

# Chemistry and Introduction to Biochemistry

## Thermodynamics 2

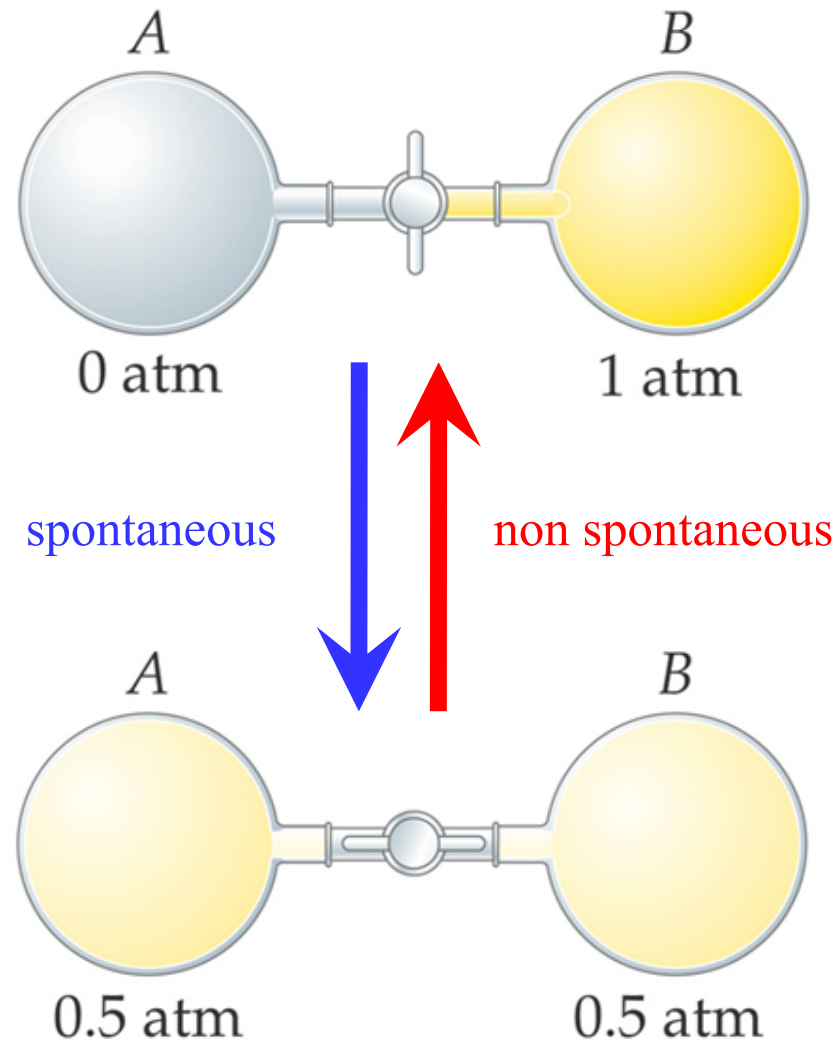
Is it possible to establish a criterion of **spontaneity** for a chemical or physical process?



It will never happen, without a contribution from the outside, that the hottest body in B heats up further and the water cools down.

## Spontaneous processes

- Those processes that take place **without any external intervention** are spontaneous
- The gas in vessel B will spontaneously escape into vessel A



# Spontaneous processes



spontaneous



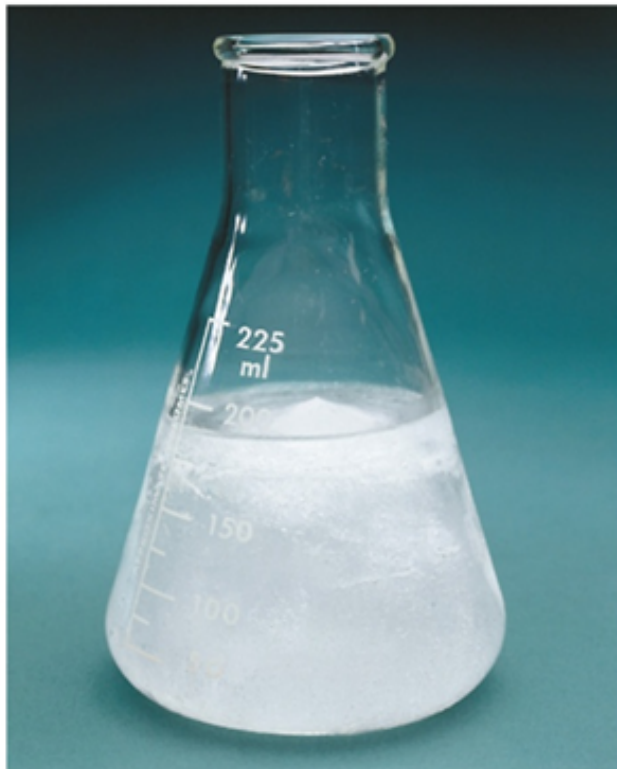
non spontaneous



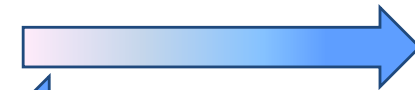
Processes which are spontaneous in one direction are non-spontaneous in the reverse direction

# Spontaneous processes

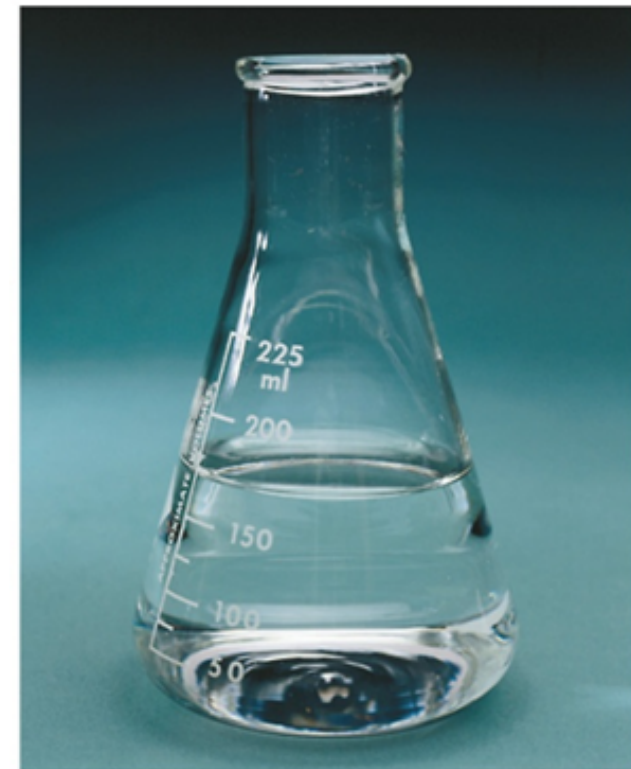
- processes that are spontaneous at one temperature can be non-spontaneous at another temperature
- above  $0\text{ }^{\circ}\text{C}$  it is natural for ice to melt
- below  $0\text{ }^{\circ}\text{C}$  the reverse process is spontaneous



spontaneous when  
 $T > 0\text{ }^{\circ}\text{C}$



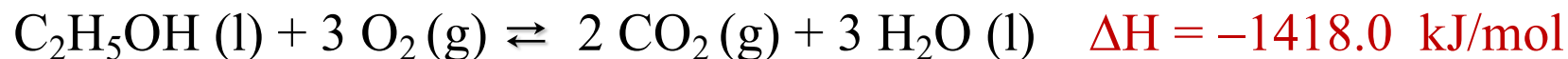
spontaneous when  
 $T < 0\text{ }^{\circ}\text{C}$





## Heat and spontaneity

Many chemical reactions proceed **spontaneously** from the reactants to the products and essentially go to completion when equilibrium is reached:



It would seem obvious, therefore, to conclude that the **emission of heat** is the **criterion that determines whether a reaction or a process is spontaneous..**

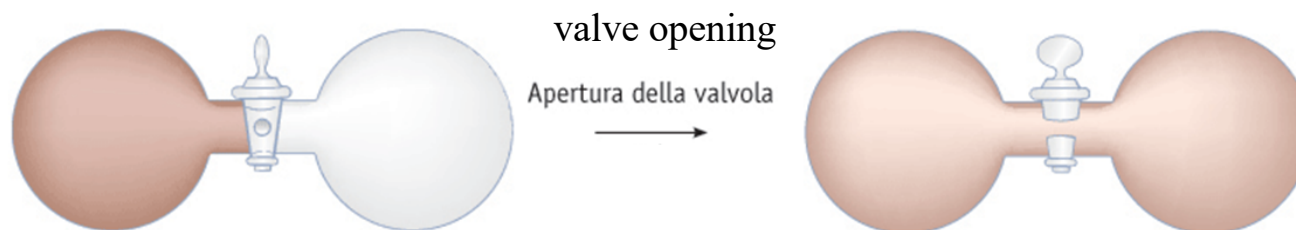
These reactions, like many others, have a common characteristic: they are **exothermic**.

**However!** There are many common physical processes in which spontaneous changes occur, but which are **endothermic** or without energetic variations.

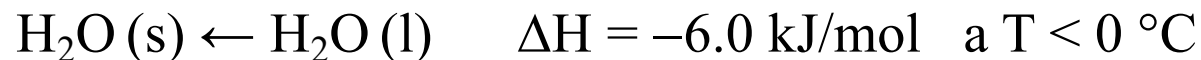
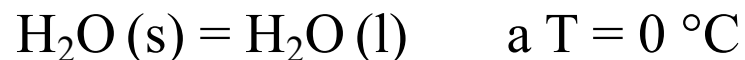
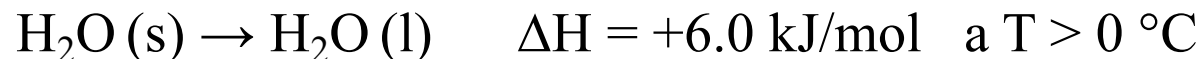
- the **dissolution** of  $\text{NH}_4\text{NO}_3$  in water is spontaneous but is endothermic



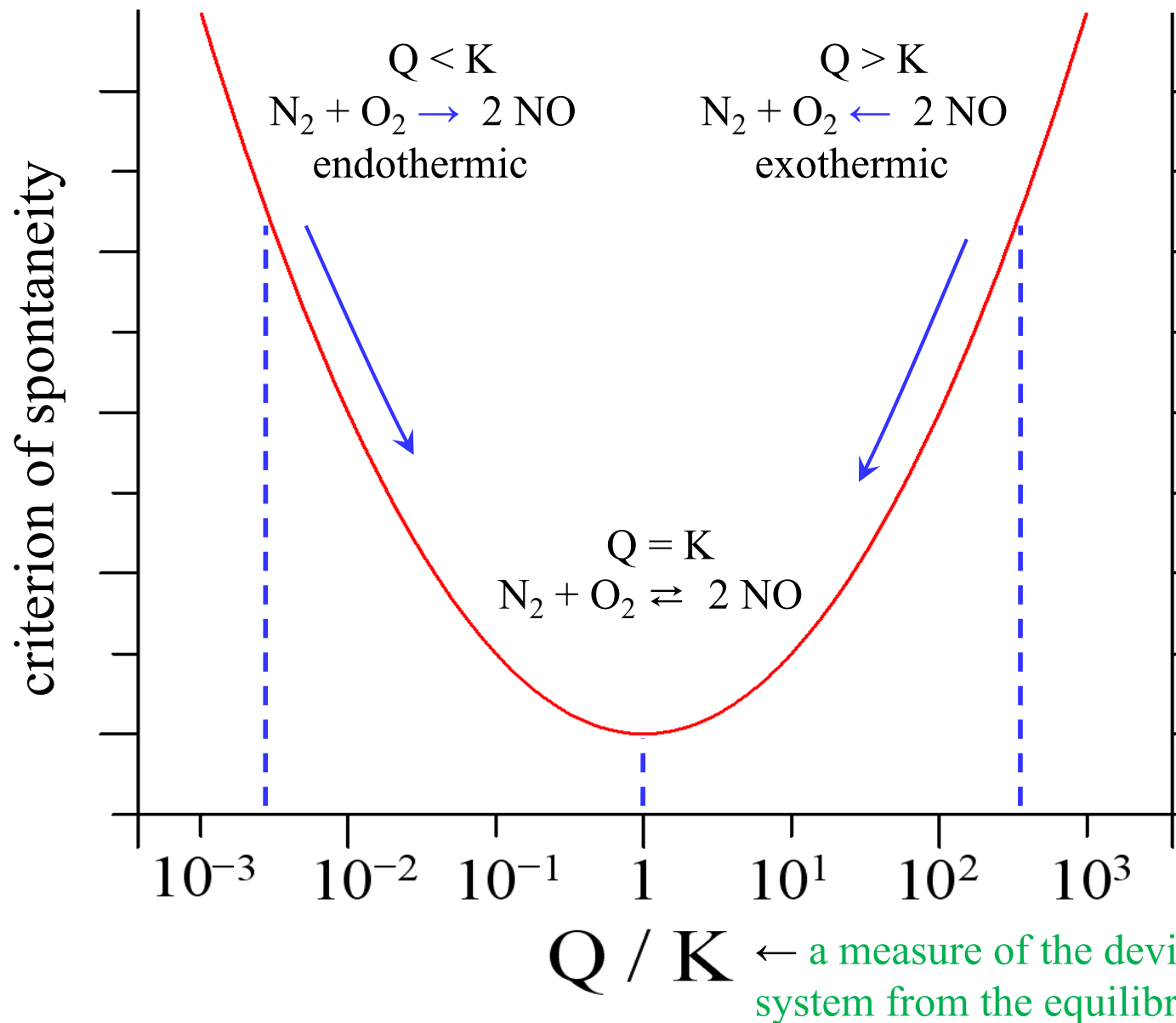
- the **expansion of a gas in a vacuum** is an **isothermal** process



- state changes**



- heat transfer**: a cold object in a hot environment will heat up to the ambient temperature in a spontaneous endothermic process.



# The second law of thermodynamics

In a spontaneous process, the **entropy** of the universe increases



**Entropy** is a:

- a state variable whose change is defined in a reversible process as  $\Delta S = q / T$
- a measure of the **amount of energy not available** to do work
- a measure of the **degree of energy dispersion**
- a measure of the **multiplicity** of a system

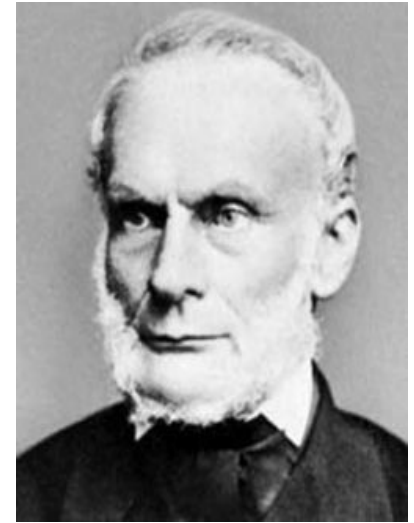


# Entropy S

Term coined by R. Clausius ( $\epsilon\nu$ , "inside", and from  $\tau\rho\omicron\pi\eta$ , "change").

The irreversibility of heat:

- heat passes naturally from hot to cold, never from cold to hot
- friction converts mechanical movement into heat, but in nature there is no comparable process to **completely transform heat in mechanical movement**.



Rudolf J. E. Clausius  
1822 –1888

He supposed that these two types of changes must have the same nature, namely that they are two different aspects of the same phenomenon: **changes in entropy**.

The natural transformations that occur spontaneously in nature must have produced an **increase in entropy**. The entropy change undergone by a system following a transformation is given by:

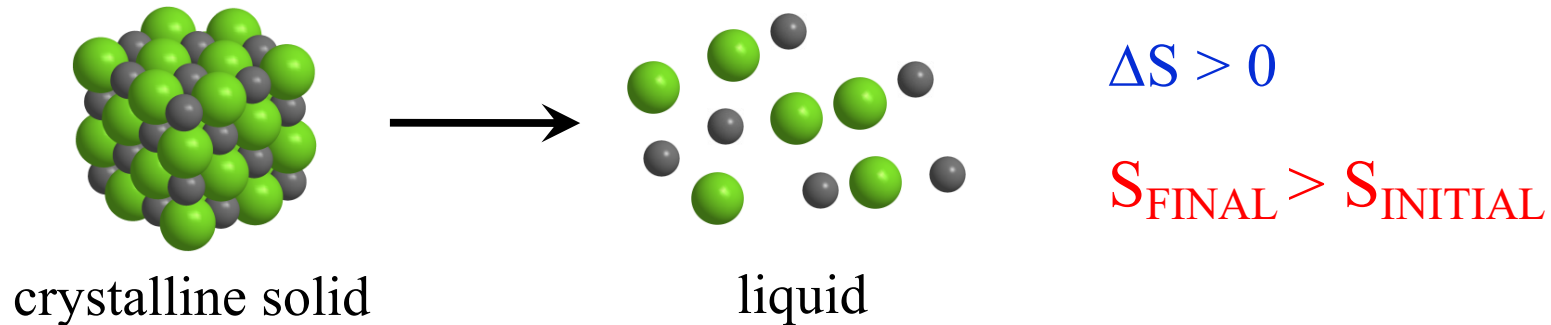
$$\Delta S = \frac{q}{T}$$

# Entropy and the second law of thermodynamics

Entropy  $S$  is a thermodynamic quantity that measures the degree of dispersion of the energy and mass of a system. This quantity is a state function and for a given process it is possible to uniquely define a change in entropy as

$$\Delta S = S_{\text{FINAL}} - S_{\text{INITIAL}}$$

The entropy change for some processes is qualitatively intuitive: for example in a melting process one must have  $\Delta S > 0$  since the degree of dispersion increases



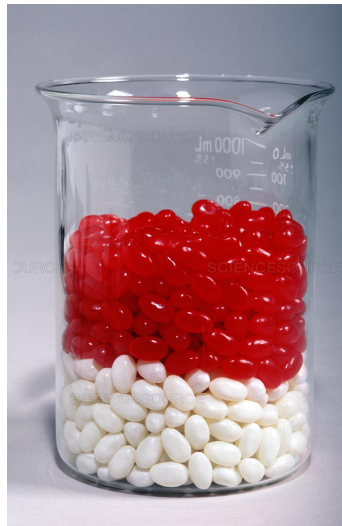
For example, melting 1 mole of  $\text{H}_2\text{O}$  results in  $\Delta S = 22 \text{ J K}^{-1} \text{ mol}^{-1}$

# Entropy and the second law of thermodynamics

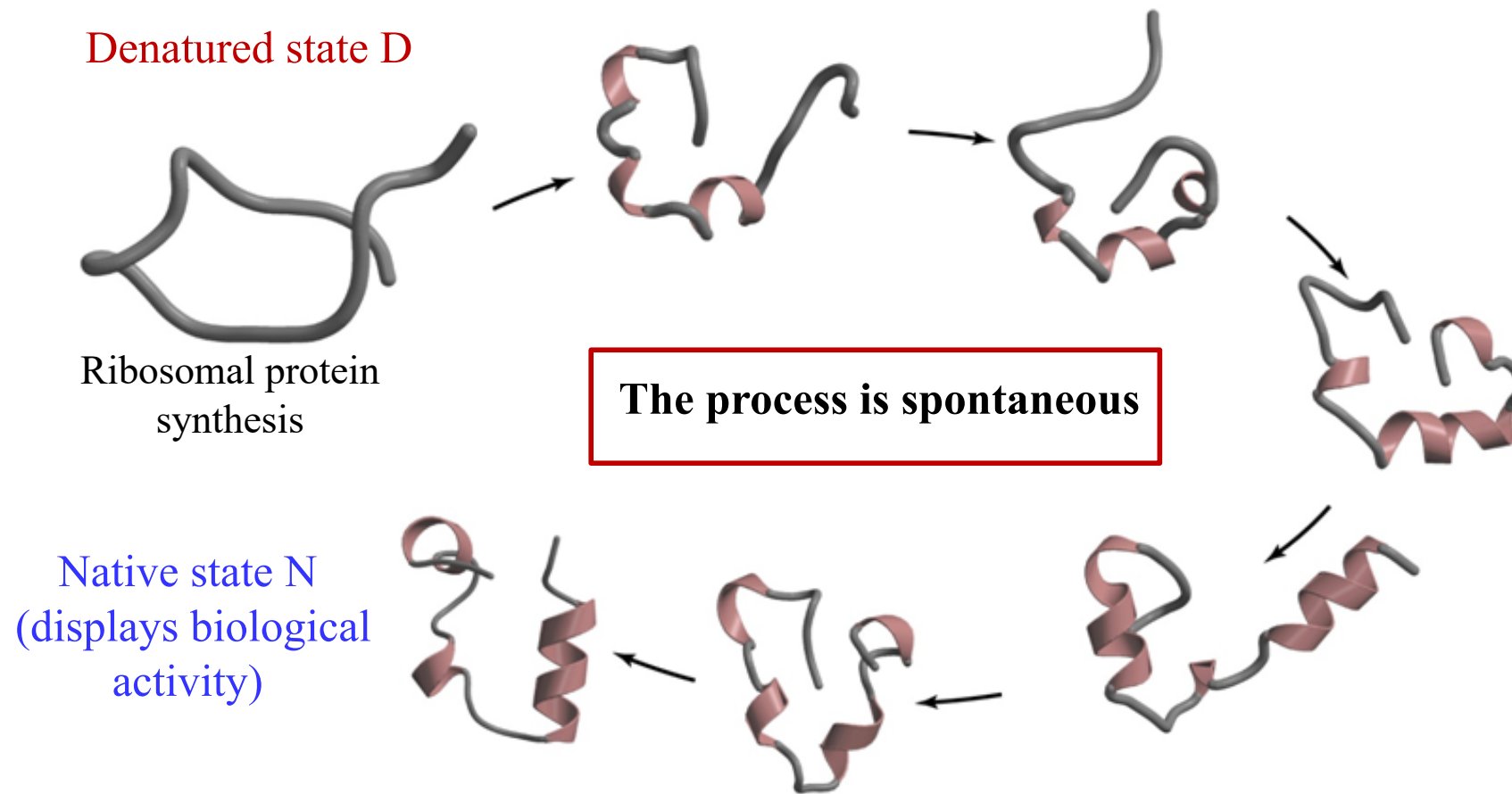
All work done on a system can be turned into heat; **conversely**, not all the heat acquired by a system can be turned into work

$$\Delta S_{universe} = \Delta S_{system} + \Delta S_{environment} > 0$$

The entropy of the universe increases and this corresponds to an increase in energy dispersion



# Protein folding ( $\Delta S < 0$ )



This process takes place *in vivo* with a decrease in entropy  $S_D > S_N$ . The fact that the **protein folds spontaneously** into the native three-dimensional structure endowed with biological activity depends on **opposite entropy variations in the aqueous solvent** (hydrophobic effect)



*Representative protein folding diseases*

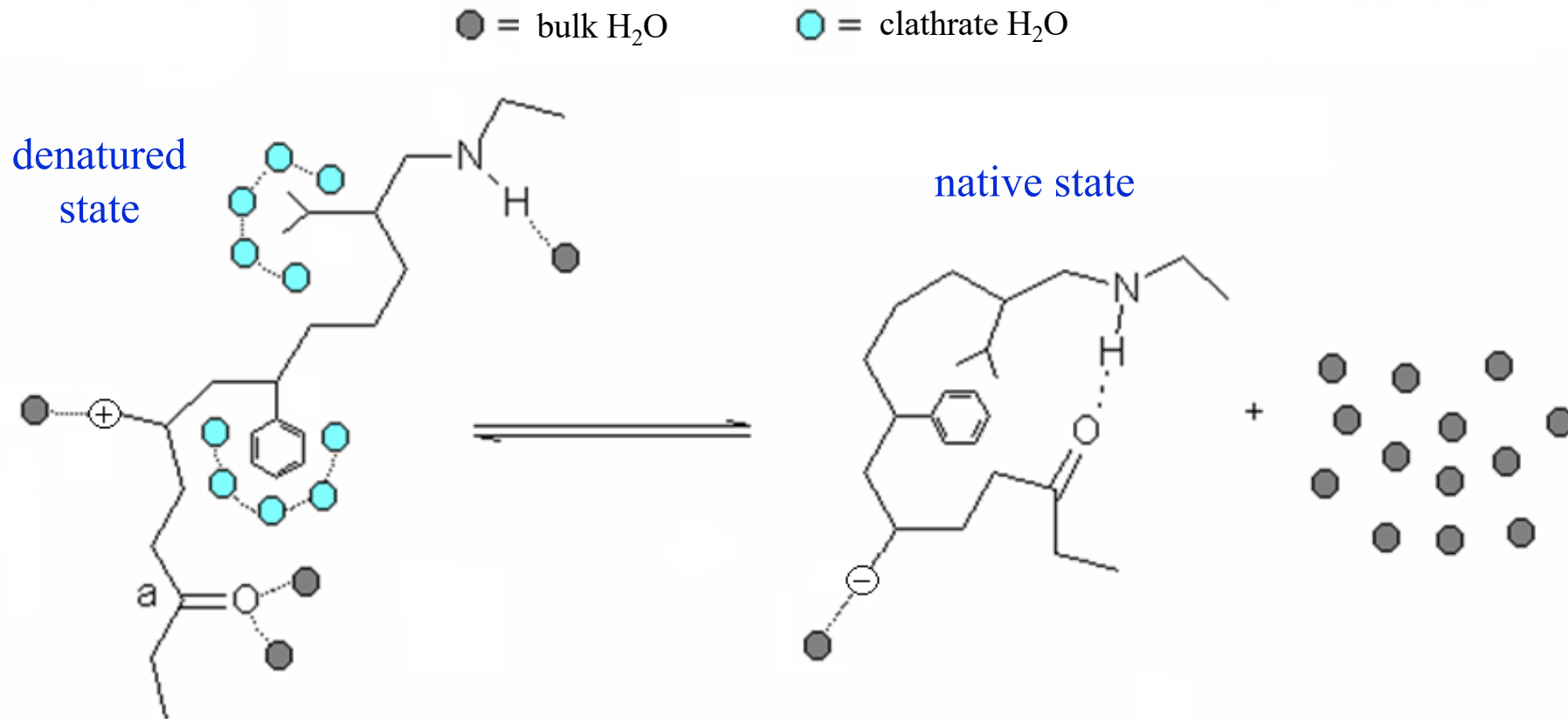
disease	protein	site of folding
hypercholesterolaemia	low-density lipoprotein receptor	ER
cystic fibrosis	cystic fibrosis trans-membrane regulator	ER
phenylketonuria	phenylalanine hydroxylase	cytosol
Huntington's disease	huntingtin	cytosol
Marfan syndrome	fibrillin	ER
osteogenesis imperfecta	procollagen	ER
sickle cell anaemia	haemoglobin	cytosol
$\alpha$ 1-antitrypsin deficiency	$\alpha$ 1-antitrypsin	ER
Tay-Sachs disease	$\beta$ -hexosaminidase	ER
scurvy	collagen	ER
Alzheimer's disease	$\beta$ -amyloid/presenilin	ER
Parkinson's disease	$\alpha$ -synuclein	cytosol
scrapie/Creutzfeldt-Jakob disease	prion protein	ER
familial amyloidoses	transthyretin/lysozyme	ER
retinitis pigmentosa	rhodopsin	ER
cataracts	crystallins	cytosol
cancer	p53	cytosol

# Clathrates



**Cages of water** (clathrates) can dissolve hydrophobic substances. Protein folding is correlated to the presence of clathrates

During the folding process, the water passes from a more orderly to a less ordered state (hydrophobic effect)



In the denatured state, the water molecules bound to the hydrophobic amino acid residues (**clathrates**) are in a much **more orderly ice-like configuration** than the other **bulk water molecules**. In the transition from the denatured to the native state, these molecules increase their degree of disorder.

## A deck of (40) Treviso cards

- suppose you initially have the deck "sorted" by suit and rank
- we shuffle the cards in such a way as to destroy the ordered arrangement



In this way we will obtain any arrangement among the  $40!$  possible without knowing which one.

In this way we have **lost all the information** we previously possessed on the arrangement of the cards in the deck.

$$(n! = n \cdot (n-1) \cdot (n-2) \cdot \dots \cdot 1 \quad \text{ex: } 40! = 40 \cdot 39 \cdot 38 \cdot \dots \cdot 3 \cdot 2 \cdot 1 = 8.1592 \cdot 10^{47})$$

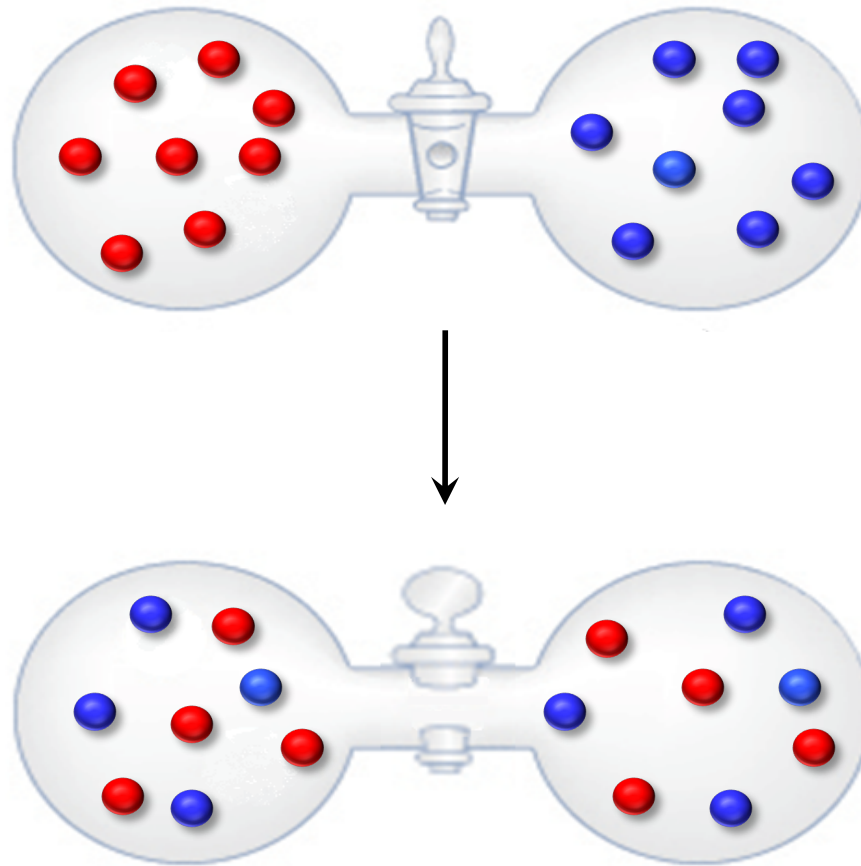
We can uncover the cards and thus regain the lost information, **but we certainly cannot hope to return to the initial situation in a reasonably short time by continuing to shuffle the deck.** As we can see, **the "disorder" that is caused by shuffling the cards is essentially irreversible.**

**Why?** The reason lies not in the fact that a particular disposition is more probable than the original one (all dispositions have equal probability,  $1/40!$ ); but on the fact **that the number of dispositions compatible with a disordered state is enormously greater than that compatible with an ordered state.**



# Mixing of two gases by diffusion.

When the valve is opened, the 2 gases mix spontaneously, but the mixture does not spontaneously return to its initial state



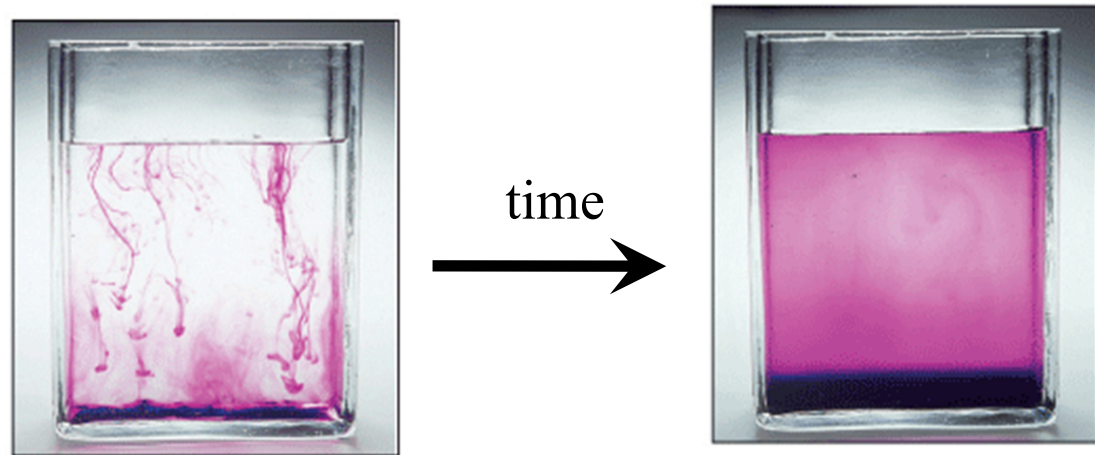
What determines the diffusion is only the entropy increase that occurs in the process.

# Dispersion of energy and matter

The concept of entropy also arises from the idea that **a spontaneous transformation leads to a dispersion of energy**. Many times a dispersion of matter is also involved in this process and this can contribute to the dispersion of energy in some systems.

- entropy can be viewed as a function that describes the number of possible arrangements of energy and matter that are available (microstates)
- nature proceeds spontaneously towards the states which have the greatest probability of existence
- these observations are the basis of statistical thermodynamics

A small amount of  $\text{KMnO}_4$  is added to the water. Over time, the solid dissolves and the intensely colored  $\text{MnO}_4^-$  ion and  $\text{K}^+$  ion are dispersed throughout the solution

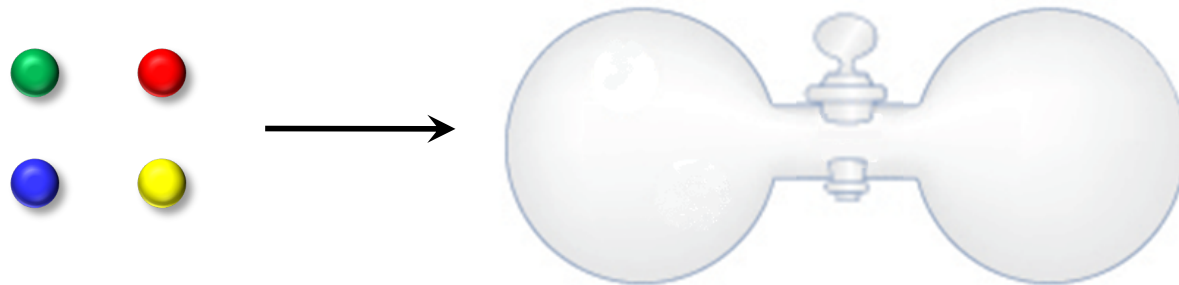


## Microstates & macrostates

- **classical thermodynamics** classifies system states on the basis of macroscopic characteristics
- **statistical thermodynamics** uses microstates (microscopic states)
  - **microstate**: position and momentum of each molecule
  - **macrostate**: (P, V, T)
- **multiplicity**: the number of microstates corresponding to a single macrostate

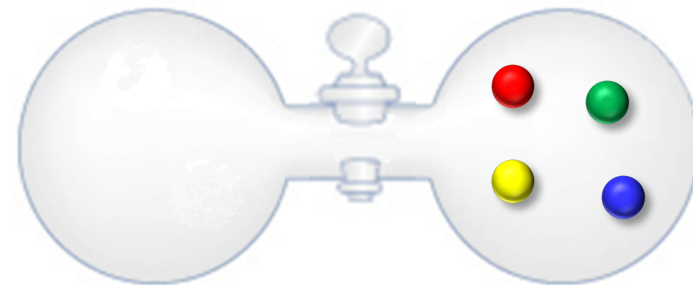
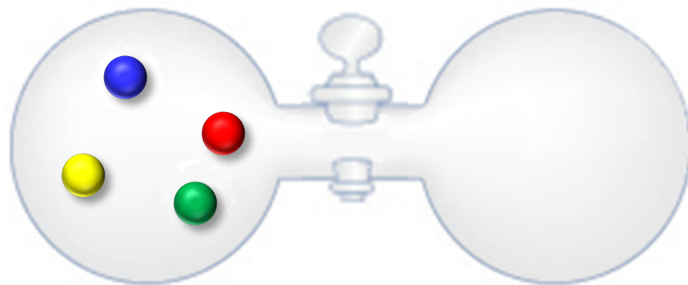
# Macrostates, microstates and probability

Let's consider 4 identical molecules (but of different color to distinguish them) to be distributed in two connected vessels. How many micro- and macrostates are there?



macrostate 4-0: 1 microstate

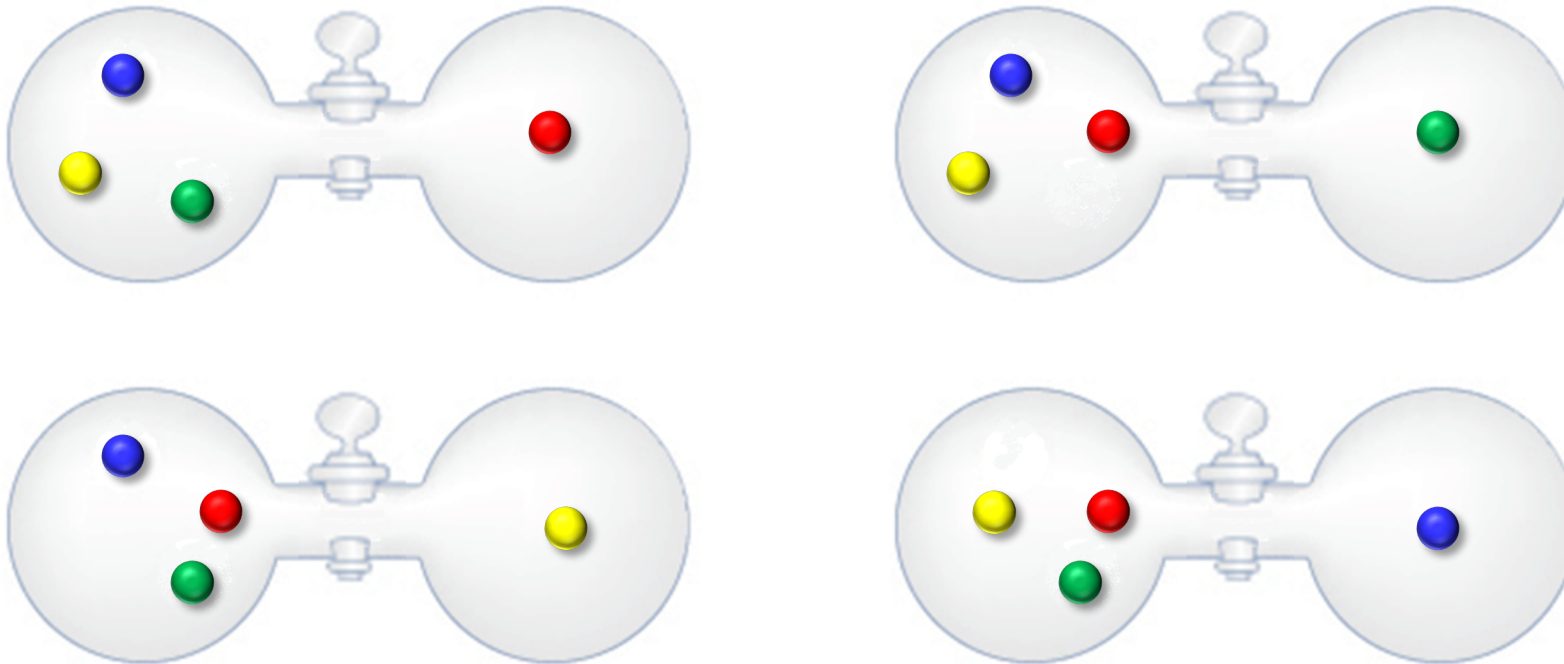
macrostate 0-4: 1 microstate



partial sum: 2 macrostates and a total of 2 microstates

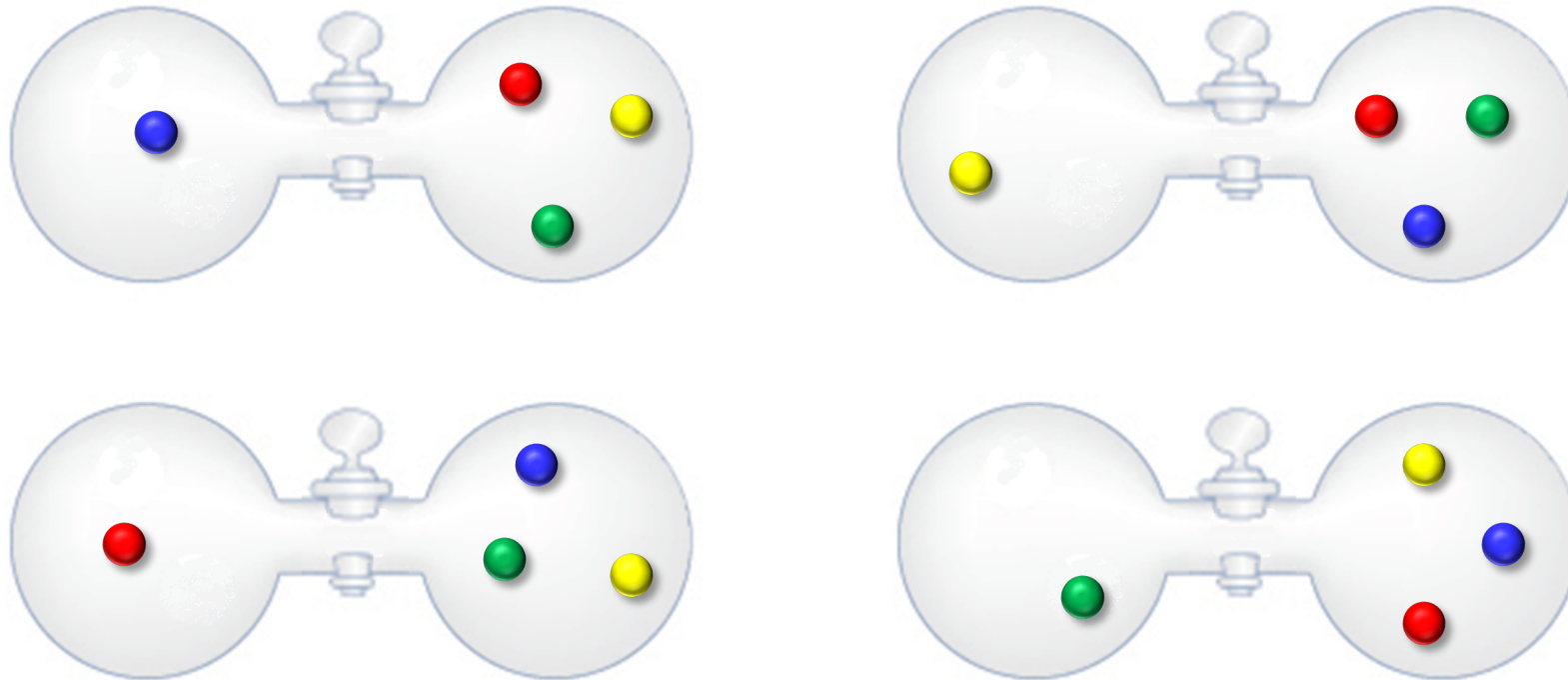


macrostate 3-1: 4 microstates



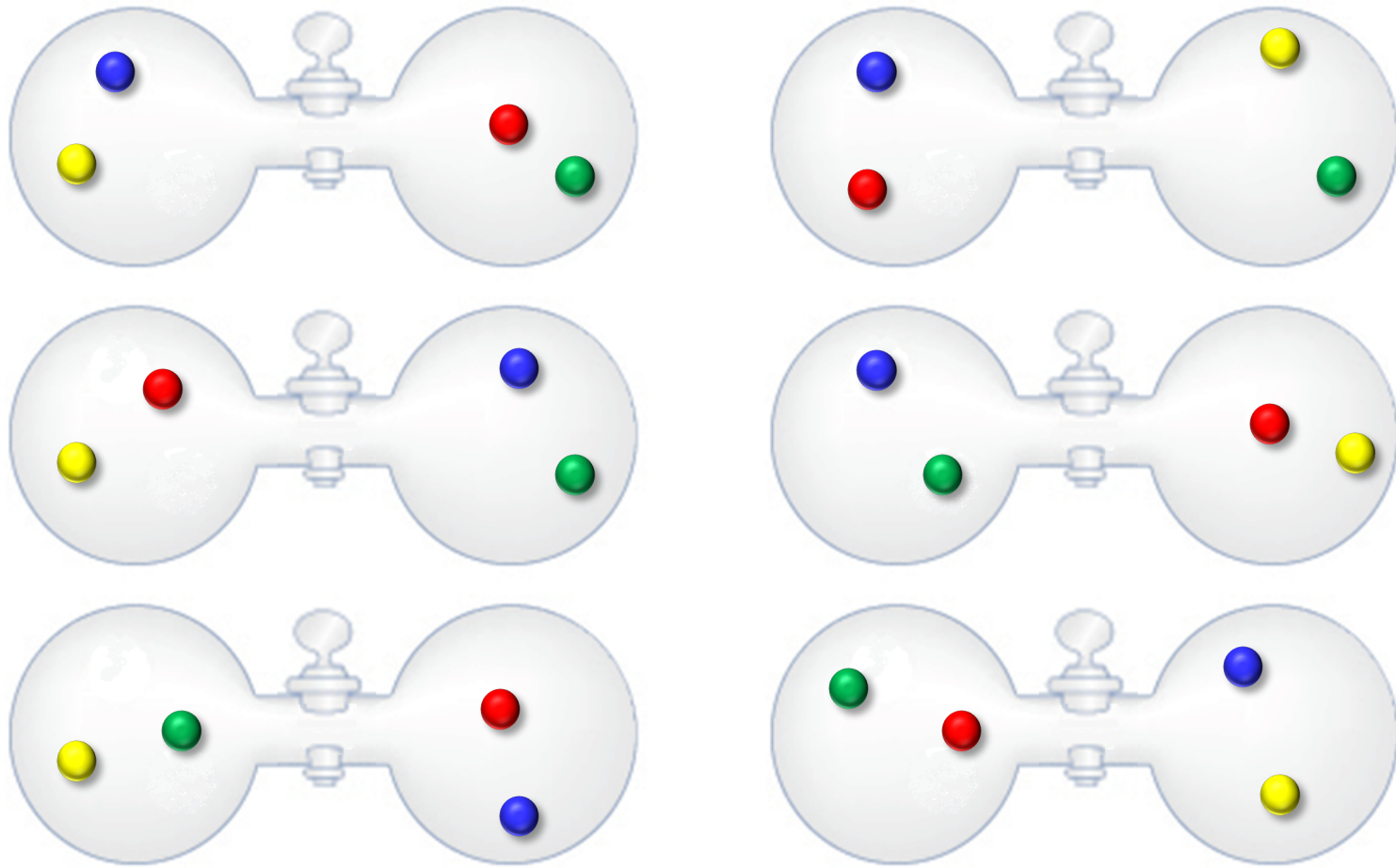
partial sum: 3 macrostates and a total of 6 microstates

macrostate 1-3: 4 microstates



partial sum: 4 macrostates and a total of 10 microstates

macrostate 2-2: 6 microstates



somma parziale: 5 macrostati e un totale di 16 microstati

partial sum: 5 macrostates and a total of 16 microstates

There are 16 possible ways in which molecules can arrange themselves in the vessel, which we have termed microstates. Some of these are equivalent.

macrostate [4,0]	→	equivalent microstates: 1
macrostate [3,1]	→	equivalent microstate: 4
<b>macrostate [2,2]</b>	<b>→</b>	<b>equivalent microstates: 6</b>
macrostate [1,3]	→	equivalent microstates: 4
macrostate [0,4]	→	equivalent microstates: 1

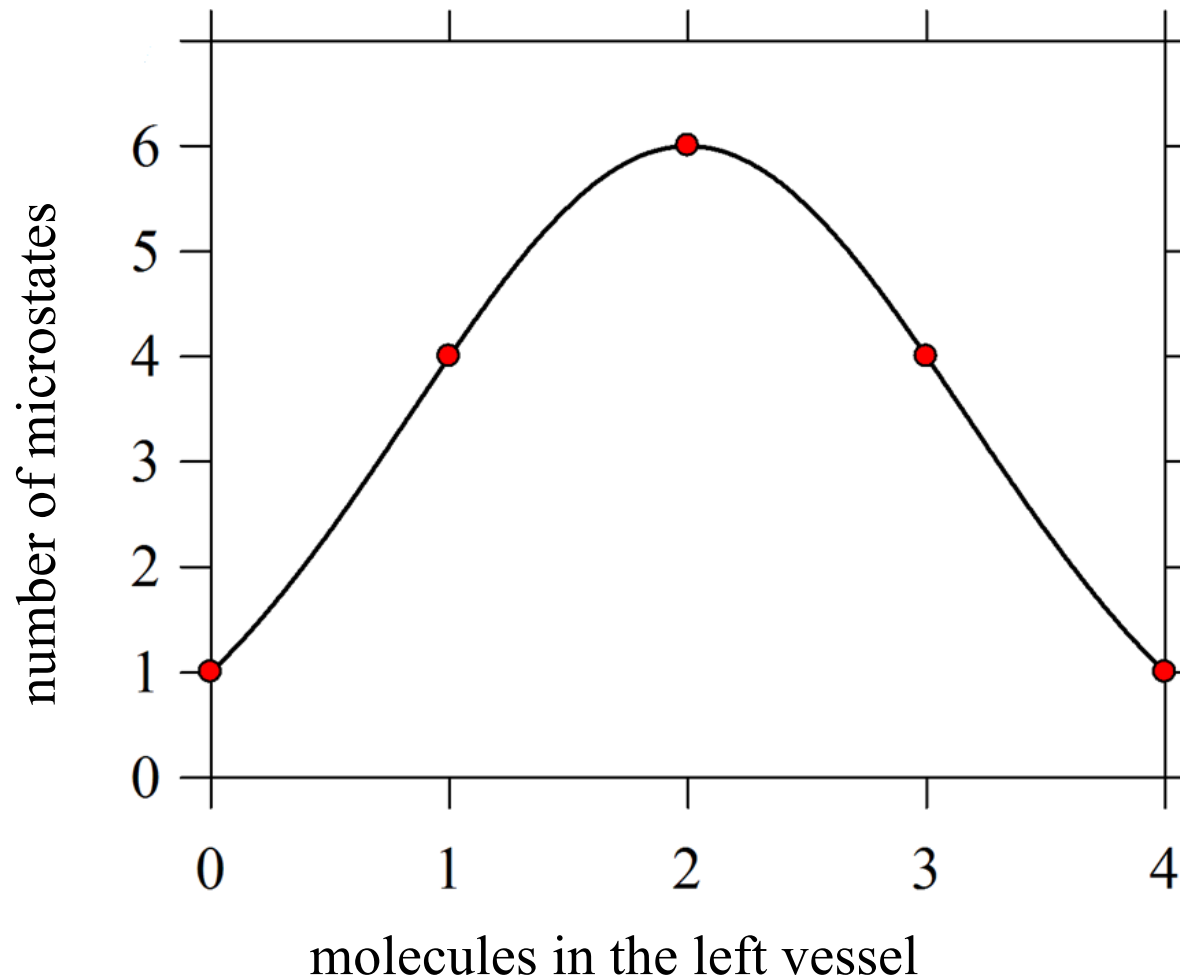
Defining **multiplicity** ( $w$ ) the number of equivalent microstates, for  **$n$  molecules**, the multiplicity of a macrostate or configuration is given by:

$$w = \frac{n!}{n_L! \cdot n_R!}$$

$n_L$  = number of molecules in the right compartment  
 $n_R$  = number of molecules in the left compartment

Configurations with greater **multiplicity** (more likely) are those with **higher entropy**.

Graphically ...



$$w = \frac{n!}{n_S \cdot n_D}$$

$$w = \frac{4!}{0! \cdot 4!} = 1$$

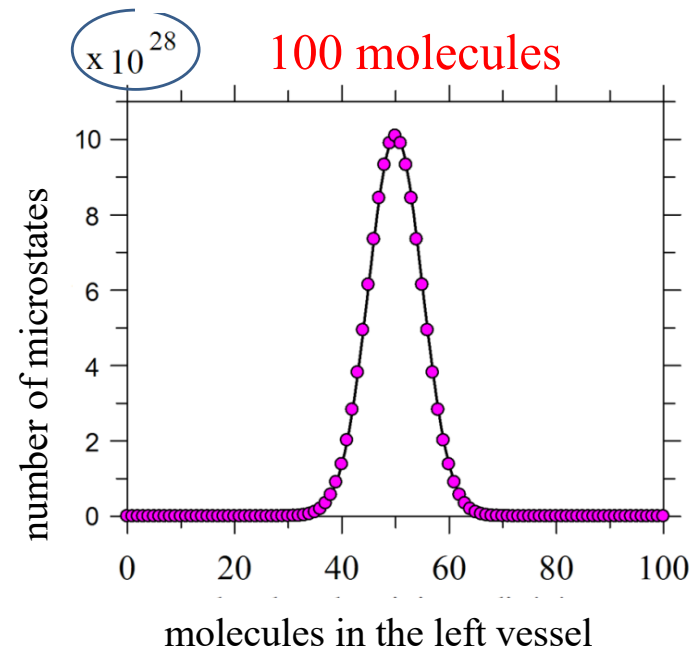
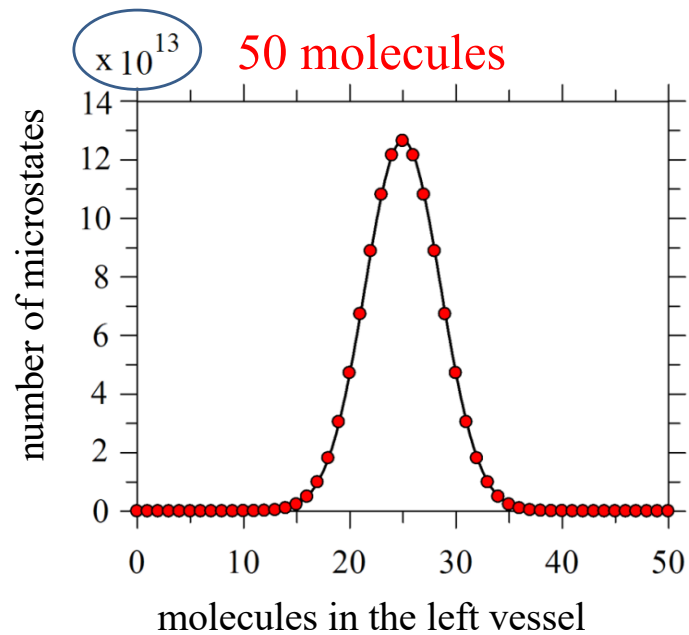
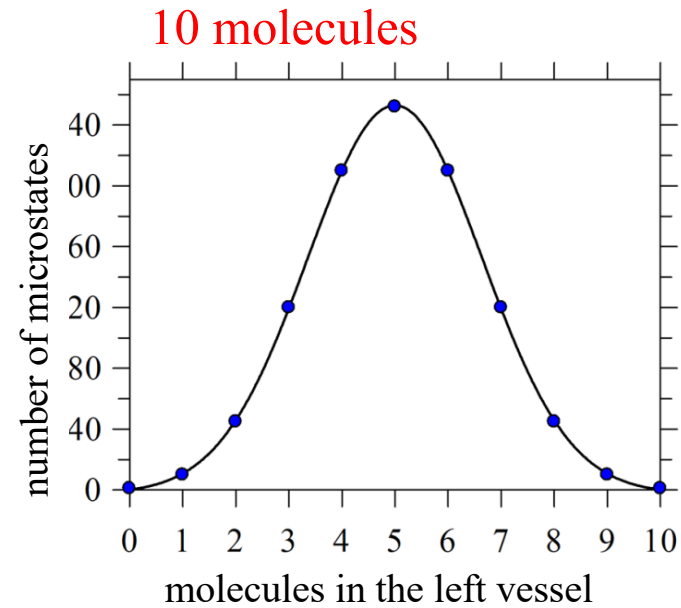
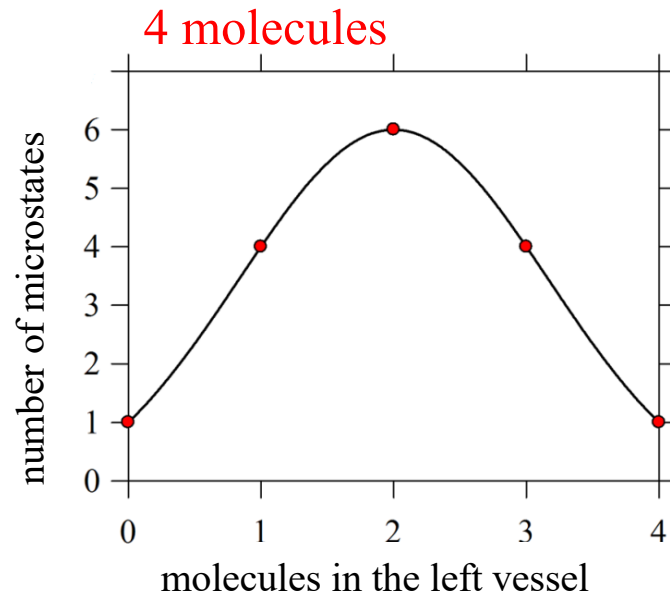
$$w = \frac{4!}{1! \cdot 3!} = 4$$

$$w = \frac{4!}{2! \cdot 2!} = 6$$

$$w = \frac{4!}{3! \cdot 1!} = 4$$

$$w = \frac{4!}{4! \cdot 0!} = 1$$

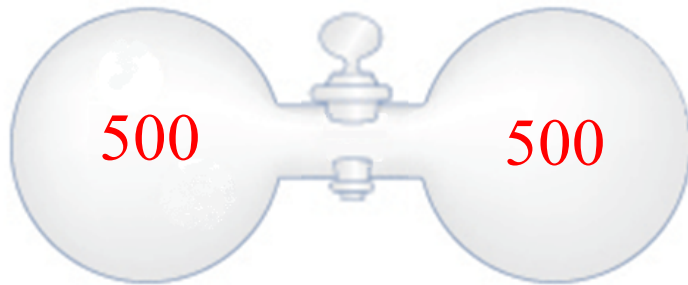
Al crescere del numero di molecole la distribuzione si assottiglia





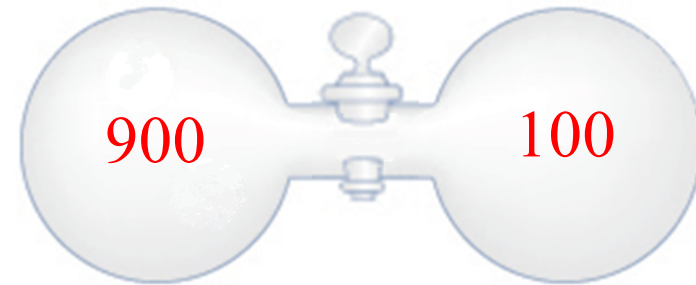
As the number of molecules increases, the number of equivalent microstates increases dramatically

1000 molecules



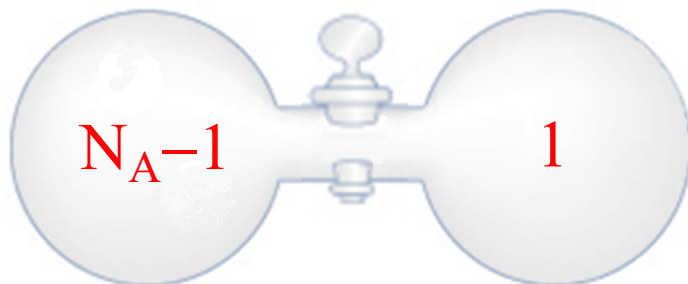
The number of microstates in the macrostate with 500 molecules in each vessel is approximately  $w = 10^{299}$

1000 molecules



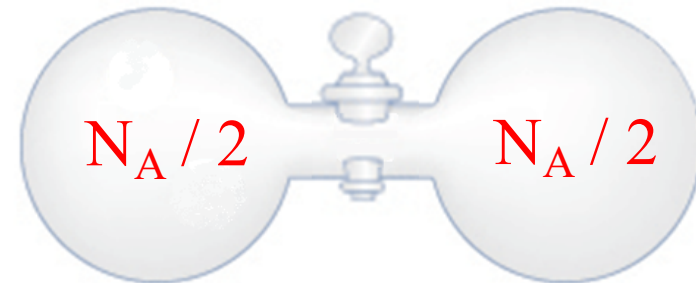
The number of microstates in the macrostate with 900 molecules in the left vessel and 100 in the right vessel is just  $w = 10^{140}$

1 mole



$$w = N_A$$

1 mole



$$w \approx 10^{2 \cdot 10^{23}}$$

# Boltzmann's entropy equation

Ludwig Boltzmann developed the idea of considering the distribution of energy in the various energy levels as a way to calculate entropy

$$S = k \log w$$

$w$  = the number of different ways in which energy can be distributed in the available energy levels

$k = 1.3807 \cdot 10^{-16}$  J/K Boltzmann's constant

In Boltzmann's original definition, multiplicity  $w$  is the initial of **wahrscheinlichkeit** which means **probability of state** (log = natural logarithm)



Zentralfriedhof, Vienna

## Some molar standard absolute entropy values at 298 K.

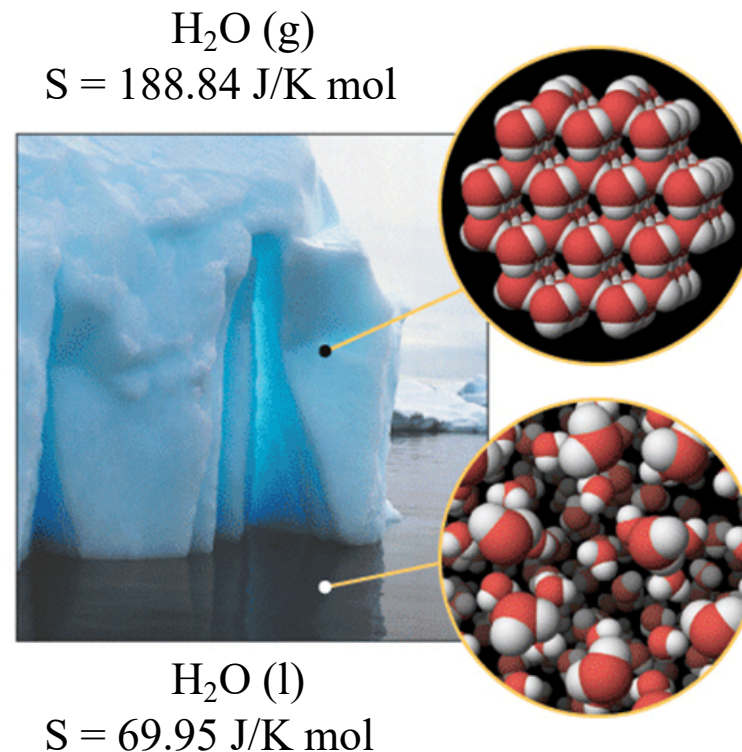
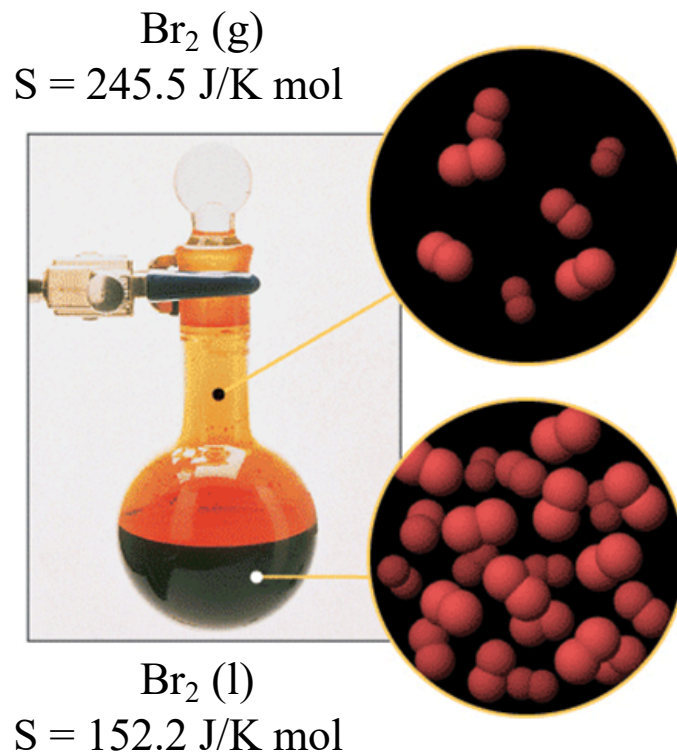
element	entropy (J/K mol)	compound	entropy (J/K mol)
C (diamond)	2.377	CH <sub>4</sub> (g)	186.3
C (graphite)	5.6	C <sub>2</sub> H <sub>6</sub> (g)	229.2
C (vapor)	158.1	C <sub>3</sub> H <sub>8</sub> (g)	270.3
Ca (s)	41.59	CH <sub>3</sub> OH (l)	127.2
Ar (g)	154.9	CO (g)	197.7
H <sub>2</sub> (g)	130.7	CO <sub>2</sub> (g)	213.7
N <sub>2</sub> (g)	205.1	H <sub>2</sub> O (g)	188.84
O <sub>2</sub> (g)	191.6	H <sub>2</sub> O (l)	69.95
F <sub>2</sub> (g)	202.8	HCl (g)	186.2
Cl <sub>2</sub> (g)	223.1	NaCl (s)	72.11
Br <sub>2</sub> (l)	152.2	MgO (s)	26.85
I <sub>2</sub> (s)	116.1	CaCO <sub>3</sub> (s)	91.7

source: NIST (<http://webbook.nist.gov>)

## Interesting and useful generalizations

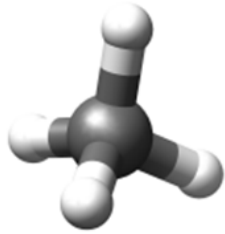
1) Comparing similar substances :  $S_{\text{GAS}} \gg S_{\text{LIQUID}} \gg S_{\text{SOLID}}$

In **solids**, the particles occupy almost exactly fixed positions around the nodes of the crystal lattice. When a **solid melts**, its particles are freer to assume different positions and this produces an increase in the degree of disorder. When a liquid evaporates, the constraints due to the forces between the particles disappear almost completely and there is a further increase in entropy.

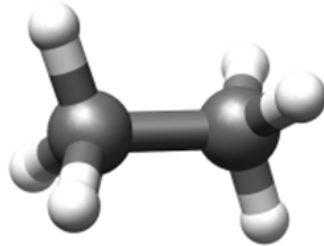


## Interesting and useful generalizations

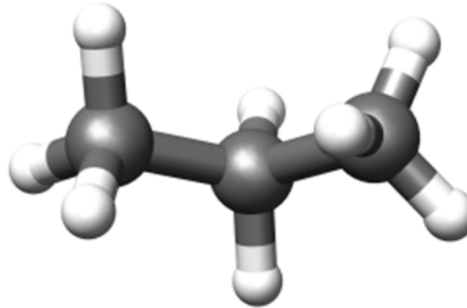
2) In general, **larger molecules** have **greater entropies** than smaller molecules



$\text{CH}_4$  (g)  
 $S = 186.3 \text{ J/K mol}$



$\text{C}_2\text{H}_6$  (g)  
 $S = 229.3 \text{ J/K mol}$



$\text{C}_3\text{H}_8$  (g)  
 $S = 270.3 \text{ J/K mol}$

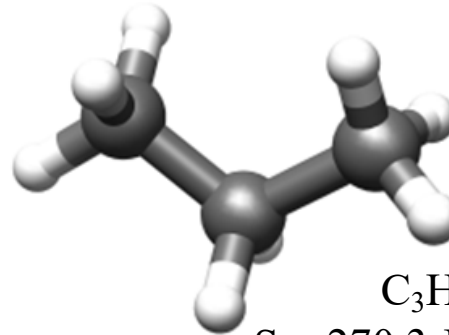
and molecules with more complex structure have larger entropies than molecules with simpler structure.



Ar (g)  
 $S = 154.9 \text{ J/K mol}$



$\text{CO}_2$  (g)  
 $S = 213.7 \text{ J/K mol}$

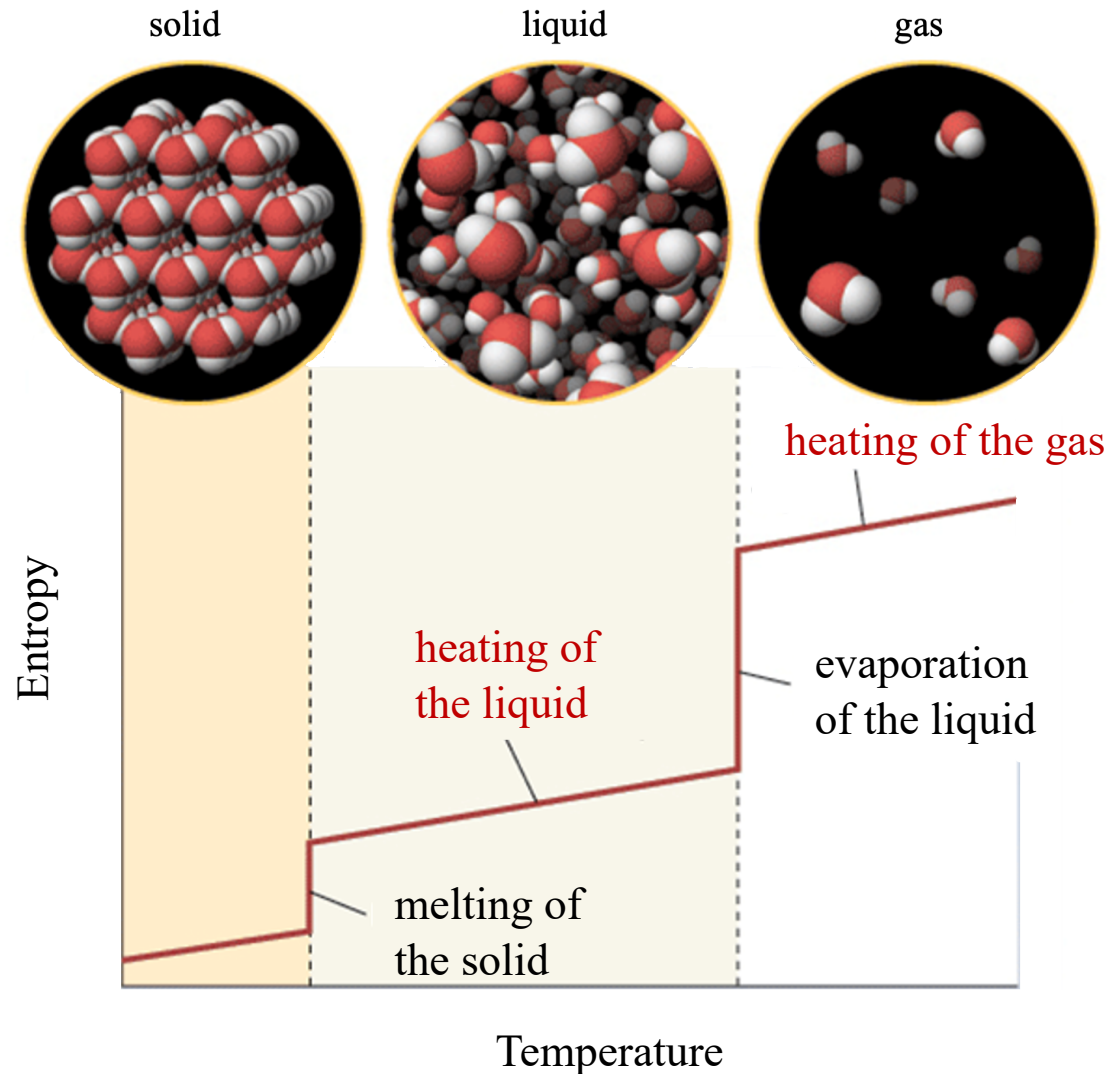


$\text{C}_3\text{H}_8$  (g)  
 $S = 270.3 \text{ J/K mol}$

**More complex molecules have more possibilities to rotate, bend and vibrate in space. This determines a greater number of energy states on which energy can be distributed.**

## Interesting and useful generalizations

3) For a certain substance, entropy increases with increasing temperature. Changes of state are accompanied by large variations in entropy.





## Free energy G

Evaluating the spontaneity of a reaction by examining the  $\Delta S$  that the system and environment undergo during a transformation can be impractical (moreover, some processes with  $\Delta S < 0$  are spontaneous, e.g. protein folding).

Ideally we want to focus our attention on some exclusive property of the system, capable of informing us on the direction of a spontaneous process. This opportunity exists and is possible by defining a new state function, called **Gibbs free energy** (G), so that:

$$G = H - TS$$

Thus for a finite transformation

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

The criterion of spontaneity of a reaction

Free energy represents the **maximum energy available to do work.**

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

when  $\Delta G > 0$  the process is non-spontaneous and **endoergonic**

when  $\Delta G = 0$  the process is at equilibrium and isoergonic

when  $\Delta G < 0$  the process is spontaneous and **exoergonic**

Different reactions can be spontaneous for different reasons.  
Spontaneity criterion:  $\Delta G < 0$  (in general reactions are favored when  $\Delta H < 0$  or  $\Delta S > 0$ )

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

Some examples

enthalpic factor	entropic factor	condition	free energy	reaction
$\Delta H > 0$	$T\Delta S > 0$	$\Delta H < T\Delta S$	$\Delta G < 0$	spontaneous
$\Delta H > 0$	$T\Delta S > 0$	$\Delta H > T\Delta S$	$\Delta G > 0$	non spontaneous
$\Delta H < 0$	$T\Delta S < 0$	$\Delta H > T\Delta S$	$\Delta G < 0$	spontaneous
$\Delta H < 0$	$T\Delta S < 0$	$\Delta H < T\Delta S$	$\Delta G > 0$	non spontaneous

## Effect of temperature on the spontaneity of reactions

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

sign of $\Delta H$	sign of $\Delta S$	is the reaction spontaneous?	example
–	+	Yes, at all temperatures	$2 \text{ O}_3 (\text{g}) \rightarrow 3 \text{ O}_2 (\text{g})$
+	+	Yes, at high temperatures (reaction is entropy driven)	$\text{H}_2\text{O} (\text{s}) \rightarrow \text{H}_2\text{O} (\text{l})$
–	–	Yes, at low temperatures (reaction is enthalpy driven)	$\text{H}_2\text{O} (\text{l}) \rightarrow \text{H}_2\text{O} (\text{s})$
+	–	No, at all temperatures (reverse reaction is spontaneous)	$3 \text{ O}_2 (\text{g}) \rightarrow 2 \text{ O}_3 (\text{g})$

# Relationship between free energy and the equilibrium constant



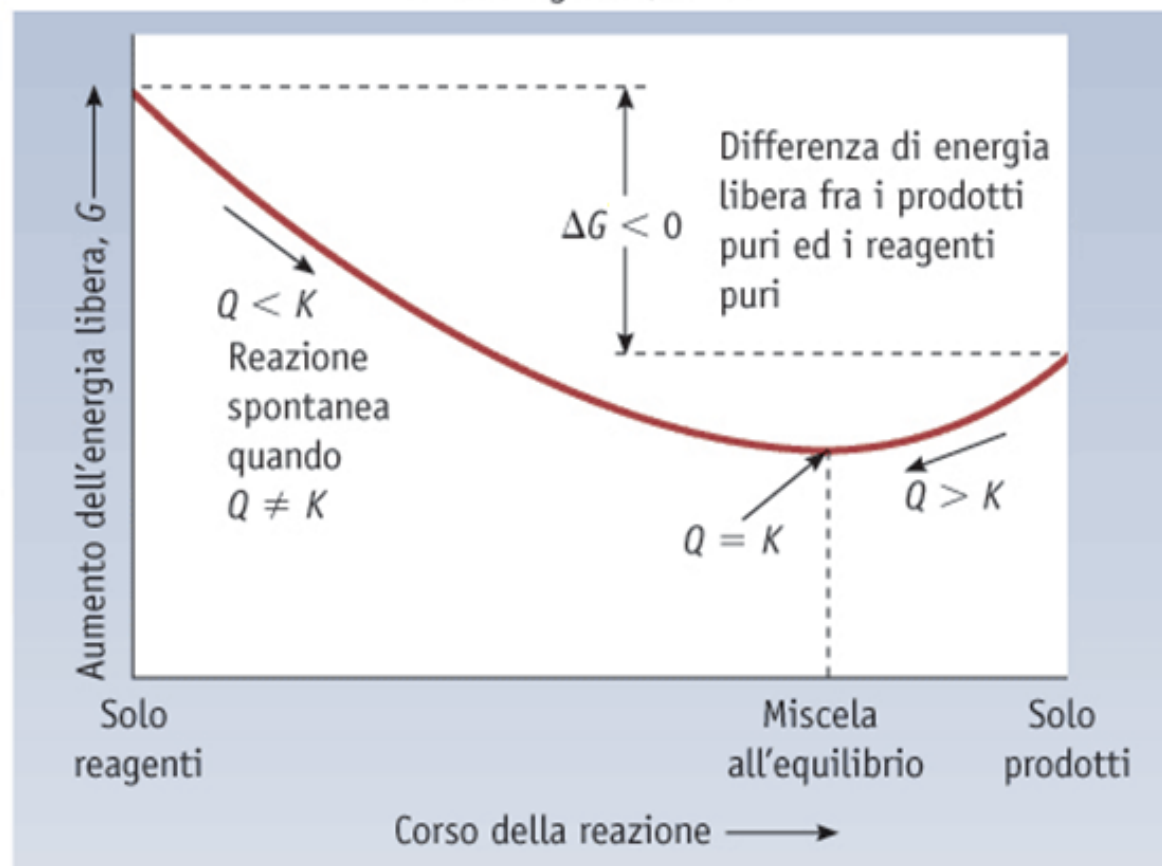
$$K_{eq} = \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

$$\Delta G = \Delta G^0 + RT \ln Q$$

The standard free energy change of a reaction ( $\Delta G^0$ ) is the increase or decrease in free energy when reactants in their standard states (1 M, 1 atm) transform into products in their standard states (1 M, 1 atm) at a given temperature.

At equilibrium  $\Delta G = 0$ ,  $Q = K_{EQ} \rightarrow$

La reazione è a favore dei prodotti,  
 $\Delta G$  è negativo,  $K > 1$



$$\Delta G^0 = -RT \ln K_{eq}$$

$$\Delta G = \Delta G^0 + RT \ln Q$$

**$\Delta G^{\circ'}$  and  $\Delta G$  for the Reactions of Glycolysis in Heart Muscle<sup>a</sup>**

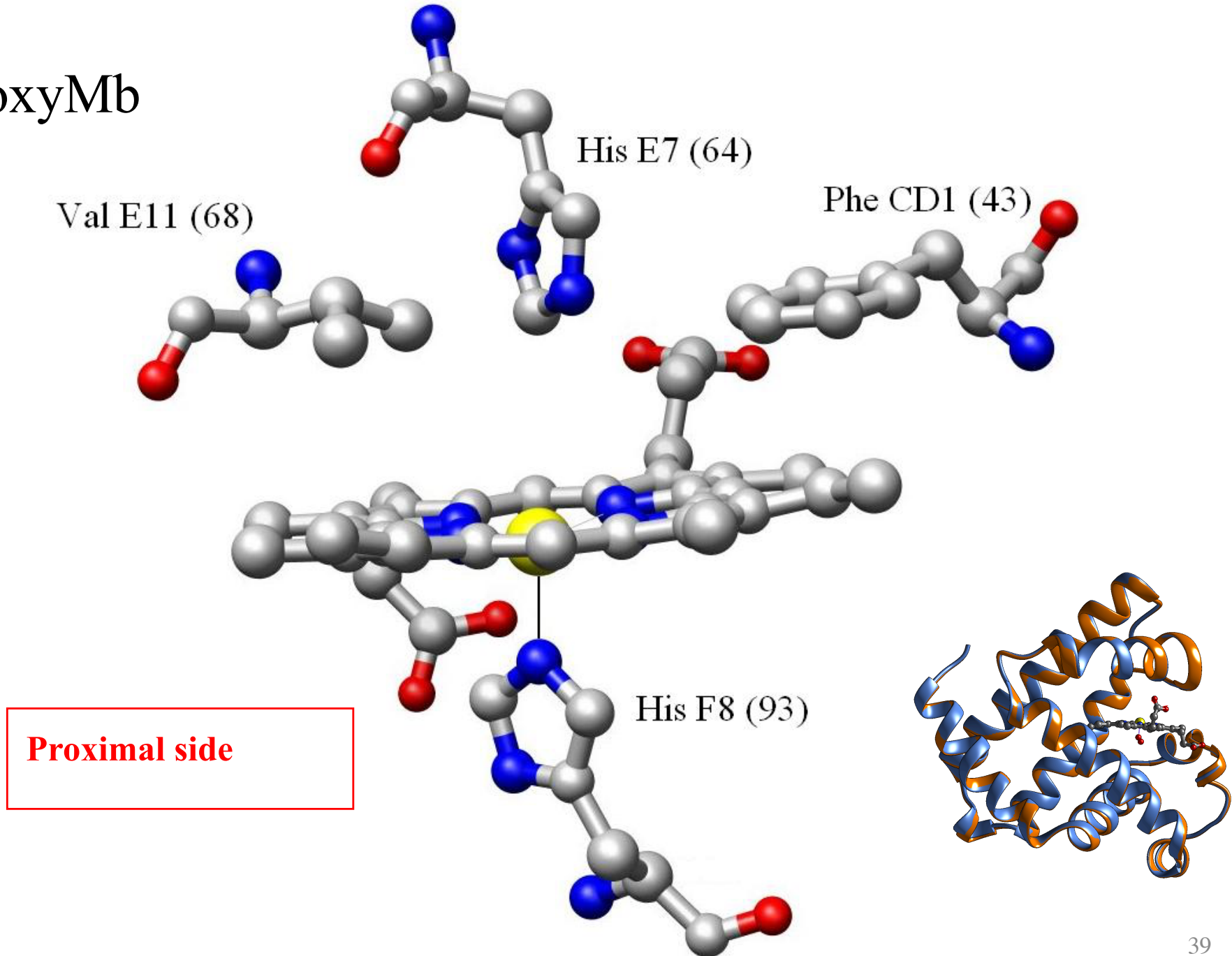
Reaction	Enzyme	$\Delta G^{\circ'}$ (kJ · mol <sup>-1</sup> )	$\Delta G$ (kJ · mol <sup>-1</sup> )
1	Hexokinase	-20.9	-27.2
2	PGI	+2.2	-1.4
3	PFK	-17.2	-25.9
4	Aldolase	+22.8	-5.9
5	TIM	+7.9	~0
6 + 7	GAPDH + PGK	-16.7	-1.1
8	PGM	+4.7	-0.6
9	Enolase	-3.2	-2.4
10	PK	-23.0	-13.9

<sup>a</sup>Calculated from data in Newsholme, E.A. and Start, C., *Regulation in Metabolism*, p. 97, Wiley (1973).

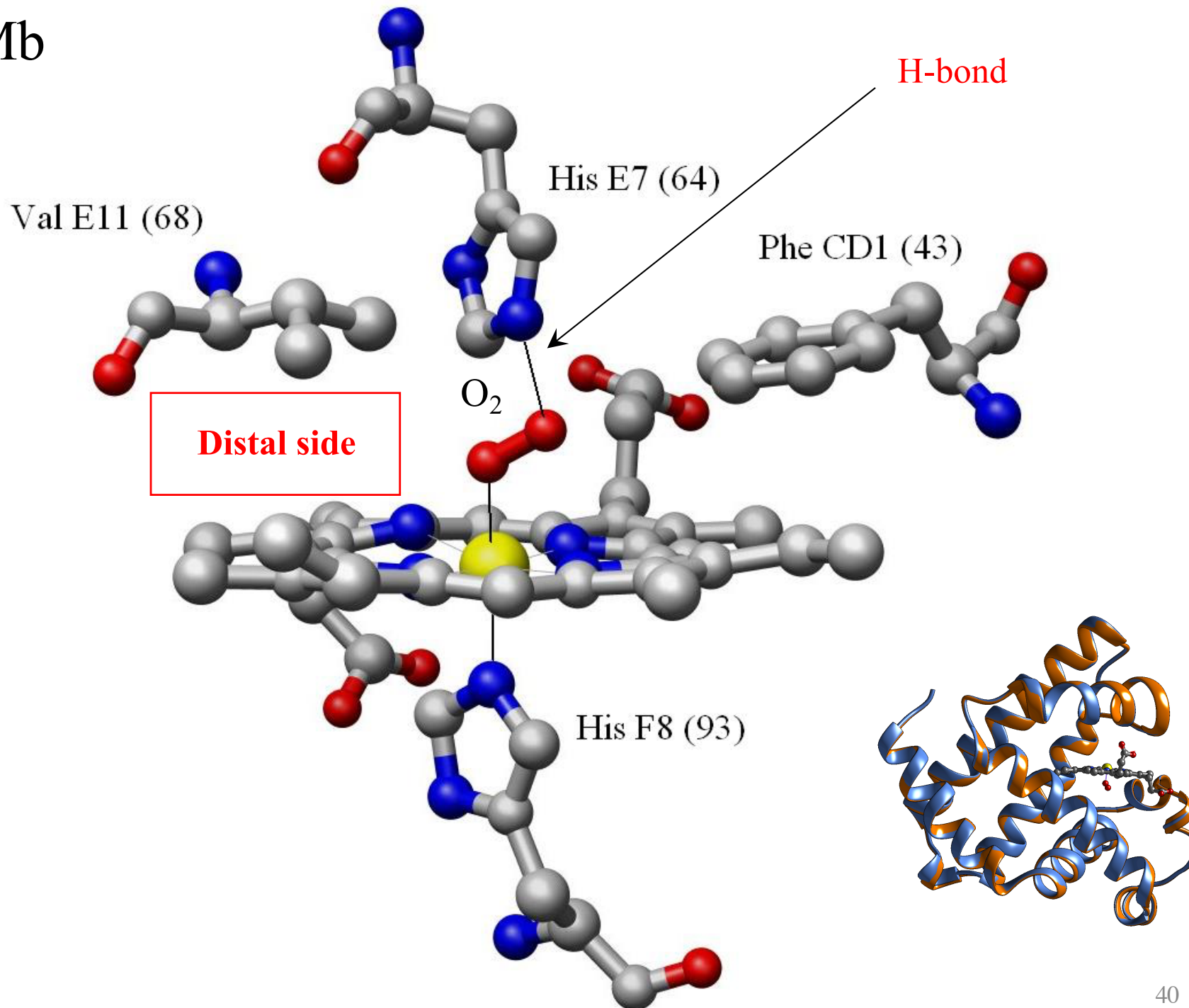


# The combination reaction of myoglobin (Mb) with O<sub>2</sub> at 25 ° C

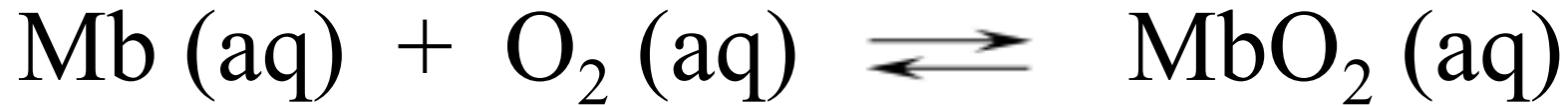
## DeoxyMb



# OxyMb



The combination reaction of myoglobin with O<sub>2</sub> at 25 ° C



$$K_{\text{O}_2} = \frac{[\text{MbO}_2]}{[\text{Mb}][\text{O}_2]} = 7.7 \cdot 10^5 \text{ M}^{-1}$$

$$\Delta G^0 = -RT \ln K_{\text{O}_2} = -8.314 \cdot 298 \cdot \ln(7.7 \cdot 10^5) = -33581.4 \text{ J/mol}$$

Note: R = 8.314 J K<sup>-1</sup> mol<sup>-1</sup>

$$\Delta H^0 = -56065.5 \text{ J/mol} \quad \Delta G^0 = \Delta H^0 - T\Delta S^0$$

$$\Delta S^0 = \frac{\Delta H^0 - \Delta G^0}{T} = -75.5 \text{ JK}^{-1}\text{mol}^{-1}$$

What is the probability of drawing 5 cards from a 52-card deck?

Tizio  
(sequence)



1 / 2598960

Caio  
(poker)



1 / 2598960

Sempronio  
(scala)



1 / 2598960

$$W = \frac{n!}{(n-r)! \cdot r!} = \frac{52!}{(52-5)! \cdot 5!} = 2598960$$

The probability of having any 5 cards is 1 in 2598960

This reasoning is valid only if, having extracted Tizio's cards, the cards are put back in the deck and re-extracted for Caio and then for Sempronio

# MACROSTATE

# MICROSTATE

# PROBABILITY



sequence  
(Tizio)



1302540 possible combinations (P = 50.1%)

one pair



1098240 possible combinations (P = 42.2 %)

two pair



123552 possible combinations (P = 4.8 %)

tris



54912 possible combinations (P = 2.1 %)



straight  
(Sempronio)



10200 possible combinations (P = 0.39 %)

flush



5108 possible combinations (P = 0.20 %)

full



3744 possible combinations (P = 0.14 %)



poker  
(Caio)



624 possible combinations (P = 0.02 %)

straight flush



36 possible combinations (P = 0.001 %)

royal flush



4 possible combinations (P = 0.0001 %)