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BIOMOLECULAR PERFECTION AND THE „COMMON DESCENT"

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Introduction

The concept of „fundamental unity of life". The concept of „fundamental unity of life" belongs to the descriptive element of biology. It contrasts with the equally empirical concept of multiplicity and diversity of living forms. „Fundamental unity of life" means that however peculiar a biological form might be, some of its essential mechanisms are exactly the same as in the rest of the biological world. It is astonishing to realize that so different beings as bacteria, plants and men manifest several evidently non fortuitous identities.

For thousands of years man has been aware, that many behavioral traits are common to all living beings. Every living being processes matter, multiplies, regenerates, adapts to its surroundings[1]. During the last century a new, impressive confirmation and amplification of these resemblances was found on the molecular and subcellular level. One may say that the previous, rather raw concepts of nutrition, reproduction, adaptation and regeneration have been replaced by the more or less direct evidence, observable within the single living cells. So the idea of „fundamental unity of life" underwent a legitimate „reduction" to the level of biochemistry[2].

The concept of „common origin". The concept of „fundamental unity of life", when analysed in its physical nature, is closely linked with the concept of „biological selectivity". Advances in biochemistry clearly show that there is a curious disproportion between the „chemical space" and the „biologically relevant space". What does this mean?

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[1] Green *et al*. (1996/2) believe that the fundamental characteristics recognized in all living organisms *„ are only the observable characteristics of the all-important properties of living material, that is, extracting, converging and using energy from the environment".* This statement is arguable for many reasons. The meaning of the word „living material" is rather obscure. The word „energy" in the biological sense has a very, very restricted meaning. One should be aware of a crucial difference between the random rain of photons, radiating from the Sun and the ATP molecules which serve as the perfect units of the intracellular energy currency. Finally the words „using energy" are nothing more than a kind of shorthand reference to the processes of development, adaptation, regeneration and multiplication. So we are sent back to the very beginning of the problem.

[2] Cfr Crick 1992/48-49, 53; Gregg *et al*., 2003; Weiner 1999/61.

> *„The chemical compounds used by biological systems represent a staggeringly small fraction of the total possible number of small carbon-based compounds with molecular masses in the same range as those of living systems (that is, less than about 500 daltons)"* (Dobson, 2004, see also Alberts *et al.*, 1994/42).

A very rough estimation of this disproportion is close to the fraction $1/10^{60}$ (cfr Bohacek *et al.*, 1996). This enormous selectivity refers to the same assortment of small carbon-based compounds, however different the nature of a biological form might be (bacterial or human). Therefore it would be difficult to attribute this kind of selectivity to many different, random, unpredictable and erractic influences. The idea of a „common origin" – meaning a single, common, stable agency affecting all the known biological forms presses into our mind. Today the idea of „common origin" is stronger and better documented than ever before. However, it does not seem to convey the same meaning as the idea of a „common descent".

> *„Are the fundamental similarities and conserved relationships discussed /.../ due to divine intervention, or do they reflect an evolutionary relatedness?"* (Gregg *et al.*, 2003).

The authors opt in favor of the Darwinian evolution, but the two questions provoked by these *„fundamental similarities and conserved relationships"* indicate the inscrutable – at present depth of the problem.

„Common origin" vs „common descent". The idea of „common origin" – as we have said – should not be confounded with the idea of a „common descent". „Common origin" requires just *the same* cause or the same set of causes, but does not indicate what kind of cause would be adequate to explain the origin of the structures and dynamisms under consideration. „Common descent", on the other hand, means that a multiplicity (and a variety) of specimens have originated via a series of generations from a „single, common ancestor"[3]. „Generation" refers to a particular biological dynamism which, in turn, is notoriously reduced back to the common, universal, almost immutable cellular system of DNA encipherment, replication and translation[4]. In other words the idea of „common descent" is liable to be used in an imprudent, presumptuous way of explanation. It seems to be loaded with the *„circulus vitiosus"* logical error.

Besides, the idea of the „common descent" has to be evaluated in reference to

- *a limited* idea of a living form,

and in reference to

- *a generalized* idea of a living form.

A limited idea of common descent. The *limited* idea of a living form, for instance, embraces all the races of dog, including wolves, foxes, jackals and coyotes. Man, with all its li-

[3] E. g. according to the Bible all the individual human beings have a „common descent", in spite of their different racial traits.

[4] *„The enzymes of metabolism and the proteins involved in the replication and expression of genes (and of course the code) are just too similar among all known species to be of independent nonliving origin. The conclusion that all contemporary organisms must have derived from a single 'form', in whose genome the ancestral versions of all these proteins were encoded, seems inescapable."* (Doolittle, 2000).

living or vanished races may provide another example of a limited idea of living form. The limited idea of „common descent" seems sufficiently evident or at least sufficiently probable.

A generalized idea of common descent. However, if we take the *generalized* idea of a *genetic descent* common to bacteria, plants, arthropods and mammals, we enter into a vague sphere of hardly substantiated extrapolations. The question emerges why and to what extent the concept of the „fundamental unity of life" together with the idea of „com-mon origin" corroborates the generalized idea of a „common descent".

In order to analyse the relations between the ideas of „fundamental unity of life", „common origin" and the „common descent" we have first to be acquainted with some details of the modern, up-to-date concept of „fundamental unity of life".

Theobald (2004) has enumerated the main empirical data which show the „fundamental unity of life" and – supposedly – call for a „common origin" of all terrestrial biological forms of life. We have slightly modified the Theobald's list.

a) In all the living bodies, starting with bacteria and ending with *Homo sapiens*, we detect the same few kinds of polymeres (polypeptides, polynucleotides and polysaccharides), and the same chirality[5] of the monomers.

b) All known biological forms produce and utilize the same set of basic 20 aminoacids. Each one of them manifests an identical, highly selective trait, i. e. the *L- form of the α-aminoacid group*[6].

c) All known biological forms utilize a set of four nucleosides (deoxyadenosine, deoxyguanosine, deoxythymidine, deoxycytidine), to produce new copies of the enciphered messages of the DNA. Each one of them has 8 possible stereoisomeres, but only one of them is produced during the replication of the cell's DNA. This means an error-free selection of just four from the 32 chemically equivalent possibilities. It has to be added that about 100 different nucleosides occur naturally and many more have been artificially synthesized. Higly selective character of the DNA nucleosides seems therefore quite evident.

d) All known biological forms (with rather few exemptions) utilize the same set of 64 codons (triplets) to denote a given common aminoacid, the same signals „stop" (UAA, UAG, UGA), which indicate the end of the enciphered message, and the same signal „start" (AUG - for methionine, or formylmethionine).

e) All known biological form utilize the same standard, „universal" carrier of chemical energy, i. e. the ATP molecule.

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[5] The notion of „chirality" refers to stereoisomers, i.e. a number of compounds which essentially have the same structure and the same purely chemical properties but differ one from another like right-hand and the left-hand glove. *„RNA has four chiral centers in its ribose ring, which means that it has 16 possible stereoisomers – but only one of these stereoisomers is found in the RNA of known living organisms."* (Theobald, 2004)

[6] Isoleucine and threonine have a second (β) assymmetric carbon atom, so their selective production in a living cell has to eliminate three, not just one stereoisomers. About 400 different L-aminoacids occur in one species or another, but as a rule they do not enter into the structure of protein molecules. Cfr Klein, 1998.

f) All known biological forms utilize the same nanomachine (F_0F_1- ATPase) refurbishing the ATP molecules from the ADP + P_i + energy stored in the proton chemiosmotic gradient.

g) All known biological form utilize the same standard, „universal" unit of stored elementary biochemical energy and structure, *the D-glucose* which is one of 16 physically possible six-carbon sugar stereoisomers. This structural selectivity is of crucial importance, because – for instance – the important enzyme glucose oxidase processes only β-D-glucose stereoisomer. Some other stereoisomers of six carbon sugar can be also processed but the rate of this processing is 100 times lower (Dixon and Webb, 1979/243-244).

h) All known biological forms utilize essentially *the same set of enzymes and organelles* to copy (replicate) and to utilize (transcript and translate) the enciphered messages of DNA into precursors of the functional RNA and protein molecules.

The above list of the „universal traits" observed in all living forms is far from being complete. It is however sufficiently complete to demonstrate the „common origin" of the biological universe. The main point of this demonstration consists in explaining the distinction between three concepts of selectivity: physico-numerical selectivity, biochemical selectivity and biological selectivity.

Three concepts of selectivity

The purely physico-numerical concept of selectivity and its empirical source. Suppose that in a series of 40 consecutive throws with the same coin one realizes (*description I*) that the „heads" were thrown 20 times. This might suggest that *no selectivity* was present. There seems to be no evidence that „head" (H) or „tail" (T) was in a privileged situation. Apparently the „chances" were even.

Selectivity means that chances are not even. In such a case some reasons *why they are not even* have to be found. The concept of selectivity primarily refers to phenomena, not to the actual conditions or causal mechanisms which can produce a difference in the „chances". From the ontological, or metaphysical point of view a selective agent leads to the selective pattern of phenomena. However, from the epistemological, and scientific point of view a selective pattern is usually recognized first, while its causal origin is discovered only later.

Suppose now, that later, the *information* concerning the above mentioned sequence of 40 throws was enriched with more detailed description (*description II*) of the whole series:

TTHTTTTHHTHTHHHTHTHHTTTHTTTTHHTHTHHHTHTHHT

We may divide the set into two halves. The identity of both halves is evident.

TTHTTTTHHTHTHHHTHTHHT
TTHTTTTHHTHTHHHTHTHHT

Consequently, in this case, the selectivity (in the common sense of the word) is obvious, flawless, unsurpassed. No more selective set of 40 throws can be imagined. We have to add, however, what is the origin of the series under consideration. The first half of the series (20 consecutive „throws") was generated by the 'randomizing function' of the *CASIO fx-85* scientific calculator. The second half is just a man-made copy of the first half.

As we see the same „object" (the sequence of 40 successive throws) was perceived in two, essentially different way. At first no selectivity was observed. Then the maximal possible selectivity was discerned. Where the roots of this difference might be found? The first way of description consisted in a *deficient, incomplete* awareness of the object, or a disregard of some empirically evident regularities. The succession of the throws was ignored. The evident repetitiveness of the pattern was ignored.

We have to add that the perfect selectivity was discernible only by the end of the series. If we had the perfectly detailed information on the first 22 or even 24 throws, we might nevertheless be unable to detect the perfect selectivity – although it was, to a certain extent, already partially realized. We have also to underline the physical character of the event under consideration. The throws of a coin are physical events. This remark, however, applies only to the first part of the series. The second part of it does not illustrate a physical event but is the result of man's conscious and deliberate intervention[7].

The repetitiveness of physical structural patterns or events requires a nonrandom set of physical causes. In other words a kind of a „cheating" super-cause, correlating the individual throws within the set is to be postulated. The „cheating super-cause" introduces *constraints in favor* of some, or *against* some other events. The „cheating" does not produce anything „above", or „beyond" the physical nature of event, but it makes the purely physical nature of relations „shrink" to a more or less „narrowed" end product.

The numerical concept of selectivity, however, does not reveal the full meaning of the biological selectivity concept.

Biochemical concept of selectivity. Dobson (2004) has introduced two, very useful concepts, which help to describe the idea of „biochemical selectivity". He distinguishes between the *'biologically relevant chemical space'* and the *'complete chemical space'* (Dobson, 2004). The term „chemical space" in Dobson's text has at least two different layers. The lower one refers to the micromolecular biological material (a micromolecule weights less than 500 daltons[8]). In the whole biological sphere fewer than 10^4 different micromolecules were discovered. However, from the purely chemical point of view there are some 10^{60} possible forms of the organic molecules. Biologically relevant micromolecules constitute, therefore, an insignificant part of the „complete chemical space".

If we climb on a higher level of biological complexity, i.e. on the level of protein molecules, the distance between the „biologically relevant chemical space" and the „complete chemical space" is even more dramatic. The selectivity on this level is about 10^5:10^{390} (Dobson, 2004).

This enormous level of selectivity calls for an explanation. Within the living forms we observe an evident *limitation* of the purely mineral dynamism.

> *„Constraints are restrictions within the realm of the physically possible. /.../ Constraints, then, refer to conditions that prohibit the realization of certain states or events, even though they are physically possible."* (Schlosser, 2004).

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[7] This „numerical" example might be replaced by a biological one. Imagine a complex random pattern of the sea bottom. It represents the first half of our series of throws. Suppose a flounder lying on this bottom, copies its random pattern, to make itself „invisible".

[8] Dalton = the weight of the hydrogen atom less the weight of a single electron.

The enormous selectivity within the macromolecular, biological sphere turns our attention to the *„conditions that prohibit the realization of certain states or events, even though they are physically possible."* The universal and perfect repetitiveness of some elements of the biochemical sphere requires a postulate of *the same set of constraints* in every single case. In other words, there is no reason to look for a different explanation in the numerically different cases. That is what the Ockham's Rule is about. But even the Dobson's idea of „biologically relevant chemical space" does not seem adequate in the attempt to give justice to the selectivity of biological forms of dynamism.

Biological concept of selectivity. Truly biological dynamism is not limited to the level of the relatively simple organic compound. It is not limited to the level of the relatively complex polymeres, and polymere macromolecules. Even such a complex chemical structure as rybosome[9] is not a truly biological object if considered apart from many other cellular structures and without a reference to the whole dynamic pattern of a cell behavior. Therefore the most primitive *biological* concept of selectivity cannot be founded on something less than the numerical pattern representing the dynamism of a single generation, meaning *a single, complete life cycle* (cfr. Plaxton, 2004).

Penny and Pole (1999) have made a step forward in the search for an adequate description of a biological being. The problem of „fundamental unity of life", in their opinion, is reducible to the concept of „the last universal common ancestor" (LUCA).

> *„The last universal common ancestor (LUCA) is the organism at the root of the 'tree of life' the ancestor of all organisms alive today. /.../ An interesting picture of the LUCA is emerging. It was a fully DNA and protein-based organism with extensive processing of RNA transcripts by RNPs /.../ It had an extensive set of proteins for DNA, RNA and protein synthesis, DNA repair, recombination, control systems for regulation of genes and cell division, chaperone proteins, and probably lacked operons."* (Penny and Poole, 1999)

The advantage of the LUCA concept seems to be this. It puts together all the structural conditions which, at present, seem absolutely necessary for a cell to survive. Nobody tried to calculate the numerical expression of the selectivity proper to the LUCA concept. The LUCA concept – in our opinion – is still far away from the apt description of a true biological being. Essentially it is a *structural* concept. Penny and Pole seem to believe that chemical structures, DNA molecules, protein molecules are the primary dynamic agents of the LUCA „organism". In other words a set of „organs" (micro-organs) is substituted for the true biological activity, i. e. the organogenesis (micro-organogenesis). Even the most elementary, primitive life cycle consists in the micro-organogenesis. Life means not just functioning or „robots", but it means producing, repairing, adapting the structures which serve as the „tools" of the biological dynamic form.

A truly biological concept of selectivity, therefore, should embrace both the spatial

[9] The *Escherichia coli* rybosome weights 2.700.000 daltons and is composed of some 55 different aminoacid polymeres, and three different RNA polymeres. Only one of these RNA polymeres (16S rRNA) is a polymer of 1542 rybonucleotides. A really rudimentary way of calculating its chemical selectivity gives the number $1/10^{928}$. A calculation of selectivity which would embrace all the components of the ribosome would give a number incomparably more astounding.

and temporal aspect of a life cycle. At present, however, our knowledge of life cycles is deficient even in the case of the simplest bacterial form. Consequently the available concept of biological selectivity should be conceived as a slowly developing awareness of the true, actual biological selectivity. Every new generation of biologists will have a more developed awareness of this selectivity.

The concept of „biological selectivity" (and not just a physical or biochemical selectivity) is to be introduced in order to prevent the deliberate conceptual omissions of the evidence, relevant to the processes of life. It should not be considered as a purely numerical value, but as an open awareness of the multiple levels and instances of the evident and qualitatively complex selectivity within a *life cycle* (which is the primary, absolutely indivisible unit of life). This awareness starts with simple organic compounds such as aminoacids, sugars and nucleosides. It develops with the evidence concerning the macromolecules and cell organelle. It increases with the organellogenesis and behavioral dynamics of the cell. The more complete is our biological knowledge, the more manifest is the amazing selectivity of life's dynamism. The attempts to put it into a numerical form usually stop at the rather low, fragmentary structural elements of the essentially dynamic pattern of life. The numbers such as $1{:}10^{500}$ or $1{:}10^{5000}$ are a far cry from the real, exquisite selectivity of a living cell.

Let us give us another example of the contrast between some physico-numerical expressions of selectivity and the real selectivity of life. The content of phosphorus (P_i) in the marine water is about 0.000007%. In the bodies of the marine crustaceans this content raises to the level of 0.13% (Mizerski, 2003/11). The concentration increases almost 20,000 times above the original concentration of P_i in the seas and oceans. It is obvious that these organisms have to select the P_i compounds from their surroundings. Someone might be impressed. But the actual selectivity of the cellular structures and dynamisms which achieve such a concentration cannot be numerically imagined.

The average concentration of P_i in the oceans.

⬇

20,000 times higher concentration of P_i in the marine organisms.

⬇

A set of the subcellular microstructures (nanomachines) which serve to attain this high level of P_i concentration.

⬇

The cellular dynamism producing, repairing, and adapting the nanomachines.

If one realizes that a simple bacterial cells, within an hour, produces hundreds of different and highly specific and perfectly functional macromolecules, and that the selectivity of this biosynthesis is close to 100%, then one may understand why the numerical language sufficient to measure the structures of the astronomic universe is too simplistic and inappropriate to describe the universe of a simplest living being (cfr. Lenartowicz, 1997).

Now we are ready to rephrase the previous, „raw" concept of the „**F**undamental **U**nity of **L**ife" (FUL), and the intellectual challenge it provokes.

The more detailed idea of FUL has two „sides". On the *descriptive* side an unimaginable selectivity of some intracellular structures is evident. On the *theoretical* side, a need for an integrated, coherent explanation of this selectivity is yawning.

Analysis of the „evidence" for the FUL

The evidence for fundamental unity of life (or „common origin") has to be sorted out. It seems that at least four different forms of the „global" unity can be distinguished.

a) One is the utmost *perfection* of some structural and dynamic „solutions" observable within any specimen of living being.

b) Next is the evident *standardization* of some elementary „solutions" upon the subcellular, biochemical level.

c) Another one is the evident identity of some *developmental signals* (homeoboxes and their products).

d) Finally it seems that one has to take apart a great number of biochemical structures which serve as *identification labels* (antigenes).

Let us reflect a little upon these four kinds of evidence involved in favor of the FUL concept.

Ad a) Biochemical *perfection* refers to the precision of a dynamism and its quantitative economy in terms of material and energy utilized. Perfection implies that a given „perfect object" cannot be improved in its efficiency, dynamic precision and economy. In this paper we will reflect upon a couple of such „perfect objects" and the theoretical consequences of this perfect pattern.

Ad b) Biochemical *standardization* means that within the living forms some structures are built in such a way that they fit into the biochemical machinery of any other living form. This refers not only to the structural aspect of these standardized structures but to their energy load as well. The idea of biochemical standardization will be discussed in a separate paper.

Ad c) Chemical signaling within a living body constitutes quite a distinct topic. There is a certain and rather odd identity between these signals produced in the apparently unrelated forms of life. Yet this seems to have nothing to do with the perfection and standardization phenomena. It will be discussed in a separate paper.

Ad d) Finally we have to do with the chemical markings which help to distinguish the elements of our own body from some „alien molecules". These „identification marks" are signaling nothing. Therefore they have to be analyzed separately.

Dynamic perfection vs „fundamental unity of life"

As we have seen, the concept of „fundamental unity of life" is founded on some fragmentary identities of biochemical structures. These structures are entangled within an integrated, much more complex and unimaginably more selective context of a single „generation", i. e. a single „life cycle". However, these „universally common" traits demonstrate so evident character of selectivity that a hypothesis of a „common origin" seems inevitable. Let us now reflect on a concrete example of the „universally common trait". The analysis of this example will illustrate the idea of *biochemical perfection*.

The concept of *perfection* is well known in the arts. There, it usually refers to paintings or sculptures estimated as *unimprovable.* Something is perfect if it cannot be further improved. Many paleolithic artists had a capacity for creating cave paintings which no other artist could have improve. It means that taking into account the circumstances (the unpolished, rough ceiling of a cave) and the pigments available, the paleolithic artist created, for instance, a perfect, unimprovable sketch of a bison.

Technical kind of perfection is also founded on the idea of unimprovability. A good illustration of this provides the most famous of Leskov's short stories, *„The Steel Flea"* (1881). The tsar of Russia during his visit in London, received as a gift a microscopic dancing flea made by English blacksmiths. Back home, tsar ordered this work of art to be improved upon in order to show that Russian products are the best. A Russian blacksmith, using nails invisible to the naked eye, contrived to shoe the dancing steel flea. The nails and the shoes, unfortunately, weigh the flea down; it was no longer able to dance[10]. The technical perfection of a structure or a dynamism means that nothing can be added or removed from it, without an essential decrease in its functioning.

The biological and biochemical instances of perfection can be quite various. Perfection of a nest woven by the *Ploceidae* bird, the perfection of mimicry of the hatchet fish *(Argyropelecus aculeatus)*, perfection of the bombardier beetle defence system may help us to realize how diverse is the dynamism discussed under the same label of „perfection". We have to select an example which fulfills two conditions: (1) it reveals a perfect dynamism and, at the same time, (2) it belongs to the relatively narrow group of the traits which are „universally common." We have therefore to limit ourselves to the level of subcellular dynamisms. There the phenomena leading to the concept of „fundamental unity of life" are the most evident. As an illustration of the subcellular, macromolecular, biochemical perfection we have selected the ATP synthase (Fig. 1). Its name means that it synthesizes ATP, a high energy compound. ATP is a sort of a universal chemical energy unit, or universal chemical energy currency, which can be utilized as a fuel whenever a living cell requires an input of energy.

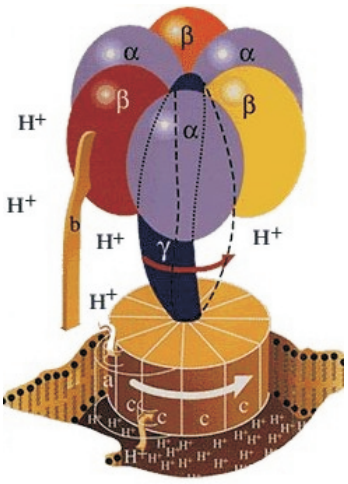

Fig. 1. A very much simplified representation of the hydrogene ATPase's structure. The rotational engine (F_0) – lower part of the picture – is driven by the chemiosmotic gradient of H^+, and this results in the rotation of the shaft γ (black). The upper (F_1) part of the molecule consists of three identical catalytic segments (αβ) in which the mechanical energy of rotation of the shaft γ is changed into the chemical energy of the ATP molecule. The F_1 can act as a motor, utilizing the energy of ATP hydrolysis. In that case the movement of the shaft forces the reverse rotation of the F_0 subunit, pumping H^+ across the intracellular membrane, which results in increasing the chemiosmotic gradient of H^+. This double-engin complex is working in many biological forms, most probably in every one of them. *Based on materials from the 1997 Nobel Poster for Chemistry. The drawing by Kjell Lundin.*

[10] Leskov Nikolaï Semenovitch (1831-1895) <http://www.gbrussia.org/archive.php?id=98>

„Adenosine triphosphate synthase (ATP synthase or F_1F_0 ATPase) is the universal enzyme in biological energy conversion that is almost three billion years old and is present in the membranes of mitochondria, chloroplasts and bacteria with amazingly similar structure and function in different species." (Nath *et al.*, 2000).

„The importance of ATP can be seen in the fact that every organism on earth uses it – from single cell bacteria to complex, multicellular organisms like plants and animals. Indeed, ATP production was probably one of the earliest cellular processes to evolve, and the synthesis of ATP from two precursor molecules is the most prevalent chemical reaction in the biological world." (Reed, 2002).

ATP synthase.

„ATP synthase comprises two rotary motors in one. The F_1 motor can generate a mechanical torque using the hydrolysis energy of ATP. The F_0 motor generates a rotary torque in the opposite direction, but it employs a transmembrane proton motive force. Each motor can be reversed: The F_0 motor can drive the F_1 motor in reverse to synthesize ATP, and the F_1 motor can drive the F_0 motor in reverse to pump protons. /.../ ATP synthase is unique amongst proteins in that it embodies two of the major cellular energy transduction mechanisms. F_1 can synthesize ATP, but it can also hydrolyze ATP to operate as a motor. F_0 can convert a transmembrane ion gradient into a rotary torque, or it can be driven in reverse to perform as an ion pump." (Oster and Wang, 2000)[11].

What is so perfect, so unimprovable, in the mechanism of the ATP synthase? Its perfection consists in its *efficiency*, in its *adaptability* and in its *miniaturization*.

The efficiency of the F_0-F_1 ATPase. The high efficiency of a biological dynamism means that a living form can work in the practically isothermal conditions. The inevitable increase in the enthropy of the system is remarkably low. During the cell's enzymatic or motor activity the loss of the utilizable energy is reduced to a nearly absolute minimum. The ATP synthase outruns all the previously known enzymatic structures. The efficiency of the – F_0-F_1 ATPase is unimprovable – i. e. perfect in a very concrete, measurable sense of the word. It was the measured level of the efficiency which indicated the road for further research and which has limited the sphere of the plausible hypotheses.

„The near 100% mechanical efficiency dictated extraordinary tight coupling between the chemistry and mechanics. This was a key constraint in analyzing the mechanism, for it forced the assumption that the binding energy of the nucleotide was translated into elastic strain, and the remainder of the cycle released this strain energy to drive rotation." (Oster and Wang, 1999)

This efficiency is so high that an observer cannot restrain his admiration. This is pretty obvious if one considers the wording of the strictly scientific reports.

„/.../ we summarize the breakthroughs in the elucidation of the structure of F_0 F_1-ATPase/synthase, and relate this information to previous and new kinetic

[11] In 1997 Paul D. Boyer and John E. Walker have received the Nobel Prize in chemistry for their elucidation of the enzymatic mechanism underlying the synthesis of adenosine triphosphate (F_0-F_1ATPase), together with Jens C. Skou, who has discovered the functioning of an ion-transporting enzyme, Na^+, K^+ – ATPase.

mechanisms and bioenergetic considerations. The emerging picture of ATP synthase is nothing less than fantastic: a rotary engine of high efficiency. /.../ As if we were not impressed enough by the structural complexity of ATP synthase, we have recently learned that it functions like a rotary engine! /.../ The mechanism of proton translocation is a good example of the wonderful inventiveness and economy of nature." (Nagyvary and Bechert, 1999).

„*Our understanding of how biomolecular motors function and of their role in the machinery of the cell is advancing rapidly. As we learn more, the wonderful complexity and effectiveness of these motors as part of cellular networks become all the more impressive."* (Karplus and Gao, 2004)

„Natural processes are extremely efficient in terms of energy and material usage and provide us with many inspiring and thought provoking designs and principles.
These bio components offer immense variety and functionality at a scale where creating a man-made material with such capabilities would be extremely difficult. These bio components have been perfected by nature through millions of years of evolution and hence these are very accurate and efficient. As noted in the review section on Molecular Machines, F_1-ATPase is known to work at efficiencies which are close to 100%. Such efficiencies, variety and form are not existent in any other form of material found today."
(Ummat *et al.*, 2004)

The adaptability of the F_0-F_1 ATPase. Adaptability means, that a biological (or a technical) entity manifests a relatively constant level of efficiency and economy within a relatively broad range of the changing external conditions (cfr. Koszteyn and Lenartowicz, 1997).

Biological adaptability has two forms. The *physiological* adaptability consists in a specific, adaptive dynamism, without any structural modification. A good example of this is the complex system of the iris which helps to keep a relatively constant level of the illumination of retina. In the process of physiological adaptation an amount of free energy is utilized, but no structure is built or destroyed (except the hydrolysis of the ATP molecule).

The *developmental* adaptability requires a structural modification of the elements involved in this process. The change of the density of fur occurring in autumn in many species of mammals[12], or the change of a caterpillar body into the butterfly body, may illustrate the concept[13]. The adaptability of the F_0-F_1 ATPase fits into the first category.

The two rotary motors of the ATPase are utilizing different principles of physical dynamism, different sources of energy and different kinds of energy. The results of their activity are also different.

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[12] A tiger's fur density varies based on climate. The Sumatran tiger has ~1,700 to 2,000 hairs/cm^2 while the winter coat of the Siberian tiger has as many as 3,000 to 3,300 hairs/cm^2 (Walvekar, 2000-1).

[13] The embryological stage of the life cycles cannot understandably manifest a physiological kind of adaptation. The adaptive organs, like the system regulating the diameter of the pupil, are still under construction.

The F_0 motor is running on the chemiosmotic gradient – the electrochemical proton gradient. So, a sufficient level of the gradient constitutes a condition of its activity. The F_1 motor runs on the chemical energy stored in the ATP molecules. A sufficiently high concentration of this molecule is a condition of its activity.

The two motors cannot work at the same time.

When the concentration of the ATP molecules is high, the F_1 motor utilizes their energy and forces the F_0 motor to rotate. In this way it pumps the H^+ ions (or protons) across the inner membrane in which the ATP complex is assembled. This results in a rise of the intermembrane chemiosmotic (H^+) gradient. The ATP molecules are depleted. The concentration of the ADP + P_i is rising[14].

When the intermembrane proton gradient is high, the F_0 motor forces the F_1 motor to rotate, and to synthesize new molecules of the ATP from the ADP and P_i material.

The perfect functional adaptability of the F_0-F_1 ATPase consists in its automatic capacity to switch from one kind of activity to another – depending on the circumstances.

It has to be added that the ATP synthase's dynamism is coupled with some other complex systems which either increase the chemiosmotic gradient (utilizing, for instance, the energy of sunlight), or liberate the energy stored in the β-D-glucose molecules. This energy is then converted into the ATP molecules.

In different biological forms some differences in the structure of F_0-F_1 ATPases were observed.

> *„While 10 identical subunits (c_{10}) compose the transmembrane rotor of yeast ATP synthase, the rotor of Ilyobacter tartaricus exhibits 11 subunits (c_{11}), and the rotor of spinach chloroplast ATP synthase is assembled from 14 subunits (III_{14})."* (Müller *et al.*, 2001)[15]

The dimensions of the F_0-F_1 ATPase.

> *„Molecular and biochemical studies revealed a complex subunit composition of the enzymes, and recent studies gave fantastic insights into the three-dimensional structure of F-ATPases. These enzymes work as molecular rotational motors, the smallest found in biology."* (Müller and Grüber, 2003)

ATP synthase is a macromolecular complex, which looks like a very short bludgeon. Its thicker part (called F_1) has a diameter of some 10 nm and a molecular weight of about 400 kDa. Its narrower part (called F_0) ATP has a molecular weight of about 100 kDa[16]. The length of the whole is not much above 15 nm. It is the smallest of the known rotating nanomachines[17]. The diameter of the ATP synthase is just about 50 times greater

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[14] In Nath *et al.* (2000) one, who is not a professional chemist, can find an intuitively very clear and detailed description of the main principles operating in the ATP synthase.

[15] See also Müller and Grüber., 2003; Devenish *et al.*, 2000; Ojaimi *et al.*, 2002.

[16] *„This large enzyme complex (with an overall molecular weight of 520,000 in Escherichia coli) consists of two major parts: a membrane-extrinsic, hydrophilic F_1 containing three a, three b, and one copy each of the g, d, and e subunits, and a membrane-embedded, hydrophobic F_0 composed of one a, two b, and twelve c subunits."* (Nath *et al.*, 2000).

[17] Cfr. Stryer 1999/582; *„As perhaps the world's smallest rotary engine, ATP synthase is fully reversible,with an energy efficiency of almost 100%."* (Bao and Suresh, 2003)

than the distance between the two carbon atoms in an organic molecule. That distance is about 0.2 nm. It puts an absolute limit for any attempt to miniaturize a nanomachine operating on the chemical, supra-atomic level. An improvement towards a further miniaturisation is hardly imaginable. So, in terms of miniaturisation the F_0-F_1 ATPase seems to be close to the absolute physico-chemical limit of perfection (Leslie and Walker, 2000).

Let us now turn back to the idea of efficiency, as it constitutes the main – in our opinion – element of biological (and technical) perfection.

Near absolute economy of the energy transformations. The relative isothermy of biological dynamism, as we have seen, imposes very narrow constraints on the attempts to reconstruct the actual, molecular dynamisms of the living cell. To illustrate the point let us reflect on the quantity of the molecular fuel utilized by the human body. Daily, an adult man utilizes some 40 kg of the ATP, that is more than 27 g/min. During a physical exercise this amount may increase to up to 500 g/min[18]. The actual amount of the ATP in our body is less than 100 grams. It means that the depletion of the ATP fuel has to be balanced by a relatively fast resynthesis of these molecules. The energy required by the resynthesis is taken from the food. This process, in turn, requires a complex series of chemical reactions catalyzed by an equally complex set of the intracellular enzymes. Although the catabolic pathways are rather complex and the intermedialy steps are quite numerous, the total amount of the inevitably dissipated energy cannot be high, as the temperature of a living body remains rather constant. So the measurement of the thermal energy produced by a living body may serve as a premise in the processes of the reconstruction of its dynamism.

> *„Natural processes are extremely efficient in terms of energy and material usage and provide us with many inspiring and thought provoking designs and principles." /.../ These bio components offer immense variety and functionality at a scale where creating a manmade material with such capabilities would be extremely difficult. /.../ F1-ATPase is known to work at efficiencies which are close to 100%. Such efficiencies, variety and form are not existent in any other form of material found today."* (Ummat *et al.*, 2004).

Stryer (1981/103) in a section entitled *„ENZYMES HAVE ENORMOUS CATALYTIC POWER"* states that they *„accelerate reactions by factors of at least a million. /.../ Even a reaction as simple as the hydration of carbon dioxide is catalyzed by an enzyme /.../ carbonic anhydrase /.../* [which] *can hydrate 10^5 molecules of CO_2 in one second. This catalyzed reaction is 10^7 faster than the uncatalyzed reaction."* In the later edition of his *„Biochemistry"* (1995) he utilizes even more enthousiastic wording. He refers to the „kinetic perfection" of the enzymes both in the text and in the title of the corresponding section[19].

The complex set of the enzymatic qualities. The machine-like enzymatic structures run the required chemical processes in the way which is amazingly efficient. The structure of the enzymes, therefore, has to be very precise. It has to meet conditions that minimize

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[18] Cfr Stryer 1981/241. *„A typical 70 kg human with a relatively sedentary lifestyle will generate around 2.0 million kg of ATP from ADP and P_i in a 75-year lifespan."* (Senior *et al.*, 2002). See also Wojtczak, 1998; Reed, 2002.

[19] Polish edition, 1999/205-206. Cfr. also Ho *et al*., 2004 and Berg *et al*., 2002/205-206, section entitled *„Kinetic Perfection in Enzymatic Catalysis: The kcat/KM Criterion"* in Biochemistry, W. H. Freeman and Company, New York.

entropy production and maximize the efficiency of energy conversions. This precision involves several distinct, irreducible correlations, namely: *synhexis, symmorphy, stechiometry, syntopy* and *synchrony. Synhexis* refers to the proper quality of the material used, the material which as a rule is synthetized within living cells. *Symmorphy* refers to the shape of the structures (for instance, only selected stereoisomeres are allowable). *Stechiometry* refers to the proper number of parts (subunits). *Syntopy* refers to the proper orientation in the space and the proper distance between the subunits. *Synchrony* refers to the temporal, strict order of the numerous and diverse chemical processes underlying any biological activity[20].

This point was aptly articulated by Bruce Alberts (1998a)[21]:

> *„Nous avons toujours sous-estimé les cellules, et nous persistons encore aujourd'hui. /.../ la plupart d'entre nous considéraient les cellules comme le siège d'une pléiade de réactions d'ordre deux: une molécule A entrait en collision avec une molecule B, au hasard, par simple diffusion libre, pour donner une molécule AB. /.../ La chimie du vivant est beaucoup plus élaborée et sophistiquée que ce que nous avions pu imaginer. /.../ au lieu d'avoir une cellule où régnent des collisions aléatoires /.../ la cellule dans son ensemble peut être comparée à une usine équipée d'un réseau élaboré de chaînes d'assemblage imbriquées les unes dans les autres, chacune d'elles étant constituée de plusieurs grandes machines protéiques.*
>
> */.../ Pourquoi désignons-nous par «machines protéiques» les assemblages complexes de protéines qui assurent une fonction cellulaire? Parce que précisement, à l'image des machines inventée par l'homme pour travailler avec efficacité dans le monde macroscopique, ces complexes protéiques contiennent de parties mobiles hautement coordonnées"*[22]

Alberts, therefore, recommends that:

> *„/.../ l'enseignement devra offrir aux étudiants en biologie les bases physico-chimiques qui leur permettront de pénétrer plus avant le fonctionnement de ces merveilleuses, mais extraordinairement complexes, machines protéiques."*

Problem of „origin" vs problem of a „common origin".

Problem of „common origin" in the case of such a complex device as F_1-F_0 ATPase is certainly intellectually provoking, especially when we realize that the perfection of these nanomachines is not more pronounced in the higher forms of life than in a simple bacteria. However, another, much more fascinating problem has to be discussed and solved *before* we attempt to handle the „common origin" of the nanomachines. This problem refers to the origins of these nanomachines within the single life cycle of a bacterium.

Any bacterial cell can construct *de novo* a daughter cell within less than a thousand seconds[23]. The new cell is equipped with new set of the nanomachines, which are necessary to sustain the biological dynamism of this form. The production of these nanoma-

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[20] These concepts were introduced by Lenartowicz, 1986/240-242. See also Lenartowicz, 1993.

[21] At that time he was the president of the USA Academy of Sciences.

[22] See also Alberts, 1998b.

[23] *„Generation times for bacterial species growing in nature may be as short as 15 minutes or as long as several days."* (Todar, 2002).

chines is fast and practically faultless. The processes of biosynthesis run efficiently, the raw material and the energy sources are exploited in a perfect, absolutely economical way. This is well documented by the observations on the starving biological forms. In other words, *the perfect economy of functioning is – to a certain extent – a kind of physico-chemical consequence of the perfection and economy of the ATPase biosynthesis.* So the main secret of the enzymatic perfection is hidden in the processes of the life-cycle epigenesis. The dynamism of the life-cycle is the smallest unit of life phenomena. Its integrative epigenesis remains the greatest challenge to biological investigation. The tremendous progress of the molecular biology does not seem to diminish the challenge. On the contrary. The greater the perfection of the molecular dynamisms, the more difficult it seems to explain them within the actual framework of biological ideas closely tied with a reductionist and monist program.

> *„/.../ a living organism, unlike any machine known or conceivable at present, makes and maintains itself and all of its components. Any serious investigation of how this can be possible implies an infinite regress in which each set of enzymes needed for the metabolic activity of the organism implies the existence of another set of enzymes to maintain them, which, in turn, implies another set, and so on indefinitely. Avoiding this implication of infinite regress represents a major challenge for future investigation."* (Cornish-Bowden *et al.*, 2004).

Conclusions.

We have distinguished between the empirical fact of „biological structural identites", the idea of a „common origin" and the idea of a „common descent". We have shown that the instances of the „fundamental biological unity" refer exclusively to the level of the subcellular structures, which just constitute a part of the life-cycle indivisible dynamism. We have also argued that the idea of the „common origin" is much broader than the idea of a „common descent". The empirically observable mechanisms which explain the processes of „descent" (heredity) are no more than one of the instances of the „fundamental biological unity". Therefore they need to be explained rather than to serve as an explanatory system of concepts. Finally we have tried to show, that some of the instances of the „fundamental biological unity" are describable in terms of perfect functional structures. Their *de novo* production puts forward the question of their „origin", and this problem of origin refers to the present time, not to some distant geological epoch.

The genetic, enciphered messages coded in a DNA molecule seem to be inadequate to provide a rational answer to the problem of the *de novo* origin of the structures which constitute the set of instances illustrating the „fundamental biological unity" (cfr. Lenartowicz, 1997; Lenartowicz and Koszteyn, 2001).

In a further, separate paper we intend to investigate the problem of biological standardization. Biological perfection and biological standardization form a rich empirical background for the idea of the „common origin".

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Jolanta KOSZTEYN

PERFEKCJA BIOMOLEKULARNA A PROBLEM „WSPÓLNEGO PRZODKA”

Streszczenie

Od niepamiętnych czasów nie tylko filozofowie, ale i „zwykli” ludzie dostrzegali pewne podobieństwa pomiędzy zupełnie odmiennymi, skądinąd, formami biologicznymi. Wszystkie te formy *rozmnażały się, przechodziły kolejne etapy rozwoju osobniczego, odżywiały się, przystosowywały się* do warunków otoczenia ... itd.

Mimo tych uderzających podobieństw, wrażenie fundamentalnej odrębności wielu organizmów było tak silne, że w Stwórcy upatrywano zarówno przyczynę owej jedności jak i odrębności. Zatem od starożytności istniała teoria wspólnego Źródła Życia (*„common origin"*) będącego przyczyną osobnych aktów stwórczych dla poszczególnych typów form żywych.

Darwinizm – w swojej fundamentalnej, materialistyczno-redukcjonistycznej postaci – na miejscu Źródła Życia umieścił hipotetyczny proces abiogenezy, na miejscu przyczyny podobieństw umieścił mechanizmy dziedziczenia (*„common descent"*), a na miejscu przyczyny różnorodności umieścił losowe mutacje i bezcelowy dobór naturalny.

Ogromny postęp wiedzy biologicznej, jaki dokonał się w XX wieku, w nadzwyczajny sposób pogłębił wrażenie podobieństw istniejących pomiędzy tak różnymi formami życia jak np. bakteria i człowiek. Okazało się też, że wszystkie, dostrzegane poprzednio podobieństwa mają swoje źródło w dynamizmach wewnątrzkomórkowych, niemożliwych do zaobserwowania bez wyrafinowanych narzędzi badawczych. W dalszej konsekwencji stało się jasne, że te wszystkie podobieństwa (a) ujawniają niewyobrażalny poziom *selektywności,* precyzji, oraz (b) stanowią jedynie *fragmenty* niepodzielnej, skądinąd, dynamiki życia osobnika (cyklu życiowego).

Selektywność, leżąca u podstaw owych podobieństw, z jednej strony przekracza wszelkie formy selektywności obserwowanej w materii mineralnej, a z drugiej strony wymaga istnienia czynników ograniczających (*constraints*). Dynamika biologiczna, w tej perspektywie, jawi się jako niewyobrażalne doprawdy *ograniczenie* możliwości zawartych w materii mineralnej. Nie ma tu sensu mówić o „przekraczaniu praw fizyki i chemii", bowiem te prawa, w organizmach żywych, są *selektywnie wykorzystywane* a nie przekraczane.

Wstępna analiza fundamentalnych podobieństw, na które powołuje się nowoczesna biologia w swojej darwinowskiej teorii *„common descent"* wskazuje, że należą one przynajmniej do czterech różnych kategorii: perfekcyjności, standardyzacji, sygnalizacji i oznakowania. W dalszej części pracy skoncentrowano się wyłącznie na aspekcie perfekcyjności.

Ilustracją perfekcyjności może być struktura i dynamika biologicznej nanomaszyny zwanej wodorową syntazą ATP (F_0-F_1 ATPase). Ta syntaza to dwa nanosilniczki, z których jeden jest napędzany prądem elektrycznym (gradientem H^+ na granicy błony wewnątrzkomórkowej), a drugi energią chemiczną pochodzącą z hydrolizy wysokoenergetycznego związku zwanego ATP. Przez centrum obu tych silniczków przechodzi wspólny trzpień (podjednostka γ). Gdy pracuje jeden z tych silniczków, wtedy drugi wykonuje pracę. Zatem albo kosztem gradientu H^+ produkowane są nowe cząsteczki ATP, albo kosztem tych cząsteczek działa pompa protonowa drugiego silniczka, zwiększając gradient H^+. Silniczek F_0 dokonuje całkowitego obrotu w 12 „małych" krokach po 30^o. Natomiast silniczek F_1 obraca się skokowo, co 120^o. Trzpień γ łączący obydwa silniczki jest najprawdopodobniej elastyczny i w ten sposób jest w stanie, bez straty energii, przekazywać obroty z jednego silniczka na drugi.

Perfekcyjność ATPazy oznacza, że nie da się tej nanomaszyny ulepszyć. Jej struktury mają takie właściwości i są tak ze sobą połączone, że jej wydajność energetyczna jest bliska 100%. Nie należy jednak zapominać, że wszystkie w ogóle procesy przekazywania energii w komórce żywej cechują się nadzwyczajną ekonomią, a nieunikniony

wzrost entropii jest ograniczony do minimum. Stanowi to równocześnie podstawowy warunek istnienia form biologicznych. Ich wewnątrzkomórkowe struktury są tak labilne i wrażliwe na chaotyczne, niekontrolowane wyładowania takich porcji energii, jakie wyzwala hydroliza ATP, że sam fakt istnienia i trwania form żywych jest równocześnie dowodem precyzyjnego i kontrolowanego przepływu energii chemicznej w komórkach.

Powróćmy teraz do problemu „wspólnego początku" i do darwinowskiej koncepcji ciągłości filogenetycznej (*„common descent"*). „Początek" wodorowej syntazy ATP nie tkwi w odległej epoce geologicznej, lecz w niezwykle złożonej i precyzyjnej dynamice biosyntezy wewnątrzkomórkowej. Synatazy ATP są budowane *de novo* z wyselekcjonowanej z otoczenia surowej materii mineralnej (autotrofy), bądź z precyzyjnie zdemontowanych, stosunkowo prostych struktur organicznych pokarmu. System, produkujący nowe egzemplarze tych nanomaszyn, to gruby pęczek wieloetapowych ścieżek biosyntetycznych, których selektywność i wzajemna korelacja w przestrzeni i w czasie jest koniecznym warunkiem powodzenia. Jeśli weźmiemy pod uwagę, że taki system jest tylko niewielkim fragmentem ogromnej liczby analogicznych systemów biosyntezy, błyskawicznie – w ciągu kilkunastu minut – budujących nową, kompletnie wyposażoną komórkę, to pojawia się oczywiste pytanie o przyczynę korelacji i integracji tych wszystkich procesów.

Wewnątrzkomórkowy mechanizm dziedziczenia jest również fragmentem tamtego, całościowego systemu biosyntezy. On sam może być ilustracją niezwykłej korelacji i integracji, a zatem sam wymaga odpowiedniego wyjaśnienia w ramach cyklu życiowego osobnika.

Z tego wynika, że sam pojedynczy cykl życiowy, najprostszej nawet komórki żywej, wymaga jakiejś teorii tłumaczącej doskonałość dynamiki biosyntetycznej. Dopóki taka zadowalająca teoria nie powstanie, nie ma sensu przerzucać ciężaru wyjaśnienia na poprzednie cykle życiowe, a tym bardziej na „wspólnego przodka". Taka procedura byłaby intelektualnym *„processus in infinitum"*, który niczego nie wyjaśnia.

Pragnę w tym miejscu podziękować prof. dr hab. Piotrowi Lenartowiczowi SJ za liczne i bardzo pomocne uwagi na temat tego artykułu.