Enhanced Sampling, Pt 2

Combining info from multiple simulations

Last time RX @ $T_1 \ldots T_N$

or umbrellas @ $Q_1 \ldots Q_N$

Showed how for US, can stitch together "by hand" and for RX just use lowest temp

Idea, combine info from all sims

One method: Weighted Histogram Analysis Method (wham)

Annoying to derive (Tuckerman 8.8)

Idea:

Sim in modified Ensemble eg

$$P_i(X) = e^{-\beta\left(U(x) + \frac{1}{2}k(Q-Q_i)^2\right)} / Z_i$$

$$Z_i = \int dX\, e^{-\beta\left(U(x) + \frac{1}{2}k(Q-Q_i)^2\right)}$$

$Q(x) =$ some function of q's

$$P_i(Q) = \int \delta(Q(x) - Q_i)\, e^{-\beta(u(x) + \frac{1}{2}k(Q-Q_i)^2)} / Z_i$$

But want $P(Q)$ ie w/o bias

suppose have cfg

$x_1^i \ldots x_t^i$, $\quad P(x_n^i) = e^{-\beta u(x_n^i)} \cdot e^{-\beta \frac{1}{2}k(Q-Q_i)^2} / Z_i$

and $P(x_n) = e^{-\beta u(x_n)} / Z$

$\Rightarrow P(x_n) = Z_i P(x_n^i)\, e^{+\beta \frac{k}{2}(Q-Q_i)^2}$ reweighting

So eg $\langle A \rangle = \frac{1}{T_i} \sum_{n=1}^{T_i} Z_i e^{\beta k/2 (Q(x)-Q_i)^2} A(x_n^i)$

idea is to estimate Z_i's by comparing data from i & j & minimizing a variance in data

Result w/ some assumptions! $\quad A_k = -k_B T \log Z_k$

$$P(Q) = \frac{\sum_{i=1}^{N} n_i P_i(Q)}{\sum_{i=1}^{N} n_i e^{-\beta \frac{1}{2}k(Q-Q_i)^2} e^{\beta(A_k - A_0)}} \quad \& \; Z_0/Z_k$$

where $\exp(-\beta(A_k - A_0)) \equiv \int dQ\, \underline{P(Q)}\, e^{-\beta \frac{1}{2}k(Q-Q_0)^2}$

This method can let us compute

$A(Q) = -k_B T \log P(Q)$

and hence $A(Q_B) - A(Q_A)$, free energy difference between 2 states if differ in coordinate

Sometimes states better described by a change in hamitonian, eg

$$Cl^- + Na^+ \longleftrightarrow Cl + Na$$

suppose state1 has $\mathcal{H}_1 = KE + U_1(x)$

and $H_2 = KE + U_2(x)$

Then $H(\lambda) = KE + (1-\lambda)U_1(x) + \lambda U_2(x)$

can be simulated to try to get free energy between states

$$Q(\lambda) = C \int dX\, e^{-\beta \mathcal{H}(x,\lambda)}$$

$$A = -k_B T \log Q(\lambda) = -k_B T \log Z(\lambda) + k.\varepsilon.$$

$$\frac{\partial A}{\partial \lambda} = -\frac{k_B T}{Q} \frac{\partial Q}{\partial \lambda} = -\frac{k_B T}{Z} \frac{\partial Z}{\partial \lambda}$$

$$\partial Z / \partial \lambda = \int dq^{3N} -\beta \frac{\partial U}{\partial \lambda} e^{-\beta U(q,\lambda)}$$

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

if liner

$$\Delta A = \int_0^1 d\lambda \frac{\partial A}{\partial \lambda} = \int_0^1 d\lambda \left\langle \frac{\partial U}{\partial \lambda} \right\rangle_\lambda = \int_0^1 \langle U_2 - U_1 \rangle_\lambda \, d\lambda$$

Thermo Integration

In practice, do simulations at diffrent λ_i in range, and then do when to get $A(\lambda)$ to compute $A(1) - A(0)$

In contrast, direct/end point swiching (Free Energy Perturbation)

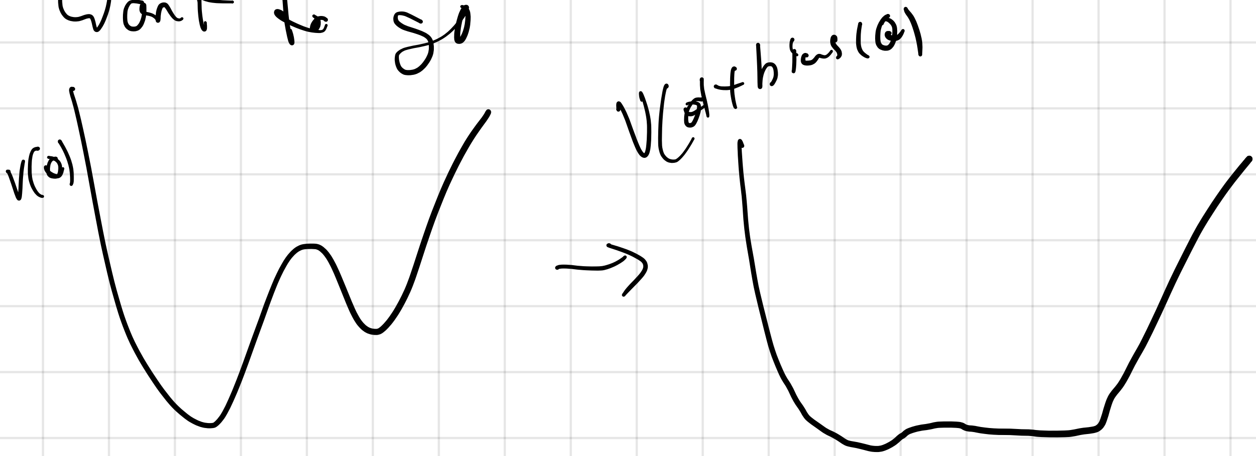
$$A_2 - A_1 = -k_B T \log Z_2 - k_B T \log Z_1$$

$$= -k_B T \log Z_2 / Z_1$$

$$= -k_B T \log\left(\left\langle e^{-\beta (U_2 - U_1)} \right\rangle_1 \right)$$

Another Idea: Metadynamics

Want to go



"ideal" bias $= -V(\theta)$

Add gaussians every Δt steps $\quad V(\theta, t+\Delta t) = V(\theta, t) + h e^{-\frac{(\theta - \theta(t))^2}{2\sigma^2}}$

h is height, σ is width

center is current CV position

Well tempered, $\quad h(\theta) = e^{-\gamma V(\theta)} h$

bias added is smaller where bias exists