Why Statistical Mechanics?

Understand & predict the physical properties of macroscopic systems from the properties of their constituents

Deterministic approach $ma = F$
- need of $6N$ coordinates at $t_0$: $r_i$ and $v_i$
- but typically $N \equiv$ moles $(10^{23})$!

“Ensemble” rather than microscopic detail
... and its surroundings
  ➢ microcanonical, canonical, grand canonical
What With Statistical Mechanics?

Averages, distributions, deviation estimates...

... of microstates: specification of the complete set of positions and momenta at any given time (points on the constant energy hypersurface for Hamiltonian dynamics)

Ensemble average & ergodic hypothesis:

\[ A = \langle a \rangle_{\text{ensemble}} = \frac{1}{N} \sum_{i=1}^{N} a(x_i) = \lim_{T \to \infty} \frac{1}{T} \int_{0}^{T} a(x(t)) dt \]

A system that is ergodic is one which, given an infinite amount of time, will visit all possible microscopic states available to it.
The First Law – Work

Work, heat & energy = basic concepts
Energy of a system = capacity to do work

➢ At the molecular level, difference in the surroundings

<table>
<thead>
<tr>
<th></th>
<th>Energy transfer that makes use of...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat</td>
<td>... chaotic molecular motion</td>
</tr>
<tr>
<td>Work</td>
<td>... organized molecular motion</td>
</tr>
</tbody>
</table>

$$\Delta U = q + w$$

state function – independent of how state was reached
Second Law – Gibbs

- Spontaneous processes increase the overall “disorder” of the universe

- Reasoning through an example
  - microstates to achieve macrostate

  **Gibbs postulate**: for an isolated system, all microstates compatible with the given constraints of the macrostate (here $E$, $V$ and $N$) are equally likely to occur

  - Here $2^N$ ways to distribute $N$ molecules into 2 bulbs
Second Law - Probability

- Number of (indistinguishable) ways of placing $L$ of the $N$ molecules in the left bulb:

$$W_L = \frac{N!}{L!(N - L)!}$$

- Probability $W_L/2^N$ maximum if $L = N/2$

  ✓ With $N = 10^{23}$, $p(L = R \pm 10^{-10}) = 10^{-434}$ possible but extremely unlikely
Second Law - Entropy

\[ S = k \ln W \]
\[ S = -\sum_{i=1}^{t} p_i \ln p_i \]

Boltzmann’s constant
\[ k = 1.38 \times 10^{-23} \text{ J.K}^{-1} \]

- Principle of Fair Apportionment

\[ W = \frac{N!}{n_1! n_2! \ldots n_t!} \]

\[ = \left( \frac{N}{e} \right)^N \left( \frac{n_1}{e} \right)^{n_1} \left( \frac{n_2}{e} \right)^{n_2} \ldots \left( \frac{n_t}{e} \right)^{n_t} = \frac{N^N}{n_1^{n_1} n_2^{n_2} \ldots n_t^{n_t}} = \frac{1}{p_1^{n_1} p_2^{n_2} \ldots p_t^{n_t}} \]

Multiplicity of outcomes
Second Law - Entropy

\[
S = k \ln W
\]

\[
\frac{S}{k} = -\sum_{i=1}^{t} p_i \ln p_i
\]

\[
\ln W = -\sum_{i=1}^{t} n_i \ln p_i
\]

\[
\frac{S}{N} = \frac{S}{Nk} = \frac{1}{N} \ln W = -\sum_{i=1}^{t} p_i \ln p_i
\]

Flat distribution ≡ high \( S \)

The absolute entropy is never negative

\[ S \geq 0 \]

\( S \) max at equilibrium

Flat distribution ≡ high \( S \)
The Boltzmann Distribution Law

- Maximum entropy principle + constraints

\[
\frac{S}{k} = -\sum_{i=1}^{t} p_i \ln p_i \quad \begin{cases} 
\langle U \rangle = \frac{E}{N} = \sum_{i=1}^{t} p_i E_i \\
\sum_{i=1}^{t} p_i = 1
\end{cases}
\]

⇒ exponential distribution

\[
p_i^* = \frac{p_i^*}{Q} = \frac{\exp\left(-\frac{E_i}{kT}\right)}{Q}
\]

Partition function \[ Q = \sum_{i=1}^{t} \exp\left(-\frac{E_i}{kT}\right) \]
The Boltzmann Distribution Law (2)

- More particles have low energy: more arrangements that way
  \[ P_i^* = \frac{\exp\left(-\frac{E_i}{kT}\right)}{Q} \]

- \( Q \equiv \) connection between microscopic models & macroscopic thermodynamic properties
  \[ U = kT^2 \left( \frac{\partial \ln Q}{\partial T} \right) \quad \text{and} \quad S = k \ln Q + kT \left( \frac{\partial \ln Q}{\partial T} \right) \]

- \( Q \equiv \) number of states effectively accessible to system
  \[ Q = \sum_{i=1}^{t} \exp\left(-\frac{E_i}{kT}\right) = 1 + e^{-E_2/kT} + e^{-E_3/kT} + \ldots + e^{-E_t/kT} \]

- \( T \to +\infty \Rightarrow \frac{E_i}{kT} \to 0 \Rightarrow Q \to 1 + 1 + 1 + \ldots + 1 = t \)
The Helmholtz Free Energy

- Systems held at constant $T \to$ minimum free energy ($\neq S_{\text{max}}$)
  Equilibrium if $F(T, V, N)$ minimum ($T$ fixed at boundaries)

<table>
<thead>
<tr>
<th>Internal energy</th>
<th>Entropy</th>
</tr>
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<tbody>
<tr>
<td>$F_{\text{dim}} = U_{\text{dim}} - TS_{\text{dim}} = -\varepsilon - kT \ln(V - 1)$</td>
<td></td>
</tr>
<tr>
<td>$W_{\text{mon}} = W_{\text{iota}} - W_{\text{dim}} = \frac{V!}{(2!)(V - 2)!} - (V - 1) = \left(\frac{V}{2} - 1\right)(V - 1)$</td>
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<td>$F_{\text{mon}} = U_{\text{mon}} - TS_{\text{mon}} = -kT \ln\left[\left(\frac{V}{2} - 1\right)(V - 1)\right]$</td>
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$F = U - TS$

Example of ‘dimerization’

\[
F_{\text{dim}} = U_{\text{dim}} - TS_{\text{dim}} = -\varepsilon - kT \ln(V - 1)
\]

\[
W_{\text{mon}} = W_{\text{iota}} - W_{\text{dim}} = \frac{V!}{(2!)(V - 2)!} - (V - 1) = \left(\frac{V}{2} - 1\right)(V - 1)
\]

\[
F_{\text{mon}} = U_{\text{mon}} - TS_{\text{mon}} = -kT \ln\left[\left(\frac{V}{2} - 1\right)(V - 1)\right]
\]

$F(T)$
## Fundamental Functions

<table>
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<tr>
<th>Function</th>
<th>Expression</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>$U(S, V, N)$</td>
<td>$dU = TdS - pdV + \sum_i \mu_i dN_i$</td>
<td>calorimetry</td>
</tr>
<tr>
<td>$S(U, V, N)$</td>
<td>$dS = \left(\frac{1}{T}\right) dU + \left(\frac{p}{T}\right) dV - \sum_i \left(\frac{\mu_i}{T}\right) dN_i$</td>
<td>cal.</td>
</tr>
<tr>
<td>$H(S, p, N)$</td>
<td>$dH = TdS + Vdp + \sum_i \mu_i dN_i$</td>
<td>calorimetry</td>
</tr>
<tr>
<td>$F(T, V, N)$</td>
<td>$dF = -SdT - pdV + \sum_i \mu_i dN_i$</td>
<td>Internal energy vs. entropy</td>
</tr>
<tr>
<td>$G(T, p, N)$</td>
<td>$dG = -SdT + Vdp + \sum_i \mu_i dN_i$</td>
<td>Enthalpy vs. entropy</td>
</tr>
</tbody>
</table>
Macromolecular Mechanics

- Why study the mechanics of biological macromolecules?
  - provide structural integrity and shape
  - coupling of geometry & dynamics ⇒ what is possible
  - importance of conformation for ion channels, pumps...
  - motility
  - mechanotransduction, signaling
The Gaussian Chain Model (Kuhn)

- Long floppy chain made of \( N \) rigid links of length \( b \) (free to swivel about joints, overlapping & crossing allowed)
- Valid for small displacements from equilibrium, not large extensions

\[
G_g = H - TS = -Tk \ln P(R, N)
\]

Entropic reasoning \( \Rightarrow \) mechanical spring
(straightening out \( \equiv \) decrease of entropy)

\[
\begin{align*}
\langle R \rangle &= 0 = \mu \\
\langle R^2 \rangle &= Nb^2 = \sigma^2
\end{align*}
\]

\[
P(R, N) = \left( \frac{3}{2\pi\sigma^2} \right)^{3/2} \exp \left( -\frac{3}{2} \cdot \frac{(|R| - \mu)^2}{\sigma^2} \right)
\]

\[
G_g = \frac{1}{2} \cdot \frac{3kT}{Nb^2} \cdot |R|^2 = \frac{1}{2} \cdot K \cdot (\ell - \ell_0)^2
\]
The Worm-like Chain Model

- Self-avoiding linear chains (Flory, 1953)
- Freely-jointed chain model (Grosberg & Khoklov, 1988)
- Worm-like chain model: Bending stiffness of polymer on short length scales

\[ E = -Fx + \int_{0}^{L} \frac{B \kappa^2}{2} \, ds \]  \hspace{1cm} \text{(Kratky-Porod)}

\[ F = \frac{kT}{16 \ell_p} \left( 1 - \frac{x}{L} \right)^{-2} \]  \hspace{1cm} \text{(diverges for } x \rightarrow L\text{)}

Persistence length
\[ \ell_p = \frac{Yl}{kT} \]

\[ s = L \]

- bending
- thermal
Experimental Validation of Models

- **Single-molecule studies of DNA mechanics:**

- **WLC interpolated:**

\[ F = \frac{kT}{\ell_p} \left[ \frac{x}{L} + \frac{1}{16} \left( 1 - \frac{x}{L} \right)^{-2} - \frac{1}{16} \right] \]

After Bustamante *et al.*, *Current Opinion in Structural Biology*, 2001
Effect of Force on Equilibrium

\[
\frac{[1]}{[2]}_{\text{no force}} = \frac{p_1}{p_2} = \frac{\exp\left(-\frac{G_1}{kT}\right)}{\exp\left(-\frac{G_2}{kT}\right)} = \exp\left(-\frac{\Delta G_{\text{no force}}^0}{kT}\right)
\]

- Force tilts energy profile
  ⇒ favors configuration
Sources

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