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## Density-Dependent Potentials and their Application to Self-Assembly

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Modeling Soft Matter: Linking Length and Time Scales  
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### Outline



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- Self-Assembly
- Development of DDIS potentials
- Application to a Surfactant System

References: Allen and GCR, J.Chem.Phys. 2008, 128, 154115.  
Allen and GCR, J.Chem.Phys. 2009, 130, 034904.  
Allen and GCR, J.Chem.Phys., 2009, 130, 204903.  
Ismail, GCR and Stephanopoulos, J. Chem. Phys. 2003, 118, 4414.  
Ismail, Stephanopoulos and GCR, J. Chem. Phys., 2003, 118, 4424.

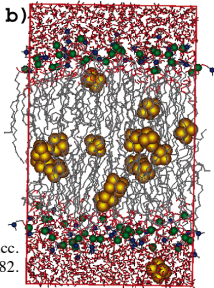
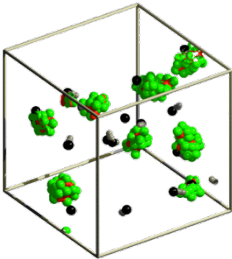
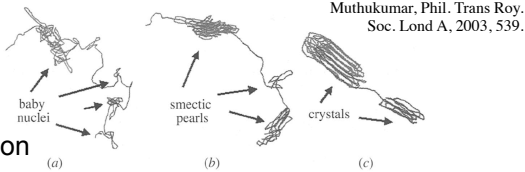
# Self-assembly



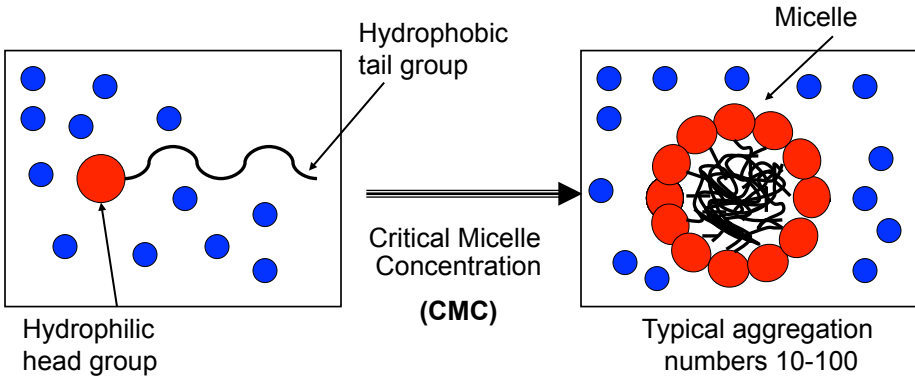
**Self-assembly** refers to the spontaneous and reversible organization of molecular units into ordered structures held together by non-covalent interactions

**Important examples:**

- Crystallization from dilute solution
- Lipid bilayers
- Protein folding
- Micellar phases



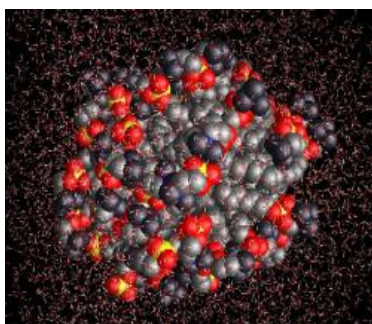
# Surfactant Background



Typically  $\mu\text{M}$  to  $\text{mM}$

$$X_{CMC} = \exp[\beta g_{mic}(n^*)]$$

## A Typical All-Atom Simulation



D. P. Tieleman, D. van der Spoel, H.J.C. Berendsen, J. Phys. Chem. B 104, 2000

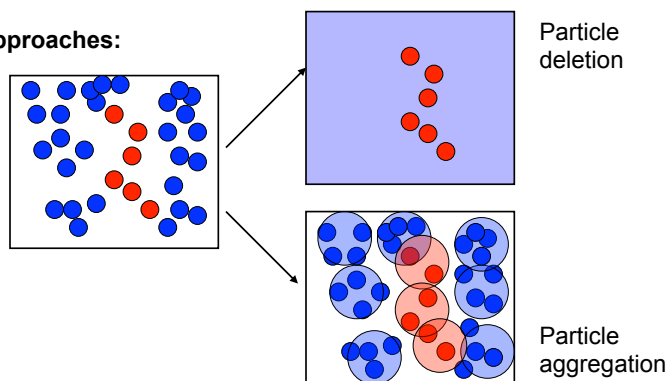
- Simulation size limited to one micelle
- Simulation times limited to <100 ns  
(1  $\mu$ s or longer needed to study aggregation properties)
- Solvent is the main culprit!

## Coarse-graining



**Coarse-graining** refers to the systematic removal of degrees of freedom (i.e. particles) from an all-atom representation in order to speed computation, while “conserving” some property or properties of the underlying all-atom system.

### 2 General Approaches:



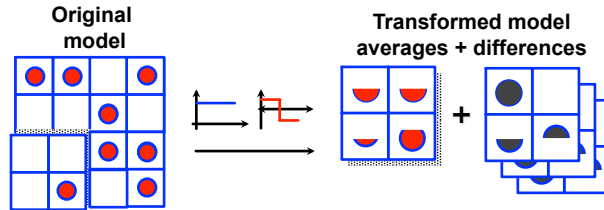
Either approach entails modification of the interaction between remaining particles to represent, in some approximate way, the influence of the lost degrees of freedom. **Information is lost.**

## A "systematic" coarse-graining illustration



- Wavelets are translation-invariant functions with useful properties (orthonormality, localization, completeness) that can be applied recursively to generate means and differences

Ex. Haar wavelet applied to Ising lattice in 2D  
(Ismail, Stephanopoulos and GCR, JCP 2003, 4414 & 4424)



The degrees of freedom ( $u_i$ ) are TRANSFORMED ( $s_i, \delta_i$ ) and DOWNSAMPLED ( $s_{i/2+1}, \delta_{i/2+1}$ ) without loss of detail

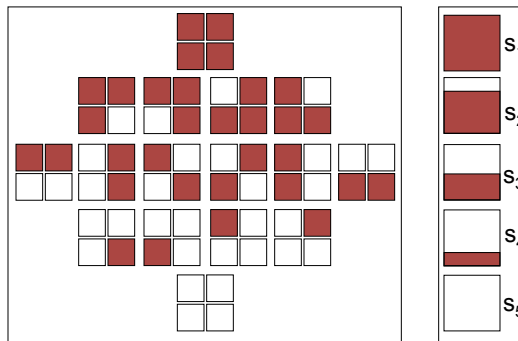
## Systematic Coarse-Graining



Entails keeping only a fraction of the transformed degrees of freedom (e.g. the averages,  $s_i$ ) and approximating the combined effect of the lost degrees of freedom (i.e. the differences,  $\delta_i$ ).

Instead of calculating the complete partition function:

$$Z = \sum_{u_i \in \Omega} \exp(-\beta H(u_i))$$



$$Z' = \sum_{s_i \in \Omega'} w(s_i) \exp(-\beta H'(s_i))$$

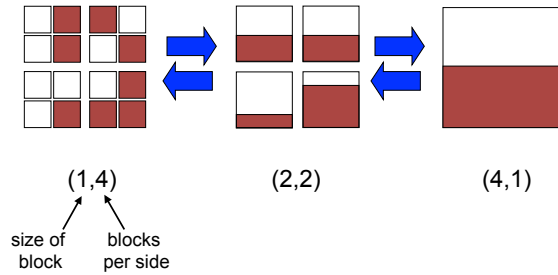
"Weight" of each configuration determined by counting or sampling (a "degeneracy")

... we approximate as a sum over partitions of configuration space.

## Multi-resolution

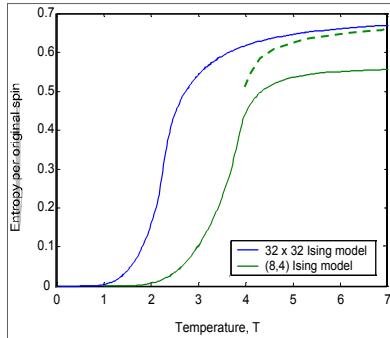


Wavelet transformation can be applied recursively.  
 Invocation of differencing functions permits reverse mapping.

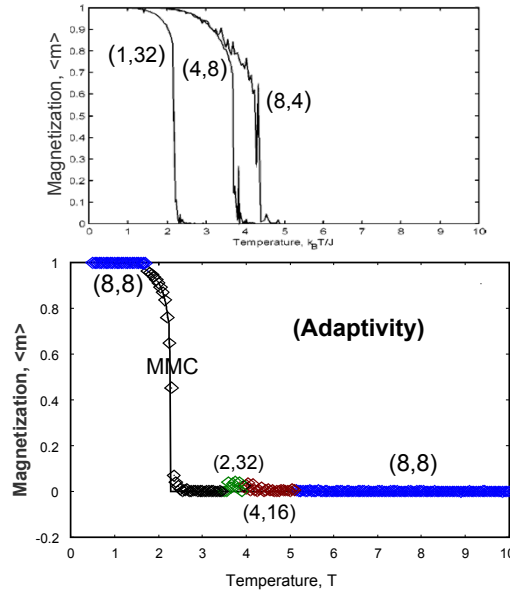


For large blocks,  $w(s)$  can be estimated through sampling:  
 → Wavelet Accelerated Monte Carlo

## Entropy error at intermediate temperatures



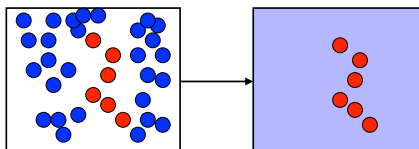
- Sources of error:
- Loss of distinct states at intermediate temperature (and subsequent use of thermodynamic integration)
  - Sampling approximation to weighting function  $w(\mathbf{s})$



## Density-dependent implicit solvent potential (DDIS)



- Solute density becomes a proxy for lost solvent degrees of freedom



$$\begin{aligned}
 Z &= \int_V dr_{\text{solv}}^{N-n} \int_V dr_S^n \exp[-\beta V(r_{\text{solv}}^{N-n}, r_S^n)] \\
 &= C_{\text{solv}}(\rho_S) \int_V dr_S^n \exp[-\beta V^{\text{eff}}(r_S^n, \rho_S)] \\
 &= \int_V dr_S^n \exp \left[ -\beta \sum_{i=1}^n \left( \underbrace{\mu(\rho_{S,i})}_{\text{1-body term}} + \sum_{j=1}^n \underbrace{V^{\text{eff}}(r_{S,ij}, \rho_{S,i})}_{\text{2-body term}} \right) \right]
 \end{aligned}$$

ensures reproduction of thermodynamic free energy (in the mean)

ensures reproduction of structure (rdf), by Henderson's Theorem

*Henderson, Phys. Lett. 1974, 197*

## Global vs. Local Density Dependence



- Global Density Dependent Potential

$$\rho_S = n / V$$

$$E_i(\rho_S) = \mu_i(\rho_S) + \frac{1}{2} \sum_{j \neq i}^n V^{\text{EFF}}(r_{ij}, \rho_S)$$

- Fitting is "easy"
- Some pathological behavior
- Not sensitive to inhomogeneities

- Local Density Dependent Potential

$$\rho_{S,i} = \sum_{j \neq i}^n \int_0^{r_D} \delta(r - r_{ij}) w(r) r^2 dr / \int_0^{r_D} w(r) r^2 dr$$

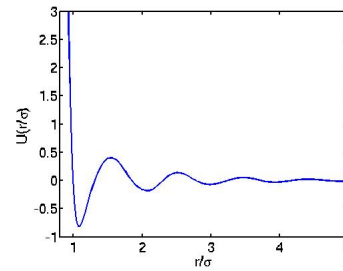
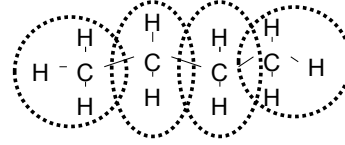
$$E_i(\rho_{S,i}) = \mu_i(\rho_{S,i}) + \frac{1}{2} \sum_j V^{\text{EFF}}(r_{ij}, \rho_{S,i})$$

- Global solution as initial guess, optimization converges readily
- Finite in range
- **More transferable?**

## Implementation



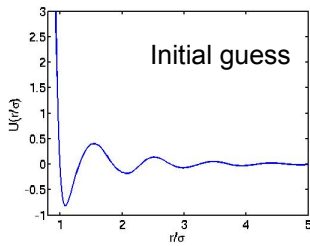
- Run short, explicit particle simulations for simple (e.g. monomeric) systems to collect training data for the range of particle densities
- Remove or assign explicit particles to CG particles
- Select a *free energy metric* ( $\mu^{ex}(\rho_S)$ ) and a *local structure function* ( $g(r, \rho_S)$ ), both to be conserved during coarse-graining
- Numerically fit  $\mu(\rho_S)$  and  $V^{eff}(r, \rho_S)$  to reproduce targets



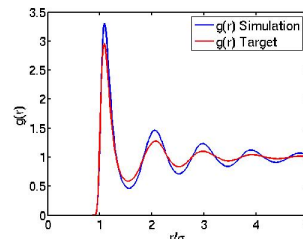
## $E(r, \rho_S)$ Solution Procedure



Schommers, *Phys. Rev. A* **28**,3559 (1983)



MD sim

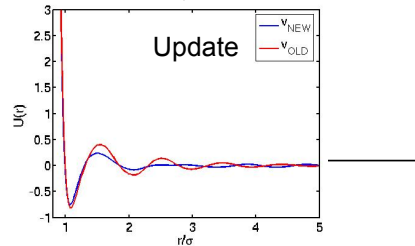


$$V_k^{eff}(r, \rho_S) = V_{k-1}^{eff}(r, \rho_S) - kT \log \left( \frac{g_{target}(r, \rho_S)}{g_k(r, \rho_S)} \right)$$

$$\Delta\mu(\rho_S) + \rho_S \frac{\partial \Delta\mu(\rho_S)}{\partial \rho_S} = \mu_{target}^{ex}(\rho_S) - \mu_{k-1}^{ex}(\rho_S)$$

$$\Delta\mu = \mu_k - \mu_{k-1}$$

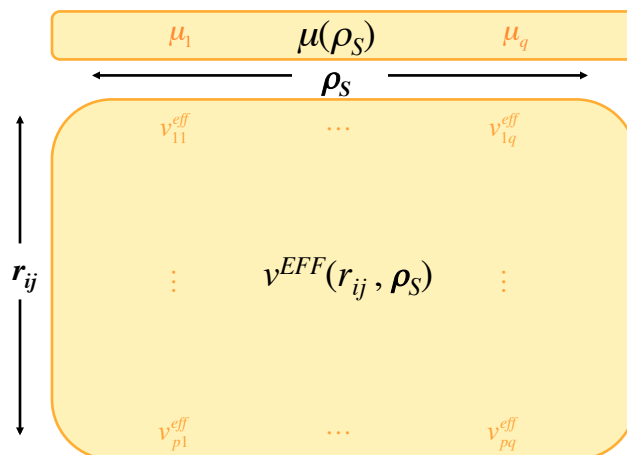
Iterate to convergence



## Structure of the DDIS Potential



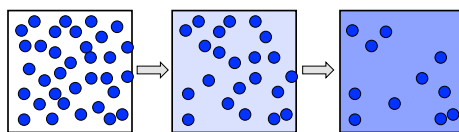
A piecewise linear potential with 1- and 2-body contributions



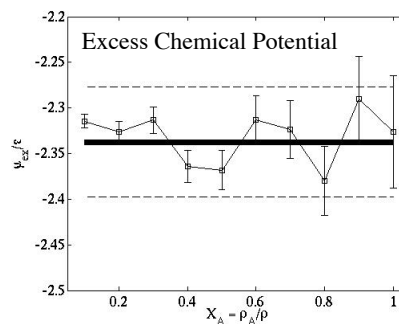
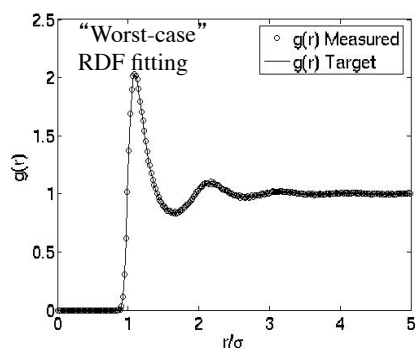
## Testing the DDIS Approach (1)



System 1: A homogeneous system of Lennard-Jonesium comprising explicit solute A within an implicit solvent Z identical to A, at various  $X_A = \rho_A / \rho$



System Specs:  
 $\epsilon_A = 1, \sigma_A = 1; \epsilon_Z = 1, \sigma_Z = 1$   
 $T^* = kT/\epsilon_A = 1.35;$   
 $\rho^* = \rho \sigma_A^3 = 0.55$



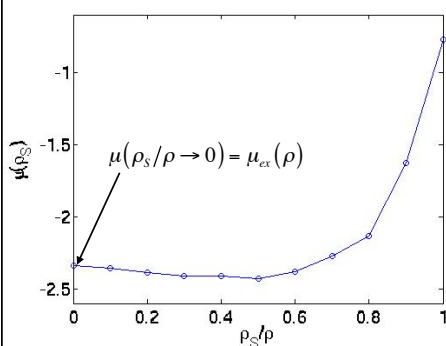
Allen and GCR, J. Chem. Phys **128** (2008), 154115.



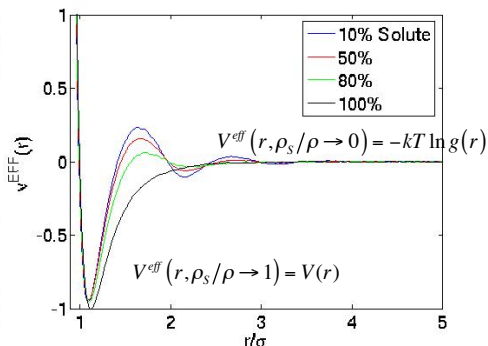
## Results for fitted DDIS Potentials



### One-Body Potential



### Two-Body Potential

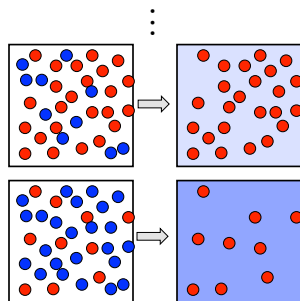


State point sensitivity: up to 10% variation in  $T^*$  or  $\rho^*$  can be sustained with <1% error in either mean particle coordination number or mean particle energy

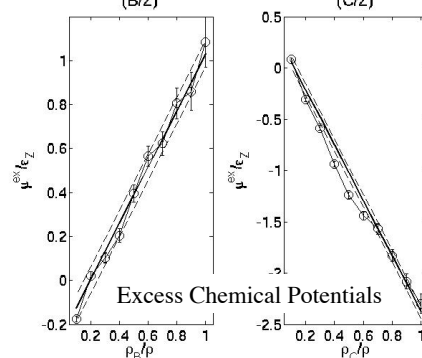
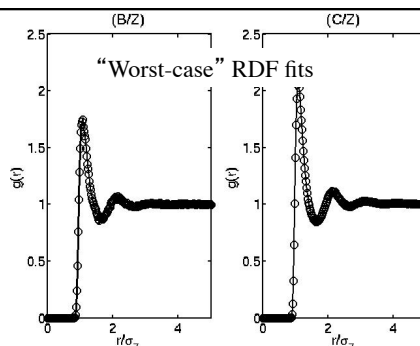
## Fitting Results for Dissimilar Particles (2)

System 2: LJ mixtures comprising explicit solute B (or C) within an implicit solvent Z identical to A, at various  $X_B = \rho_B/\rho$

B = Solvo-philic } ●  
 C = Solvo-phobic } ●  
 A, Z = Solvent } ●



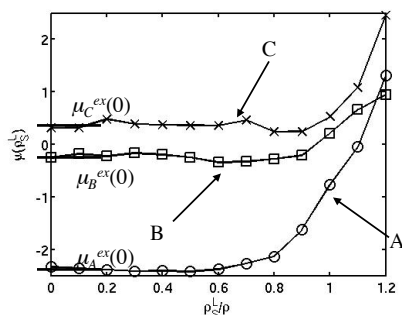
Allen and GCR, J. Chem. Phys **130** (2009), 024904



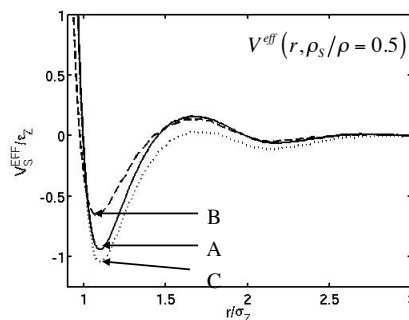
## Solvo-philic and Solvo-phobic particle potentials



### One-Body Potential



### Two-Body Potential



## DDIS Summary

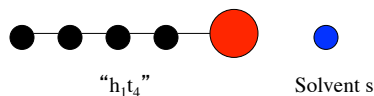


- In implicit solvent simulations, a density-dependent potential with both 1-body and 2-body terms is indicated
- Using such a two-term potential, we can reproduce both the excess chemical potential and the radial distribution function over a wide range of composition
- Transferability to mixtures, chains, and chains of mixed composition (e.g. surfactants) is acceptable, especially at low (global) concentrations relevant to micellar self-assembly
- DDIS potentials follow predictable relationships depending on the solvent-philic or solvent-phobic nature of the solute

## Application to Surfactant Self-Assembly



- “Smit”<sup>1</sup> (nonionic) surfactant model



- $\epsilon_t = \epsilon_h = \epsilon_s = 1.0$

- $\alpha_t = \alpha_s = 1.0$ ,  $\alpha_h = 2.0$

$$V_{ij}^{TS}(r_{ij}; \epsilon_{ij}, \sigma_{ij}, R_{c,ij}) = \begin{cases} V_{ij}^{LJ}(r_{ij}; \epsilon_{ij}, \sigma_{ij}) - V_{ij}^{LJ}(R_{c,ij}; \epsilon_{ij}, \sigma_{ij}) & r_{ij} \leq R_{c,ij} \\ 0 & r_{ij} > R_{c,ij} \end{cases}$$

- Particles interact via truncated and shifted Lennard-Jones potential

- $T^* = 1.0$ ;  $\rho^* = 0.6$

- Pool and Bolhuis (all-atom simulations)<sup>2</sup>

- $h_1 t_4$ :  $\rho^{\text{CMC}} \sim 5 \times 10^{-6}$ ,  $N_{\text{AGG}} \sim 20$

- $h_1 t_5$ :  $\rho^{\text{CMC}} \sim 5 \times 10^{-7}$ ,  $N_{\text{AGG}} \sim 30$

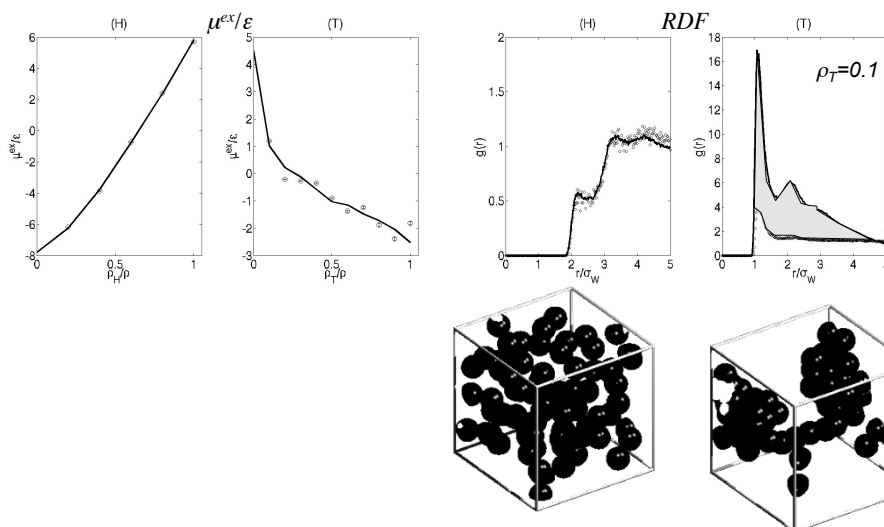
$R_c/\sigma_{ij}$	s	h	t
s	2.5	2.5	$2^{1/6}$
h	2.5	$2^{1/6}$	$2^{1/6}$
t	$2^{1/6}$	$2^{1/6}$	2.5

1. Smit, Phys. Rev. A. **37** (1988), 343.
2. Pool and Bolhuis, J. Phys. Chem. B **109** (2005), 6650.

## Fitting results for Head and Tail particles



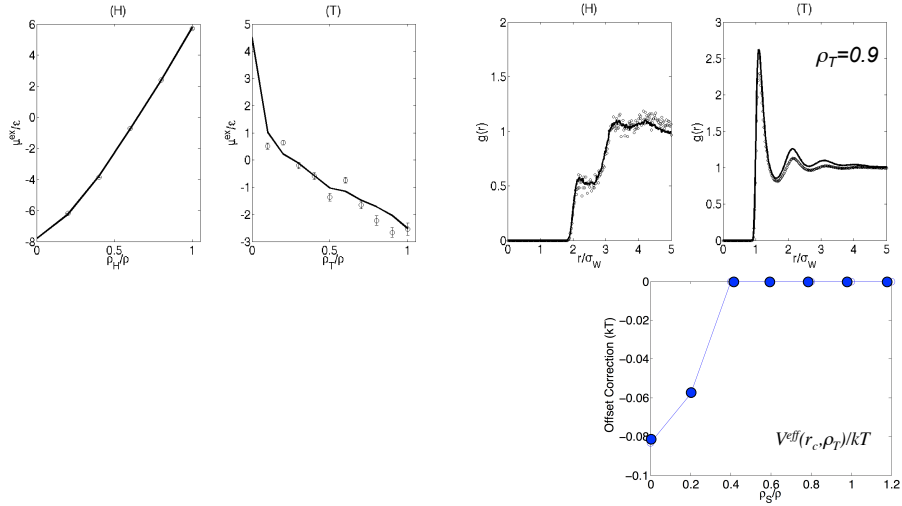
Already in explicit T/W simulations, clustering is observed



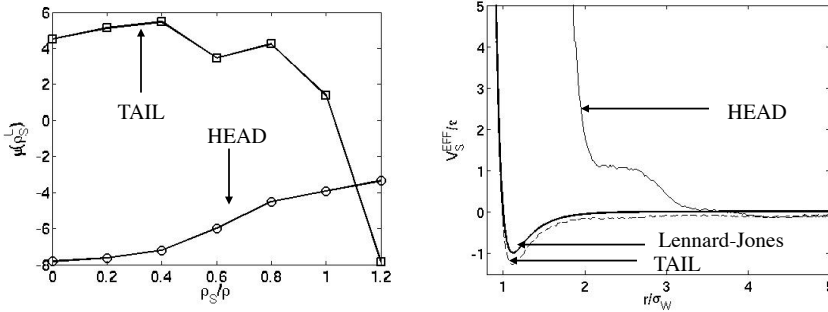
## Fitting results for Head and Tail particles

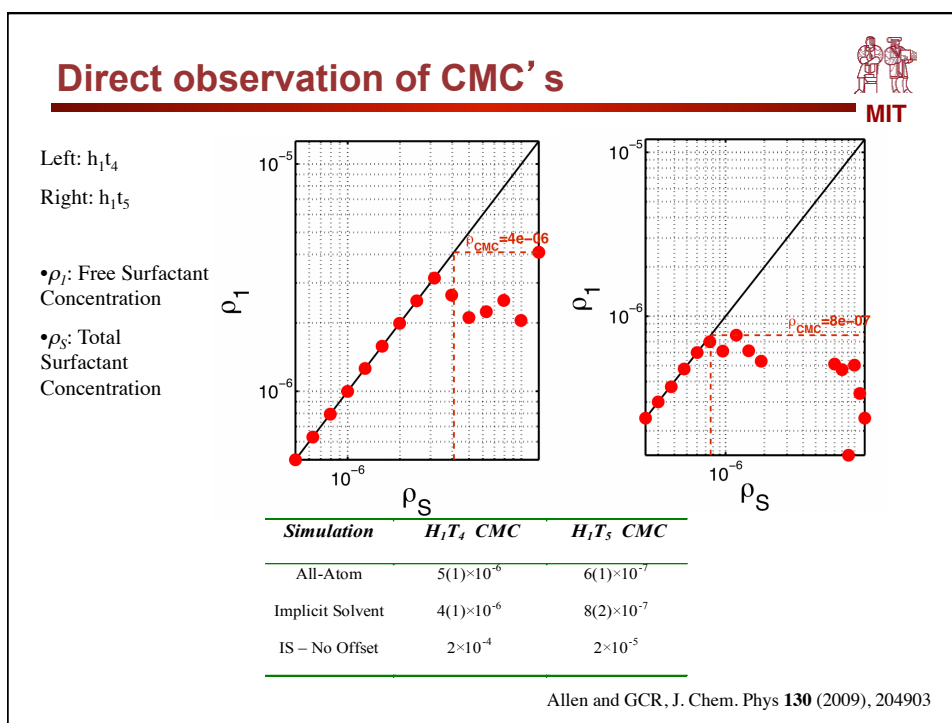
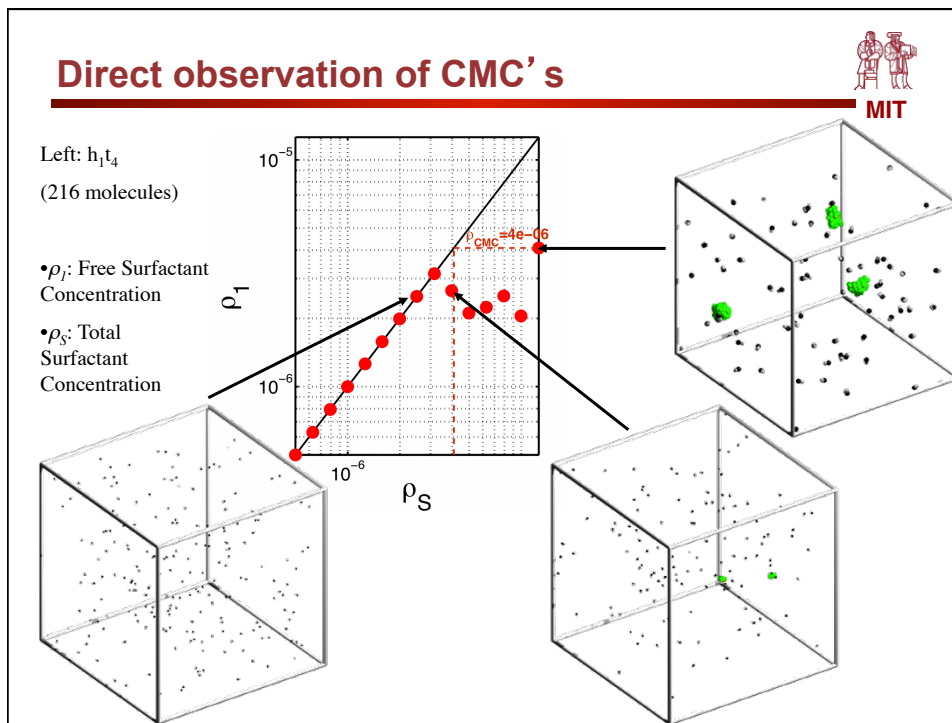


Allowing the offsets at  $r_C$  to vary accounts for this

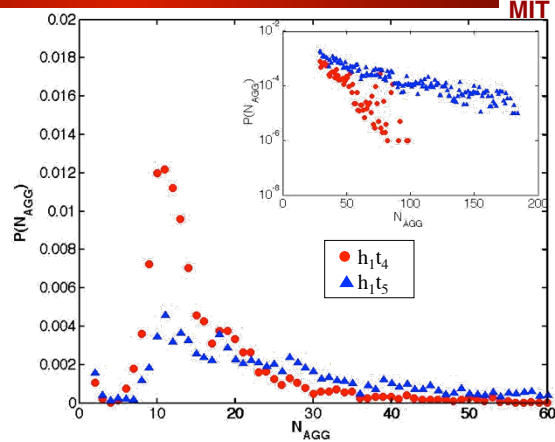


## Head and Tail Potentials





## Average Aggregation Number



<i>Simulation</i>	$H_1T_4 N_{AGG}$	$H_1T_5 N_{AGG}$
All-Atom	~20	~30
Implicit Solvent	16	34

$N_{AGG}$ : Micelle aggregation size as determined by a clustering algorithm

## Computational Performance



<i>Simulation</i>	<i># Atoms</i>	<i>Simulation Time</i> (Days)
All-Atom (est)	$2.5 \times 10^8$	$4.6 \times 10^7$
Implicit Solvent	1080	2

## Summary



- Self-assembly involves simulation across a broad range of local densities (compositions)
- Coarse-graining inevitably implies a tradeoff between speed and accuracy (in selected quantities). The challenge is to find a form that optimizes this tradeoff.
- Local solute density as a proxy for the number of lost configurations
- Density-dependent implicit solvent (DDIS) potentials with both 1- and 2-body terms offer a particularly simple form that permits to retain some approximation of both thermodynamics ( $\mu_{ex}$ ) and structure,  $g(r)$  simultaneously
- Direct simulation of micellar self-assembly for a simple, nonionic surfactant demonstrated, with promising results.