

## Lecture 2:

# Thermodynamics and Statistical Mechanics

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**Course website:**

**[www.physics.drexel.edu/~brigita/COURSES/BIOPHYS\\_2011-2012/](http://www.physics.drexel.edu/~brigita/COURSES/BIOPHYS_2011-2012/)**

# Laws of Thermodynamics

## First Law:

→ energy cannot be created or destroyed:  $\Delta E = E_{\text{in}} - E_{\text{out}}$

$$\Delta U = Q - W$$

U ... internal energy of a system

Q ... heat the system receives from the environment

W ... work done by the system

→ heat is treated separately from other forms of E:

-historically (heat engine: motor that converts heat into E)

-results from kinetic energy and random motion of molecules

-least organized form of energy

→ *system* is a part of the universe under study, the rest is *surroundings*

→ Units: *calorie*=energy needed to heat 1g H<sub>2</sub>O from 14.5 to 15.5 C at atmospheric pressure; 1 cal = 4.184 J

## **Enthalpy H:**

→ **Classic thermodynamic property of a system:**

$$\mathbf{H = U + pV}$$

**U ... internal energy of a system**

**p ... external pressure**

**V ... volume of the system**

→ **Changes:  $\Delta H = \Delta(U + pV) = \Delta U + \Delta p V + p \Delta V$**

**or**

$$\mathbf{\Delta U = \Delta H - \Delta p V - p \Delta V = Q - W, \text{ where } W = p \Delta V}$$

**(W ... work done by the system:  $W = \int F dx$ )**

**so**

$$\mathbf{Q = \Delta H - V \Delta p}$$

**The heat which is provided to the system is associated with:**

- the change in the enthalpy of a system**
- the energy needed to change the pressure of the system**

$$\mathbf{\Delta H = Q + V \Delta p}$$

**Most biological processes occur at  $p = \text{const.}$ , thus  $\Delta H \approx Q$ .**

## Entropy S:

→ Rudolf Clausius and heat machines to convert heat into work (~1%)

Where is the remaining 99% of energy?

-if the change occurs at a constant T:

$$\Delta S = Q/T$$

S ... entropy of a system

T ... absolute temperature of a system [K]

-if the heat flows from  $T_1$  to  $T_2$  ( $T_1 > T_2$ ):

$$\Delta S = Q/T_2 - Q/T_1$$

→ S: *trope* [Greek] ... transformation & energy → entropy

*S is a measure of disorder in a system and is associated with a number of different ways a system can be in one energy state:*

-only a few ways to arrange molecules at a given temperature →  
ordered system with a low S

-many possible ways to arrange molecules at a given temperature →  
disordered system with a high S

## Gibbs Free Energy G:

- Gibbs used Clausius's definition of S to define *available energy* that can be converted into work: **free energy** (as opposed to the energy lost through dissipation):

$$G = H - TS$$

G ... the energy that remains in the system after the energy losses due to dissipation are accounted for

- Gibbs energy change during a process occurring at constant T:

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

*For a process that occurs spontaneously,  $\Delta G < 0$ , that is the final state has always a lower free energy than the initial state!*

- This principle is in a way analogous to  $F=ma$  (Newons's 2<sup>nd</sup> law) as it drives all spontaneous processes, including chemical reactions.
- The process that takes the system from state A to state B will occur spontaneously only if  $\Delta G < 0$

## The Second Law of Thermodynamics

→ One way to state the second law is:

*In any process, when considering a system with its surroundings, the entropy will either remain constant or increase.*

→ DISCUSSION:

*Does a life form violate the second law of thermodynamics?*

**Life form:**

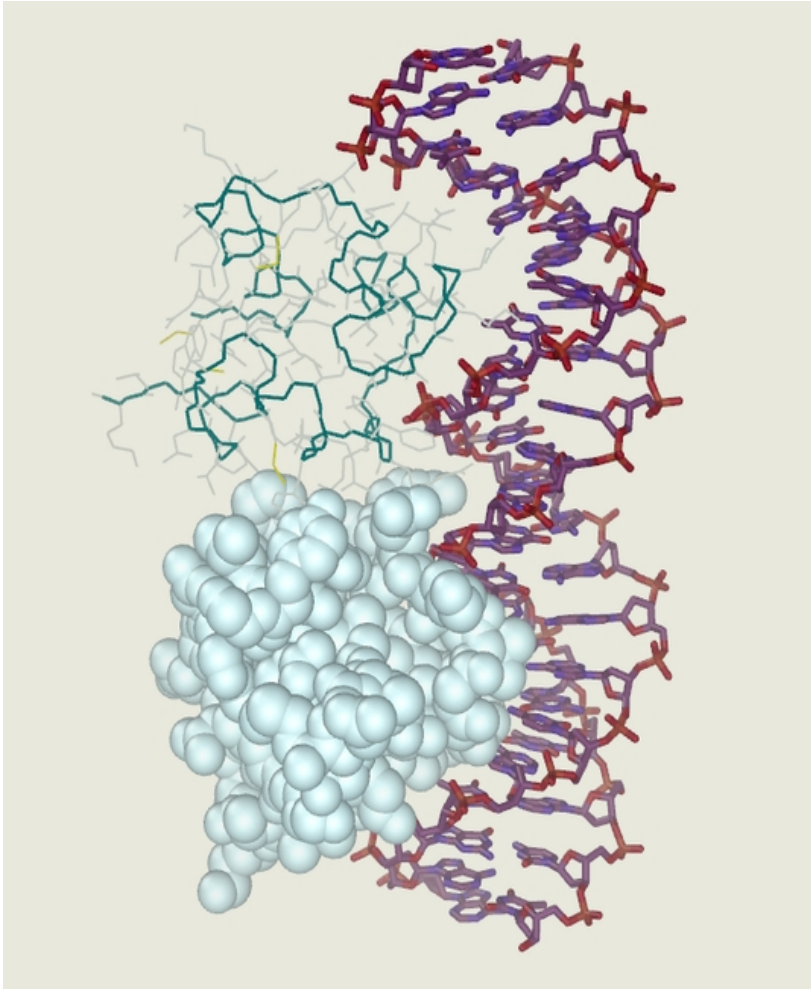
1. take energy from outside and create order
2. propagate the order by having offspring

→ *The Gibbs function principle  $\Delta G < 0$  has the second law of TD build in.*

**What drives the process forward?**

- a system releases energy,  $\Delta H < 0$ , process *enthalpy driven*
- increasing disorder,  $\Delta S > 0$ , process *entropy driven*
- changing temperature, if  $\Delta S > 0$ , then  $\Delta T > 0$  will result in  $\Delta G < 0$ ;  
if  $\Delta S < 0$ , then  $\Delta T < 0$  will result in  $\Delta G < 0$

## Example:



When a certain protein binds to DNA, the entropy decreases by 2 kcal/K. At the same time, the system releases 700 kcal of enthalpy.

-What is the Gibbs free energy change for this binding process occurring at  $T=310\text{K}$  (37 Celsius)?

-Is this process spontaneous?

# Statistical Mechanics

**provides a mathematical framework to explain TD quantities of a system at the molecular level**

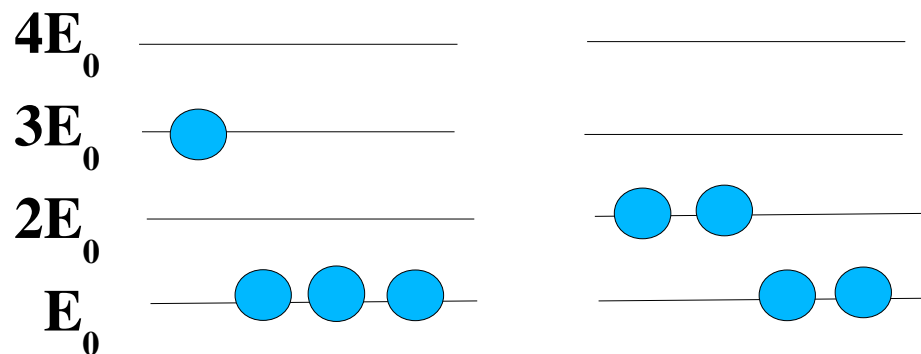
- **For example: temperature is directly related to an average kinetic energy of atoms/molecules in the system**
- **How is SM applied?**
  - devise a model* that defines all possible microscopic states of the system (e.g., 5 states of hemoglobin molecule: # of O-atoms 0-4)
  - assign energy differences* between different microscopic states (preferably based on some experimental data)
  - determine the number of different ways* the molecules can distribute themselves among those energy states
  - determine which of the above distributions are most likely to occur* (mathematics of probability and distribution)
  - knowing the distribution of energy and a probability of a molecule to be in each of the possible (allowed) energy states, we can derive all TD quantities*



## A SIMPLE EXAMPLE:

Our system has 4 molecules, each of which can have an energy that is a multiple of one energy unit  $E_0$  of  $10^{-20}$  J (but not zero). Assume that the total energy of the system is  $6 E_0$ .

*In how many ways can you distribute the total energy among the 4 molecules?*



**There are two states of the 4-molecule system with a total  $E$  of  $6 E_0$ .**

Each of the two above distributions of molecules into the energy levels can be realized in several ways. *How many permutations of molecules lead to each of the two distributions?*

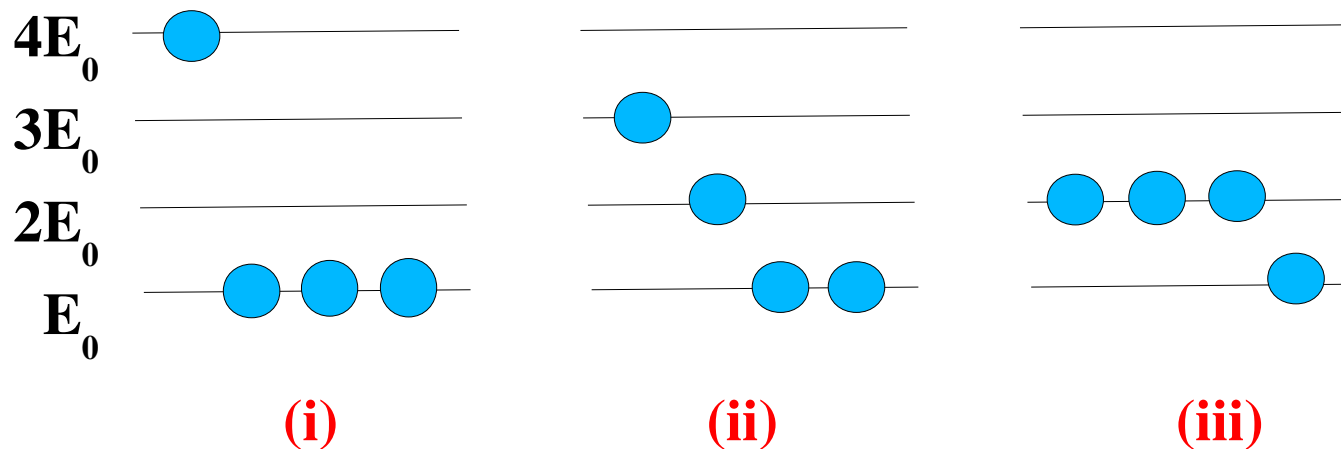
**left distribution: 4 permutations**  
**right distribution: 6 permutations**

There are in total 10 *permutations* of molecules to be arranged into the energy levels, which are all *equally likely to occur*. Of the two distributions, the left one has thus 0.4 and the right one has 0.6 occurrence probability.

**A SIMPLE EXAMPLE WITH A SLIGHTLY HIGHER TOTAL E:**

Consider the same example with a *total energy of  $7E_0$*  (instead of  $6E_0$ ).

*How many distributions of 4 molecules into energy levels exist?*



*In how many ways (permutations) can molecules be arranged into each of the three distributions?*

**How do we calculate the total number of permutations, that is, different ways to arrange molecules in any given distribution?**

$$W = \frac{N!}{n_1! n_2! n_3! \dots n_L!}$$

**N ... total number of molecules**

**L ... total number of energy levels**

**$n_l$  ... number of molecules on the energy level l**

$$N = \sum_{l=1}^L n_l$$

**Remember:  $0!=1$ ;  $1!=1$ ;  $2!=2 \times 1=2$ ;  $3!=3 \times 2 \times 1=6$ ; ...**

## EXAMPLE – INCREASE ENERGY AND NUMBER OF MOLECULES

What happens if we increase both the total energy and the number of molecules? Consider *10 molecules with a total energy of  $18 E_0$* .

- (1) *Determine the maximal number of energy levels  $L$ .* **A: 9**
- (2) *Find all possible distributions of molecules into  $L$  energy levels.* **A:22**
- (3) *Calculate the number of permutations for each distribution.*

9 1 1 1 1 1 1 1 1 1	<b>(10)</b>	5 2 2 2 2 1 1 1 1 1	<b>(1260)</b>
8 2 1 1 1 1 1 1 1 1	<b>(90)</b>	4 4 3 1 1 1 1 1 1 1	<b>(360)</b>
7 3 1 1 1 1 1 1 1 1	<b>(90)</b>	4 4 2 2 1 1 1 1 1 1	<b>(1260)</b>
7 2 2 1 1 1 1 1 1 1	<b>(300)</b>	4 3 3 2 1 1 1 1 1 1	<b>(2520)</b>
6 4 1 1 1 1 1 1 1 1	<b>(90)</b>	4 3 2 2 2 1 1 1 1 1	<b>(5040)</b>
6 3 2 1 1 1 1 1 1 1	<b>(720)</b>	4 2 2 2 2 2 1 1 1 1	<b>(1260)</b>
6 2 2 2 1 1 1 1 1 1	<b>(840)</b>	3 3 3 3 1 1 1 1 1 1	<b>(210)</b>
5 5 1 1 1 1 1 1 1 1	<b>(45)</b>	3 3 3 2 2 1 1 1 1 1	<b>(2520)</b>
5 4 2 1 1 1 1 1 1 1	<b>(720)</b>	3 3 2 2 2 2 1 1 1 1	<b>(3150)</b>
5 3 3 1 1 1 1 1 1 1	<b>(360)</b>	3 2 2 2 2 2 2 1 1 1	<b>(840)</b>
5 3 2 2 1 1 1 1 1 1	<b>(2520)</b>	2 2 2 2 2 2 2 2 1 1	<b>(45)</b>

All *permutations* are equally likely regardless of which *distribution* they belong to. If we have a distribution with 100 permutations and distribution B with 5 permutations, then it is 20-times more likely that we will find the system in distribution A rather than in distribution B.

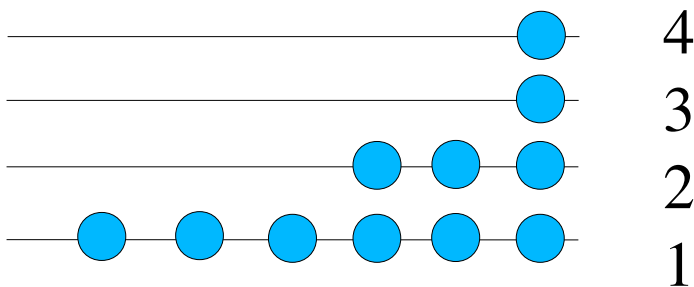
The total number of permutations in our example is 24,310:

(1) the least permutations (10) corresponds to the distribution

9 1 1 1 1 1 1 1 1 1 (occurrence probability  $p=4.1 \times 10^{-4}$ )

(2) the most permutations (5,040) corresponds to the distribution

4 3 2 2 2 1 1 1 1 1 (occurrence probability  $p=0.21$ )



**It could be shown that ignoring the 4 least probable distributions, the error is 1.5%!**

**Ignoring 45% of all distributions, we would still capture the correct distributions with 85% probability (15% error).**

<i># of Molecules [Total Energy]</i>	<i># of Energy Levels</i>	<i># of States (Distributions)</i>	<i># of Permutations</i>
<i>4 [ 6 units]</i>	<i>3</i>	<i>2</i>	<i>10</i>
<i>4 [ 7 units]</i>	<i>4</i>	<i>3</i>	<i>20</i>
<i>10 [18 units]</i>	<i>9</i>	<i>22</i>	<i>24,310</i>

**Biophysical system: # of molecules at least 1,000 and up to  $10^{20}$  !**

**For a fixed average energy per molecule,  $1.8 E_0$  per molecule, then:**

<i># of Molecules</i>	<i># of Levels</i>	<i># of Distributions</i>	<i>% Ignored Dists [error &lt; 5%]</i>
<i>5</i>	<i>5</i>	<i>9</i>	<i>14.0%</i>
<i>10</i>	<i>22</i>	<i>24,310</i>	<i>37.0%</i>
<i>20</i>	<i>231</i>	<i><math>4.1 \times 10^9</math></i>	<i>71.0%</i>
<i>...</i>			
<i>100</i>	<i><math>15.8 \times 10^6</math></i>	<i><math>1.7 \times 10^{52}</math></i>	<i>99.9%</i>

# Boltzmann Distribution

In the limit  $N \rightarrow \infty$ , the most probable distribution is Boltzmann distribution. We find it, if we can find  $n_i$  for all energy levels  $i$  from 1 to  $L$ .

We assume that all energy levels between 1 and  $L$  are available and that  $L$  is the total number of available energy levels.

$$N = \sum_{i=1}^L n_i \qquad W = \frac{N!}{n_1! n_2! n_3! \dots n_L!}$$

Mathematically, to find the most probable distribution means to maximize  $W$ . The set of  $n_i$  that maximizes  $W$  is:

$$N_i = N/Z \exp(-\beta E_i) \quad \text{and} \quad Z = \sum \exp(-\beta E_i) \quad i=\{1, \dots, L\}$$

## **Things to remember about the Boltzmann distribution (derived in 1860s):**

- the most probable distribution of  $N$  molecules over  $L$  energy levels**
- for any reasonable # of molecules and total energy, the Boltzmann distribution overshadows all other distributions**
- derivation of the functional form of the Boltzmann distribution uses Stirling's approximation [  $\log(N!) \approx N \log(N)$  ], assuming  $N$  is a large number (at least 60)**

### **Statistical Mechanical Calculations:**

- the fraction of molecules,  $F_i$ , in a particular energy level:**

$$F_i = N_i/N = \exp(-\beta E_i) / Z \text{ (is also a probability)}$$

- The average energy:**

$$\langle E \rangle = \sum E_i F_i = 1/Z \sum E_i \exp(-\beta E_i)$$



## Degeneracy of Energy Levels:

- atoms/molecules exist in different states (e.g. a particular conformation of a macromolecule, a mode of vibration, ...)
- in many cases, each state (of a macromolecule) has a unique energy level
- sometimes, 2 or more *distinct* states (conformations, vibration modes) happen to have the same energy level: *how do we deal with such cases?*
  - distinct states occupying the same energy level are *degenerate*
  - degeneracy* of the E level = # of distinct states with this E level
- partition function  $Z$  can be then expressed as:
$$Z = \sum \omega_i \exp(-\beta E_i) \text{ with } \beta = 1/(k_B T),$$
where the sum is over *all energy levels* (not all states) and  $\omega_i$  denotes the degeneracy of the energy level  $i$ .

## Reference State and Relative Energy:

- define a reference state  $E_{\text{ref}}$  ( $E_{\text{ref}}$  does not need to be known!)
- define all energy levels relative to  $E_{\text{ref}}$  (in most cases the lowest energy state = ground state)
- *example*: double-helix state of DNA as a reference state, partially or fully unwound states that are relevant to the situation under study defined with respect to this reference state

$$\Delta E_i = E_i - E_{\text{ref}}$$

$$Z = \omega_{\text{ref}} + \sum \omega_i \exp(-\beta \Delta E_i)$$

Here we considered a possibility of a reference state to be degenerate.

Biophysics with Gibbs free energy :  $Z = 1 + \sum \omega_i \exp(-\beta \Delta G_i)$