Free Energy Calculation

Outline

- Free energies: classical thermodynamics
- Free energies: statistical thermodynamics
- Monte Carlo simulations: what went wrong?
- Experiments: how to make a chemical potential-meter?
- Free energy techniques:
    - Thermodynamic integration
    - Krikwood coupling parameter
    - Widom test particle insertion
    - Overlapping distribution
    - Histogram method
    - Umbrella sampling

Chemical potential

Until now we have assumed that most of our systems are closed: NVE

Let us now assume that our system can exchange matter

First law

$$dU = TdS - pdV + \sum_i \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j} dn_i$$

Change in U if we add one mole of component i at constant S, V, n_j

Chemical potential

$$\mu_i \equiv \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j}$$

How is the chemical potential is defined in term of A,G,H

$$A \equiv U - TS$$

$$dA = dU - TdS - SdT$$

Using

$$dU = TdS - pdV + \sum_i \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j} dn_i$$

$$dA = -SdT - pdV + \sum_i \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j} dn_i$$

$$dA = -SdT - pdV + \sum_i \left(\frac{\partial A}{\partial n_i}\right)_{T,V,n_j} dn_i$$

Chemical potential

$$\mu_i \equiv \left(\frac{\partial A}{\partial n_i}\right)_{T,V,n_j} = \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j}$$

Energy $$dU = TdS - pdV + \sum_i \mu_i dn_i$$

Enthalpy $$dH = TdS + Vdp + \sum_i \mu_i dn_i$$

Helmholtz free energy $$dA = -SdT - pdV + \sum_i \mu_i dn_i$$

Gibbs free energy $$dG = -SdT + Vdp + \sum_i \mu_i dn_i$$

Chemical potential

$$\mu_i \equiv \left(\frac{\partial U}{\partial n_i}\right)_{S,V,n_j} = \left(\frac{\partial H}{\partial n_i}\right)_{S,p,n_j} = \left(\frac{\partial A}{\partial n_i}\right)_{T,V,n_j} = \left(\frac{\partial G}{\partial n_i}\right)_{T,p,n_j}$$

G is extensive

How does the Gibbs free energy change if the system is increased by a factor k?

$$\Delta G = kG - G = (k-1)G$$

$$dG = -SdT + Vdp + \sum_i \mu_i dn_i$$

Integration gives

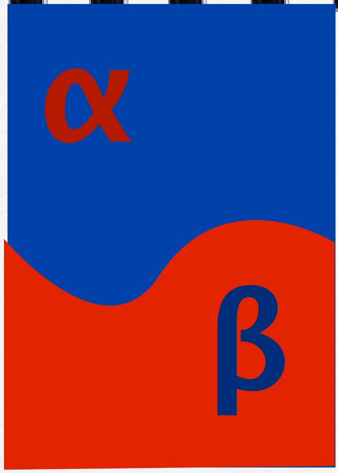
$$\Delta G = 0 + 0 + \sum_i \mu_i \Delta n_i$$

$$\Delta G = 0 + 0 + \sum_i \mu_i (k-1) n_i$$

Which gives:

$$G = \sum_i \mu_i n_i$$

Equilibrium



Let us consider a system with a constant number of particles, volume, and energy.

This system consists of two phases α and β

Question: When are these two systems in equilibrium?

$$dS = dS^{\alpha} + dS^{\beta} = 0 \qquad dS^{\alpha} = \frac{dU^{\alpha}}{T^{\alpha}} + \frac{p^{\alpha}}{T^{\alpha}} dV^{\alpha} - \sum_i \frac{\mu_i^{\alpha}}{T^{\alpha}} dn_i^{\alpha}$$

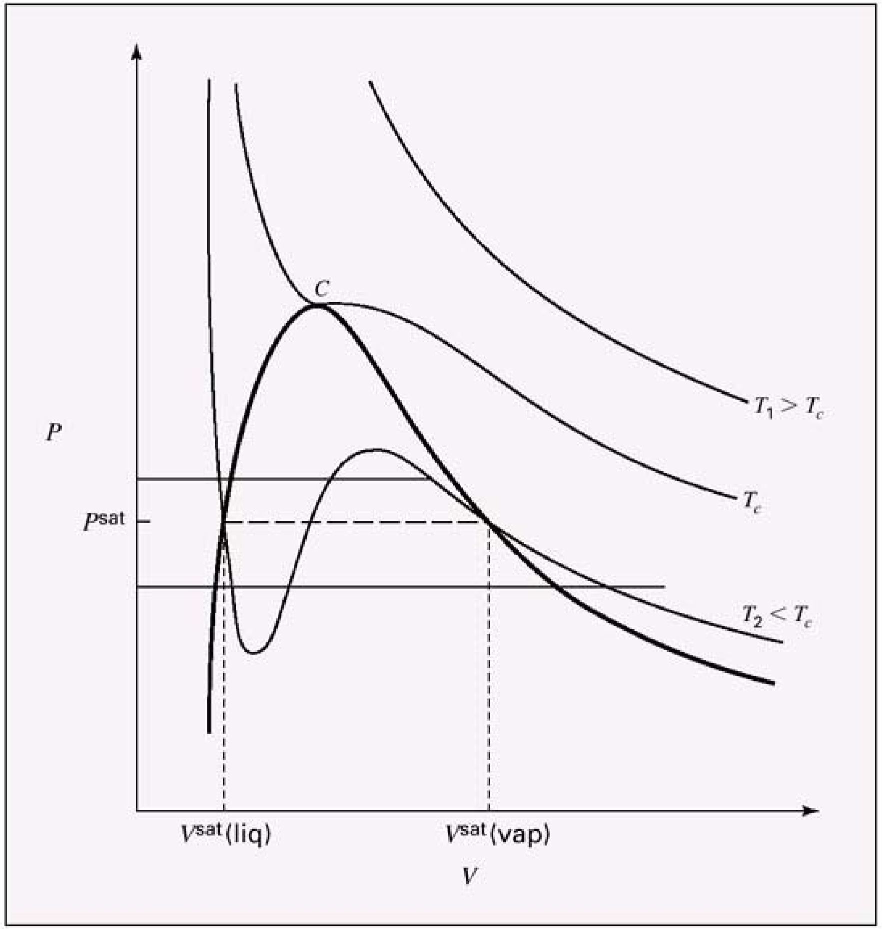
$$dS^{\alpha} + dS^{\beta} = \left(\frac{1}{T^{\alpha}} - \frac{1}{T^{\beta}}\right) dU^{\alpha} + \left(\frac{p^{\alpha}}{T^{\alpha}} - \frac{p^{\beta}}{T^{\beta}}\right) dV^{\alpha}$$

$$- \sum_i \left(\frac{\mu_i^{\alpha}}{T^{\alpha}} - \frac{\mu_i^{\beta}}{T^{\beta}}\right) dn_i^{\alpha}$$

Equilibrium: $T^{\alpha} = T^{\beta} \wedge p^{\alpha} = p^{\beta} \wedge \mu_i^{\alpha} = \mu_i^{\beta}$

Vapor-liquid equilibria

Equilibrium: $T^\alpha = T^\beta \wedge p^\alpha = p^\beta \wedge \mu^\alpha = \mu^\beta$



Van der Waals equation of

$$P = \frac{k_B T}{v - b} - \frac{a}{v^2}$$

We need to compute the chemical potential

Chemical potential

In equilibrium we have: $\mu^{\alpha}(T, V^{\alpha}) = \mu^{\beta}(T, V^{\beta})$

$$\Delta\mu^{\alpha\beta} = \mu^{\alpha}(T, V^{\alpha}) - \mu^{\beta}(T, V^{\beta})$$

Equilibrium if:

$$\Delta\mu^{\alpha\beta} = \int_{\beta}^{\alpha} dV \left(\frac{\partial\mu}{\partial V}\right)_{T,n} = 0$$

How to relate this to the equation of state?

Recall that we derived the relation between changes in the chemical potential and temperature and pressure (Gibbs-Duhem)

$G = \sum_i \mu_i n_i$ or, for a pure component $G = n\mu$

$\sum_i n_i d\mu_i = -SdT + Vdp$ or $n d\mu = -SdT + Vdp$

$$d\mu = -sdT + vdp$$

$$\Delta\mu^{\alpha\beta} = \int_\beta^\alpha dv \left(\frac{\partial\mu}{\partial v}\right)_{T,n} = 0$$

$$d\mu = -sdT + vdp$$

$$\mu = \mu(T, P)$$

We need to find $\left(\frac{\partial\mu}{\partial v}\right)_T$

$$\left(\frac{\partial\mu}{\partial v}\right)_T = \left(\frac{\partial\mu}{\partial T}\right)_p \left(\frac{\partial T}{\partial v}\right)_T + \left(\frac{\partial\mu}{\partial p}\right)_T \left(\frac{\partial p}{\partial v}\right)_T$$

=0 =v

$$\left(\frac{\partial\mu}{\partial v}\right)_T = 0 + v\left(\frac{\partial p}{\partial v}\right)_T$$

Equation of state gives us the chemical potential

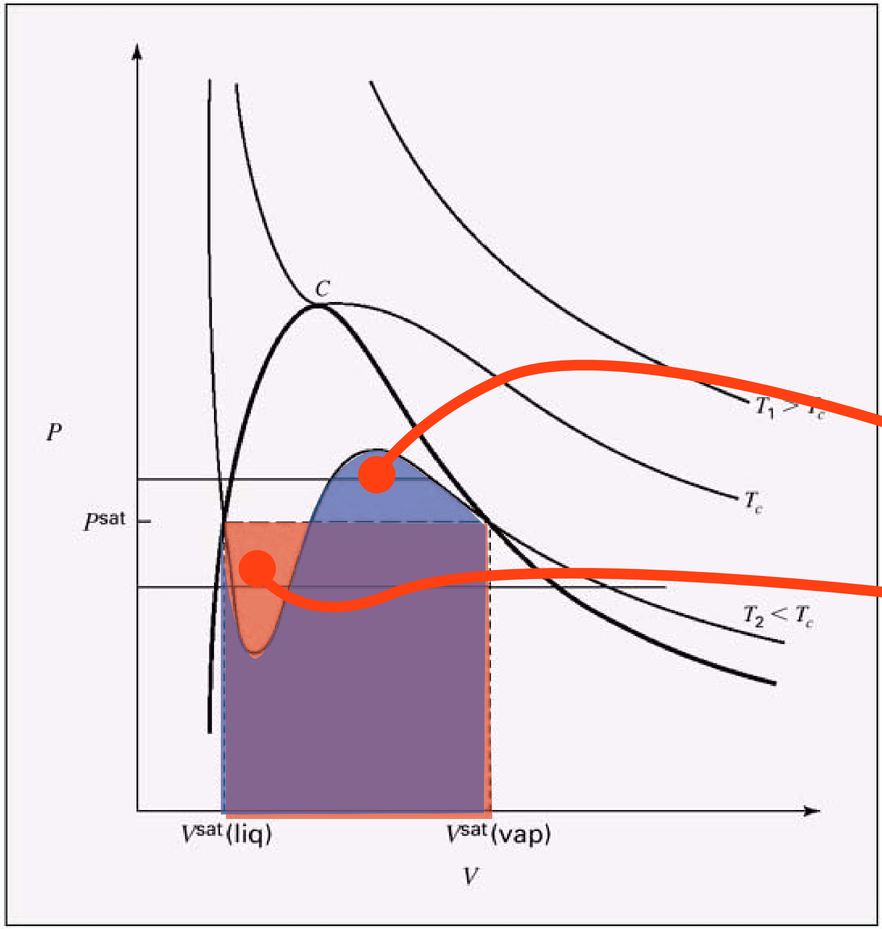
Which gives:

$$\Delta\mu^{\alpha\beta} = \int_\beta^\alpha dv v \left(\frac{\partial p}{\partial v}\right)_T = vp|_\alpha^\beta - \int_\beta^\alpha p dv$$

$$= -\int_\beta^\alpha (p - p_{\text{coex}}) dv$$

Vapor-liquid equilibria

Equilibrium: $T^{\alpha} = T^{\beta} \wedge p^{\alpha} = p^{\beta} \wedge \mu^{\alpha} = \mu^{\beta}$



Equal chemical potential if

$$\int_{\beta}^{\alpha} (p - p_{\mathrm{coex}}) dv = 0$$

Equilibrium if these areas are equal

NVT ensemble

Define de Broglie wave length:

$$\Lambda \equiv \left(\frac{h^2 \beta}{2\pi m} \right)^{1/2}$$

Partition function:

$$Q(N,V,T) = \frac{1}{\Lambda^{3N} N!} \int \mathrm{d}\mathbf{r}^N \exp\left[-\beta U\left(r^N\right) \right]$$

Free energy:

$$F = -\frac{1}{\beta} \ln Q(N,V,T)$$

Example: ideal gas

$$Q(N,V,T) = \frac{1}{\Lambda^{3N} N!} \int d\mathbf{r}^N \exp\left[-\beta U\left(r^N\right)\right]$$

$$= \frac{1}{\Lambda^{3N} N!} \int d\mathbf{r}^N 1 = \frac{V^N}{\Lambda^{3N} N!}$$

Free energy:

$$\beta F = -\ln\left(\frac{V^N}{\Lambda^{3N} N!}\right)$$

$$\approx N \ln \Lambda^3 + N \ln\left(\frac{N}{V}\right) = N \ln \Lambda^3 + N \ln \rho$$

Thermo recall (3)

Helmholtz Free energy:

$$\mathrm{d}F = -S\mathrm{d}T - p\mathrm{d}V$$

Pressure

$$\left(\frac{\partial F}{\partial V}\right)_T = -P$$

Energy:

$$\left(\frac{\partial F/T}{\partial 1/T}\right) = \left(\frac{\partial \beta F}{\partial \beta}\right) = E$$

Free energy: $$\beta F = N \ln \Lambda^3 + N \ln\left(\frac{N}{V}\right)$$

Pressure: $$P = -\left(\frac{\partial F}{\partial V}\right)_T = \frac{N}{\beta V}$$

Energy: $$E = \left(\frac{\partial \beta F}{\partial \beta}\right) = \frac{3N}{\Lambda}\frac{\partial \Lambda}{\partial \beta} = \frac{3}{2} N k_B T$$

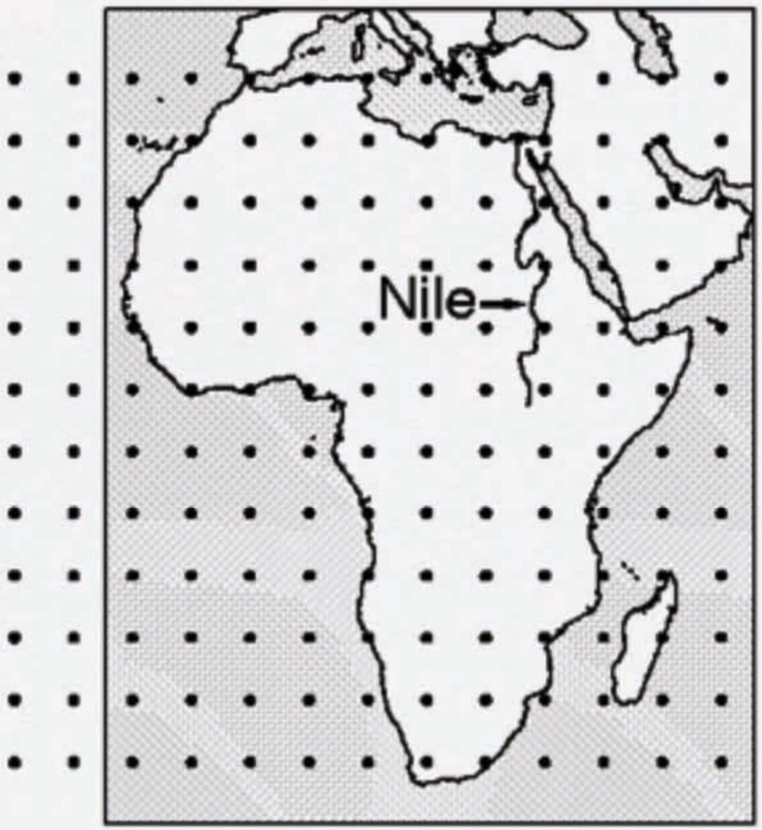
Chemical potential: $$\mu_{\mathrm{i}} = \left(\frac{\partial \mathrm{F}}{\partial N_i}\right)_{T,V,N_j}$$

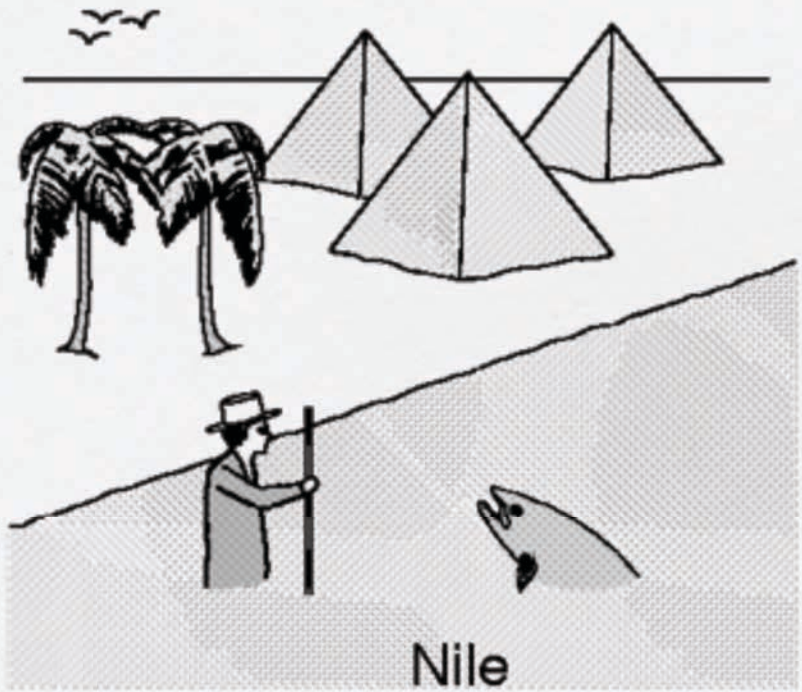
$$\beta\mu^{IG} = \ln \Lambda^3 + \ln \rho + 1$$

$$\beta\mu^{IG} = \beta\mu^0 + \ln \rho$$

Monte Carlo simulation

What is the difference between <A> and F?





The price of importance sampling

$$\langle A \rangle_{NVT} = \frac{1}{Q_{NVT}} \frac{1}{\Lambda^{3N} N!} \int d\mathbf{r}^N A(\mathbf{r}^N) \exp\left[-\beta U(\mathbf{r}^N)\right]$$

$$= \int d\mathbf{r}^N A(\mathbf{r}^N) P(\mathbf{r}^N) = \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) P(\mathbf{r}^N)}{\int d\mathbf{r}^N P(\mathbf{r}^N)}$$

$$P(\mathbf{r}^N) = \frac{\exp\left[-\beta U(\mathbf{r}^N)\right]}{Q_{NVT} \Lambda^{3N} N!}$$

$$= \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) C \exp\left[-\beta U(\mathbf{r}^N)\right]}{\int d\mathbf{r}^N C \exp\left[-\beta U(\mathbf{r}^N)\right]} = \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) \exp\left[-\beta U(\mathbf{r}^N)\right]}{\int d\mathbf{r}^N \exp\left[-\beta U(\mathbf{r}^N)\right]}$$

Generate configuration using MC:

$$\left\{ \mathbf{r}_1^N, \mathbf{r}_2^N, \mathbf{r}_3^N, \mathbf{r}_4^N \cdots, \mathbf{r}_M^N \right\}$$

$$\bar{A} = \frac{1}{M} \sum_{i=1}^{M} A(\mathbf{r}_i^N) = \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) P^{MC}(\mathbf{r}^N)}{\int d\mathbf{r}^N P^{MC}(\mathbf{r}^N)}$$

with

$$P^{MC}(\mathbf{r}^N) = C^{MC} \exp\left[-\beta U(\mathbf{r}^N)\right]$$

$$= \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) C^{MC} \exp\left[-\beta U(\mathbf{r}^N)\right]}{\int d\mathbf{r}^N C^{MC} \exp\left[-\beta U(\mathbf{r}^N)\right]}$$

$$= \frac{\int d\mathbf{r}^N A(\mathbf{r}^N) \exp\left[-\beta U(\mathbf{r}^N)\right]}{\int d\mathbf{r}^N \exp\left[-\beta U(\mathbf{r}^N)\right]}$$

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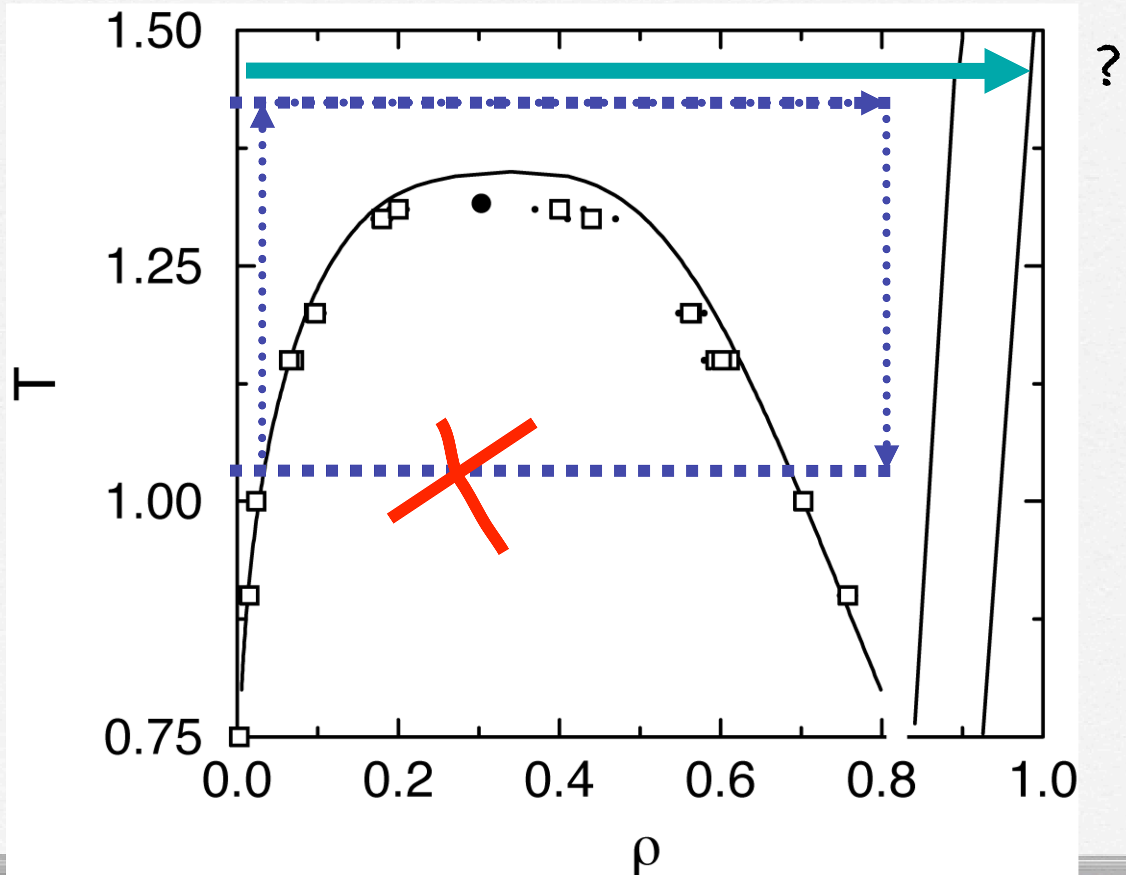
Experimental (2)

$$\left(\frac{\partial F}{\partial V}\right)_{N,T} = -P \qquad F(P) - F(P_0) = -\int_{V_0}^{V} \left(\frac{\partial F}{\partial V}\right)_{N,T} \mathrm{d}V$$



- Works always for vapor-liquid
- Requires a large number of simulations to fit the equation of state
- Does not work for solid-liquid

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Thermodynamic integration

Coupling parameter

$$U(\lambda) = (1-\lambda)U_I + \lambda U_{II}$$

$$U(\lambda) = U^{LJ} + \lambda U^{\text{dipole-dipole}}$$

$U(0) = U^{LJ}$ Lennard-Jones

$U(1) = U^{\text{Stockm}}$ Stockmayer

$$Q_{NVT}(\lambda) = \frac{1}{\Lambda^{3N} N!} \int \mathrm{d}\mathbf{r}^N \exp\left[-\beta U(\lambda)\right]$$

$$Q_{NVT}(\lambda) = \frac{1}{\Lambda^{3N} N!} \int \mathrm{d}r^N \exp\left[-\beta U(\lambda)\right]$$

$$F = -\frac{1}{\beta} \ln\left(Q_{NVT}\right)$$

$$\left(\frac{\partial F(\lambda)}{\partial \lambda}\right)_{N,T} = -\frac{1}{\beta}\frac{\partial}{\partial \lambda}\ln(Q) = -\frac{1}{\beta}\frac{1}{Q}\frac{\partial Q}{\partial \lambda}$$

$$= \frac{\int \mathrm{d}r^N \left(\partial U(\lambda)/\partial \lambda\right)\exp\left[-\beta U(\lambda)\right]}{\int \mathrm{d}r^N \exp\left[-\beta U(\lambda)\right]} = \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_\lambda$$

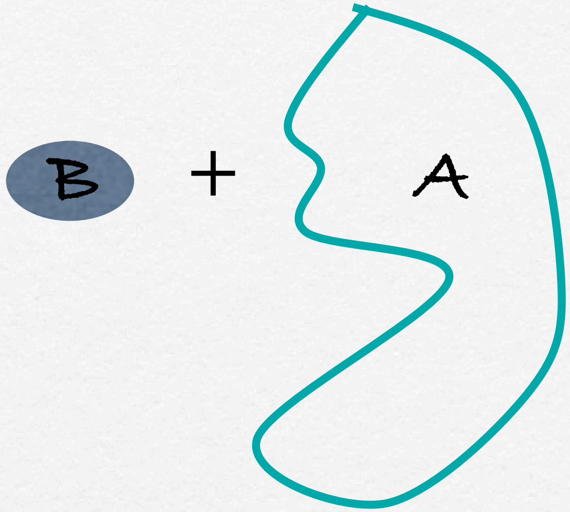
Free energy as ensemble average!

$$F(\lambda = 1) - F(\lambda = 0) = \int \mathrm{d}\lambda \left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_\lambda$$

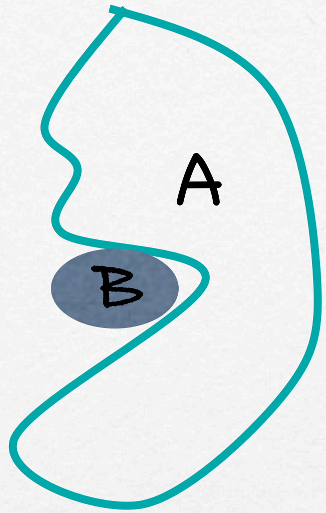
$$U(\lambda) = (1-\lambda)U_I + \lambda U_{II}$$

$$\left\langle \frac{\partial U(\lambda)}{\partial \lambda} \right\rangle_\lambda = \left\langle U_{II} - U_I \right\rangle_\lambda$$

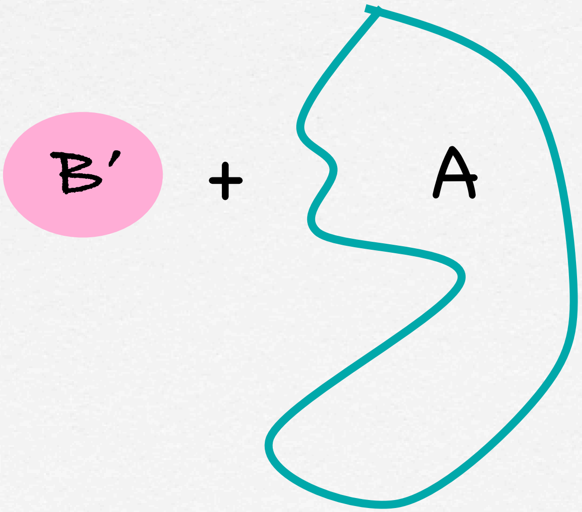
Molecular association



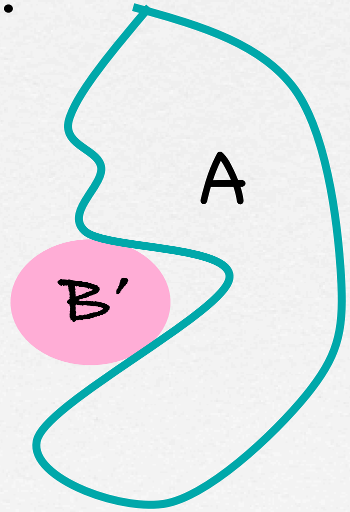
ΔG_1 →



Experimentally we can measure the free energies of association.



ΔG_2 →



We would like to have the molecule which has the optimal free energy of association

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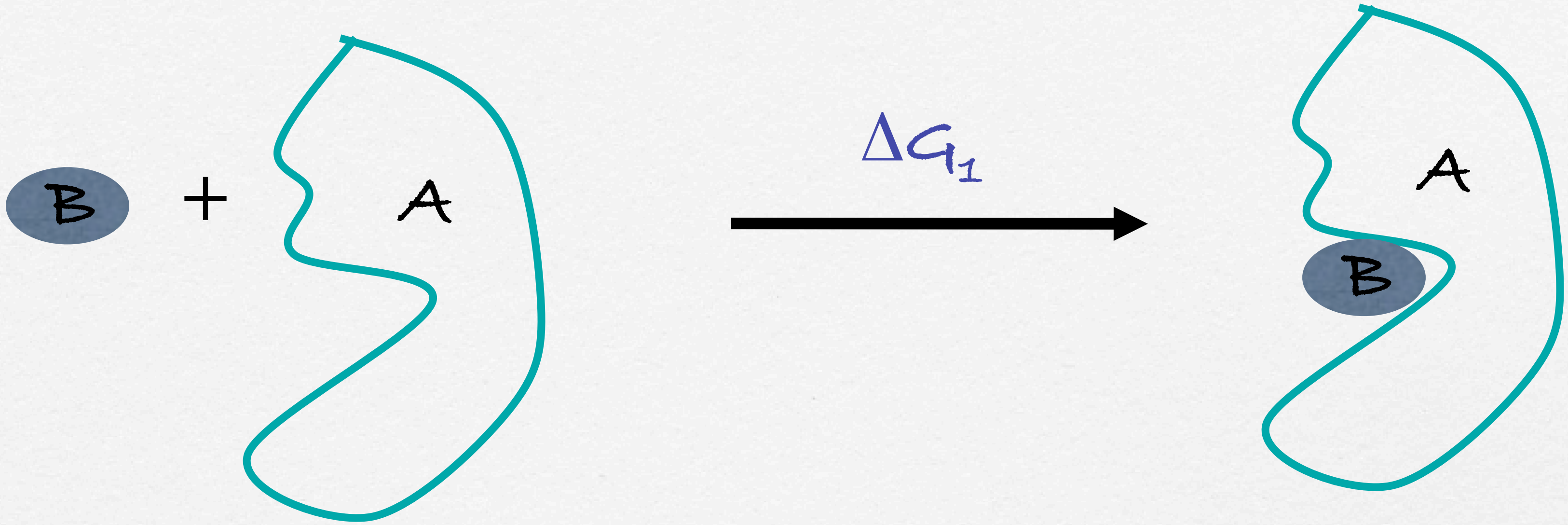
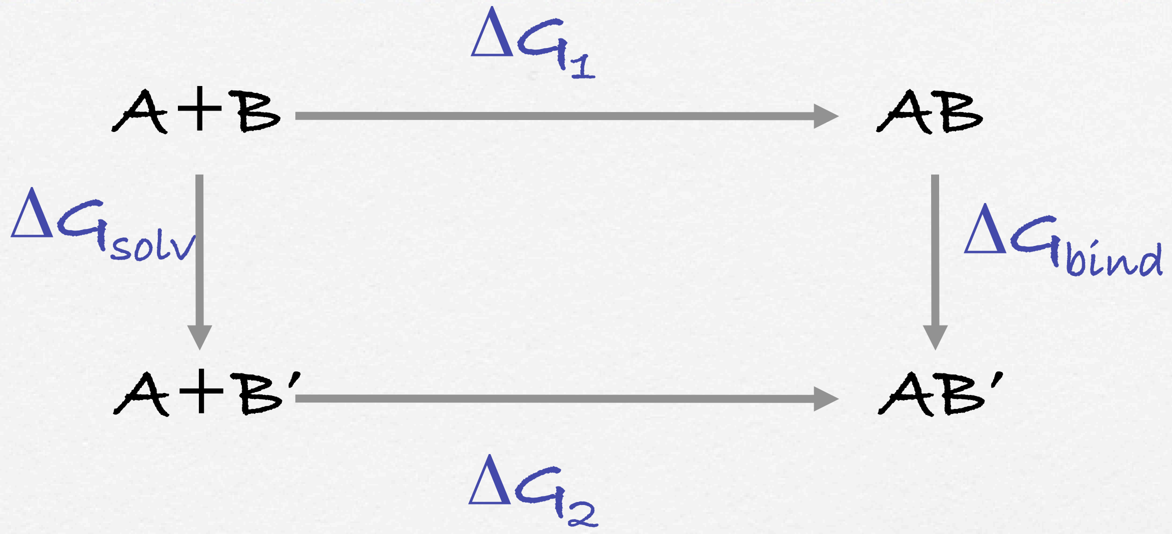
How to compute the free energy of association?



Solution: compute the **potential of mean force** =
the reversible work required to bring B to the host



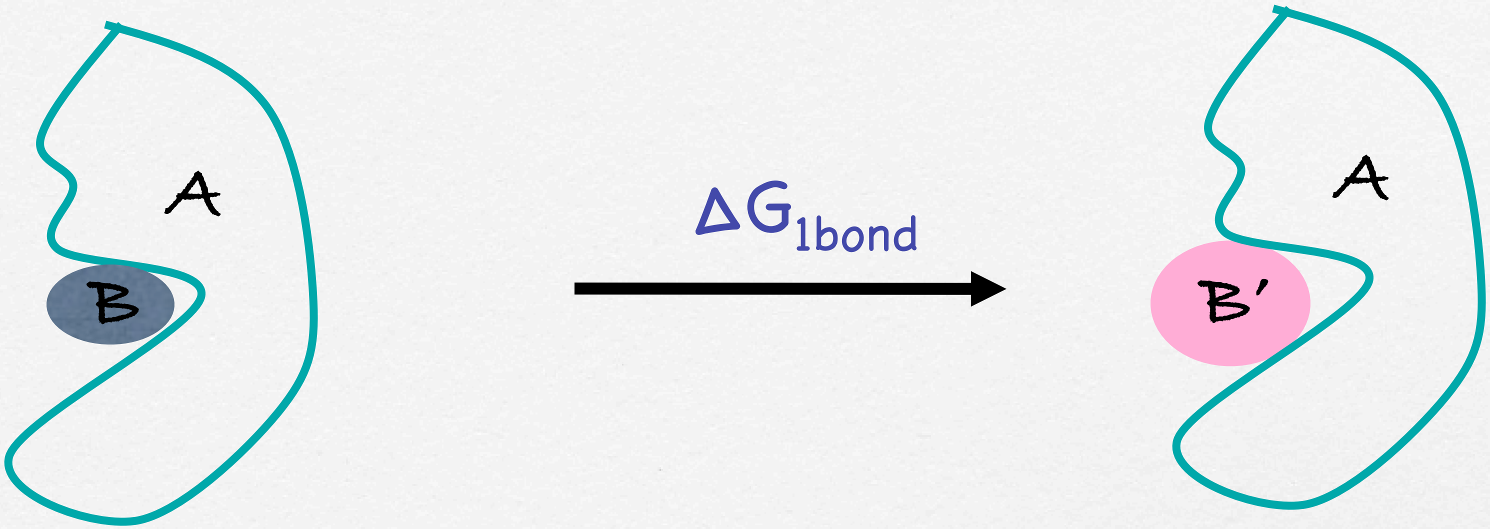
We do not need to know the absolute value, but to see whether B or B′ is better we need to know only:

$$\Delta\Delta G = \Delta G_1 - \Delta G_2$$

$$U(\lambda) = U(B) + \lambda\left[U(B') - U(B)\right]$$

In a simulation it is easier to compute:

$$\Delta\Delta G = \Delta G_{bind} - \Delta G_{solv}$$



$$U(\lambda)=U(B)+\lambda\left[U(B')-U(B)\right]$$

$$F(\lambda=1)-F(\lambda=0)=\int d\lambda\left\langle\frac{\partial U(\lambda)}{\partial\lambda}\right\rangle_{\lambda}$$

When will this computation be accurate?

Chemical potential

$$Q_{NVT} = \frac{1}{\Lambda^{3N} N!} \int d\mathrm{r}^N \exp\left[-\beta U\left(\mathrm{r}^N\right)\right]$$

Scaled coordinates: s=r/L

$$Q_{NVT} = \frac{V^N}{\Lambda^{3N} N!} \int d\mathrm{s}^N \exp\left[-\beta U\left(\mathrm{s}^N; L\right)\right]$$

$$\beta F = -\ln\left(Q_{NVT}\right)$$

$$= -\ln\left(\frac{V^N}{\Lambda^{3N} N!}\right) - \ln\left(\int d\mathrm{s}^N \exp\left[-\beta U\left(\mathrm{s}^N; L\right)\right]\right)$$

$$= -N \ln\left(\frac{1}{\Lambda^3 \rho}\right) - \ln\left(\int d\mathrm{s}^N \exp\left[-\beta U\left(\mathrm{s}^N; L\right)\right]\right)$$

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Chemical potential: Widom test particle method

$$\beta F = -\ln\left(Q_{NVT}\right)$$

$$= -N\ln\left(\frac{1}{\Lambda^3\rho}\right) - \ln\left(\int \mathrm{ds}^N \exp\left[-\beta U\left(\mathrm{s}^N;L\right)\right]\right)$$

$$\left.\begin{array}{l} \beta F = \beta F^{IG} + \beta F^{ex} \\ \mu \equiv \left(\dfrac{\partial F}{\partial N}\right)_{V,T} \end{array}\right\} \quad \beta\mu = \beta\mu^{IG} + \beta\mu^{ex}$$

$$\beta\mu^{IG} \equiv \left(\frac{\partial \beta F^{IG}}{\partial N}\right)_{V,T} \quad \beta\mu^{ex} \equiv \left(\frac{\partial \beta F^{ex}}{\partial N}\right)_{V,T}$$

$$\beta\mu \equiv \left(\frac{\partial \beta F}{\partial N}\right)_{V,T} \qquad \beta\mu = \frac{\beta F(N+1)) - \beta F(N))}{N+1-N}$$

$$= -\ln \frac{Q(N+1)}{Q(N)}$$

$$= -\ln \left(\frac{\dfrac{V^{N+1}}{\Lambda^{3N+3}(N+1)!}}{\dfrac{V^N}{\Lambda^{3N} N!}} \right) - \ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$= -\ln \left(\frac{V}{\Lambda^3 (N+1)} \right) - \ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu = \beta\mu^{IG} + \beta\mu^{ex}$$

$$\beta\mu^{ex} = -\ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu^{ex} = -\ln\left(\frac{\int ds^{N+1}\exp\left[-\beta U\left(s^{N+1};L\right)\right]}{\int ds^{N}\exp\left[-\beta U\left(s^{N};L\right)\right]}\right)$$

$$U\left(s^{N+1};L\right) = \Delta U^{+} + U\left(s^{N};L\right)$$

$$\beta\mu^{ex} = -\ln\left(\frac{\int ds^{N}\int ds_{N+1}\exp\left[-\beta\left(\Delta U^{+} + U\left(s^{N};L\right)\right)\right]}{\int ds^{N}\exp\left[-\beta U\left(s^{N};L\right)\right]}\right)$$

$$= -\ln\left(\frac{\int ds_{N+1}\int ds^{N}\left\{\exp\left[-\beta\Delta U^{+}\right]\right\}\exp\left[-\beta U\left(s^{N};L\right)\right]}{\int ds^{N}\exp\left[-\beta U\left(s^{N};L\right)\right]}\right)$$

$$= -\ln\left(\int ds_{N+1}\left\langle\exp\left[-\beta\Delta U^{+}\right]\right\rangle_{NVT}\right)$$

Ghost particle!

Algorithm 16 (Widom Test Particle Insertion)

```
      subroutine Widom           excess chemical potential
                                 via the addition of test particles
      xtest=box*ranf()           generate a random position
      call ener(xtest,entest)    determine energy
      wtest=wtest                update Boltzmann factor in (7.2.5)
     +      +exp(-beta*entest)
      return
      end
```

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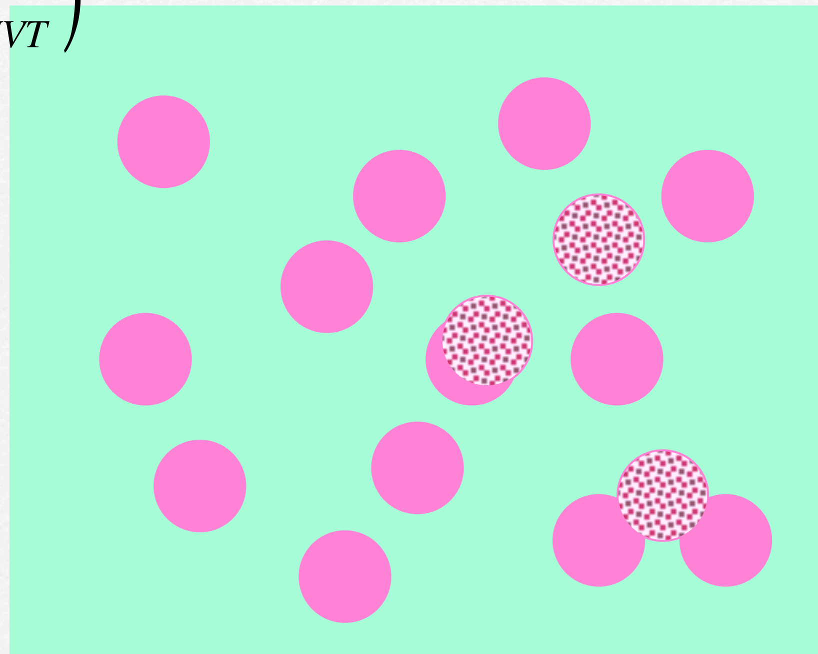
Hard spheres

$$\beta\mu^{ex} = -\ln\left(\int ds_{N+1} \left\langle \exp\left[-\beta\Delta U^{+}\right]\right\rangle_{NVT}\right)$$

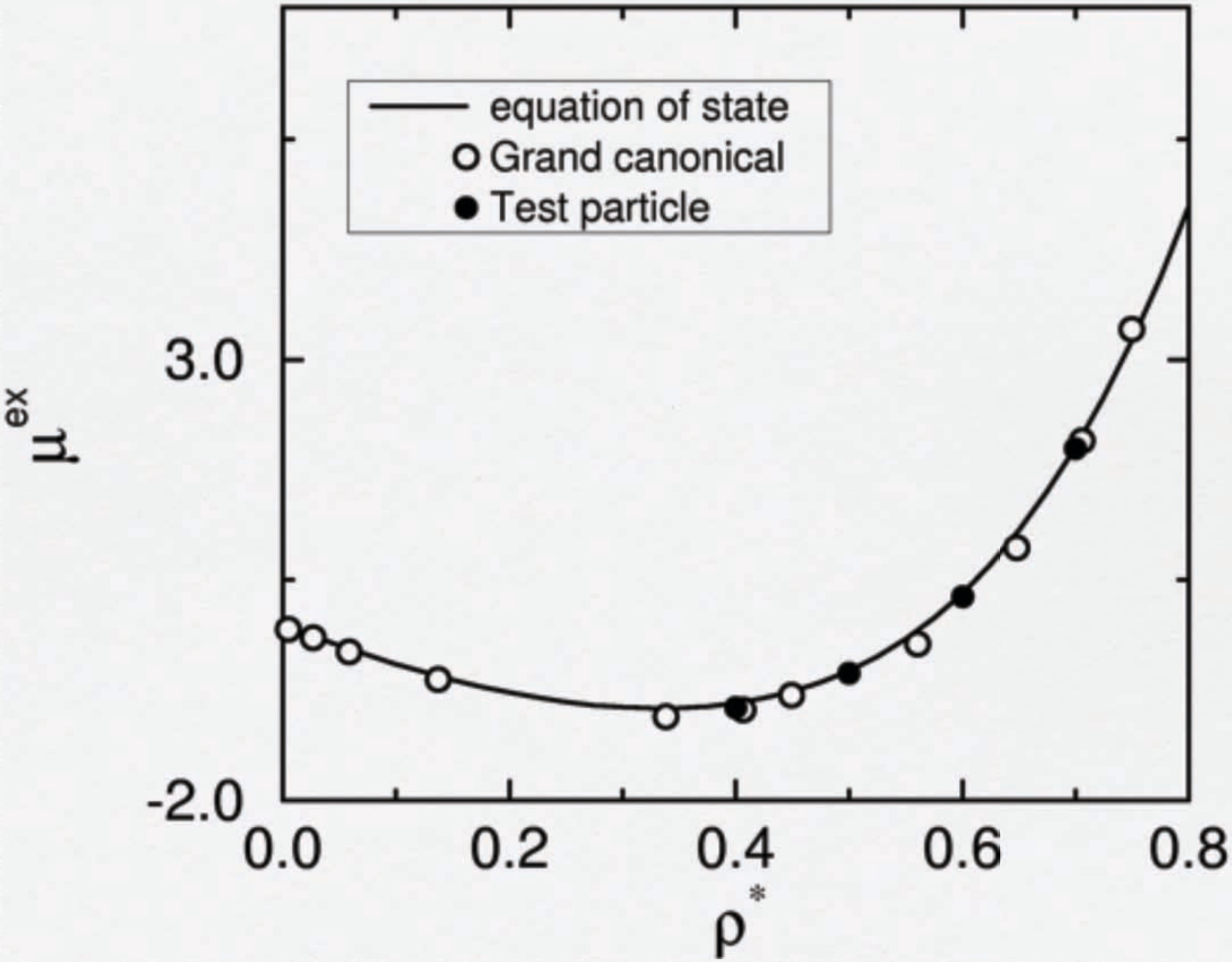
$$U(r) = \begin{cases} \infty & r \le \sigma \\ 0 & r > \sigma \end{cases}$$

$$\left\langle \exp\left[-\beta\Delta U^{+}\right]\right\rangle = \begin{cases} 0 & \text{if overlap} \\ 1 & \text{no overlap} \end{cases}$$



Probability to insert a test particle!

Lennard-Jones fluid



Real-particle method

$$\beta\mu \equiv \left(\frac{\partial \beta F}{\partial N}\right)_{V,T} \qquad \beta\mu = \frac{\beta F(N+1) - \beta F(N)}{N+1-N}$$

$$= -\ln \frac{Q(N+1)}{Q(N)}$$

$$= -\ln \left(\frac{\dfrac{V^{N+1}}{\Lambda^{3N+3}(N+1)!}}{\dfrac{V^N}{\Lambda^{3N} N!}} \right) - \ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$= -\ln \left(\frac{V}{\Lambda^3 (N+1)} \right) - \ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu = \beta\mu^{IG} + \beta\mu^{ex}$$

$$\beta\mu^{ex} = -\ln \left(\frac{\int \mathrm{ds}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu^{ex} = -\ln\left(\frac{\int d\mathrm{s}^{N+1}\exp\left[-\beta U\left(\mathrm{s}^{N+1};L\right)\right]}{\int d\mathrm{s}^{N}\exp\left[-\beta U\left(\mathrm{s}^{N};L\right)\right]}\right)$$

$$U\left(\mathrm{s}^{N+1};L\right) = \Delta U^{+} + U\left(\mathrm{s}^{N};L\right) \qquad U\left(\mathrm{s}^{N};L\right) = U\left(\mathrm{s}^{N+1};L\right) - \Delta U^{+}$$

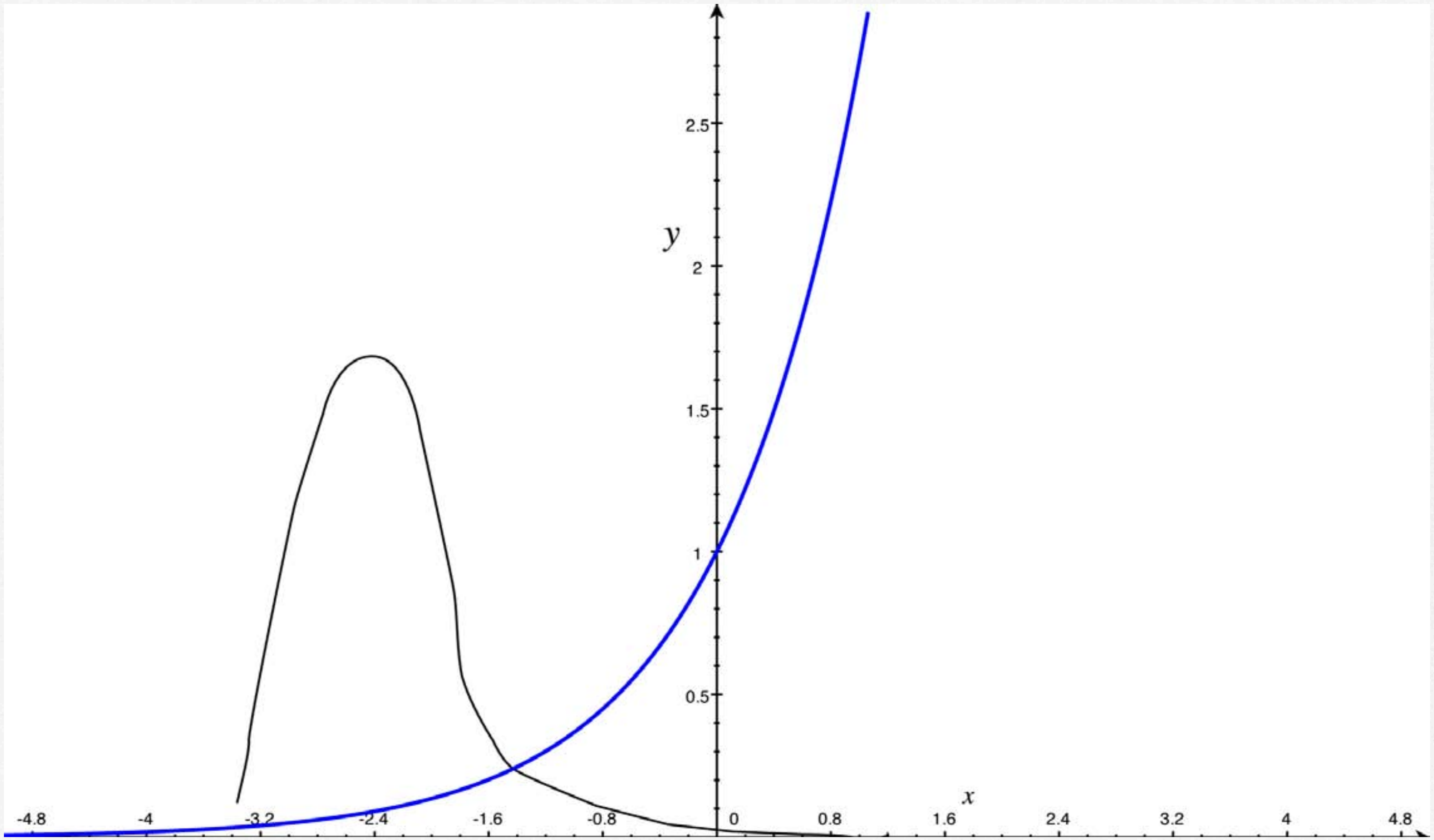
$$\beta\mu^{ex} = -\ln\left(\frac{\int d\mathrm{s}^{N+1}\exp\left[-\beta U\left(\mathrm{s}^{N+1};L\right)\right]}{\int d\mathrm{s}^{N+1}\exp\left[+\beta\Delta U^{+} - \beta U\left(\mathrm{s}^{N+1};L\right)\right]}\right)$$

$$= -\ln\left(\frac{\int d\mathrm{s}^{N+1}\exp\left[-\beta U\left(\mathrm{s}^{N+1};L\right)\right]}{\int d\mathrm{s}^{N+1}\exp\left[+\beta\Delta U^{+}\right]\exp\left[-\beta U\left(\mathrm{s}^{N+1};L\right)\right]}\right)$$

$$= +\ln\left(\left\langle \exp\left[+\beta\Delta U^{+}\right]\right\rangle_{N+1VT}\right)$$

real particle!

Real particle energy



Other ensembles: NPT

NVT: Helmholtz free energy

$$\mu \equiv \left(\frac{\partial F}{\partial N}\right)_{V,T}$$

NPT: Gibbs free energy

$$\mu \equiv \left(\frac{\partial G}{\partial N}\right)_{P,T}$$

$$\beta G = -\ln\left(Q_{NPT}\right)$$

$$Q_{NPT} = \frac{1}{\Lambda^{3N} N!}\int \mathrm{d}V V^{N} \exp(-\beta VP)\int \mathrm{ds}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N};L\right)\right]$$

$$\beta\mu = \frac{\beta G(N+1)) - \beta G(N))}{N+1-N}$$

$$\beta\mu = -\ln\frac{Q(N+1)}{Q(N)}$$

$$\beta\mu = -\ln \frac{Q(N+1)}{Q(N)}$$

$$\beta\mu = -\ln \frac{\dfrac{1}{\Lambda^{3N+3}(N+1)!}}{\dfrac{1}{\Lambda^{3N}N!}} \left(\frac{\int \mathrm{d}V V^{N+1} \exp(-\beta VP) \int \mathrm{d}\mathrm{s}^{N+1} \exp\left[-\beta U\left(\mathrm{s}^{N+1}; L\right)\right]}{\int \mathrm{d}V V^{N} \exp(-\beta VP) \int \mathrm{d}\mathrm{s}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu = -\ln \frac{1}{\Lambda^{3}(N+1)} \left(\frac{\int \mathrm{d}V V^{N} \exp(-\beta VP) V \int \mathrm{d}\mathrm{s}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right] \int \mathrm{d}\mathrm{s}_{N+1} \exp\left(-\beta \Delta U^{+}\right)}{\int \mathrm{d}V V^{N} \exp(-\beta VP) \int \mathrm{d}\mathrm{s}^{N} \exp\left[-\beta U\left(\mathrm{s}^{N}; L\right)\right]} \right)$$

$$\beta\mu = -\ln\frac{1}{\Lambda^3(N+1)}\left(\frac{\int dV V^N \exp(-\beta VP) V \int ds^N \exp\left[-\beta U\left(s^N;L\right)\right]\int ds_{N+1}\exp\left(-\beta\Delta U^+\right)}{\int dV V^N \exp(-\beta VP)\int ds^N \exp\left[-\beta U\left(s^N;L\right)\right]}\right)$$

$$\beta\mu = \ln\left(\Lambda^3\beta P\right) - \ln\left(\frac{\beta P}{N+1}\frac{\int dV V^N \exp(-\beta VP)\int ds^N \exp\left[-\beta U\left(s^N;L\right)\right]\int ds_{N+1} V \exp\left(-\beta\Delta U^+\right)}{\int dV V^N \exp(-\beta VP)\int ds^N \exp\left[-\beta U\left(s^N;L\right)\right]}\right)$$

The volume fluctuates!

$$\left\langle \frac{\beta PV}{N+1}\int ds_{N+1}\exp\left(-\beta\Delta U^+\right)\right\rangle \neq \left\langle\frac{\beta PV}{N+1}\right\rangle\left\langle\int ds_{N+1}\exp\left(-\beta\Delta U^+\right)\right\rangle$$

$$\beta\mu = \ln\left(\Lambda^3\beta P\right) - \ln\left\langle\frac{\beta PV}{N+1}\int ds_{N+1}\exp\left(-\beta\Delta U^+\right)\right\rangle$$

NVT versus NPT

NVT:

$$\beta\mu = \beta\ln(\rho) - \ln\left\langle \int \mathrm{ds}_{N+1} \exp\left[-\beta\Delta U^{+}\right]\right\rangle_{NVT}$$

NPT:

$$\beta\mu = \ln\left(\Lambda^{3}\beta P\right) - \ln\left\langle \frac{\beta P V}{N+1} \int \mathrm{ds}_{N+1} \exp\left(-\beta\Delta U^{+}\right)\right\rangle$$

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Overlapping Distribution Method

Two systems:

System 0: N, V,T, U_0

System 1: N, V,T, U_1

$$Q_0 = \frac{V^N}{\Lambda^{3N} N!} \int d\mathbf{s}^N \exp(-\beta U_0)$$

$$Q_1 = \frac{V^N}{\Lambda^{3N} N!} \int d\mathbf{s}^N \exp(-\beta U_1)$$

$$\Delta\beta F = \beta F_1 - \beta F_0 = -\ln(Q_1/Q_0)$$

$$= -\ln\left(\frac{\int d\mathbf{s}^N \exp(-\beta U_1)}{\int d\mathbf{s}^N \exp(-\beta U_0)}\right) = -\ln\left(\frac{q_1}{q_0}\right)$$

$$\int d\mathbf{s}^N \exp(-\beta U_1) = \frac{q_1}{q_0} \int d\mathbf{s}^N \exp(-\beta U_0)$$

System 0: N, V,T, U_0 System 1: N, V,T, U_1

Let us define

$$p_1(\Delta U) \equiv \frac{\int d\mathbf{s}^N \exp(-\beta U_1)\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_1)}$$

and

$$p_0(\Delta U) \equiv \frac{\int d\mathbf{s}^N \exp(-\beta U_0)\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_0)}$$

$$\Delta\beta F = -\ln\left(\frac{\int d\mathbf{s}^N \exp(-\beta U_1)}{\int d\mathbf{s}^N \exp(-\beta U_0)}\right) = -\ln\left(\frac{q_1}{q_0}\right)$$

$$p_1(\Delta U) = \frac{\int d\mathbf{s}^N \exp(-\beta U_1)\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_1)} \quad p_0(\Delta U) = \frac{\int d\mathbf{s}^N \exp(-\beta U_0)\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_0)}$$

=ΔU: Because of the δ function it can be taken outside the integration

$$p_1(\Delta U) = \frac{\int d\mathbf{s}^N \exp[-\beta(U_1 - U_0)]\exp[-\beta U_0]\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_1)}$$

$$= \frac{\exp[-\beta\Delta U]\int d\mathbf{s}^N \exp[-\beta U_0]\delta(U_1 - U_0 - \Delta U)}{\int d\mathbf{s}^N \exp(-\beta U_1)}$$

$$\int d\mathbf{s}^N \exp(-\beta U_1) = \frac{q_1}{q_0}\int d\mathbf{s}^N \exp(-\beta U_0)$$

Overlapping Distribution Method

$$p_1(\Delta U) = \frac{\exp[-\beta\Delta U]\int ds^N \exp[-\beta U_0]\delta(U_1 - U_0 - \Delta U)}{\int ds^N \exp(-\beta U_1)}$$

$$= \frac{q_0}{q_1}\exp(-\beta\Delta U)\frac{\int ds^N \exp[-\beta U_0]\delta(U_1 - U_0 - \Delta U)}{\int ds^N \exp(-\beta U_0)}$$

$$\int ds^N \exp(-\beta U_1) = \frac{q_1}{q_0}\int ds^N \exp(-\beta U_0)$$

$$\frac{q_0}{q_1} = \exp(\beta\Delta F)$$

$$p_1(\Delta U) = \frac{q_0}{q_1}\exp(-\beta\Delta U)p_0(\Delta U)$$

$$\ln p_1(\Delta U) = \beta(\Delta F - \Delta U) + \ln p_0(\Delta U)$$

$$\ln p_1(\Delta U) = \beta(\Delta F - \Delta U) + \ln p_0(\Delta U)$$

Let us define two new functions:

$$f_0(\Delta U) \equiv \ln p_0(\Delta U) - 0.5\beta\Delta U$$

$$\beta\Delta F = f_1(\Delta U) - f_0(\Delta U)$$

$$f_1(\Delta U) \equiv \ln p_1(\Delta U) + 0.5\beta\Delta U$$

Fit f_0 and f_1 to two polynomials that only differ by the offset.

$$f_1(\Delta U) \equiv C_1 + a\Delta U + b\Delta U^2 + c\Delta U^3$$

$$\beta\Delta F = C_1 - C_0$$

$$f_0(\Delta U) \equiv C_0 + a\Delta U + b\Delta U^2 + c\Delta U^3$$

Simulate system 0: compute f_0

Simulate system 1: compute f_1

System 0: N–1, V,T, U

+ 1 ideal gas

$$\Delta\beta F = \beta F_1 - \beta F_0 \equiv \beta\mu^{ex}$$

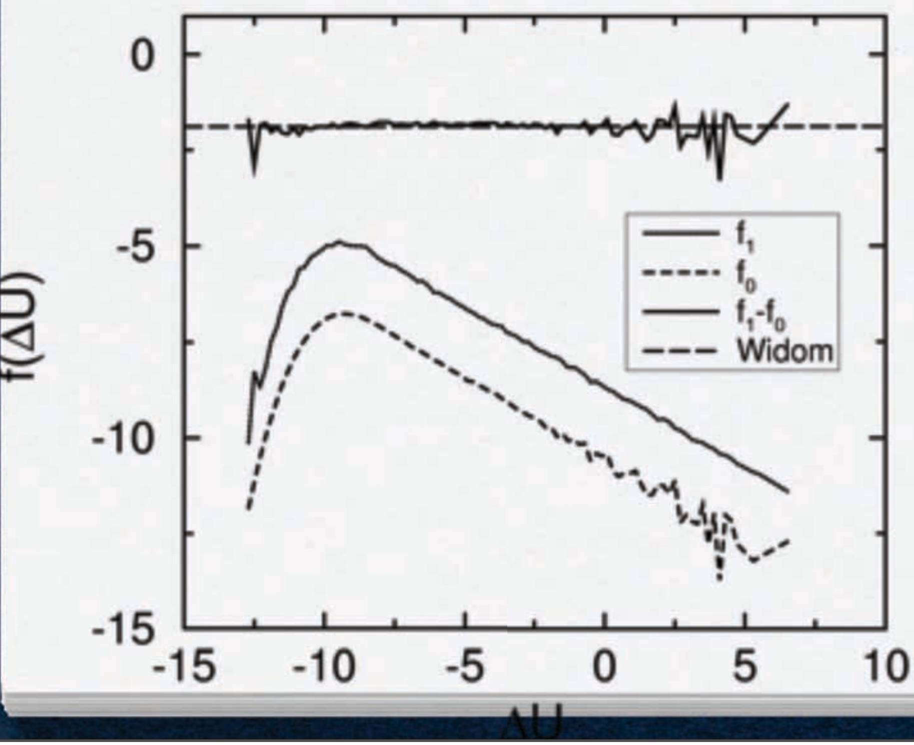
System 1: N, V,T, U

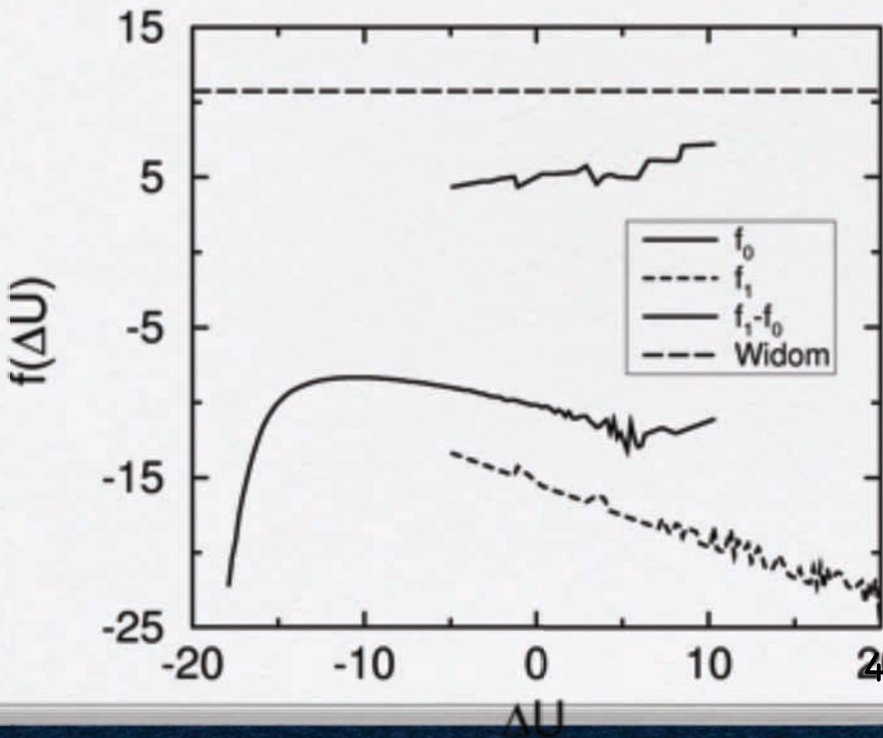
$$\Delta U = U_1 - U_0$$

System 0: test particle energy

System 1: real particle energy

$$\beta\mu^{ex} = f_1(\Delta U) - f_0(\Delta U)$$





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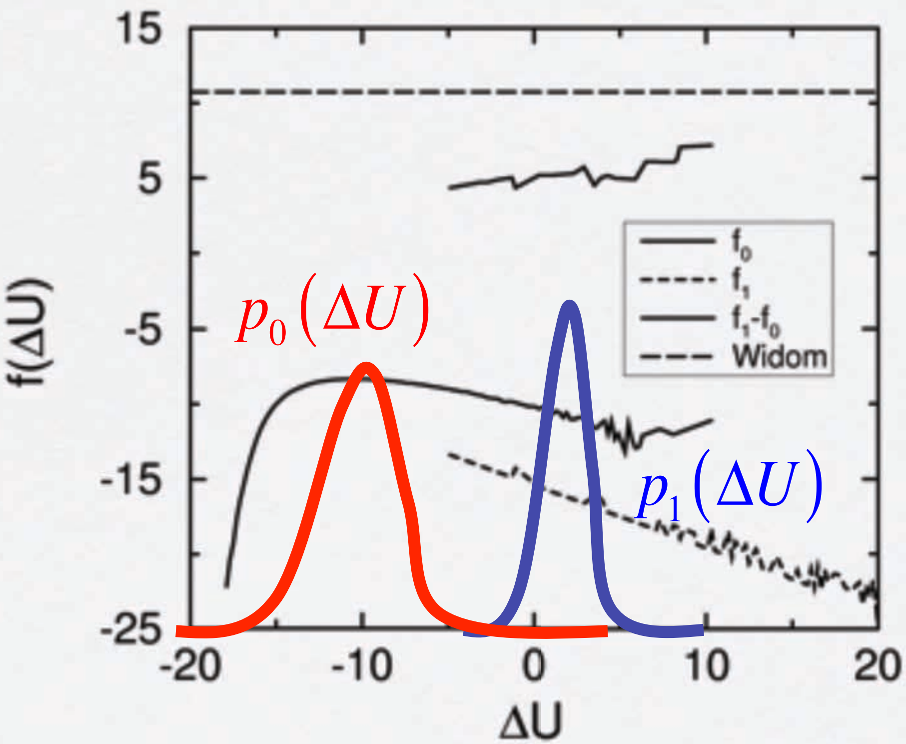
System 0: N-1, V,T, U
+ 1 ideal gas

System 1: N, V,T, U

$$f_0(\Delta U) \equiv \ln p_0(\Delta U) - 0.5\beta\Delta U$$

$$f_1(\Delta U) \equiv \ln p_1(\Delta U) + 0.5\beta\Delta U$$



- Accurate sampling only if there is overlap between the two distributions
- How to create this overlap?

Intermezzo: order parameters and Landau Free energies (1)

Landau free energy density:

$$\beta f(q) = -\ln \frac{1}{\Lambda^{3N} N!} \int \delta\left(q - q\left(\mathbf{r}^N\right)\right) \exp\left[-\beta U\left(\mathbf{r}^N\right)\right] \mathrm{d}\mathbf{r}^N$$

Probability to find the system with order parameter q

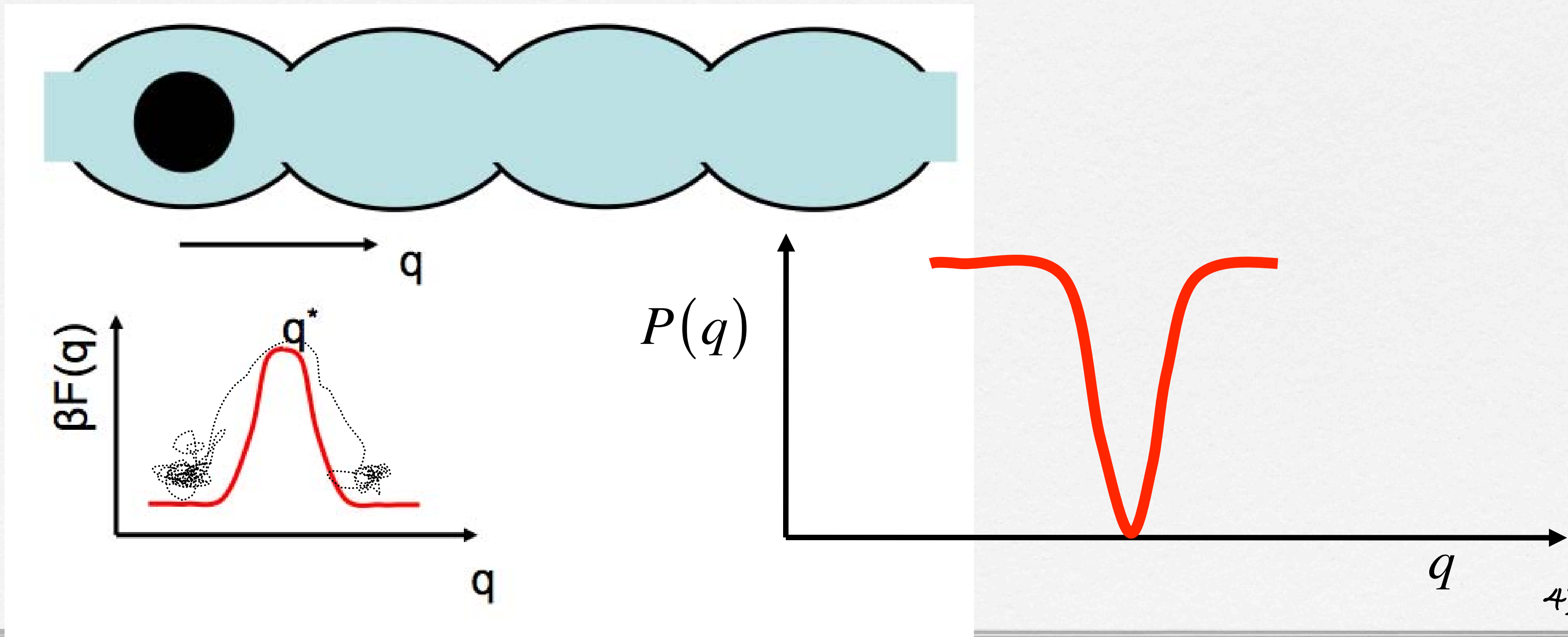
$$P(q)\mathrm{d}q \propto \exp\left[-\beta f(q)\right]\mathrm{d}q$$

Free energy:

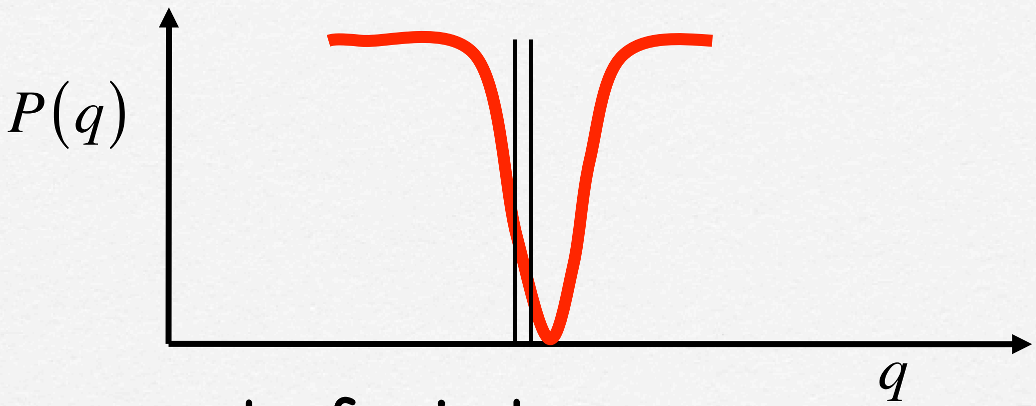
$$F = \int f(q)\mathrm{d}q$$

Probability to find the system with order parameter q

$$P(q)\mathrm{d}q \propto \exp\left[-\beta f(q)\right]\mathrm{d}q$$



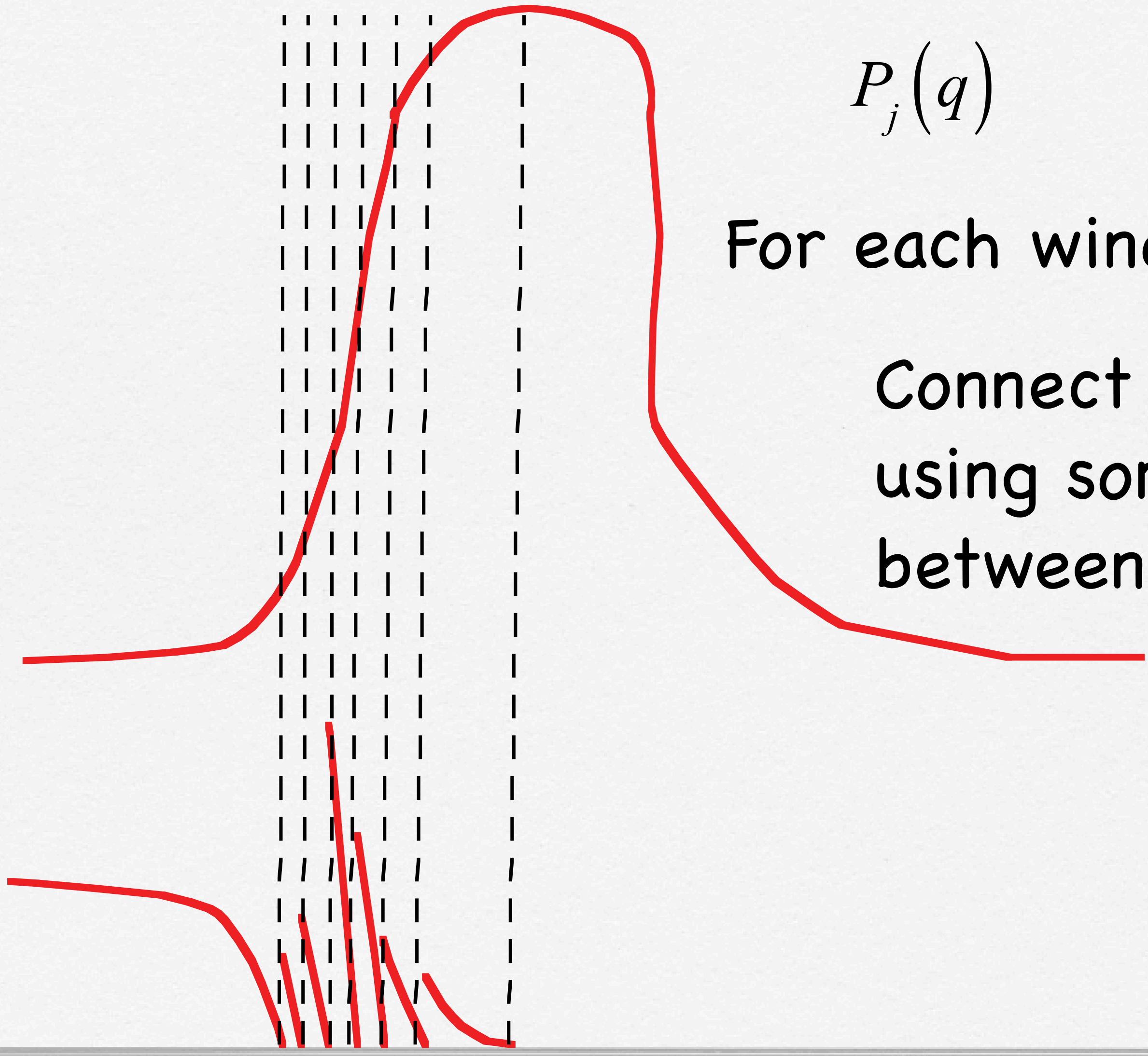
Histogram method (1)



Define a set of windows:

$$U_j(q) = \begin{cases} \infty & \text{if} \quad q < q_j^{\min} \\ 0 & \text{if} \quad q_j^{\min} < q < q_j^{\max} \\ \infty & \text{if} \quad q > q_j^{\max} \end{cases}$$

For each window determine: $P_j(q)$



$P_j(q)$

For each window separately

Connect the windows using some overlap between Windows

Umbrella sampling (1)

$$\exp\left[-\beta f(q)\right] = \frac{1}{\Lambda^{3N} N!} \int \delta\left(q - q\left(\mathbf{r}^N\right)\right) \exp\left[-\beta U\left(\mathbf{r}^N\right)\right] d\mathbf{r}^N$$

$$\Delta f(q) = f(q) - f^{IG}(q)$$

$$\exp\left[-\beta \Delta f(q)\right] = \frac{\int \delta\left(q - q\left(\mathbf{r}^N\right)\right) \exp\left[-\beta U\left(\mathbf{r}^N\right)\right] d\mathbf{r}^N}{\int \delta\left(q - q\left(\mathbf{r}^N\right)\right) d\mathbf{r}^N}$$

$$\exp\left[-\beta \Delta f(q)\right] = \frac{\int \pi\left(\mathbf{r}^N\right) \pi^{-1}\left(\mathbf{r}^N\right) \delta\left(q - q\left(\mathbf{r}^N\right)\right) \exp\left[-\beta U\left(\mathbf{r}^N\right)\right] d\mathbf{r}^N}{\int \pi\left(\mathbf{r}^N\right) \pi^{-1}\left(\mathbf{r}^N\right) \delta\left(q - q\left(\mathbf{r}^N\right)\right) d\mathbf{r}^N}$$

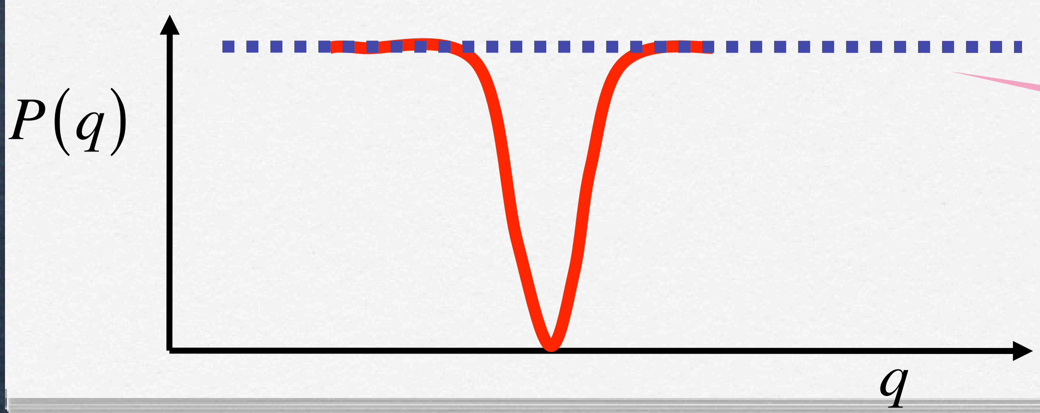
$$\exp\left[-\beta \Delta f(q)\right] = \frac{\int \pi^{-1}\left(\mathbf{r}^N\right) \delta\left(q - q\left(\mathbf{r}^N\right)\right) \exp\left[-\beta U\left(\mathbf{r}^N\right)\right] \pi\left(\mathbf{r}^N\right) d\mathbf{r}^N}{\int \pi^{-1}\left(\mathbf{r}^N\right) \delta\left(q - q\left(\mathbf{r}^N\right)\right) \pi\left(\mathbf{r}^N\right) d\mathbf{r}^N}$$

$$\exp\left[-\beta\Delta f(q)\right] = \frac{\int \pi^{-1}(\mathbf{r}^N)\,\delta\left(q - q(\mathbf{r}^N)\right)\exp\left[-\beta U(\mathbf{r}^N)\right]\pi(\mathbf{r}^N)\,\mathrm{d}\mathbf{r}^N}{\int \pi^{-1}(\mathbf{r}^N)\,\delta\left(q - q(\mathbf{r}^N)\right)\pi(\mathbf{r}^N)\,\mathrm{d}\mathbf{r}^N}$$

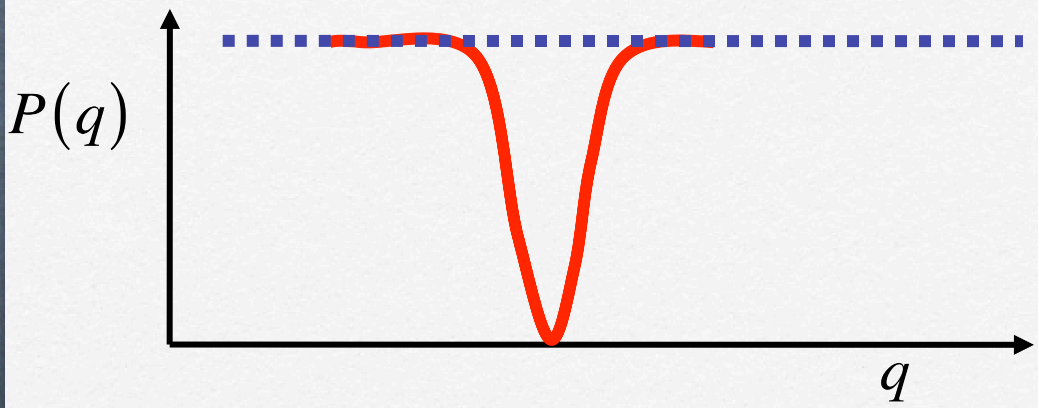
This is NOT a Boltzmann distribution

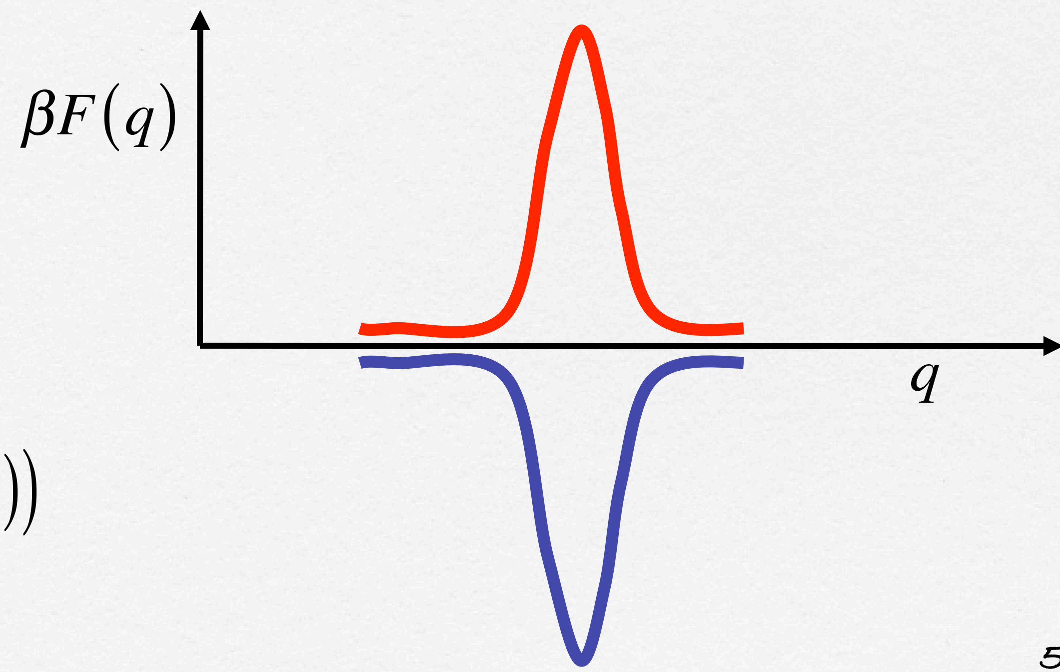
$$\exp\left[-\beta\Delta f(q)\right] = \frac{\left\langle \delta\left(q - q(\mathbf{r}^N)\right)\exp\left[-\beta U(\mathbf{r}^N)\right]\pi^{-1}(\mathbf{r}^N)\right\rangle_\pi}{\left\langle \delta\left(q - q(\mathbf{r}^N)\right)\pi^{-1}(\mathbf{r}^N)\right\rangle_\pi}$$

How to choose π?



Ideal sampling





$$\pi\left(\mathbf{r}^N\right) = \exp\left(-\beta \tilde{F}^{est}(q)\right)$$