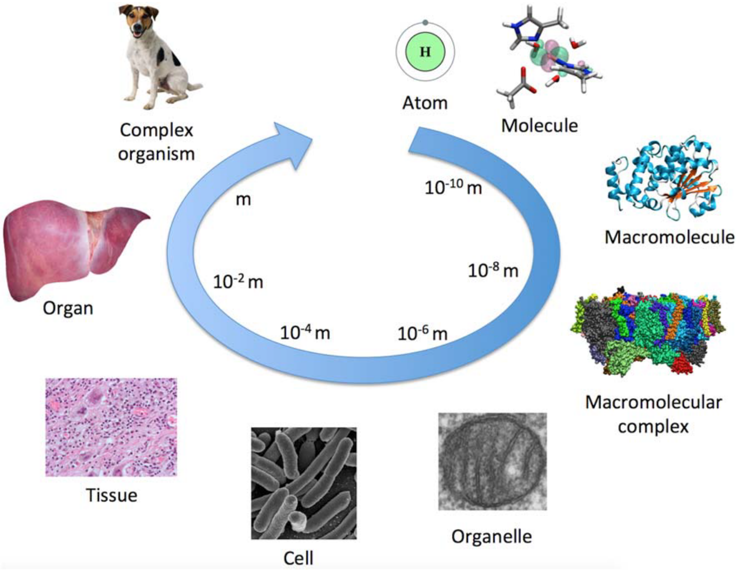
Hybrid particle-field molecular dynamics for biological systems

Sigbjørn Løland Bore
University of Oslo, Norway

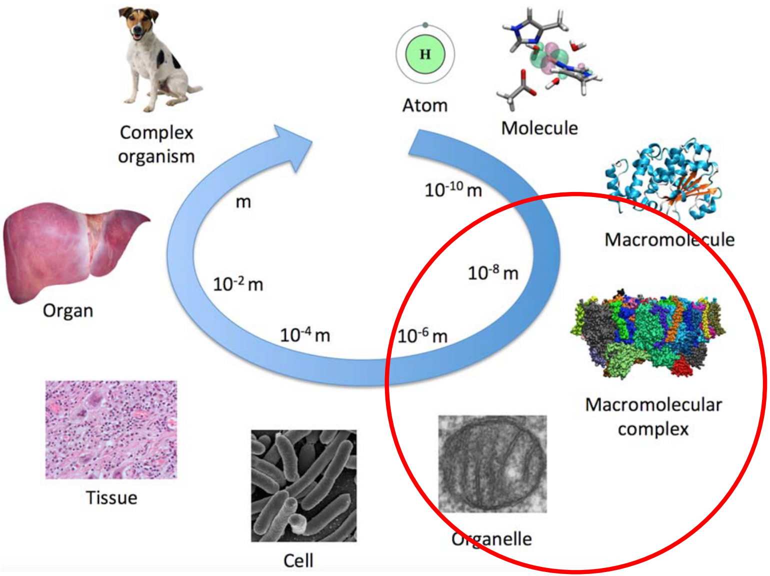
Monday, September 30, 2019

Biological scales



*M. Cascella and S. Vanni, Chem. Modell., (**2016**), 12*

Biological scales



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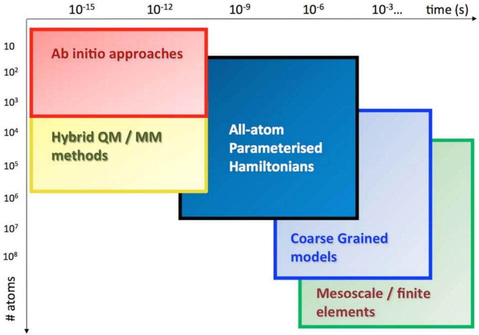
Coarse-graining



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*T. A. Soares, et al., J. Phys. Chem. Lett., (**2017**) 8(15)*

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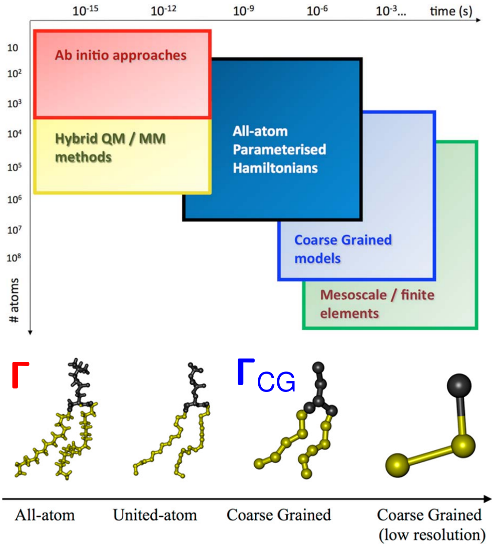

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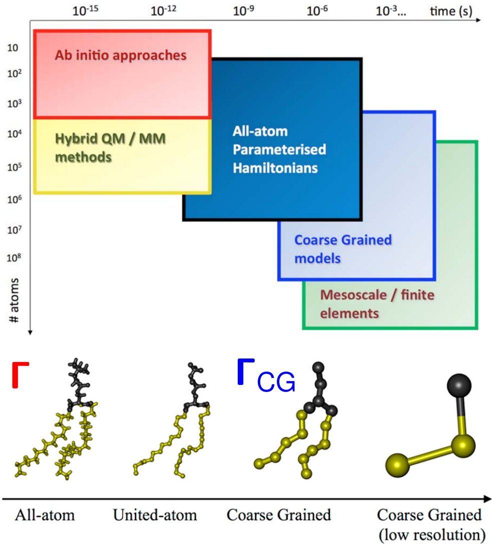

$$Z = \int d\mathbf{\Gamma}\; e^{-\beta H(\mathbf{\Gamma})}$$

$$\downarrow$$

$$Z \simeq \int d\mathbf{\Gamma}_{CG}\; e^{-\beta H(\mathbf{\Gamma}_{CG})}$$

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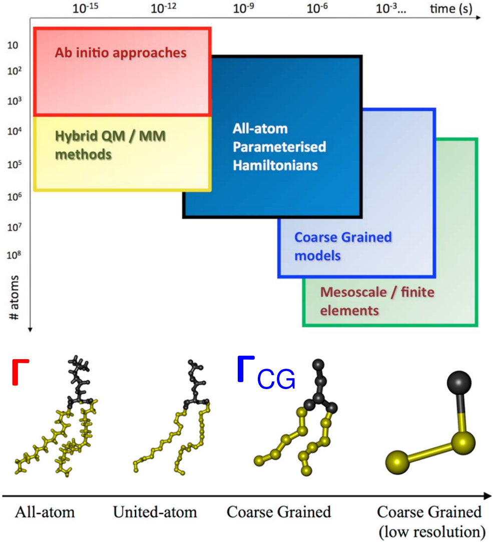

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$$Z \simeq \int d\mathbf{\Gamma}_{CG}\; e^{-\beta H(\mathbf{\Gamma}_{CG})}$$

- Fewer degrees of freedom
- Speedup of dynamics

*M. Cascella and S. Vanni, Chem. Modell., (**2016**), 12*
*T. A. Soares, et al., J. Phys. Chem. Lett., (**2017**) 8(15)*

Hybrid Particle-field method

$$H(\{\mathbf{r}\}) = \sum_{m=1}^{N_{\text{mol}}} \underbrace{H_0(\{\mathbf{r}_m\})}_{\text{Intra-molecular}} + \underbrace{W[\{\phi(\mathbf{r})\}]}_{\text{Inter-molecular}}$$

$\{\phi\} \equiv \{\phi_1, \ldots, \phi_M\}$, *particle-type number densities*.

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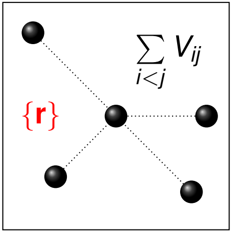
Intermolecular interactions

Particle-particle



$\{\mathbf{r}\} \equiv \{\mathbf{r}_1, \ldots, \mathbf{r}_N\}$, *particle positions*.

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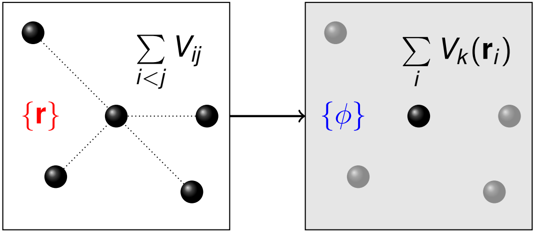

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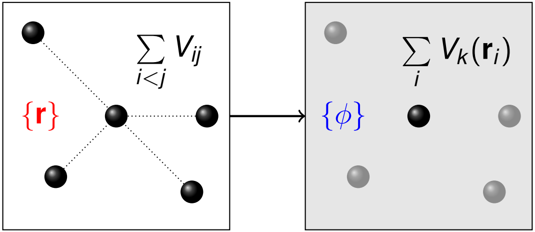

$$V_k(\mathbf{r}) = \frac{\delta W[\{\phi\}]}{\delta \phi_k(\mathbf{r})}$$

$$\mathbf{F}_i = -\nabla_i V_k(\mathbf{r}_i)$$

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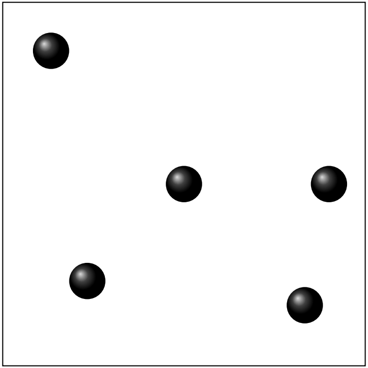
Force computation: Particle-mesh



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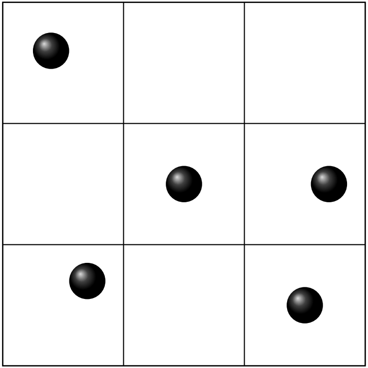
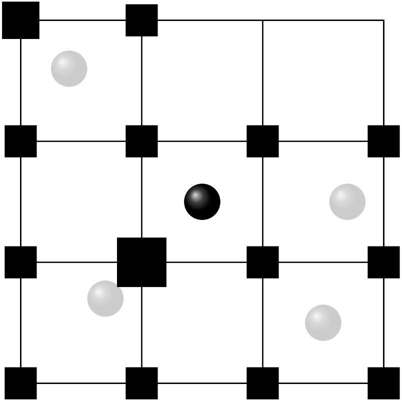


1) Linear interpolation:

$\{\mathbf{r}\} \to \{\phi_{nml}\}$

Force computation: Particle-mesh



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■ : ϕ_{nml}

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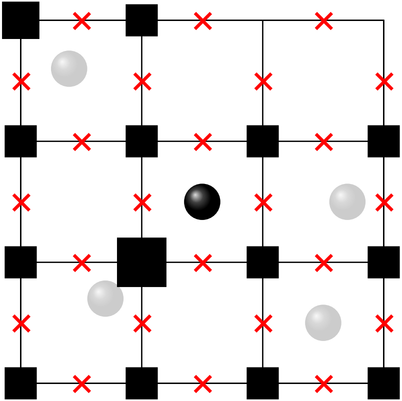


1) Linear interpolation:

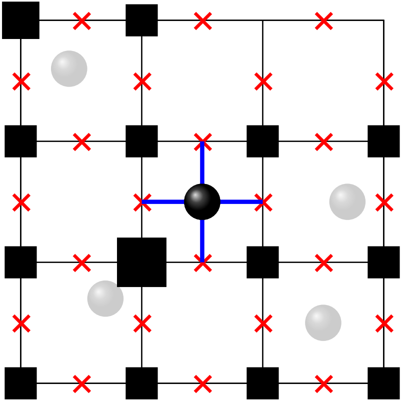
$\{\mathbf{r}\} \rightarrow \{\phi_{nml}\}$

2) Finite-differences:

$\{\phi_{nml}\} \rightarrow \{\nabla\phi_{nml}\} \rightarrow \{\nabla V_{nml}\}$

■ : ϕ_{nml} ✕ : ∇V_{nml}

Force computation: Particle-mesh



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2) Finite-differences:

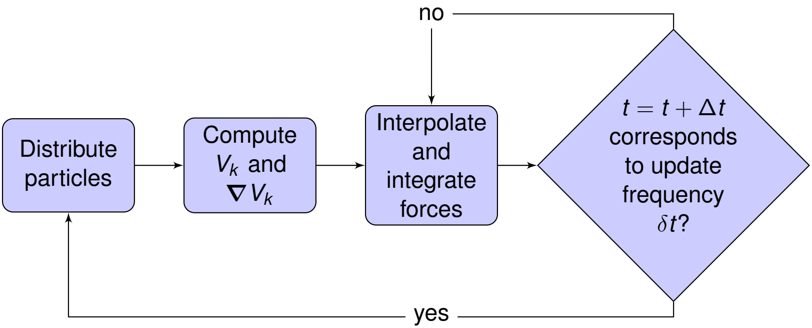
$\{\phi_{nml}\} \rightarrow \{\boldsymbol{\nabla}\phi_{nml}\} \rightarrow \{\boldsymbol{\nabla} V_{nml}\}$

3) Force interpolation:

$\{\boldsymbol{\nabla} V_{nml}\} \rightarrow \mathbf{F}_i$

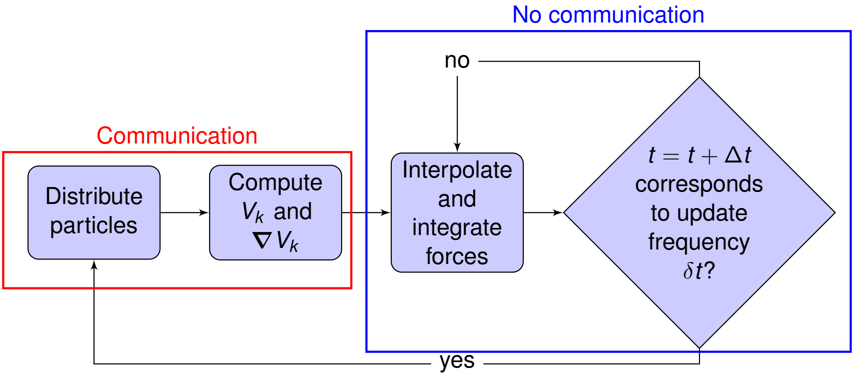
■ : ϕ_{nml} ✕ : $\boldsymbol{\nabla} V_{nml}$

Implementation and parallelization



*Y. Zhao et al., J. Comput. Chem., (**2012**) 33*

Implementation and parallelization



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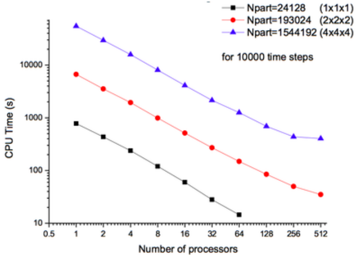
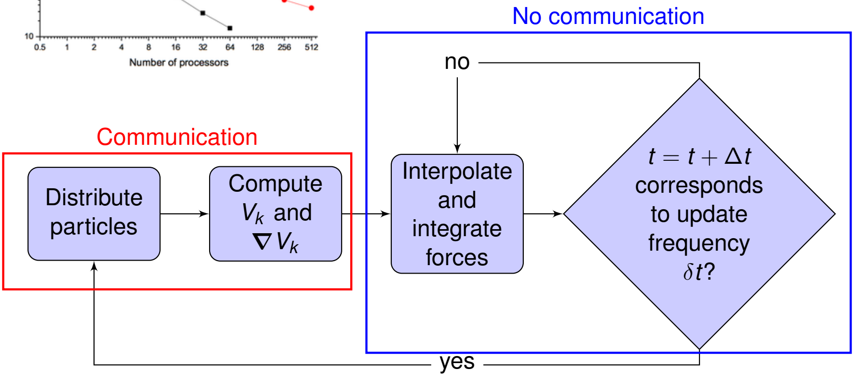


Excellent scaling for small and large systems!

OCCAM Molecular Dynamics



*Y. Zhao et al., J. Comput. Chem., (**2012**) 33*

Interaction energy: Polymer-theory

$$W[\phi] = \int d\mathbf{r}\ \frac{1}{\rho_0}\left(\sum_{k\ell} \frac{\tilde{\chi}_{k\ell}}{2}\phi_k(\mathbf{r})\phi_\ell(\mathbf{r}) + \frac{1}{\kappa}\left(\sum_\ell \phi_\ell(\mathbf{r}) - \rho_0\right)^2 \right)$$

ρ_0: *density-parameter related to the volume per bead.*

*G. Milano and T. Kawakatsu, J. Chem. Phys., (**2009**) 130 (21)*

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$\tilde{\chi}_{k\ell} > 0 \rightarrow$ *Likes not* to mix
$\tilde{\chi}_{k\ell} \leq 0 \rightarrow$ *Likes* to mix

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$\tilde{\chi}_{k\ell} > 0 \rightarrow$ *Likes not* to mix $\quad \kappa \sim 0 \rightarrow$ incompressible

$\tilde{\chi}_{k\ell} \leq 0 \rightarrow$ *Likes* to mix $\quad \kappa \gg 0 \rightarrow$ very compressible

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$$\overset{\text{Net effect}}{\Longrightarrow} V_k(\mathbf{r}) = \frac{1}{\rho_0}\left(\sum_\ell \tilde{\chi}_{k\ell}\phi_\ell(\mathbf{r}) + \frac{1}{\kappa}\left(\sum_\ell \phi_\ell(\mathbf{r}) - \rho_0\right)\right)$$

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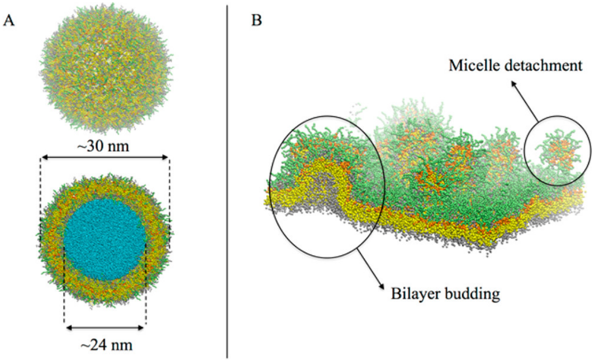
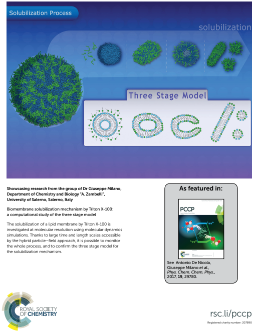
*G. Milano and T. Kawakatsu, J. Chem. Phys., (**2009**) 130 (21)*

Prototypic application

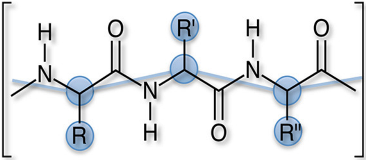
Large lipid vesicles interacting with surfactants



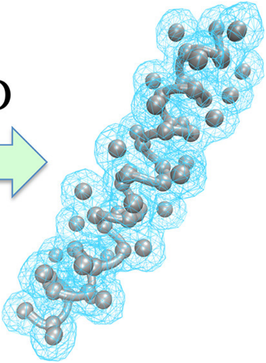


T. A. Soares et al., JPCL ***2017***   *A. Pizzirusso et al., PCCP* ***2017***

Hybrid Particle-Field Model for Conformational Dynamics of Peptide Chains



hPF-MD



$$\boxed{H = H_0(\{\mathbf{r}\}) + W[\rho(\mathbf{r})]}$$

S.L Bore et al., JCTC, ***2018***

Underlying model

Michele Cascella

JCTC 2008

JCTC 2010

JCTC 2013

Underlying model

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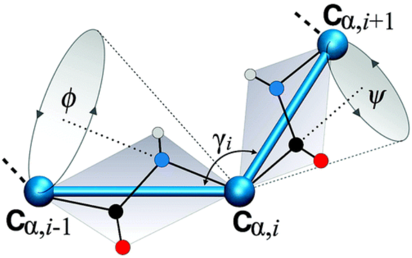
$C\alpha$-representation



Underlying model

Michele Cascella

JCTC 2008

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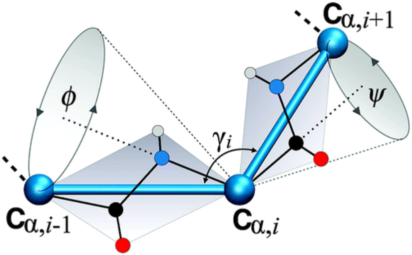
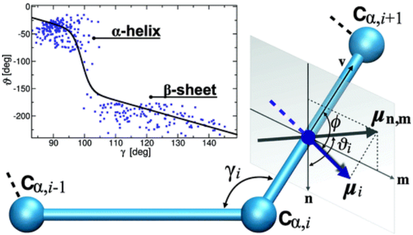
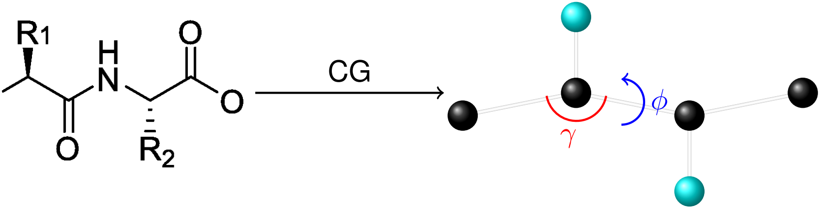
Cα-representation



Reconstruction of dipole



Extension of the model: Two-bead representation



*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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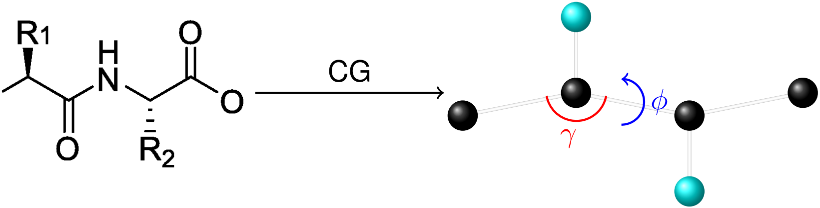

$$V(\gamma, \phi) = V_1(\gamma) + V_2(\phi)?$$

*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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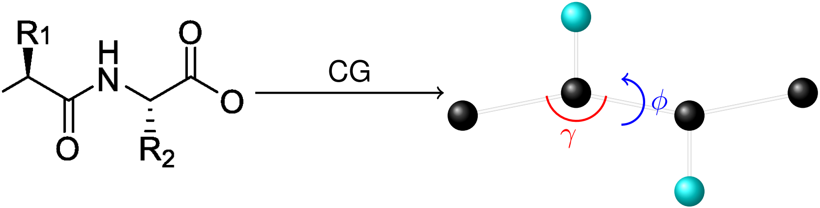
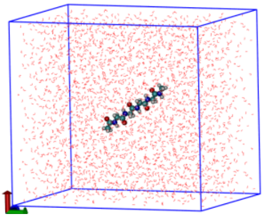


$$V(\gamma, \phi) = V_1(\gamma) + V_2(\phi)?$$

4-Alanine



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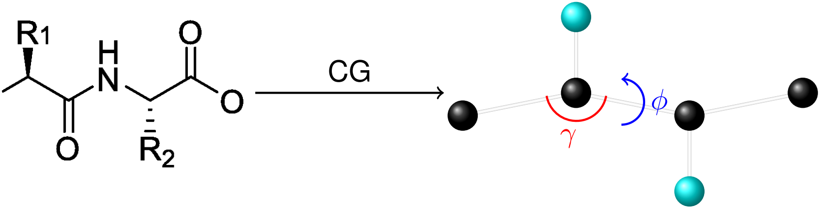
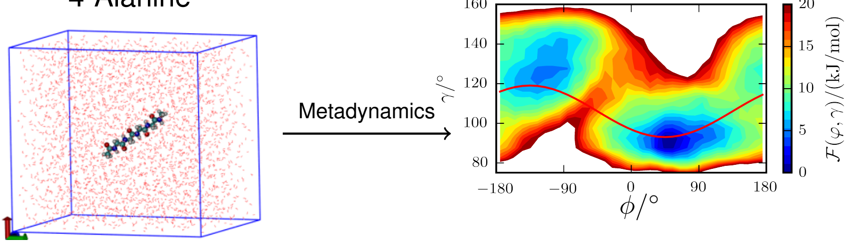


$$V(\gamma, \phi) = V_1(\gamma) + V_2(\phi) \quad \text{X}$$

4-Alanine



S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)

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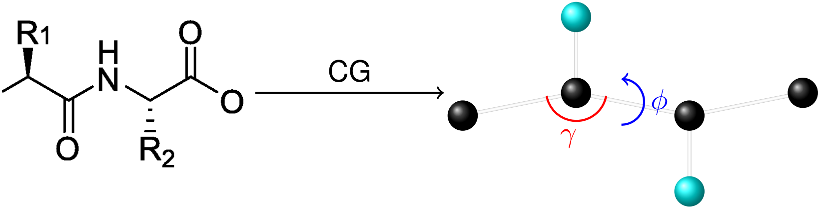
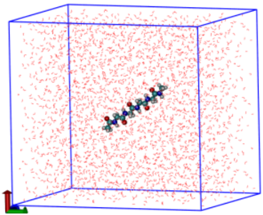
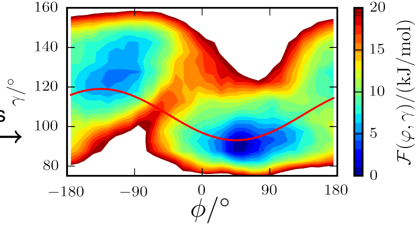


$$V(\gamma,\phi) = \frac{1}{2}k(\phi)\left(\gamma - \gamma_0(\phi)\right)^2 + V_{\mathrm{prop}}(\phi,\lambda) \quad \checkmark$$

4-Alanine



Metadynamics

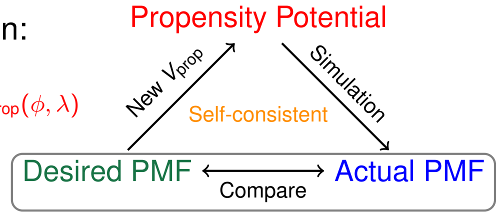


*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

Extension of the model: Propensity potential

Iterative Boltzmann-inversion:

$$V(\gamma,\phi) = \frac{1}{2}k(\phi)\left(\gamma-\gamma_0(\phi)\right)^2 + V_{\text{prop}}(\phi,\lambda)$$



*D. Reith, et al. J. Comput. Chem. (**2003**), 24 (13)*

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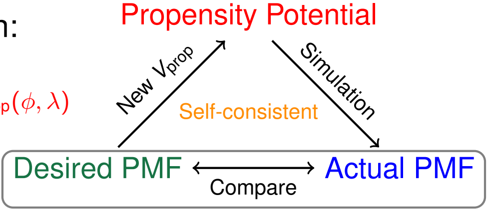
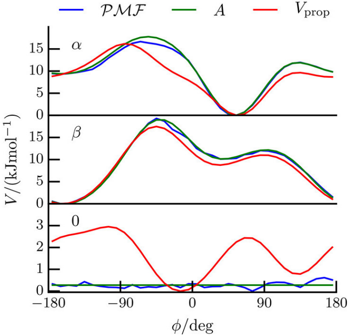
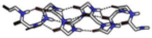




$\lambda = -1 \implies$ Helical



Propensity λ: Linear interpolation between $V_\alpha - V_0 - V_\beta$

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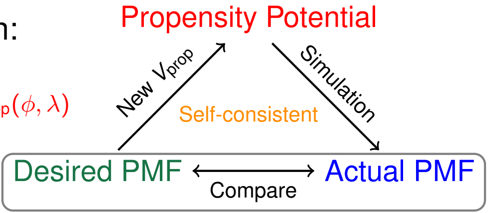

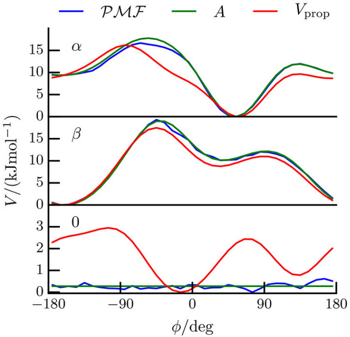

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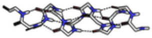
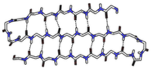


$\lambda = 1 \implies$ Extended



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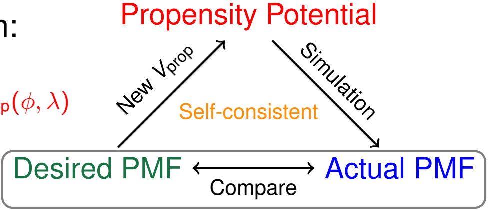

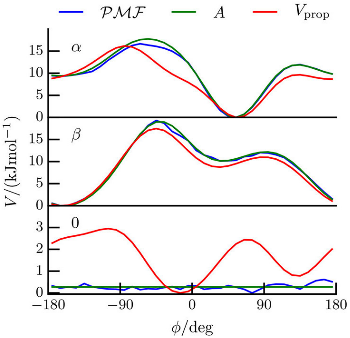

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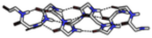
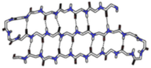
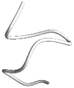


$\lambda = 1 \implies$ Extended



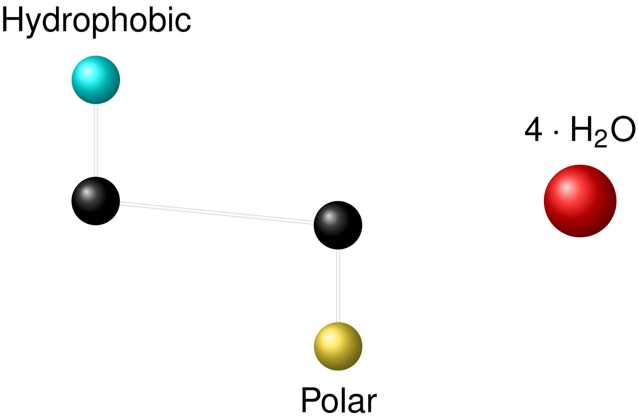
$\lambda = 0 \implies$ Random



Propensity λ: Linear interpolation between $V_\alpha - V_0 - V_\beta$

*D. Reith, et al. J. Comput. Chem. (**2003**), 24 (13)*

Extension of model: χ_{kl}-interactions



$$\boxed{V_k(\mathbf{r}) = \frac{1}{\rho_0}\left(\sum_{\ell} \tilde{\chi}_{k\ell}\phi_\ell(\mathbf{r}) + \frac{1}{\kappa}\left(\sum_{\ell}\phi_\ell(\mathbf{r}) - \rho_0\right)\right)}$$

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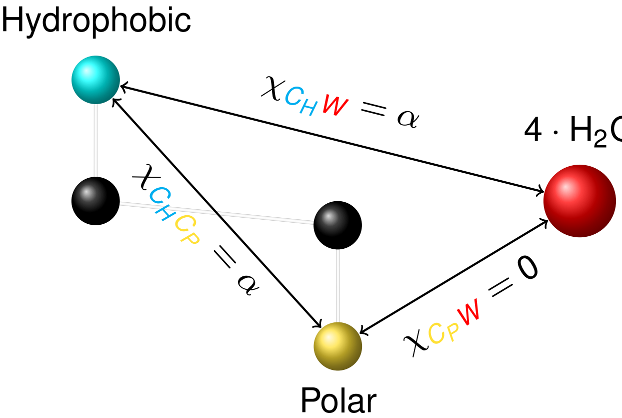

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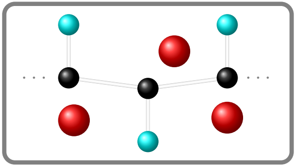
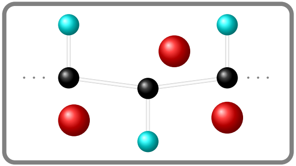
Phase-diagram: Solvated homo-poly-peptide



Phase-diagram: Solvated homo-poly-peptide

$\tilde{\chi}_{k\ell}$	CB	$4{\cdot}H_2O$
CB	0	α
$4{\cdot}H_2O$	α	0



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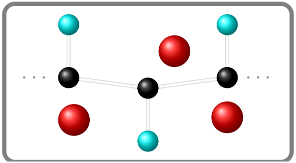

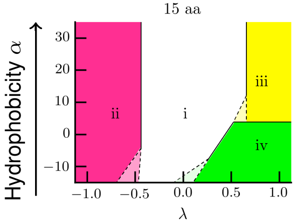

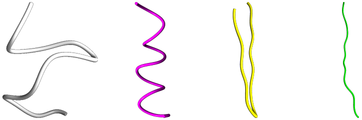

i: Random coil ii: α-helix iii: β-hairpin iv: Extended

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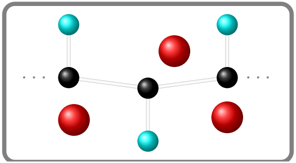

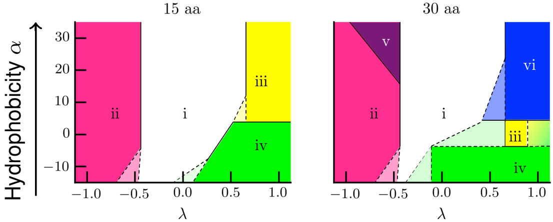

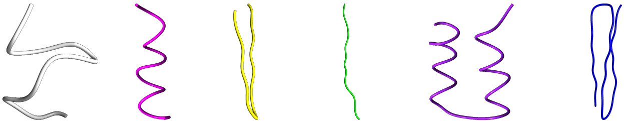

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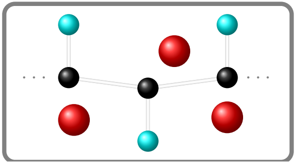

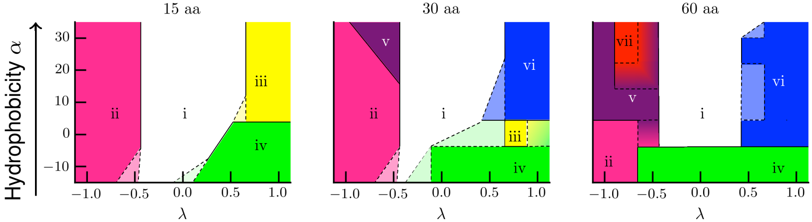

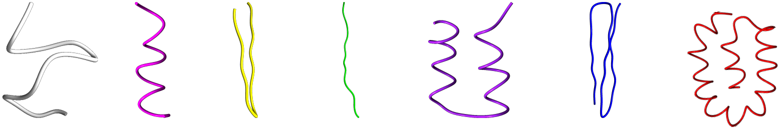

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Amphilic polypeptides: hydrophobic-polar

$\tilde{\chi}_{k\ell}$	CB_P	CB_H	$4{\cdot}H_2O$
CB_P	0	α	0
CB_H	α	0	α
$4{\cdot}H_2O$	0	α	0

*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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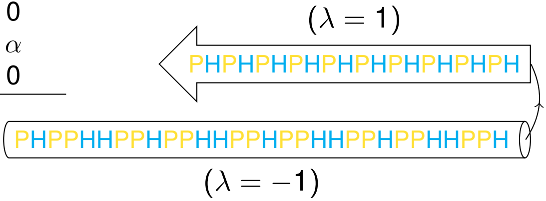

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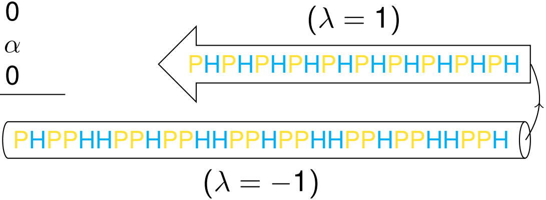

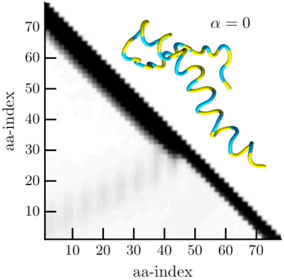

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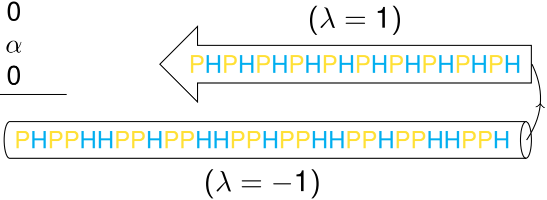

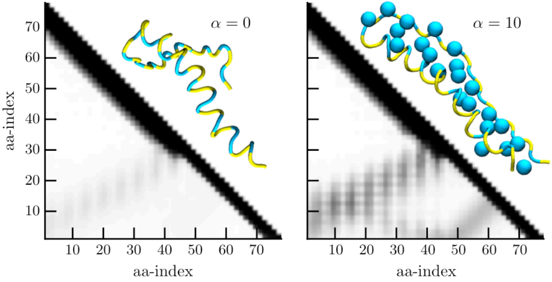

*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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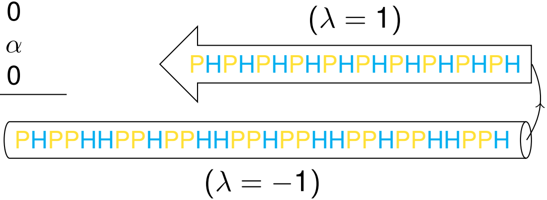
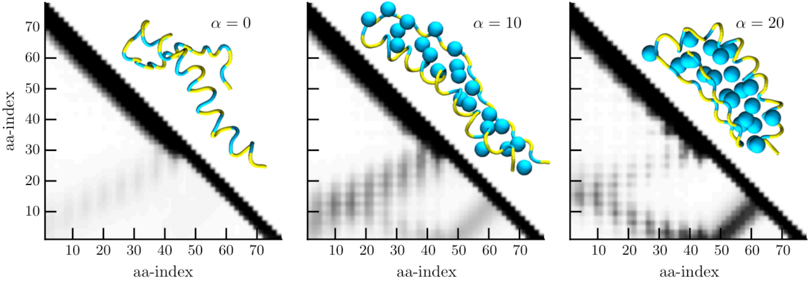
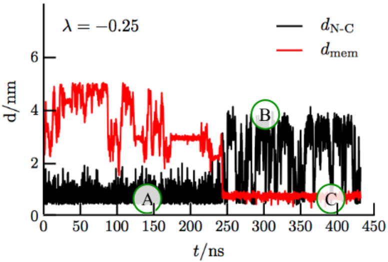
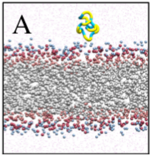




*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

HP-polymer interacting with membrane





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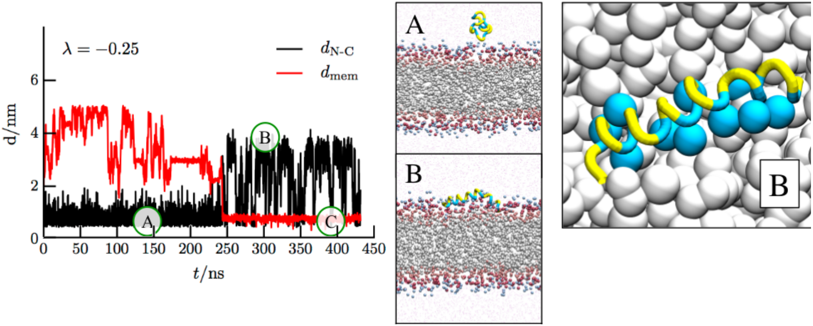

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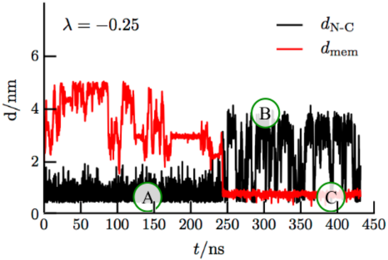

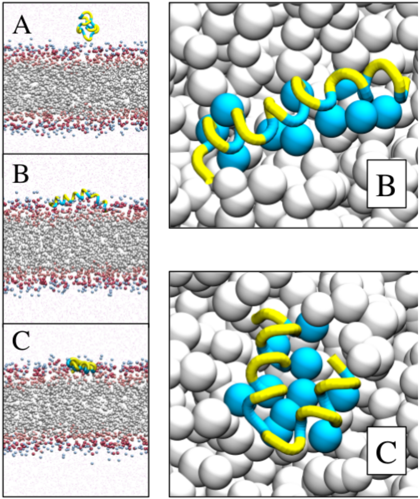

*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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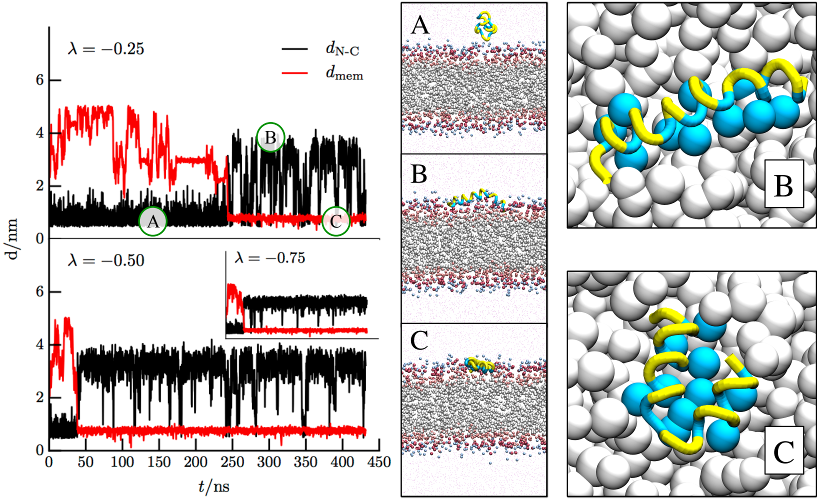

S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)

Outlook

- Parametrization: Toy-model $\rightarrow$ 20 amino-acids

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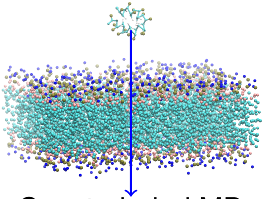

Constrainded MD

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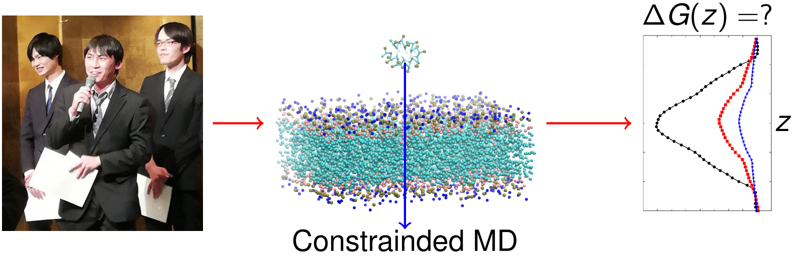
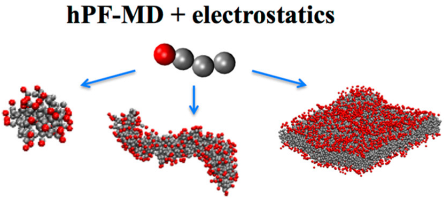
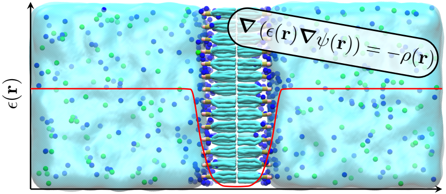


Electrostatics in Hybrid particle-field



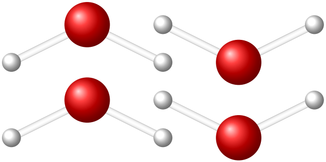
*H. B. Kolli et al. JCTC, **2018***



*S. L. Bore et al., JCTC, **2018***

Electrostatic screening: Atomistic vs coarse-grained

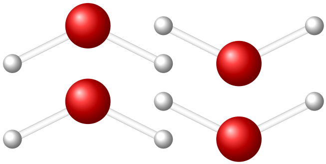
Atomistic molecular dynamics:



Electrostatic screening: Atomistic vs coarse-grained

Atomistic molecular dynamics:

- *Charges are resolved*
- *Screening is modeled directly*



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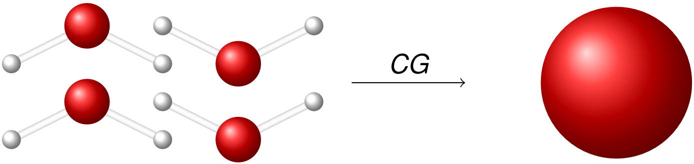

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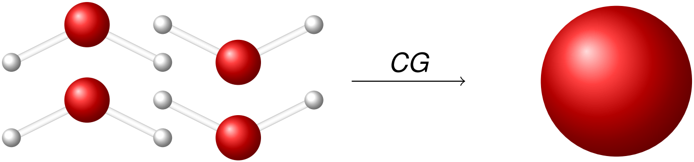

$$\text{Idea}: \quad \boldsymbol{\nabla} \cdot (\epsilon(\mathbf{r})\boldsymbol{\nabla}\psi(\mathbf{r})) = -\rho(\mathbf{r}) \quad \text{(Generalized Poisson equation)}$$

External potential in a density dependent dielectric

Electrostatic interaction energy:

$$W_{\mathrm{elec}}[\{\phi(\mathbf{r})\}] = \frac{1}{2}\int \mathrm{d}\mathbf{r}\,\frac{\mathbf{D}(\mathbf{r})\cdot\mathbf{D}(\mathbf{r})}{\epsilon(\mathbf{r})},$$

$\{\phi\}$*: number densities.* $\mathbf{D}$*: displacement field.* ϵ*: permittivity.*

S. L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)

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Potential felt by particles of type K:

$$V_{\mathrm{ext},K}(\mathbf{r}) = \frac{\delta W_{\mathrm{elec}}}{\delta\phi_K(\mathbf{r})}$$

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ψ*: electrostatic potential.* $\mathbf{E}$*: electrostatic field* ($\mathbf{E} = -\nabla\psi = \epsilon\mathbf{D}$).

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*S. L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)*

Modelling: density dependence of the dielectric

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Density weighted average:

$$\epsilon(\{\phi(\mathbf{r})\}) = \frac{\sum_K^M \epsilon_K \phi_K(\mathbf{r})}{\phi_0(\mathbf{r})},$$

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Forces on particle of type K:

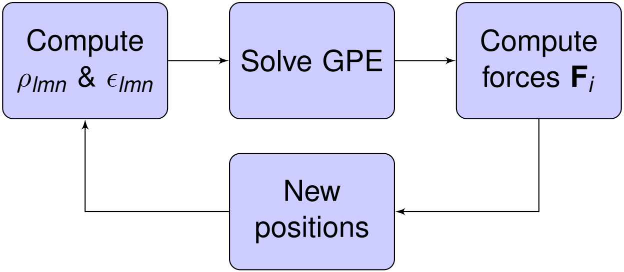
$$\mathbf{F}_K = -\boldsymbol{\nabla} V_{\text{ext},K}(\mathbf{r}) = q_K \mathbf{E}(\mathbf{r}) + \frac{1}{2} \boldsymbol{\nabla} \left(\frac{\epsilon_K - \epsilon(\mathbf{r})}{\phi_0(\mathbf{r})} |\mathbf{E}(\mathbf{r})|^2 \right)$$

*S. L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)*

Force computation and molecular dynamics

*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)*

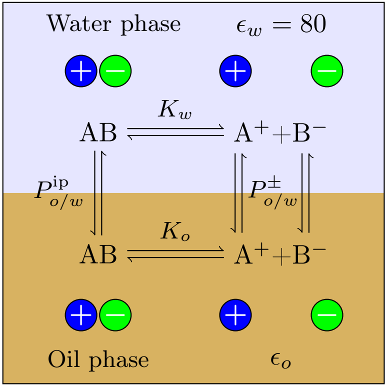
Force computation and molecular dynamics



*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)*

Partitioning of ions (1)

Ions in a phase separated oil/water mixture of ϵ_o and ϵ_w. ($RT \times \chi_{ow}$ =30 kJ mol^{-1})



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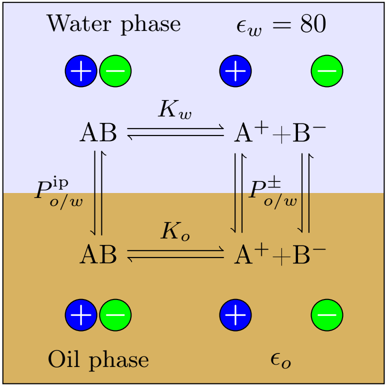
Distribution coefficient:

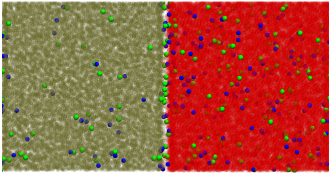
$$D_{o/w} = \frac{c_o}{c_w}$$

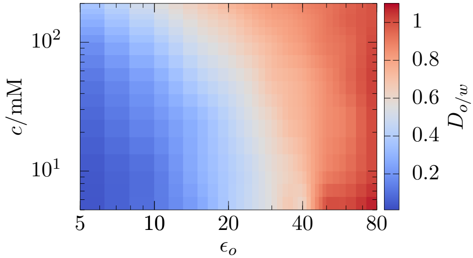
c_0 and c_w: concentration of ions within each phase.



S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 15 (3)

Partitioning of ions (2)





$$D_{o/w} = f(c, P^{\pm}_{o,w}, P^{\mathrm{ip}}_{o,w}, K_w)$$

c: concentration of ions.

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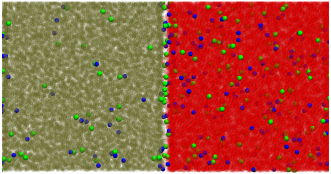

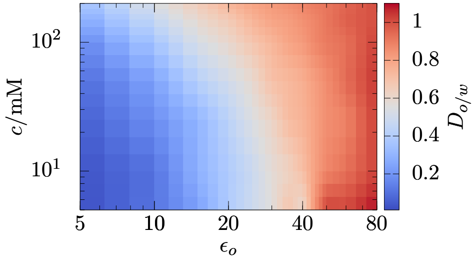

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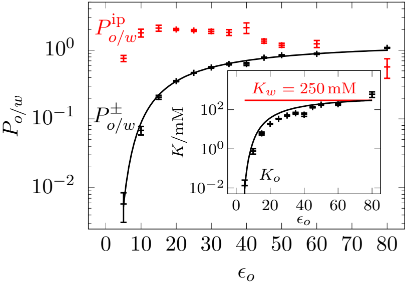

Born theory of ions:

$$\log P^{\pm}_{o/w} = \gamma \left(\frac{1}{\epsilon_w} - \frac{1}{\epsilon_o} \right)$$

Outlook

Applications

- Antonio De Nicola: Model for charged lipids
- Ken Schäfer: Molecular packing of charged surfactants
- Victoria Ariel Bjørnestad: Simulation and experiments on charged surfactants

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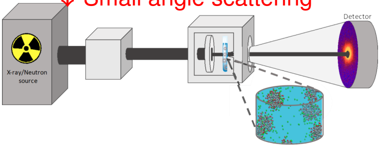
→ OCCAM

↓ Small angle scattering



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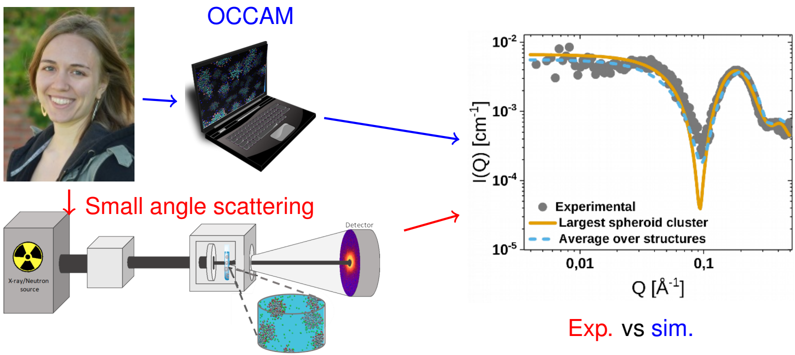

Exp. vs sim.

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