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On the Basics of Biochemistry (An edited and shortened version of the presentation given on 12 September 2012 in the 10th semester of the Open University of Szeged)

Biochemistry is one of the relatively new fields in natural sciences. Biochemistry is the study of the structure of living organisms and their vital processes at the level of molecules, chemical compounds and their reactions. Justus Liebig was the first scientist to describe it first in the middle of the 19th century, and he wrote about the chemical properties of living organisms in two of his books.

Figure 1. Justus von Liebig (1803–1873)

The first independent biochemistry departments, institutes and societies were founded and the first biochemistry journals launched in the first decades of the 20th century in German speaking countries followed by English speaking countries. There are two fields of sciences in the background of biochemistry: organic chemistry and physiology. Researchers in the field of organic chemistry working with macromolecules and biopolymers started to identify themselves as biochemists. Physiologists who tried to search down to the level of molecules when describing vital processes were also the forerunners of biochemists. Even nowadays, several universities have a department for molecular physiology and have the subject in the curriculum under this name.

It is an interesting issue what the development of biochemistry targets. Most probably it develops toward two further scientific fields, and they may take over the place of physiology in some generations.

Biophysics makes us possible to understand faster and more delicate changes of even smaller units with the development of the analytical approach. It is quite difficult even nowadays to draw a borderline between the two fields. "Omic" sciences will be the other option in further development due to their integrative approach and the technical development, especially in combinatorial chemistry. These sciences such as genomics, transcriptomics, proteomics, or metabolomics try to answer the essential questions of life by studying the complete DNA and RNA of the cells, tissues or the organism or studying their overall metabolic systems instead of characterizing a certain nucleic acid or protein. Processing and assessment of the unbelievable amount of data that can be gained by the new approach is possible only by the help of bioinformatics, and the systematization requires the methods of systems biology (systeomics).

During chemical, biochemical examinations of living organisms, nobody has been able to identify a compound or chemical process that could not be created or performed in non-living systems as well if the appropriate circumstances are given. Therefore, the apparent differences between living and non-living systems cannot be described by one or some chemical characteristics or substances. The essence of the difference can be found in the highly organized chemical processes and molecular systems, their regulation and adaptability.

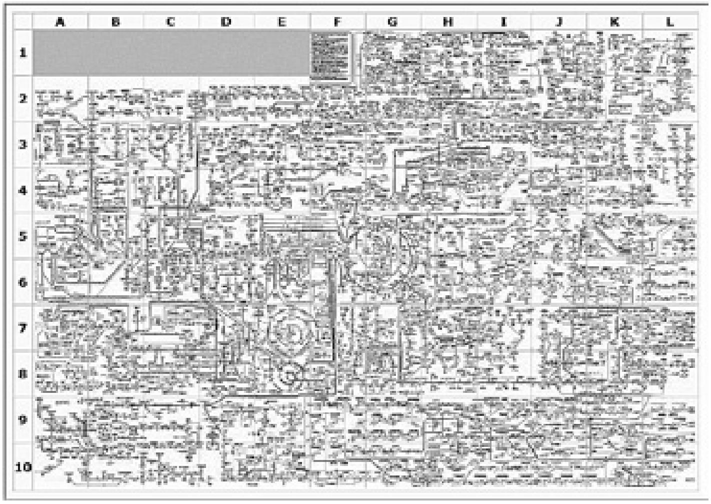
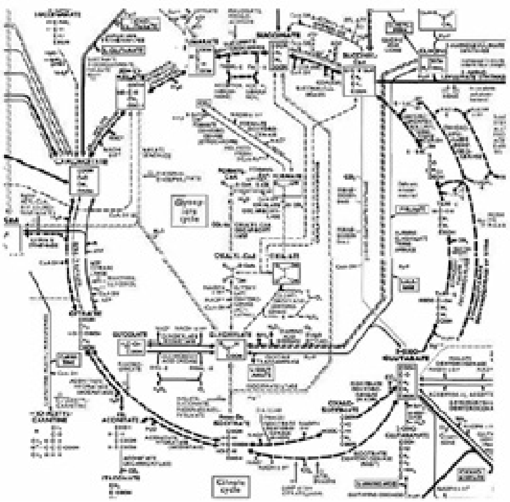


Figure 2. a) Organization of biochemical processes and metabolic pathways (http://biochemical-pathways.com)



b) The citrate cycle (http://biochemical-pathways.com)

Figure 2 presents in a simplified way the structural features of this network. It is a simplified presentation as it shows in a single plane, in two dimensions what happens in living systems based on strict structures in three dimensions. However, the role of the fourth dimension, time, should also be kept in mind as the system works differently in an infant, young adult or elderly subject, and it is different before breakfast, during meals or when doing sports. The regulation of biochemical systems are also expressed by our short and long term adaptability. An example for short term accommodation is that people in the room have their blood glucose level in the same range, except for diabetics, irrespective of the fact that they have had dinner or they will have it only after the lecture. Whereas long term accommodation refers to the different survival rate of certain groups and individuals, mainly related to the genetic variability among changing external circumstances, in the molecular-biological evolution process.

However wide and rich is the accommodation capacity of living systems, their limitations should also be considered. The amplitude or measure of the changes may exceed the limits of the survival range in case of any parameters, but the speed and frequency of the changes should not be underestimated either in determining the capacities of survival. One of the sources of risks in the modern societies is the acceleration of changes, which may reach or exceed the upper limit of the speed of accommodation capacities. Let us just remember the fact that our ancestors lived in the same cave for some ten thousand years, which covers at least 500 to 1000 generations compared to the fact that currently there are unbelievably huge changes even within the life of 2 or 3 generations in energetics, informatics, transportation or chemicalization. These changes would be hardly tolerated by people who lived 36 or 37 generations ago in the age of the Landtaking in Hungary.

Two of the most important thermodynamic features of living systems are that on the one hand, they are open systems so there is constant material, energy and information interchange between them and their environment; on the other hand, they keep up a higher level of organization, i.e., a lower level of entropy. The higher level of organization in an open system can be maintained only by continuous energy input. The oxidation of reduced carbon atoms of nutrients provides the necessary energy source to it (and to all other life functions) in both human and animal organisms, and due to our oxidizing atmosphere, it is a spontaneous process. Most of the reduction of carbon atoms with high energy need is performed by the photosynthesizing green plants during which sugars, starch or even vegetable oils are performed from carbon dioxide by the help of light energy from fusion processes in the Sun.

In the first decades of the 20th century, the basic question in bioenergetics was established about the activation that results in a reaction between the reduced carbon atom of living organisms and atmospheric oxygen. One of the positions was represented by a German biochemist, Heinrich Wieland, who considered the pre-activation of foodstuff molecules essential according to the hydrogen activation theory. Otto Warburg and his followers, however, favored the oxygen activation theory, which considered the development of a form of atmospheric oxygen with higher reactivity to be predominant.

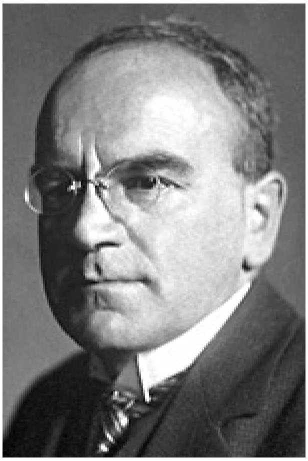


Figure 3. Heinrich Otto Wieland
(1883–1970)
Nobel Prize in Chemistry – 1927

Figure 4. Otto Heinrich Warburg
(1877–1957)
Nobel Prize in Physiology or Medicine – 1931

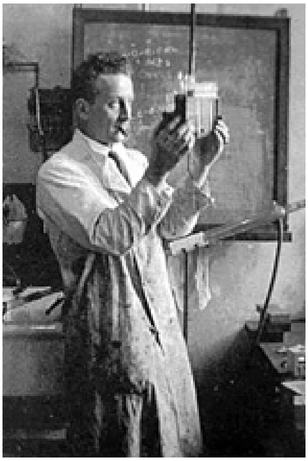
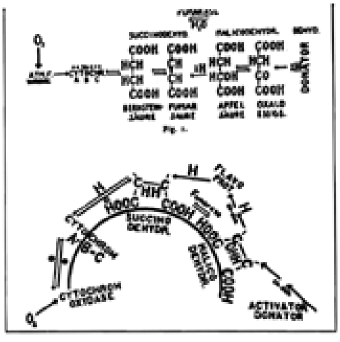


Figure 5. Albert Szent-Györgyi at the end of the 1920s

During this period of time, the young Albert Szent-Györgyi started travelling around Europe after leaving the University of Pozsony, which was taken from Hungary at the end of the war. First, he worked at the University of Leiden and then of Groningen, the Netherlands, where he revealed that the positions of the two disputing researchers (Warburg and Wieland, both of them are Nobel prize winners, too) are possible to be combined if the oxidation-reduction (redox) reaction is performed not in a single step, but being gradually performed from the more reduced carbon atom to the more oxidized form. To prove that his theory was right, he described the oxidation cycle of succinic, fumaric, malic, oxaloacetic acids, which was proven in a couple of years to be the second half of the citrate cycle. In 1937, Szent-Györgyi won the Nobel prize with special reference to the catalysis of fumaric acid.



Figs. 1 and 2 of Szent-Györgyi's Nobel Lecture.

Figure 6. Figures 1 and 2 of Szent-Györgyi's Nobel Prize Lecture

CAMBRIDGE
SZEGED

KUNGL.
KAROLINSKA
MEDIKO-KIRURGISKA
INSTITUTET
VILKET, ENLIGT TESTAMENTE, SOM DEN
27 NOVEMBER 1895 UPPRÄTTATS AV
ALFRED NOBEL
ÄGER ATT MED

NOBELPRIS
BELÖNA DEN VIKTIGASTE UPPTÄCKT, VARMED DE FYSIOLOGISKA OCH MEDICINSKA
VETENSKAPERNA UNDER SENASTE TIDEN
RIKTATS, HAR DENNA DAG BESLUTIT
ATT TILLERKÄNNA DET ÅR 1937
UTGÅENDE PRISET ÅT
ALBERT SZENT-GYÖRGYI
FÖR HANS UPPTÄCKTER RÖRANDE DE BIOLOGISKA FÖRBRÄNNINGSPROCESSERNA
MED SÄRSKILD HÄNSYN TILL VITAMIN C
OCH FUMARSYREKATALASEN

STOCKHOLM DEN 28 OKTOBER 1937

Figure 7. Certificate of the Nobel Prize in Physiology or Medicine - 28 October 1937

To show evidence for the cyclic feature of the complete citrate cycle, Hans Krebs, who was awarded by the Nobel Prize in 1953, also repeated Szent-Györgyi's fumaric acid catalysis experiment in the presence of malic acid that prevents the change of succinic acid and fumaric acid into both directions. Thus we do not make a mistake if we refer to the citrate cycle as the Szent-Györgyi–Krebs cycle at least in Szeged.

Figure 8. Sir Hans Adolf Krebs (1900–1981) Nobel Prize in Physiology or Medicine – 1953

Warburg's theory on oxygen activation was not incorrect as well. It is widely known that because of the specific electron shell structure of the oxygen molecule, especially in the presence of metals with variable valencies, it tends to produce so called oxygen free radicals, i.e., reactive oxygen derivatives, which may oxidize the reduced substances they get into contact with. It may cause the development of various diseases, or their progression, but it might be due to the normal aging process as well.

The other major reason why Szent-Györgyi was awarded the Nobel Prize has an interesting relation to oxygen activation. The discovery of vitamin C, as it is widely known, is a genuine explanation for the common observation that the cut or injured surface of the fruits and vegetables gets brownish or black. However, this discoloration develops slowly or not at all in certain crops. On the basis of this phenomenon, Szent-Györgyi suggested that the cause of the slower discoloration might be the presence of a strongly reductive agent that slowed or prevented the reaction developing in the presence of oxygen in the air. This reductive agent was identified as hexuronic acid, later renamed as ascorbic acid, and then described as vitamin C. These works are mostly related to Szeged and the paprika of Szeged.

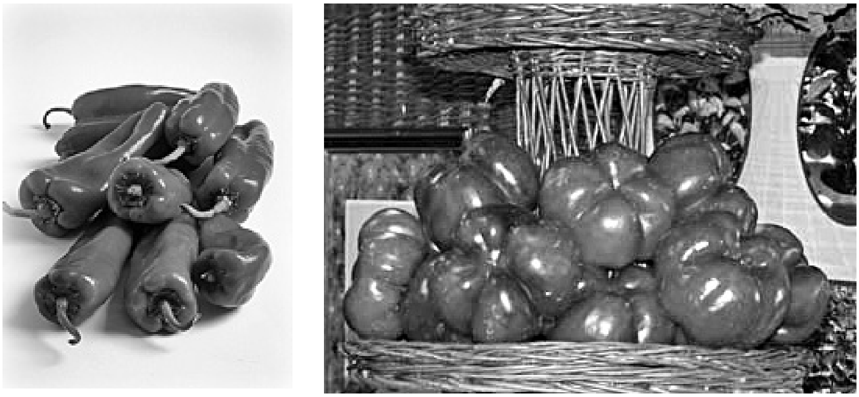


Figure 9. The paprika of Szeged

Chemical processes in living structures are almost exclusively performed in catalysis with enzymes. Catalysis makes the development of biochemical reactions possible with appropriate intensity even at a relatively low temperature specific for warm-blooded animals. Catalysis enables the decrease in activation energy, the regulation of processes, their relation to structures, the distinction between energy releasing, spontaneous (exergonic) and energy needing (endergonic) processes, and their switch if necessary. The energy adaptability of living organisms and the differentiation of energy storing and releasing processes in time and space may be due to the appearance of macroergic phosphate-binding nucleotides, primarily to adenosine triphosphate (ATP). The highly polarized phosphate group of these compounds is able to store the energy that is released during the breakdown of food. This process is the oxidative phosphorylation pathway in the mitochondria, which are the cells' miniature power plants, driven by the proton gradient power produced during respiration. The ATP energy gained in this process is utilized in chemical synthesis processes. We should also bear in mind (especially in winter time) the energy reserve that is not bound in ATP, which is responsible for the thermogenesis being essential in maintaining the constant body temperature. The biological catalysts, the enzymes are mainly proteins or protein derivatives, but it has been proven that ribonucleic acid may also employ biocatalytic mechanisms.

Living organisms are able to transform chemical energy into two other types of energy. One of them is the transport pump system playing a role in developing the unequal distribution of ions. Their mechanism is fundamental in the maintenance of electrochemical features of cells. It is the so called chemiosmotic energy transfer, which means that the gradients developed by the utilization of energy increase order in the system, and as a result they provide higher energy level and work capacity. The other type is the transformation of chemical energy to mechanical energy, which can be studied in its most developed form during muscle contraction.

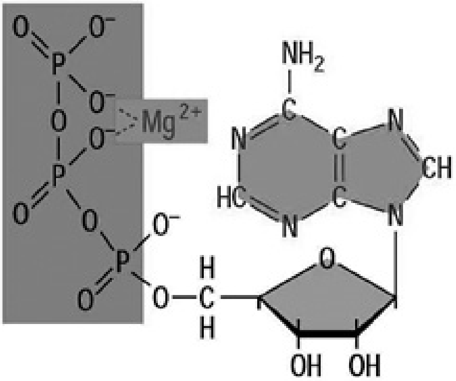


Figure 10. The molecular structure of ATP

The molecular features of it were also studied first in Szeged in the former Szent-Györgyi Institute. This research worth another Nobel Prize according to several researchers initiated the biochemical research on muscles in our

Institute. At the beginning of the 1940s, Szent-Györgyi and two of his outstanding students, Ilona Banga and Brunó F. Straub, described the explanation for the highly different behavior of the protein extracted from muscles (that they called myosin) depending on the timing of the extraction: right after the animal's death or only a couple of hours later.

While the solution of myosin A that can be obtained by fast extraction keeps its liquid form, the slowly extracted solution of myosin B becomes a gum like gel mass. The difference between the two solutions is explained by the fact that ATP present in the muscles is broken down during slow extraction, and in its absence, another protein being present permanently activates myosin. This protein was called actin, and it was first derived in its pure form by Brunó F. Straub in Szeged, in 1942. Actin is known as one of the most basic scaffold proteins in living creatures. The development of rigor mortis in the muscles can also be explained by the permanent actin-myosin interaction after the disintegration of ATP stores.

Figure 11.
Ilona Banga (1906–1998)

Figure 12.
Brunó F. Straub (1914–1996)

The last figure gives a summary of the chemistry of living organisms. One model for performing the processes with high energy uptake is that of the autotrophic organisms that are mainly green plants. They build up their simple organic compounds from basic, simple inorganic molecules such as carbon dioxide, water and minerals by the help of solar energy, and then the complex macromolecules and molecular systems are built up from them. The disintegrating processes are active even here, and part of the energy transferred during them is also utilized in the energy resources of the living organism.

The other model is the animal one, the heterotrophic metabolism, which is characteristic for the human body as well. The energy needed for build-up processes and other life functions is released by the uptake of small organic molecules and the oxidation of reduced carbon molecules in them. The living organism's energy resources are supplied by further energy release provided by the breakdown of previously built complex systems.

These systems would be able to balance the rate of oxidized and reduced forms of carbon atoms in the ecosystems. Unfortunately, this balance has been lost since the industrial revolution as a result of increased carbon dioxide emission. The reduced carbon atoms of fossil energy resources, which are also products of former photosynthesis themselves, are oxidized annually at a rate of normal reduction processes of 2000 years because of their use in the industry and transportation. The capacity of biological systems is by far not enough to reduce this amount of oxidation, especially considering that the rain forests are being destroyed, and erupting volcanoes also hinder the transfer of solar energy.

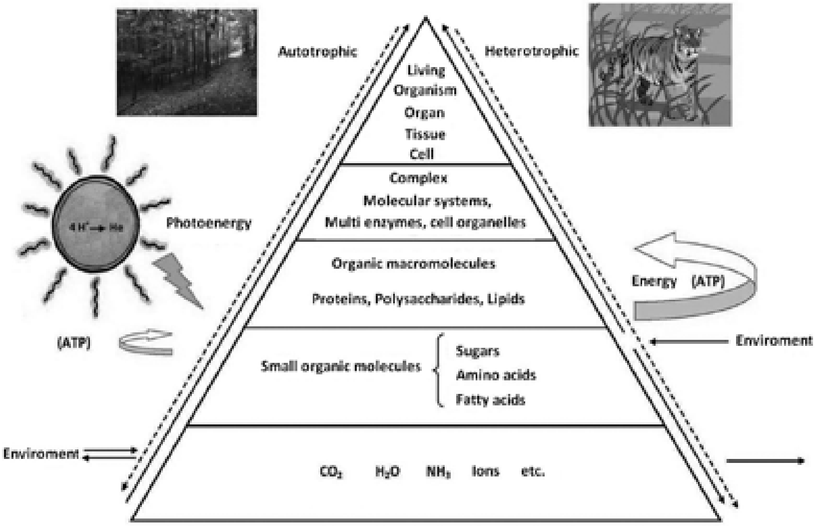


Figure 13. The pyramid model of substance and energy flow in living organisms

The end of metabolic, energy and information changes results in the death of living systems, i.e., the open thermodynamic feature of the systems are ceased, and they become isolated systems. After that no further build-up processes with high energy need are completed. However, breakdown processes are still performed. The main motive power of these processes is the entropy difference between the space occupied by the former living organism and its surroundings, and the processes will be continued until the equilibrium is reached between the two systems. Entropy balance equation, the speed at which the chaotic level of the surroundings is reached, mainly depends on the surrounding factors. In a cremated dead body, this balance equation is fully reached at the high temperature in a couple of minutes. It might not be fully reached even in thousands of years at temperatures below freezing point, or under specific pressure, moisture, or chemical conditions, as it has been seen in recent years when corpses were found in glaciers or moorland.