Notes S - Statistical mechanics and thermodynamics: from two simple assumptions to the free energy

Chapter 1. From mechanics to statistical mechanics

Mechanics is very powerful. Equations such as $F=ma$ or $H\dot{\Psi}=E\Psi$ allow us to calculate how a system of particles evolves in time. Both equations conserve energy for isolated system. In classical mechanics, the state of an isolated system is specified by the positions and momenta of all the particles. In quantum mechanics, the state is specified by a wavefunction, which depends only on the positions of the particles: you might think you need only half as many variables, but in reality, it’s the same number because the wavefunction is a complex function (has a real and imaginary part) to make up for it. As we saw in quantum mechanics, the big difference between solving $F=ma$ and solving $H\dot{\Psi}=E\Psi$ is that classical particles behave like points that can congregate arbitrarily close, while quantum particles occupy an ‘area’ $\Delta \chi \Delta p = \hbar/2$ - The Heisenberg Principle - and certain particles, called Fermions, can’t share that area - the Pauli Exclusion Principle.

Very often, we don’t want to know what every single particle does. For example, in a chemical reaction in a flask, there are many molecules reacting, and we may be interested only in what the equilibrium constant of the reaction is, or whether the reaction will go spontaneously or not.

Statistical mechanics makes the connection between microscopic dynamics and macroscopic dynamics. For example, while thermodynamics can manipulate equations of state such as $PV=nRT$, it cannot be used to derive them. Statistical mechanics can derive such equations and show how they arise from the world of atoms and molecules. Our overall goal in chapters S1-6 is to start with two simple postulates in Chapter 2, and derive the equilibrium constant $K$ and that the Gibbs free energy satisfies $\Delta G<0$ for a spontaneous chemical reaction, all from first principles. Then we’ll have a quick look at how molecules move by diffusing.

Important definitions:

**Isolated system:** A collection of particles with their time-independent Hamiltonian $H$ specified. ($H$ may include constraints such as potential energy walls that confine the particles to a volume $V$.)

**Microstate:** A state of the system fully specified, i.e. the exact positions/momenta (classical), or the exact wavefunction (quantum) of all particles in the system are known.

**Macrostate:** A state of the system uniquely specified by macroscopic variables such as: $U$ (total energy), $V$ (volume), $n$ (particle number), etc.

**State functions:** The macroscopic variables that specify the unique macrostate of a system are called state functions.

**Reversible:** two macrostates that differ only by an infinitesimal change in state functions are said to be connected by a reversible process. A series of such infinitesimal transformations therefore is also reversible. **Irreversible** describes all other processes.

**Example:** A box filled with argon atoms is nearly an ideal gas. If you know where every atom is located and how fast it is moving, you know the microstate. If you know only average quantities like the energy $E$ of the gas, volume $V$ of the box, and total number of particles $n$, you know only the macrostate.

**Thought experiment:** If a typical human looked at a jar of red and blue marbles of equal luminance, and all the red ones were at the bottom, and another where they are mixed, would we call them different macrostates? Assume for a moment that we are dogs with gray-scale vision. ‘Woofd’ we call them different macrostates? These definitions are not absolute, and observers need to agree what they consider ‘macroscopic variables’ before we can rigorously compare experiments!
For the first five chapters of statistical thermodynamics, we will compare only equilibrium states or states that differ by an infinitesimal change. Some of the equalities we derive for such reversible transformations would become inequalities for an irreversible process (a process that, even when sliced into infinitesimal steps, still contains steps with large changes – say an explosion, or suddenly lifting a weight instead of gradually reducing weight).

**IMPORTANT CONCEPT: Density or “probability density”**
The most fundamental object in statistical mechanics is the density. What is this mysterious ‘density’? It is simply the probability $\rho_j$ that a macroscopic system will be in a specific microstate “$j$”. Statistical mechanics deals with this probability instead of every individual particle.

Three cases are common: discrete, classical and quantum system:

a. **Discrete systems**: an example would be rolling dice. The die sitting on the table is the macrostate. Which face points up is the microstate. A die has 6 faces, each of which is a “microstate.” Each outcome is equally likely if the die is fair, so

$$P = \rho_j = \frac{1}{W} = \frac{1}{6}$$

is the probability of being in microstate “$j$” where $W=6$ is the total number of microstates and $j$ ranges from 1 to 6, depending on which face of the die is pointing up.

**Homework Problem S1.1**: For two dice, what is the probability of being in macrostate “7”? What function does the probability distribution approach when I roll many dice at once in each roll, and add up the numbers? Make a plot, starting with the uniform distribution (dice have equal probability of 1/6 for each face) for N=2 dice and N=20 dice using

http://195.134.76.37/applets/AppletCentralLimit/Appl_CentralLimit2.html

Figure: Here are all the microstates of two dice for being in macrostate “4”

b. **Classical systems**: here the microstate has to be specified by the positions $x_i$ and the momenta $p_i$ of all particles in the system, so

$$P(x_i, p_i, t) = \rho(x_i, p_i, t)$$

is the probability of finding the particles at positions $x_i$ and with momenta $p_i$ at time $t$.

c. **Quantum systems**: here the probability of microstate $j$ is specified by the square of the wavefunction $\psi_j$, or

$$P(x, t) = |\psi_j(x, t)|^2.$$ 

In all three cases, statistical mechanics attempts to evaluate the probability $\rho(t)$ from first principles, using the conserved energy (Hamiltonian) of the isolated system.

**In-class exercise**: For any observable $A_j$ known in every microstate “$j$”, if we also know the probability $\rho_j$, what is the average value (expectation value) of the observable? [Hint: the answer is in the Overview - goals of chem chapter and in next chapter, if you need to look it up.]
Homework problem S1.2: A bag contains two 1 dollar coins and 4 quarters. If you draw a single coin from the bag many times in a row, what is the average value of a draw? Could you ever draw that amount in a single attempt? If the bag contained a dollar coin, a half dollar and 2 quarters, what would be the answer to the same two questions? Beware: experiments can, but do not always, give the ‘average’ value as a result when you do them!
Chapter 2. Postulates of statistical mechanics, entropy, and thermodynamic laws

1. Postulates and the ergodic approximation

Thermodynamics puts constraints on the behavior of macroscopic systems without talking about the underlying microscopic properties. It does not provide a connection to the microscopic origin of its fundamental quantities $E$ (energy) and $S$ (entropy). For $E$, this is less of a problem because energy is a more intuitive quantity and we know from mechanics that

$$E = \sum \frac{1}{2m} p_i^2 + V(x_i),$$

and the macroscopic formula for $E$ arises by integrating over most coordinates and velocities.

Statistical mechanics makes the macro-micro connection and provides a quantitative description of $E$ and $S$ in terms of microscopic quantities. For large systems (except near the critical point), its results are in agreement with thermodynamics: one can derive the laws of thermodynamics from statistical mechanics, and we will do so. For systems undergoing large fluctuations (small systems, or systems near a critical point), the predictions of statistical mechanics are different from thermodynamics and more accurate.

Important definitions:

An ensemble is a collection of all the microstates of a system consistent with the macrostate as specified by the system’s state functions such as $E$, $V$, $N$, ...

A partition function of a system is the average number of microstates accessible to the system in a given macrostate.

An extensive state function or variable scales linearly with the size of the system (e.g. total mass)

An intensive state function or variable is independent of the size of the system (e.g. density)

The goal of statistical mechanics:

- Given a system of many particles “$i$” with positions $x_i$ and momenta $p_i$ (or with wavefunction $\Psi(x_i)$), find the average value $A$ of any observable $A(x_i, p_i)$ (or of any operator $\hat{A}$) as particles move about, averaged over the ensemble. At equilibrium, the average value $A$ does not change with time.

The two main postulates of statistical mechanics are:

**Postulate I: Extension of microscopic laws to macroscopic systems**

Microscopic dynamics (e.g. $F=ma$) applies to any finite isolated system whose macrostate is uniquely specified by its Hamiltonian and its extensive state functions ($E$, $V$, $N$, ... are constant).

Here $E$ is the energy, $V$ the volume, and $N$ the number of particles. You may need to specify other state functions, such as length $L$ if the system is one-dimensional, but we’ll use $E$, $V$, $N$ as examples (or instead of $N$, mole number $n= N / 6.02214076 \times 10^{23}$, if $N$ is inconveniently large).

**Postulate II: Principle of equal probabilities**

The principle of equal probabilities in ensemble (weak) form and time (strong) form is:

i) Weak form: All $W$ microstates “$j$” of a system satisfying Postulate I have equal probability $\rho_j = 1/W$. These $W$ microstates are called the microcanonical ensemble, $W(E, V, n ...)$ is called the microcanonical partition function; it counts the number of microstates in the macrostate of postulate I.

ii) Strong form: for any ensemble satisfying i) at equilibrium, $\langle \rho_j \rangle_t = \langle \rho_j \rangle_E$ (ergodic principle). This states that averaging a single system over time is equivalent to averaging over the ensemble of all $W$ microstates.
From these two postulates, we can calculate any average property \( A \) of the system in a macrostate by averaging over all its microstates. Thus for the microcanonical ensemble of \( W \) microstates “\( j \)”, each of which has value \( A_j \) for the observable \( A \), the average value or expectation value of \( A \) is simply, as we saw in our introduction to pchem,

\[
A = \sum_j \rho_j A_j = \frac{1}{W} \sum_j A_j
\]

(discrete probability density) or \( A = \int \rho(x,p) A(x,p) \, dx \, dp \) (continuous probability density). Note that we deal with averages like \( E \) or \( A \) so much that we will leave out the bar as in \( \bar{E} \), whereas the unaveraged quantities will be labeled \( E(x,p) \) or \( E_j \).

Before we use them, these postulates require some discussion.

I) This is a strong statement; the system often has >10\(^20\) coordinates, and we assume that the dynamics are the same as for a few particles!

In an “isolated system,” the Hamiltonian \( \hat{H} \) is independent of time (the energy \( E \) is constant). Therefore the first law of thermodynamics is automatically satisfied. In an isolated system, the volume is also constant, so is the particle number, etc. Thus we can write the microcanonical partition function \( W(E, V, n, …) \), as a function of all the conserved quantities needed to describe our isolated system.

II-i) Classically, this says that two configurations ‘\( j \)’ and ‘\( k \)’ of a system with different values of \( x_i \) and \( p_i \) of the individual particles are equally likely to be occupied as long as the energy \( E \) and other specified state functions of the two configurations are the same: \( \rho_j = \rho_k \)

Quantum-mechanically, this means that two states \( \Psi_j \) and \( \Psi_k \) with the same energy \( E \) are equally likely to be occupied.

II-ii) This is also a strong statement: it says that we could take a single initial microstate of a system (with one a specific set of \( x_i \) and \( p_i \)) and evolve it in time, eventually that system will visit all of the microstates at the same energy (and other state functions) as the initial microstate. This property is known as ‘ergodicity.’ In practice, ergodicity cannot really be satisfied, but we can use ii) for ‘all practical purposes’ instead of i) if the system visits enough typical microstates that the time average is not too different from the true ensemble average.

**Homework problem S2.1:** A measurement of the ammonia out-of-plane bending angle by the “Coulomb explosion technique” yields values -27°, +16°, +20°, -12°, +8°, -12°. Calculate the average by assigning a weight to each distinct value (e.g. 1/6 for +18°). Are any actual measurements near the average value? Remembering what you learned about tunneling in quantum mechanics, why are none of the measurements near the average?

**Homework problem S2.2:** How many distinguishable ways are there of arranging \( N=3 \) different-colored balls in a box with three compartments? Draw all the configurations, and express your answer in terms of a factorials. What if all balls are blue and you can’t tell the difference between them, how many distinguishable ways are there then? Write your answer in terms of a ratio of factorials. What if 2 balls are red, and 1 is blue?
Example showing why ergodicity cannot be satisfied in reality:
We will use a discrete system to illustrate. Consider a box with 
\( M = V/V_0 \) cells, filled with \( N \ll M \) particles of volume \( V_0 \). The 
dynamics is that the particles hop randomly to unoccupied 
neighboring cells at each time step \( \Delta t \). This model is called a 
lattice-ideal gas. The number of arrangements for \( N \) identical 
particles is
\[
W = \frac{M!}{(M-N)!} \cdot \frac{1}{N!}
\]
Large factorials \( n! \) (or gamma functions \( \Gamma(n-1) = N! \)) can be approximated by 
Stirling’s formula
\[
n! \sim n^n e^{-n}, \text{ or } \ln[n!] = n\ln[n] - n
\]
Thus,
\[
W = \frac{M!}{(M-N)!} \cdot \frac{1}{N!} = M^M (M-N)^{N-M} N^{-N} = \left( \frac{M}{N} \right)^N.
\]
Let us plug realistic numbers into this:
\( V_0 = 10 \, \text{Å}^3, \ V = 1 \, \text{cm}^3 \Rightarrow M = \frac{V}{V_0} = 10^{23} \).
For \( N = 10^{19} \) gas molecules (~1 atm) \( \Rightarrow \frac{M}{N} = 10^4 \)
\[
v_{\text{gas}} = \left( \frac{U_0}{m} \right)^{1/2} \approx 300 \, \text{m/s} \text{ (O}_2\text{ at R.T.)} \Rightarrow \Delta t \sim \frac{L_0}{v} = \frac{V^{1/3}}{v} \sim 10^{-12} \, \text{s} = 1 \, \text{ps}
\]
Lifetime of universe: \( < 10^{11} \text{ a} \sim 10^{18} \text{ s} \)
\[
W_{\text{possible}} \sim \frac{10^{18} \, \text{s}}{10^{12} \, \text{s}} \sim 10^{30}
\]
\[
W_{\text{actual}} = (10^4)^{10^{19}} \approx 1 \text{ boogol} \gg 10^{30}
\]
The possible \( W \) that can be visited during the lifetime of the universe is a mere \( 10^{30} \), 
negligible compared to the actual number of microstates \( W_{\text{actual}} \) at constant energy.

2. A calculation with \( W \) and its properties
In principle, we can perform all statistical mechanical calculations if we know \( W \), and thus the total 
number of microstates, and the probability of a microstate.

In-class exercise: Consider again the example of particles filling cells in a box. Consider 2 boxes, 
each with \( M \) cells of volume \( V_0 \), connected by a wall. The volume of each box is \( V = MV_0 \). Let the left 
box contain \( N \) identical particles, let the right box be empty. The particles hop randomly form cell to 
cell at each time step \( \Delta t \). Now the wall is removed, so the total volume is \( 2V \). What is the probability 
that the particles remain on the left side of the box?

Answer: Before the wall is removed, \( W_{\text{left}} = M!/(M-N)! \, N! \), and \( W_{\text{right}} = 1 \) since there is only one way 
to arrange no particles in the right box. Thus the total number of microstates before the wall is 
removed is \( W_{\text{before}} = W_{\text{left}} \, W_{\text{right}} = M!/(M-N)! \, N! \). After the wall is removed, \( W_{\text{after}} = (2M)!/(2M-N)! \, N! \).
Thus the probability that the particles remain on the left side is, if all microstates have equal probability (Postulate II)

\[ \rho_{\text{left}} = \frac{W_{\text{left}}}{W_{\text{after}}} = \frac{W_{\text{left}}}{W_{\text{after}}} = \frac{M!(2M - N)!}{(2M)!(M - N)!} \]

If \( M \) and \( N \) are large (see example in a!), we can use Stirling’s formula again. And

\[ \rho_{\text{left}} = \frac{M^M (2M - N)^{2M - N}}{(2M)^{2M} (M - N)^{M - N}} e^{-M - 2M + N + 2M + M - N} \]

\[ \approx \frac{M^N}{(2M)^N} = \frac{1}{2^N} \]

For a large number of particles, this is an incredibly small probability, so the particles will never stay on the left side. They are going to fill the whole volume \( 2V \) after the wall is removed, and the chance that they will all spontaneously go back to the left side is \( 2^{-N} = 2^{-10^{19}} \) for 1 cm\(^3\) of gas particles at 1 atmosphere.

No matter what our system looks like, it is clear that removing constraints always produces an increase in \( W \), the number of available microstates. If the number of particles is large, \( W \) increases astronomically when the constraint is removed, scaling as \( e^N \). Thus we can deduce in general the following law for \( W \) whenever the number of particles is large enough, Postulate II holds, and a constraint is removed at \( t=0 \):

\[ W(t>0) > W(t=0). \]

The fewer constraints a system has, the more disordered it is. Thus \( W \) is a measure of disorder: disorder is the quantity that always increases when constraints are removed.

3. \( W \) and the entropy

However, \( W \) has a property that is not very desirable from a thermodynamic point of view. Recall that in thermodynamics, we prefer to work with intensive or extensive quantities: intensive quantities are independent of the size of the system. Extensive quantities increase linearly with the size of the system. Consider two identical systems from our microcanonical ensemble, each at energy \( E_1=E_2=E \), and each with \( W_1=W_2=W \) possible microstates. Clearly for two isolated systems combined into a new isolated system, \( E_{\text{total}}=E_1+E_2=2E \) because energy is conserved (Postulate I, from which follows the first law of thermodynamics). The total energy is twice the energy. But \( W_{\text{total}}=W_1 W_2 \). For example, if there are 10 arrangements of the particles in each system, there are \( 10 \times 10 = 100 \) arrangements of the particles in the two systems. Thus \( W \) is neither an intensive quantity, nor an extensive quantity. It is a multiplicative quantity.

We can easily fix this: any function \( a f(W) \) that increases monotonically with \( W \) will also satisfy

\[ a f(W(t>0)) > a f(W(t=0)) \]

In particular, the logarithm function is monotonically increasing AND has the property \( \ln(ab)=\ln(a)+\ln(b) \). The logarithm turns multiplicative functions into additive functions.

We now define the new function

\[ S=k_B \ln(W), \]

(so we let \( a=k_B \)). It is then always true that

\[ S(t>0) > S(t=0), \]

and \( S \) is an intensive function. This is known as the second law of thermodynamics, and the new function is called the entropy. The entropy also measures the disorder of a system, but in an
extensive (additive) way. Note that we do not need to work with $S$. We could always calculate $W$ to solve any problem in statistical mechanics, such as what the average value of any observable $A$ is. But the entropy is very convenient: it is an extensive function, and it always increases in time for a closed system whose energy is conserved.

Now a word about the units of entropy. In other fields, like information science, entropy is defined with $a=1$. As you can see, the entropy defined above has units of $k_B=1.38 \times 10^{-23}$ J/K. If chemists of the 19th century had understood that temperature is just the average energy per active degree of freedom of a system, the entropy would be unitless because temperature and energy would have the same units of Joules. But in the 19th century, people were confused about what temperature really is, coming up with ‘bad’ scales (like °C, which allows negative values of $T$) because they did not know that there is a minimum temperature reached when the average available energy per active degree of freedom goes to zero (all energy is extracted from the system). So in chemistry, temperature and energy have different units, and the ratio of these units is given by Boltzmann’s constant $k_B$ ($\approx 1.38 \times 10^{-23}$ J/K). As we will see later, so that $TS$ has units of energy, we thus define $S=k_B \ln(W)$.

We already know that the 2nd law of thermodynamics that we derived above is independent of the choice of the constant $a$, as long as $a>0$ so $S(t>0) > S(t=0)$. As long as $a$ is a positive number, $W$ can be recovered uniquely from $S$ because the logarithm increases monotonically with its argument, and $S$ increases when constraints are removed.

**Homework problem S2.3:** Using the boxed example two pages ago, show that $S\approx Nk_B \ln(V/V_0) - Nk_B \ln(N)$ if $M$ (number of volume elements $V_0$ in the box) is much larger than $N$ (the number of particles). If I double the size of a box containing $6.2\times10^{20}$ molecules (roughly 1 mMole), by how much does the entropy increase in units of J/K? What if I increase the volume by a factor of 1000? As you can see, entropy grows very slowly with volume, but it does increase because more volume => more arrangements => more disorder is possible.

We can also write the formula above in a slightly different way that can be more useful for general calculations:

$$S = k_B \ln(W) = -W \cdot \frac{1}{W} \ln\left(\frac{1}{W}\right)$$

$$S = -\sum_{i=1}^{W} \frac{1}{W} \ln\left(\frac{1}{W}\right)$$

$$S = -\sum_{i=1}^{W} \rho_i \ln(\rho_i)$$

This last formula writes the entropy explicitly in terms of the probability of each microstate. It could also be applied in cases where the probability of states in the sum is not the same (although it is required to be the same by postulate II in the microcanonical ensemble).
Finally, consider the case where all possible energy has been removed from the system. It can be proved from Postulate I that the ground state of any Hamiltonian of the type
\[ H = \sum_i \frac{p_i^2}{2m_i} + V(x_i) \]
where \( V \) is finite at finite \( x \) is singly degenerate. Thus when \( E \) approaches its minimum value \( W=1 \), there can be only one microstate. Clearly, we must then have \( S = k_B \ln(1) = 0 \). The entropy of a system approaches 0 when all the available energy is extracted from the system:
\[ \lim_{E \to \text{min}} S = 0. \]

This is known as the third law of thermodynamics (microcanonical version = constant energy version).

Figure: Entropy \( S \) increases monotonically as energy increases, i.e. \( \frac{\partial S}{\partial E} > 0 \) always. Only processes at constant entropy are reversible according to the second law \( S(t>0) > S(t=0) \). A quasistatic process is one done slowly enough so the system’s trajectory lies on an ‘equation of state’ surface \( S=S(E, V, n) \) that specifies what \( W \) (and thus \( S \)) is at a given energy, volume, particle number, etc. of the system.

Thus the postulates of statistical mechanics secure for \( S \) all the properties in the second and third laws of thermodynamics, and for \( E \) in a closed system the first law of thermodynamics (energy conservation). We thus have now proved the laws of thermodynamics based on the microscopic properties of the Hamiltonian and the assumption of equal probability of states of equal energy. Note that statistical mechanics only has two postulates, one fewer than thermodynamics, and that we can prove the postulates of thermodynamics in the framework of statistical mechanics. This tells us that statistical mechanics is a more generally valid theory than thermodynamics, like quantum mechanics or special relativity are more generally valid than Newtonian mechanics.
Chapter 3. Entropy, temperature, and the microcanonical partition function: how to calculate results with statistical mechanics.

The goal of equilibrium statistical mechanics is to calculate the ‘density’ (probability) $\hat{\rho}_{eq}$ so we can evaluate average observables $A$ that give us fundamental relations or equations of state.

Just as thermodynamics has its potentials $E$, $H$, $F$, and $G$, so statistical mechanics has its ensembles. So far we only considered the microcanonical ensemble. The microcanonical ensemble is the one directly defined in postulate II of statistical mechanics. In the microcanonical ensemble $E$ is fixed (Postulate I), and the other constraints that are fixed are the volume $V$ and mole number $n$ (for a simple system), or other extensive parameters (for more complicated systems).

1. How do we define temperature (and other variables) intuitively?

a. Monotonicity of $S(E)$ and $E(S)$. We saw in chapter 2 that $S=k_B\ln(W(E,V,n...))$, and that $W$ increases monotonically with $U$: the higher the energy, the more microstates are accessible to the system. But the logarithm is also a monotonically increasing function, so $S(E,V,n)$ is a monotonically increasing function of $E$: as the energy goes up, so does the entropy (or disorder) of a system because more microstates are available. More microstates means more disorder. Only 1 microstate means complete order ($S=0$), as we saw in chapter 2. We can thus invert the function uniquely, and $E(S,V,n)$ is a monotonically increasing function of $S$: the more disorder a system has, the higher its energy must be:

$$\frac{\partial E}{\partial S}_{v,n,...} \geq 0$$

b. Derivatives of the energy and entropy. If the energy changes a little bit, we have the differential change

$$dE = \left(\frac{\partial E}{\partial S}\right)_{v,n} dS + \left(\frac{\partial E}{\partial V}\right)_{s,n} dV + \left(\frac{\partial E}{\partial n}\right)_{s,v} dn + \cdots$$

$$= T dS + (-P) dV + \mu dn + \cdots$$

The derivatives are intensive variables (independent of system size). Solving for $dS$ we also have

$$dS = \frac{1}{T} dE + \frac{P}{T} dV - \mu dn + \cdots$$

so

$$\left(\frac{\partial S}{\partial E}\right)_{v,n} = \frac{1}{T}, \left(\frac{\partial S}{\partial V}\right)_{v,n} = \frac{P}{T}, \text{ etc.}$$

Note that we are giving these derivatives names, like $T$ and $-P$ and $\mu$, but we usually reserve these names for temperature and pressure and chemical potential. Are they actually the temperature and pressure and chemical potential?!! Let’s find out.

What is this quantity $T$? Consider a closed composite system $\{\text{Sys}\}$ made of two subsystems $\{\text{Sys}_1\}$ and $\{\text{Sys}_2\}$ separated by a diathermal wall. A diathermal wall allows only allows energy to flow back and forth in the form of heat, so $dV=0$ and $dn=0$. At equilibrium, the number of microstates of the composite system $\{\text{Sys}\}$ is not changing, so

$$dS = 0 = \left(\frac{\partial S_1}{\partial E_1}\right)_{v,n} dE_1 + \left(\frac{\partial S_2}{\partial E_2}\right)_{v,n} dE_2$$

or

$$dS = \frac{1}{T_1} dE_1 + \frac{1}{T_2} dE_2.$$  

But $dE=0$ for a closed system because of energy conservation, from which follows that

$$dE_2 = -dE_1 \quad \text{or} \quad 0 = \left(\frac{1}{T_1} - \frac{1}{T_2}\right) dE_1$$

at equilibrium.
This equation can only be true if
\[
\left( \frac{1}{T_1} - \frac{1}{T_2} \right) = 0 \quad \text{and therefore} \quad T_1 = T_2
\]

Thus, \( T \) is the intensive quantity that is equalized between two subsystems when heat is allowed to flow between them.

**Thought experiment:** Intuitively, what thing is the same between to objects if heat does not flow between them when in contact? For example, if I have two glasses of water and hold them together, but no heat flows from one glass to the other, what can we say about the water in the two glasses.

That’s the definition of temperature: the thing that becomes equal when heat stops flowing between two places. We can thus identify the intensive variable \( T \) as the temperature of the system. Temperature is always guaranteed to be positive because we saw in a. that \( E \) is a monotonically increasing function of \( S \) and \( T = (\partial E / \partial S) \).

![Molecules exchange kinetic energy](image1)

**Figure:** molecules exchange kinetic energy through collisions when in contact: heat flows (from left to right in our example). Once the energy per molecule has been equalized on averaged heat no longer flows. We say ‘the temperature is the same on both sides.’ Temperature difference acts like a driving force for heat flow.

**Homework problem S3.1:** Use the same logic to prove that \( P \) must be the pressure. Pressure is the quantity that is equalized when two systems connected by a movable wall reach equilibrium by changing their volumes. Note that the derivative \( \partial E / \partial V \) is defined as \(-P\) to agree with our intuition that volume decreases (\( dV \) is negative) by squeezing on the system, its energy increases (\( dE \) is positive) because we are doing work on the system.

**Homework problem S3.2:** Now prove that \( \mu \), the chemical potential, is the quantity that is equalized between two subsystems when particles flow back and forth (or react) and their particle numbers come to equilibrium. You could go on and on proving such relationships for other intensive (derivative) variables.

We call pairs of variables such as \( S \) and \( T \), or \( P \) and \( V \), or \( \mu \) and \( n \) ‘thermodynamically conjugate state functions,’ or simply ‘conjugate,’ not to be confused with the same word used for quantum variables that obey the Fourier principle! These state functions describe the macroscopic equilibrium state of a system. Note that some of them are independent of system size (pressure, temporarily, chemical potential) while others increase linearly with the system size (entropy, volume, mole number). We call them ‘extensive’ and ‘intensive,’ respectively.
c. **An explicit formula for the energy.** In b., we are giving a formula for energy change. Can we derive one for the energy $E(S, V, n\ldots)$ explicitly? Since $E, S, V, n\ldots$ are all extensive quantities, it must be true for any positive multiplier $\lambda$ that

$$E(\lambda S, \lambda V, \lambda n\ldots) = \lambda E(S, V, n\ldots)$$

This simply states if I increase the size of the system by $\lambda$, so $S\rightarrow \lambda S$ and so forth, the new energy must equal $\lambda E$. Taking the derivative with respect to $\lambda$ on both sides,

$$
\left(\frac{\partial E}{\partial \lambda S}\right) \frac{\partial S}{\partial \lambda} + \left(\frac{\partial E}{\partial \lambda V}\right) \frac{\partial V}{\partial \lambda} + \cdots = E(S, V, n\ldots) \quad \text{or}
$$

$$
\left(\frac{\partial E}{\partial \lambda S}\right) S + \left(\frac{\partial E}{\partial \lambda V}\right) V + \cdots = E(S, V, n\ldots).
$$

This must hold for $\lambda=1$ in particular, so

$$
\left(\frac{\partial E}{\partial S}\right) S + \left(\frac{\partial E}{\partial V}\right) V + \cdots = E(S, V, n\ldots) \quad \text{or}
$$

$$
TS - PV + \mu n + \cdots = E(S, V, n\ldots)
$$

This remarkably simple and universally true formula says that energy is simply a sum over the product of conjugate variable pairs that describe the macrostates of our system. It is known as ‘bilinear form’ or ‘Euler’s form’ of the energy in terms of intensive and extensive thermodynamic state functions. It is always true, no matter how complicated the system!

Systems that are more complicated than a gas need additional pairs of conjugate variables added: for a spring extended by length $L$ when a force $F$ is applied, a “-FL” term is added to the energy instead of “-PV”; for a soap bubble of surface area $A$ and surface tension $\sigma$, a term “-A\sigma” has to be added. And so on, but the energy is always ‘bilinear’ in terms of thermodynamic variables, and this is not an approximation.

**Thought experiment:** Other systems may of course have other variables besides $V, n$, etc. What about a protein of charge $q$ in an electric potential $V_e$?

2. **Thermodynamic potentials $E, F, G$, and $H$ are equivalent to $S$ and $W$.**

We started with postulate II about $W(E, V, n\ldots)$, and showed that the functions $S(E, V, n\ldots)$ (basically the log of $W$) and $E(S, V, n\ldots)$ contain the same information, but may be more convenient because the logarithm makes them less humongous. More such functions, or “thermodynamic potentials,” can be devised that also contain the same information as $E$.

**Thought experiment:** (see Figure) Let’s say we want $E$ as a function of temperature, not entropy. Why can’t we just calculate $T(S) = \partial E/\partial S = $ solve for $S(T)$, plug into $E(S)$ to get $E(T)$? That would give us $E$ as a function of $T$, wouldn’t it? **Answer: nope**

![Diagram](image)

Figure: Changing $y(x)$ to the equivalent function intercept(slope) = $\varphi(m)$. Note that you cannot uniquely define $y(m)$, you really need $\varphi(m)$ to replace $y(x)$: for example, the function $z(x) = y(x-c)$ is different from $y(x)$, but produces the same $z(m) = y(m)$, so $z(m)$ and $y(m)$ cannot be used to reconstruct the original and different $y(x)$ and $z(x)$!
**Homework problem S3.3:** Illustrate this for the two functions \( y(x) = x^2 \) and \( z(x) = (x-5)^2 \). First, calculate \( m(x) = \partial y/\partial x \), solve for \( x(m) \), and insert back into \( y \) to get \( y(m) = \) ?. The then do the same thing for \( z(m) \). The functions \( y(m) \) and \( z(m) \) are identical. So no way, if I give you \( y(m) \) or \( z(m) \), can you tell me what the original different functions \( y(x) \) and \( z(x) \) were.

So how do we do this right? Consider a function \( y(x) \). We could calculate its slope \( m(x) = \partial y/\partial x \) and its intercept \( \varphi = y(x) - mx \), and then express the intercept as a function of slope, \( \varphi(m) = y(x(m)) - mx(m) \) by solving \( m(x) \) for \( x(m) \) and inserting. The function \( \varphi(m) \) does contain the same information as \( y(x) \), we can go back from \( \varphi(m) \) to \( y(x) \). \( \varphi(m) \) is called the Legendre transform of \( y(x) \). Let us apply this to \( y = E, x = S \) and \( m = \partial E/\partial S = T \), and let’s call the resulting intercept “\( F \)”. \( F \) will be a function of the ‘slope’ \( T \) instead of \( S \).

\[
F(T, V, n, \cdots) = E - TS.
\]

We can also easily see the change of variables by using the chain rule on the differentials:

\[
F(T, V, n, \cdots) = E - TS \Rightarrow dA = dE - Tds - SdT
\]
\[
dF = Tds - Pdv + \mu dn + \cdots - Tds - SdT
\]
\[
dF = SdT - Pdv + \mu dn + \cdots
\]

Clearly, \( F \) is now a function of \( T, V, \cdots \) instead of \( S, V, \cdots \). It contains information equivalent to \( E \) because we can always transform back from \( F(T) \) to \( E(S) \). \( F \) is called the Helmholtz free energy.

Similarly, if we want \( P \) as our variable instead of \( V \), we can let \( y = E, x = V \) and \( m = \partial E/\partial V = -P \):

\[
H(S, V, n, \cdots) = E + PV \Rightarrow dH = Tds - Vdp + \mu dn + \cdots
\]

\( H \) is called the enthalpy. Just like the Helmholtz free energy, the enthalpy is also equivalent to \( E \). We could even do it twice in a row, first for \( S \) and then for \( V \), getting

\[
G(T, P, n, \cdots) = E + PV - TS = H - TS \Rightarrow dG = -SdT + Vdp + \mu dn + \cdots
\]

\( G-H-TS \) is called the Gibbs free energy. It is a function of \( T \) and \( P \), but it also contains equivalent knowledge to \( E \) that can be traced back to \( S \) and ultimately to \( W \). Using the explicit formula for the energy from \( c_n \), and applying it to a system with several components of mole number \( n_i \), we can see that \( G \) has a particularly simple formula:

\[
E = TS - PV + \sum \mu_i n_i \quad \text{and} \quad G = E + PV - TS \Rightarrow G = \sum \mu_i n_i
\]

The Gibbs free energy is just the sum over the chemical potentials of the individual chemicals “\( i \)”, \( \mu_i = (\partial G/\partial n_i)_V, S, \cdots \). We will find the Gibbs free energy very useful in Chapter 5 when we want to know the equilibrium concentrations of reactants and products in a chemical reaction at constant temperature and pressure.

We’ll also find the chemical potential very useful. Based on the above equation, evidently we also have \( \mu_i = (\partial G/\partial n_i)_{T, P} \). And since \( (\partial G/\partial T) = -S \) and \( (\partial S/\partial n_i) = s_i \) is the change of entropy per mole of substance “\( i \)”, \( (\partial \mu_i/\partial T) = -s_i \) and similarly \( (\partial \mu_i/\partial P) = v_i \) and so forth. We call \( s_i \) the ‘molar entropy’ of substance “\( i \)” \( v_i \) its ‘molar volume,’ and so on. For an ideal substance, the molar volume is just the volume of one mole of substance. But in non-ideal situations in a mixture, this may not be true!

**Thought experiment:** When some ions, such as Mg++, are dissolved in water, the volume of the resulting solution actually shrinks! That would mean (Le Chatelier’s principle) that the applying pressure should lower the chemical potential of Mg++ even more, so more will dissolve: \( (\partial \mu_i/\partial P) = v_i < 0 \). So the molar volume of Mg++ in water is actually negative. What could be the reason?

### 3. Heat flow and heat capacity

**Entropy change, heat flow, and temperature** Here’s one more useful formula involving the entropy and temperature. If our system is not allowed to exchange particles \( (dn=0) \) and the volume is fixed \( (dV=0) \), no work can be done. The only way to change its energy is by adding heat. Therefore
\[ dq_{V,n} = dE = TdS - PdV + \mu dn = TdS , \]
\[ dS = \frac{dq_{V,n}}{T} . \]

**Homework problem S3.4:** You already learned about the enthalpy \( H=E+PV \): it is the heat flow when pressure is constant (\( dn=0 \) and \( dP=0 \) instead of \( dn=0 \) and \( dV=0 \)). Using \( dH=dE+PdV+VdP \), write down a formula like the above one for \( S, q_{P,n} \) and \( T \) when pressure is constant: how is entropy change \( dS \) related to heat flow at constant pressure? Look familiar compared to the equation above?

**Temperature dependence of the energy, enthalpy and entropy: the heat capacity.** The Helmholtz and Gibbs free energies are already functions of temperature. \( E, S \) and \( H \) are not, but frequently it is useful to know how they depend on temperature. For example,

\[ \left( \frac{\partial E}{\partial T} \right)_V = C_V(T) \Rightarrow dE = C_V(T) dT \]
\[ \left( \frac{\partial H}{\partial T} \right)_P = C_P(T) \Rightarrow dH = C_P(T) dT \]

\[ dS = \frac{dq}{T} \Rightarrow dS = \frac{dH}{T} \quad \text{(at constant } P) \]

\[ \Rightarrow dS = \frac{C_P(T) dT}{T} \]

\[ dS = \frac{dq}{T} \Rightarrow dS = \frac{dU}{T} \quad \text{(at constant } V) \]

\[ \Rightarrow dS = \frac{C_V(T) dT}{T} \]

**Homework problem S3.5:** If \( S=ns^{(0)} \) at concentration \( c^{(0)}=1 \) and at the standard reference temperature \( T^{(0)} \) (for example 298 K), show that at some other temperature, \( S=ns^{(0)}+\int dTC_P(T)/T \) where the integration limits are \( T^{(0)} \) and the other temperature. Derive a similar formula for \( H \). We’ll see later that this is useful for studying protein denaturation because disorder (entropy) of a protein increases as it unfolds at high temperature.

So, if we want to know how \( S, H, \) and \( E \) depend on temperature, we need to figure out what the two functions \( C_V \) and \( C_P \) are. They tell us how much \( E \) or \( H \) increase when the temperature of our system increases. \( C_V \) is given by a second derivative as follows: \( (\partial^2 E/\partial S^2)_V \), since \( T=(\partial E/\partial S)_V \). Also \( (\partial S/\partial T)= (\partial T/\partial S)^{-1} \). But we showed above that \( (\partial S/\partial T)=C_V/T \), so \( C_V=\int (\partial^2 E/\partial S^2)_V \).

**Homework problem S3.6:** By Legendre transforming from \( E \) to \( H \) so we have a function of pressure, play the same game with the second derivative \( (\partial^2 H/\partial S^2)_P \) to derive the analogous formula for \( C_P \).

The important concept here is that heat capacities are second derivatives of energy or enthalpy because the temperature \( T=(\partial E/\partial S)_V \) or \( (\partial H/\partial S)_P \) is already a first derivative. Note that analysis of second derivatives could be of interest if we want to prove whether a quantity is minimized or maximized, since a zero derivative only tells us that either of the two is happening, but a negative second derivative (negative curvature) tells us that we are near a minimum of the function.

4. **Calculation of thermodynamic quantities from \( W(U) \) and \( S(U) \)

**Example:** Fundamental relation for a “lattice gas” model: entropy-volume part.
Consider again the model system of a box with \(M = V/V_0\) volume elements \(V_0\) and \(N\) particles of volume \(V_0\), so each particle can fill one volume element. The particles can randomly hop among unoccupied volume elements to randomly sample the full volume of the box. This is a simple model of an ideal gas. As shown in the last chapter,

\[
W = \frac{M!}{(M-N)!N!}
\]

for identical particles, and we can approximate this, if \(M \ll N\) by

\[
W \approx \frac{1}{N!} \left( \frac{V}{V_0} \right)^N
\]

since \(M!/(M-N)! \approx M^\prime\) in that case. Assuming the hopping samples all microstates so the system is at equilibrium, we compute the equilibrium entropy, as derived in chapter 2 as

\[
S = k_B \ln W = -Nk_B \ln N + Nk_B + Nk_B \ln(V/V_0)
\]

\[
\approx Nk_B (1 - \ln(V_0)) - Nk_B \ln(N/V)
\]

\[
= nR(1 - \ln(V_0)) - nR \ln(nN_A/V)
\]

\[
= nS_0 - nR \ln(n/V) = nS_0 - nR \ln(c)
\]

In the first line, we used the definition of \(S\) in terms of \(W\) and Stirling’s approximation for the factorial \(\ln(N!) \approx N \ln N - N\). In the second line, we rearranged terms. In the third line, we converted from particle number \(N\) to mole number \(n\): \(N = nN_A\), where \(N_A\) is Avogadro’s number. \(R = k_B N_A \approx 8.31\) Joules/(mole·Kelvin). This constant is known as the “gas constant,” and you can see that it is just Boltzmann’s constant times Avogadro’s number. Both \(k_B\) and \(R\) are just conversion factors between energy and temperature because 150 years ago, scientists did not yet understand that temperature is just average energy per active degree of freedom, and should really have units of Joules! In the last line, we collected terms into ones that are constant, and ones that depend on concentration \(c = n/V\).

Thus the entropy of a randomly moving gas (and also of an ideal solution, where solutes do not interact with one another) depends on the logarithm of the concentration of the particles.

**Homework problem S3.7:** In the above formula, \(S_0\) in the last line lumps together all the constants. What is \(S_0\)? Could \(S_0\) become negative? Should it be able to if we worked with the exact equation?

**In-class exercise:** By taking the derivative \((\partial S/\partial V)\) in the above formula, and comparing to the derivative \((\partial S/\partial V)\) defined in b., let’s derive a familiar law that is obeyed by particles randomly moving around in a box.

Now you see the power of statistical mechanics: we assume energy is conserved (Postulate I) and all microstates of the same energy have same probability (Postulate II). Then we specify a system: ‘particles randomly hopping around in a box.’ Those three, two postulates and specifying our system, we can derive the ideal gas law - and any other law describing molecules. You can see now that the ideal gas law is much more general than the way it is usually derived - the assumption ‘particles randomly hopping in a box’ is all that’s required to have an ideal gas, nevermind all that stuff about forces, bouncing into container walls, etc.

**Homework problem S3.8:** Mechanical work \(dw = PdV\). Show that \(w = TdS\) when only the volume of an ideal gas, not its temperature, is changed. [Hint: integrate \(dw\) from \(V_1\) to \(V_2\) using the ideal gas law, and show that \(\Delta S = S_2 - S_1 = nR\ln(V_2/V_1)\).]
Chapter 4: Working at constant temperature - the Canonical Ensemble

All calculations in statistical mechanics can be done in the ‘microcanonical ensemble’ that we used so far, where all copies of the system are in microstates of the same energy with well-defined volume and particle number (isolated system). We saw that with just two postulates and some calculus, relations like $PV = nRT$ or $dS = dq/T$ can be derived. In particular, we were able to define a new variable “temperature” as the ‘quantity that is equal when two systems, between which heat is allowed to flow, come to equilibrium.’ Similarly, we defined what pressure and chemical potential are.

In reality, a system is never isolated; there is always a larger environment around the system that can exchange heat, or work, or volume, or particles in some combination or other. We could always treat the systems + environment as one larger closed system, and apply the microcanonical ensemble and Postulate 2 directly. This works just fine, but it can be very cumbersome if you have to treat the environment explicitly all the time. Often it is more practical to just treat the system explicitly, and leave out the environment as much as possible. That’s the philosophy behind this chapter.

Consider heat flow as an example. Many reaction are done in open flasks, where heat can flow in and out. Thus at equilibrium, or if the reaction does not generate heat too rapidly (often the case in biochemistry) not the energy in the flask will be constant, but the temperature will be constant – the same temperature as the much larger lab environment, from/into which heat can flow to/from the flask, so thermal equilibrium is approximately maintained during the reaction.

Thus it would be nice to have formulas for systems at constant temperature. Such systems are called “canonical” in statistical mechanics, while systems at constant energy are called “microcanonical.” The ensemble of microstates of a system at constant temperature that belong to the same macrostate are called the “canonical ensemble,” in analogy to the “microcanonical ensemble” that we saw in Chapter 2.

To discuss a system at constant T, we need to embed the system inside a heat bath (the environment) and connect the system by a diathermal wall (that allows heat to flow) to the heat bath.

**Thought experiment:** Does this apply to single molecule experiments? A: Only the bath needs to be large so that $W_{tot}$ and $W_{bath}$ satisfy the large number approximations necessary for thermodynamics. $W \equiv W_{sys}$ can be small. So the system could be a single molecule on a big surface, and if heat can flow from the molecule to the surface and vice versa, the molecule will still have the same temperature as the surface.

1. Deriving the canonical partition function from Postulate 2
Remember the definition of a partition function in Chapter 2: it is the number of microstates accessible on average when the system is in a given macrostate. For example, in the microcanononical ensemble, \( W \) is the microcanononical partition function; it is the number of microstates at constant energy \( E \). What about the number of microstates in a macrostate at constant temperature, instead of constant energy? That would be called the “canonical partition function” since the ensemble at constant temperature is the “canonical ensemble.”

**Homework problem S4.1:** What is the microcanononical partition function of an electron spin, when there is no magnetic field applied? (spin up and spin down have the same energy)?

Let the system and environment together have constant energy \( E_{\text{tot}} \) (overall isolated system+environment). Then the number of ways the system can be at energy \( E_j \) is \( W(E_j) \cdot W_{\text{env}}(E_{\text{tot}} - E_j) \). The number of ways the system can be at any energy is simply \( W_{\text{env}}(E_{\text{tot}}) \).

From this follows for the probability \( \rho \) of the system of being at energy \( E_j \) that
\[
\rho_j^{(eq)} = \frac{W(E_j) W_{\text{env}}(E_{\text{tot}} - E_j)}{W_{\text{tot}}(E_{\text{tot}})}; \quad \text{using } S = k_B \ln W \implies \\
\rho_j^{(eq)} = W(E_j) e^{(S_{\text{env}}(E_{\text{tot}} - E_j) - S_{\text{tot}}(E_{\text{tot}}))/k_B}
\]

where we used the ‘log trick’ in the second line to replace the multiplicative microcanononical partition function by the additive entropy.

We can simplify the exponent as follows: Let \( E \) be the (as yet unknown) average energy \( E = \langle E_j \rangle_s \) of the canonical ensemble of systems (= the ensemble at constant temperature). Let \( T \) be the temperature of the bath (and the system, since heat can flow). Calling the system’s entropy simply “\( S \)” instead of “\( S_{\text{sys}} \)” for simplicity,

(a) \( \implies S_{\text{tot}}(E_{\text{tot}}) = S(E) + S_{\text{env}}(E_{\text{tot}} - E) \) (true at energy \( E \) for any other energy)

Taylor-expanding \( S_{\text{env}}(E_{\text{tot}} - E_j) \) around the average energy \( E \) of the system, i.e. \( j(x) = j(x_0) + \partial j/\partial x \mid_{x_0} (x - x_0) + \cdots \), where \( j = S_{\text{env}}, x = E_j \) and \( x_0 = E \);

(b) \( \implies S_{\text{env}}(E_{\text{tot}} - E_j) = S_{\text{env}}(E_{\text{tot}} - E) + \left( \frac{\partial S_{\text{bath}}}{\partial E_j} \right)_{E_j=E} (E_j - E) + \cdots \)

\[
= S_{\text{env}}(E_{\text{tot}} - E) + \left( \frac{\partial S_{\text{bath}}}{\partial E_{\text{bath}}} \right) \left( \frac{\partial E_{\text{bath}}}{\partial E_j} \right) (E_j - E) + \cdots \\
= S_{\text{env}}(E_{\text{tot}} - E) - \frac{1}{T} (E_j - E) + \cdots
\]

In the last step, we used \( 1/T = \partial S/\partial E \) and \( dE_{\text{bath}} = -dE_{\text{sys}} \) (first law of thermodynamics = energy conservation) to simplify the second term.

**In-class exercise:** Why are the higher order terms negligible? A: Usually in a Taylor series, it is because \( x=E_j-E \) is small. This is true for a large system (central limit theorem) but not necessarily for a small system. Here the reason is that the bath is assumed to be huge. This causes the 0th order term \( S_{\text{bath}} \) to be large compared to the first order term, but it also causes the second derivative \( \partial^2 (1/T)/\partial E_{\text{bath}} \) to be negligible compared to the first derivative \( 1/T \): the temperature of an infinite environment is not going to change just because you add some energy to the bath.

Inserting both (a) and (b) into the formula for \( \rho_j^{(eq)} \),
\[
\rho_j^{(eq)} = W(E_j) e^{(-1/T_E + 1/\tau - S)/k_B}
\]
\[ W(E_j) = e^{\frac{1}{k_B T} \left[ (-E_j + E - TS) \right]} \]
\[ = W(E_j) e^{\frac{1}{k_B T}(-E_j + E)} \]
\[ = W(E_j) e^{\frac{-E_j}{k_B T}} \]
\[ = W_j \frac{e^{-E_j/k_B T}}{Z} \]

In the third line, we used \( F = E - TS \), the Helmholtz free energy from Chapter 3, and in the fourth line, we define \( W_j = W(E_j) \) and \( Z = e^{-E/k_B T} \) as short-hand notations for the microcanonical partition function as the exponential of the Helmholtz free energy.

So what is \( \rho_j^{(eq)} \) in words? It is the probability of the system being in state \( j \) with energy \( E_j \) when the temperature is held constant at \( T \). We call \( e^{-E_j/k_B T} \) the ‘Boltzmann factor. It says that the higher the energy \( E_j \), the less likely the system will be at that energy; but as \( T \) increases, it becomes more likely that the system is at high energy.

To obtain the physical meaning of \( Z \), we can derive an alternate formula for the normalization factor \( Z \) by realizing that the total probability has to add up to 1:

\[ \sum_j \rho_j = 1 \Rightarrow \frac{1}{Z} \sum_j W_j e^{-E_j/k_B T} = 1 \text{ or } Z = \sum_j W_j e^{-E_j/k_B T}. \]

The meaning of the canonical partition function. \( Z \) is called the canonical partition function, in analogy to the microcanonical partition function \( W \). It is given by the sum over all microcanonical partition functions weighted by a Boltzmann factor that takes into account that at a given temperature \( T \), higher energy microstates are less likely to be populated. Sometimes the notation”\( Q \)” is used for \( Z \).

Just like \( W \) counts the number of microstates accessible to an isolated system at constant energy, \( Z \) counts the number of microstates accessible to a system at constant temperature. For example, if \( T=0 \), then \( Z=W_0 \), the microcanonical partition function or “degeneracy” of the lowest energy level. This degeneracy is usually equal to 1: usually there is only one microstate without extractable energy (3\(^{rd}\) law of thermodynamics in Chapter 2). Thus \( Z=1 \) at very low temperature because only the one lowest energy microstate can be populated. As the temperature increases, \( Z \) increases because more microstates can be populated. When \( k_B T \gg E_j \), a state at energy \( E_j \) makes a full contribution

\[ \lim_{x=E_j/k_B T \to 0} e^x = 1 \]

to \( Z \). If a state has \( E_j >> k_B T \), then it makes a small contribution to \( Z \). Thus \( Z \) counts the effective number of accessible microstates, including the ones that are partially accessible.

For practical use, the important consequence of the derivation given above is that

\[ Z = \sum_j W_j e^{-E_j/k_B T} = e^{-E_j/k_B T} = e^{-\beta F} \text{ if we define } \beta = 1/k_B T \text{ (often convenient!)}. \]

This formula connects the microscopic world of individual energy levels \( E_j \) and their degeneracies (degeneracy = microcanonical partition function) with the macroscopic world of thermodynamic potentials, in this case \( F \), which is the potential useful at constant temperature, called the Helmholtz potential. Once the microcanonical partition functions \( W(E_j)=W_j \) are known for each energy \( E_j \), \( Z \) can
be calculated. Once $Z$ is known, $F$ can be calculated, and from $F$ all other thermodynamics quantities can be calculated, since $F$ is equivalent to $W$, $S$, and $U$ as we saw in Chapter 3.

**Note 1:** If $E$ is continuous, we replace the sum by an integration $Z = \int_0^\infty dE W(E) e^{-E/k_BT}$, where $W(E)$ is the continuous density of states.

**Note 2:** $Z$ is sometimes written as a sum over every single state, instead of over degenerate energy levels:

$$Z = \sum_{i=1}^\infty e^{-\beta E_i} \quad \hat{\rho}_{eq}(T,V) = \frac{1}{Z} e^{-\beta \hat{\mu}}$$

For example, if energy level $i=5$ is 3-fold degenerate, this sum would have to contain the term three times, rather than explicitly writing out $W_i = 3$.

2. **Computation of thermodynamic quantities from $Z$**

We saw in the last chapter how to prove useful thermodynamic formulas like $dS = dq/T$, or $PV = nRT$. We can use the same method to calculate any average quantity we want from $Z$.

**In-class exercise: What is the heat capacity of an RNA hairpin?**

Consider the following simple model for the reaction that interconverts a folded RNA hairpin to an unfolded RNA hairpin. The figure below shows a simple 2-D lattice model for an RNA with four bases, two of which can base pair in the “stem.” In this model, we can count all the states that are non-superimposable by 2-D rotation:

![Figure: Folding/unfolding reaction of an RNA hairpin in a simple 2-D lattice model that allows only 90° hinge motions of the bases, and counts only one interaction energy (base pairing energy), between the two black bases.](image)

Let the base pairing energy between the two black bases be $-\varepsilon$ kJ/mole. Renormalizing the minimum energy to 0, we have $E_F = 0$ $W_F = 1$ and $E_U = +\varepsilon$ and $W_U = 5$. The partition function for this system is

$$Z = W_F + W_U e^{-\varepsilon/RT}.$$  

The probability of being in states $F$ and $U$ is

$$\rho_F = \frac{W_F}{Z}, \quad \rho_U = \frac{W_U e^{-\varepsilon/RT}}{Z},$$

and the ratio of concentrations for the above reaction is therefore

$$K = \frac{[U]}{[F]} = \frac{\rho_U}{\rho_F}.$$  

We will prove in chapter 5 that this ratio, known as the equilibrium constant $K$, can be calculated directly from the Gibbs free energy introduced in chapter 3.

The average energy of the system is given by
We now have the energy as a function of temperature and the parameters $W_F$, $W_U$ and $\varepsilon$. Now take the derivative of the energy as in with respect to temperature to obtain

$$ C_V = \left( \frac{\partial E}{\partial T} \right)_V = \left( \frac{1}{R} \right) \left( \frac{\varepsilon}{T} \right)^2 \rho_U \rho_F $$

This heat capacity has a maximum at $\rho_U = \rho_F = 1/2$, in the middle of the folding/unfolding transition. Thus the ‘melting temperature’ of an RNA piece could be determined by calorimetry by looking for the heat capacity maximum.

Let’s calculate this melting temperature $T_m$, where $\rho_U = \rho_F = 1/2$: according to the definition of $\rho_F$ above, at the melting temperature $1/2 = 1/Z$ (since $W_F = 1$) or $2 = 1 + W_U \exp(-\varepsilon RT_m)$, or $T_m = \varepsilon (R \ln(W_U))$. This should make sense: the higher the interaction energy $\varepsilon$, the harder it will be to melt the RNA; the more unfolded microstates are available, the easier it will be to melt the RNA.

Note that a simple model like the above will not be perfectly accurate. For example, by making it 2-D, we are grossly underestimating the number of unfolded configurations compared to the folded ones. We could easily remedy this by writing $\rho_U$ as

$$ \rho_U = 1 - \rho_F = \frac{W_U/W_F e^{-\varepsilon/RT}}{1 + W_U/W_F e^{-\varepsilon/RT}} $$

and making the ratio $W_U/W_F$ an adjustable parameter in our fitting model. Or we could do a better calculation by, say, running molecular dynamics to count configurations and evaluate energies. The important thing is that statistical mechanics lets you derive realistic model functions for your experiment, instead of fitting the data by a polynomial or some other function that has no physical meaning and provides no physical insight. In the above equation for $C_V$, the physical insight is that the heat capacity is directly related to the base pairing energy $\varepsilon$, depends on the ratio $(\varepsilon T)^2$, has a peak, and depends on the ratio $W_U/W_F$ (which is probably much larger than 5 in reality), and that the RNA melts at a temperature $T_m = \varepsilon (R \ln(W_U))$. That’s a lot of useful things you have already learned about RNA folding just by thinking about a simple model before even toughing the calorimeter to do the experiment.

![Figure: Plot of the unfolded state fraction $\rho_U$ as a function of temperature. The curve is sigmoidal or ‘cooperative’ with a maximum slope shown by the dotted line. We say the RNA hairpin ‘unfolds at temperature $T_m$’, that is, unfolding is defined as the midpoint of the transition.](image)

**Homework problem S4.2:** Derive a simple formula for the average energy of a system at constant temperature. Start with $Z = e^{-\beta F}$, write out $F$ in terms of $E$ and $S$ in the exponent, then take the derivative of $Z$ with respect to $\beta$ and solve for $E$. 

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In-class exercise: What is the energy and heat capacity for \( n \) moles of ideal (= non-interacting) gas particles? A: To do this, let’s (1) realize that a quantum particle-in-a-box with energy \( E = \hbar^2 \{ n_x^2 + n_y^2 + n_z^2 \}/(8mL^2) \) from the quantum part of the course is an ideal gas particle in a box of volume \( V = L^3 \). (2) Write \( Z \) by summing over all possible values of the quantum numbers \( n_x, n_y, \) and \( n_z \) from 0 to \( \infty \). (3) Since the energy level spacing goes to 0 as \( L \) gets large (macroscopic box), we can approximate the summation by an integral and get a simple formula for \( Z_{1D} = (2\pi \hbar k_b T/\hbar^2)^{1/2}L \). For a particle in 3-D, this then becomes \( Z = Z_{1D}^3 \). (4) Use the formula for getting \( E \) from \( Z \) that you are deriving on the homework to get \( E(T) \). Finally, use the definition of heat capacity \( C_V \) from Chapter 3 to calculate the heat capacity. Do these formulas look familiar?

From the above, we conclude for a gas that the highest randomness (equilibrium) is achieved when energy is distributed completely randomly among particles, so on average each ‘degree of freedom’ that can store energy has \( \frac{1}{2}k_bT \) of energy. That’s why a monatomic gas particle has energy \( \frac{3}{2}k_bT \), a mole of such particles has energy \( \frac{3}{2}nRT \), and a spring, which can store energy as potential and kinetic energy has energy \( \frac{1}{2}k_bT = k_bT \). Although we proved it here just for an ideal gas, this principle can be proven valid at high temperatures for any system where we can replace the quantum sums by integrals, and treat the energy levels as a ‘continuum’. It is perhaps one of the most important principles in science, useful in discussing anything from Maxwell’s demons (see below) to global warming (see next chapter):

**Equi-partition principle:** in a classical system at temperature \( T \), every degree of freedom on averages stores an energy \( \frac{1}{2}k_bT \).

**Homework problem S4.3:** Derive a formula for average pressure in a system at constant temperature that directly related \( P \) to \( Z \). Hint: remember from chapter 3 that \( P = -(\partial E/\partial V) \). The analogous formula is still true for the Helmholtz potential \( F \), and \( F \) is related to \( Z \) as we proved earlier in this chapter.

**Homework problem S4.4:** Derive a formula for the entropy of a system at constant temperature in terms of \( Z \). Hint: Once we have \( E \) and \( F \), it is easy to obtain \( S \)!

Remember that \( F \) is a function of \( T \) and \( S \) is a function of \( E \), so to get a proper fundamental relation, you have to substitute \( T = \partial E/\partial S \) as a function of \( E \) and/or \( S \) everywhere. Thermodynamics provides us with the manipulations to get any variable we want once we have computed the partition function. \( Z \) (or \( W \)) contain all knowledge about the equilibrium properties of a system, just like \( E(S) \) and \( F(T) \) do.

**In-class exercise:** A diatomic molecule with spring constant \( k \) is heated to a temperature \( T \). What is the average (root-mean-squared) length \( L \) by which the molecule is compressed or expanded because of heating?

**Answer:** The applied force that stretches the spring is \( f = kL \), where \( L \) is the displacement from the equilibrium bond distance. Instead of \( E = TS - PV \) for a 3-D system, we have \( E = TS - fL \) for a 1-D spring. Note that \( fL = kL^2 \), not \( \frac{1}{2}kL^2 \). \( E \) is not the potential energy, but the total energy, and when the spring is heated, half the energy is stored in potential energy, the other half in kinetic energy (the classical equipartition principle). I use lower case \( f \) for the force here so we don’t confuse it with free energy \( F \).

From our study of quantum mechanics, the energy of the spring is \( E_n = \hbar \omega n \), if we shift to the zero point energy as our reference energy. Now we can calculate \( Z \)
\[ Z = \sum_{n=0}^{\infty} 1 \cdot e^{-\frac{\omega_n}{k_B T}} = \sum_{n=0}^{\infty} e^{-\frac{\omega}{k_B T}^n} = \frac{1}{1 - e^{-\frac{\omega}{k_B T}}} \]

\[ \Rightarrow F = -k_B T \ln Z = +k_B T \ln \left(1 - e^{-\frac{\omega}{k_B T}}\right) \]

And since \( E = TS - fL \) for a spring

\[ \Rightarrow F = E - TS = -fL; f = kL \Rightarrow F = -kL^2 \Rightarrow L^2 = -\frac{F}{k} = +k_B \frac{T}{k} \ln Z \]

\( E = TS - fL \) for a spring, where “-fL” replaces “-PV” for a gas because the spring is one-dimensional. So \( F = E - TS = -fL \), and since \( f = kL \) we can write \( F \) as \( F = -kL^2 \). Solving for \( L^2 \), we get \( L^2 = -F/k = (k_B T/k) \ln Z \). Therefore we have for the root-mean-square displacement of the spring

\[ L_{rms} = \sqrt{\frac{k_B T}{k} \ln Z} \]

This remarkable result tells us how the root-mean-square thermal fluctuations of a diatomic molecule depend on temperature \( T \), spring constant \( k \) and number of states populated \( Z \). For a macroscopic spring, \( L_{rms} \) would be rather small compared to the length of a spring, but for a molecule-sized spring, it could be quite large relative to the length of the spring. This is the reason we cannot build a Maxwell Daemon by making a little door between two chambers held tight by a spring on one side so “particles can only go through one way.” In reality, the random thermal motion of all the particles would also make the spring vibrate so much that particles could get through either way (or if \( k \) is too large, neither way). Equipartition of energy between particles and springs messes up the daemon. There’s just no escaping the Second Law!

We’ve come a long way. Using just two assumptions about Nature, (1) Newton’s equations, or if needed for accuracy, the Schrödinger equation, are true, and (2) states of equal energy have equal probability, we are able to derive at what temperature an RNA molecule unfolds, or how much the bond length of a molecule vibrates at temperature \( T \), or that a gas has energy \( \frac{3}{2} nRT \). In the next Chapter, we’ll continue our brief tour of statistical mechanics and thermodynamics by looking closely at the Gibbs free energy, and what it tells us about equilibria of chemical reactions at constant temperature and pressure. Of course, you already know the answer from freshman chemistry: we can calculate an ‘equilibrium constant’ that tells us how much of each chemical we’ll get at the end of the reaction.
Chapter 5. Chemical equilibrium and the free energy.

1. Rewriting the second law for an open system (reaction)
In chapter 2 we derived the second law of thermodynamics from statistical mechanics:
\[ S^{\text{tot}}(t>0) > S^{\text{tot}}(t=0), \]
or
\[ dS^{\text{tot}} > 0 \]
for a spontaneous process in an isolated system (constant \( E, V, \ldots \)) with entropy \( S^{\text{tot}} \). But in many chemical reactions, the system is open, and \( T \) and \( P \) are constant, not \( E \) and \( V \). \( T \) and \( P \) are constant because the system (like a beaker) is connected to a large environment (like a lab) kept at constant \( T \) and \( P \); so when equilibrium has been reached, \( T \) and \( P \) in the beaker are the same as in the lab, and even during the reaction, if the reaction runs slowly enough.

Can we find a specific version of the second law for the case of an open system, when heat can flow? Why would it be useful? We’ll consider two examples in this chapter, heat trapping in the atmosphere and RNA or protein folding.

Consider a solar photon as our open system, and the Earth as its environment. Photons actually undergo very simple reactions on Earth and in the atmosphere by being ‘absorbed’ (used up) and ‘emitted’ (newly made).

**Homework problem S5.1:** When a visible solar photon of energy \( h\nu \sim k_B T_{\text{solar}} \) \((T_{\text{solar}} \sim 6000 \, \text{K})\) hits the Earth’s surface, it is absorbed, but the energy does not disappear. Instead, it is re-emitted as several ‘thermal’ photons with energy \( \sim k_B T \) \((T \sim 300 \, \text{K})\), or transferred as heat energy, also in packets \( \sim k_B T \) by the equipartition principle. Let’s assume for a moment the photon just splits into equal lower energy \( \sim k_B T \) photons. The reaction here is \( v_{\text{solar}} \rightarrow N v_{\text{solar}} \). How many \( N \) ‘thermal’ photons can be made from a solar photon by energy conservation?

**Homework problem S5.2:** Assume that the photons behave like an ideal gas in a box, which we’ll take to be unit volume \( V=1 \). Use the formula for \( Z \) of a gas from the last chapter, Planck’s law \( E=h\nu \), and Einstein’s formula \( E/c^2 = m \) to write down the partition function for a photon per unit volume in terms of only \( k_B, T, c, \nu \), and \( h \). [Note: your formula is a ballpark estimate because photons really are massless and really \( E/c^2 = (m^2 + (p/c)^2)^{1/2} \); but it will be very close to the right answer below.]

**In class problem:** Let’s say 20 infrared photons are made out of one solar photon, and remember that \( Z_{\text{tot}} = Z_1 Z_2 Z_3 \ldots Z_N/N! \) for \( N \) indistinguishable particles. (Entropy adds, partition function multiplies, indistinguishable particles reduces \( Z \) by a factor \( N! \)). With the partition function per unit volume of one thermal photon being \( 8\pi (k_B T/c^3) \), how much does the number of microstates go up when a solar photon is converted to infrared photons? Is it better to do that calculation with entropy, which is additive? A: use 300 K for \( T \) to get \( Z \approx 2\times10^{14} \, \text{m}^{-3} \), and compare \( Z^N/N! \) to \( Z \) for the original photon at 6000 K. \( S \) would do this with more manageable-sized numbers.

CO\(_2\) molecules absorb strongly in the infrared, whereas O\(_2\) and N\(_2\) do not. So thermal photons re-emitted from the Earth’s surface towards space can be absorbed by CO\(_2\) in the atmosphere and re-emitted in a random direction, warming the Earth’s surface rather than letting the photon escape.

**Thought experiment:** If a photon is re-emitted in a random direction in the atmosphere near the Earth’s surface, what is the probability it will reach space?

Going back to our question: Can we find a specific version of the second law for the case of an open system, when heat can flow? The answer is yes. We will consider a closed system, containing a
large environment and a reaction, which is coupled to the environment only by heat flow. Thus $T$ in the reaction and environment is the same, and it will remain the same even if the reaction releases heat because the environment is large (it is a heat ‘bath’). First, split the entropy of the closed system into the reaction and environment parts:

$$dS_{tot}=dS_{rx} + dS_{env} > 0$$

We derived in chapter 2 that $dS=dq/T$ is the change of entropy due only to heat flow at either constant pressure (when $dq=dH$) or constant volume (when $dq=dE$). If the reaction is run near equilibrium conditions at constant $T$, we can also integrate this so $\Delta S=q/T$. We can only do this integration if we let the reaction in our beaker run slowly enough so the environment always keeps the beaker at temperature $T$; if we run it too fast, the beaker may heat up or cool down. So the assumption made here is that the reaction is run slowly enough so $T$ is constant. We can use this to eliminate $dS_{env}$ from the equation:

$$dS_{tot}=dS_{rx} + dS_{env} > 0 \Rightarrow dS_{rx} + \frac{dq_{env}}{T} > 0.$$ 

It is important to note that we cannot substitute $dS_{rx}$ by $dq_{rx}/T$. The entropy change in the reaction has many sources, not just the heat flow, whereas the entropy change in the environment has only one source: heat flow from the reaction. For example, if the reaction consisted of mixing two inert gases, the entropy $S_{rx}$ would increase ($dS_{rx}>0$), but $dq_{rx}=0$ in that case. Or if the reaction consisted of making a bond, $dS_{rx}<0$ (two atoms move together afterwards), but $dq_{rx}<0$ (making the bond releases energy, say in the form of a photon released into the environment since heat flow is allowed).

Now we can use energy conservation to remove $dq_{rx}$ from the above equation: the heat that flows into the environment must be the opposite of the heat that flowed out of the reaction, or $dq_{env}=-dq_{rx}$.

At constant volume, $dq_{rx}=dE_{rx}$. Therefore

$$dS_{rx} + \frac{dq_{env}}{T} > 0 \Rightarrow dS_{rx} + \frac{dE_{rx}}{T} > 0 \Rightarrow -TdS_{tot} = dE_{rx} - TdS_{rx} < 0.$$ 

In the last equation, we multiplied by $-T$, so the $>$ flipped to $<$. If we had done the same derivation also allowing volume exchange between system and bath, then the pressure would be constant instead of the volume, and the heat exchange would be $dq_{rx}=dH_{rx}$. We would then get

$$dS_{rx} + \frac{dq_{env}}{T} > 0 \Rightarrow dS_{rx} + \frac{dH_{rx}}{T} > 0 \Rightarrow -TdS_{tot} = dH_{rx} - TdS_{rx} < 0.$$ 

We already defined the Helmholtz free energy $F=E-TS$ and the Gibbs free energy $G=H-TS$, which contain the same information as $E$ and $S$. Thus

$$dE_{rx} - TdS_{rx} < 0 \Rightarrow -TdS_{tot} = dE_{rx} < 0 \text{ (const. } T \text{ and } V)$$

$$dH_{rx} - TdS_{rx} < 0 \Rightarrow -TdS_{tot} = dG_{rx} < 0 \text{ (const. } T \text{ and } P)$$

This is the second law of thermodynamics for open systems embedded in an environment that allows heat to flow, and pressure to equilibrate. It expresses the total change of entropy, which must be positive according the the second law, in terms of only reaction quantities: reaction entropy and heat released, or reaction Helmholtz free energy/Gibbs free energy. The $-TdS_{rx}$ term accounts for the entropy change of the reaction, and the $dE_{rx}$ or $dH_{rx}$ term accounts for the entropy change of the environment, assuming only heat flow from the reaction affects the entropy of the environment.

The above is the reason thermodynamics is such a versatile theory, and can set bounds on quantities, such as global warming, using very general formulas. One just has to make sure one has all the important reactions included.
Figure: How the free energy $G$ (top), and the derivative of the free energy with respect to reaction progress, $\partial G/\partial x$, often called $\Delta G$ (bottom) depends on the reaction progress “x”. In this example, we are looking at the reaction $N_2+3H_2\rightarrow2NH_3$ and we have $1.66 = 5/3$ moles of $H_2$ at the start of the reaction.

If the reaction progresses by $x$ moles of a product when the free energy changes by $dG_{rx}$, we can write this as

$$
\left( \frac{\partial G_{rx}}{\partial x} \right)_{T,P} = \left( \frac{\partial H_{rx}}{\partial x} \right)_{T,P} - T \left( \frac{\partial S_{rx}}{\partial x} \right)_{T,P} < 0 \text{ or }
$$

$$
\Delta G = \Delta H - T \Delta S < 0
$$

where the derivatives are defined as $\Delta G = (\partial G/\partial x)$ etc., and have units of kJoules/mole. In the second equation, we dropped the subscript “rx” because it is understood from now on that we are talking about the reaction (open system), not the environment or the overall closed system (reaction + environment).

Since $\Delta G = -T \Delta S_{tot}$, it follows that for a reaction at constant temperature and pressure,

$$
\Delta G(P,T) < 0 \text{ (spontaneous reaction)}
$$

$$
\Delta G(P,T) = 0 \text{ (equilibrium)}
$$

$$
\Delta G(P,T) > 0 \text{ (spontaneous reverse reaction)}
$$

$\Delta G$ tells us how much the free energy $G$ changes if the reaction proceeds by some small amount “x”. Thus if $G$ has units of Joules, $\Delta G$ has units of Joules/mole. This is just another statement of the second law of thermodynamics, but for the special case of an open system (reaction) at constant temperature and pressure. It says that the free energy will decrease in any spontaneous reaction, until the spontaneous reaction ends (equilibrium is reached), at which point $\Delta G = 0$ (the reaction goes neither forward nor backward). Of course if our reaction does not satisfy these assumptions, we can always go back the the full statistical mechanical analysis to check if $S(t>0) > S(t=0)$ to see if the reaction is spontaneous.

**Homework problem S5.3:** On the figure above, mark with an arrow a place where the reaction spontaneously makes more ammonia, and a place where it makes more nitrogen and hydrogen? What is the slope of $G$ in each case, positive or negative? Are there more places in the plot where ammonia will be made, or hydrogen will be made. So if I pick random concentrations between 0 and 1 moles/l of hydrogen, nitrogen and ammonia as starting conditions, will the reaction most likely go forward or backward?
ΔG is made up of two pieces, an enthalpy change, and an entropy change: the more the enthalpy is lowered, the more negative the derivative; the more the entropy increases, the more negative the derivative. Thus systems tend to either go towards lower enthalpy (or energy at constant volume), or towards higher disorder, and these two effects always compete and balance. Going towards lower energy occurs because then heat is released into the environment, making it more disordered; going towards higher entropy, or more microstates $W$, occurs because the system then directly occupies more microstates, which is more likely.

2. Concentration dependence of the free energy $G$ in the ideal case

For a mole of ideal gas or an ideal solution (noninteracting particles that move around randomly in a box), we proved in Chapter 3 that $s=s^{(0)}+R\ln(V)=s^{(0)}-R\ln(c)$ for a mole of substance (the ‘molar entropy’).

**Thought experiment:** If you have a solution filled with ions that can react individually, but they are far enough apart so they do not attract each other strongly and so heat flow can keep the temperature constant, will the energy released by the reaction of one ion affect another?

Also for noninteracting particles, the enthalpy does not depend on volume, so $h=h^{(0)}$, where $h^{(0)}$ is the enthalpy for one mole of particles. Note that $s^{(0)}$ and $h^{(0)}$ could still depend on temperature, as discussed already in chapter 3. Consider the free energy for a mixture of different noninteracting particles “i” obeying the reaction

$$v_i A + v_B B + \cdots \rightarrow v_C C + v_B D + \cdots \text{ or } 0 \rightarrow \sum_i v_i X_i .$$

In the general notation for a reaction on the right, $X=A,B,C,\ldots$ and the stoichiometric coefficients $v_i$ are positive for products, negative for reactants. Don’t mix up stoichiometric coefficients with frequency $v$, although books (and I!) use the same Greek letter.

If the reaction starts at mole numbers $n_i^{(0)}$ and is allowed to advance by $x$ moles,

$$G_{rx} = \sum_i n_i \mu_i$$

$$= \sum_i (n_i^{(0)} + v_i x_i) \mu_i$$

Taking the derivative with respect to $x$, to get the change of free energy as the reaction proceeds,

$$\left( \frac{\partial G_{rx}}{\partial x} \right)_{T,P} = \Delta G = \sum_i v_i \mu_i$$

Now replacing $\mu_i=h_i-Ts_i$ for each reactant/product and simplifying,

$$\Delta G = \sum_i v_i h_i - T \sum_i v_i s_i$$

$$\Delta G \approx \sum_i v_i h_i^{(0)} - T \sum_i v_i s_i^{(0)} - v_i R \ln(c_i)$$

$$\Delta G \approx \sum_i v_i \mu_i^{(0)} + T \sum_i v_i R \ln(c_i)$$

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The approximation of the “ideal” case occurs between lines 1 and 2. In line 3, we just combined \( \mu_i^{(0)} = h_i^{(0)} - TS_i^{(0)} \).

**Homework problem S5.4:** Since \( \mu_i = h_i - TS_i \), insert the formula for \( s_i = s_i^{(0)} - R \ln(c) \) to show directly that the chemical potential for chemical species “i” can be written as \( \mu_i = \mu_i^{(0)} - R T \ln(c) \), and what is the constant \( \mu_i^{(0)} \). Note that this strictly applies only for ideal solutions or gases we discussed at the end of Chapter 3.

If we call the first sum \( \Delta G_{rx}^{(0)} \) (how much, in kJ/mole, the free energy of the reaction changes at the initial condition “(0)” when \( x \) changes by a small amount), and in the second term, we put the sum over \( \nu_i \) into the logarithm:

\[
\left( \frac{\partial G_{rx}}{\partial x} \right)_{T,P} = \Delta G = \Delta G_{rx}^{(0)} + RT \ln(Q); \quad Q = \prod_i c_i^\nu_i.
\]

Here, \( Q \) is the mass action law coefficient, and the above equation is the mass action law. It allows you to compute the free energy change if a reaction proceeds by a small amount given the concentrations of reactants and products, and their free energies at \( T \) and \( P \). Values of \( \Delta G_{rx}^{(0)} \) are usually tabulated under ‘standard conditions’ (temperature \( T = T^{(0)} = 298 \text{ K} \), \( P = P^{(0)} = 1 \text{ atm} \), and concentration \( c^{(0)} = 1 \text{ molar} \)).

The free energy has units of Joules. Its derivative \( \Delta G \) has units of Joules/mole, and tells us how much the free energy changes per mole when the reaction proceeds by an infinitesimal amount. At equilibrium, \( G \) has reached a minimum, and \( \partial G/\partial x = 0 \). Thus \( \partial G/\partial x = \Delta G \) is just the same “change in free energy for a small amount of reaction” we discussed at the beginning of this chapter, calculated explicitly for reaction among noninteracting (between the reactive collision) particles:

\[
\Delta G = \Delta G_{rx}^{(0)} + RT \ln(Q).
\]

At equilibrium, the reaction stops because \( \Delta G = 0 \) exactly; if \( \Delta G \) were \( < 0 \), the reaction would go forward; if \( \Delta G \) were \( > 0 \), it would have ‘overshot’ equilibrium and go backward. Thus at equilibrium,

\[
0 = \Delta G_{rx}^{(0)} + RT \ln(Q_{eq}) \Rightarrow K_{eq} \equiv Q_{eq} = e^{-\frac{\Delta G_{rx}^{(0)}}{RT}}.
\]

Note that at equilibrium, we like to give the mass action coefficient a special name, “\( K_{eq} \)”. We call it the “equilibrium constant.” Note that we have one last missing ingredient in our statistical mechanical theory of reaction equilibria: \( K_{eq} \) or equivalently \( \Delta G^{(0)} \) have not yet been derived from first principles.

3. **Calculating the equilibrium constant from molecular properties by using statistical mechanics**

We won’t do it here in detail, but you can probably imagine by now that we don’t have to measure the free energy or rate coefficient \( k \) experimentally, we can actually calculate them from statistical mechanics. The way you do it is that the chemical potential (like anything else!) can be calculated if you know the partition function of the molecules (reactants and products) participating in the reaction. At constant volume (so we can use the Helmholtz potential \( F \)), as we saw in Chapter 4,

\[
\mu_i = \left( \frac{\partial F}{\partial n_i} \right)_{T,V} = -k_B T \left( \frac{\partial \ln Z_i}{\partial N_i} \right)_{T,V} = -k_B T \frac{\partial}{\partial N_i} (N_i \ln z_i - N_i \ln N_i + N_i) = -k_B T \ln \left( \frac{z_i}{N_i} \right)
\]

And of course we saw above that \( \Delta G^{(0)} = \Sigma v_i \mu_i^{(0)} \) and \( K_{eq} = e^{-\Delta G^{(0)}/RT} \), if one just evaluates the chemical potential at standard conditions (\( T = 298 \text{ K} \), etc.).
So as long as I know the stoichiometric coefficients of my reaction and the energy levels of each of my molecules from quantum mechanics, I can just calculate

\[ z_i = \sum W_j e^{\frac{E_j}{k_B T}} \]

for molecule “i”, and voila - plug in to get \( K_{eq} \). This is often more accurate than doing the experiment, although for some reactions, the quantum calculations are still not good enough. For a typical organic reaction, electronic structure calculations now provide an accuracy of about 1 kcal/mole ~ 1 kJ/mole, the main limiting factor being approximations made to solve the many-electron Schrödinger equation accurately. We saw it’s a bear without a computer when we were doing quantum mechanics!

**Homework problem S5.5:** Let’s do one simple example, the folding of the RNA from macrostate U to macrostate F in the reaction \( U \leftrightarrow F \) in the previous chapter, so \( \nu_F = +1 \) and \( \nu_U = -1 \) for the stoichiometric coefficients going towards folded product. Using the partition function \( Z \) for the folded RNA in the previous Chapter as \( Z_F = W_F \), and for the unfolded RNA as \( Z_U = W_U e^{-e/RT} \), write down the formula for \( \Delta F \) and the equilibrium constant \( K_{eq} \). These are two of the most important equations to describe at what temperature an RNA molecule or a protein folds. [Note: it’s \( \Delta F \) instead of \( \Delta G \) because our canonical partition function formula from the last chapter is at constant temperature and volume, not temperature and pressure; but protein solutions are not very pressure sensitive, so the formula for \( \Delta G \) is almost the same.]
Chapter 6. Out of equilibrium: Brownian motion and drift velocity

While we are interested in seeing where reactions will go in equilibrium, eventually that equilibrium is going to be perturbed, and we will go to a new equilibrium. It’s just a matter of time.

Thought experiment: the pencil I just put on the table is in mechanical equilibrium. How likely do you think it will be in equilibrium 10 seconds from now? How about tomorrow?

Clearly, perfect equilibrium is never reached in reality, although it may be reached long enough that we can do useful calculations like in the last Chapter. Eventually, though, things get moving. Specifically, how do molecules tend to move around? We can of course fling molecules around, so they follow a trajectory like Newton’s law. But even if we don’t touch them, we notice they actually move about. Why? Because of equipartition, at least classically there is energy $k_B T/2$ in every degree of freedom, and molecules constantly kick each other randomly to maintain or evolve towards that average.

1. Brownian motion Let us consider the trajectory of a ‘test’ particle in a heat bath of solvent particles: for example, a protein molecule surrounded by water molecules that can bump into the protein randomly due to heat. On average the forces from the solvent particles cancel, but at any instant a few more may hit the test particle from one side than from the other side. The test particle is getting buffeted around by solvent particles.

At very short times, the motion is predictable by Newtonian mechanics $F=ma$:

$$x(\Delta t) = x(0) + v(0)\Delta t; \quad v(\Delta t) = \frac{F(0)}{m} \Delta t + v(0),$$

After many such events, the motion becomes unpredictable because the forces $F(0), F(\Delta t), F(z\Delta t)$... change randomly with each collision, see BD Simulation:

![Fig. 19.1 Random walk of a test particle in one dimension. At each time step $\Delta t$ the particle receives a kick. After many kicks, the position of the particle is the sum of many random variables, thus it is a Gaussian random variable.](image)

Each of the hops $\Delta x$ the particles makes during the mean collision time $\Delta t$ is random. Thus, $\delta x = x - x_0 = \Sigma \Delta x$ sampled at a time $t \gg \Delta t$ is a Gaussian random variable by the central limit theorem (C.L.T.). This is true NO MATTER WHAT the probability distribution of $\Delta x$ looks like, so we need to know nothing about it. Thus, if
If we rename the constant \( \frac{\Delta x^2}{\Delta t} = 2D \), we obtain
\[
\langle \Delta x^2 \rangle = 2Dt.
\]
This is the law of Brownian motion, which states that the mean square displacement of a particle grows linearly with time, i.e. the root mean square displacement only grows as the square root of time. \( D \) is known as the diffusion coefficient; the larger \( D \) is, the more rapidly the particle moves away from the initial position. It has units of length\(^2\)/time. Whatever the exact functional form of the probability distribution is for a particle to move by an amount \( d\alpha_\tau \) starting at \( x \), it must satisfy
\[
\int d(\delta x) P(x,\delta x) = 1
\]
\[
\int d(\delta x) \delta x P(x,\delta x) = \langle \delta x \rangle = 0
\]
\[
\int d(\delta x) \delta x^2 P(x,\delta x) = \langle \delta x^2 \rangle = 2Dt
\]
In three dimensions, there are 3 opportunities to move away from the center and
\[
\langle \delta x^2 \rangle = 6Dt.
\]
**Homework problem S6.1**: A protein has a diffusion coefficient of 10 \( \mu\text{m}^2/\text{s} \). A human cell has a diameter of 30 \( \mu\text{m} \). On average how long does it take a protein to diffuse across a cell?

**In-class exercise**: Assuming a small drug from a dermal patch needs to diffuse through 2 mm of skin to get to the target blood vessels, how long would that take if \( D=100 \mu\text{m}^2/\text{s} \)? A: \( \sim 2 \text{ h} \).

2. Drift velocity Now let’s assume that there is an applied force acting on the particle, in addition to the random force \( F_{\text{random}} \) from the collisions. For example, our protein might be undergoing gel electrophoresis. It sits in a gel, where it gets bumped randomly by water molecules, but there is also an applied potential or ‘voltage’ \( \Psi \). The applied potential causes the potential energy \( \mu \) of the charged protein to depend on position as \( \mu(x) = -qxe^\Psi \), where \( q \) is the charge of the protein, \( x \) is its position between the electrodes, and \( E \) is the electric field in V/m, related to the applied potential \( \Psi \) and electrode separation by \( E = -\Psi/\Delta L \). We use \( \Psi \) for the voltage instead of ‘V’ to avoid confusion with the volume \( V \) elsewhere! Thus the applied force acting on the protein is \( F_{\text{applied}} = -\frac{\partial \mu}{\partial x} = qE \). The minus signs are defined so the electric field points from the positive electrode (anode) to the negative electrode (cathode), and the potential energy of a negatively charged protein will be lowered by moving towards the anode.

The dragging of the protein by the electric field is resisted by a friction force \( F_{\text{friction}} \). The friction is caused by the protein bumping into the gel molecules. The faster the protein moves, the more often it bumps and the more friction, so the frictional force increases with velocity \( \nu \) and opposes the motion of the protein, or \( F_{\text{friction}} = -\gamma \nu \). \( \gamma=1/\mu \) is the friction coefficient in units of force/velocity or Ns/m, and its inverse ‘\( \mu ' \) is known as Einstein’s mobility.

Let’s put those words into an equation, the first step for constructing a model in physical chemistry:
\[
F = ma
\]
\[
F_{\text{applied}} + F_{\text{friction}} + F_{\text{random}} = ma
\]
\[
-\frac{\partial \mu}{\partial x} - \gamma \nu + F_{\text{random}} = ma
\]
If the frictional force is large enough, the inertial acceleration term \( ma \) can even be neglected. In that case, the equation simplifies to...
\[
\frac{\partial \mu}{\partial x} = -\gamma v + F_{\text{random}}.
\]
This equation is known as the Langevin equation. If we set \(\mu\) to a constant in this equation so \(\frac{\partial \mu}{\partial x} = 0\) (no applied force), we again just have a particle moving by random Brownian motion, and we get the same answer we already found above
\[
\langle \delta x^2 \rangle = 6 \frac{k_B T}{\gamma} t.
\]
The bonus of solving the Langevin equation, taking into account that the random force of bumping water molecules increases with temperature \(T\), is that we obtain an expression for the diffusion coefficient \(D = k_B T / \gamma\): so the diffusion coefficient should increase when it gets hotter, and decrease if the friction gets bigger. Those trends make sense intuitively, it’s always a good thing to check.

Now let’s do the opposite, and set \(F_{\text{random}} = 0\) and keep the other two terms,
\[
\frac{\partial \mu}{\partial x} = -\gamma v = -qE
\]
if we insert the electric potential energy \(\mu(x) = -q x E\) into the equation. Don’t confuse electric field here with energy, although an ‘\(E\)’ is usually used for both! So we find that
\[
v = \frac{q}{\gamma} E = v_{\text{drift}}.
\]
This is a very important equation for gel electrophoresis: it tells us that the protein drifts through the gel at a constant velocity \(v_{\text{drift}}\). The higher the electric field or charge of the protein, the higher the drift velocity. The higher the friction coefficient, the lower the drift velocity. Bulkier proteins experience higher friction so they drift more slowly and produce a band closer to the origin than smaller proteins. Note that the friction caused by a gel or solution is directly proportional to its viscosity. We won’t prove it here (we could!), but for a spherical particle of radius \(r\), \(\gamma = 6\pi r \cdot \eta\), where \(\eta\) is the viscosity of the solution. Again, this should be intuitive: the bigger the particle, the larger its friction, and the more viscous the solution, the larger its friction. For water at room temperature, \(\eta = 0.001 \text{ Pa} \cdot \text{s}\) (pressure x time units).

The ancient Greek scientist and philosopher Aristotle believed that particles had to be pushed by a force, or would come to rest. In the 1600s, Newton turned the table on him by showing that \(F_{\text{applied}} = ma\), so acceleration is zero without force, but velocity remains constant. This is true for simple systems of particles that do not encounter any significant friction, like planets moving in the solar system. But Aristotle was kind of right in the end. He guessed that in any real, frictional environment, the Langevin equation would describe motion, not Newton’s \(F_{\text{applied}} = ma\). And the Langevin equation does not even have \(ma\) in it! This sometimes happens in science: we come up with a theory, later we think it’s wrong, but even later we realize that it was right after all, just in a different context.

**Homework problem 6.2:** A voltage of 100 V is applied to an electrophoresis gel of 10 cm length. The protein phosphoglycerate kinase (PGK) has charge +2e and in a 1% polyacrylamide gel at room temperature, its diffusion coefficient is \(D = 100 \mu \text{m}^2/\text{s}\). What is the drift velocity of PGK in mm/s? How long should you plan on running the gel if you want the protein to move across half the length of the gel?

### 3. Flux and continuity equation
When particles drift with a velocity \(v\) due to a potential energy \(\mu(x)\) (provides a driving force) and friction (provides a counter force), there is a flux \(J\) of particles, measured in units of moles/s/m\(^2\). The flux is proportional to the velocity, and to the concentration of particles \(c\) in moles/m\(^3\), or
\[
J = vc
\]
But we saw above that \(\frac{\partial \mu}{\partial x} = -\gamma v\) and that \(\gamma = 1/U\), so we can also write this equation as
\[ J = -Uc \frac{\partial \mu}{\partial x}. \]

This equation tells us that the flux of particles (such as proteins on the gel) increases with mobility, concentration, and the applied force given by the derivative of the potential.

There is also another important relation between flux and concentration. To derive it, we’ll use something from Calc 3 that actually has its uses: Gauss’ theorem. The number of particles leaving a volume \( V \) per unit time, given by \( \frac{\partial}{\partial t} \iiint c dV \), is equal to the flux of particles through the surface around the volume, \( \iint J dA \), because particle number is conserved, or
\[
\frac{\partial}{\partial t} \iint c(x) dV = \iint J \cdot dA.
\]

Gauss’ theorem states
\[
\iint J \cdot dA = \iiint \nabla \cdot J dV.
\]
Combining the two equations, using the fact that if the integrals are the same, the integrands are the same, and just replacing \( \nabla \cdot J \) by \( \frac{\partial}{\partial x} J \) in one dimension, we have.
\[
\frac{\partial}{\partial t} c(x, t) = \frac{\partial}{\partial x} J(x, t).
\]
This is the continuity equation. Although it looks pretty abstract, it says something pretty straightforward: if the concentration in a volume is decreasing with time, there must be a position-dependent flux so more molecules flow out of the volume than into the volume. We’ll use this when discussing chemical transport and various associated laws in the final part of our tour of pchem.