Free energy calculations (cont.)

F+S Chaps. 7 + 14
H-T Chap. 9

Direct simulation? $F = -kT \ln Z_N$ (fixed N)

$$Z_N = \frac{1}{N!\,\lambda_{TH}^{3N}} \int \prod_1^N d^3r_i \; e^{-U_N/kT}$$

$$= \frac{V^N}{N!\,\lambda_{TH}^{3N}} \left[\int \prod_1^N d^3r_i \; \frac{e^{-U_N/kT}}{\int \prod_1^N d^3r_i \; e^{-U_N/kT}} \cdot e^{+U_N/kT} \right]^{-1}$$

$$= \frac{V^N}{N!\,\lambda_{TH}^{3N}} \left\langle e^{+U_N/kT} \right\rangle_{NVT}^{-1}$$

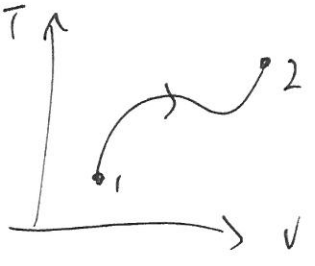
Nice formula but numerically unstable for some reason as "Widom deletion"

– + –

Thermodynamic integration

Since $dF = -S\,dT - p\,dV$

$$F_1 - F_2 = -\int_1^2 S(V,T)\,dT - \int_1^2 p(V,T)\,dV$$



along some path in the (T,V) plane

– independent of path because F is a state function.

What's S in this calc?

$dS = \frac{1}{T} dE + \frac{P}{T} dV$ so could integrate this first to get $S(E,V)$ using simulations for dE

but this is { time-consuming
not so accurate

Instead: $\left.\frac{\partial (F/T)}{\partial (1/T)}\right|_V = F + \frac{1}{T}\left.\frac{\partial F}{\partial (1/T)}\right|_V = F - T\left(\frac{\partial F}{\partial T}\right)_V$

$= F + TS = E$

so $d\left(\frac{F}{T}\right) = \left(\frac{\partial (F/T)}{\partial V}\right)_T dV + \left(\frac{\partial (F/T)}{\partial (1/T)}\right)_V d\left(\frac{1}{T}\right)$

$= -\frac{P}{T} dV + E\, d\left(\frac{1}{T}\right)$

$\rightarrow \frac{F_2}{T_2} - \frac{F_1}{T_1} = \int_1^2 \left(-\frac{P}{T} dV + E\, d\left(\frac{1}{T}\right)\right)$

↑ directly measured

This assumes equilibrium values for E & p so the "motion" $1 \rightsquigarrow 2$ must be slow & reversible

Use: start at high (V,T) where system is an ideal gas where F is known, integrate in small steps through equilibrium states where E & p can be found by MC.

Related example: nano-particle in a liquid in a tube

Where does the particle sit in equilibrium?

At the wall? center? elsewhere?

→ Compute $F(r)$

MC simulation: tube = cylindrical shell of atoms fixed in space

liquid = LJ

particle = rigid spherical section of a lattice

liquid interacts with all atoms, variable strength

$dF = -S\,dT - p\,dV + \underline{f}\cdot d\underline{r}$ ← work done when particle moves

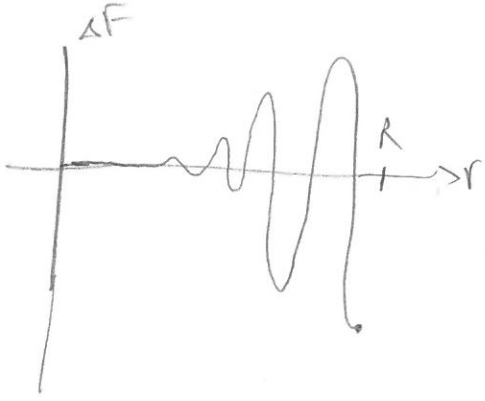
$\underline{f}$ = force exerted by liquid (+ solid if close by)

NVT simulation: $dT = dV = 0$

move particle "slowly" from center to wall, compute $\underline{f}$ at each $\underline{r}$

$$\Delta F = \int_1^2 \underline{f}(\underline{r})\cdot d\underline{r} \approx \sum \underline{f}_i \cdot \Delta \underline{r}_i$$

Result



oscillations result from liq. density osc. near a wall, $\Delta F(R)$ depends on int. strength

Nice feature of Nerno int is independence of path — F depends only on current values of $V, T, \bar{\lambda}$.

→ some result if any parameter is varied reversibly

→ "Hamiltonian integration"

let $U(\lambda) = (1-\lambda) U_1 + \lambda U_2$ so $U: U_1 \to U_2$ if $\lambda: 0 \to 1$

choose $U_1 = U$ for a system where F is known

e.g. $F = F_{ideal}$ when $U_1 = 0$

Then

$$\left.\frac{\partial F(\lambda)}{\partial \lambda}\right|_{NVT} = -kT \frac{\partial}{\partial \lambda} \ln Z(NVT, \lambda)$$

$$= \frac{-kT}{Z} \int \prod_i^N d^3 r_i \, e^{-U/kT} \left(-\frac{1}{kT} \frac{\partial U(\lambda)}{\partial \lambda}\right)$$

$$= \left\langle \frac{\partial U}{\partial \lambda} \right\rangle_{NVT}$$

so $F_2 - F_1 = \int_0^1 d\lambda \frac{\partial F}{\partial \lambda} = \int_0^1 d\lambda \underbrace{\left\langle \frac{\partial U}{\partial \lambda} \right\rangle_{NVT}}_{\text{average this in an MC sim.}} = \sum \cdots$

Convenient to have $U(\lambda)$ linear in λ (not rqd.)

so $\frac{\partial U}{\partial \lambda} = U_2 - U_1$ and

$$\left(\frac{\partial^2 F}{\partial \lambda^2}\right)_{NVT}^{*} = -\frac{1}{kT}\left[\left\langle (U_2 - U_1)^2 \right\rangle - \left\langle U_2 - U_1 \right\rangle^2\right] \le 0$$: check on calc.

Related method - free energy perturbation theory

think of $U_2 - U_1$ as a pert. of U_1:

$$F_2 - F_1 = -kT \log \frac{\int \prod_i d^3 r_i \, e^{-U_1/kT} \cdot e^{-(U_2 - U_1)/kT}}{\int \prod d^3 r_i \, e^{-U_1/kT}}$$

$$= -kT \log \left\langle e^{-(U_2 - U_1)/kT} \right\rangle_{U_1}$$

Doesn't necessarily require $U_2 - U_1$ small, but could have a problem if U_2 is only large in regions where U_1 has a small population

Fix: use small steps in $\Delta U \to \sum (U_{i+1} - U_i)$

$$F_2 - F_1 = -kT \sum_i \log \left\langle e^{-(U_{i+1} - U_i)/kT} \right\rangle$$

This reduces to Hamiltonian int if $\Delta U_i / kT$ is small.

Issue with these methods:

The result is some number $F_2 - F_1$, no idea if it's right

Better to have an internal consistency check and/or compute ΔF over a range of parameters to see if it's reasonable

Overlapping distribution method:

gives ΔF for any 2 systems, with a check

Suppose system 1 with PE $U_1(\{r_i\}) \to F_1$

" 2 " U_2 " F_2

In system 1, compute the pdf of $U_2 - U_1$:

$$p_1(\Delta U) = \frac{1}{Q_1} \int \prod_i^N d^3 r_i \, e^{-U_1/kT} \, \delta\left(U_2(\{r_i\}) - U_1(\{r_i\}) - \Delta U \right)$$

($U_2(\{r_i\})$: fcns. of r_i; ΔU: number)

in practice: MC simulation in system #1

at each state, record ΔU = energy difference

$\to$ histogram of ΔU's

$$p_1(\Delta U) = \frac{1}{Q_1} \int \prod d^3 r_i \, e^{-(U_2 - \Delta U)/kT} \, \delta[U_2 - U_1 - \Delta U]$$

$$= \frac{Q_2}{Q_1} e^{+\Delta U/kT} \cdot \frac{1}{Q_2} \int \prod d^3 r_i \, e^{-U_2/kT} \, \delta[U_2 - U_1 - \Delta U]$$

$$= \frac{Q_2}{Q_1} e^{\Delta U/kT} \, p_2(\Delta U)$$

$\downarrow$

in system 2 compute the histogram of ΔU

$$\log p_1(\Delta U) = \frac{1}{kT}(\Delta U - \Delta F) + \log p_2(\Delta U)$$

Consistency check: $\Delta \log p$ should be a linear function of ΔU.

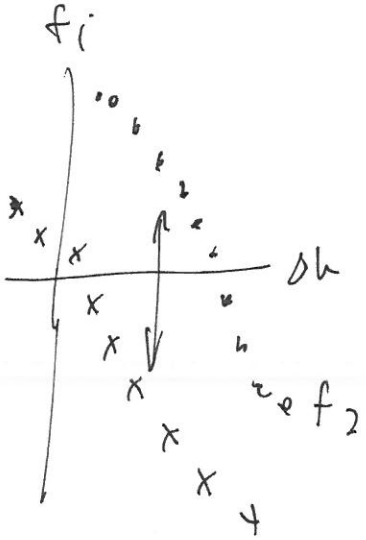
Cleaner way to evaluate: let $f_1(\Delta u) = \log p_1(\Delta u) - \Delta u/kT$

$f_2(\Delta u) = \log p_2 + \Delta u/kT$

$\rightarrow \Delta F = kT\left[f_2(\Delta u) - f_1(\Delta u) \right]$

So: compute f_1 & f_2 in 2 MC calculations, should see

$f_2 - f_1 = \text{const} \rightarrow \Delta F/kT$



In practice Δf not exactly constant

$\rightarrow$ fit $\Delta f_i = \sum_{0}^{N} a_i^{(n)} \Delta u^n$

& say $\Delta F = kT\left(a_{02}^{(0)} - a_1^{(0)} \right)$

To get μ: #2 = N-particle interacting system of interest

#1 = (N-1) interacting particles + 1 ideal gas

$\rightarrow \Delta F$ = extra F when a particle is added

$= \mu$

In the MC simulation of #1 must use N-1 particles since the other does not affect it.

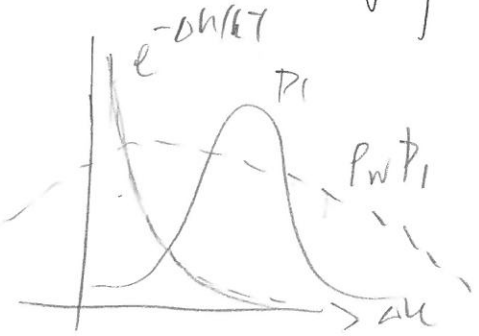
In a sense, this is the right way to do "particle deletion".

Umbrella sampling:

Metropolis version of importance sampling in MC integration

look at $F_2 - F_1 = -kT \log\left(e^{-\Delta U/kT}\right)_1 \quad \Delta U = U_2 - U_1$

If $U_{1,2}$ are very different, U_2 may be large & $e^{-\Delta U/kT}$ small in the configurations that are well-sampled by U_1



→ bias p_1 by p_W which forms an "umbrella" over the peaks in p_1 & p_2

replace $p_1 = \dfrac{e^{-U_1/kT}}{\int \prod d^3r_i\, e^{-U_1/kT}}$ by $p_W = \dfrac{W(\{\vec{r}_i\})\, e^{-U_1/kT}}{\int \prod d^3r_i\, W e^{-U_1/kT}}$

so that

$$\langle f(\{\vec{r}_i\})\rangle_{p_1} = \int \prod d^3r_i\, p_1 f(\{\vec{r}_i\})$$

$$= \int \prod d^3r_i\, W e^{-U_1/kT} \cdot f/W \Big/ \int \prod d^3r_i\, W e^{-U_1/kT} \cdot 1/W$$

$$= \langle f/W\rangle_{p_W} \Big/ \langle 1/W\rangle_{p_W}$$

MC implementation: accept moves $i \to j$ with probability

$$p = \min\left\{1, \frac{W_j}{W_i} e^{-(U_j - U_i)/kT}\right\}$$

because $We^{-U/kT}$ is the new "equil" pdf

then $\langle f \rangle_{p_1} = \sum_n (f/w)_{w,n} \Big/ \sum_n (1/w)_{w,n}$

value of f/w in state n_1 in a biased simulation with w

Choice of w? should "include" both p_1 & p_2

e.g. $w = e^{-(u_2-u_1)/kT}$ so $p_1 w \propto e^{-(u_1+u_2)/2kT}$

Still have problem that $\langle 1/w \rangle_w$ may be hard to evaluate.

→ work in small steps

$$F_2 - F_1 = \sum_{n=1}^{N} -kT \log \frac{Z_n}{Z_{n-1}} \qquad Z_n = \int \prod d^3 r_i \, e^{-(u_1 + \frac{k}{n}\Delta u)/kT}$$

so $$\frac{Z_n}{Z_{n-1}} = \left\langle e^{-\Delta u/nkT} \right\rangle_{n-1}$$

: effectively Δu lowered by $1/n$

Acceptance ratio method:

$$e^{(F_2-F_1)/kT} = \frac{Q_1}{Q_2} \cdot \frac{\int \prod^N d^3 r_i \, w(\{r_i\}) e^{-(u_1+u_2)/kT}}{\text{II}} \quad \text{for any } w(\{r_i\})$$

$$= \frac{\langle w e^{-u_1/kT} \rangle_2}{\langle w e^{-u_2/kT} \rangle_1}$$

trick w to minimize the error:

$$\sigma^2 = \frac{\langle w^2 e^{-2u_1/kT} \rangle_2 - \langle w e^{-u_1/kT} \rangle_2^2}{N_2 \langle w e^{-u_1/kT} \rangle^2} + (1 \leftrightarrow 2)$$

details in F+S

Umbrella sampling uses a bias potential to explore a region of phase space that would otherwise be poorly sampled.

Generalization: suppose $s(\Gamma) = s(\{\underline{r}_i, \underline{p}_i\})$
= some collective coordinate

could be density at $\underline{r}_0$, int energy w/ ext. field, force on a suspended particle, ...

& you want to know $p(s)$.

Formally $p(s) = \frac{1}{Z} \int d\Gamma\, e^{-H(\Gamma)}\, \delta(s - s(\Gamma))$

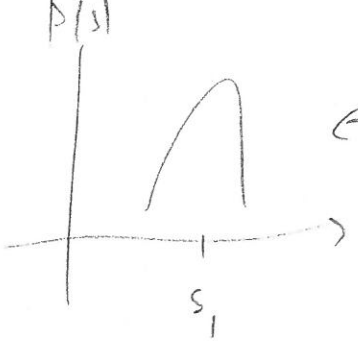
. with $p(s) \geq 0$, $\int ds\, p(s) = 1$

in a simulation $p(s) = N(s)/N_{MST}$ = fraction of config. at that s

but s tends to stick at local minima & the whole pdf isn't sampled

→ Add a bias potential like $\tilde{U}(s) = -\frac{k}{2}(s - s(\Gamma))^2$

so if k is large the simulation explores the region about s (only).



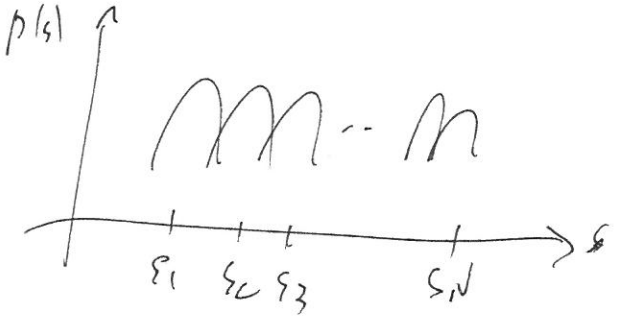
$\leftrightarrow U(s)$ $\quad \hat{p}(s) = \frac{1}{\tilde{Z}} \int d\Gamma\, e^{-\beta(U+\tilde{U})}\, \delta(s - s(\Gamma))$

$= \hat{N}(s)/\tilde{N}_{MST}$ in a simulation

Notice $\hat{p}(\xi) = \frac{1}{\tilde{Z}} e^{-\hat{u}(\xi)/kT} \int \prod_i dr_i \, e^{-u/kT} \delta(\xi - s(r))$

$= e^{-\hat{u}/kT} p(\xi) \cdot \underbrace{\frac{\tilde{Z}}{\tilde{Z}}}_{\text{unknown constant}}$

Repeat the calc over the full range of ξs:



assuming $\Delta\xi$ chosen so the p_i overlap in their tails

$$\rightarrow \quad p(\xi) = \sum_i \bar{p}_i(\xi) = \sum_i e^{\hat{u}_i/kT} \underbrace{\hat{N}_i(\xi)}_{\tilde{N}_{i,[r]}} \cdot \underbrace{\frac{\hat{Z}_i}{\tilde{Z}}}_{\text{unknown} \equiv w_i}$$

treat the w_i as parameters & choose them to minimize the variance in $p(\xi)$

→ weighted histogram acceptance method

Details in HW 5.

Histogram Method 2:

convert results at temperature T_1 to T_2

At T_1, $\beta_1 \equiv 1/k_B T_1$ use an MC simulation to find

$$p_1(u)\,du = \frac{1}{Q_1}\,\Omega(u)\,e^{-\beta_1 u}\,du \;\cong\; \frac{1}{N}\,H_1(u)\,\Delta u$$

$p_1(u)$: pdf of u; Q_1: Q at T_1; N: # steps; $H_1(u)$: # times a value in $[u, u+\Delta u]$ is found

At $T_2 \neq T_1$ the pdf changes to

$$p_2(u) = \frac{1}{Q_2}\,\Omega(u)\,e^{-\beta_2 u}$$

$$= \frac{\Omega(u)\,e^{-\beta_1 u}\,e^{-(\beta_2-\beta_1)u}}{\sum_u \Omega(u)\,e^{-\beta_1 u}\,e^{-(\beta_2-\beta_1)u}} \cdot \frac{1/\sum_u \Omega(u)\,e^{-\beta_1 u}}{1/\sum_u \Omega(u)\,e^{-\beta_1 u}}$$

$$= \frac{p_1(u)\,e^{-(\beta_2-\beta_1)u}}{\sum_u p_1(u)\,e^{-(\beta_2-\beta_1)u}}$$

$$\cong \frac{H_1(u)\,e^{-(\beta_2-\beta_1)u}}{\sum_u H_1(u)\,e^{-(\beta_2-\beta_1)u}}$$

∴ new pdf is an "transform" of the old one.

As usual, works if old pdf well-samples the new region of energies, needs $\beta_2 - \beta_1$ not too large