2013 WAS THE 75TH ANNIVERSARY OF ERVIN BAUER'S DEATH

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Introduction

Science minded people commonly remember *Lotka, Rashevsky, Bertalanffy* and *Haldane* etc. when they are speaking about the foundation of theoretical biology (see *Alt* et al. *2010*). In similar Russian (or Hungarian) works *Ervin Bauer*'s name is perhaps mentioned too (see *Tokin 1965*). Why is Bauer omitted in most cases? The usual explanation is that Bauer's principal work: Theoretical Biology (*Бауэр 2002)* did not enter the pool of widely known scientific books due to its publication in Russian**.** The political system in the earlier Soviet Union (and the author's tragic life) banned not only the translation but also even the circulation of this work (see *Müller 2005*) before the fifties of the last century.

This explanation can be accepted. Bauer, however, published a short and early version of his theoretical work in German (*Grundprinzipien…*in the following *Fundamentals, Bauer 1920),* which already in 1920 contained his significant principle about permanent non-equilibrium of living matter (see *Elek and Müller 2013*). How could it happen, that Bauer's memory totally faded away from the western biological literature? This is the question I attempt to answer in the following.

The colloid chemistry became dominant in biology in the 20s of last century

Bauer was not an acknowledged scientific person yet when he put down the first version of his principle. In the early 20th Century there was no generally adopted theory of the organism. Nevertheless we need to remember that this period saw high theoretical activities and intense debates in the last resort between the adherents of vitalism and those of mechanicism. A thousand different individual opinions, personally coloured in varying degrees between vitalists and mechanics, confronted one another among which a given reasoner could choose according to his personal taste and the requirements of his special sphere (see *Bertalanffy 1932* 1-4., 44-47.). Following the pioneering work of *Driesch* a number of 'theoretical biology's' were penned, this became a fashionable enterprise. Some were multivolume treatises and some were thin, less than 100 pages long. The theoretical biology was, however, by no means generally recognised science yet. Voices were often raised in rejection of theoretical biology as 'merely philosophical' or 'speculative' and superfluous. The experimentation was thought to be something superior and only the adjoining experimental approach could overcome the aversion to a theory and lend to it the legitimate pride.

Bauer in this stage of his life was neither an experimentalist nor a theoretician yet; he was pathologist. He abandoned, however, his career *(Elek- Müller 2006)* and he was an expatriate in search of a position. Therefore his *Fundamentals (Bauer 1920)* could not have significant immediate effect on the above debate. Its immediate effect was possibly that it helped Bauer to secure a place at the Institute of General Biology and Experimental Morphology of the Charles University in Prague where he worked as a research associate. A new period of his life began. These were the years when he had to learn through the practice of a subordinate position the leading principles employed in the biological research. These principles themselves underwent a significant alteration at the twenties in the last Century.

It has become accepted to explain life phenomena by molecular processes. At the end of the 19th Century in the development of the cell theory the dynamic position of the cell became the protoplasm, whose most characteristic property was the resemblance to albumin. This approach required, however, some knowledge of the chemical structure of albumin like molecules.

The albuminoidal substances – albumin, casein, fibrin – later to be known as proteins, were considered as labile uncristallisable substances susceptible to alteration by heat or mild chemical treatment and their elementary composition suggested chemical complexity. Such materials could not be fitted into the fabric of the contemporary structural organic chemistry – and the proper, real biochemistry did not yet exist. Some chemists had excluded these compounds from organic chemistry and had denoted them 'organised substances' rather than organic compounds. The new domain of physical chemistry called colloid chemistry, however, offered some possibilities for investigating the forces working among such large sub-microscopic particles, the so-called colloids *(Ostwald, Wo. 1919; Buzágh 1931).* The choice for interpretation of life was between the uncertain structural theory of organic chemistry and the popular physical chemistry as sources of inspiration. The colloid chemistry of protoplasm offered to biologists a more satisfying guide to the molecular explanation of physiological phenomena than did organic chemistry. "*There are animals, e.g. amoebae that can hardly be distinguished morphologically from some colloidal mixture of liquids and there are plants, such as small bacteria that cannot be distinguished from small structures present in certain disperse systems (colloids)."* (*Hartmann 1953 18.).* Cell organelles were explained as a jellified (gel) state of spongoid protoplasm-sol, secretion by its syneresis (shrinkage) and enzyme activity by adsorption on its semi-permeable membranes, etc *(Ostwald 1919* 129-147.*; Buzágh 1931 33.).*

The albuminoids were therefore largely pursued in medical laboratories rather than in chemical institutes, thus accentuating the separation of organic chemistry from physiology *(*see *Fruton 1976).* Such type of physiological laboratory was Růžička's institute in Prague, the Institute of General Biology and Experimental Morphology of the Charles University. *Ružička*'s main efforts were based on the postulate that dissimilation leads to the accumulation of an increasing amount of insoluble albuminoidal products – as he called them – 'plastin' during ontogenesis. Aging according to Ružička was nothing else than the jellification of the sol state of the protoplasm. He used the term hysteresis for the production of plastin by the living tissue and regarded it as an expression of entropy increase in the organisms. Accordingly, he accepted the validity of the second law of thermodynamics in living cells *(Ružička* 1924*).* Physical – energetic – explanation of hysteresis therefore was fully acceptable to Ružička. Bauer obtained an attractive possibility to apply his permanent non-equilibrium principle to Růžička's colloid model of aging.

Bauer's principle in the language of colloid nature of the living matter

The following train of thoughts is totally foreign for the today biology – there are expressions and notions of colloid chemical biology. The colloidal state of matter is defined as a dynamical state of matter, the crystalloid state being the static condition. Also the colloid possesses 'energy' (*Zwaardemaker 1927* pp 229-239; *Buzágh 1931* 5, 23, 62.). According to *Keller'*s opinion the most important sort of the energies in the living cell is the electric one *(Keller 1918).* Its total is estimated $\boldsymbol{E} = \frac{1}{2}\,QV = \frac{1}{2}\boldsymbol{CV^2}$ *(Zwaardemaker 1927* 235.). This is the formula for capacitors, where $\boldsymbol{C}$ is the capacitance and $\boldsymbol{V}$ the 'potential difference' (i.e. a potential). Since the capacitance of a plate condenser is: $C=\varepsilon\ (F/d)$, where ε is the dielectric constant of the dispersant, $E=\frac{1}{2}\ (\varepsilon F/d)\ V^2$ (see *Kugler* and *Kugler 1962* 173.). The living colloid was to imaginated as solid particles dispersed in the liquid phase. These solid particles were Ružička's 'plastin' carrying on their surface electric charges. Each pair of these particles is supposed as a small condenser. The average distance of the particles is d, the total of their charges Q, and the total of their surface F. The electric energy of the 'living' colloid is thus the product of the *surface* of the dispersed phase and the 'potential difference' (i.e. a *potential*). The living organism uses this electric energy to perform work, leading to a temporary decrease of E.

The original Bauer's principle (principle of permanent non-equilibrium of living systems) says: "*All living organisms are characterized by being a system that is not in equilibrium in its environment and is so organised that it transforms the sources and forms of energy taken up from its environment into such state that acts against the establishment of equilibrium in the given environment. – All the energy taken up by the organism from the environment must be fully used to deviate from the equilibrium state. All life functions are necessarily regulatory"* (in *Fundamentals*, *Bauer 1920* 10, 12-13.; see *Elek-Müller 2013).*

The process of taking up energy (food) from the environment needs energy in itself; therefore the organisms' own energy (E) ought to decrease by means of potential (V) drop during the whole life. The organism – however – has to possess energy for its primary activities. This ominous decrease of E should be compensated for a life in accordance with the Bauer's principle. In order to maintain constancy of E– taking account the $E=\frac{1}{2}\ (\varepsilon F/d)\ V^2$ formula – (according to the rules of algebra) d should become smaller or F larger in the course of time. Which possibility will be realised? The average distance (d) of particles – that is the dispersion of the colloid – is in itself potential (V) dependent, therefore only F might become larger and this is ensured by the above mentioned 'regulatory' life functions. But as F is no other than Růžička's 'plastin' – that is Bauer's theory clearly explains and theoretically proves Ružička's 'hysteresis' *(Bauer 1924).*

Bauer's physicochemical model of the protoplasm colloid was welcome to Bauer's principal. Although Ružička does not mention at all the 'principle of permanent non-equilibrium' he refers four times *(Ružička 1924*) to Bauer's paper that is Bauer's just discussed colloid model of his principle *(Bauer 1924).* Co-workers of Ružička also quote Bauer *(Bergauer 1924; Kříženecký 1924)* and Bauer became known as biologist *(Przibram 1926 1090.; Lepeschkin 1937* 45.) educated in a leading school of colloid chemistry. This was a considerable change in Bauer's sphere of thought but this was not the most determinant source of his development.

Electric field in biological phenomena

Bauer sets out to use electric notions in addition to thermodynamic ones in his logical constructions. Although colloid chemistry speaks many times about electric charge, the change in Bauer's viewpoint is not only the effect of his workplace, of Ružička's-school. Prague had a special feature concerning biological colloid chemistry – this was the so-called 'School of Prague' (see *Bertalanffy 1932* 181.).

It was evident already that the living organism cannot be regarded a thermal machine. In Prague small group of specialist went into the electric aspects of energetic organisation of living beings. According to contemporary physics (*Rutherford, Bohr,* etc) bodies are composed of atoms (or ions) and contemporary atom physics has proved that atoms/ions are built with elementary particles moving in field of force, which is dynamically but not statically equilibrated. There are potential differences between various ions or contacting phases (bodies) too (cohesive attraction, valence). In fluids these potential differences can equalize and statistical equilibrium ensues. Such equalization, however, in solids (crystals) is impossible, the potential differences create electric field, which is also dynamically and not statistically equilibrated. In living creatures – which are partially jellified – external factors (nutrients and oxygen) recreate such potentials over and over and the final effect is a permanently produced electric field. The equilibrium of this field in living organisms is seemingly stationary (steady state) but periodical processes (assimilation, dissimilation, circulation, excretion, etc) are superposed over it so the end result is a quasi-stationary equilibrium. Consequently vital processes are in the last analysis electromagnetic processes, living beings are electromagnetic systems and biology is – strictly speaking – 'electric biology' (*Fürth 1928; 1928a; Zwaardemaker 1927* 261-263.).

The electric charge of various tissue-points might be estimated by vital staining. According to *Rudolf Keller* the cathode points (negative poles) in tissue shall be coloured by positively charged stain molecules and the anode ones (positive poles) by negative stains (electric histochemistry, *Keller 1929*). Keller, a publishing company owner, was the central figure of the 'school of Prague' group. He did belong to neither a state university nor an academic research laboratory – he called himself 'unofficial' (private) researcher

Table: Comparison of Bauer and Keller's opinion about the electrostatic phenomena in some vital processes

The hypotheses	Keller 1918	Bauer 1935
	Page numbers in parentheses are from the two books mentioned in the following row	
Numbering is arbitrary	Keller: Die Elektrizität in der Zelle (Electricity in the cell) 1918, Wien	Bauer: Теоретическая Биология (Theoretical Biology) 2002 edition, SanktPeterburg
1. Origin of the static electricity	In the living tissue there are many electrically charged points, which are positives or negatives compared to one another (1, 16, 84-93, 172-178).	Some protein molecules are electric dipoles, which have differently large from each other moment (202-203, 228-230).
2. Origin of the potential energy	The distribution of these charged points forms an electric field whose spatial arrangement is characteristic of species, gender, age, etc (22, 103-106, 121-124).	The various protein electric dipoles are parallel ordered in a quasi crystal lattice (micelle). Moments cannot extinguish each other as their seize is different on the proteins with unlike molecular weights. The living crystal matrix is full of characteristically distributed defects (194-198, 245).
3. Performance of work	The change of charges or rather of the electric field results in doing work (142-145). This change is always depending on the direction (vectorial quantity). Material- (80-84), solutiontransport (137-141), electrophoresis (168-172).	The decrease of the size of the dipole moment (shortening of some protein molecules) results in doing work (202-203). Specificity of the work is canalised by the systemic forces (as for example by force of inertia in physics 100-102).
4. Assimilation and dissimilation	Distribution of the charges characteristic of assimilation is changed to its opposite by the dissimilation, that is the inverse (complementary) pattern of the charged points emerges. The energetic equilibrium of the system is always statistical (73-89, 140-142).	Although assimilation diminishes the size of the dipole moment of these proteins, the polarity is maintained, it does not change in its inverse. The energy deliberated by dissimilation restores the original size of the dipole moment (the length of he protein molecule) almost completely. Therefore the energetic non-equilibrium of the system is permanent (134, 196, 223).

5. Enzymatic action	Biochemical transformation of a molecule (that is enzymatic action, biological oxidation) takes place as a result of vectorial change of the electric field of tissues and cells (79-84). The role of the enzymes is not accepted in the theory (87, 106-108, 111).	The protein molecule associates the substrate and shortens. Due to the shortening its dipole moment diminishes, that is it lends energy to the substrate. This energy promotes the transformation of the substrate. The energy deliberated from the transformed substrate almost completely regenerates the original length and dipole moment of the protein (222-226). The specificity of the enzymes is not accepted in the theory (220).
6. Excitability	Some tissue components are forming consecutive microscopic condensers in the nerve or in the muscle (16-24, 40). The dielectric isolation between the lamellas of this condenser may become conductive for a short time (35). Excitation does not spread by trans-mission of electrons as in the electric current, but by consecutive discharge of the elements of this condenser series (20-35, 75).	Action (or injure) potential is explained (in the nerve or muscle) by consecutive and transitional deformation of series of the protein molecules, which provisionally alters their dipole moment, and as a result their potential energy (194, 312-317).
7. The difference of living from the non living	The transport of materials across the membrane of the living cell may take place against the forces of the diffusion too, that is the living cell is selecting. The organisation controls all factors according to its requirement (113-114).	The living system always and in its entirety works for the maintaining and caring of its working capacity (133-134). On behalf of the preserving its working power – when it is necessary – it may reorganise the internal conditions its activity (135).

Let us compare Keller's idea with Bauer's one (*Table*). Keller's book was not a theoretical biology yet, but only an attempt to verify the biological role of a single physical phenomenon – the electricity – by morphological methods *(Keller 1918*). On the other hand Bauer's concept – detailed 17 years later – was a theoretical biology on the highest level of abstraction (see 7th row of the Table). All the same if we set the two authors' conclusions side by side the impression will be gained that the static electricity of Bauer's 'living matter' is nothing else than the improved and more closely reasoned variant of Keller's idea (see rows from 1 – to 6 of Table). Bauer's model differs from the Keller's one first of all in using electric *dipoles* instead of electric points, which allows him the seminal final conclusion about permanent non-equilibrium of living (see 4th row of Table). With the passing of 17 years the knowledge of the vital staining increased – it was documented that not only electric attraction but phagocytosis of the dye as well might produce the colour (*Höber 1927* 441-455.). Meanwhile x-ray diffraction of some proteins (fibres, crystalline enzymes) revealed their bipolar and micellar (crystal like) organisation (see *Buzágh 1931* 40-60.).

Bauer probably came across Keller's book only in Prague. From this time onward he invoked however electric dipoles in all his life in the maintenance of the permanent non-equilibrium state. He explained all biological phenomena on molecular level by the modification of the extent of electric dipoles.

The supposition is obvious that the static electricity was the influence of 'School of Prague' on Bauer's intellectual horizon at the beginning. This supposition is however hard to prove because Bauer newer quoted Keller. In general Bauer used quotations only sparsely. It is also possible it had not been welcome to quote Keller in Růžička's team. Keller's theory had officially not been considered acceptable by most of his contemporaries (see *Keller 1918* 76-77.). There are however indirect evidences. Bauer referred to Fürth's article *(Bauer 1923).* We read on the first page of Fürth's article: „*My experiments were carried out on Rudof Keller's initiative... The examined materials had ben selected by Rudolf Keller according to biological point of view...“ (Fürth 1923).* Reinhold Fürth was the second prominent person in the 'School of Prague', assistant and later docent in the Physical Institute of the University.

Bauer probably became acquainted with the ideas of the 'School of Prague' only after having been finished the *Fundamentals (Bauer 1920),* for neither bioelectrical nor colloid chemical ideas were even mentioned in this earlier booklet. The *Fundamentals* was theoretical biology also, though it carried a different title. Bauer (formally) followed Driesch' more than a decade old example and starting from his own principle derived the fundamental phenomena of biology: the concepts of life, conditions of life, excitability and adaptability, etc. Bauer's work differs from Driesch' one in materialistic way of looking. Molecular, supramolecular (and historical) view of biology is missing from the *Fundamentals*. The little book did not draw much attention to itself. The colloid chemical trend in biology had been a laboratory practice on supramolecular level in Bauer's days. The practicing biologists of Bauer's era did not found employable ideas for his daily work among the '*Fundamentals'* macroscopic notions. It had been regarded rather a philosophical writing about general knowledge. For this reason had it faded from the scientific consciousness. This is the *first part* of the answer to the question raised in my introduction.

Colloid chemistry became an obstacle for biology in the thirties

At the beginning of the twentieth century the protoplasm was regarded as a single 'living protein' common to all form of life. Proteins could not exist as real solutions for colloid chemists, but consisted aggregates in water (suspensions) with various degree of association (polymerization) without distinct molecular weight (*Buzágh 1931* 134-137.). The view that enzymes are proteins was questioned (see first half of the 5th row in Table) and the prevailing idea was that enzyme catalysis is a phenomenon arising from physical adsorption on surfaces rather than from specific chemical combination (*Keller 1921, 1921a)*. Enzymes were considered as artefacts arising from the transformation and decomposition of the single homogenous substance present in life.

Since generations had been discussions about proteins between colloid chemists and earlier biochemists (*Emil Fisher*) without clear transition points. After 1930 however many proteins – among them enzymes – were crystallized and in water solution they proved to be homogenous (molecular) with well-defined molecular weight excluding the colloid (suspension) state. The decade lasting dispute – proteins were molecules or colloids – became strained (see *Laszlo 1986* 145-153.). Bauer severely criticized a representative (*Martin Fischer*) of the biological colloid theory too (see *Bauer and Tschukitschewa 1929*). His criticism however, did not deal with the most essential point of protein dispute – he never used biochemical ideas but remained at the physiological level. Because of this he was not able to draw the line between colloid chemistry and biochemistry. His critique was directed against the mechanical aspects of the cellular protoplasm as organ-colloid. Sometimes his irresistible logic connected the seemingly most remote experimental facts. By way of illustration he linked up the inactivation of complement with the decrease of the surface tension of the serum *(Bauer 1923)*. According to Bauer both events are the consequences of the reduction of energetic non-equilibrium of vital processes. This example can be read even in Теоретическая Биология (Theoretical Biology) (*Бауэр 2002* 201-205.). In our time we know there is really a common factor in the background of two processes but it is the denaturalisation (of proteins). The macromolecules are loosing their secondary and tertiary structures and in this coil state their dipole moments become less. In Bauer's time, however, not only the details of denaturalisation were unknown, but the effect of denaturising on surface tension was proved experimentally only in the thirties (*Loughlin 1933*). Although the impact of colloid chemistry concerning the protein structure was nothing, the physical chemistry, on which it had been based, continued to influence the development of the research on the structure of proteins and other macromolecules, on biological oxidations and on the enzyme actions. Theoretical elements of protein structure were elaborated merely in the thirties *(Mirsky and Pauling 1936),* and that of the enzyme actions in the late forties *(Pauling and Delbrück 1940)*. It can be attributed to this delayed date that Bauer's interpretation about enzymatic action remained incomplete (see second half of the 5th row in Table).

As we know the general outcome of the colloid chemical – biochemical discussion was that colloid chemistry retarded the knowledge of the proteins. The elaboration of the modern concept of biochemistry was beginning. But biochemists on the whole vigorously rejected philosophizing of any sort *(*see *Kohler 1975)*. Bauer's German publication is connected with a closed chapter of biology. Its significance is far less than his activity in Russia (see *Зотин and Зотина 1993* 10-24., 41.). This is the other reason he has been forgotten in the western scientific literature. This might be the *second part* of the answer to the question raised in my introduction.

Conclusion of the commemoration

So the statement is that Bauer's work is theoretical achievement of a closed period of biology. His conception might have been self-evident for a contemporaneous scientific reader but it needs competent interpretation, historical background for a today inquiring person. In spite of this he has message for us. The fraction of the principle of permanent non-equilibrium worded and italicized above from the *Fundamentals* is prevalent even today. It was highly estimated by *Bertalanffy* the founder of the modern theoretical biology as well (see *Elek - Müller 2013*). It is valid in modern models of living systems too (see *Abonyi – Elek 1970*), except it is not regarded as the definition of life (or living). Even in our days there is a hypothesis that a basic biological imperative of all organisms is to maximise energy intensity by covering chemical potential energy into circuits of electromagnetic energy comprising electric charge, photons and excited electrons *(Milewsky and Mills 2010)*. This line of reasoning formally reminds us of Bauer's old theory at a further (Russian) stage of its development (see 3rd column of Table and *Elek - Müller 2013*).

In our days the *Fundamentals* is more easily readable than Bauer's other works, it is devoid of colloid chemist's outmoded biological ideas and terminology. Some parts of the booklet might have been written still in Budapest (see *Müller 2005; Elek and Müller 2006*). This is one more reason for keeping in evidence his memory in Hungary as well as one of the founders of theoretical biology.

Some biographical notes

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[1] Hungarian posthumous edition of Theoretical Biology (Akadémiai Kiadó, 1967, Budapest, see 2. footnote) contains the Grundprinzipien (*Fundamentals*) in Hungarian too.

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ÖSSZEFOGLALÁS

Bauer Ervint az orosz tudománytörténet az elméleti biológia egyik megalapítójának tartja. A nyugati tudományos irodalom mit sem tud erről, mert fő művét, az *Elméleti Biológiát* (Теоретическая Биология) oroszul írta és ez a szovjet korszakban hozzáférhetetlen volt. Életének azonban több mint a felét Közép-Európában és Magyarországon töltötte. Német nyelven írt tudományos cikkei mára jórészt elavultak, mert ezekben még nem volt képes leszámolni a sejtplazma kolloidkémiai szemléletével, melyet a biokémia későbbi fejlődése feleslegessé tett. Főműve jellegzetes elemét – a molekuláris elektromos erőteret – még Prágában ismerte fel. A nevéhez fűződő permanens non-ekvilibrium tétel bármilyen biológiai modellben – a maiakban is – érvényes, de nem csupán élőlényekre áll, és így nem a biológia alaptörvénye, mint ahogy Bauer gondolta. Úgy is mondhatnánk, hogy az élet szükséges, de nem elégséges feltétele. E tétel már első elméleti munkájában a *Grundprinzipien*-ben (*Fundamentals*) is szerepel, melyet akkor írt, amikor még nem volt biológus kutató. E kis írása azért nem keltett nagyobb figyelmet, mert szemlélete nem volt az 1920-as években divatos kolloidkémiai és molekuláris. Számunkra ma éppen ezért könnyebben olvasható. Egyes részei még Budapesten íródhattak. Ezért Bauer Ervint mint az elméleti biológia egyik megalapítóját Magyarországon is joggal tarthatjuk számon.

[2] There are other posthumous editions. *In Hungarian:* (1967) Akadémiai Kiadó, Budapest. *In Russian withan extended summary in English:* (1982) Eds. Frank, G.M., Tigyi, J., Shnol, E.S., Yamyatsin, A.A., Akadémiai Kiadó, Budapest. *This latter volume includes in English an article by Shnol on Bauer's principle of 'permanent non-equilibrium', and a bibliography of Bauer's works.*