



Systematic coarse graining using reversible work potentials

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Outline

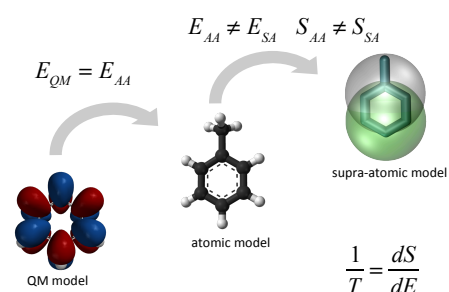
Monday, April 9

- Recap of free energy calculation methods
- Conditional Reversible Work (**CRW**) coarse graining

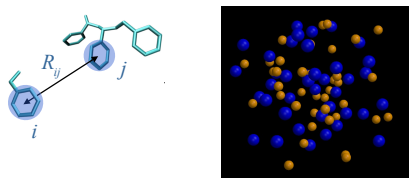
Tuesday, April 10

- Applications to soft matter problems
- Dynamically-consistent coarse-grained models

Systematic coarse graining



Systematic coarse graining



Recap of free energy calculation methods

Potential of mean force

- Thermodynamic integration (TI)
- Free energy perturbation (FEP)

Free energy

- Single-component systems

$$A(T, V, N) \quad G(T, P, N)$$

- Multicomponent systems

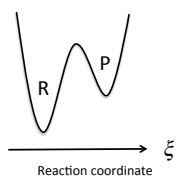
$$A(T, V, N_1, \dots, N_c) \quad G(T, P, N_1, \dots, N_c) \quad C \text{ components}$$

- Typically, we are only interested in the dependence of these free energies along a single parameter

$$A(V), G(P), G(T), \text{ etc.}$$

Potential of mean force (PMF)

- Free energy surface
- Internal coordinate ("reaction coordinate"): $\xi(\mathbf{R}^N)$



Potential of mean force (PMF)

Partition function

$$Q = c \int d\mathbf{R}^N e^{-\beta U(\mathbf{R}^N)} \quad \beta = \frac{1}{k_B T}$$

$$= c \int d\xi \int d\mathbf{R}^N e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi)$$

$$= \int d\xi Q(\xi)$$

Potential of mean force (free energy along ξ)

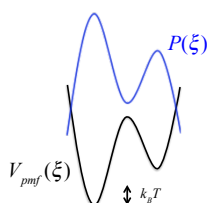
$$V_{pmf}(\xi) \equiv -k_B T \ln Q(\xi)$$

$$= -k_B T \ln \left[c \int d\mathbf{R}^N e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi) \right]$$

$$= -k_B T \ln P(\xi) + const.$$

Calculating the PMF

- Run MD or MC and sample $P(\xi)$
- Problematic if energy barriers are large ($> k_B T$)



Deriving the PMF

- Thermodynamic integration (TI)
- Thermodynamic (free energy) perturbation (FEP)
- Umbrella sampling
- Metadynamics
- ...

Thermodynamic integration (TI)

$$\begin{aligned} \frac{dV_{pmf}(\xi)}{d\xi} &= -k_B T \frac{d}{d\xi} \ln \int d\mathbf{R}^N e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi) \\ &= \dots \\ &= - \frac{\int d\mathbf{R}^N f_\xi e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi)}{\int d\mathbf{R}^N e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi)} \\ &= - \langle f_\xi \rangle_\xi \end{aligned}$$

Average over constrained ensemble

f_ξ : force along the direction ξ

den Otter & Briels, J. Chem. Phys. 109, 4139 (1998)

Thermodynamic integration (TI)

- Constrained equilibrium simulation
- Feasible only for low-dimensional PMFs
- Numerical integration of average constraint forces

$$V_{pmf}(\xi) = - \int_{\xi_0}^{\xi} \langle f_{\xi'} \rangle_{\xi'} d\xi'$$

Free energy perturbation (FEP)

- Split \mathbf{R}^N in internal coordinate ξ and all other degrees of freedom \mathbf{R}'

$$U(\mathbf{R}^N) \Rightarrow U(\xi, \mathbf{R}')$$

$$V_{pmf}(\xi) = -k_B T \ln \int d\mathbf{R}' e^{-\beta U(\mathbf{R}^N)} \delta(\xi(\mathbf{R}^N) - \xi)$$

$$= -k_B T \ln \int d\mathbf{R}' e^{-\beta U(\xi, \mathbf{R}')}$$

- Consider a small perturbation $\xi \rightarrow \xi + \Delta\xi$

Free energy perturbation (FEP)

$$V_{pmf}(\xi + \Delta\xi) - V_{pmf}(\xi) = -k_B T \ln \frac{\int d\mathbf{R}' e^{-\beta U(\xi + \Delta\xi, \mathbf{R}')}}{\int d\mathbf{R}' e^{-\beta U(\xi, \mathbf{R}')}}$$

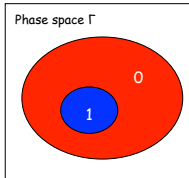
$$= -k_B T \ln \frac{\int d\mathbf{R}' e^{-\beta U(\xi + \Delta\xi, \mathbf{R}')} e^{-\beta U(\xi, \mathbf{R}')} e^{+\beta U(\xi, \mathbf{R}')}}{\int d\mathbf{R}' e^{-\beta U(\xi, \mathbf{R}')}}$$

$$= -k_B T \ln \frac{\int d\mathbf{R}' e^{-\beta[U(\xi + \Delta\xi, \mathbf{R}') - U(\xi, \mathbf{R}')] } e^{-\beta U(\xi, \mathbf{R}')}}{\int d\mathbf{R}' e^{-\beta U(\xi, \mathbf{R}')}}$$

$$= -k_B T \ln \left\langle e^{-\beta[U(\xi + \Delta\xi, \mathbf{R}') - U(\xi, \mathbf{R}')] } \right\rangle_{\xi}$$

Free energy perturbation (FEP)

Important regions in phase space Choice of reference and target states:



Forward

$$\Delta A_{0 \rightarrow 1} = A_1 - A_0 = -k_B T \ln \langle \exp[-\beta \Delta U] \rangle_0$$

$$= \int_{-\infty}^{\infty} P_0(\Delta U) \exp[-\beta \Delta U] d\Delta U$$

Reverse

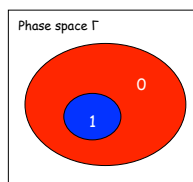
$$\Delta A_{0 \leftarrow 1} = A_1 - A_0 = k_B T \ln \langle \exp[\beta \Delta U] \rangle_1$$

$$= \int_{-\infty}^{\infty} P_1(\Delta U) \exp[\beta \Delta U] d\Delta U$$

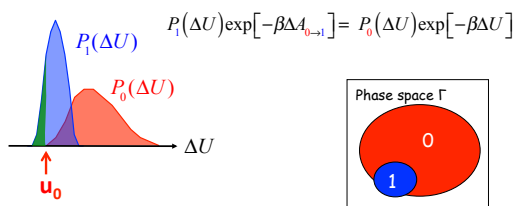
Choice of reference and target states

$$P_1(\Delta U) \exp[-\beta \Delta A_{0 \rightarrow 1}] = P_0(\Delta U) \exp[-\beta \Delta U]$$

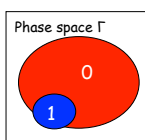
- We can invert them
- HS liquid – very precise but terribly inaccurate
- Choice forward or reverse: high to low entropy
- Averaging “forward” and “backward” result is not allowed



N. Lu, D.A. Kofke *J. Chem. Phys.* **114**, 7303 (2001)

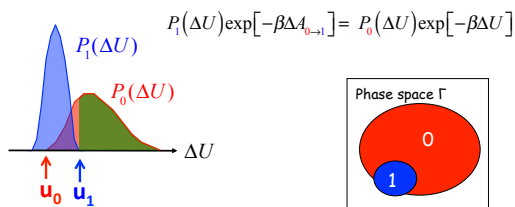


$$P_1(\Delta U) \exp[-\beta \Delta A_{0 \rightarrow 1}] = P_0(\Delta U) \exp[-\beta \Delta U]$$

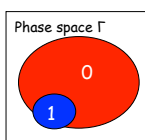


$$\frac{\exp[-\beta \Delta A^{exact}] - \exp[-\beta \Delta A_{0 \rightarrow 1}^{sim}]}{\exp[-\beta \Delta A^{exact}]} = \int_{-\infty}^{u_0} P_1(\Delta U) d\Delta U$$

Green area: Relative error in the $0 \rightarrow 1$ calculation



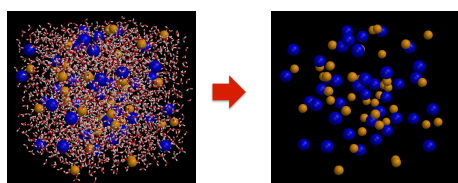
$$P_1(\Delta U) \exp[-\beta \Delta A_{0 \rightarrow 1}] = P_0(\Delta U) \exp[-\beta \Delta U]$$



$$\frac{\exp[\beta \Delta A^{exact}] - \exp[\beta \Delta A_{0 \leftarrow 1}^{sim}]}{\exp[\beta \Delta A^{exact}]} = \int_{u_1}^{\infty} P_0(\Delta U) d\Delta U$$

Green area: Relative error in the $0 \leftarrow 1$ calculation

Coarse graining



Coarse graining: effective potentials

- Ions (\mathbf{R}) and water (\mathbf{r})

$$Q = \int \int e^{-\beta V(\mathbf{R}, \mathbf{r})} d\mathbf{R} d\mathbf{r} = \int d\mathbf{R} \left[\int e^{-\beta V(\mathbf{R}, \mathbf{r})} d\mathbf{r} \right] \quad \beta = 1/k_B T$$

- If we define:

$$V^{eff}(\mathbf{R}) = -k_B T \ln \left[\int d\mathbf{r} e^{-\beta V(\mathbf{R}, \mathbf{r})} \right] \quad \text{multibody potential of mean force}$$

- We preserve thermodynamics (and structure \mathbf{R}):

$$Q = \int e^{-\beta V^{eff}(\mathbf{R})} d\mathbf{R}$$

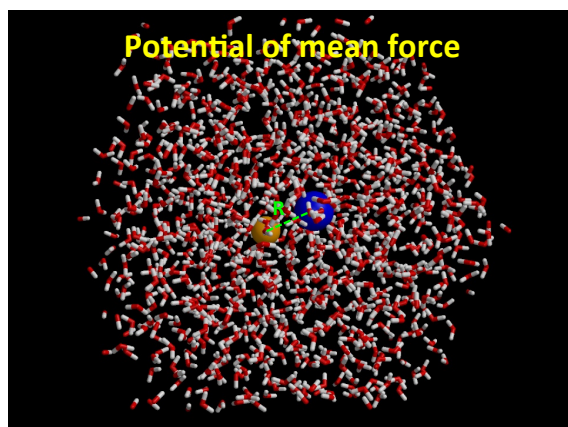
Effective pair potential

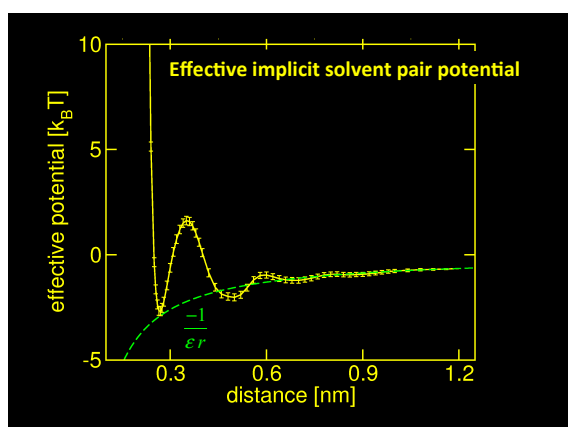
$$V^{eff}(\mathbf{R}) = \sum_{i < j} V_2(\mathbf{R}_i, \mathbf{R}_j) + \sum_{i < j < k} V_3(\mathbf{R}_i, \mathbf{R}_j, \mathbf{R}_k) + \dots$$

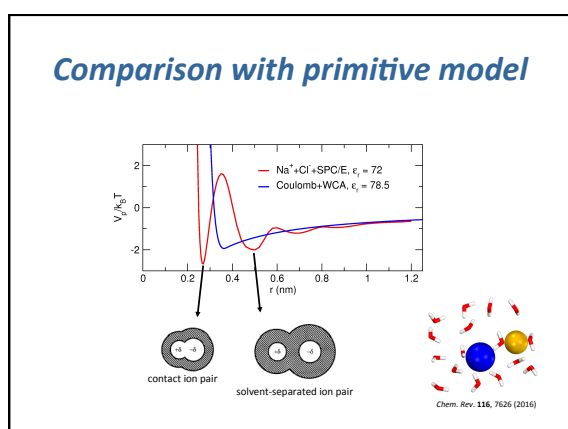
$$\approx \sum_{i < j} u^{eff}(|\mathbf{R}_i - \mathbf{R}_j|)$$

u^{eff} accounts for average multibody effects:

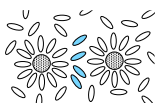
- Ion multiplet correlations
- Solvent-mediated correlations
- State dependent



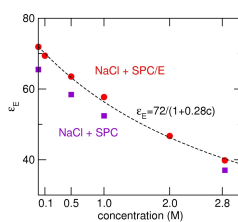




Solvent-mediated multibody effects



Solvent-mediated multibody effects



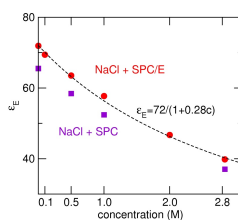
Transferable pair potential

$$V_c^{eff}(r, c) = V_p(r) + \frac{q_1 q_2}{4\pi\epsilon_0} \left(\frac{1}{\epsilon_E(c)} - \frac{1}{\epsilon_E(0)} \right) \frac{1}{r}$$

Solvent-mediated multibody effects

Adelman (1976), Friedman (1982), Levesque, Weis and Patey (1980)

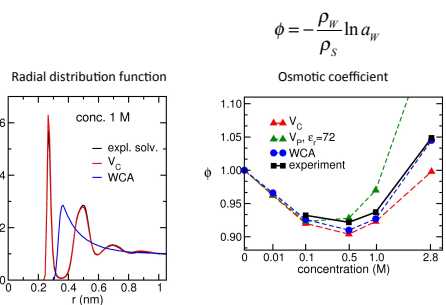
“... in any MM-level model for ionic solutions in which pairwise additivity is assumed, comparison with data for real solutions can only be made if the dielectric constant is replaced with one that depends on ion concentrations”



Transferable pair potential

$$V_c^{eff}(r, c) = V_p(r) + \frac{q_1 q_2}{4\pi\epsilon_0} \left(\frac{1}{\epsilon_E(c)} - \frac{1}{\epsilon_E(0)} \right) \frac{1}{r}$$

Electrolyte structure & thermodynamics



B. Hess, C. Holm, N.F.A. van der Vegt
Phys. Rev. Lett. **96**, 147801 (2006) *J. Chem. Phys.* **124**, 164509 (2006)

