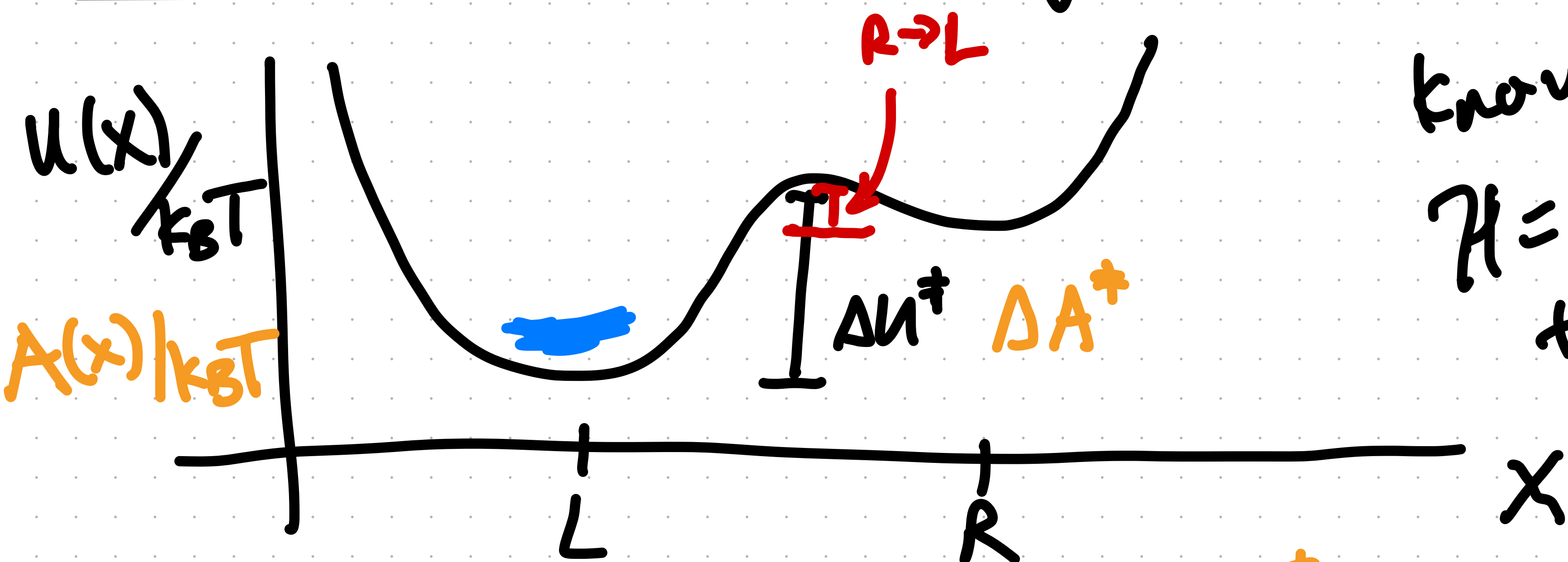
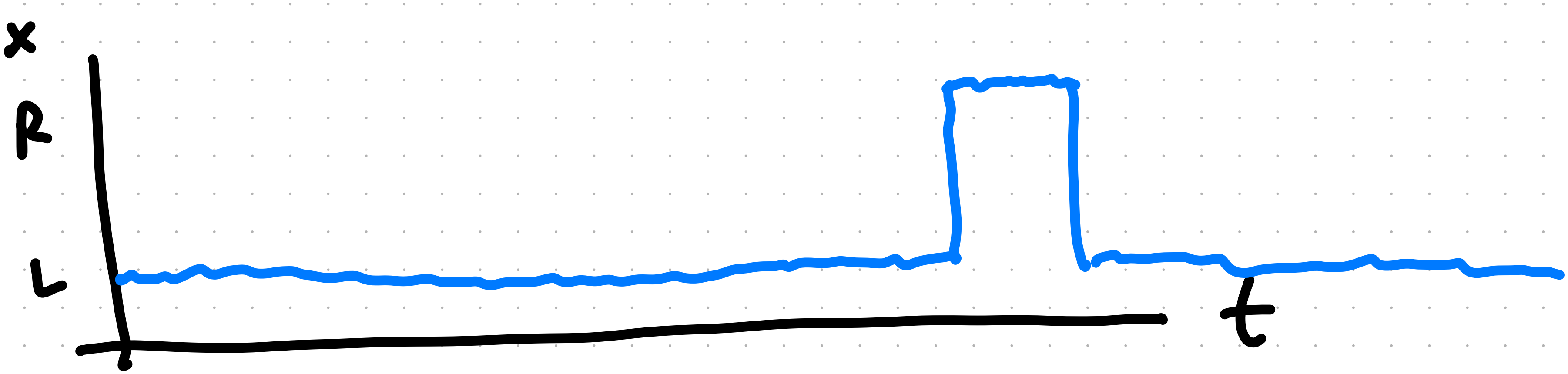
Enhanced Sampling Simulations



know

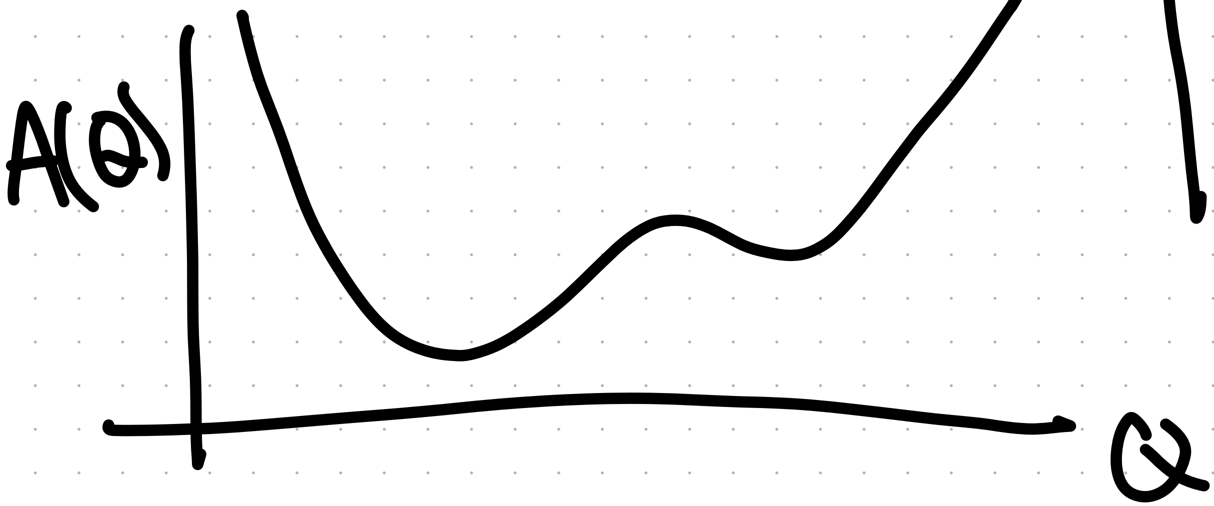
$\mathcal{H} = KE + PE$

$$\text{Rate}_{L \to R} \propto e^{-\beta \Delta U^{\ddagger}} \quad \left(e^{-\beta \Delta A^{\ddagger}}\right)$$



$$A(Q) = -k_B T \log \int d\vec{X}\, \delta(M(\vec{X}) - Q)\, e^{-\beta U(X)} \;) \quad - A_0$$

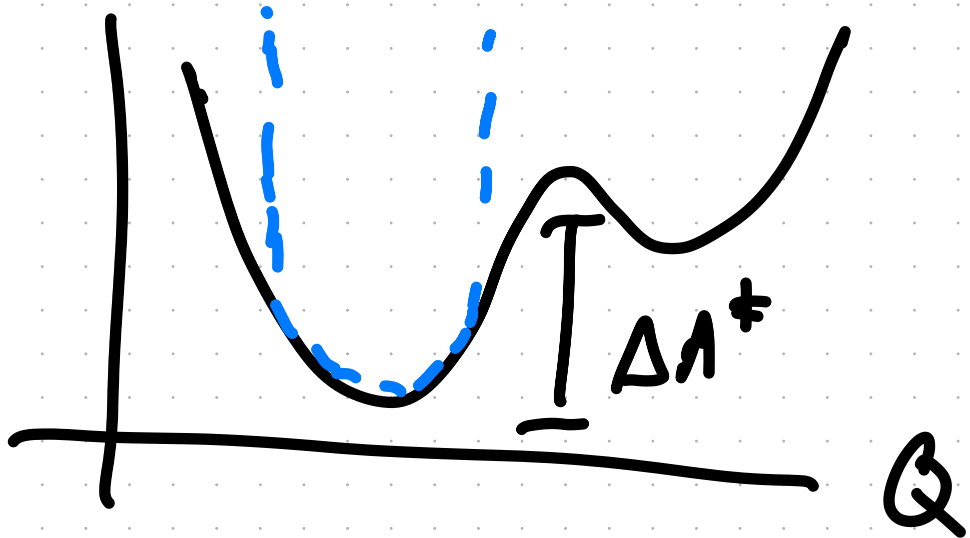
PMF



Q "collective variable", "reaction coordinate"

$M(\vec{X})$ "mapping" - $3N \to$ several dof

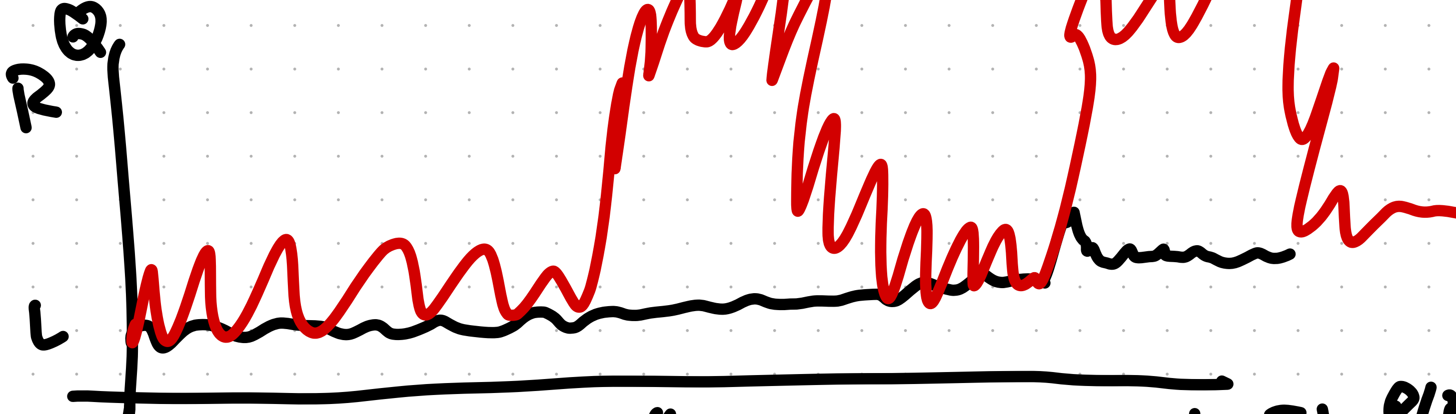
True FES:



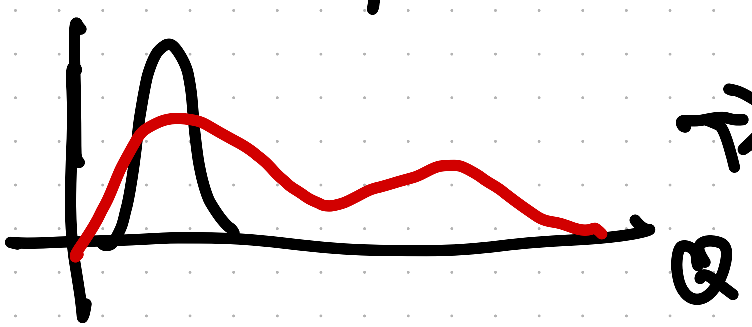
Simulation start on left, and $k_BT << \Delta A^\ddagger$

simulate

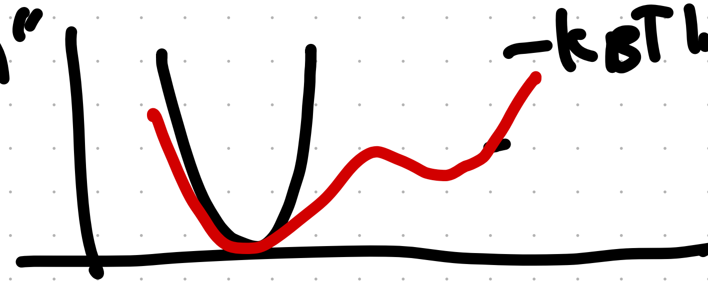
$k_BT \sim \Delta A^\ddagger$



P(Q)



→ "A"



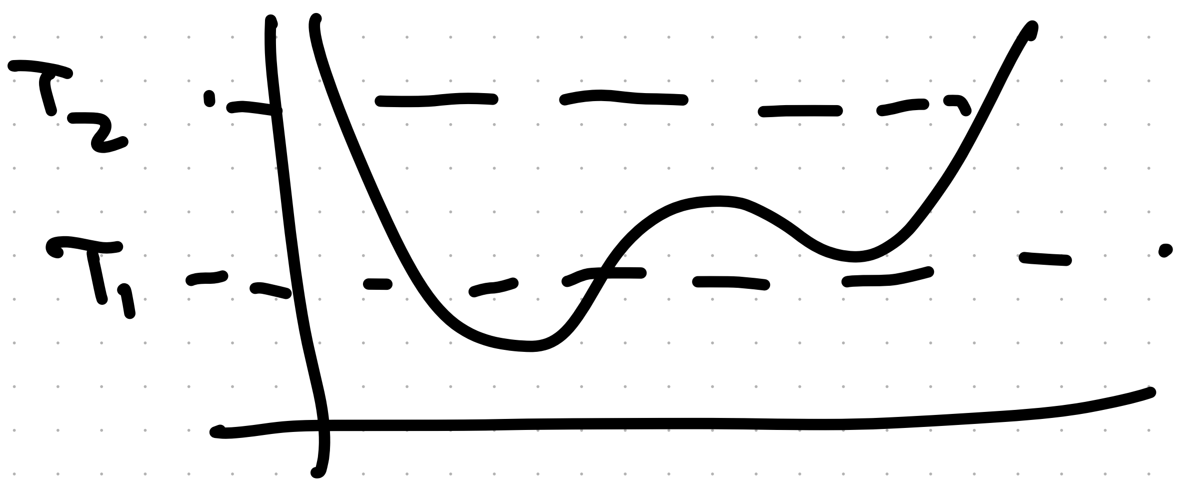
$-k_BT \ln P(Q)$

How sample a surface don't know

1) run simulation and histogram Q

$$Q(t) \rightarrow \underline{P(Q)} \Rightarrow -k_B T \ln P(Q) \approx A(Q)$$

Idea 1: increase T



$T \propto \langle KE \rangle$

$$\langle A\rangle_{T_1} = \int d\vec{x}\, P_{T_1}(\vec{x})\, A(\vec{x})$$

$$P_1(x) = \underbrace{e^{-U(x)/k_B T_1}}_{} \Big/ Z_1 \qquad \omega_1(x)$$

$$Z_1 = \int d\vec{x}\, e^{-U(x)/k_B T_1}$$

$$= \int d\vec{x} \left[\frac{\omega_1(x)}{Z_1} A(x)\right] \cdot \frac{\omega_2(x)/Z_2}{\omega_2(x)/Z_2}$$

$$= \frac{Z_2}{Z_1} \int dx \left(A(x)\, \frac{\omega_1(x)}{\omega_2(x)} \right) \underbrace{\frac{\omega_2(x)}{Z_2}}_{P_2(x)}$$

$$\langle A \rangle_{T_1} = \underbrace{\frac{Z_2}{Z_1} \int dx \left(A(x) \frac{\omega_1(x)}{\omega_2(x)} \right) \frac{\omega_2(x)}{Z_2}}_{=\ \frac{Z_2}{Z_1} \left\langle A\, \omega_1/\omega_2 \right\rangle_{T_2}} = \frac{\left\langle A\, \omega_1/\omega_2 \right\rangle_{T_2}}{\left\langle \omega_1/\omega_2 \right\rangle_{T_2}}$$

$$Z_1/Z_2 = \left\langle \omega_1/\omega_2 \right\rangle_{T_2}$$

$$\langle A \rangle_{T_1} = \langle A \, w_1/w_2 \rangle_{T_2} \Big/ \langle w_1/w_2 \rangle_{T_2}$$

Simulate at T_2

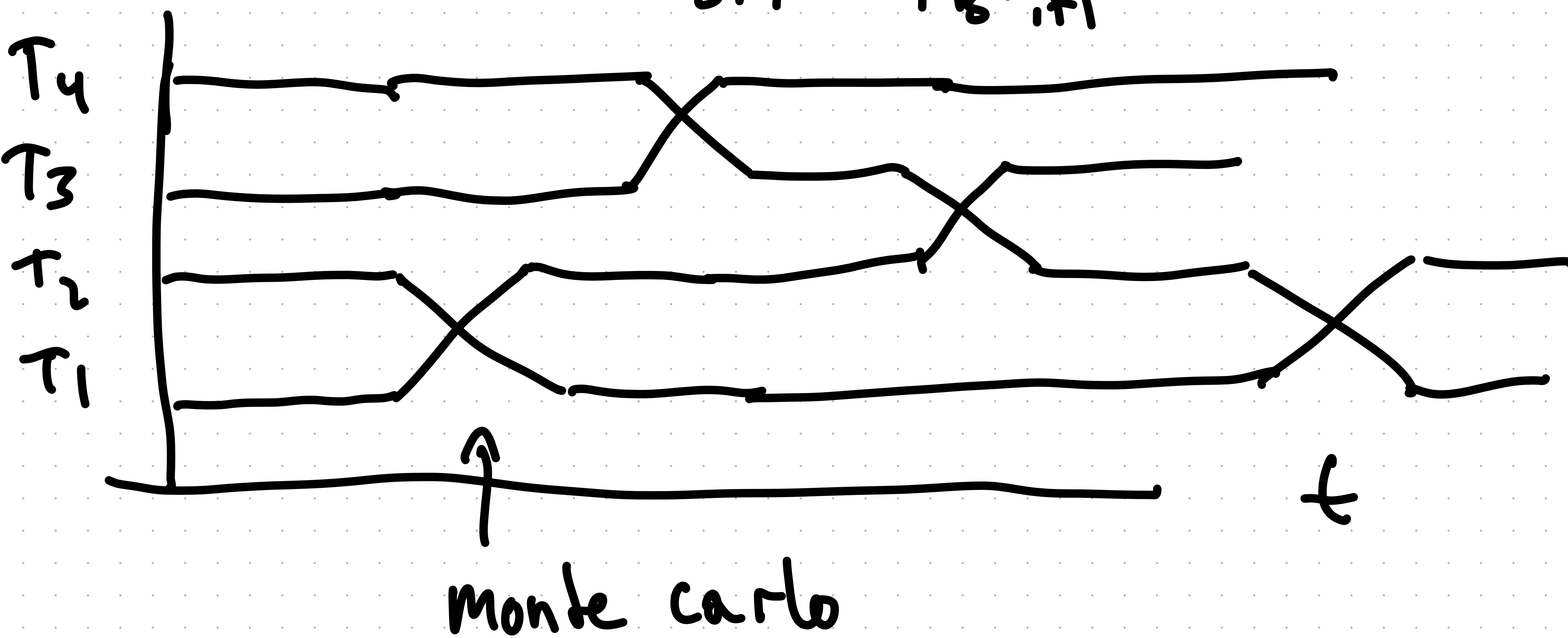
$$w_1^{(x)}/w_2^{(x)} = e^{-U(x)/k_B T_1} \Big/ e^{-U(x)/k_B T_2}$$

$$= e^{-U(x)\cdot\left[\frac{1}{k_B T_1} - \frac{1}{k_B T_2}\right]}$$

Replica Exchange / Parallel Tempering

if many $T_1, T_2, \ldots, T_N$

so that if $\frac{1}{k_B T_i} \sim \frac{1}{k_B T_{i+1}}$



If we do monte carlo exchanges

$$X_{T_1}(t) \propto P_{T_1}(x)$$

Need detailed balance

$$P(A \to B)\, P(A) = P(B)\, P(A \to B)$$

$$A = \{ \vec{x} @ T_i \,,\; \vec{y} @ T_{i+1} \}$$

$$B = \{ \vec{y} @ T_i \,,\; \vec{x} @ t_{i+1} \}$$

$$P(A \to B)\, P(A) = P(B)\, P(A \to B)$$

$$A = \{ \vec{x} @ T_i \, , \; \vec{y} @ T_{i+1} \}$$

$$B = \{ \vec{y} @ T_i \, , \; \vec{x} @ t_{i+1} \}$$

Metropolis Rule

$$P(A \to B) = \min\left\{ 1, \; \frac{P(B)}{P(A)} \right\}$$

$$\frac{P(B)}{P(A)} = \frac{e^{-U(y)/k_B T_i} \; e^{-U(x)/k_B T_{i+1}}}{e^{-U(x)/k_B T_i} \; e^{-U(y)/k_B T_{i+1}}}$$

$$P(A \to B) = \min\left\{1, e^{-\left[\frac{U(x)-U(y)}{k_B}\right]\left[\frac{1}{T_{i+1}} - \frac{1}{T_i}\right]}\right\}$$

if $T_i < T_{i+1}$, $\frac{1}{T_{i+1}} - \frac{1}{T_i} < 0$

$U(x) - U(y)$ <u>probably</u> < 0

most of the time, acceptance prob < 1

$$X_i^{T_1} \propto P(X_i) = e^{-U(X_i)/k_B T}$$

$$\langle A \rangle = \frac{1}{N} \sum_{i=1}^{N} A(x_i^{T_1})$$

$$P(X;\mu_1,\mu_2,\ldots,\mu_N)$$

$$\{\mu\}^i$$

$$\{\mu\}^j$$

$$\mathcal{H}(X) = \sum p_i^2/2m_i + U(X,\lambda_1,\lambda_2,\ldots,\lambda_N)$$

$$P(X) = e^{-\beta\mathcal{H}(X)}/Z$$

Statistics $P(\text{data}, \text{parameters})$

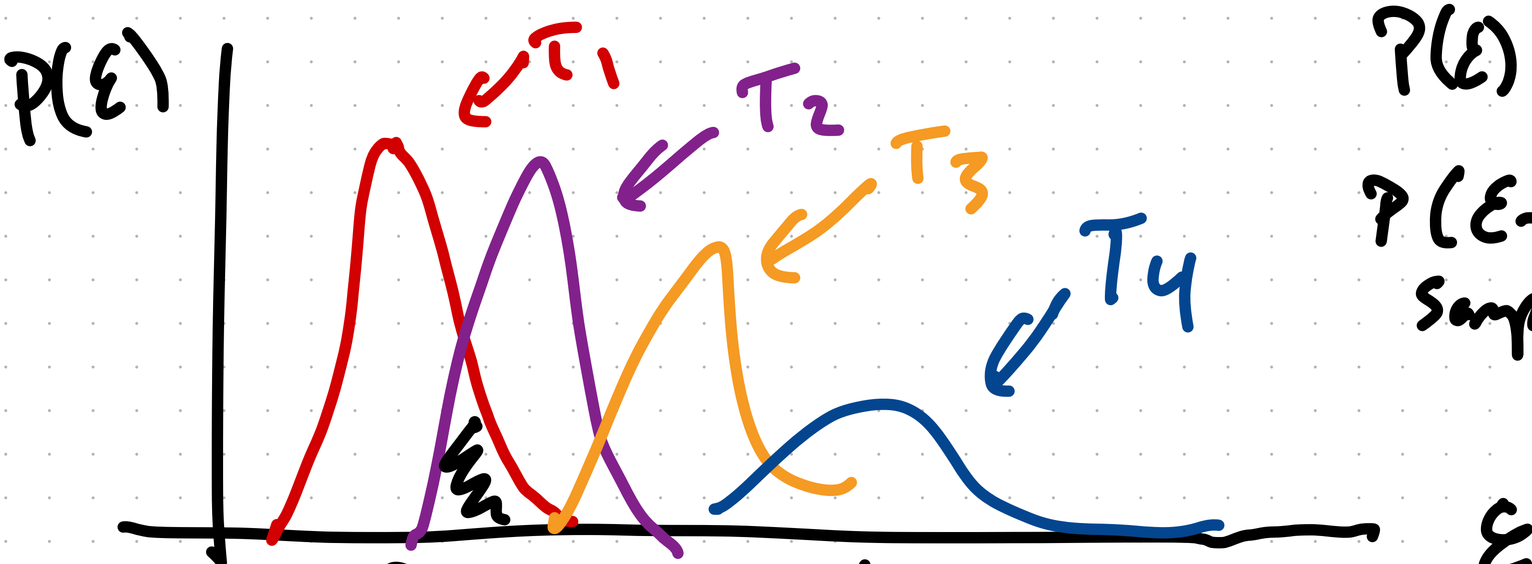
$$P(\text{data}; \text{parameters})$$

$$= e^{+\log(P(\text{data}; \text{parameters}))}$$

$$\log P(\text{data}) = -A(\text{data})/k_BT$$

$$C_V \propto N$$

$$\frac{\sigma_E}{E} \sim \frac{1}{\sqrt{N}}$$



$P_{swap} \propto$ overlap

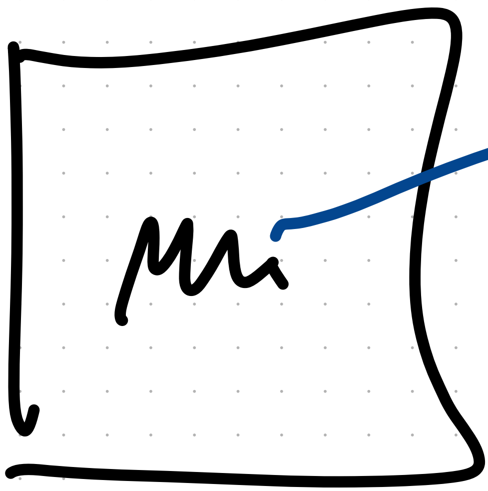
$$P(E) \propto e^{-E/k_BT}$$

$P(E - \langle E \rangle)$ gaussian sampled

$$\sigma^2 = \operatorname{Var} E \propto C_V$$

Replica Exchange w/ Solute Tempering

(REST)



$\rightarrow T_1, T_2, T_3 \ldots$

$$\varepsilon_{sol} + \varepsilon_{sol \sim solu} + \varepsilon_{solu}$$