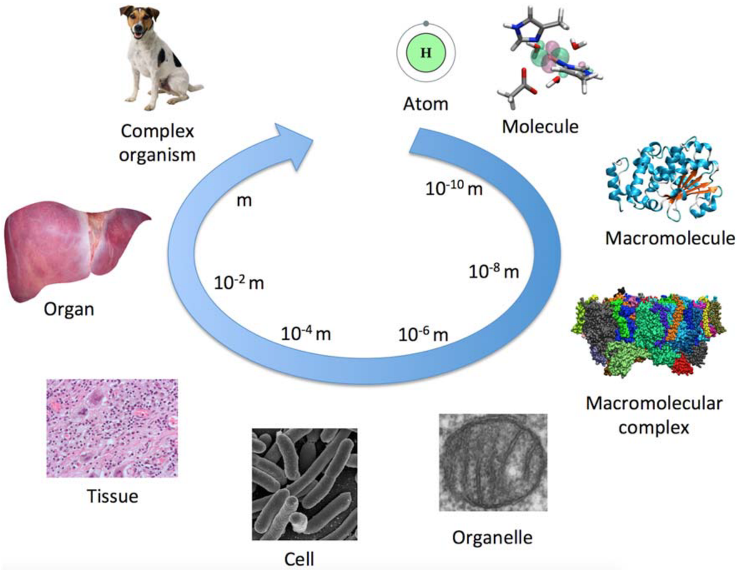
Hybrid particle-field molecular dynamics for biological systems

Hylleårs seminar

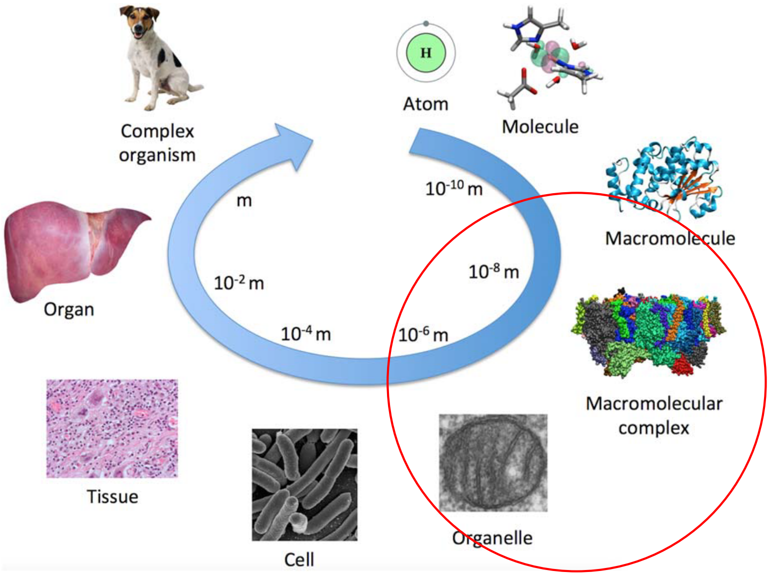
Sigbjørn Løland Bore
University of Oslo, Norway

Friday, September 6, 2019

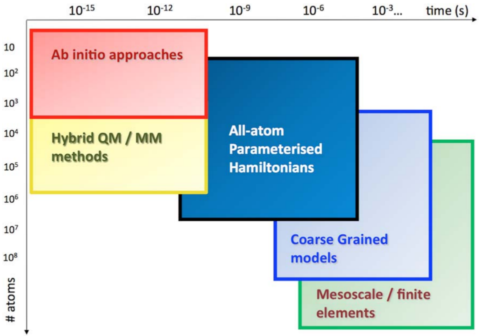
Biological scale



Biological scale



Coarse-graining



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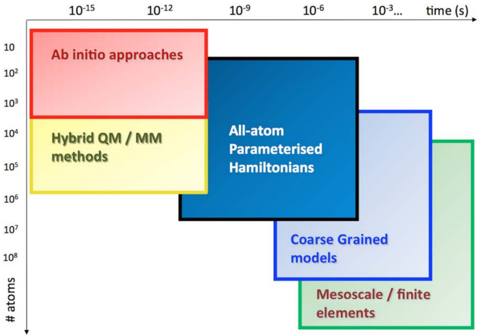

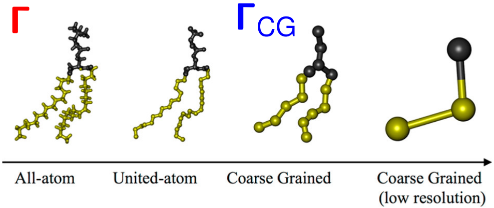

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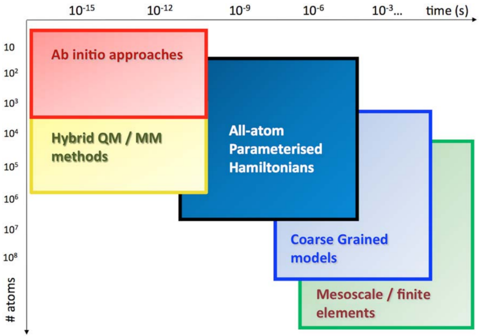
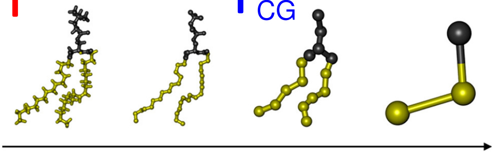


$$Z = \int \mathrm{d}\boldsymbol{\Gamma}\; e^{-\beta H(\boldsymbol{\Gamma})}$$

$$\downarrow$$

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

$\boldsymbol{\Gamma}$ $\boldsymbol{\Gamma}_{CG}$



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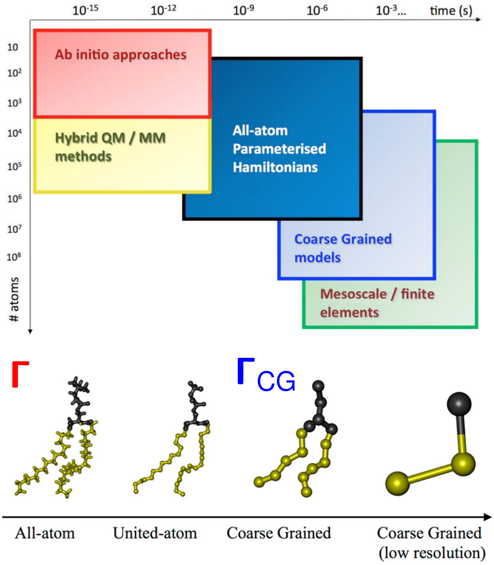

$$Z = \int \mathrm{d}\mathbf{\Gamma}\ e^{-\beta H(\mathbf{\Gamma})}$$

$$\downarrow$$

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

- Fewer degrees of freedom
- Speedup of dynamics

The hybrid particle-field method

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

Particle-particle-Hamiltonian   Density-field interaction-energy

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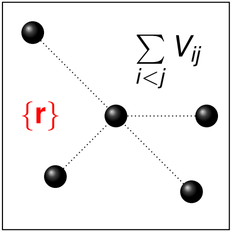

$\{\mathbf{r}\} \equiv \{\mathbf{r}_1, \ldots, \mathbf{r}_N\}$, *particle positions*.

The hybrid particle-field method

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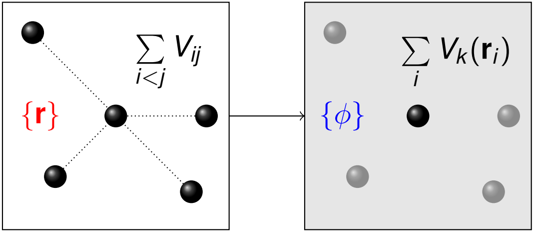
Particle-particle-Hamiltonian Density-field interaction-energy



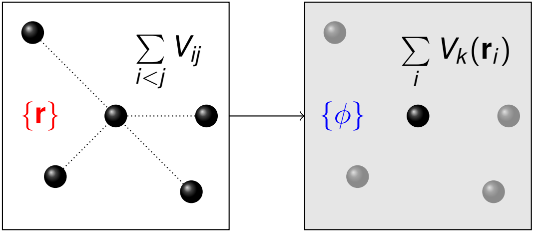
$\{\mathbf{r}\} \equiv \{\mathbf{r}_1, \ldots, \mathbf{r}_N\}$, *particle positions*.

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

The hybrid particle-field method

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

Particle-particle-Hamiltonian   Density-field interaction-energy



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

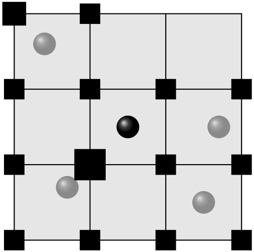
$$\mathbf{F}_i = -\nabla_i V_k(\mathbf{r}_i)$$

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

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

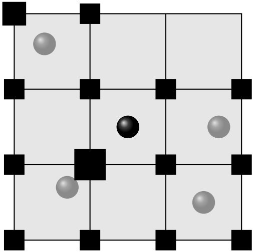
Computation of forces

Particle-mesh



Computation of forces

Particle-mesh

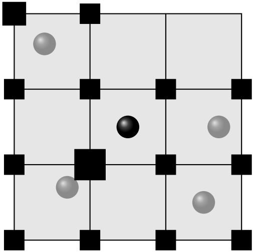


1) Linear interpolation:

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

Computation of forces

Particle-mesh



1) Linear interpolation:

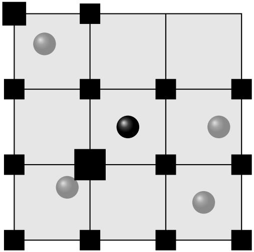
$\{\mathbf{r}\} \rightarrow \{\phi_{nml}\}$

2) Finite-differences:

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

Computation of forces

Particle-mesh



1) Linear interpolation:

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

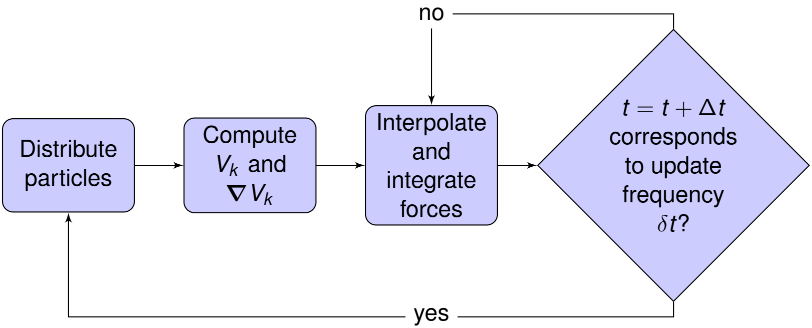
2) Finite-differences:

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

3) Force interpolation:

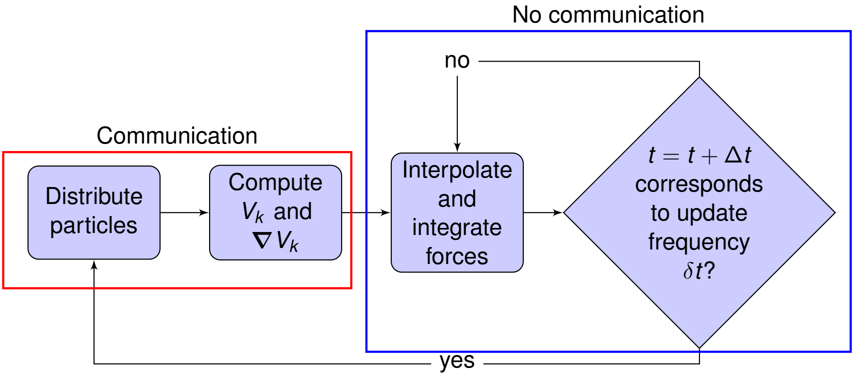
$\{\boldsymbol{\nabla} V_{nml}\} \rightarrow \mathbf{F}_i$

Implementation and parallelization



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

Implementation and parallelization



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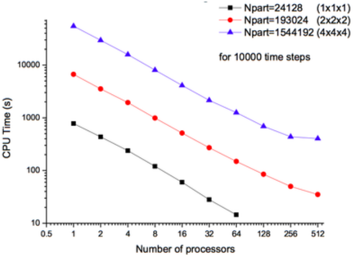
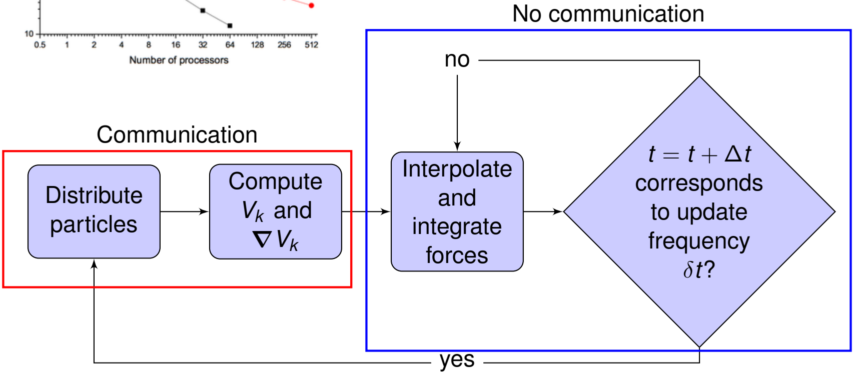
Implementation and parallelization



Excellent scaling for small and large systems!

OCCAM
Molecular Dynamics



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

Interaction energy: Polymer-theory

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

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

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

Interaction energy: Polymer-theory

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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 $\kappa \sim 0 \rightarrow$ incompressible

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

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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

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

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

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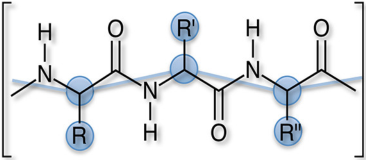
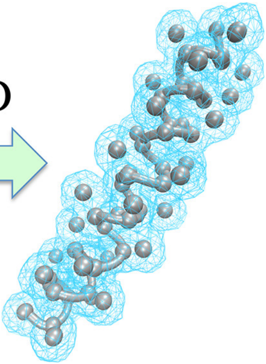
Hybrid Particle-Field Model for Conformational Dynamics of Peptide Chains



hPF-MD



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

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

Previous work

JCTC 2008

JCTC 2010

JCTC 2013

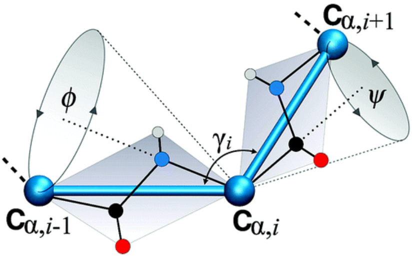
Previous work

JCTC 2008

JCTC 2010

JCTC 2013

Cα-representation



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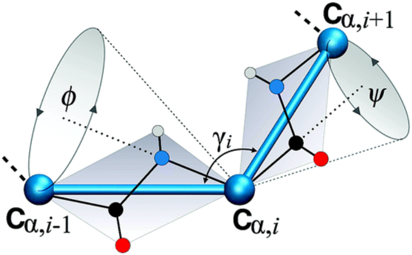
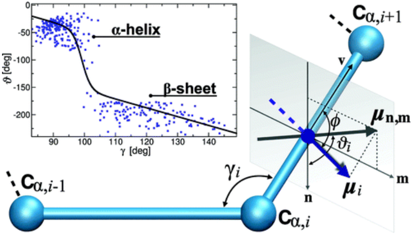
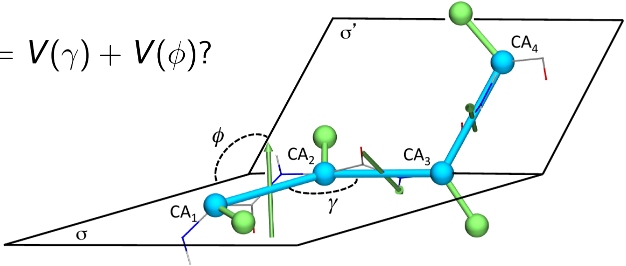


Reconstruction of dipole



Two-bead model

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



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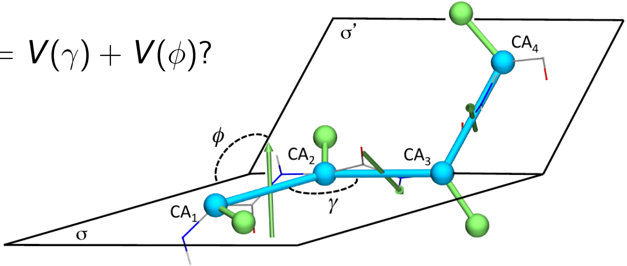
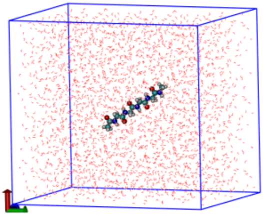


4-Alanine



Two-bead model

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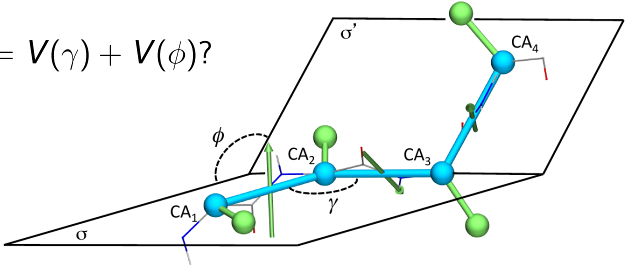
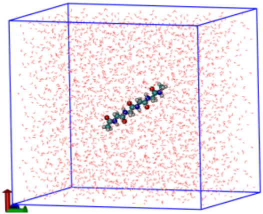
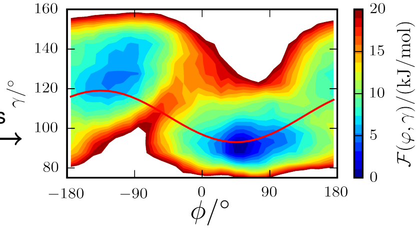


4-Alanine



Metadynamics



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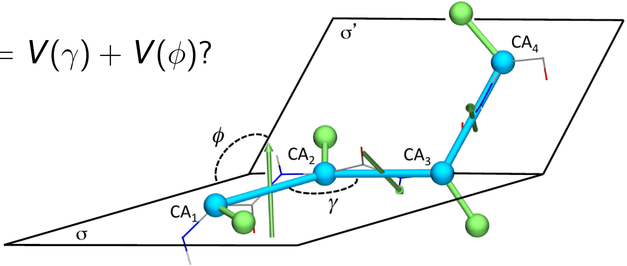

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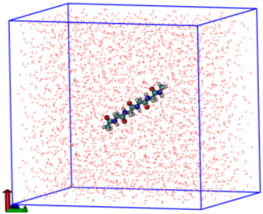
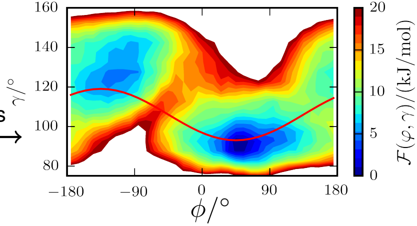


Metadynamics



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

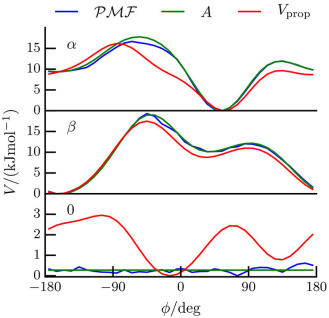
Propensity potential

$$\begin{tikzcd}
A \arrow[r] & \mathcal{PMF} \arrow[r] & V_{\text{prop}} \arrow[ll, bend right, "\text{Boltzmann Inversion}"'] \\
\text{Desired PMF} & \text{Actual PMF} & \text{Propensity potential}
\end{tikzcd}$$

Propensity potential

$$\begin{tikzcd} A \arrow[r] & \mathcal{PMF} \arrow[r] & V_{\text{prop}} \arrow[ll, bend right, "\text{Boltzmann Inversion}"'] \end{tikzcd}$$

Desired PMF — Actual PMF — Propensity potential



Propensity potential

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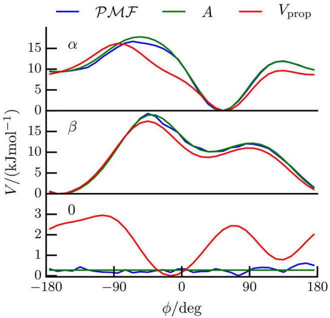
Desired PMF | Actual PMF | Propensity potential



$$V_{prop}(\phi, \lambda) = \frac{1}{2}\left(\left(|\lambda| - \lambda\right) V_\alpha(\phi) + \left(|\lambda| + \lambda\right) V_\beta(\phi) + \left(1 - |\lambda|\right) V_0(\phi)\right)$$

Propensity potential

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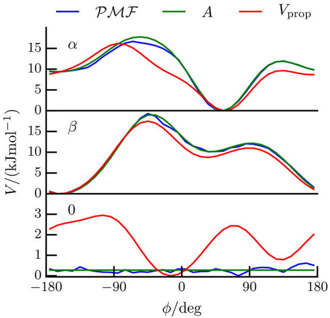
Desired PMF | Actual PMF | Propensity potential



$-1 \leq \lambda < 0 \implies$ Helical

$$V_{prop}(\phi, \lambda) = \frac{1}{2}\left(\left(|\lambda| - \lambda\right) V_\alpha(\phi) + \left(|\lambda| + \lambda\right) V_\beta(\phi) + \left(1 - |\lambda|\right) V_0(\phi)\right)$$

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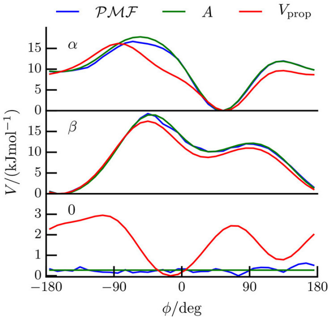
Desired PMF   Actual PMF   Propensity potential



$$-1 \leq \lambda < 0 \implies \text{Helical}$$

$$0 < \lambda < 1 \implies \text{Extended}$$

$$V_{prop}(\phi, \lambda) = \frac{1}{2}\left(\left(|\lambda| - \lambda\right) V_\alpha(\phi) + \left(|\lambda| + \lambda\right) V_\beta(\phi) + \left(1 - |\lambda|\right) V_0(\phi)\right)$$

Propensity potential

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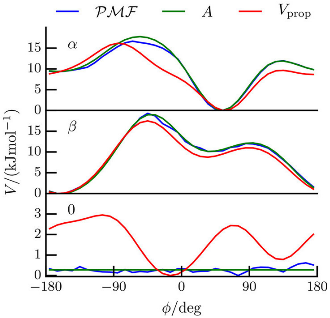
Desired PMF　　Actual PMF　　Propensity potential



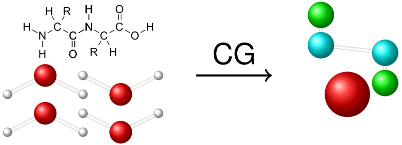
$-1 \leq \lambda < 0 \implies$ Helical

$0 < \lambda < 1 \implies$ Extended

$\lambda = 0 \implies$ Random

$$V_{prop}(\phi, \lambda) = \frac{1}{2}\left(\left(|\lambda| - \lambda\right) V_\alpha(\phi) + \left(|\lambda| + \lambda\right) V_\beta(\phi) + \left(1 - |\lambda|\right) V_0(\phi)\right)$$

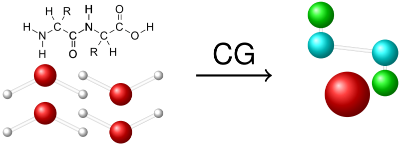
Phase-diagram: homo-poly-peptide



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

Phase-diagram: homo-poly-peptide

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



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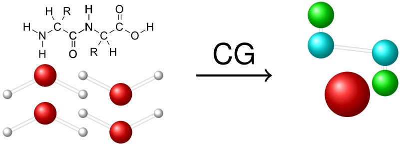
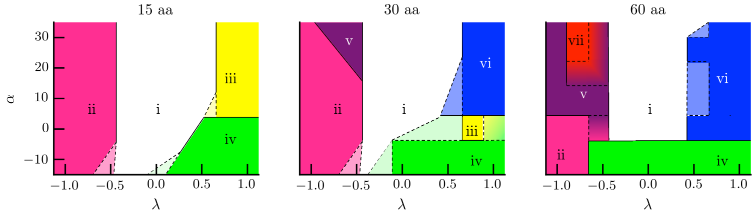
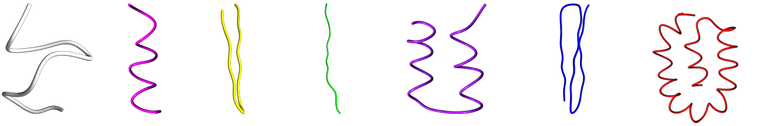






i: Random coil ii: α-helix iii: β-hairpin iv: Extended v: Helix-coil-helix vi: β-floor/helix vii: Helical bundle

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

HP-model

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

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

HP-model

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

α-part: PHPPHHPPHPPHHP

β-part: PHPHPHPHPHPHPH

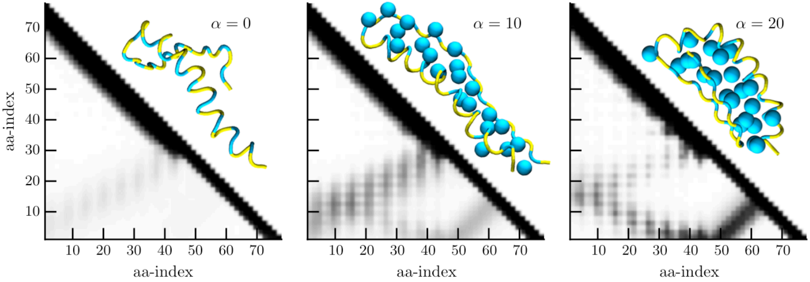
*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

HP-model

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

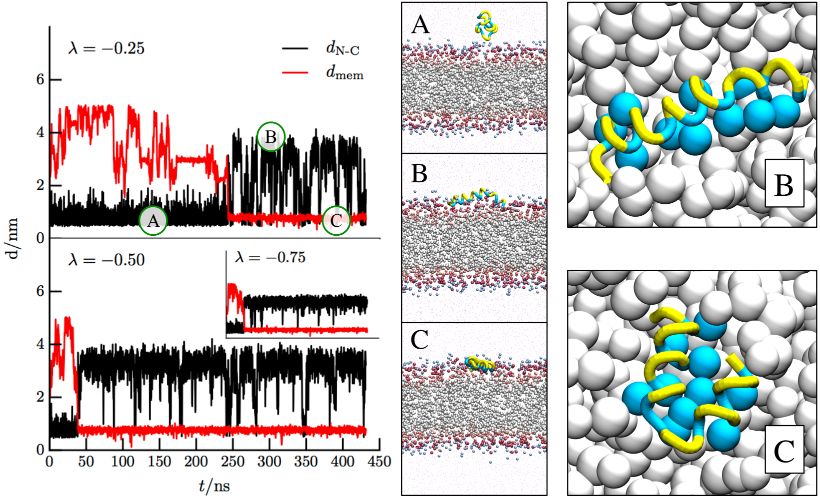
α-part: PHPPHHPPHPPHHP

β-part: PHPHPHPHPHPHPH



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

HP-polymer interacting with membrane



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

Outlook

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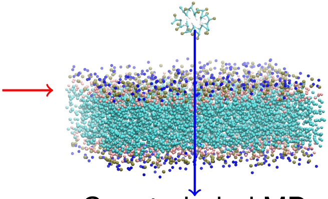

Constrainded MD

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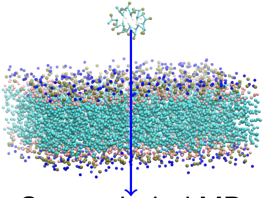
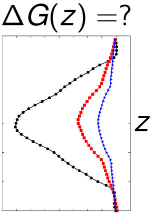
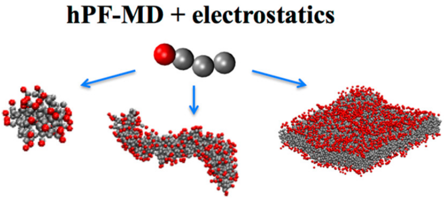


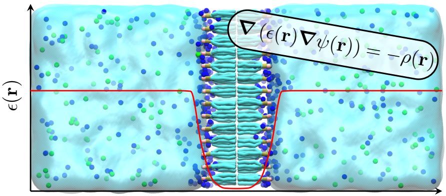
Constrained MD



Electrostatics in Hybrid particle-field



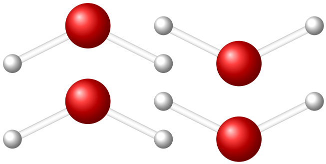
*H.B. Kolli et al. JCTC, **2018***



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

Electrostatic screening: Atomistic vs coarse-grained

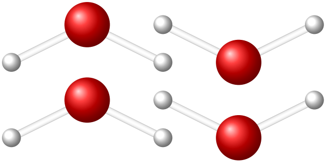
Atomistic molecular dynamics:



Electrostatic screening: Atomistic vs coarse-grained

Atomistic molecular dynamics:

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



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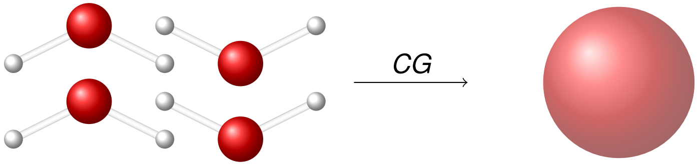

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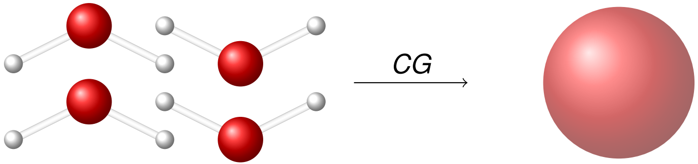

$$\text{Idea}: \quad \boldsymbol{\nabla}\cdot(\epsilon(\mathbf{r})\boldsymbol{\nabla}\psi(\mathbf{r})) = -\rho(\mathbf{r}) \quad \text{(Generalized Poisson equation)}$$

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*: permitivity.*

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

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Modelling: density dependence of the dielectric

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Density weighted average:

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

ϵ_K*: dielectric of particle type K.* ϕ_0*: local total particle density.*

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

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Forces on particle of type K:

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

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Force computation and molecular dynamics

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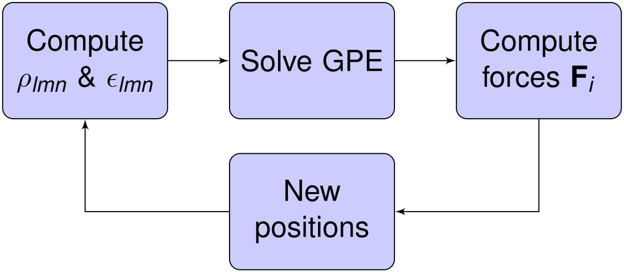

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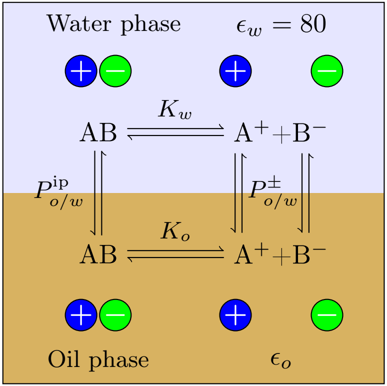
Partitioning of ions (1)

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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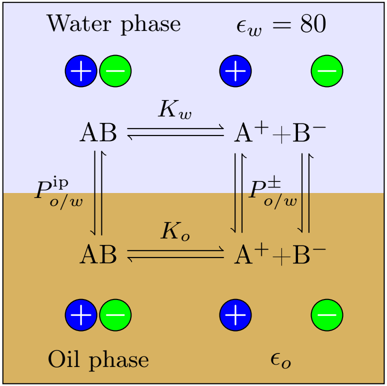
Distribution coefficient:

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

c_0 and c_w: concentration of ions within each phase.



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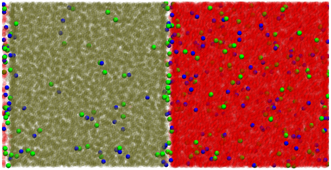
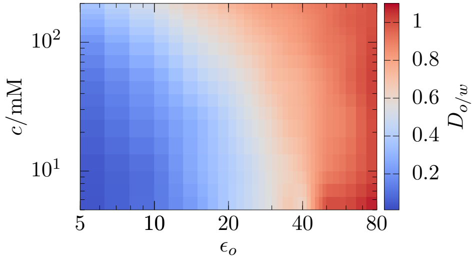
Partitioning of ions (2)

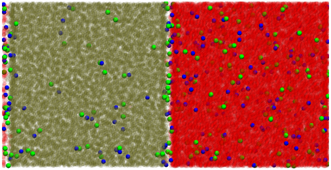


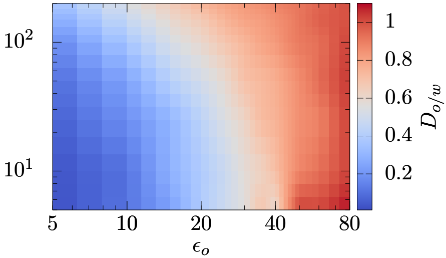


$$D_{o/w} = f(c, P^{\pm}_{o,w}, P^{\text{ip}}_{o,w}, K_w)$$

c: concentration of ions.

Partitioning of ions (2)





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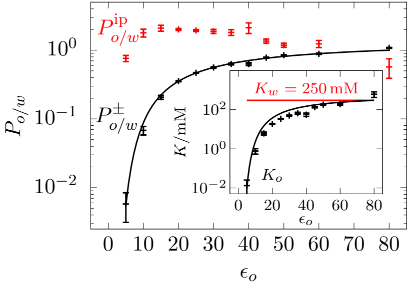

Born theory of ions:

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

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  - Parallel version
  - Improve on accuracy

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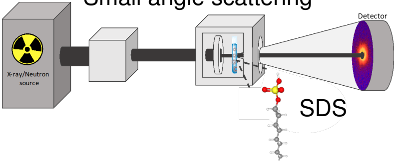
Small angle scattering



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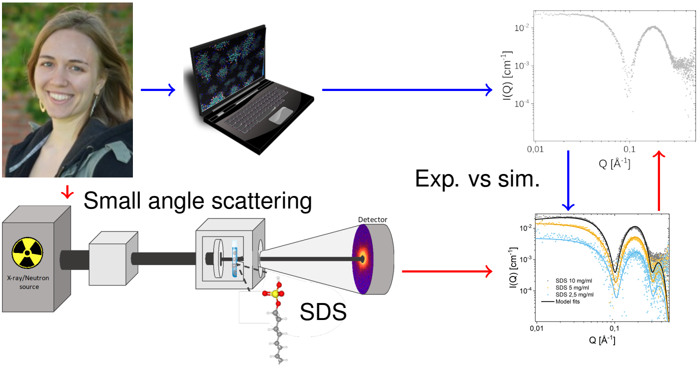

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- Tsudo Yamanaka

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