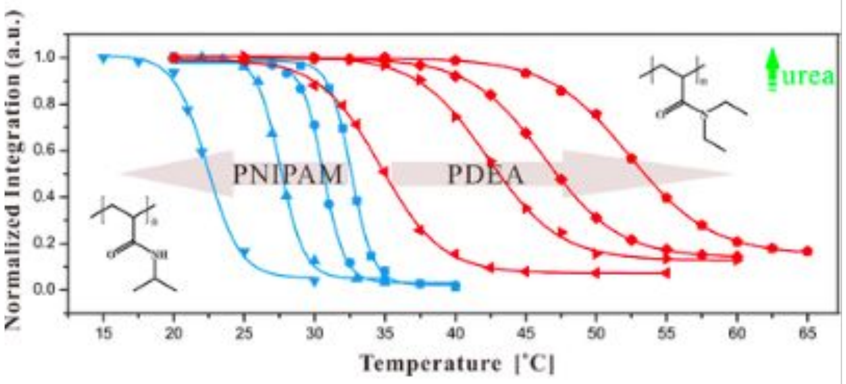
Hydration shell: small sub volume region defined from the center of the heavy atoms to the first solvation layer of water
Virtual sites: COM of water





To do

- NMR spectroscopy,
- control LCST by urea concentration - water density fluctuations



Macromolecules 2016, 49, 1, 234-243

Summary

Water density fluctuations are an important statistical mechanical observable- related to hydrophobic hydration and hydrophobic interactions

Measure of hydrophobicity: local density fluctuations near solid water surface

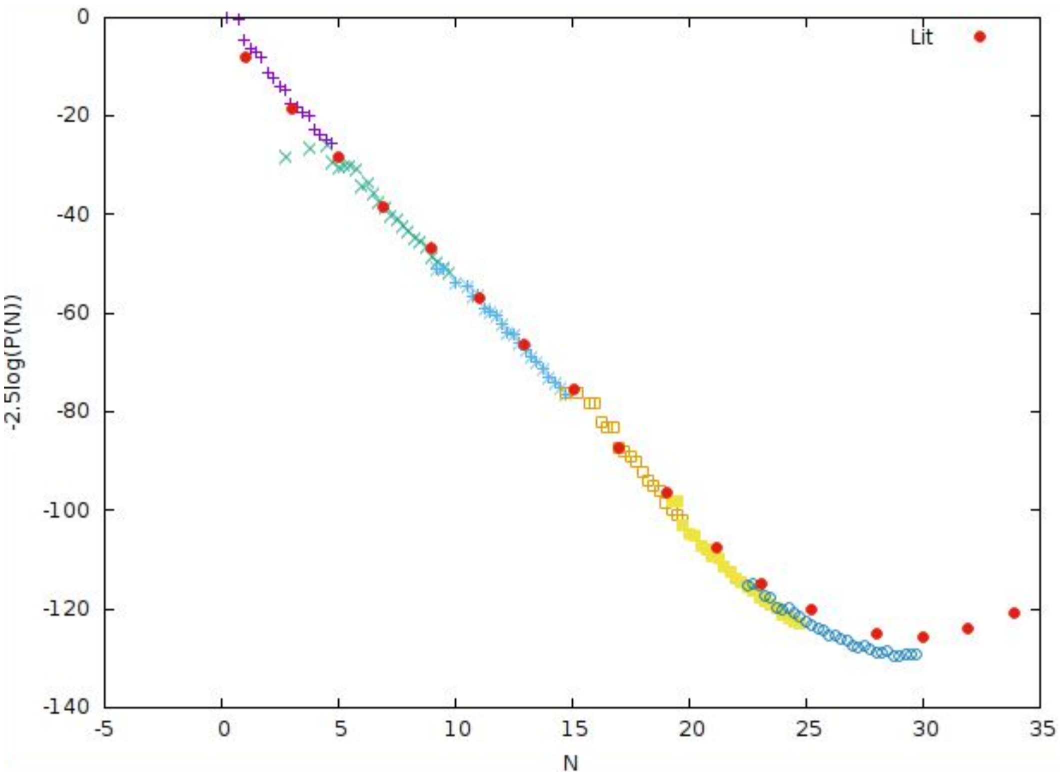
Quantified: calculating the probability of observing N waters in a probe volume of interest

Backup slides

WHAM - Weighted histogram analysis method

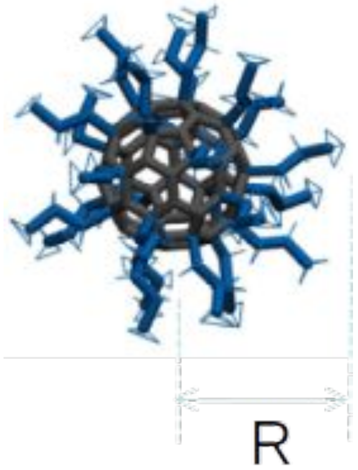
Step5: Do this in each biased simulation and you plot the free energy obtained in each of the biased simulation separately.

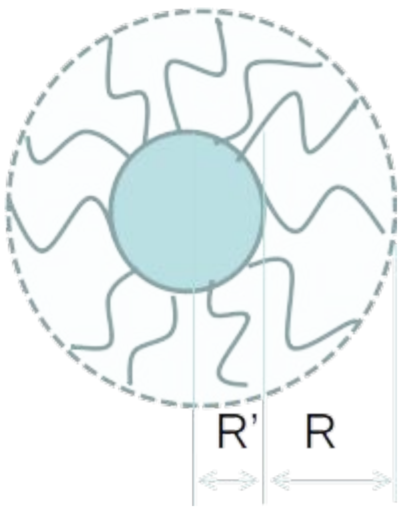
Step6: Stitching - Now add a weight to the free energy in such a way the final free energy would overlap with each other.

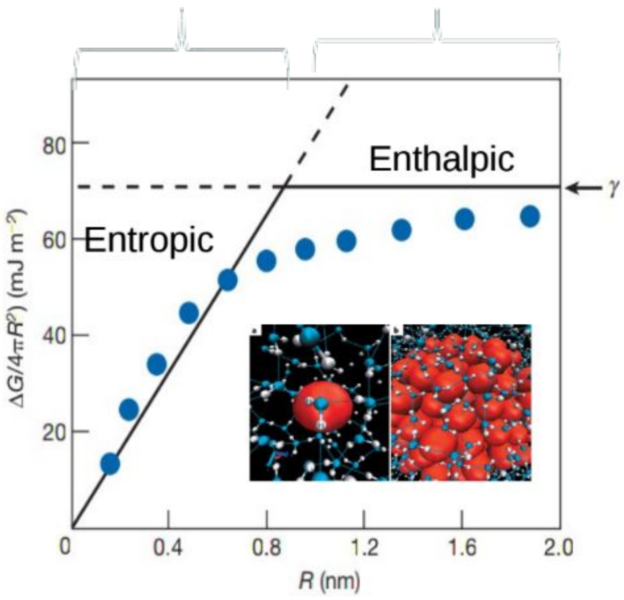


Characterizing **length**, hydrophobicity & local density

Bigger particle regime of hydrophobic hydration

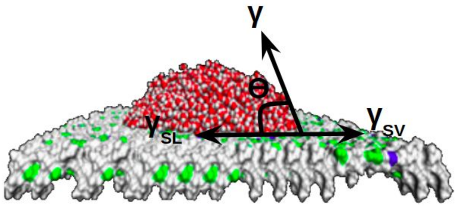






Characterizing length, **hydrophobicity** & local

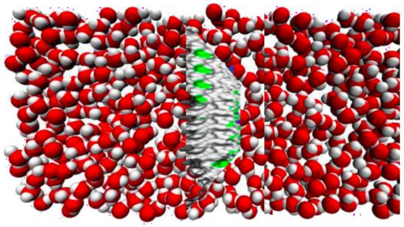
Macroscopic wetting thermodynamics



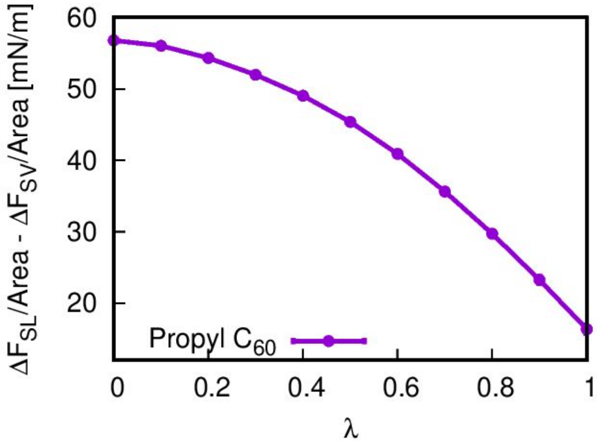
$\gamma_{SL} - \gamma_{SV} = -\gamma \cos\Theta$

≡

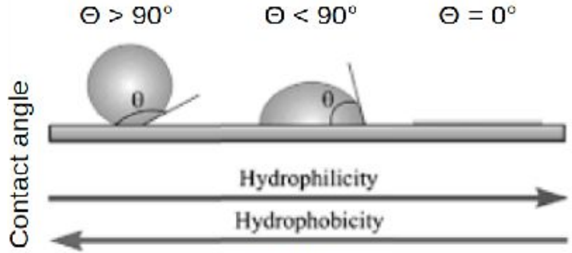
Thermodynamic Integration route



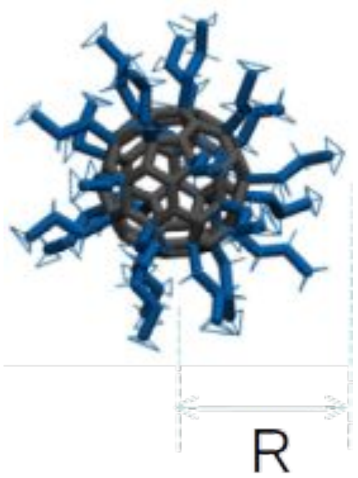
$\Delta F_{SL}/Area_s - \Delta F_{SV}/Area_s = -\gamma \cos\Theta$

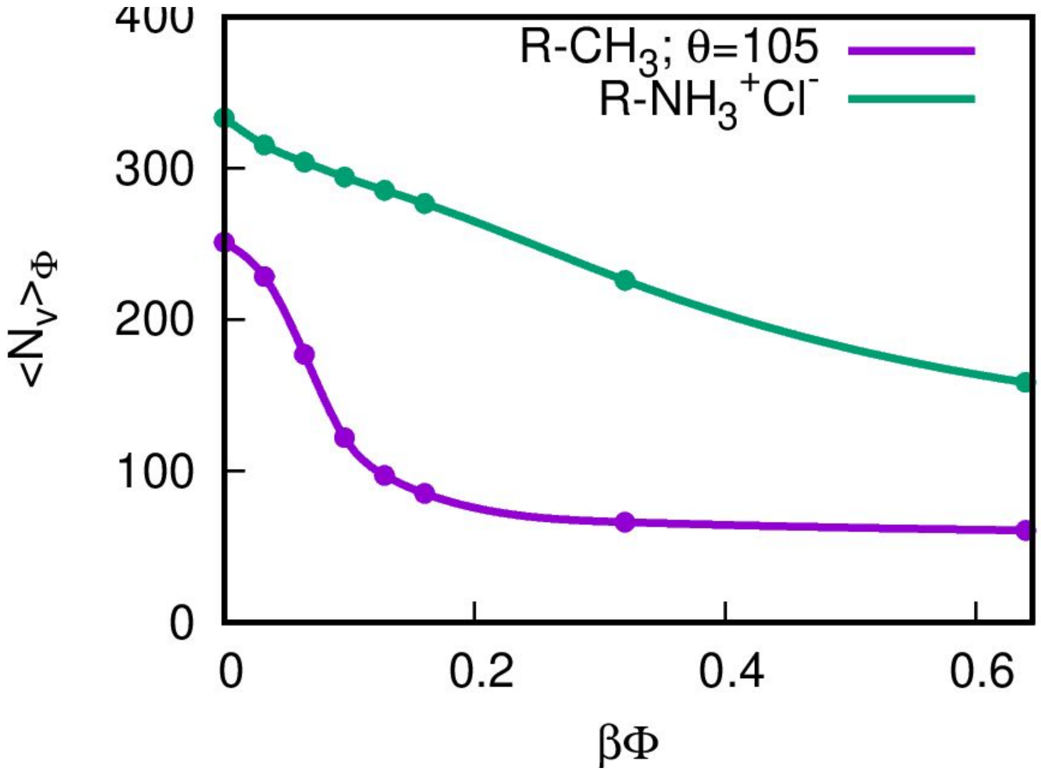


Propylated	$\gamma_{sl} - \gamma_{sv}$	γ_{lv}	$\Theta^{\circ}_{This work}$	Θ°_{Lit}
C_{60}	16.3	63.5	104.9	
Graphane	21.1	63.5	109.4	110^{3}

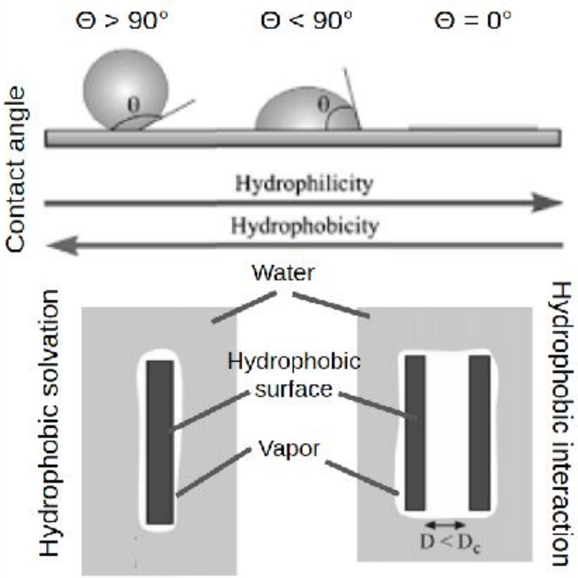


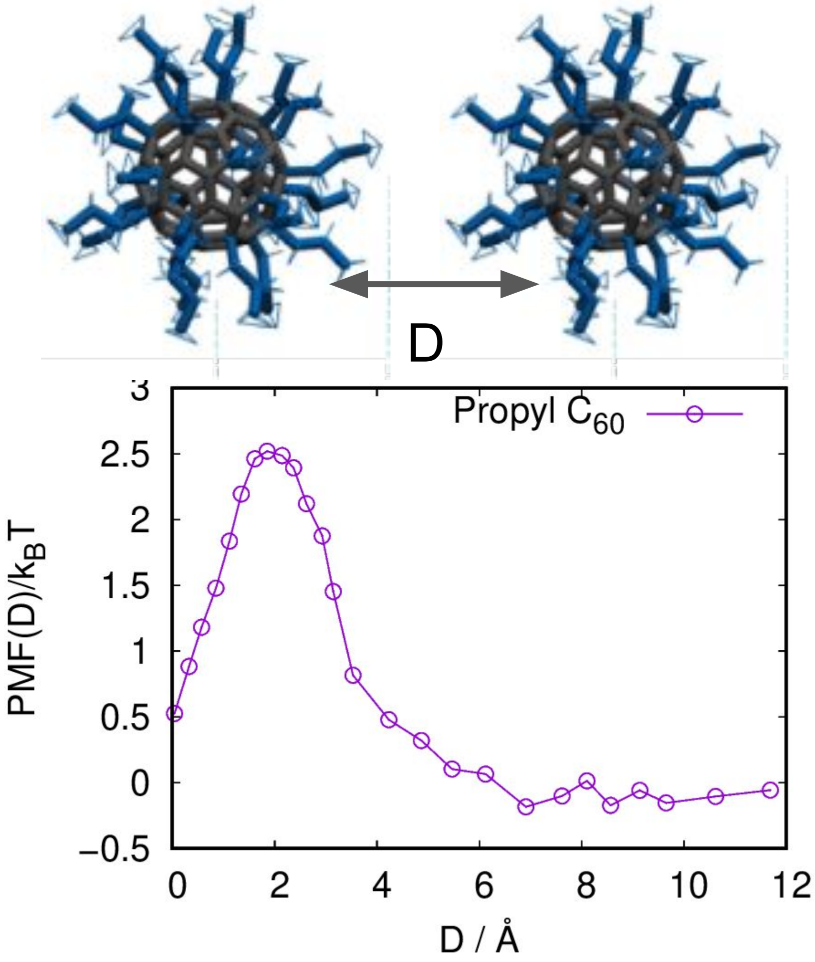
Characterizing length, hydrophobicity & **local density**



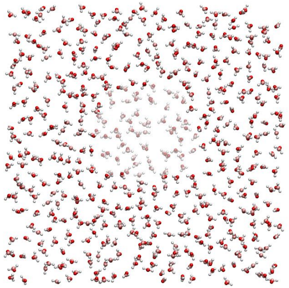


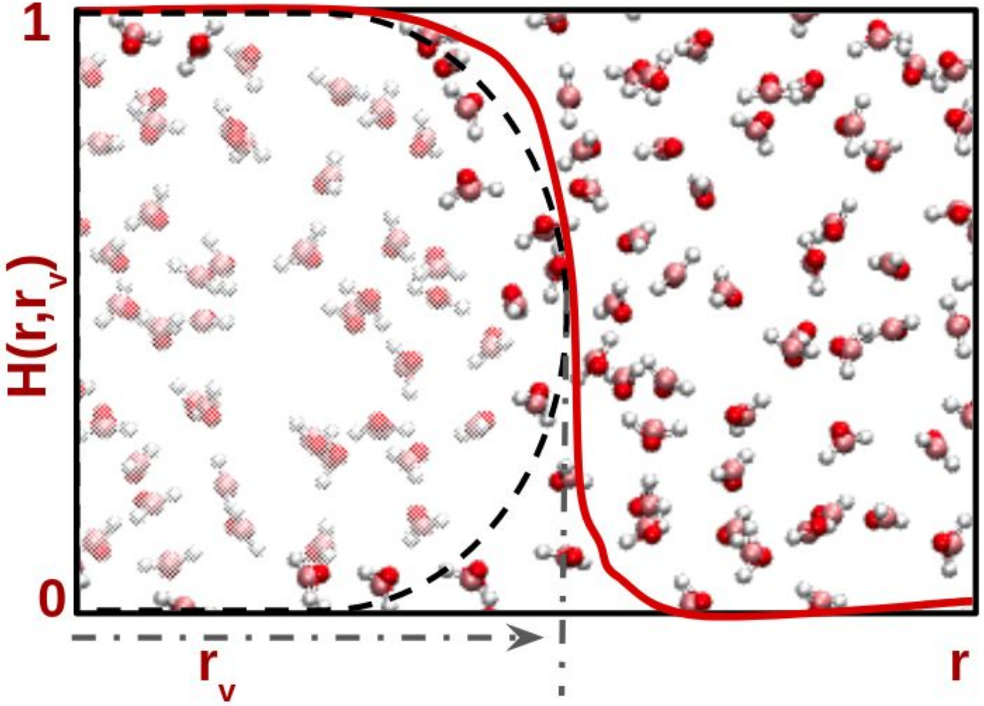
Hydrophobic interaction



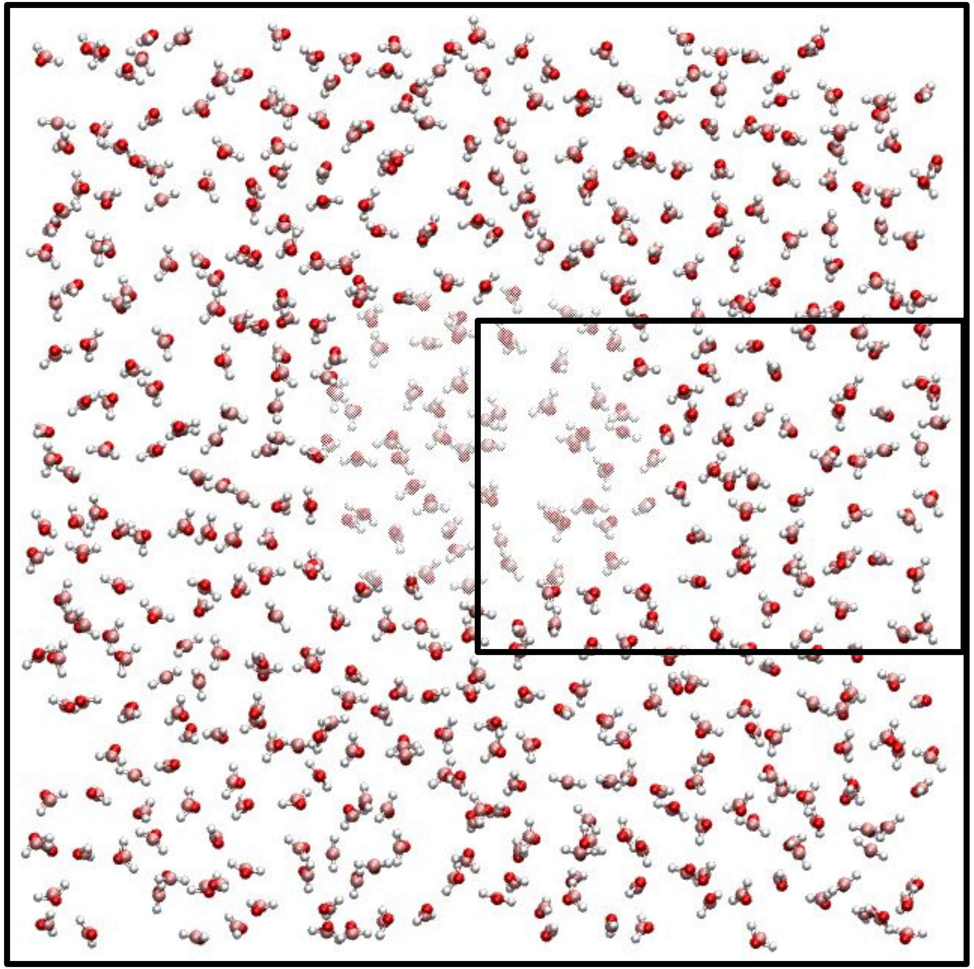


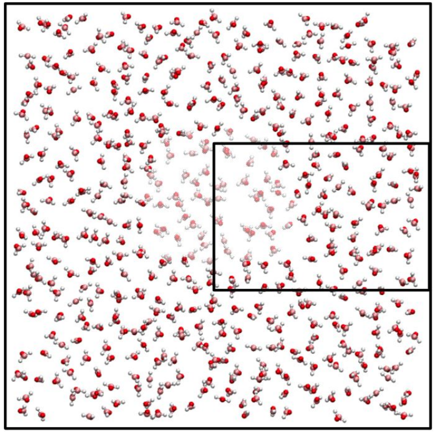
*J. Phys. Chem. Lett.*2016, 7, 16, 3158-3163

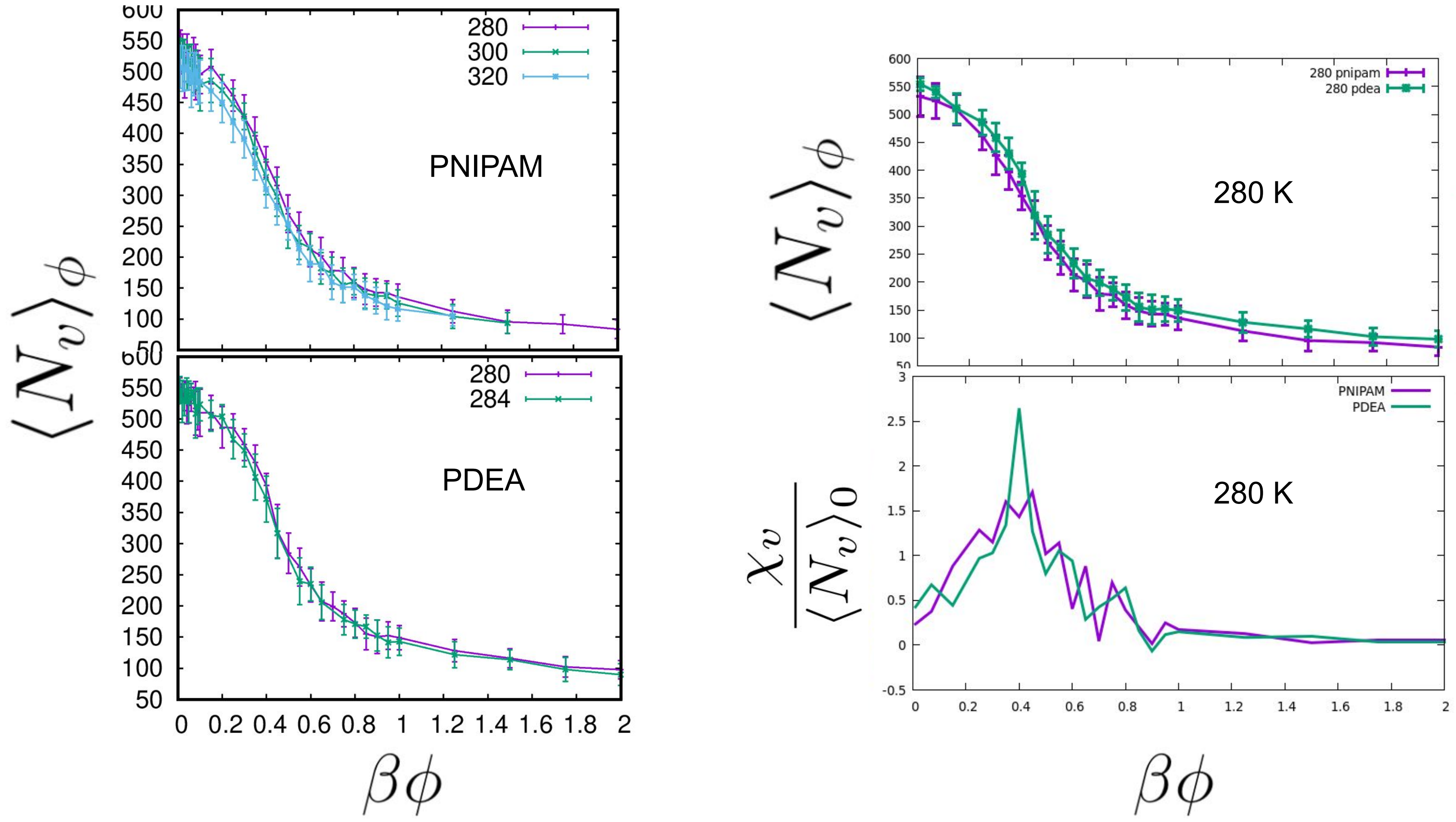




1
0
H(r,r_v)
r_v
r







280
300
320
PNIPAM
280
284
PDEA
$\langle N_v \rangle_\phi$
$\beta\phi$
280 pnipam
280 pdea
280 K
PNIPAM
PDEA
280 K
$\frac{\chi_v}{\langle N_v \rangle_0}$
$\beta\phi$

Test of the method

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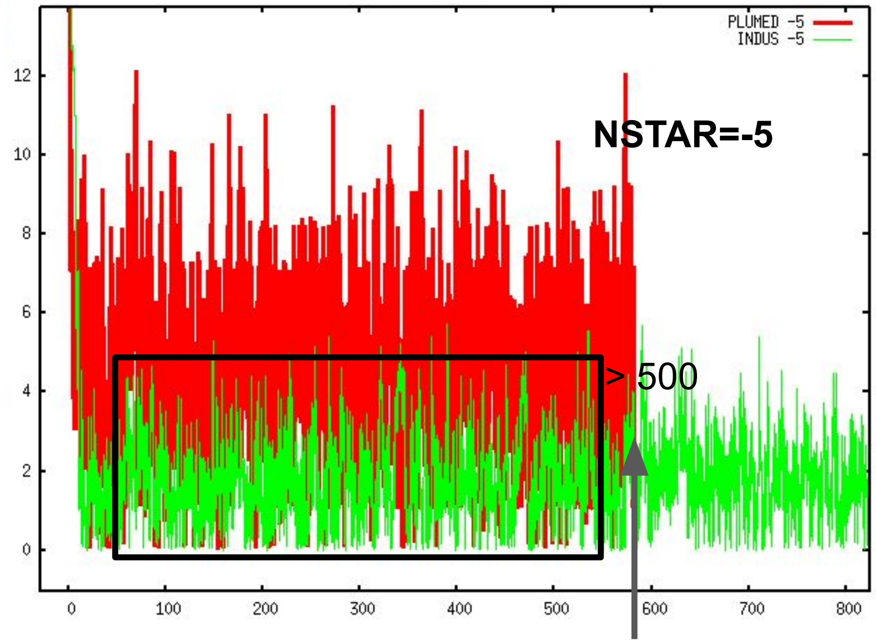
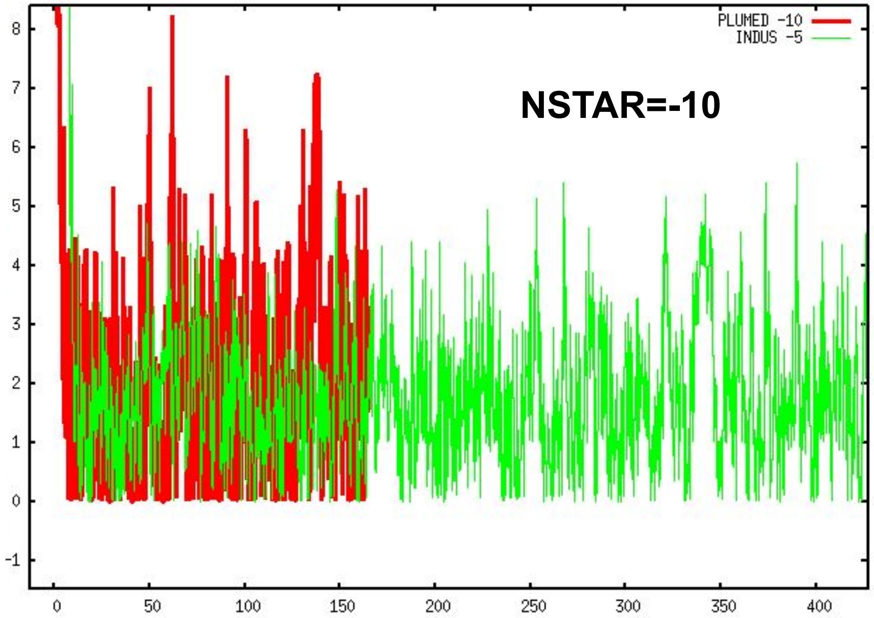
J. Phys. Chem. B 2010, 114, 1632–1637

Plumed: GPU, N_biasing

Dynamic Observation volume

B. Shadrack Jabes & Swaminath





Functional form samples the n range captured by indus

Method: Unfavorable Biasing potential

Linear bias potential

$$U_{\text{linear}} = \phi \tilde{N}_{\nu},$$

Harmonic bias potential

$$U_{\text{Harmonic}} = k\left(\tilde{N}_{\nu} - \tilde{N}_{\nu,\text{fix}}\right)^{2},$$

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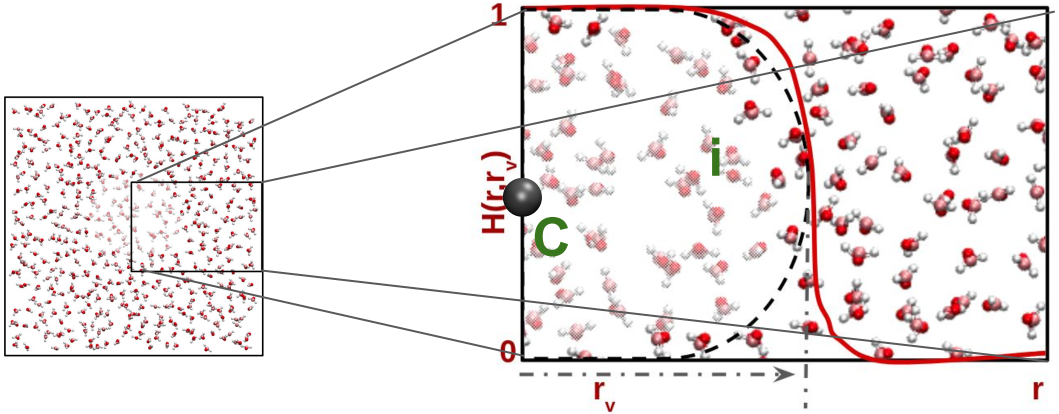

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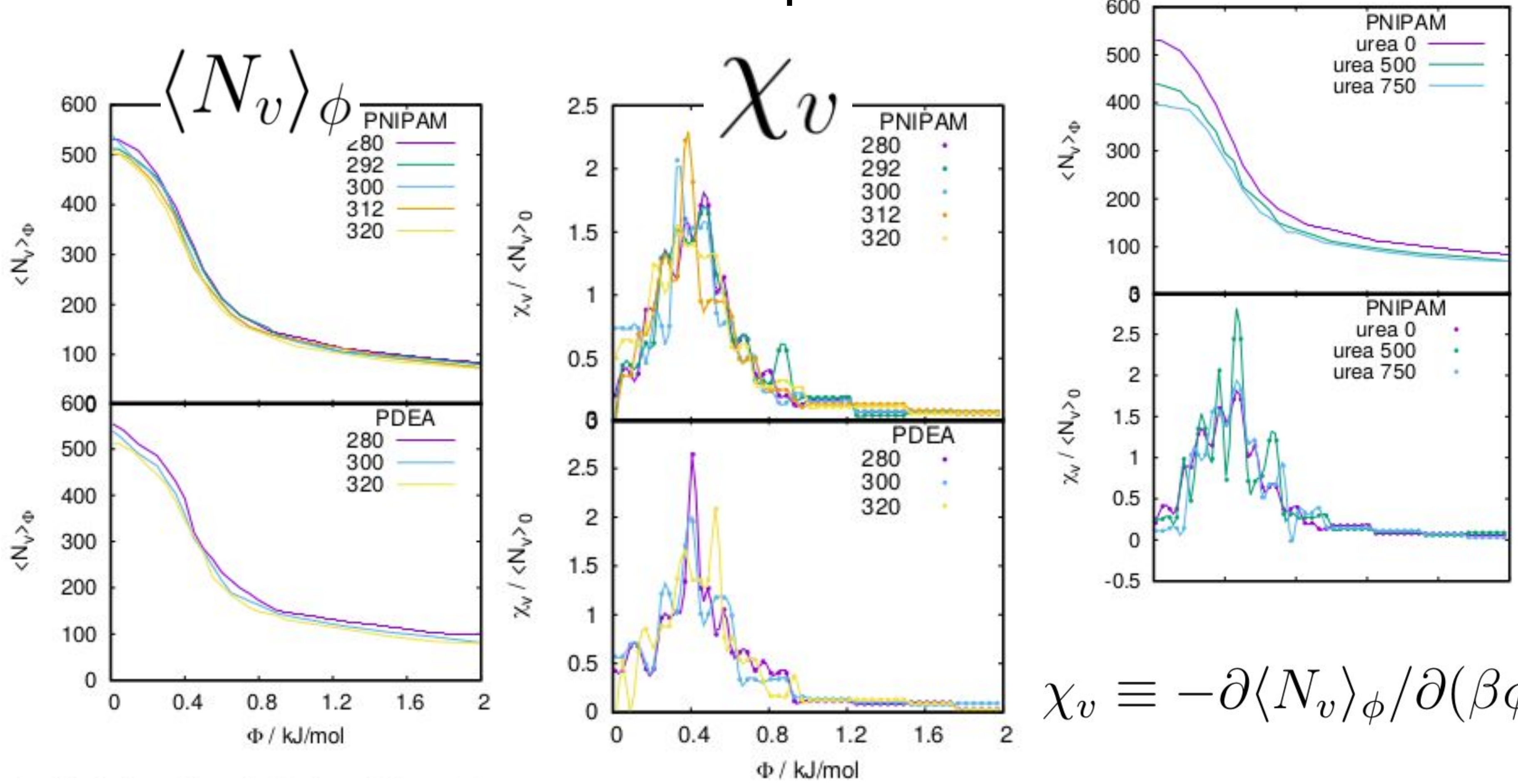
INDUS : indirect umbrella sampling

Linear bias potential



$$\chi_v \equiv -\partial \langle N_v \rangle_\phi / \partial(\beta\phi)$$

Harmonic bias potential

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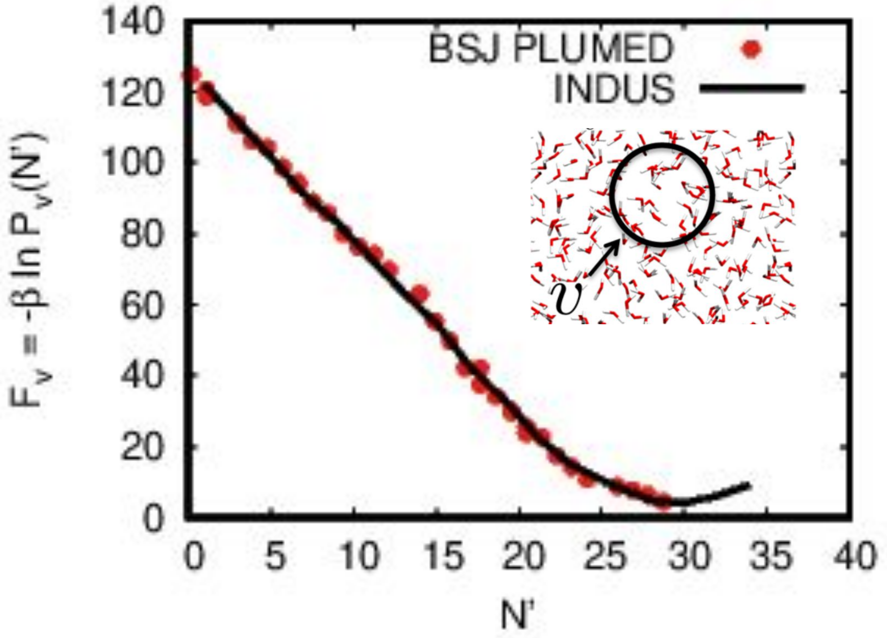
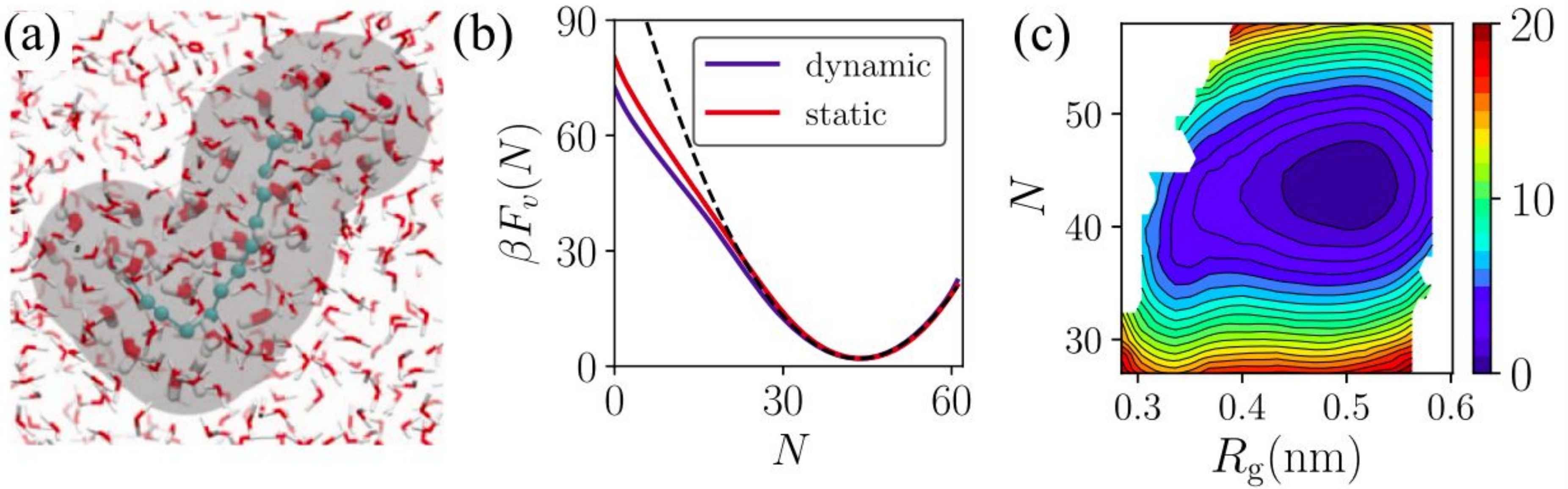


J. Phys. Chem. B 2010, 114, 1632–1637

PLUMED(GPU) 88.566 ns/day, on 1 GPU, 4 MPI threads
PLUMED(CPU) 13.316 ns/day, on 1 CPU, 8 MPI threads

Dynamic bias potential



J. Phys. Chem. B 2019, 123, 1650−1661