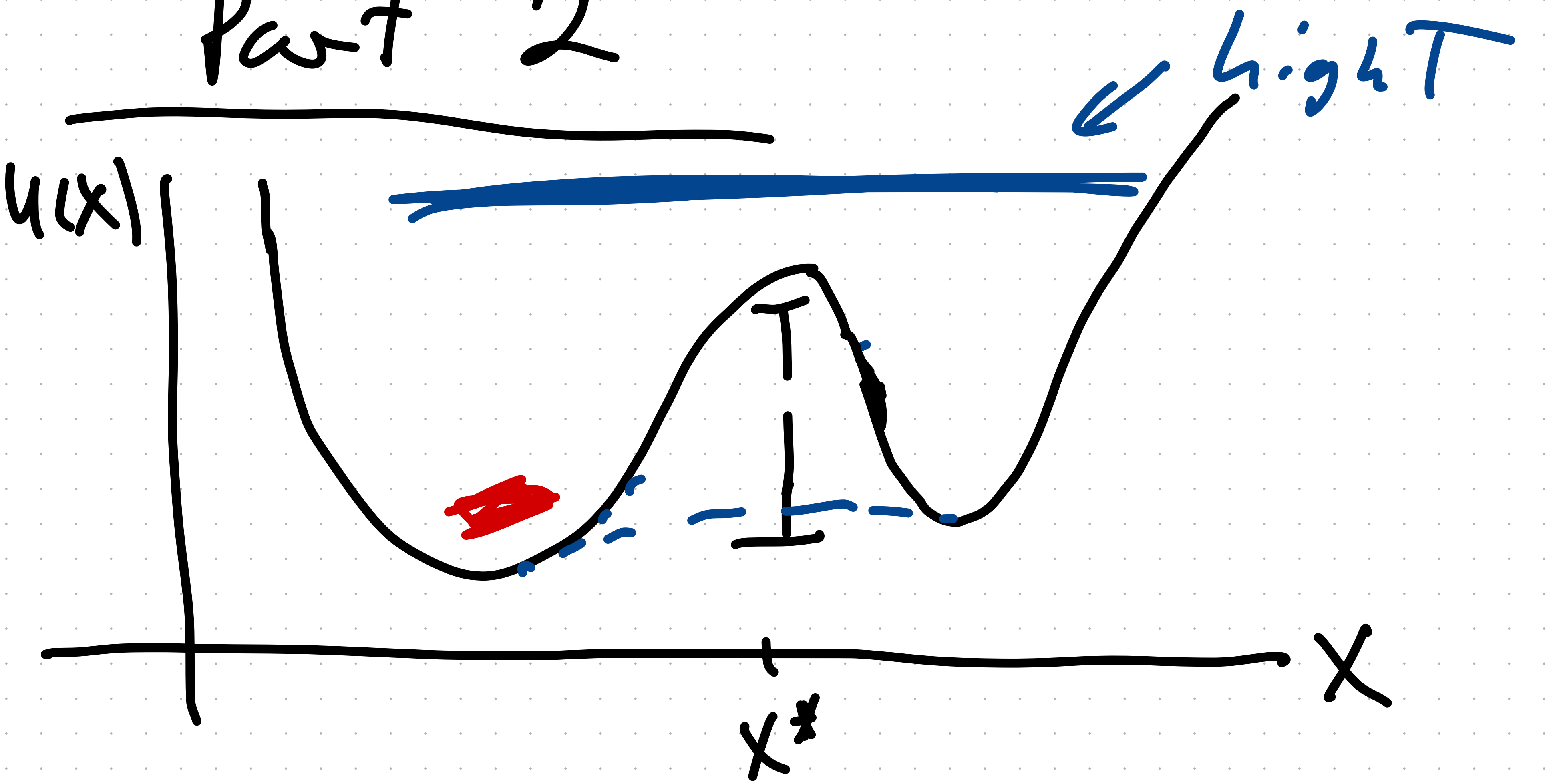
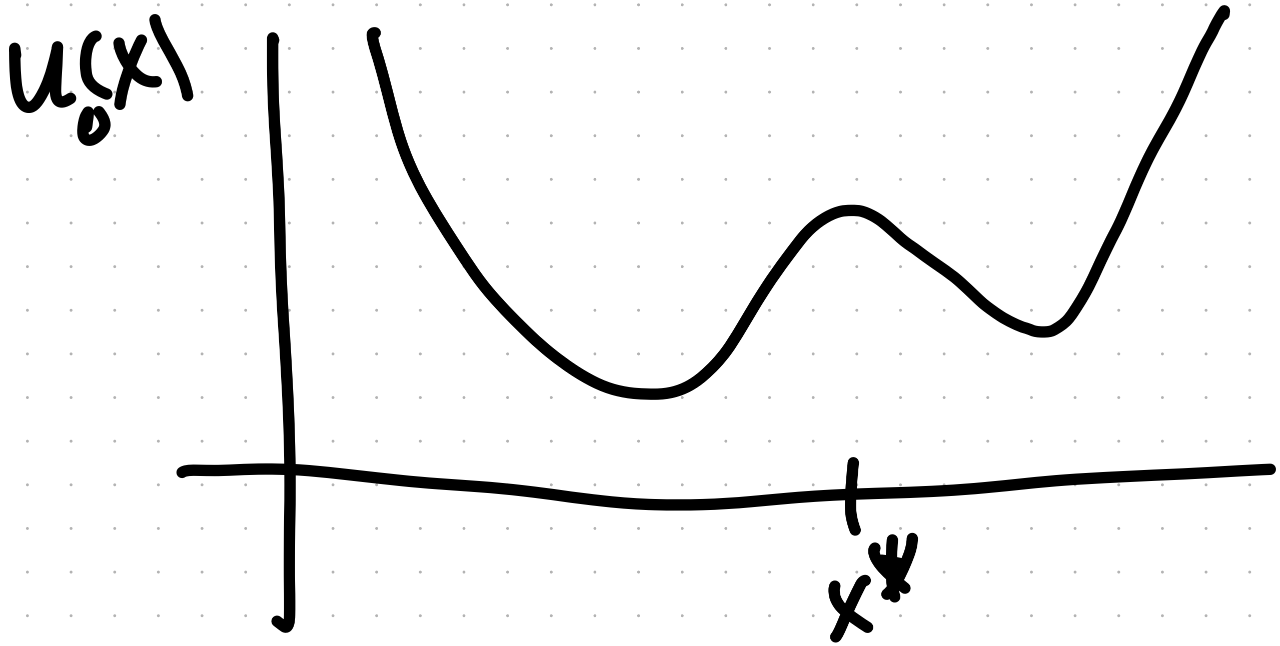
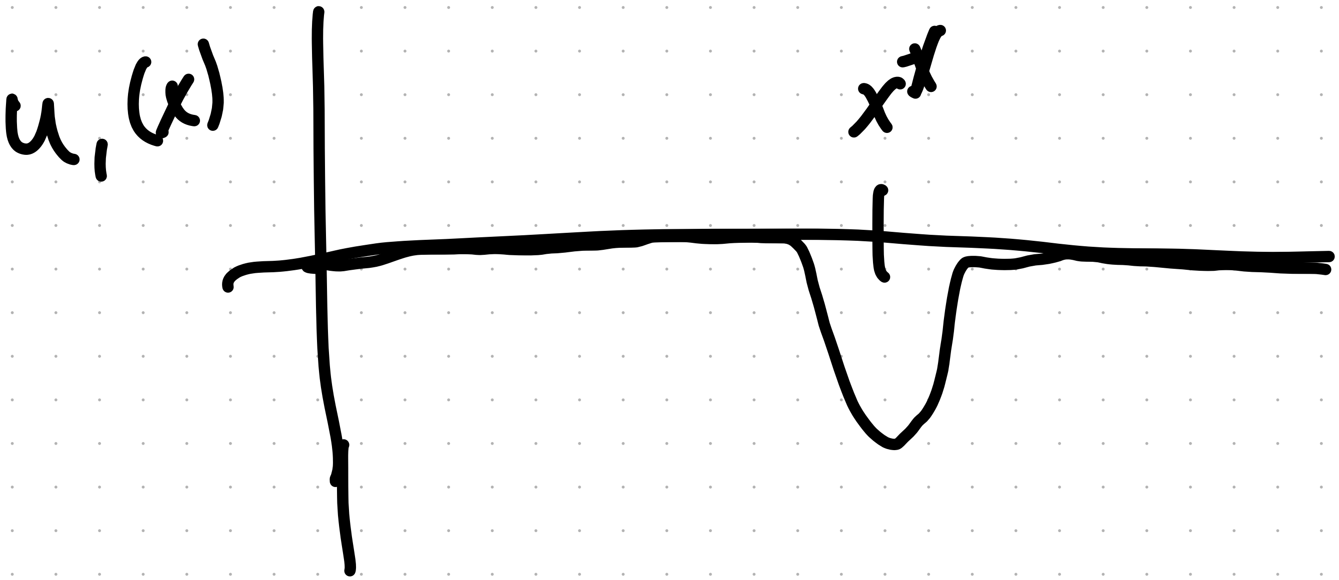
Free energies / enhanced sampling

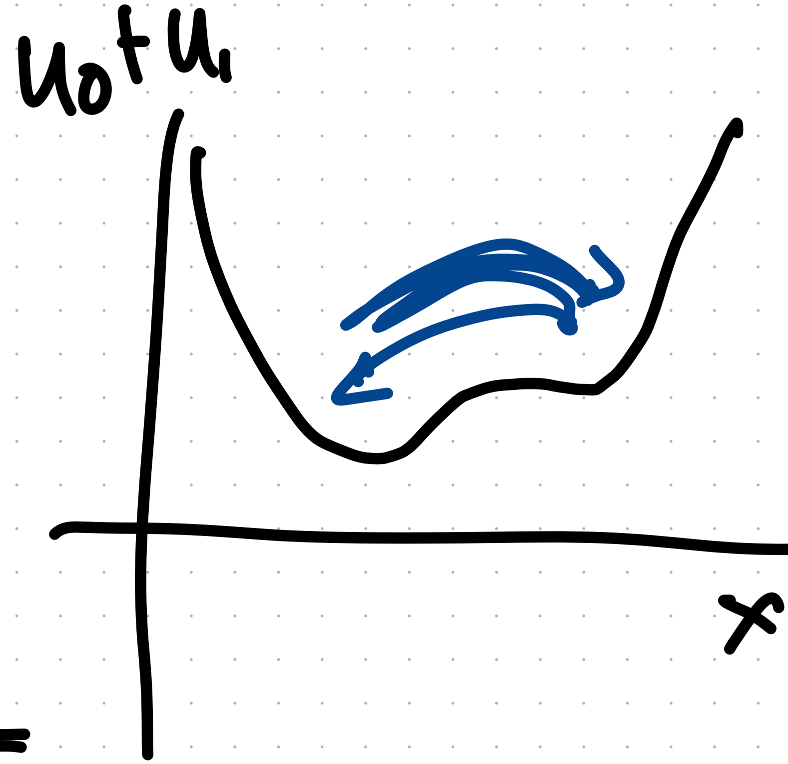
Part 2



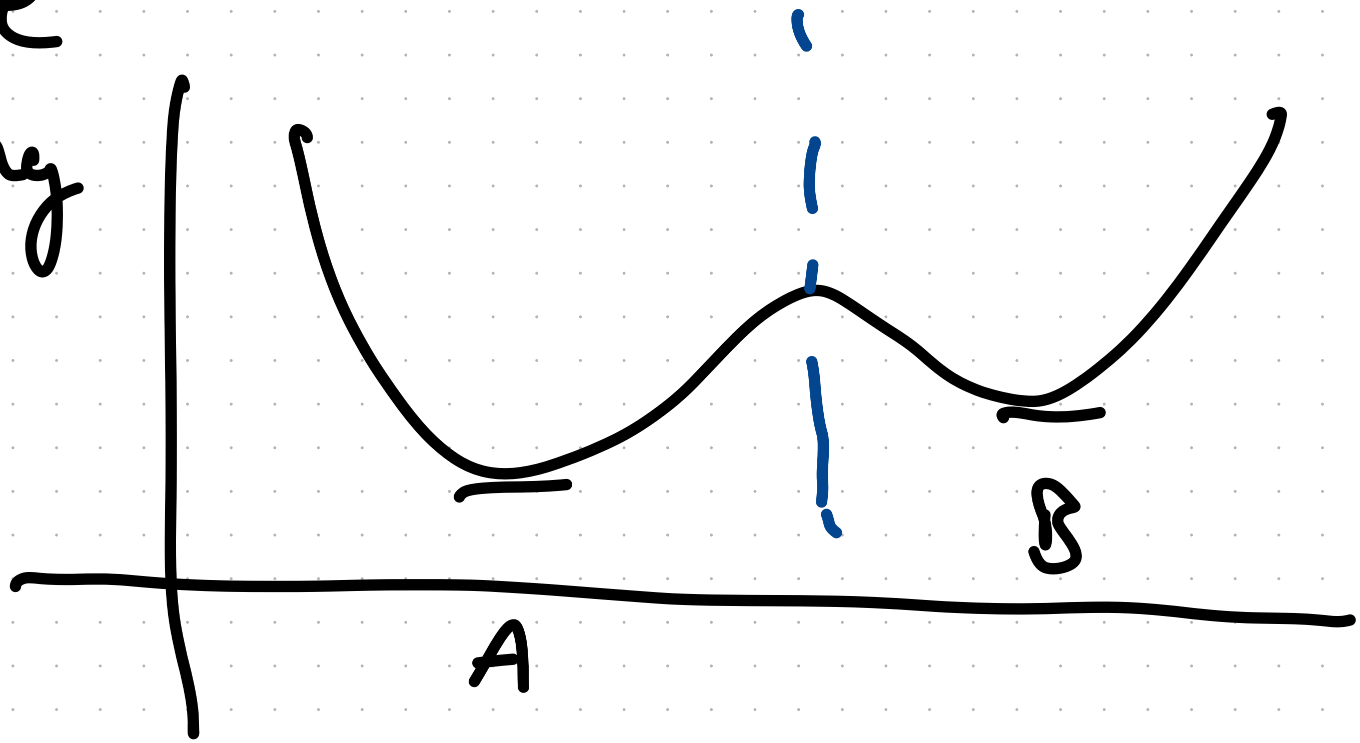
Torrie Valleau 1977







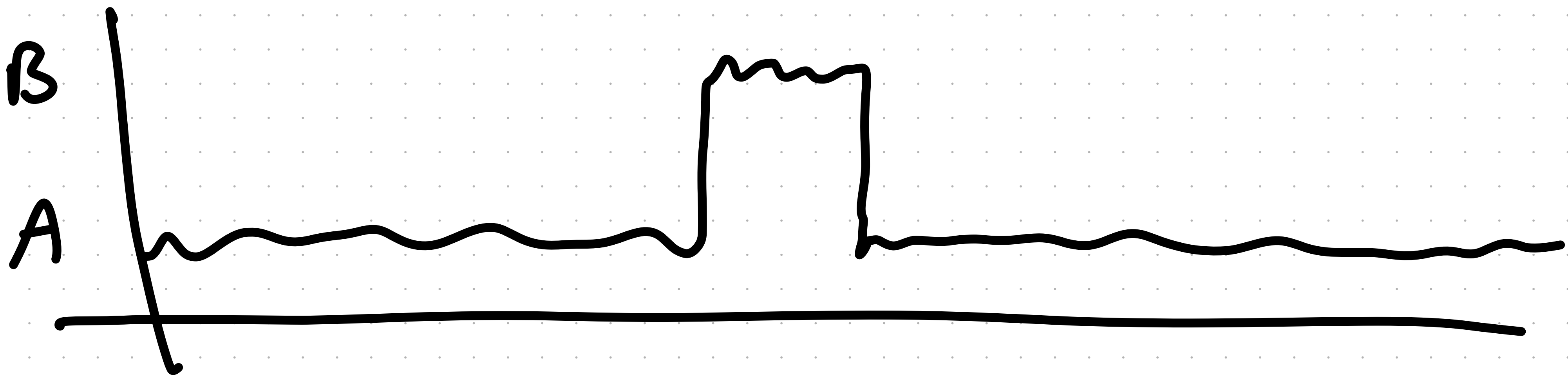
Side note
sampling



$$\Delta A = -k_B T \ln \frac{Q_B}{Q_A}$$

$$A(\text{state } A) = -k_B T \ln \overbrace{\int dx\, e^{-\beta U(x)} \chi_A(x)}^{Q_A}$$

from trajectories

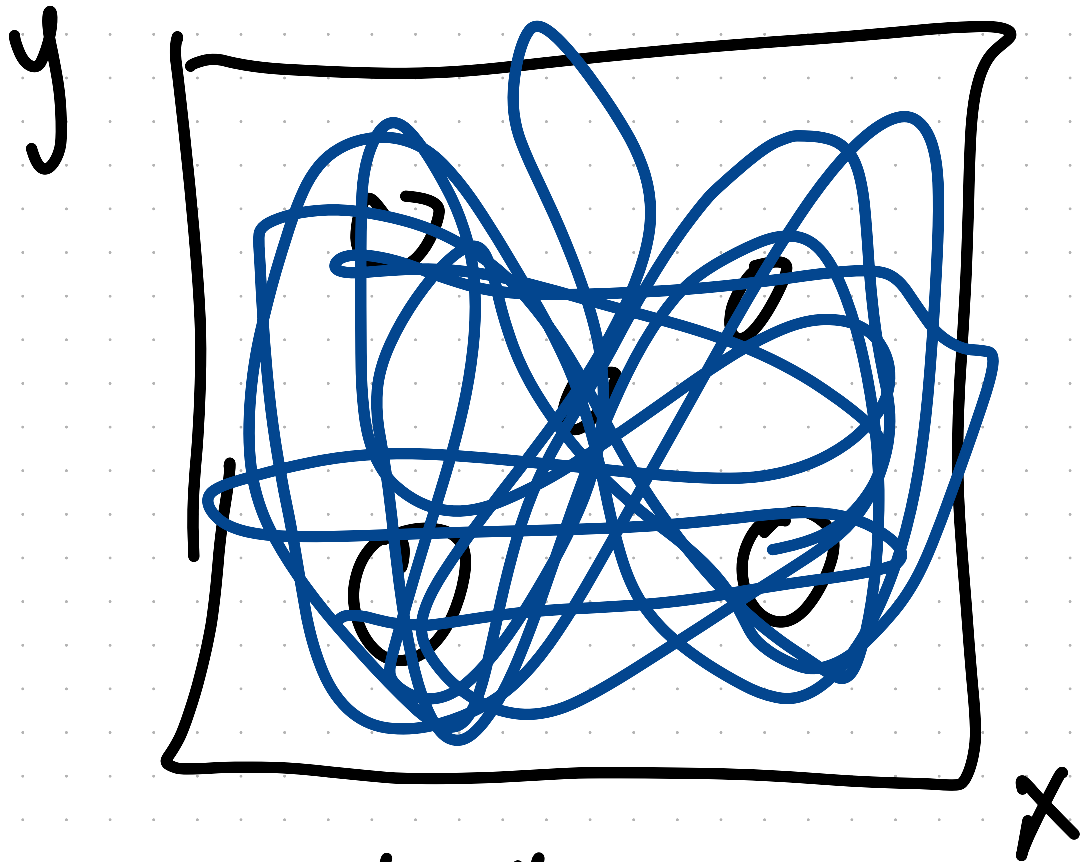


Prob $A \approx 0.8$

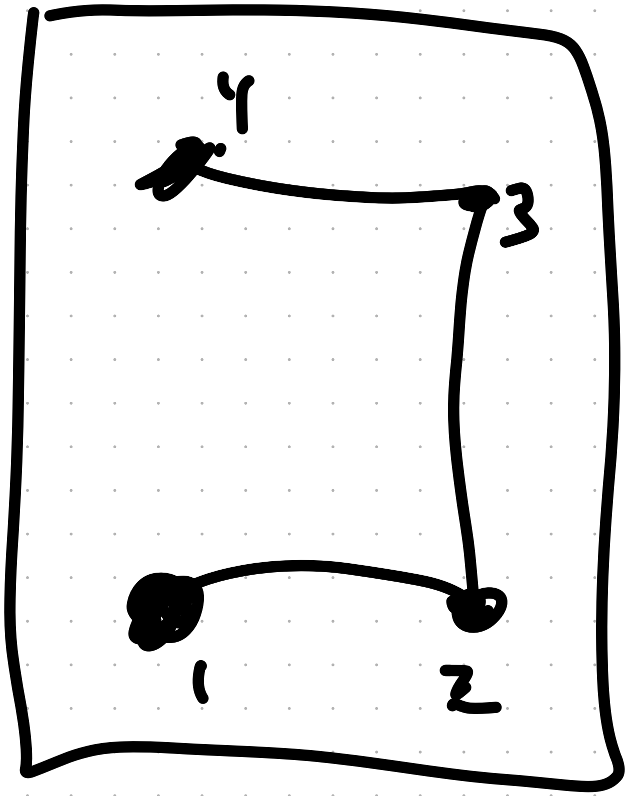
Prob $B \approx 0.2$ ← hard to estimate if rare

Need to be correct is many "crossings" from $A \to B \to A$

Good trajectory



better

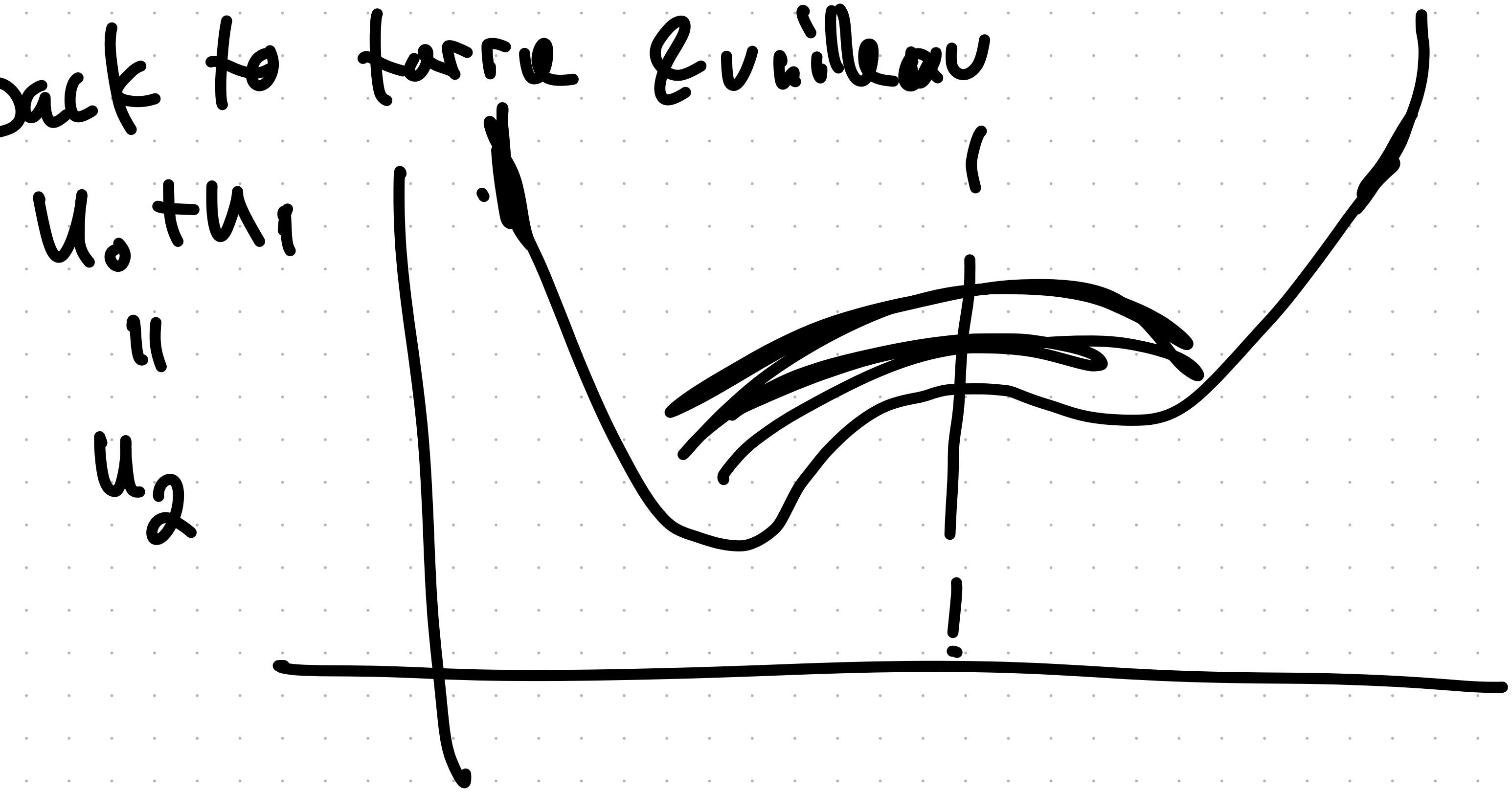


bad

reality $P(x) \propto e^{-\beta U(x)}$

$U \to \infty$ for big "x"

back to torrie & valleau



want

$$\langle A \rangle = \int dx\, P_0(x)\, A(x)$$

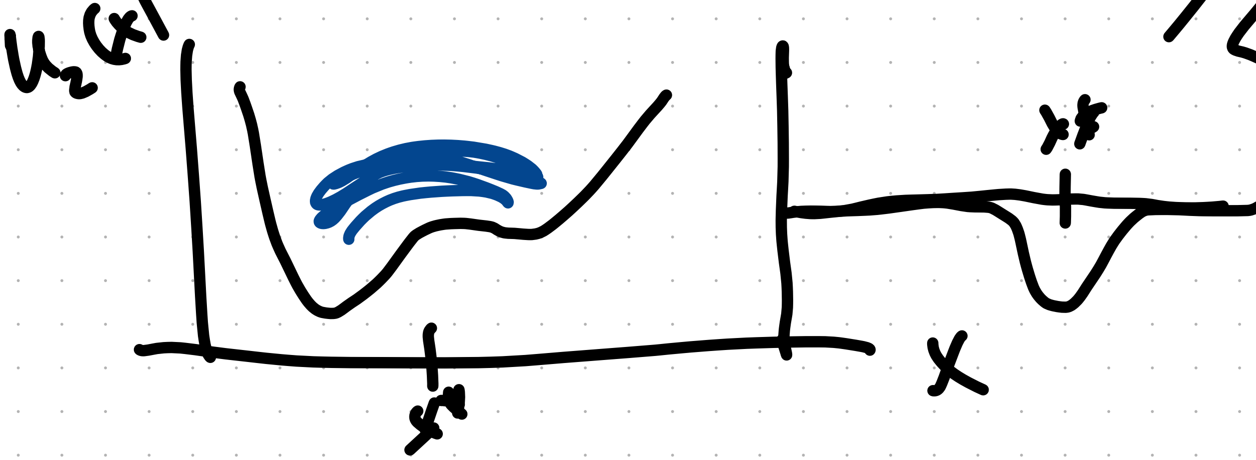
$$P_0 = e^{-\beta U_0(x)} / Z_0$$

$$\langle A \rangle_0 = \frac{1}{Z_0} \int dx \, A(x) \, e^{-\beta U_0(x)} \leftarrow w_0$$

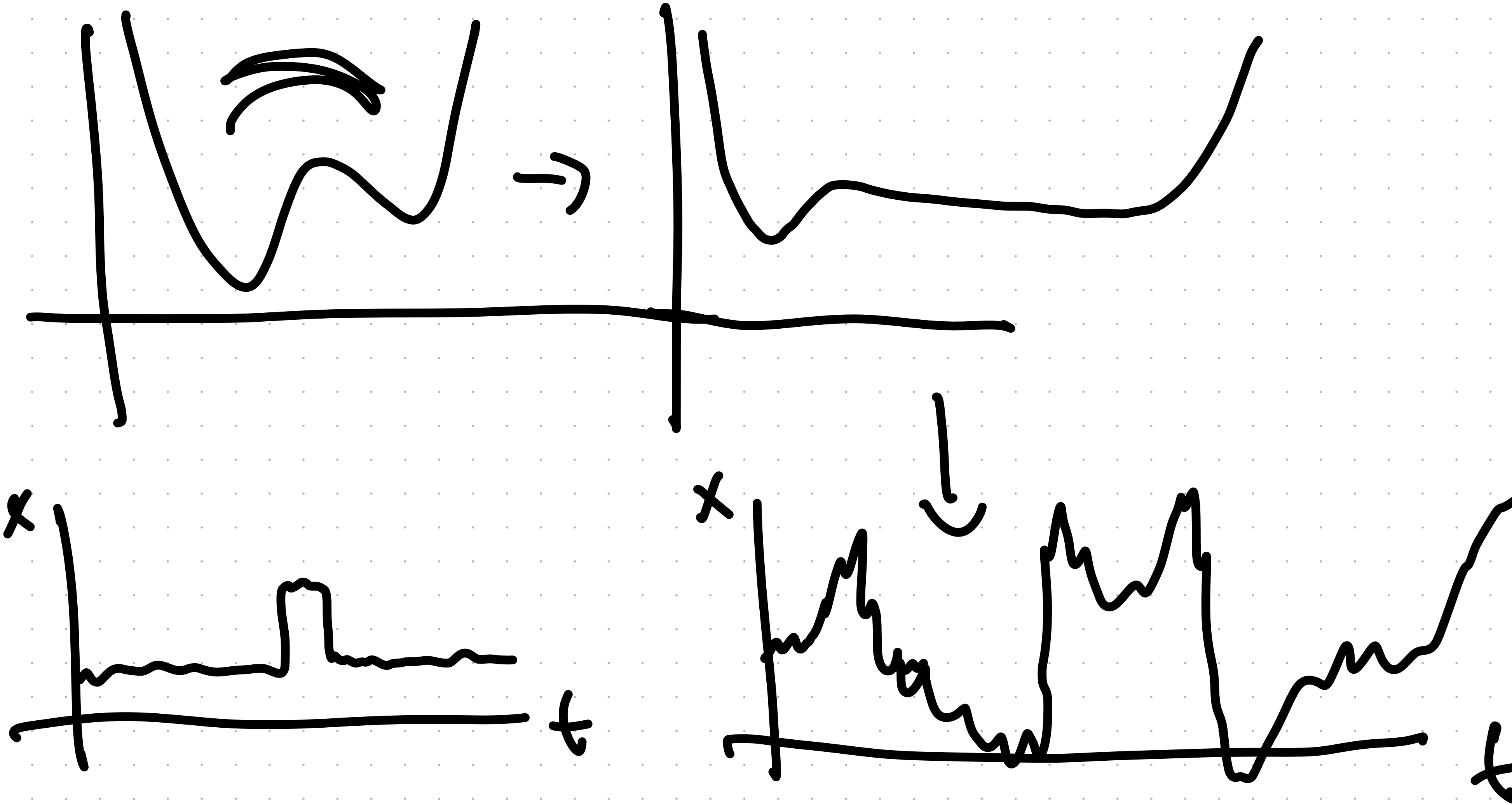
multiply and divide by $e^{-\beta U_2(x)} / Z_2$

$\uparrow w_1$

$$\ldots = \langle A e^{\beta U_1(x)} \rangle_2 \Big/ \langle e^{\beta U_1(x)} \rangle_2$$



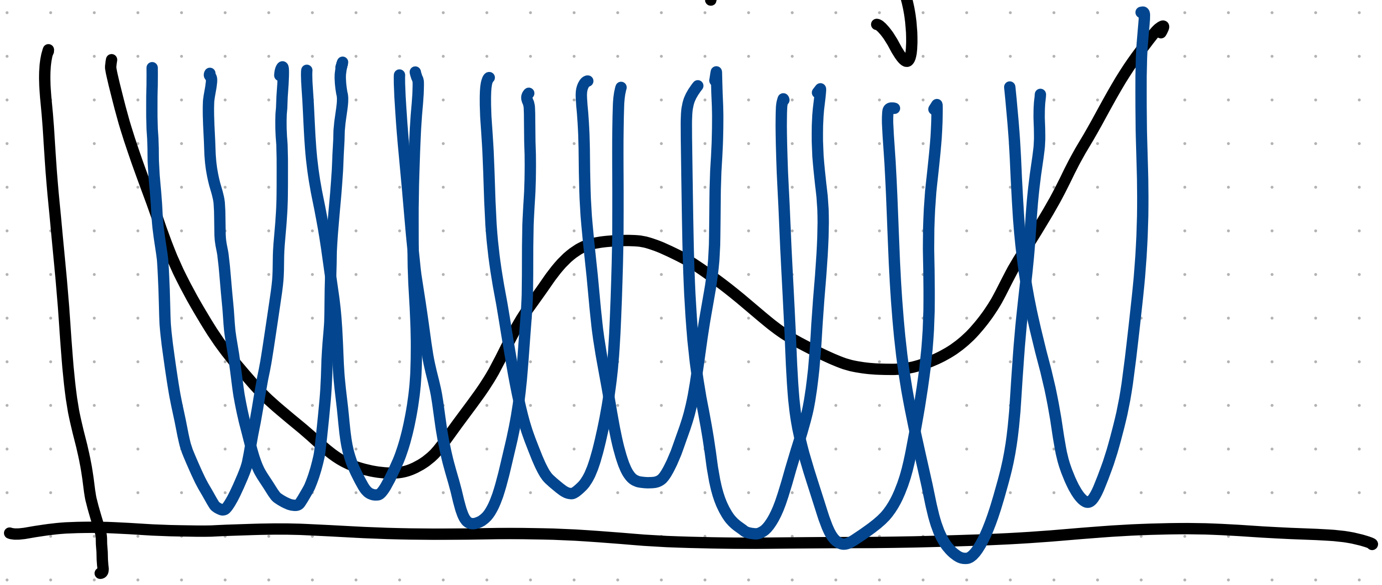
low weight near x^*



$$\langle \delta x^2 \rangle \propto D t \cdot d \quad \sim \quad t \sim L^2 / dD$$

low D problems, can take a long time

Umbrella Sampling (modern)

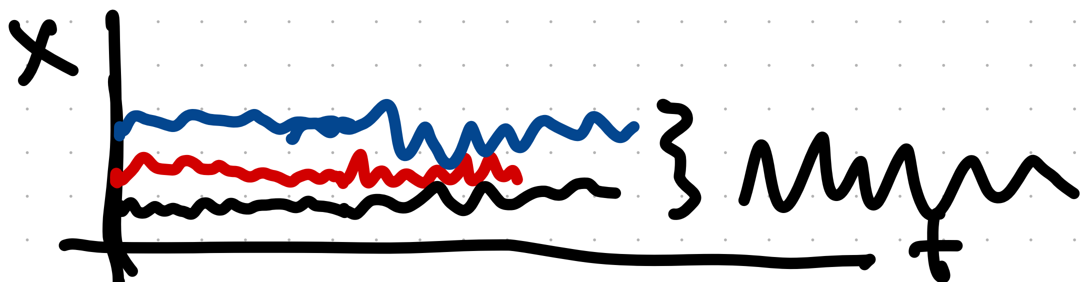


add restraint at positions x_i

$$R_i(x) = \frac{1}{2} k (x - x_i)^2$$

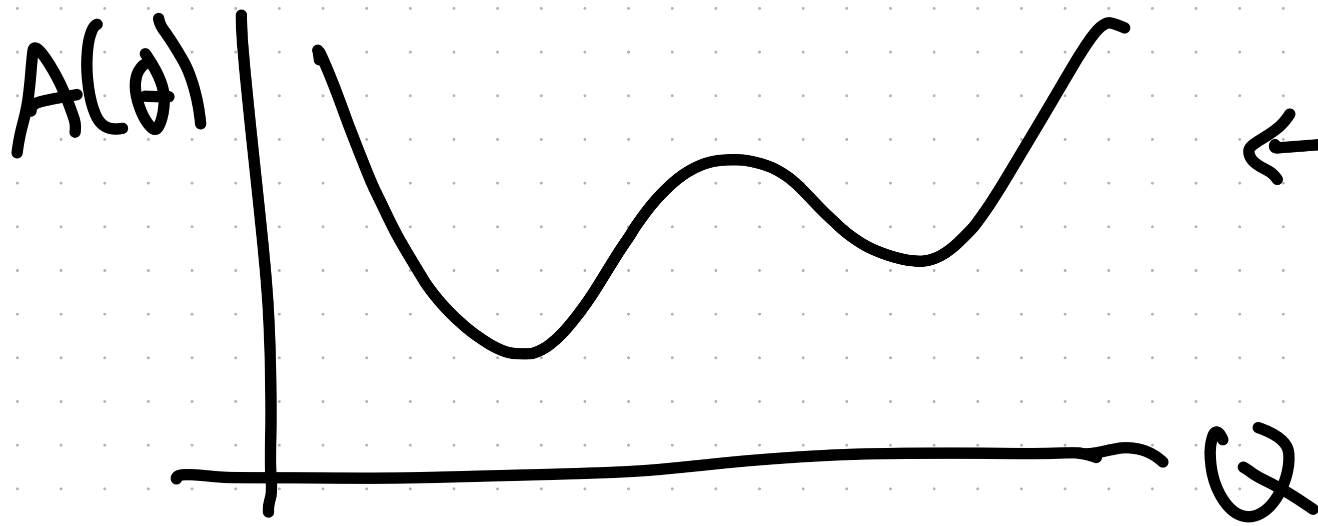
$$U_i = U_0 + R_i$$

Result



know $U(x)$

in $d > 1, 2$ we don't know $A(\theta)$



← don't know

Simplest conceptual umbrella sampling

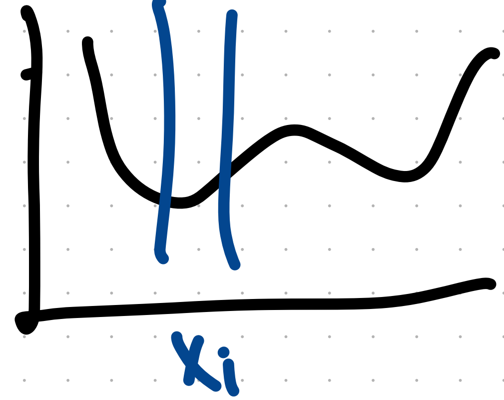
$$R_i(x) = \begin{cases} 0 & |x - x_i| < a \\ \infty & \end{cases}$$

$$U_i(x) = \begin{cases} U_0(x) & |x_i - x| < a \\ \infty & \end{cases}$$

simulation in potential U_i samples

$$P(x) \propto e^{-\beta U_i(x)} \propto e^{-\beta U_0(x)} \quad \text{if } |x - x_i| < a$$

$$\chi_i = \begin{cases} 1 & |x-x_i| < a \\ 0 & |x-x_i| \geq a \end{cases}$$



$$A_i = -k_B T \log\left[\int dx\, e^{-\beta u_i(x)} \Big/ z_i\right]$$

$$= -k_B T \log\left[\int dx\, \chi_i\, e^{-\beta u_0(x)} \Big/ \underbrace{\int dx\, e^{-\beta u_0(x)}}_{Z}\right]$$

$$+ \text{constant}_i$$

$$C_i = -k_B T \ln\left(z_i / z_0\right)$$

run a simulation in U_i, N differenti

get $A_i(x) = -k_B T \ln \Big[\int dx\, \underbrace{e^{-\beta u_0} \chi_i}_{P_i(x)} \Big]$

$+ \text{const}$

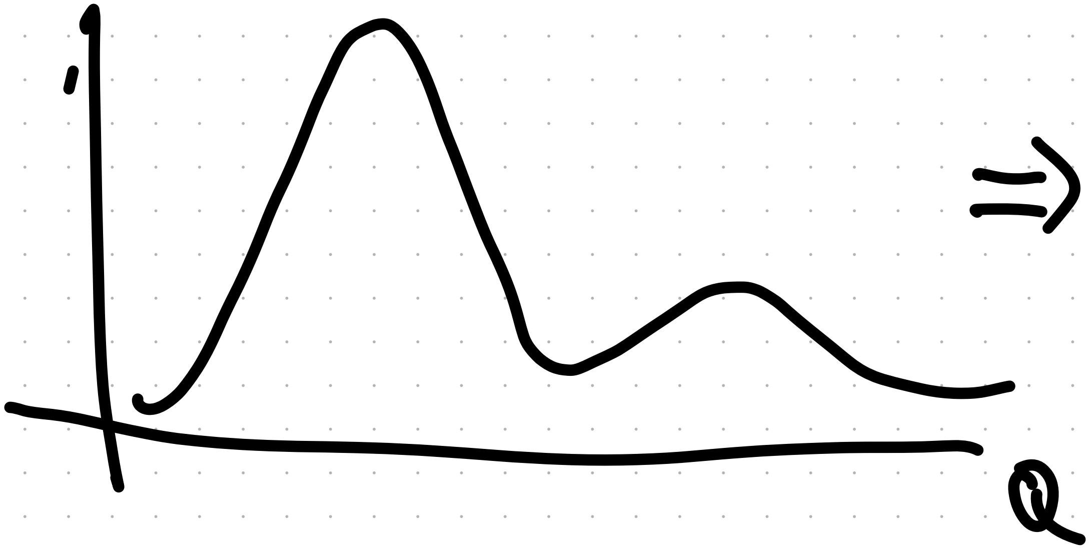
$P_i(x) = e^{-\beta A_i(x)} \cdot \text{const}$

$\approx$ histogram , MD trajectory

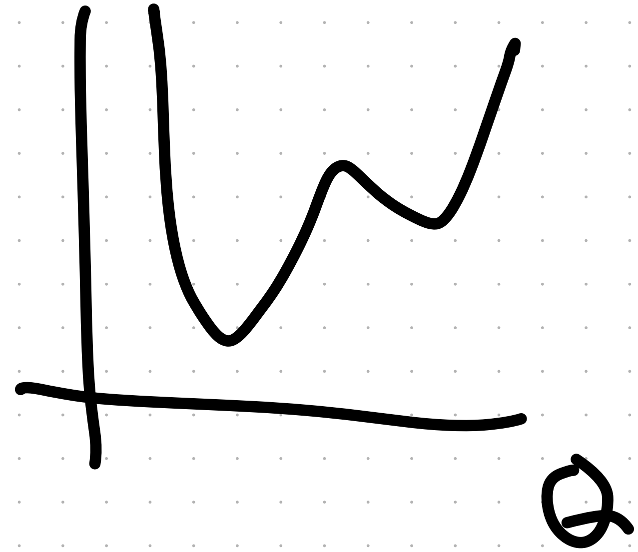
impose

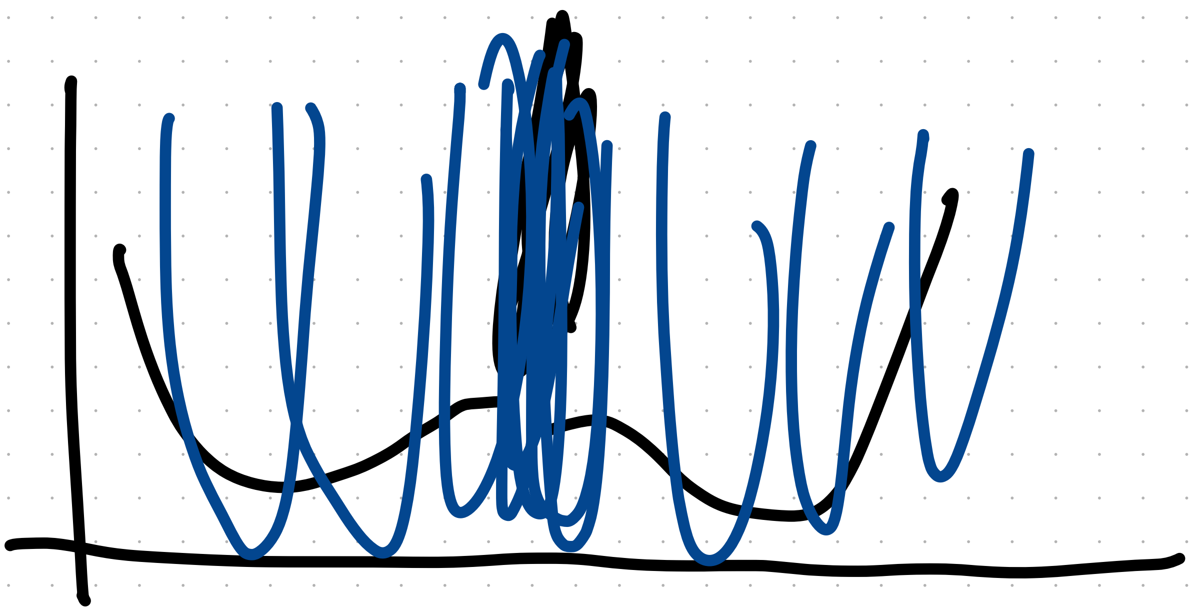
P(x) must be smooth

combine $p_i(x) \rightarrow P(x)$



$\Rightarrow A = -k_B T \log P(x)$





In practice: $R_i(Q) = \frac{1}{2} k (Q - Q_i)^2$

$$Q_j = M_j(\vec{X})$$

high dimensions

$$\Delta Q = L / N_{boxes}^{1/d}$$

$$N_{boxes} = (L/\Delta Q)^d$$
$$= e^{d \log(L/\Delta Q)}$$

histogram our MD sim

in potential U_i

$$P_i(\vec{x}) = e^{-\beta U_0(x) + \frac{1}{2}k(Q-Q_i)^2} / Z_i$$

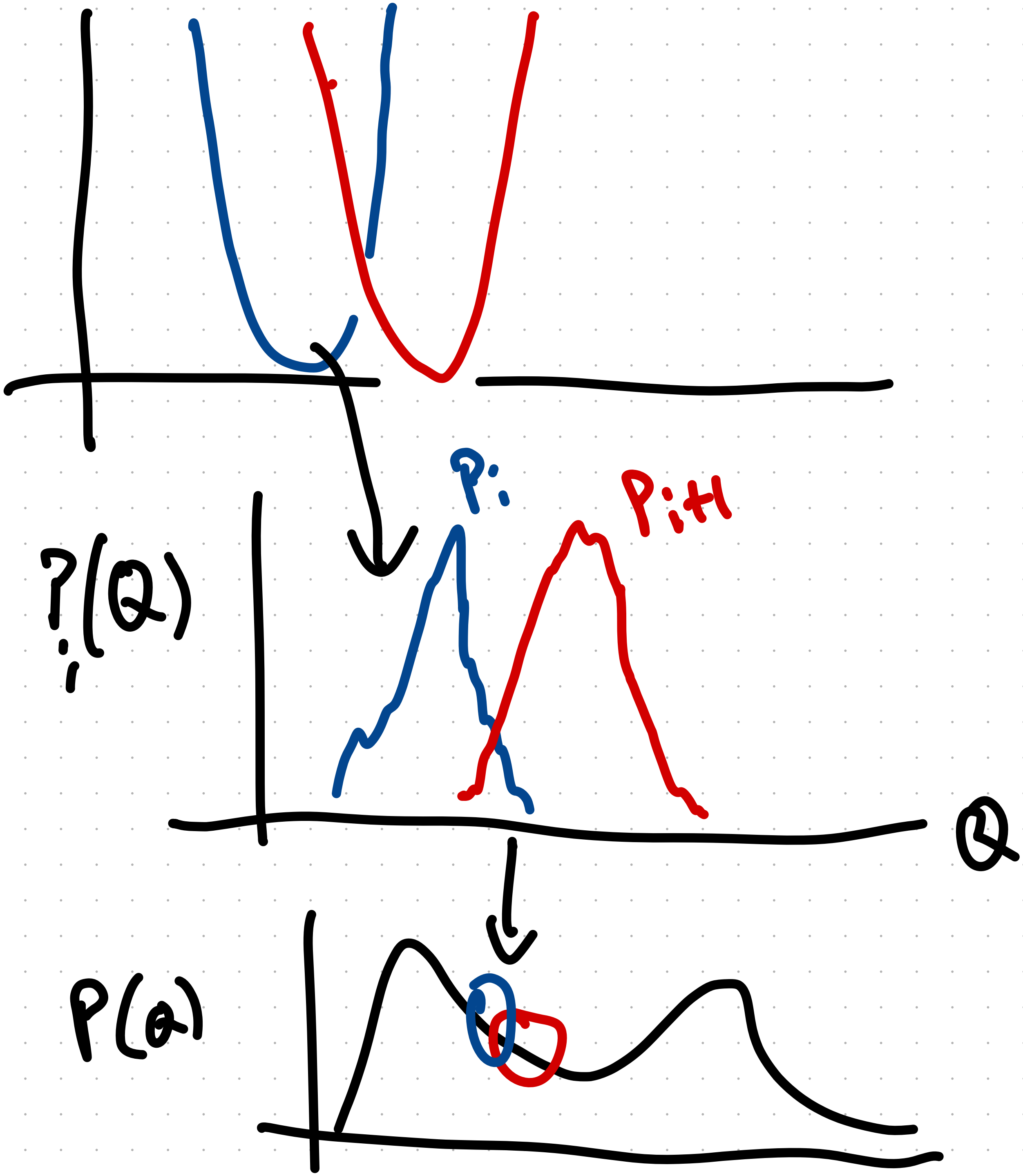
what want is $A(Q)$

need $P(Q)$

$$P_i(Q) = \int dx\, P_i(x)\, \underline{\delta(M_i(x) - Q)}$$

to get $P(Q)$ combining info from N simulations

Wham - weighted histogram analysis method (Tuckerman 8.8)



minimize variance in our estimate of $P(Q)$

Solve by iteration

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

$$e^{\beta(A_k - A_0)} \sim z_0 / z_K$$

$$A_K = -k_B T \log z_K$$

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

don't know this

Learned about free energy in
"Real" coordinate

Also do it for an abstract
reaction coordinate

H_2O

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

$$U(x,\lambda) = (1-\lambda)\, U_1(x) + \lambda\, U_2(x)$$

want to know $A(\lambda=1) - A(\lambda=0)$

$$Q(\lambda) = \frac{\overset{\text{const}}{1}}{Z_\lambda} \int dx\, e^{-\beta U(x,\lambda)}$$

$$A(\lambda) = -k_B T \ln Q(\lambda)$$

$$\frac{dA}{d\lambda} = -k_B T \frac{1}{Q_\lambda} \frac{\partial Q(\lambda)}{d\lambda}$$

$$\frac{\partial Q}{\partial \lambda} = \int dx \; -\beta \frac{\partial u}{\partial \lambda} e^{-\beta u(x,\lambda)}$$

$$\frac{\partial A}{\partial \lambda} = \frac{1}{Q_\lambda} \cdot (-k_B T)(-\beta) \int dx \; \frac{\partial u}{\partial \lambda} e^{-\beta u(x,\lambda)}$$

$$= \left\langle \frac{\partial u}{d\lambda} \right\rangle_\lambda$$

thermodynamic integration

if linear

$$\Delta A = \int_0^1 d\lambda \frac{\partial A}{\partial \lambda} = \int_0^1 d\lambda \left\langle \frac{\partial u}{\partial \lambda} \right\rangle_\lambda = \int_0^1 d\lambda \langle u_2 - u_1 \rangle_\lambda$$

do like umbrella sampling

N simulations at λ_i

In contrast

Free Energy Perturbation

$$A_2 - A_1 = -k_B T \log \left(\langle e^{-\beta(U_2 - U_1)} \rangle_1 \right)$$