Course review (up to now)

I. System states: \( n = 1, 2, \ldots \)

State properties: \( E_n, V_n, H_n = E_n + PV_n, N \)

State probability: \( P_n(t), \sum_n P_n(t) = 1 \)

Averages: \( \langle E \rangle_t = E(t) = \sum_n P_n(t) E_n \), etc.

II. Transition properties:

\[ \Omega_{mn} = \text{rate } n \rightarrow m \quad (m \neq n) \]
\[ \Omega_{nn} = -\text{(escape rate from } n) = -\sum_{m \neq n} \Omega_{mn} \]

\[ P_{mn}(t) = \text{joint prob. of } n \text{ at } t, \ m \text{ at } t + \delta t \]

\[
\begin{cases}
\Omega_{mn} \delta t \cdot P_n(t) & m \neq n \\
(1 + \Omega_{nn} \delta t) \cdot P_n(t) & m = n
\end{cases}
\]

\[ \sum_{m, n} P_{mn}(t) = 1, \sum_m P_{mn}(t) = P_n(t), \sum_n P_{mn}(t) = P_m(t + \delta t) \]

Current \( J_{mn}(t) = \text{current from } n \rightarrow m \quad (m \neq n) \)

\[ J_{mn}(t) = \frac{1}{\delta t} \left[ P_{mn}(t) - P_{nm}(t) \right] \]

\[ J_{mn}(t) = -J_{nm}(t) \]

III. Equation of motion: [i.e. how to take time derivatives]

\[ \frac{dp_n}{dt} = \sum_m \Omega_{mn} P_m(t) = \sum_{m \neq n} J_{nm}(t) \]

Solve this equation \( \Rightarrow \) get currents \( J_{nm}(t) \)
The time derivatives of state variable averages are:

\[ \dot{E} = \frac{dE}{dt} = \sum_{n} \frac{dp_{n}}{dt} E_{n} = \sum_{n} \sum_{m \neq n} J_{nm}(t) E_{n} = \sum_{n} \sum_{m > n} J_{nm}(t) [E_{n} - E_{m}] \]

can use notational shortcut 
\[ \sum_{n} \sum_{m > n} = \sum_{(n, m)} = \text{sum over distinct pairs} \]

[Same thing as jump moment!]

The time derivatives of transition variable averages are:

\[ W_{nm} = \text{work done in transition from } m \rightarrow n = -W_{mn} \]

(may not apply to all transitions, only those coupled to ext. potential)

\[ \dot{W} = \frac{1}{8t} \langle \dot{W} \rangle_{t} = \frac{1}{8t} \sum_{n, m} P_{nm}(t) W_{nm} \]

\[ = \sum_{n} \sum_{m > n} J_{nm}(t) W_{nm} \]

Example: chemical work involved in exchanging particle type \( \alpha \) w/ environment

\[ W_{\text{chem}}^{\beta, \alpha} = -\mu_{\alpha}(N_{\alpha n} - N_{\alpha m}) \]

for transition \( m \rightarrow n \) where particle \( \alpha \) enters/leaves system from env.

\[ \dot{W}_{\text{chem}}^{\alpha} = \frac{1}{8t} \langle \dot{W}_{\text{chem}}^{\alpha} \rangle_{t} = -\sum_{n} \sum_{m > n} J_{nm}(t) \mu_{\alpha}(N_{\alpha n} - N_{\alpha m}) \]

Sum restricted to \((m, n)\) pairs where part. \( \alpha \) enters/leaves system
IV. Thermodynamics (single temp. \( T \))

\[
\frac{\Omega_{mn}}{\Omega_{nm}} = e^{-\beta Q_{mn}} \quad Q_{mn} = \text{heat from reservoir during } n \rightarrow m \text{ transition}
\]

\[
\dot{Q} = \frac{1}{\delta t} \langle Q \rangle_t = \sum_n \sum_{m > n} J_{nm}(t) Q_{nm}
\]

1st law:

\[
Q_{mn} = H_m - H_n + W_{mn}
\]

\[
\text{or} \quad \dot{Q} = \dot{H} + \dot{W}
\]

2nd law:

\[
\dot{S} = \frac{\dot{Q}}{T} + \dot{S^i} \quad \text{or} \quad \dot{G} = -\dot{W} - TS^i
\]

where \( G = H - TS \)

\[
S(t) = -k_B \sum_n p_n(t) \ln p_n(t)
\]

\[
\dot{S^i} = k_B \langle I \rangle_t = k_B \sum_n \sum_{m > n} J_{nm}(t) I_{nm}(t)
\]

\[
I_{nm}(t) = \sum \frac{\ln P_{nm}(t)}{P_{nm}(t+\delta t)}
\]

\[
\dot{S^i} \geq 0 \quad \text{irreversibility of } m \rightarrow n \text{ transition}
\]

note:

\[
\dot{S}(t) = -k_B \sum_n \frac{p_n(t)}{p_n(t)} \ln p_n(t)
\]

\[
- k_B \sum_n \frac{p_n(t)}{p_n(t)} \frac{\dot{p}_n(t)}{p_n(t)} \quad \text{subject to } \quad \sum_n p_n(t) = 1
\]

\[
\Rightarrow \dot{S}(t) = -k_B \sum_n \frac{\dot{p}_n(t)}{p_n(t)} \ln p_n(t)
\]
\[
\Rightarrow \dot{S}(t) = -k_B \sum_n \sum_{m \neq n} J_{nm}(t) \ln p_n(t)
\]
\[
= -k_B \sum_n \sum_{m > n} J_{nm}(t) \left[ \ln p_n - \ln p_m \right]
\]
\[
\Rightarrow \dot{S}(t) = -k_B \sum_n \sum_{m > n} J_{nm}(t) \ln \frac{p_n(t)}{p_m(t)}
\]
V. Long-time limit:

stationary state

\[ P_n(t) \to P_n^s \]

\[ J_{nm}(t) = \Omega_{nm} P_m^s - \Omega_{mn} P_n^s \]

\[ \equiv J_{nm}^s \]

\[ \frac{dP_n}{dt} = 0 \Rightarrow \sum_{m \neq n} J_{nm}^s = 0 \]

a) if \( J_{nm}^s = 0 \) for all \((n,m)\) \(\Rightarrow\) equilibrium \((s \to eq)\)

\[ \frac{P_n^{eq}}{P_m^{eq}} = \frac{\Omega_{nm}}{\Omega_{mn}} = e^{-\beta Q_{nm}} \]

\[ \Rightarrow \frac{I_{nm}}{I_{mn}} = 0 \text{ for all } (m,n) \]
If $W_{mn} = 0$ for all $(m,n)$, $Q_{mn} = H_m - H_n$ and hence $p_n^{eq} = \frac{e^{-\beta H_n}}{Z}$ (Boltzmann).

b) if $J_{nm}^S \neq 0$.

Equilibrium: $k_B \frac{\langle I \rangle_t}{S_t} = \dot{\langle I \rangle} = 0$

In fact, since $J_{nm}^{eq} = 0 \Rightarrow$ all time derivatives are zero.

b) if $J_{nm}^S \neq 0$ for at least one $(n,m)$

⇒ non-equilibrium stat. state

Example: single loop $J_{21}^S = J_{32}^S = J_{13}^S = J > 0$

by current conservation

Certain time derivatives always zero:

$\dot{H} = \sum_n \sum_{m>n} J_{mn}^S (H_m - H_n)$

$= J \left[ (H_2 - H_1) + (H_3 - H_2) + (H_1 - H_3) \right]$ 

$= 0$

Similarly $\dot{S} = k_B J \sum_n \sum_{m>n} \left[ \ln p_n^S - \ln p_m^S \right] = 0$

But $\dot{W} = -J W_{in} + J W_{out}$ not zero if $W_{in} \neq W_{out}$

$= P_{out} - P_{in}$

where $-W_{in} = W_{21}$

$W_{out} = W_{13}$
Hence: \[ \dot{S} = \frac{\dot{Q}}{T} + \dot{S}^i \]
\[ \dot{Q} = \dot{H} + \dot{W} \]

implies in this case: \[ \dot{Q} = \dot{W} = -T \dot{S}^i \leq 0 \]

\[ P_{out} = P_{in} - T \dot{S}^i \]
\[ = P_{in} - P_{diss} \]
\[ \Rightarrow \text{heat dissip. into environment} \]

To get NESS, we need to couple diff. parts of loop to diff. amounts of work, that do not sum to zero over one cycle.

Bad idea: make \( W_{mn} = U_m - U_n \) (diff. int. ext. potential energy)

then \[ \dot{W} = J \sum_n \sum_{m<n} (U_m - U_n) \]
\[ = 0 = \dot{Q} = -T \dot{S}^i \Rightarrow \text{equilibrium} \]

Note: since \( Q_{nm} = -k_B T \ln \frac{P_{n}^{eq}}{P_{m}^{eq}} \)

then \( I_{nm} = -\frac{Q_{nm}}{k_B T} - \ln \frac{P_{n}(t)}{P_{m}(t)} \)

Irreversibility directly related to how far \( P_n(t) \) is from equil. value \( P_n^{eq} \)

\[
I_{nm} = \ln \left( \frac{P_m(t)}{P_m^{eq}} \right) - \ln \left( \frac{P_n(t)}{P_n^{eq}} \right) \\
= \ln \left[ \frac{P_m(t)}{P_m^{eq}} \cdot \frac{P_n^{eq}}{P_n(t)} \right]
\]
• More specifically if we have mech. work

\[ W_{mn} = f(x_m - x_n) \]

we should not have this term for every transition in the cycle.

[i.e. a myosin doing work on actin cannot be attached to the actin throughout whole cycle]

• Similarly we should not allow exchange of particle type \( \alpha \) with environment during every transition, leading to

\[ W_{mn} = -\mu_\alpha (N_{am} - N_{an}) \]

\[ \Rightarrow \text{we cannot drive system by simple binding/unbinding of a single particle type} \]

How can we prevent this \( \Rightarrow \) we need to convert particle type into something else.

Example:

generic enzyme that hydrolyzes mechanical

\[ \text{ATP to ADP + P to do work} \]

NESS involves some current \( J \neq 0 \)

(cycle can be arbitrarily complicated with many internal states)
Details irrelevant, except we know that:

along direction \( J > 0 \):

One step involves work \(-M_{\text{ATP}}\) (addition of ATP)

\[ \text{work} = -M_{\text{ATP}} + M_{\text{ADP}} \] (ADP ejected)

\[ = -M_{\text{ADP}} + M_{\text{P}} \] (P ejected)

\[ = W_{\text{mech}} \]

Hence:

\[ \dot{W} = J(W_{\text{mech}} - M_{\text{ATP}} + M_{\text{ADP}} + M_{\text{P}}) \]

\[ = J W_{\text{mech}} - J \Delta \mu \text{ where } \Delta \mu = M_{\text{ATP}} \]

\[ \uparrow \text{mech. power} \quad \uparrow \text{chem. power} \]

\[ \text{out} \quad \text{in} \]

NESS \( \Rightarrow \)

\[ \dot{Q} = \dot{W} = -T \dot{S} \leq 0 \]

\[ \Rightarrow J W_{\text{mech}} = J \Delta \mu - T \dot{S} \leq J \Delta \mu \]

or \( W_{\text{mech}} \leq \frac{T}{J} \Delta \mu \)

The maximum bound on the work \( W_{\text{mech}} \) the enzyme can do in one cycle is set by \( \Delta \mu \) which only depends on relative concentrations of ATP vs. ADP + P

\[ \Rightarrow M_{\text{ATP}} = k_B T \ln \frac{K_{\text{ATP}} C_{\text{ATP}}}{K_{d,\text{ATP}}} \]

similarly for \( M_{\text{ADP}}, M_{\text{P}} \)

+ also the affinity of the molecules for the pocket (good to have large \( K_{\text{ATP}} \) + low \( K_{d,\text{ATP}} \))
If ADP + P as likely to reach binding pocket as ATP \( \Rightarrow \) \( \mu_{\text{ATP}} = \mu_{\text{ADP}} + \mu_p \)

then \( \Delta \mu = 0 \) & enzyme can do no work

So cell needs to maintain sufficiently high supply of ATP, & keep ADP + P concentrations small.