Development of Complex Curricula for Molecular Bionics and Infobionics Programs within a consortial* framework**

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**Molekuláris bionika és Infobionika Szakok tananyagának komplex fejlesztése konzorciumi keretben

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INTRODUCTION TO BIOPHYSICS

(Bevezetés a biofizikába)

THERMODYNAMICS

(Termodinamika)

GYÖRFFY DÁNIEL, ZÁVODSZKY PÉTER

Introduction

- phenomenological thermodynamics describes macroscopic properties of physical systems
- rudiments of phenomenological thermodynamics
- materials can be characterized by thermodynamic variables
- thermodynamic state functions only depend on the state itself rather than the routes toward it
- state functions have an extremum at the equilibrium of the system

- the first law of thermodynamics reflects the principle of energy conservation and conversion
- the second law of thermodynamics reflects the principle of maximal multiplicity
- free energy determines the direction of reactions
- macroscopic properties of a thermodynamic system can be derived from atomic structure of it
- the Boltzmann-equation of entropy connects the classical and statistical thermodynamics

- physical behaviour of biological macromolecules can also be described by statistical thermodynamics

Phenomenological thermodynamics

- phenomenological thermodynamics studies processes occurs in macroscopic systems which are accompanied by heat transmission and mechanical work
- a physical system can be characterized by thermodynamic variables:
  - temperature
  - pressure
  - volume
  - amount of substance

- thermodynamic variables are not independent of each other:
  - in equilibrium, if the amount of substance is constant the state of the system can be accurately characterized by only two thermodynamic variables
- the ideal gas law describes the relationship among variables:

$$pV = nRT$$

- where *p* is the pressure, *V* is the volume, *n* is the number of moles, *T* is the temperature and *R* is the gas constant

Rudiments

- **DEF** thermodynamic system: it is under consideration
- **DEF** environment: which surrounds the system
- **DEF** open system: it can exchange both matter and heat with its environment
- **DEF** closed system: it can exchange only heat with its environment
- **DEF** isolated system: it can exchange neither matter nor heat with its environment

- **DEF** thermodynamic variables: Measures that characterize the state of a macroscopic system. Their values only depend on the state itself regardless of the route through which the system reaches it. Mathematically, they are *exact differentials*. They can be *extensive* or *intensive* properties.

- **DEF** extensive properties: Their value is proportional to the amount of substance. They are additive.

- **DEF** intensive properties: Their value does not depend on the amount of substance. They are scale-invariant.
- **DEF** state functions: They are functions of thermodynamic variables, the value of which depends only on the state at which the system stays. They have an extremum at the equilibrium of the system. Such functions are: *internal energy (U), enthalpy (H), entropy (S), Helmholtz free energy (A), Gibbs free energy (G)*

- **DEF** process functions: They are functions that describe a process carrying the system from one equilibrium to another one. Such functions are *heat* and *work.*

First Law of thermodynamics

- in mathematical form:

$$dU = \delta Q + \delta W$$

where dU is an infinitesimal change of internal energy, δQ is the heat and δW is the work

- This law claims that the energy can change due to heat transmission and work and these measures can be converted into each other.

Work

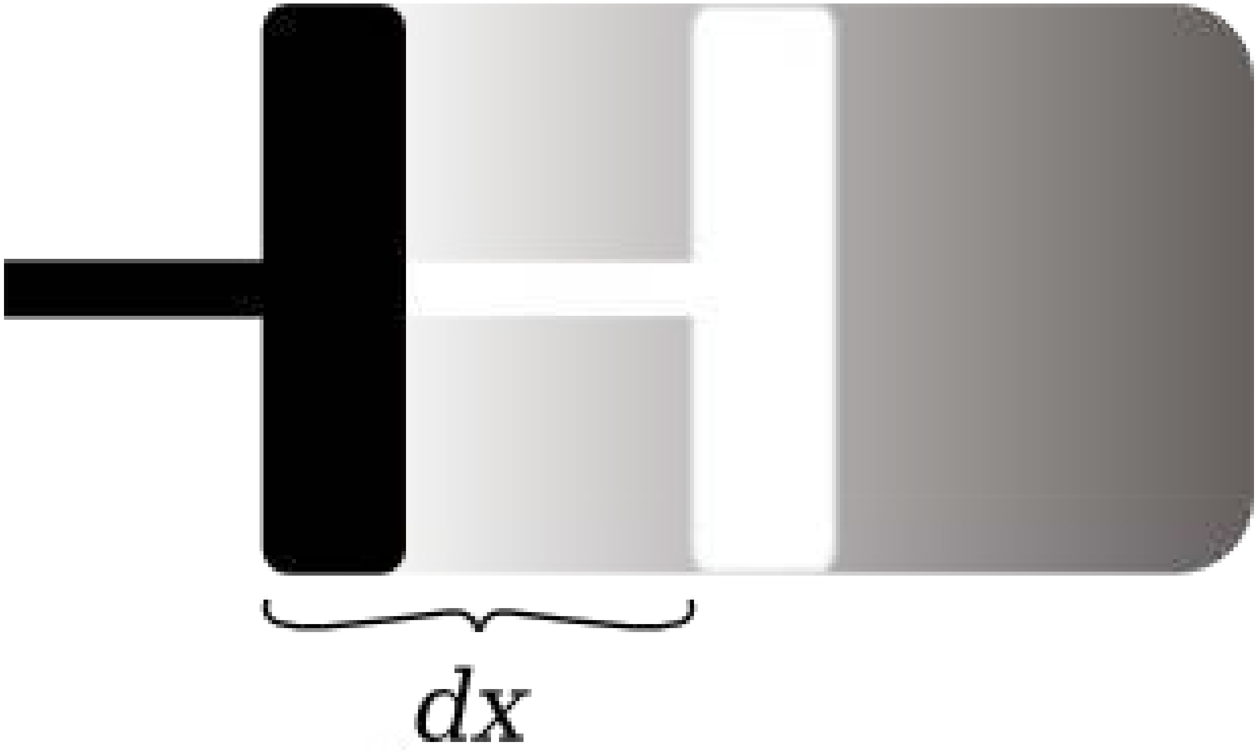


Figure 1.

- If we move the piston by *dx* (figure 1.) such that the system is in equilibrium at any time, then the elementary work we perform is:

$$\delta W = -pAdx = -pdV$$

where δW is the elementary work, p is the pressure of gas in the piston, A is the surface area of the piston and hence dV is an infinitesimal change of the volume of the gas

- the total work performed through transition of the system from p_1,V_1 state to p_2,V_2 state is:

$$W = -\int_{V_1}^{V_2} p\,dV$$

Enthalpy

- the first law if we consider only the work *-pdV* is:

$$\delta Q = dU + pdV$$

where δQ is the elementary heat flowing into or from the system and dU is the elementary change of internal energy of the system

- so at constant volume every heat we transfer increases the internal energy

- **DEF** enthalpy: A state function. Mathematically the enthalpy is:

$$H = U + pV$$

- so the first law expressed with enthalpy:

$$\delta Q = dH - V dp$$

- at constant pressure (*dp*=0*)* every heat we transfer will increase enthalpy:

$$\delta Q = dH$$

$$d(p \cdot V) = V \cdot dp + p \cdot dV$$

and after rearrangement

$$p \cdot dV = d(p \cdot V) - V \cdot dp$$

Assuming that the pressure is constant,

$$dp = 0$$

so the expression above becomes to

$$p \cdot dV = d(p \cdot V)$$

Heat, heat capacity

- if we warm a body its temperature grows and if we cool it its temperature drops
- if no work is performed then the system gains or loses *heat* proportional to the change of temperature

$$\Delta Q \propto \Delta T$$

where *ΔQ* is the total heat flowing into or from the system and *ΔT* is the change of temperature

- the coefficient of proportionality is the *heat capacity*

$$C = \frac{\delta Q}{\delta T}$$

where C is the heat capacity, *δQ* is the elementary heat flowing into or from the system and *δT* is the elementary change of temperature

- if internal energy is the function of *temperature* and *volume*, then:

$$dQ = \left(\frac{\partial U}{\partial V}\right)_T dV + \left(\frac{\partial U}{\partial T}\right)_V dT$$

- at constant volume ($dV=0$) the heat capacity is:

$$C_V = \left(\frac{\partial U}{\partial T}\right)_V$$

- at constant pressure (*dp*=0) the heat capacity is:

$$C_p = \left(\frac{\partial H}{\partial T} \right)_p$$

$$\delta Q = dU + p \cdot dV = dH - V \cdot dp$$

where *δQ* is the elementary heat flowing into or from the system, *dU* is the elementary change of internal energy of the system, *pdV* is the work performed on or by the system and *dH* is the elementary change of enthalpy of the system

$$dH = \left(\frac{\partial H}{\partial T}\right)_p dT + \left(\frac{\partial H}{\partial p}\right)_T dp$$

Because the pressure is constant, that is

$$dp = 0$$

We get the expression

$$\frac{\delta Q}{\delta T} = C_p = \left(\frac{\partial H}{\partial T} \right)_p$$

Types of thermodynamic processes

- **DEF** isobaric process: process occurring at constant pressure
- **DEF** isothermal process: process occurring at constant temperature
- **DEF** isochoric process: process occurring at constant volume
- **DEF** adiabatic process: process with no energy transfer

Carnot cycle and entropy

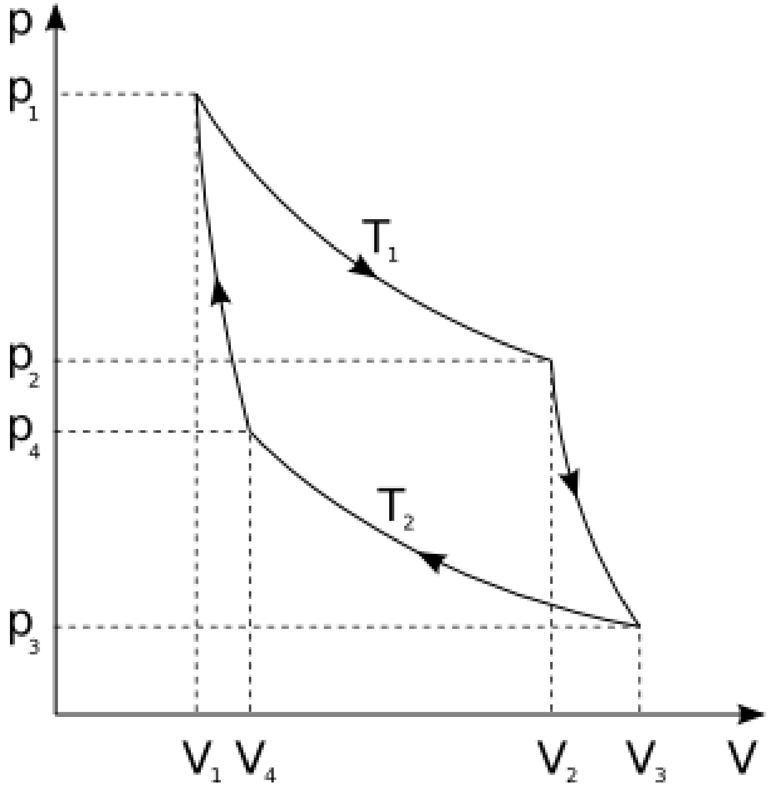


Figure 2.

- Carnot cycle consists of four steps:
  1. isothermal step from p_1,V_1 to p_2,V_2 state at T_1 temperature where the system absorbs Q_1 heat
  2. adiabatic step from p_2,V_2 to p_3,V_3 state while temperature drops from T_1 to T_2
  3. isothermal step from p_3,V_3 to p_4,V_4 state at T_2 temperature where the system loses Q_2 heat
  4. adiabatic step from p_4,V_4 to p_1,V_1 state while temperature increases from T_2 to T_1

- it can be verified that for a reversible Carnot cycle:

$$\frac{Q_1}{T_1}+\frac{Q_2}{T_2}=0$$

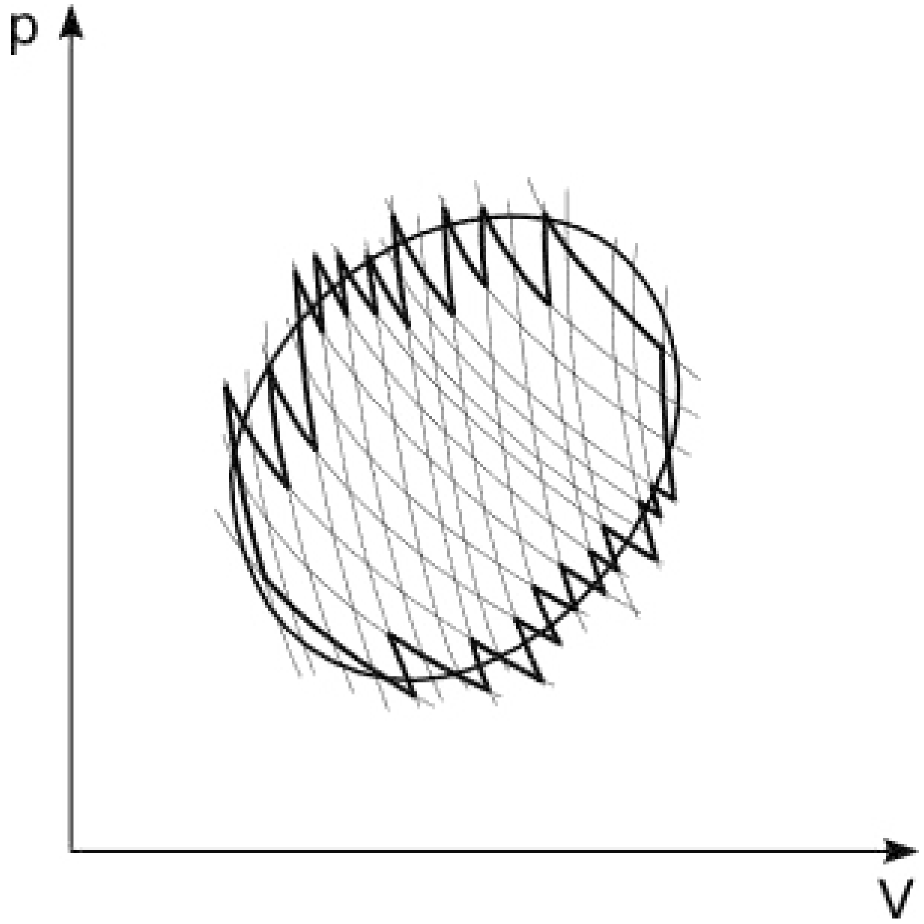


Figure 3.

- any reversible cycle on the *p-V* diagram can be approximated by several reversible Carnot cycles (Figure 3) for which:

$$\sum_i \frac{Q_i}{T_i} = 0$$

- if approximation is infinitely fine the sum transforms to an integral:

$$\oint \frac{dQ}{T} = 0$$

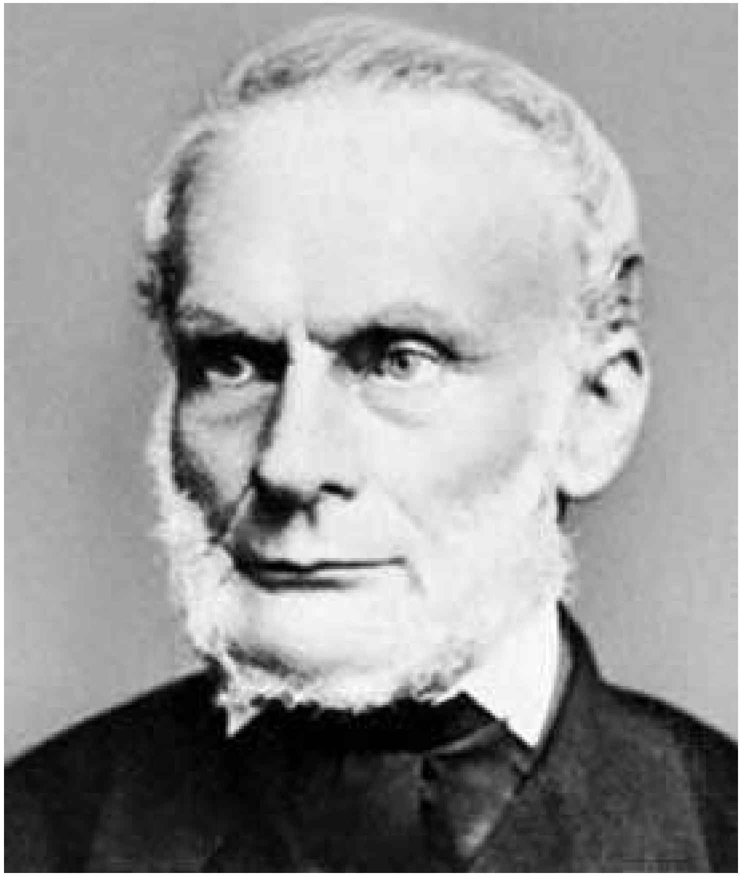
- **DEF** entropy (thermodynamic): a state function mathematically expressed:

$$dS = \frac{\delta Q}{T}$$

where *dS* is the elementary change of entropy of the system, *δQ* is the heat flowing into or from the system and T is the temperature

Sadi Carnot
(1796-1832)

Rudolf Clausius
(1822-1888)



Second law of thermodynamics

- heat can flow only from a warmer place to a cooler one
- in an isolated system, the entropy never decreases in a spontaneous process:

$$dS \geq 0$$

- equality sign applies to a reversible while > applies to an irreversible process

Thermodynamic equilibrium

- as a consequence of the first and the second laws of thermodynamics:

$$dU \leq T \cdot dS - p \cdot dV$$

- if we consider not only the pressure-volume work the equation above is:

$$dU - T \cdot dS + p \cdot dV - \sum_{k=1}^{f} X_k \, d\xi_k \leq 0$$

- where X_k is a generalized force and $d\xi_k$ the corresponding generalized coordinate

1. in the case of an isolated system where $dU=0$, $dV=0$ and $d\xi_k=0$:

$$dS \geq 0$$

so in equilibrium, the *entropy* is maximal

2. in the case of isothermal processes we introduce a new thermodynamic variable called *Helmholtz free energy* (F)

$$F = U - TS$$

the second law with the use of free energy:

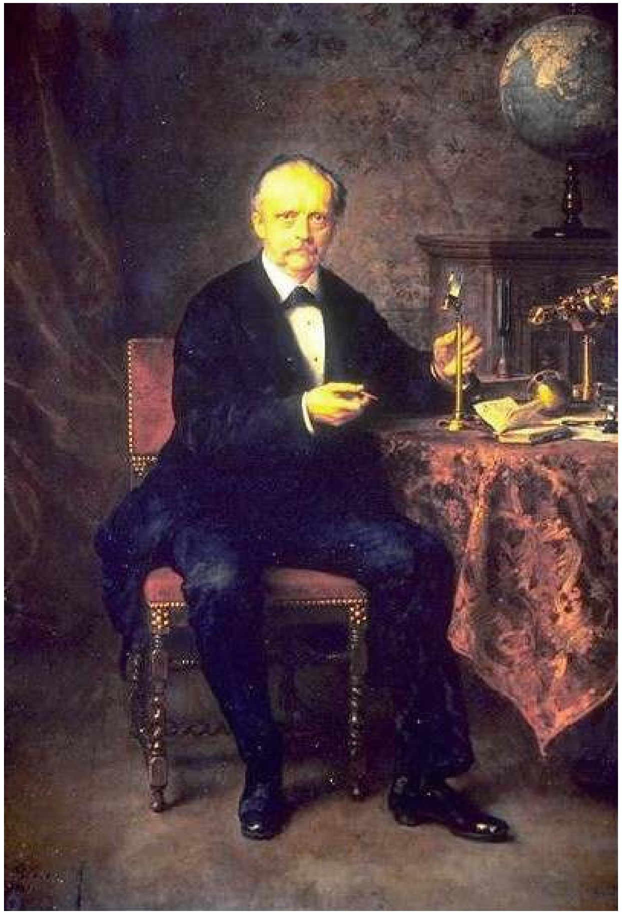
$$dF + S \cdot dT - \delta W \leq 0$$

because *dT*=0

$$dF \geq \delta W$$

so the *Helmholtz free energy* is the maximal work which can be gained from a thermodynamic process

Hermann von Helmholtz (1821-1894)



3. in the case of isothermal processes where *pressure* is also constant we introduce a new thermodynamic variable called Gibbs free energy:

$$G = H - TS$$

the second law with the use of Gibbs free energy:

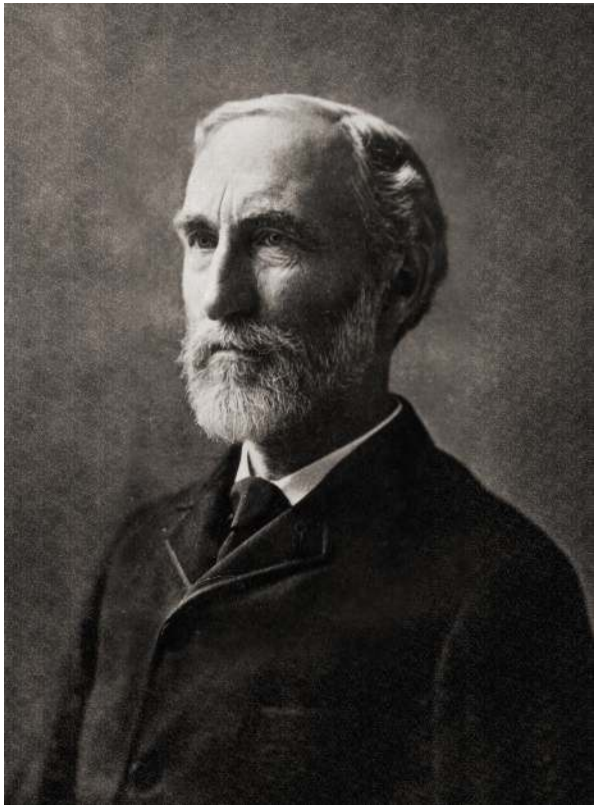
$$dG - V \cdot dp + S \cdot dT \leq 0$$

because *dT*=0 and *dp*=0

$$dG \leq 0$$

so in equilibrium the *Gibbs free energy* is minimal

Josiah Willard Gibbs
(1839-1903)



Chemical equilibrium

- let us consider a chemical reaction $A \rightleftarrows B$
- the *equilibrium constant* is:

$$K = \frac{[B]_{eq}}{[A]_{eq}}$$

where $[A]_{eq}$ and $[B]_{eq}$ denote the equilibrium concentration of the corresponding reactant or product

- the free energy change of a reaction is:

$$\Delta G_r = \Delta G_r^\circ + RT \ln \frac{[B]}{[A]}$$

where ΔG° the standard Gibbs free energy change is:

$$\Delta G_r^\circ = -RT \ln K$$

and [B] and [A] denote the current concentrations rather than equilibrium concentrations

- it is obvious that in equilibrium:

$$\Delta G_r = RT \ln \frac{[B]_{eq}}{[A]_{eq}} - RT \ln \frac{[B]_{eq}}{[A]_{eq}} = 0$$

- if $\Delta G_r < 0$ the A → B reaction occurs spontaneously
- if $\Delta G_r > 0$ the B → A reaction occurs spontaneously
- if $\Delta G_r = 0$ the system in equilibrium and no reaction occurs spontaneously

Natural variables of thermodynamic potentials

dU	$TdS-pdV$
dH	$TdS-Vdp$
dF	$-pdV-SdT$
dG	$Vdp-SdT$

Table 1

Ludwig Boltzmann
(1844-1906)

Statistical thermodynamics

- understanding phenomena of thermodynamics requires microscopic description
- fundamental principle of statistical physics is that a *macroscopic state* (macrostate) can be composed by several *microscopic states* (microstates)
- *a priori* every microstate has the same probability
- **DEF** density of states: the number of microstates at a given energy level

Boltzmann equation

- statistical thermodynamics can be connected with the phenomenological thermodynamics by *Boltzmann equation*

$$S = -k \ln \Omega$$

where *S* is *entropy*, *k* is the *Boltzmann constant* and Ω is the *density of states* (this equation is valid only in the case of *isolated systems*)

- more generally entropy is:

$$S = -k \sum_i p_i \ln p_i$$

- let ξ denote a random variable with $(x_1, x_2 \ldots x_k)$ possible values
- let $(p_1, p_2 \ldots p_k)$ denote the corresponding probabilities of $(x_1, x_2 \ldots x_k)$
- information content of specifying the value of ξ derived from the *Hartley formula*:

$$H(\xi = x_i) = \log p_i$$

where log represents logarithm of any base but the most used is 2

- so the expected value of information content when specifying any value of □ is:

$$H(\xi) = -\sum_i p_i \log p_i$$

- the equation above is called *Shannon formula*
- the logarithm can be on any base, in statistical physics $\log_e$ (ln) is used
- to gain *Boltzmann* entropy, Shannon formula is scaled by the *Boltzmann constant*, *k*

- because in an *isolated system, a priori* every microstate have the same probability, the macrostate being composed of the largest number of microstates will be the most probable one
- so equilibrium can be characterized by the maximum of entropy
- so equilibrium state is the most probable state of the system
  - it reflects the principle of maximal multiplicity

- with small but not zero probability, the system can escape the equilibrium state which explains fluctuations

Canonical ensemble

- let us consider an *isolated* system consisting of a body as a *closed* (energy transfer is allowed) subsystem and the environment surrounding it
- in the current macrostate, subsystem can be in several microstates but meanwhile current macrostate of the environment can be composed by several microstates as well, so the density of states the whole system is:

$$\Omega_{total} = \Omega_{subsystem} \cdot \Omega_{environment}$$

- the probability of a given *i* state with energy E_i according to the Boltzmann distribution is:

$$p_i(E_i) = \frac{1}{Z} e^{-\frac{E_i}{kT}}$$

where

$$Z = \sum_i e^{-\frac{E_i}{kT}}$$

the *partition function*

- total energy of the system is:

$$E_{total} = E_{subsystem} + E_{environment}$$

- let us consider the volume, the temperature and the number of particles of both the subsystem and the environment constant
- the probability that the subsystem is in a microstate with $E_{subsystem}$ is proportional to the number of microstates with energy $E_{environment}$ which can be attained by the environment

$$p_i\left(E_{subsystem}\right) \propto \Omega_{environment}\left(E_{environment}\right)$$

$$S_{environment} = k \ln \Omega_{environment}$$

$$\frac{p_i}{p_j} = \frac{e^{\frac{S_{environment}(i)}{k}}}{e^{\frac{S_{environment}(j)}{k}}}$$

$$dS = \frac{1}{T}(dU + pdV + \mu\, dN)$$

$$dV = 0 \quad \text{and} \quad dN = 0$$

$$dS = \frac{1}{T} dU$$

$$\int_i^j dS = \frac{1}{T}\int_i^j dU$$

$$\Delta S_{environment} = \frac{1}{T}\Delta U_{environment} = -\frac{1}{T}\Delta E_{subsystem}$$

$$\frac{p_i}{p_j} = \frac{e^{-\frac{E_i}{kT}}}{e^{-\frac{E_j}{kT}}}$$

$$p_i = \frac{e^{-\frac{E_i}{kT}}}{\sum_j e^{-\frac{E_j}{kT}}}$$

Statistical interpretation of free energy

- free energy of a macrostate of the whole system is:

$$F = -kT \ln Z$$

where

$$Z = \sum_{i=1}^{\Omega_{total}} e^{-\frac{E_i}{kT}}$$

- in system interacting thermally with its environment (closed system), equilibrium is characterized by the minimum of free energy (Figure 5)
- because of the equation above the partition function has its maximum value at equilibrium (Figure 6)

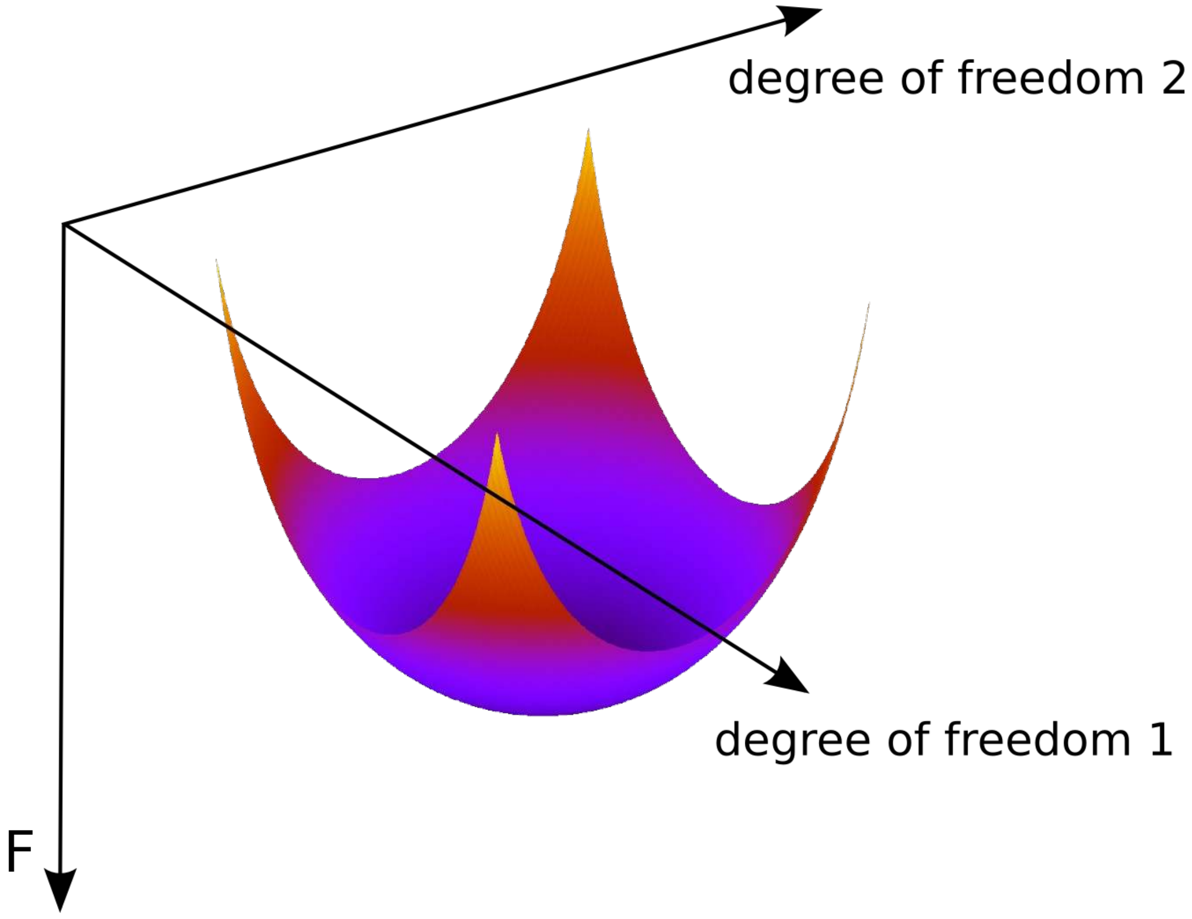


Figure 5

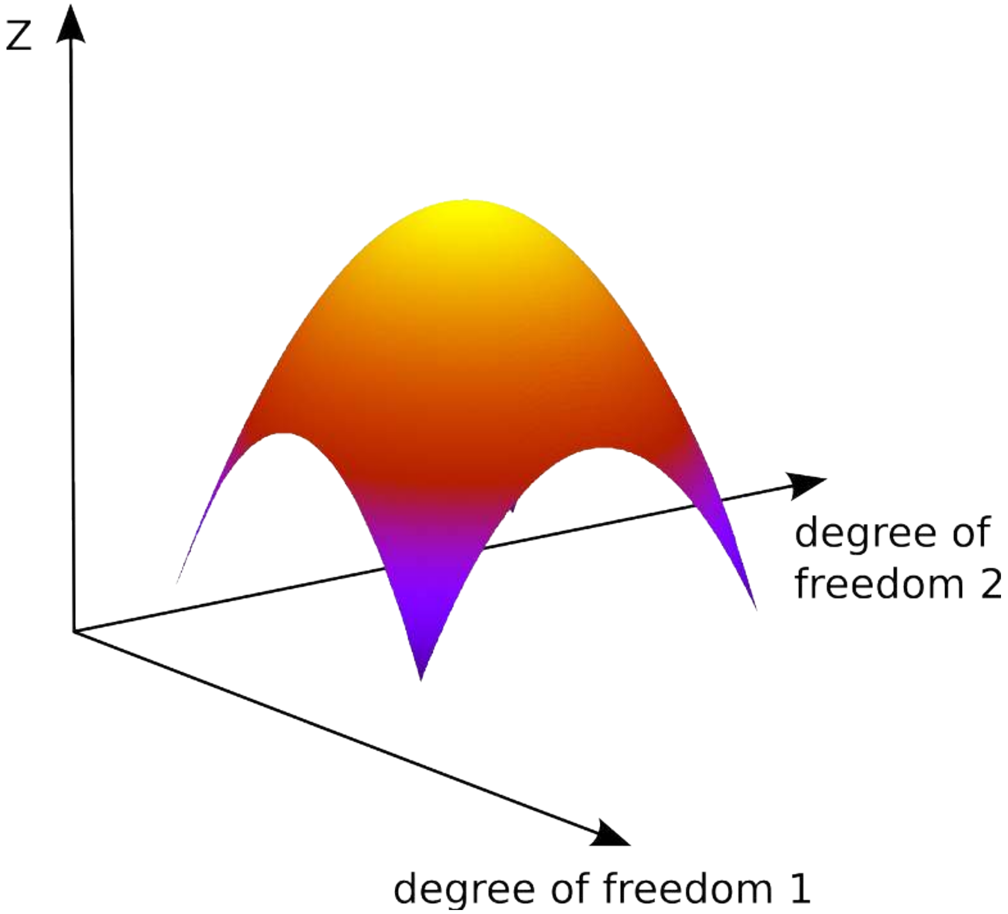


Figure 6

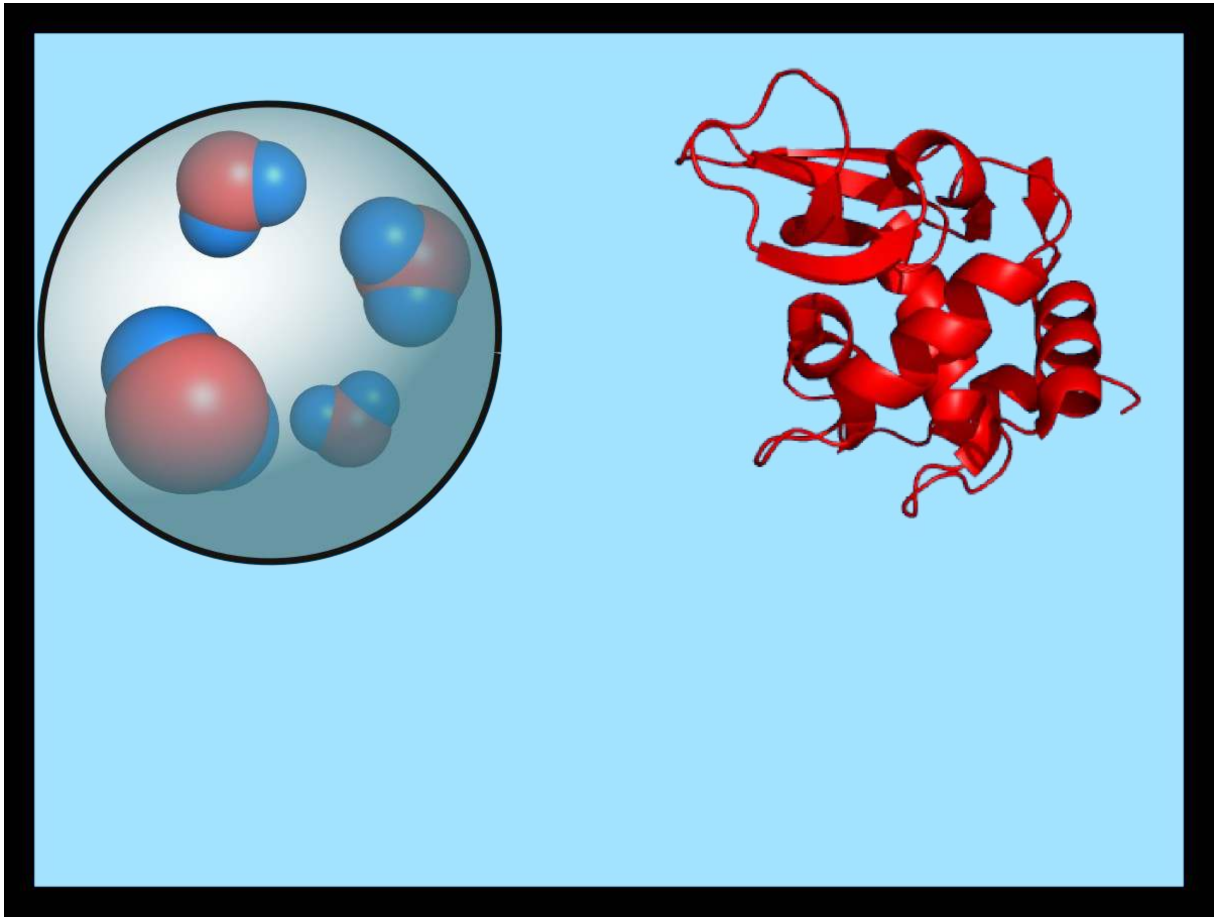


Figure 7

- in a biological example, let a protein (red in figure 7) and water surrounding the protein (visible with the help of magnifying glass in figure 7) be the subsystem
- let an environment be which surrounds the protein-water subsystem
- let us consider the whole system as isolated so neither material nor energy transport is allowed

- let degrees of freedom determining the microstate of the protein be the Cartesian coordinates of its atoms
- let degrees of freedom determining the microstate of water be the Cartesian coordinates of atoms forming water molecules
- both energy of the protein and energy of the water are a function of degrees of freedom

- the free energy of a given microstate of protein is determined by four factors:
  - energy of the protein conformation and water conformations
  - number of microstates that water molecules can attain, that is the entropy of solvent and the conformational entropy of the protein

$$E_{protein}\left(df_{p1}, df_{p2} \dots df_{pn}\right)$$

$$S_{environment}\left(df_{e1}, df_{e2} \dots df_{en}\right)$$