

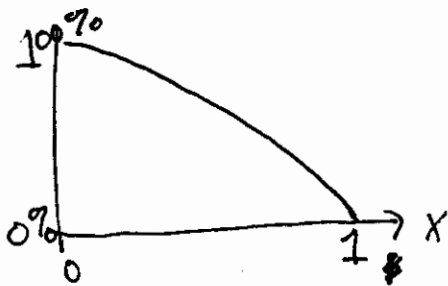
Topic 6 Entropy Continued & Boltzmann Dist'n P347

Heat Engine continued:

- for the piston that raised the weight, what is the efficiency?

$$\text{efficiency} \equiv \frac{\text{mechanical work done}}{\text{Free energy used}} = \frac{W}{\Delta F}$$

- For the piston: $\text{efficiency} = \frac{X}{-\ln(1-X)}$



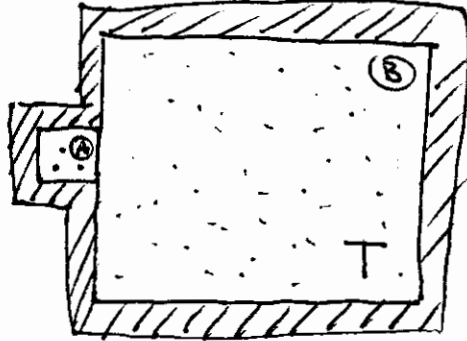
- Get best efficiency when X is small \rightarrow corresponds to small steps of engine

- However taking a bunch of small steps takes time!
- Compromise efficiency for speed of operation.

Microscopic Systems:

- So far we have been talking about macroscopic objects like engines & pistons.
- What about the properties of biological molecules which are tiny?
- Key: small molecule is interacting with large thermal bath @ temperature T.

Consider a small collection of molecules in contact with a thermal bath:



• Both systems @ temp T

• $E_{tot} = E_A + E_B$

- A can exist in a range of states, each with a different energy E_a . What is the probability of each state? Will high energy states be less probable than low energy states?
- Statistical postulate: All states of combined system are equally probable.
- Let's use this idea to compute $P(E_a)$.
- For \textcircled{A} fixed in a state E_A , how many states does \textcircled{B} have?

$$S_B(E_B) = k_B \ln \Omega(E_B)$$

↑ # of states

so

$$\Omega(E_B) = e^{S_B(E_B)/k_B}$$

but $E_B = E_{tot} - E_A \Rightarrow \Omega(E_{tot} - E_A) = e^{S_B(E_{tot} - E_A)/k_B}$

- Thus the # of states in \textcircled{B} depends on \textcircled{A} energy E_a .

(3)

• From statistical postulate, every state has prob, P_0 .

• So prob of \textcircled{A} being in E_A is $\sim P_0 \cdot (\# \text{ of B states})$

$$\text{or } P(E_A) \propto P_0 \Omega(E_{\text{tot}} - E_A) = P_0 e^{S_B(E_{\text{tot}} - E_A)/k_B}$$

• Since $E_A \ll E_{\text{tot}}$, we can expand $S_B(E_{\text{tot}} - E_A)$:

$$S_B(E_{\text{tot}} - E_A) \approx S_B(E_{\text{tot}}) - E_A \frac{dS_B}{dE_B} \leftarrow \text{temperature, } \frac{1}{T_B}$$

• So

$$P(E_A) \propto \left(P_0 e^{S_B(E_{\text{tot}})/k_B} \right) e^{-E_A/k_B T_B}$$

↑
indep of E_A

or

$$P(E_A) = A e^{-E_A/k_B T}$$

• Find \textcircled{A} by normalizing. $\sum_{E_A} P(E_A) = 1$

$$\Rightarrow A = \left(\sum_{E_A} e^{-E_A/k_B T} \right)^{-1}$$

or

$$A = \frac{1}{Z}$$

where

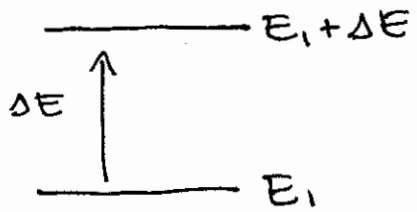
$$Z = \sum_{E_A} e^{-E_A/k_B T}$$

$Z \equiv$ Partition function.

$$P(E_A) = \frac{1}{Z} e^{-E_A/k_B T} \equiv \text{Boltzmann distribution}$$

- Thus the probability of our small system having an energy $E_A \sim e^{-E_A/k_B T}$ where the only influence of the big system (B) is through T

Two-state System: Suppose (A) can exist in 2 states

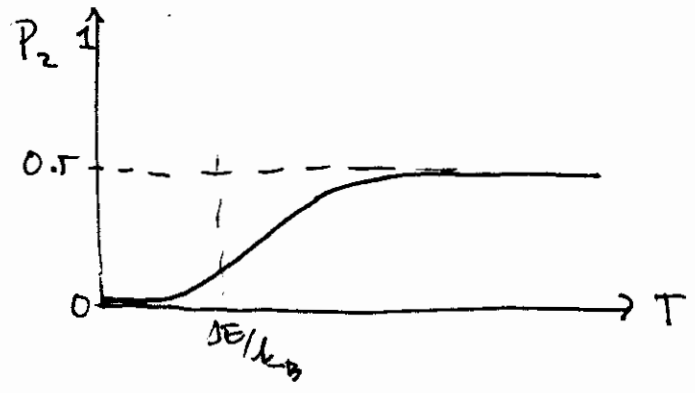
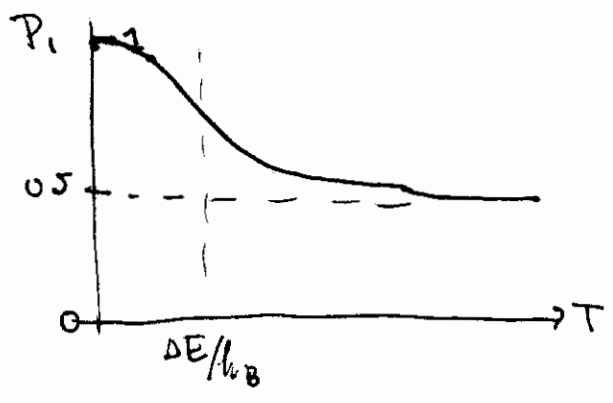


$$\textcircled{1} \frac{P_1}{P_2} = \frac{e^{-E_1/k_B T}}{e^{-(E_1 + \Delta E)/k_B T}} = e^{\Delta E/k_B T}$$

$$\textcircled{2} P_1 + P_2 = 1$$

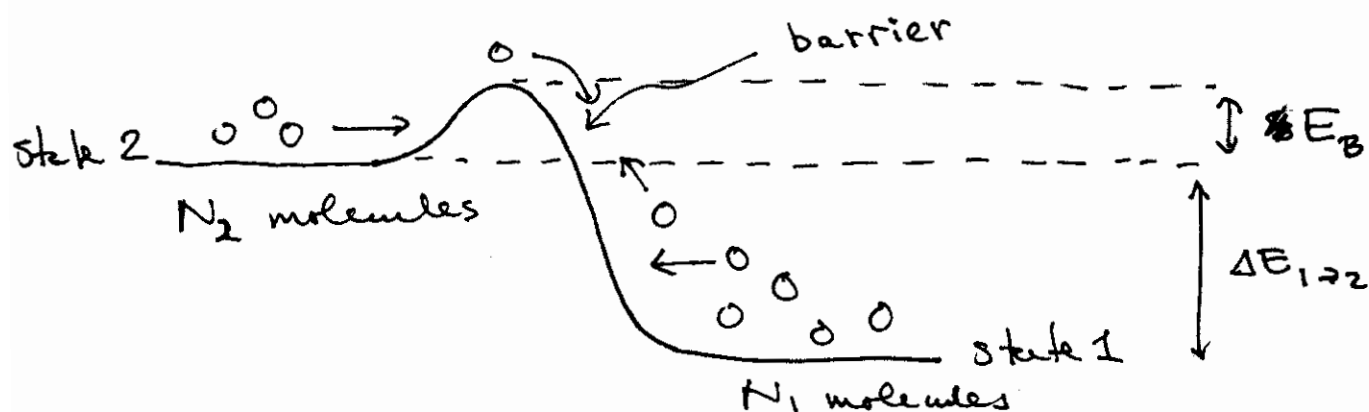
combining $\textcircled{1}$ & $\textcircled{2}$ gives:

$$P_1 = \frac{1}{1 + e^{-\Delta E/k_B T}} \quad ; \quad P_2 = \frac{1}{1 + e^{\Delta E/k_B T}}$$

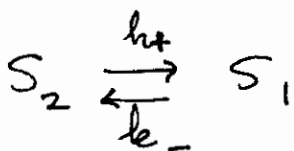


- @ low T , system is in lowest energy state, E_1
- as T rises, both states become equally likely.

Boltzmann & Chemical kinetics:



- Equilibrium occurs when the flow of particles from state ② \rightarrow state ① is balanced by the flow from state ① \rightarrow state ②



- k_+ \equiv prob of going from S_2 to S_1 (chance of going over barrier) / unit time

so $k_+ = C e^{-E_B/kT}$ \leftarrow chance of having an energy that would get you over the barrier

\uparrow
constant

- So ~~approx~~ the # of N_2 molecules going to S_1 is

$$N_2 k_+ = N_2 C e^{-E_B/kT}$$

- What about $S_1 \rightarrow S_2$? To go from $S_1 \rightarrow S_2$ requires going over a barrier of $\Delta E = \Delta E_{1 \rightarrow 2} + E_B$
so

$$k_- = c e^{-(\Delta E_{12} + E_B)/kT}$$

- # of N_1 molecules making transition $S_1 \rightarrow S_2$

$$N_1 k_- = N_1 c e^{-(\Delta E + E_B)/kT}$$

- Equilibrium: $N_2 k_+ = N_1 k_-$

or
$$\frac{N_{2,eq}}{N_{1,eq}} = e^{-\Delta E_{12}/kT} \equiv \frac{P_2}{P_1}$$

- Thus @ equilibrium, the final distribution of particles only depends on ΔE_{12} & not E_B .
- What role does the barrier play then? It influences how long it will take to reach equilibrium.
Large $E_B \rightarrow$ long time to reach equilibrium.

Dwell Times:

- Consider a molecule in S_2 , how long will it spend there before going to S_1 ?
- Ans, sometimes this dwell time will be short & some times it will be long.

$$P_{2 \rightarrow 1}(t) \equiv \text{probability of dwell time, } t.$$

Find $P_{2 \rightarrow 1}(t)$:

Start: ① @ time t there are $N(t)$ molecules in S_2

② after a time dt , $-k_+ dt N(t)$ will have left
so

$$N(t+dt) = (1 - k_+ dt) N(t) \quad (\text{with } N(0) = N_0)$$

so/ve:

$$N(t) = N_0 e^{-k_+ t}$$

$$P_{2 \rightarrow 1}(t) dt = (\text{prob of surviving in } S_2 \text{ till } t) (\text{prob of jumping in } dt)$$

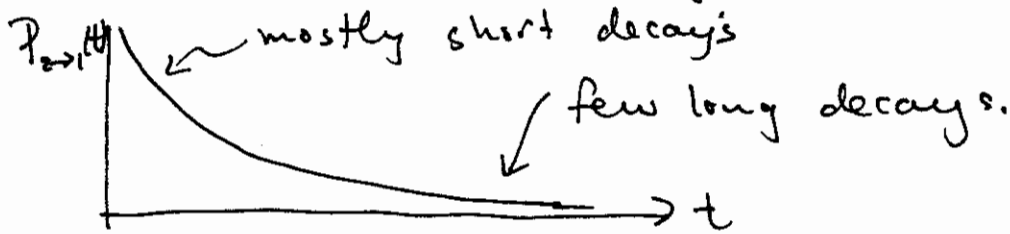
or

$$P_{2 \rightarrow 1}(t) dt = \left(\frac{N(t)}{N_0} \right) (k_+ dt)$$

so

$$P_{2 \rightarrow 1}(t) = k_+ e^{-k_+ t}$$

→ times are exponentially distributed



But, $P_{2 \rightarrow 1}(t)$ depends on $k_+ \sim e^{-E_B/kT}$

So the bigger E_B , the smaller the k_+ and hence the longer on average that a molecule will spend in S_2 !

Calculating Average Properties using Boltzman:

Energy: $\langle E_a \rangle = \sum_j E_j P_j = \sum_j \frac{E_j e^{-E_j/kT}}{\sum_h e^{-E_h/kT}}$

Entropy:

$$S = -k_B \sum_j P_j \ln P_j$$

Free energy:

$$F = -k_B T \ln Z = E_a - TS_a$$

Generalizing to Complex Systems:

————— E_2

————— E_1

(simple, systems in E_1 or E_2)

\Rightarrow
complex

Ⓜ ————— F_{II} (entropy, S_2)

Ⓜ ————— F_{I} (entropy, S_1)

(how there are internal degrees which give each system entropy)

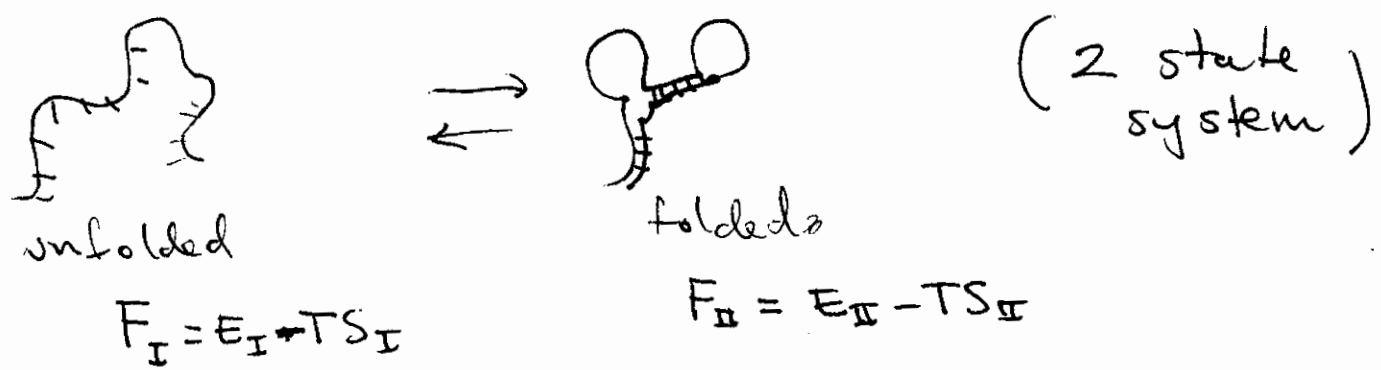
So for complex systems:

$$\frac{P_{\text{I}}}{P_{\text{II}}} = e^{-\Delta F/kT}$$

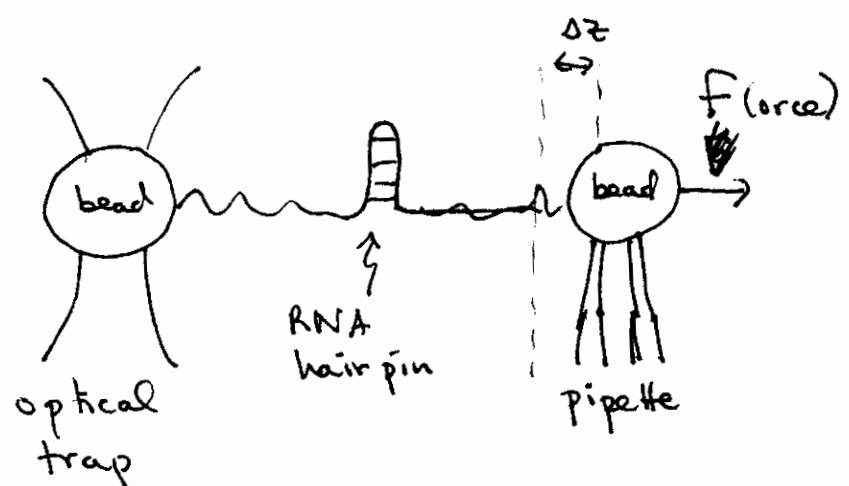
where

$$\Delta F = \Delta E - T\Delta S$$

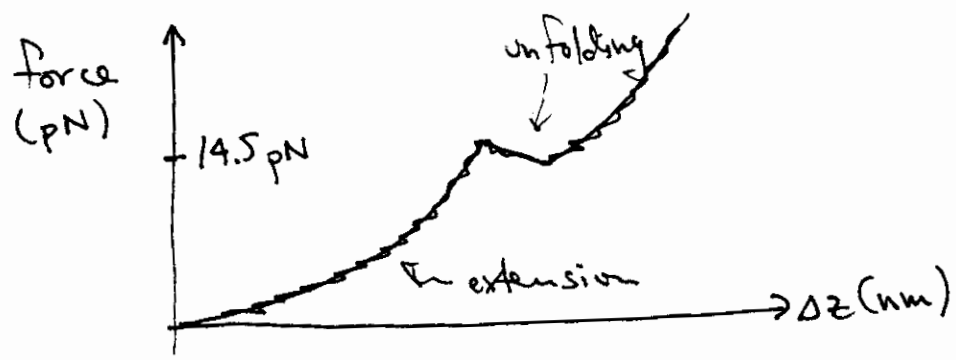
Application to RNA folding:



Expt:



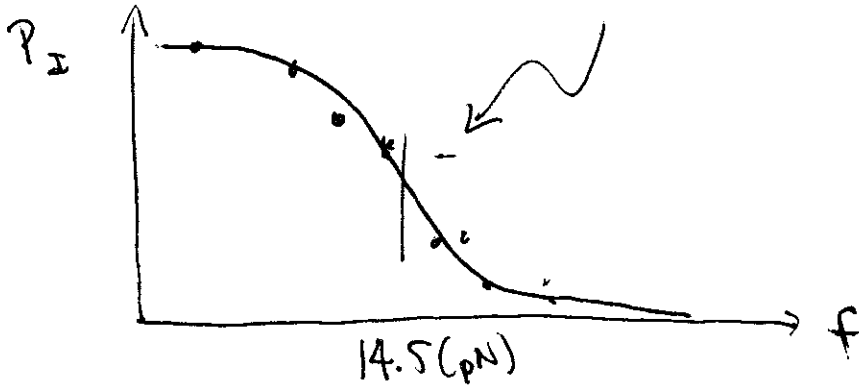
- How much force, f , ~~is~~ needs to be applied to unfold the RNA hair pin?



- In expt: $\Delta F = (F_{II} - F_I) - f \Delta z$
 \uparrow work done by trap.
- Applying more force favours the open state

From 2 state model:

$$P_{\text{fold}} = P(\text{fold}) = \frac{1}{1 + e^{-(\Delta F_0 - f\Delta z)/kT}}$$



From expt:
(J. Liphardt &
C. Bustamante,
Berkeley)

- Thus @ high forces, molecule spends all of its time in unfolded state.

See attached experimental data.

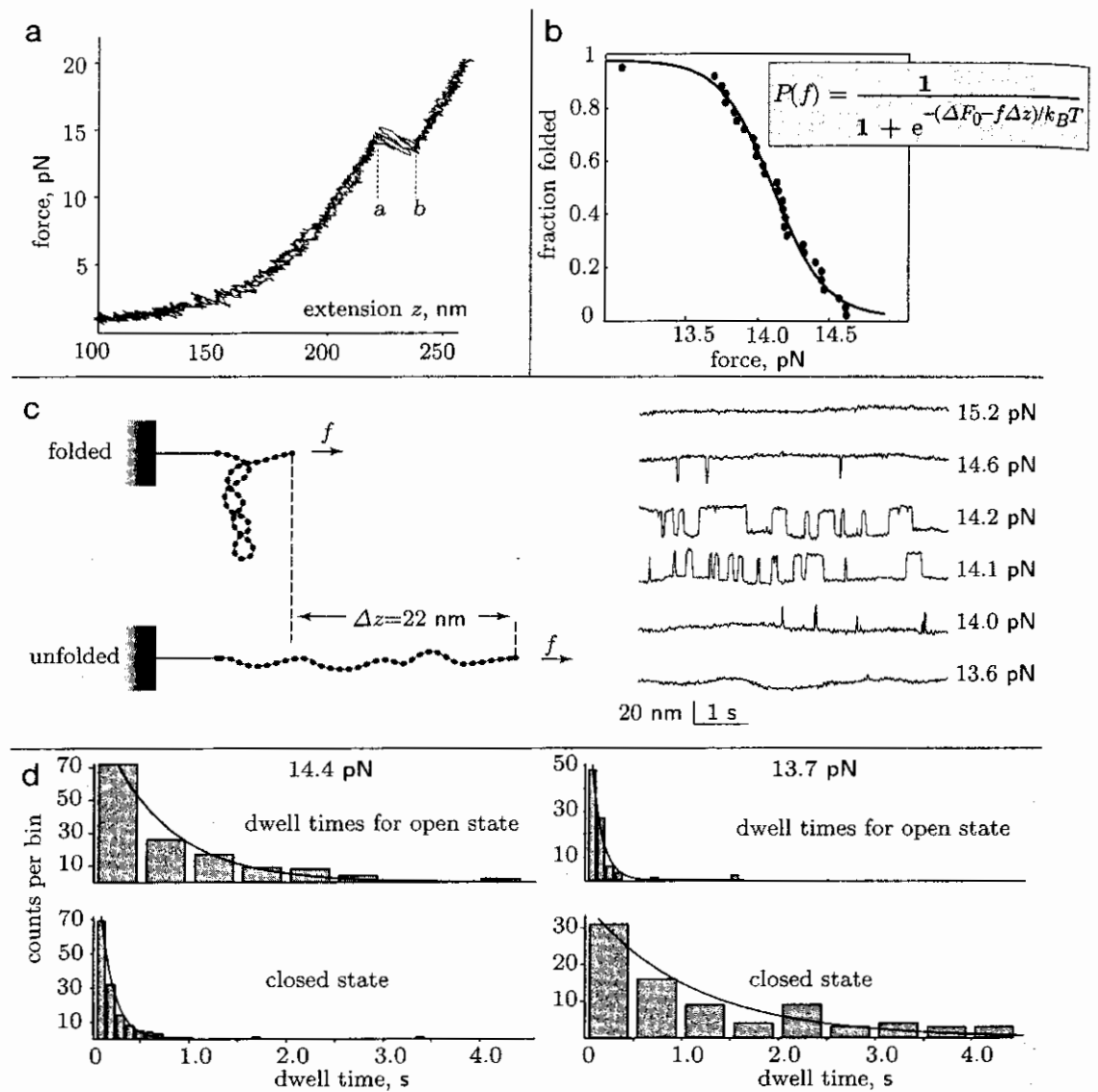


Figure 6.10: (Experimental data) (a) Force-extension curves of an RNA hairpin with handles. Stretching (*black*) and relaxing (*gray*) curves are superimposed. Hairpin unfolding occurs at about 14.5 pN (labeled *a*). (b) Fraction $P(f)$ of hairpins folded versus force. Data (*filled circles*) are from 36 consecutive pulls of a single RNA hairpin. *Solid line*, probability versus force for a two-state system (see Equation 6.34 on page 225). Best-fit values, $\Delta F_0 = 79k_B T$, $\Delta z = 22$ nm, consistent with the observed Δz seen in panel (a). (c) Effect of mechanical force on the rate of RNA folding. Length versus time traces of the RNA hairpin at various constant forces. Increasing the external force increases the rate of unfolding and decreases the rate of folding. (d) Histograms of the dwell times in the open and closed states of the RNA hairpin at two different forces ($f = 14.4$ and 13.7 pN). The solid lines are exponential functions fit to the data (see Equation 6.31), giving rate constants for folding and unfolding. At 13.7 pN, the molecule is mostly folded, with $k_{\text{open}} = 0.9 \text{ s}^{-1}$, and $k_{\text{fold}} = 8.5 \text{ s}^{-1}$. At 14.4 pN, the unfolded state predominates, with $k_{\text{open}} = 7 \text{ s}^{-1}$ and $k_{\text{fold}} = 1.5 \text{ s}^{-1}$. [Figure kindly supplied by J. Liphardt.]