Physical Biology of the Cell

Lecture 4
Boltzmann Distribution and its Application to Biological Problems
5. Boltzmann Distribution

Probability of different microstates is determined by their energy.

Assume that the system $A$ is in contact with a heat reservoir $A'$. Under the condition of equilibrium, what is the probability $P_r$ of finding the system $A$ in any one particular microstate $r$ of energy $E_r$. Note that there may be multiple accessible states at $E_r$ (degeneracy).

$$A \ll A' \quad E_r + E' = E_0 \text{ and } E_r \ll E_0$$

Since $A$ is in one definite microstate ($\Omega = 1$), probability of occurrence is proportional to the number of accessible states available to the $A'$ under this condition.

$$P_r = C'.\Omega(E_0 - E_r)$$

$$\ln\Omega'(E_0 - E_r) = \ln\Omega'(E_0) - \frac{d\ln\Omega'(E_0)}{dE'} E_r$$

$$\ln\Omega'(E_0 - E_r) = \ln\Omega'(E_0) - \beta E_r$$

$$\Omega'(E_0 - E_r) = \Omega'(E_0) e^{-\beta E_r}$$

$$P_r = Z^{-1}.e^{-\beta E_r}, \text{ where } Z^{-1} = C'.\Omega'(E_0) \text{ constant}$$

$$Z = \sum_r e^{-\beta E_r} = \sum_{E_r} \Omega(E_r)e^{-\beta E_r} \quad \text{sum of all states (also called partition function)}$$
If A is in a state $r$ with energy $E_r$, the number of states available to the reservoir (A') is lower if $E_r$ is high. Exponential decay of $P_r$ as a function of $E_r$ just expresses this fact in math.

The probability $P(E)$ that A has energy between $E$ and $E + \delta E$ is the sum of probabilities of all states in $E$.

$$P(E) = C\Omega(E)e^{-\beta E}$$

$\Omega(E)$ sharply increases with $E$, and $e^{-\beta E}$ sharply decreases. The resulting probability distribution is a sharp peak around $E = \tilde{E}$.

We can group the terms

$$Z = \sum_{E_r} \Omega(E_r)e^{-\beta E_r}$$

$Z$ is extremely useful in studying systems at fixed $T$. 

![Energy vs. Probability Graph with $E_{\text{average}} = 500$]
Example 1. Partition of Quantized Energy among Particles

Consider the number of ways of partitioning N energy units among n particles

\[ N \gg n \]

1. Energy is quantized.

\[ \sum_{i}^{n} E_i = N \varepsilon \]

\( E_i \) is integer multiple units of energy \( \varepsilon \).

2. Any partitioning of the energy among particles is equally likely.

What is the probability of a chosen particle to have \( E = m\varepsilon \)?

If a chosen particle has energy of \( m\varepsilon \) we reduce the number of ways \( n-1 \) particles can distribute energies of \((N-m)\varepsilon\)

\[ p(m) = \frac{W(N - m, n - 1)}{W(N, n)} \]
• Suppose each battery is $\varepsilon$ units of energy.
• Draw $n+1$ dividers.
• We have $N$ ones and $n+1$ zeros.
• First and last digit must be zero. We have $n-1$ zeros left to distribute.
• We converted the problem into repetitive permutation.

\[
W(N, n) = \frac{(N + n - 1)!}{(n - 1)! (N)!}
\]

\[
W(N - m, n - 1) = \frac{(N - m + (n - 1 - 1))!}{(n - 2)! (N - m)!}
\]
Probability of a chosen particle energy of $m\varepsilon$.

$N=10000$ units of energy is distributed among $n = 100$ particles.

$$p(m) = \frac{W(N-m,n-1)}{W(N,n)} = \frac{W(N-m,n-1)}{W(N,n)}$$

$$p(m) = \frac{(N + n - 1 - (m + 1))! (n - 1)! N!}{(N - m)! (n - 2)! (N + n - 1)!} = \frac{(n - 1)N^m}{(N + n - 1)^{m+1}}$$

$$= \frac{n - 1}{N + n - 1} \left(\frac{N + n - 1}{N}\right)^{-m}$$

$$= e^{-mln(N+n-1/N)} \approx e^{-mln(1+n/N)}$$

$$ln(1 + n/N) \approx \frac{n}{N} \quad n \ll N \text{ (Taylor Series Expansion)}$$

$$p(m) = \frac{n}{N} e^{-mn/N} \quad < E > = N\varepsilon/n \quad E = m\varepsilon \quad <E> \text{ is average energy per particle}$$

$$p(E) = \frac{\varepsilon}{<E>} e^{-E/<E>} \quad \text{Boltzmann Distribution.}$$
Example 2: Control of Gene Expression

RNA polymerase (RNAP) recognizes a promoter sequence preceding the gene of interest.

Consider there are $N$ nonspecific binding sites and 1 specific binding site on a DNA for $P$ RNAP molecules ($N \gg P$) at a room temperature $T$.

Energy for specific binding is $\varepsilon_s$ and for nonspecific binding is $\varepsilon_n$. Find the probability of the specific site to be occupied.

All RNAPs are bound to DNA.
Case 1. unoccupied. $E = P\,\varepsilon_n$ 

$$\Omega(N, P) = \frac{N!}{P!(N-P)!}$$

Case 2: Occupied $E = \varepsilon_s + (P-1)\,\varepsilon_n$ 

$$\Omega(N, P - 1) = \frac{N!}{(P-1)!(N-P+1)!}$$

**IMPORTANT.** Each molecule in the unbound state has the same energy. So, it is reduced to simple counting problem!

Statistical weight of each state is the multiplication of $\Omega$ by the Boltzmann factor.

Probability is the ratio of statistical weight divided by total partition function.

$$p_{\text{bound}} = \frac{\frac{N!}{(P-1)!(N-P+1)!} e^{-\beta (\varepsilon_s + (P-1)\varepsilon_n)}}{\sum_{\text{states}} e^{-\beta \Delta \varepsilon}} = \frac{1}{1+\frac{P}{N} e^{-\beta \Delta \varepsilon}}$$

$$\Delta \varepsilon = \varepsilon_s - \varepsilon_n$$

$$p_{\text{bound}} = \frac{\sum_{\text{states}} e^{-\beta \Delta \varepsilon}}{1+\frac{P}{N} e^{-\beta \Delta \varepsilon}}$$

Figure 6.12 Physical Biology of the Cell (© Garland Science 2009)
Example 3: Ligand–Receptor Binding

\[
\begin{align*}
\text{STATE} & \quad \text{ENERGY} & \quad \text{MULTIPLICITY} & \quad \text{WEIGHT} \\
& \quad L \varepsilon_{\text{sol}} & \quad \frac{\Omega!}{L!(\Omega-L)!} & \approx \frac{\Omega^L}{L!} & \frac{\Omega^L}{L!} e^{-\beta L \varepsilon_{\text{sol}}} \\
& \quad (L-1) \varepsilon_{\text{sol}} + \varepsilon_b & \quad \frac{\Omega!}{(L-1)!(\Omega-L+1)!} & \approx \frac{\Omega^{L-1}}{(L-1)!} & \frac{\Omega^{L-1}}{(L-1)!} e^{-\beta (L-1) \varepsilon_{\text{sol}} + \varepsilon_b} \\
\end{align*}
\]

\[
\begin{align*}
p_{\text{bound}} &= \frac{\Omega!}{(L-1)!(\Omega-L+1)!} e^{-\beta (\varepsilon_b + (L-1) \varepsilon_{\text{sol}})} \\
&= \frac{\Omega!}{(L-1)!(\Omega-L+1)!} e^{-\beta \varepsilon_b} + \frac{\Omega!}{L!(\Omega-L)!} e^{-\beta L \varepsilon_{\text{sol}}} \\
&= \frac{L/\Omega e^{-\beta \Delta \varepsilon}}{1 + L/\Omega e^{-\beta \Delta \varepsilon}} = \frac{(c/c_0) e^{-\beta \Delta \varepsilon}}{1 + (c/c_0) e^{-\beta \Delta \varepsilon}} \\
L/V_{\text{box}} &= c \text{ (ligand concentration)} \\
\Omega/V_{\text{box}} &= c_0 \text{ (standard state)}
\end{align*}
\]
Probability of Ligand Binding per Receptor Depends on its Concentration

- Lattice size is 1 nm\(^3\). \(c_0 \approx 0.6\) M
- Entropy is lost by stealing one of the ligands from solution.
- Energy is gained by \(\Delta\varepsilon\)
- If \(\Delta\varepsilon\) is positive, ligand will not bind. If \(\Delta\varepsilon\) is negative, energy and entropy will compete for free energy minimization.
- Half occupancy concentration depends on \(\Delta\varepsilon\)
- At low \(c\), entropy dominates
- At high \(c\), energy dominates

\[
p_{\text{bound}} = \frac{(c/c_0)e^{-\beta\Delta\varepsilon}}{1 + (c/c_0)e^{-\beta\Delta\varepsilon}}
\]