

The slide features five light purple circles. Two are solid and positioned below the title. Three are hollow with a thin purple outline, arranged around the title: one above the first word, one above the second word, and one to the right of the second line of the title.

Comparison of Methods to Compute the Potential of Mean Force

Hasan Pašalić



Overview

- Introduction into Force Field Methods
- Articles
 - **Change of Free Energy during Adsorption of a Molecule**
(W. Billes, F. Bazant-Hegemark, M. Mecke, M. Wendland, J. Fischer, American Chemical Society **2003**)
 - **A Comparison of Methods to Compute the Potential of Mean Force**
(D. Trzesniak, A.-P. E. Kunz, W. F. van Gunsteren, ChemPhysChem **2007**)
 - **Pathway dependence of the efficiency of calculating free energy and entropy of solute-solute association in water**
(D. Trzesniak, W. F. van Gunsteren, Chemical Physics **2006**)

Force Field Methods



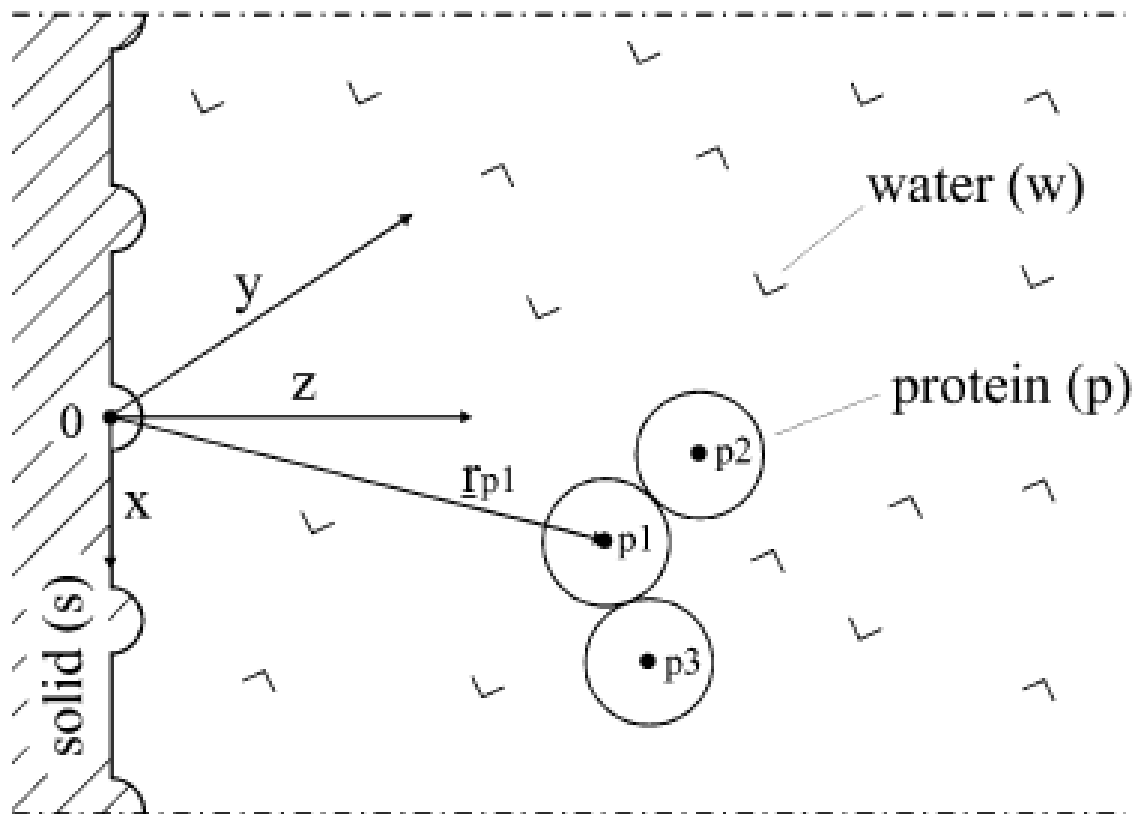
- different types of atoms
- Force Field Energy

$$E_{FF} = E_{str} + E_{bend} + E_{tors} + E_{vdw} + E_{el} + E_{cross}$$

- different types of Force Fields
- many parameters → reduction
- many particles → solvent

Change of Free Energy during Adsorption of a Molecule

- calculating the Helmholtz free energy ΔA



Change of Free Energy during Adsorption of a Molecule

- Route of the Mean Force

$$U = U_{pp} + U_{pw} + U_{ww} + U_{sp} + U_{sw}$$

$$Q_c = \int \exp\{-\beta U\} dr_{p2} \dots dr_{pM} dr_{w1} \dots dr_{wN}$$

$$A_c(r_{p1}) = -kT \ln Q_c(r_{p1})$$

$$\partial U / \partial r_{p1} = -F_{p1}$$

$$\partial A / \partial r_{p1} = \langle \partial U / \partial r_{p1} \rangle = -\langle F_{p1} \rangle$$

$$\langle F_{p1} \rangle = F_{sp1} + \langle \sum_j F_{pip1} + \sum_j F_{wjpl} \rangle$$

$$\Delta A = \int (\partial A / \partial r_{p1}) ds = -\int \langle F_{p1} \rangle ds$$

Change of Free Energy during Adsorption of a Molecule

- Route of the Local Density

$$n(r_{p1}) = (1/Z) \int \exp\{-\beta U\} dr_{p2} \dots dr_{pM} dr_{w1} \dots dr_{wN}$$

$$Z = \int \exp\{-\beta U\} dr_{p1} \dots dr_{pM} dr_{w1} \dots dr_{wN}$$

$$n(r_{p1}) = Q_c / Z$$

$$\exp(-\beta w) = V n(r_{p1})$$

$$\Delta w = -kT \Delta \ln n(r_{p1})$$

$$\partial w / \partial r_{p1} = -kT \partial \ln n(r_{p1}) / \partial r_{p1} = -kT \partial \ln Q_c / \partial r_{p1}$$

$$\partial w / \partial r_{p1} = \partial A / \partial r_{p1}$$

Change of Free Energy during Adsorption of a Molecule

- Link of both Route

$$\Delta A = \Delta w$$

$$\Delta \ln n(r_{pl}) = \beta \int \langle F_{pl} \rangle ds$$

→ Path Integral Route recommended

A Comparison of Methods to Compute the Potential of Mean Force

- (absolute) free energy F

$$F = -kT \ln Z$$

$$Z = (h^{3N} N!)^{-1} \int \int e^{-H(\mathbf{p}, \mathbf{q})/kT} d\mathbf{p} d\mathbf{q}$$

$$\pi(\mathbf{p}, \mathbf{q}) = \frac{e^{-H(\mathbf{p}, \mathbf{q})/kT}}{\int \int e^{-H(\mathbf{p}, \mathbf{q})/kT} d\mathbf{p} d\mathbf{q}}$$

$$P_R(R') = \frac{\int \int e^{-H(\mathbf{p}, \mathbf{q})/kT} \delta(R' - R(\mathbf{q})) d\mathbf{p} d\mathbf{q}}{\int \int e^{-H(\mathbf{p}, \mathbf{q})/kT} d\mathbf{p} d\mathbf{q}}$$

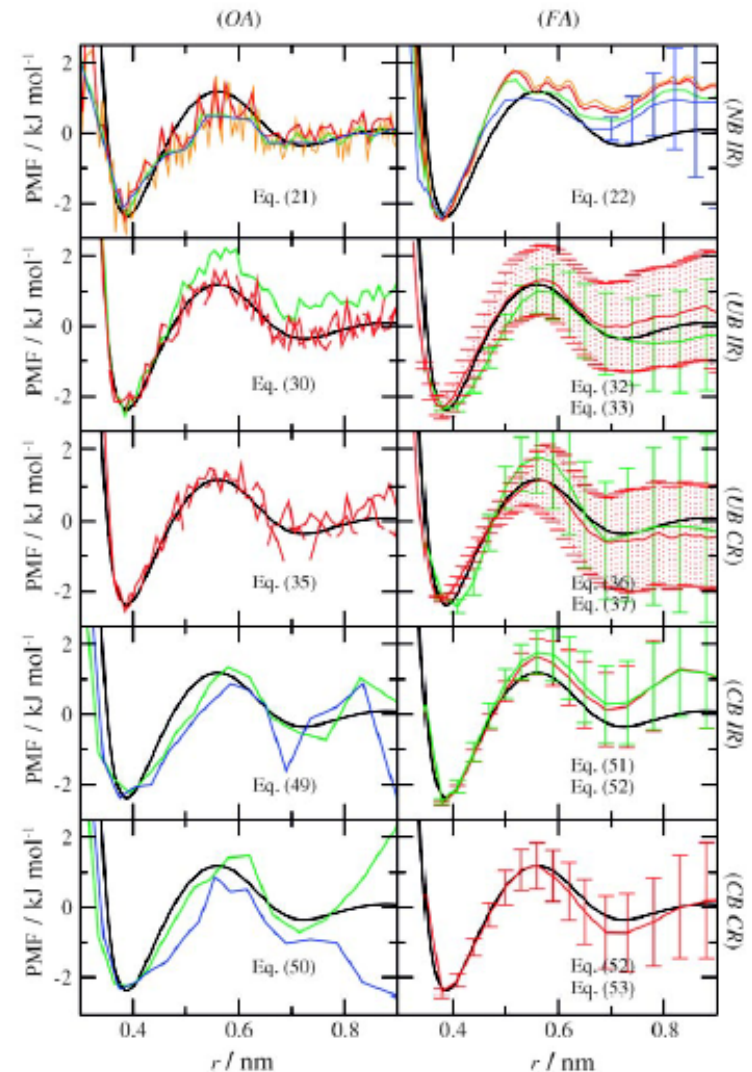
$$F_R(R') = -kT \ln P_R(R') - kT \ln Z$$

A Comparison of Methods to Compute the Potential of Mean Force

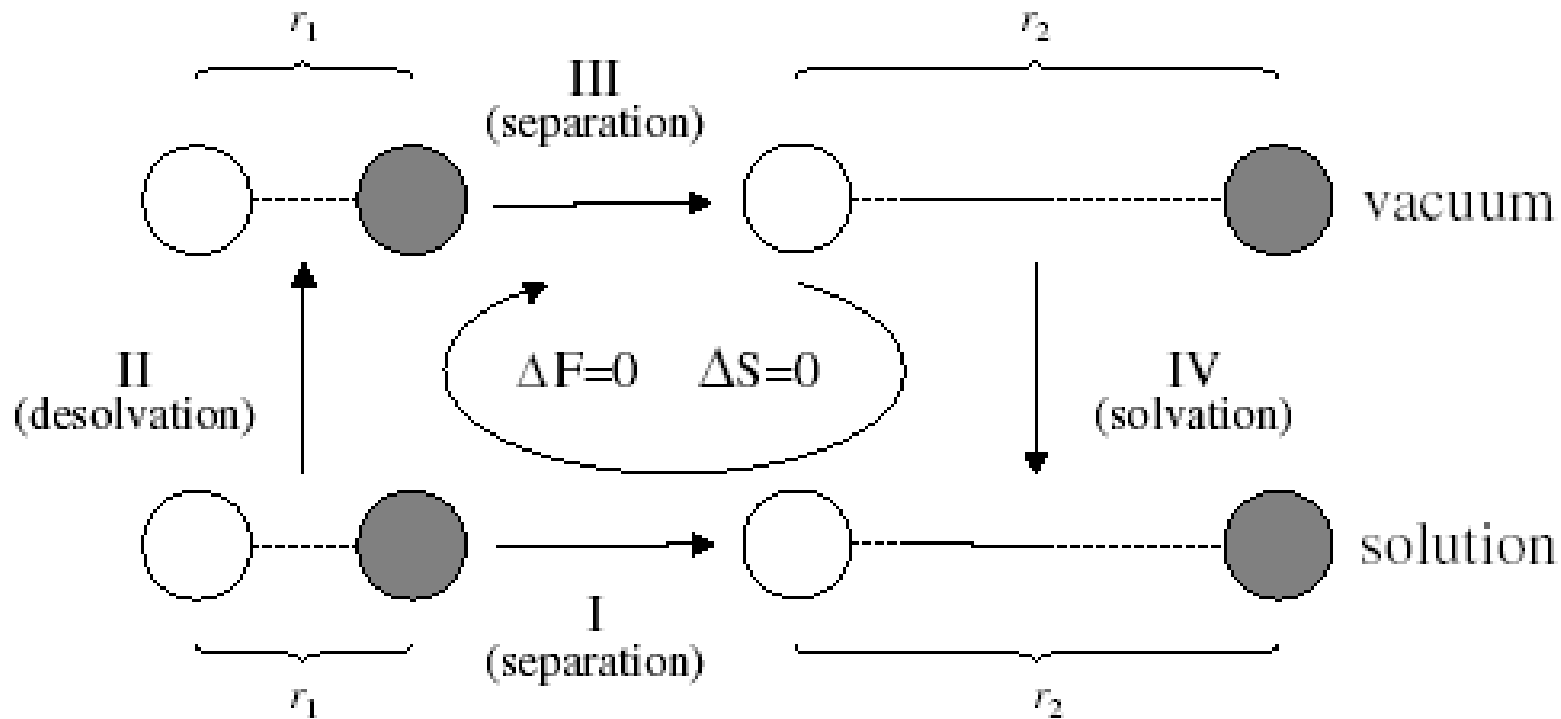
$$F_R(R') = F_R(\infty) + \int_{\infty}^{R'} \frac{dF_R(R'')}{dR''} dR''$$

Simulations

- no bias
- umbrella bias
- Constraint bias



Pathway dependence of the efficiency of calculating free energy and entropy of solute-solute association in water



Pathway dependence of the efficiency of calculating free energy and entropy of solute-solute association in water

Thermodynamic Integration

$$\Delta F_{\text{assoc}}^{r_1 \rightarrow r} = \int_{r_1}^r \left\langle \frac{\partial E}{\partial R} \right\rangle_R dR$$

$$T \Delta S_{\text{assoc}}^{r_1 \rightarrow r} = -\frac{1}{kT} \int_{r_1}^r \left[\left\langle E \frac{\partial E}{\partial R} \right\rangle_R - \langle E \rangle_R \left\langle \frac{\partial E}{\partial R} \right\rangle_R \right] dR$$

$$= -\frac{1}{kT} \int_{r_1}^r \left[\left\langle E_{uu,uv} \frac{\partial E_{uu,uv}}{\partial R} \right\rangle_R - \langle E_{uu,uv} \rangle_R \left\langle \frac{\partial E_{uu,uv}}{\partial R} \right\rangle_R \right] dR + [\langle E_{vv} \rangle_r - \langle E_{vv} \rangle_{r_1}]$$

Pathway dependence of the efficiency of calculating free energy and entropy of solute-solute association in water

- Coupling Parameter λ

$$\Delta F_{\text{solv}}^{r_i} = \int_0^1 \left\langle \frac{\partial E}{\partial \lambda} \right\rangle_{r_i; \lambda} d\lambda$$

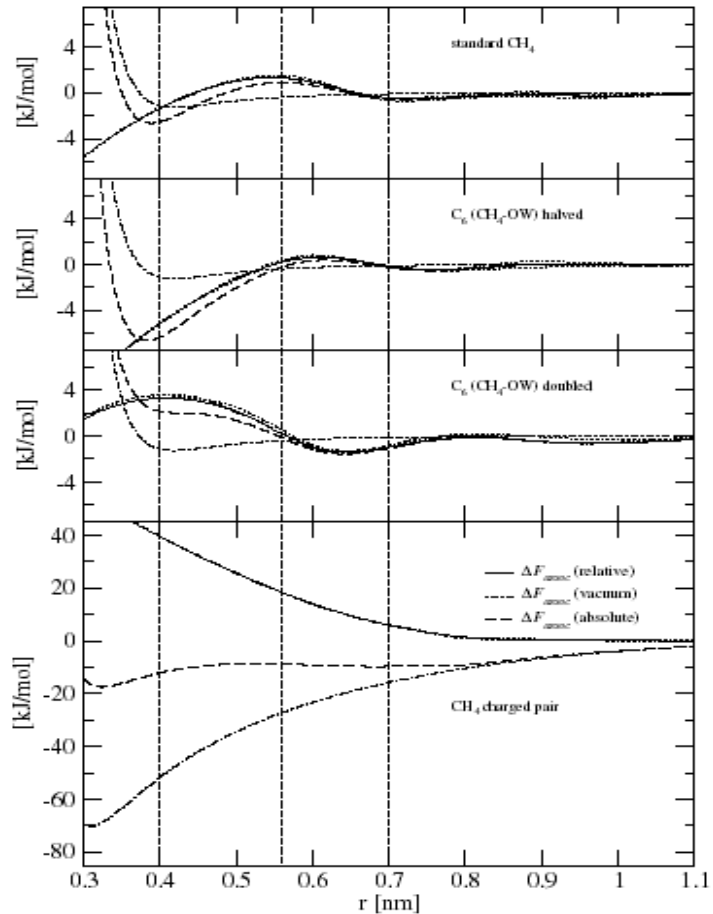
$$T\Delta S_{\text{solv}}^{r_i} = -\frac{1}{kT} \int_0^1 \left[\left\langle E \frac{\partial E}{\partial \lambda} \right\rangle_{r_i; \lambda} - \langle E \rangle_{r_i; \lambda} \left\langle \frac{\partial E}{\partial \lambda} \right\rangle_{r_i; \lambda} \right] d\lambda,$$

$$= -\frac{1}{kT} \int_0^1 \left[\left\langle E_{uu,uv} \frac{\partial E_{uu,uv}}{\partial \lambda} \right\rangle_{r_i; \lambda} \right.$$

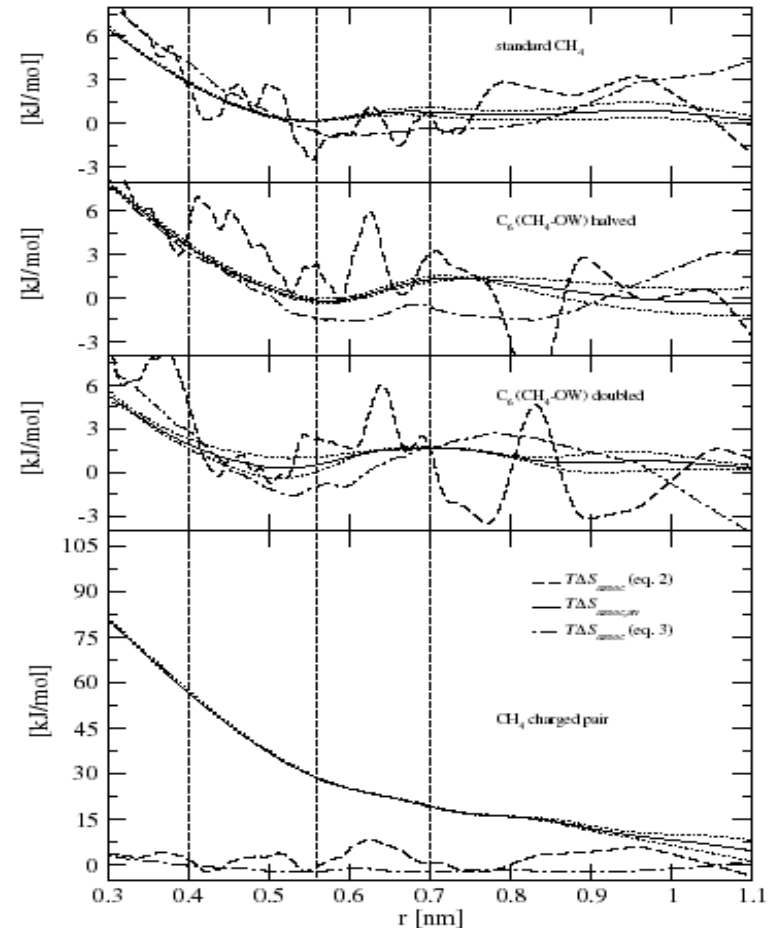
$$\left. - \langle E_{uu,uv} \rangle_{r_i; \lambda} \left\langle \frac{\partial E_{uu,uv}}{\partial \lambda} \right\rangle_{r_i; \lambda} \right] d\lambda$$

$$+ [\langle E_{vv} \rangle_{r_i; \lambda=1} - \langle E_{vv} \rangle_{r_i; \lambda=0}],$$

Pathway dependence of the efficiency of calculating free energy and entropy of solute-solute association in water



Free energy



Entropy



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