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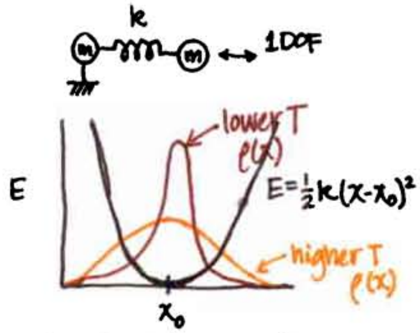
LECTURE 11: STATISTICAL MECHANICS

THURSDAY 16 MARCH 2006



Imagine a dense system of these packed together → see probability distributions above

$$\rho(x) = \text{probability of finding a copy of the system with configuration } x = \frac{e^{-\frac{E(x)}{k_BT}}}{\int_{-\infty}^{\infty} e^{-\frac{E(x')}{k_BT}}\,dx'}$$

$\int_{-\infty}^{\infty} e^{-\frac{E(x')}{k_BT}}\,dx'$ = Q Configurational Partition Function

K_B = Boltzmann Constant $= 1.987 \cdot 10^{-3} \frac{\text{kcal}}{\text{mol}\cdot\text{K}}$

T = Absolute Temperature $= 273.15 + t$ K, t (°C)

Note:

$$\int_{-\infty}^{\infty} \rho(x)dx = \int_{-\infty}^{\infty} \frac{e^{-\frac{E(x)}{k_BT}}}{Q}dx = \frac{1}{Q}Q = 1$$

What is average position?

$$\bar{x} = \sum_{\substack{\text{all possible}\\\text{configurational}\\\text{states}}} (\text{probability of } x)\cdot(\text{value at that position}, x)$$

GENERAL — SPECIFIC

$$= \int_{-\infty}^{\infty}\rho(x)\,x\,dx = \int_{-\infty}^{\infty}\frac{xe^{-\frac{E(x)}{k_BT}}}{Q}dx = \frac{\int_{-\infty}^{\infty} xe^{-\frac{k(x-x_0)^2}{2k_BT}}dx}{Q}$$

Change of variables: $y = x - x_0$, $dy = dx$

$$= \frac{1}{Q}\int_{-\infty}^{\infty}(y+x_0)e^{-\frac{ky^2}{2k_BT}}dy$$

$$= \frac{1}{Q}\underbrace{\int_{-\infty}^{\infty} ye^{-\frac{ky^2}{2k_BT}}dy}_{0} + \frac{x_0}{Q}\underbrace{\int_{-\infty}^{\infty} e^{-\frac{ky^2}{2k_BT}}dy}_{Q}$$

$$= x_0$$

Computing Average Fluctuation:

$$\sqrt{\overline{(x-\bar{x})^2}} = \sqrt{\frac{1}{Q}\int_{-\infty}^{\infty}(x-x_0)^2e^{-\frac{k(x-x_0)^2}{2k_BT}}dx}$$

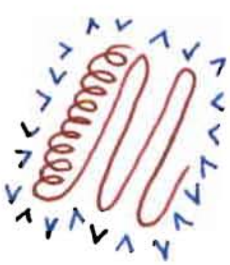
$$= \sqrt{\frac{k_BT}{k}}$$

k_BT → higher T ⇒ greater fluctuation
k → higher k ⇒ lower fluctuation

Computing Average Potential Energy

$$\bar{E} = \langle E\rangle = \frac{1}{Q}\int_{-\infty}^{\infty}E(x)e^{-\frac{k(x-x_0)^2}{2k_BT}}dx = \frac{1}{Q}\int_{-\infty}^{\infty}\frac{k}{2}(x-x_0)^2e^{-\frac{k(x-x_0)^2}{2k_BT}}dx$$

$$= \frac{k_BT}{2}$$



~3,000 atoms of protein
~10,000 atoms of solvent

N ~13,000 particles ⇒ ~39,000 degrees of freedom

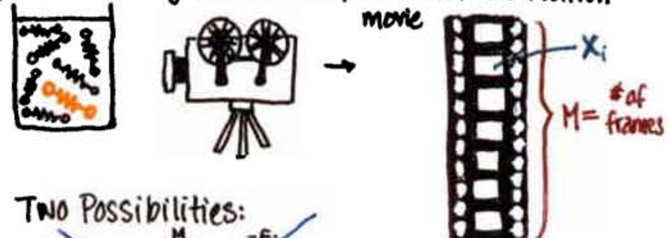
Compute Average Str. of Protein

$$\langle \vec{X}^{3N}\rangle = \frac{\int_{-\infty}^{\infty}\cdots\int_{-\infty}^{\infty}\vec{X}^{3N}e^{-\frac{E(\vec{X}^{3N})}{k_BT}}d\vec{X}^{3N}}{\int_{-\infty}^{\infty}\cdots\int_{-\infty}^{\infty}e^{-\frac{E(\vec{X}^{3N})}{k_BT}}d\vec{X}^{3N}}$$

first problem: $E(\vec{X}^{3N})$ is not analytically integrable → must do it numerically

second problem: 0.1 Å on a 100 Å grid
1000 points per dimension
$(1000)^{39{,}000}$ points total

Imagine Constructing $\rho(x)$ from Experimental Observation



Two Possibilities:

1.) ~~$\langle E\rangle = \frac{\sum_{i=1}^{M} E_i e^{-\frac{E_i}{k_BT}}}{\sum_{i=1}^{M} e^{-\frac{E_i}{k_BT}}}$~~

or

2.) $\langle E\rangle = \frac{\sum_{i=1}^{M} E_i}{M}$

If we use a molecular dynamics simulation as the movie:

Geometric Quantity: $\langle |\vec{r}_{i\ldots j}|\rangle = \frac{1}{M}\sum_{k=1}^{M}|\vec{r}_{i\ldots j}(\vec{x}_k)|$

Interaction Energy: $\langle u_{i\ldots j}\rangle = \frac{1}{M}\sum_{k=1}^{M}u_{i\ldots j}(\vec{x}_k)$

Total Potential Energy: $\langle u\rangle = \frac{1}{M}\sum_{k=1}^{M}u(\vec{x}_k)$

Metropolis Monte Carlo, like MD, also produces a trajectory that converges to a statistical mechanical ensemble
Metropolis et al, *J Chem Phys* 21: 1087-1092 (1953).

Problem trying to get the free energy...

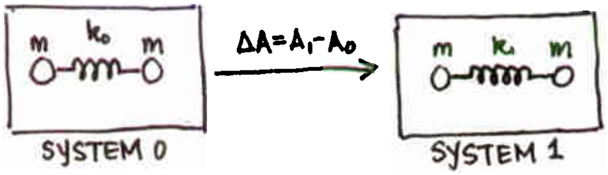
~~I attempted to write: $\langle A\rangle = \frac{1}{M}\sum_{i=1}^{M}A_i$~~ ← this doesn't exist

A ← free energy

Statistical Mechanics gives us a definition:

$$A = -k_BT\ln Q = -k_BT\ln\left[\int_{-\infty}^{\infty} e^{-\frac{u(\vec{x}^{3N})}{k_BT}}d\vec{x}^{3N}\right]$$

Doesn't help, because Q is 1000^{39,000}-dimensional integral



Thermodynamic Integration (Kirkwood, 1934)

1.) Construct a "hybrid" potential that smoothly connects $0 \mapsto 1$.

$$U(\lambda) = (1-\lambda)U_0 + \lambda U_1 \qquad \begin{array}{l} \lambda : (0 \to 1) \\ U : (U_0 \to U_1) \end{array}$$

2.) Fundamental Theorem of Integral Calculus

$$\Delta A = A_1 - A_0 = \int_0^1 \frac{\partial A}{\partial \lambda'} d\lambda'$$

$$A(\lambda) = -k_B T \ln\left[\int e^{\frac{-U(\vec{x}^{3N},\lambda)}{k_B T}} d\vec{x}^{3N}\right]$$

$$\frac{\partial A(\lambda)}{\partial \lambda} = \frac{\cancel{-k_B T} \int e^{\frac{-U(\vec{x}^{3N},\lambda)}{k_B T}} d\vec{x}^{3N} \left[\frac{-1}{\cancel{k_B T}} \frac{\partial U(\vec{x}^{3N},\lambda)}{\partial \lambda}\right]}{\int e^{\frac{-U(\vec{x}^{3N},\lambda)}{k_B T}} d\vec{x}^{3N}} = \left\langle \frac{\partial U}{\partial \lambda} \right\rangle_\lambda = \langle U_1 - U_0 \rangle_\lambda = \langle \Delta U \rangle_\lambda$$

$\rho_\lambda(\vec{x}^{3N})$

$$\Delta A = A_1 - A_0 = \int_0^1 \langle \Delta U \rangle_{\lambda'} d\lambda'$$