Hybrid particle-field molecular dynamics for biological systems

Hyllerås seminar

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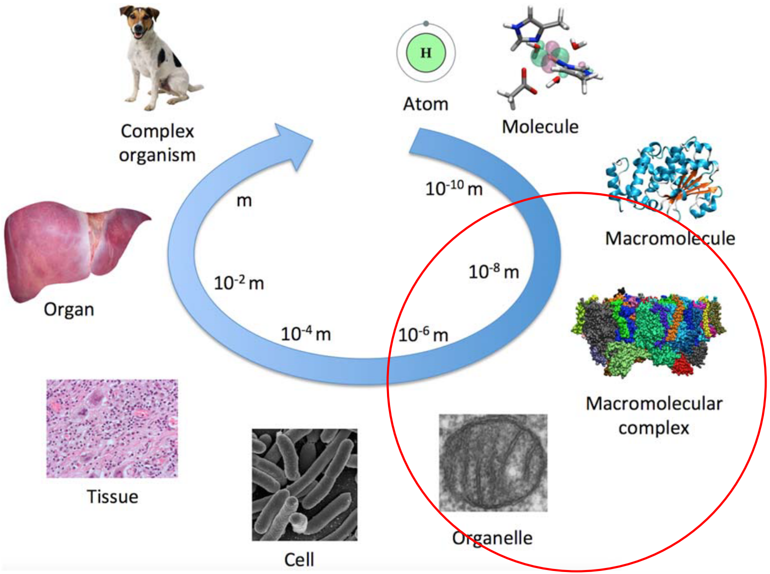
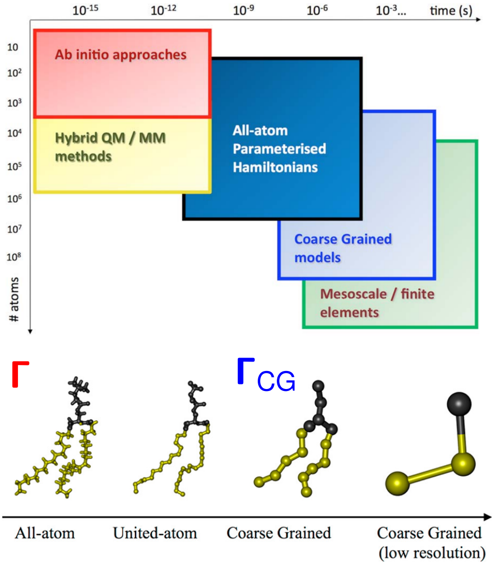
Friday, September 6, 2019

Biological scale



Coarse-graining



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

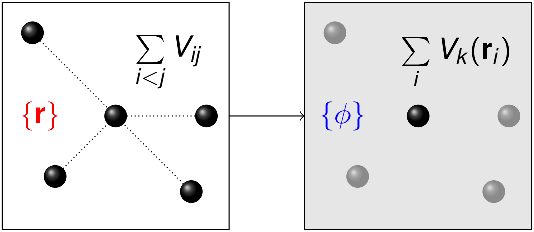
$$Z \simeq \int d\boldsymbol{\Gamma}_{CG}\ e^{-\beta H(\boldsymbol{\Gamma}_{CG})}$$

- 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



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

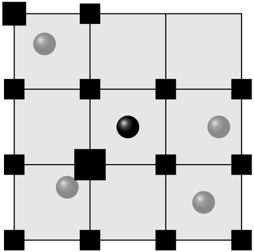
$$\mathbf{F}_i = -\nabla_i V_k(\mathbf{r}_i)$$

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

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

Computation of forces

Particle-mesh



1) Linear interpolation:

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

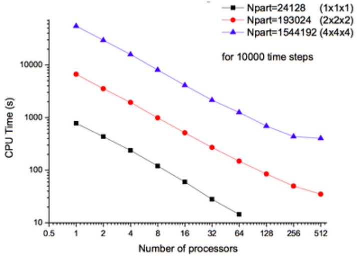
2) Finite-differences:

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

3) Force interpolation:

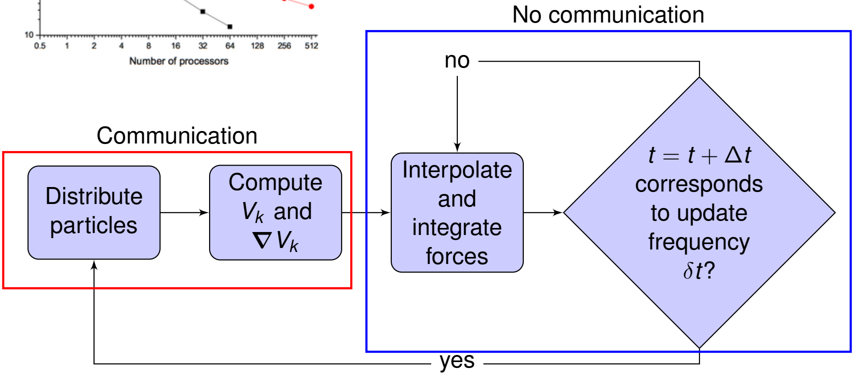
$\{\nabla V_{nml}\} \rightarrow \mathbf{F}_i$

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

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

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

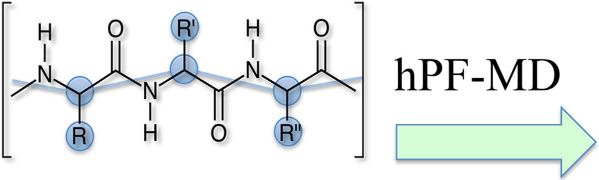
$\tilde{\chi}_{k\ell} \leq 0 \rightarrow$ *Likes* to mix $\quad \kappa \gg 0 \rightarrow$ very compressible

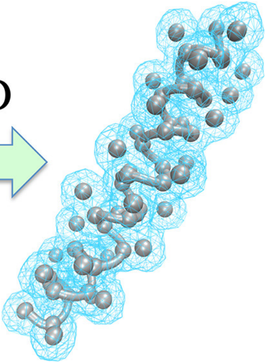
$$\xRightarrow{\text{Net effect}} V_k(\mathbf{r}) = \frac{1}{\rho_0} \left(\sum_{\ell} \tilde{\chi}_{k\ell} \phi_\ell(\mathbf{r}) + \frac{1}{\kappa} \left(\sum_{\ell} \phi_\ell(\mathbf{r}) - \rho_0 \right) \right)$$

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

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

Hybrid Particle-Field Model for Conformational Dynamics of Peptide Chains





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

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

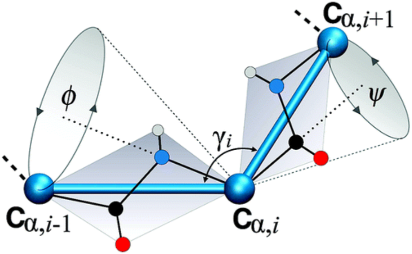
Previous work

JCTC 2008

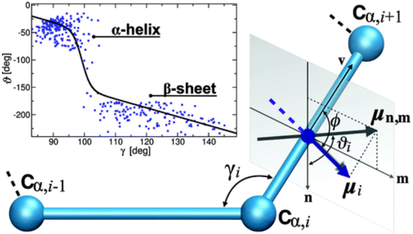
JCTC 2010

JCTC 2013

Cα-representation

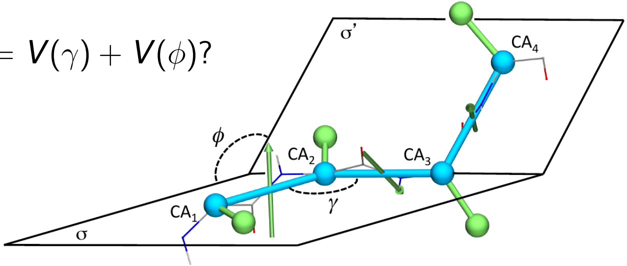


Reconstruction of dipole

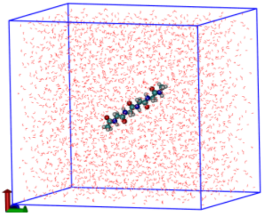


Two-bead model

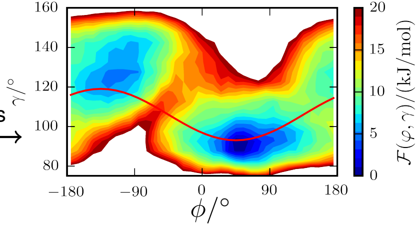
$$V(\gamma, \phi) = V(\gamma) + V(\phi)?$$



4-Alanine



Metadynamics

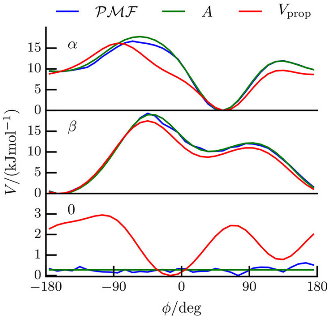


$$\rightarrow V(\gamma, \phi) = \frac{1}{2}k(\phi)\left(\gamma - \gamma_0(\phi)\right)^2 + V_{\text{prop}}(\phi, \lambda)$$

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



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

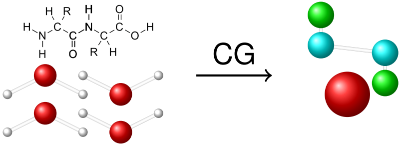
$$0 < \lambda < 1 \implies \text{Extended}$$

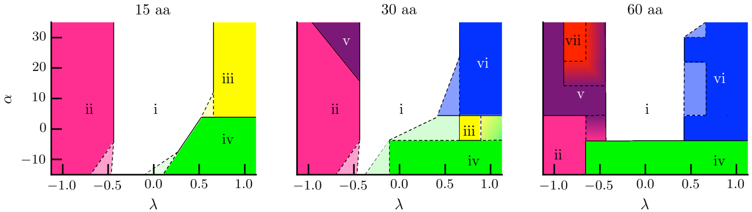
$$\lambda = 0 \implies \text{Random}$$

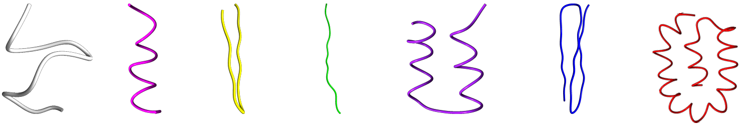
$$V_{prop}(\phi, \lambda) = \frac{1}{2}\left(\left(|\lambda| - \lambda\right) V_{\alpha}(\phi) + \left(|\lambda| + \lambda\right) V_{\beta}(\phi) + \left(1 - |\lambda|\right) V_0(\phi)\right)$$

Phase-diagram: homo-poly-peptide

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







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

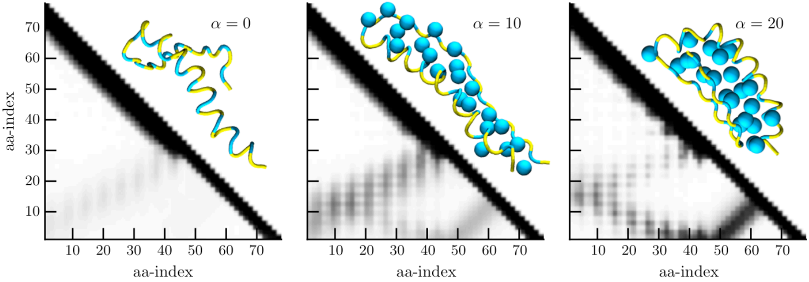
*S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)*

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

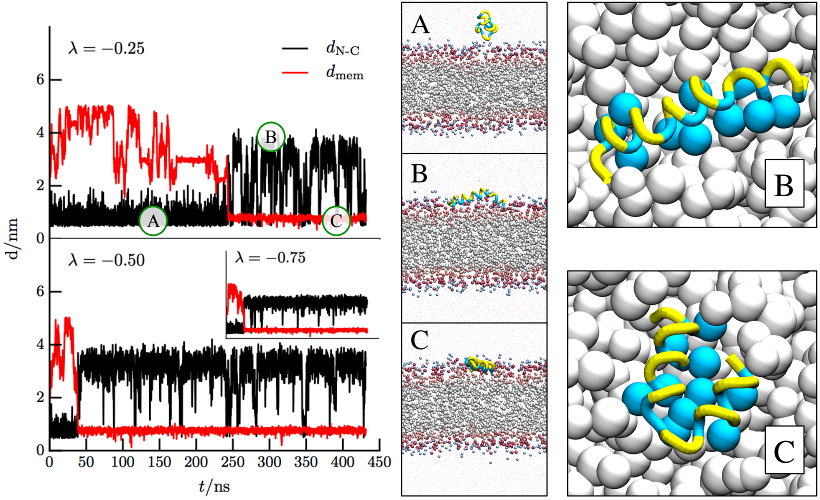
α-part: PHPPHHPPHPPHHP

β-part: PHPHPHPHPHPHPH



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

HP-polymer interacting with membrane

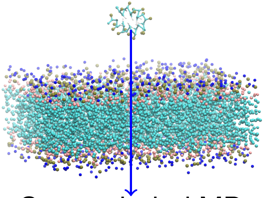


S.L. Bore et al., J. Chem. Theory Comput., (**2018**) 14 (2)

Outlook

- Parametrization: Toy-model $\rightarrow$ 20 amino-acids
  - Chemical specific $\tilde{\chi}_{k\ell}$-parameter
  - Strategies for modeling $V(\phi, \gamma)$
  - Machine-learning?
  - New PhD-student Manuel Carrera
- Electrostatics
  - Particle-field method for electrostatics
- Application of current model
  - Tsudo Yamanaka, Yamagata Univeristy, Japan

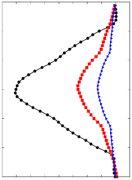
$\rightarrow$



Constrained MD

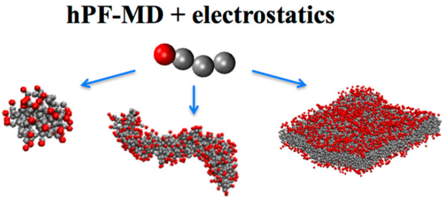
$\rightarrow$

$\Delta G(z) = ?$

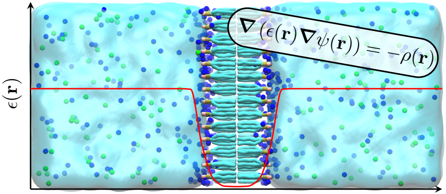


z

Electrostatics in Hybrid particle-field



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



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

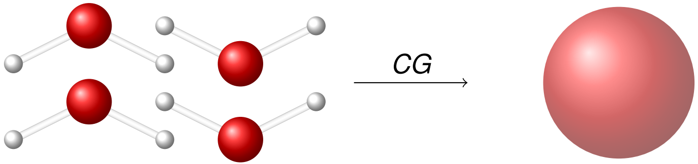
Electrostatic screening: Atomistic vs coarse-grained

Atomistic molecular dynamics:

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

Coarse-grained molecular dynamics:

- *Charge resolution is lost*
- *Screening modeled modelled indirectly*



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

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.*

Potential felt by particles of type K:

$$V_{\mathrm{ext},K}(\mathbf{r}) = \frac{\delta W_{\mathrm{elec}}}{\delta\phi_K(\mathbf{r})} = \underbrace{\int \mathrm{d}\mathbf{r}'\,\frac{\delta W_{\mathrm{elec}}}{\delta\mathbf{D}(\mathbf{r}')}\frac{\delta\mathbf{D}(\mathbf{r}')}{\delta\phi_K(\mathbf{r})}}_{q_K\psi(\mathbf{r})} + \underbrace{\frac{\delta W_{\mathrm{elec}}}{\delta\epsilon(\mathbf{r})}\frac{\partial\epsilon(\mathbf{r})}{\partial\phi_K(\mathbf{r})}}_{-\frac{1}{2}\frac{\partial\epsilon(\mathbf{r})}{\partial\phi_K(\mathbf{r})}|\mathbf{E}(\mathbf{r})|^2}$$

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

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

Modelling: density dependence of the dielectric

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.

Potential felt by particle of type K:

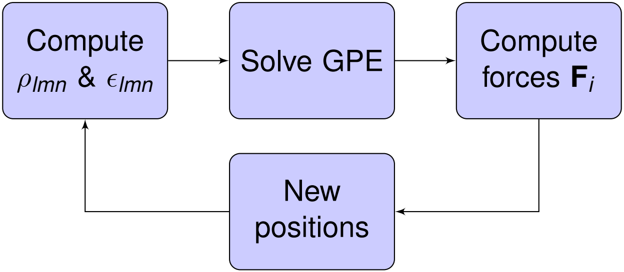
$$V_{\text{ext},K}(\mathbf{r}) = q_K \psi(\mathbf{r}) - \frac{1}{2} \frac{\epsilon_K - \epsilon(\mathbf{r})}{\phi_0(\mathbf{r})} |\mathbf{E}(\mathbf{r})|^2 ,$$

Forces on particle of type K:

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

*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)*

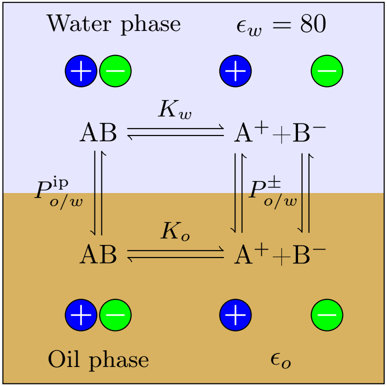
Partitioning of ions (1)

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

Distribution coefficient:

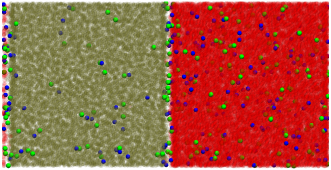
$$D_{o/w} = \frac{c_o}{c_w}$$

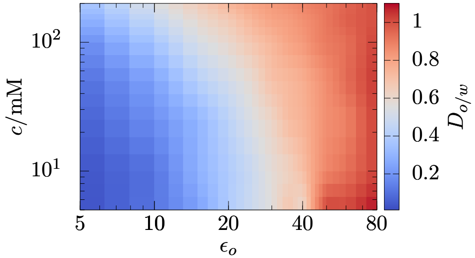
c_0 and c_w: concentration of ions within each phase.



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

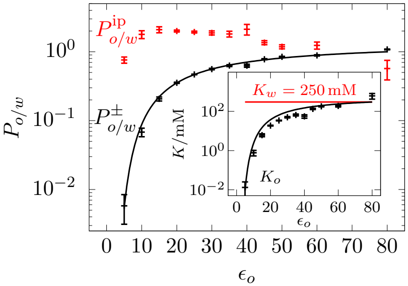
Partitioning of ions (2)





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

c: concentration of ions.

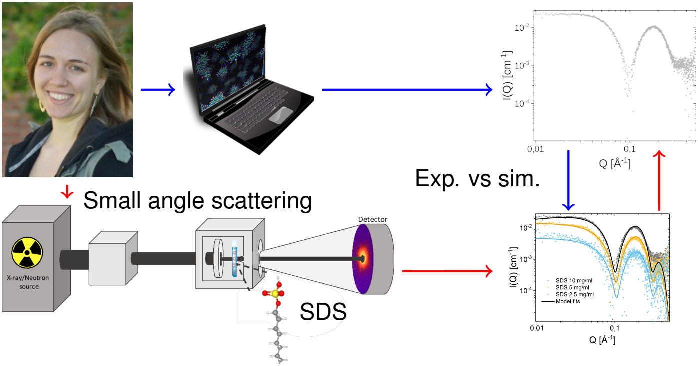


Born theory of ions:

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

Outlook

- Implementation
  - Parallel version
  - Improve on accuracy
- Application
  - Antonio De Nicola: Charged lipids
  - Ken Schafer: Molecular packing of SDS
  - Victoria Ariel Bjørnestad



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