The Universal Principle of Biology: Determinism, Quantum Physics and Spontaneity

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ABSTRACT

For the last four centuries, physics became the pre-eminent natural science. Now it is widely believed that biology will replace physics in prominence. However, systematic efforts to develop a science of theoretical biology on a par with modern theoretical physics in depth and explanatory power have failed. In this paper, we introduce the most promising effort to achieve a fundamental theory of biology, the framework of Ervin Bauer, which includes three requirements for life. The universal principle of biology, which is Bauer's principle, is introduced and presented in mathematical form. Because he was able to derive all fundamental life phenomena from this single principle, we propose that Bauer's principle is the first and foundational principle of biology. It can play a central role in biology similar to the one played in physics by the least action principle. We posit that this new picture will open the possibility to achieve an exact theoretical biology. Expanding the conceptual framework of theoretical physics in the most suitable way that is necessary and sufficient for an exact theoretical biology is a challenging task. We also clarify some significant conceptual difficulties of Bauer's requirements in the context of modern biology, and we fundamentally connect Bauer's theory to quantum physics. In conclusion, we strongly believe that the only version of modern theoretical biology capable of following in the footsteps of modern physics is Bauer's theory.

Key Words: theoretical biology, exact biology, action principle, spontaneity, quantum physics, indeterminism

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1. Introduction

As Carl Woese formulated in his famous article, "*A new biology for a new century*" biology today is at a crossroads. The mechanistic, reductionist understanding of biology does not work because it is misleading and it fails to capture biology's essence. As he remarks, a new, deeper, more invigorating representation of reality is called for. To fulfill biology's promise, it must reach a new and inspiring vision of the living world, one that addresses the major problems in the field that 20th-century biology, namely molecular biology, could not handle and, so, ended up avoiding. If such a vision emerges, it has the potential to lead biology to a fundamental role in science, along with physics, which will define and explore the nature of reality (Woese, 2004).

Unlike current science in general, contemporary biology in its theoretical foundations is built on descriptive and relatively natural-language terms. This runs contrary to the trend of building on the relevant aspects of achievements in physics, which found universal laws of physical changes. In order for biology to become a genuine theoretical science, as well

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founded as modern physics, and just as reliably predictive, its theoretical foundations should be revised (Brent and Bruck, 2006).

Today a minimal requirement for respectability of any physical theory is to admit a variational principle (Edelen, 1971). Variational principles of physics determine from all possible trajectories between an initial configuration A and a final configuration B corresponding to a specifed time, the one that is actually occurring is distinguished by the smallest value of a physical quantity, in comparison to every possible slightly modified paths. In physics, the least action principle plays this role, since all the fundamental laws of physics can be derived from it (Feynman, 1985; pp.104-105; Zee 1986; p.109). The pivotal role of the least action principle was first recognized in the 18th century by Maupertuis and Euler (there was the ancient precedent in Heron of Alexandria, a Greek mathematician and physicist of the 1st century). The central role of the least action principle in physics corresponds to unsolved conceptual problems related to a mechanical version of teleology (Grandpierre, 2012a). “There is absolutely no doubt that every effect in the universe can be explained as satisfactorily from final causes, by the aid of the method of maxima and minima, as it can from the effective causes” (Euler, 1744; in Lemons, 1997, x). Variational principles like the one expressing that light travels between any point A to B on the path corresponding to the least traveling time (Fermat’s principle), are the contemporary descendants of final causes (Lemons, 1997, x).

Given that biology has moved to the fore in the 21st century, which has even been dubbed “the century of biology,” is it plausible to search for its own first principle? The least action principle can become the ideal tool of biology when generalized to allow for free endpoint selection suitable for biological purposes. For example, a bird descending from a height beginning at initial point A, can freely select where it lands (endpoint B), such as the branch of a neighborhood tree. For a living organism, the endpoint B is not pre-fixed, as it would be for a stone dropped from a height. The endpoint is, to a significant extent, freely selectable, open to biological determinations.

Biological determinations have two sources. One is the living organism itself, having an independent biological autonomy (Grandpierre and Kafatos, 2012; 2013). The other is the biological principle (Bauer, 1967) arising from the basic fact that all living organisms must maintain themselves high above thermodynamic equilibrium. In biology, therefore, it is not the principle of least action that determines the gross behavior of living organisms. Living organisms must continuously select the endpoints of their processes according to the requirements of remaining alive. Since being alive involves a tendency to maintain life as long as possible, and as far above thermodynamic equilibrium as possible, the selection of biological endpoints corresponds to a maximal principle, termed the greatest action principle (Grandpierre, 2007). Moreover, such a generalization would provide a way to build biology on the complete theoretical framework worked out by theoretical physics. The least action principle only needs to be generalized by one step that allows for biologically determined endpoints: biological teleology.

The prevailing attitude toward a potential first principle in biology has historically been highly controversial. However, Ervin Bauer (1967), in deriving his version of the universal principle of life, pointed out that the behavior of living organisms is not governed by physical laws. For example, a cat does not move on the basis of Newton’s laws of motion. A cat - or a single cell, for that matter – that is in a state of rest doesn’t tend to remain at rest, even in the absence of external forces acting upon it. Instead, it spontaneously initiates internal biological forces that continuously change its state. The significance of this elementary biological fact isn’t recognized, however, because the related biological theory to supplant theories of physics hasn’t been formulated. Today, the dominant opinion is that since all living organisms consist of material particles that are governed by physical laws, there is no room for an additional, independent biological principle (Kim, 1989; Davies, 2006; p.266).

In contrast, we would point out that a non-deterministic type of spontaneity does exist in physics (Grandpierre and Kafatos, 2012; 2013). For example, quantum physics cannot determine which atom of a radioactive clump of matter will be the one to decay next. The quantum revolution introduced a fundamental uncertainty in the microworld. Therefore, not all details of physical processes are determined within any given physical condition. Rather than claiming that biology must first follow the deterministic model of physics, one must recognize that non-determinism plays a pivotal role in quantum mechanics and, prominently, in biology. The freedom and spontaneity observed in living organisms doesn't contradict physics. But the question remains open of how to make the two truly compatible. Spontaneous action offers an intriguing clue, but its implications are not easily followed up.

If biological determination is possible at all, it must work on the possibilities that physics left open - and in some respects indeterminate - at the quantum level. Possibilities aren't pre-fixed by any means. This implies that there is a place in Nature for biological determinations, and these can either occur at the quantum level or utilize it for higher level action. Since quantum indeterminism operates at small, nano-scales, as seen from the Heisenberg uncertainty relation, it may not at first glance seem suitable for large-amplitude biological changes. Nevertheless, while quantum indeterminism occurs at a very deep level of Nature, biological determinism may simultaneously act on a macroscopic number of particles, and, consecutively, on a large number of time steps. Quantum indeterminism has a random character, and while this randomness may arise from a large number of independent subsystems, non-randomness results when the subsystems are not independent but closely connected. In living organisms the hierarchy of subsystems are finely orchestrated together; this means that they are not independent but highly dependent on each other instead. Therefore, in the presence of biological organization, quantum indeterminism may well become non-random, additive, and organized. If living organisms intervene in their physical processes and modify them into biological paths at the quantum level, they must not do it randomly but systematically, according to biological demands. This is the reason, we think, that a cat, although subject to Newton's laws, can spontaneously change its behavior in a systematic manner. Cats, like other living things, have independent biological autonomy (Grandpierre and Kafatos, 2012; 2013) making them capable of initiating newly beginning causal chains. Therefore, they may initiate a cumulatively increasing difference between biological and physical behavior, modifying the effects of Newton's laws on their state of motion.

Unfortunately, despite repeated attempts of Bohr, Heisenberg, Schrödinger, Wigner and other founders of quantum physics, the fundamental connection between quantum physics and biology has remained largely unexplored. Instead of building itself up systematically from exact grounds, modern biology has decoupled itself from the main branch of natural sciences and built itself on some phenomenal, descriptive terms. Thus the usual method of today's biology (e.g. Abercrombie *et al.,* 1990; Alberts *et al.,* 2004; Campbell *et al.,* 2008) is to start defining life by metabolism, reproduction, and other basic phenomena. Biologists then attempt to answer fundamental questions about the nature of life on the basis of metabolism and reproduction (Cleland, 2006).

In reality, this becomes a circular argument: According to the "metabolism first" hypothesis (*i.e., "The peculiarity which distinguishes life qualitatively from all other forms of motion of matter... is metabolism"* Oparin, 2010; Schrödinger, 1948; p.71), life is defined by metabolism. Yet at the same time metabolism is explained by life (metabolism is the "sum of the physical and chemical processes occurring within a living organism", e.g., Abercrombie *et al.,* 1990; p.357). The question of how to define life is begged in such circular reasoning. Cleland (2006) has pointed out that the solution to this problem is to develop an *adequately general scientific theory of life*. To our knowledge, such a theory was developed only once in the history of modern science, by Ervin Bauer (1967). Unfortunately, Bauer's landmark oeuvre is practically unknown in the English speaking world. First, we present a concise introduction to Bauer's work that led to a first principle of life, the Bauer principle.

2. Bauer's Principle

Ervin Bauer (1890-1938) was a far-seeing Hungarian biologist who worked in his native land but also Germany, Czechoslovakia, and ultimately the Soviet Union. He wrote his fundamental works in 1920 and 1935 (Bauer, 1920a, b; 1935/1967) before being killed in Stalinist purges in 1938 (Müller, 2005). His work was banned in the Soviet Union on ideological grounds. It took considerable courage to preserve a few remaining copies of Bauer's book, Theoretical Biology, and to discuss his theory. Yet Boris P. Tokin (1965) and others kept his memory alive, and in 1967

Tokin's book about Bauer was published in Hungarian (Bauer, 1967, see also Russia publications, 1982; 1993; 2002). Today Bauer is often presented in the Russian and Hungarian literature as a scientist who was much ahead of his time; he is regarded now as one of the founders of theoretical biology (Müller, 2005), which aims to achieve something like Einstein's great goal, to unify all of physics in one grand equation.

In our view, Bauer succeeded in solving a greater problem than Einstein faced the unification of all fundamental biological phenomena in one equation. At the very least, a growing number of papers indicate the timeliness of Bauer's work (e.g. Levich, 1993; Brauckmann, 2000; Alt, 2002; Reeben, 2008; Volkenstein, 2009; Grandpierre, 1988; 2002; 2007; 2008a; 2011a; 2011b; 2012b; 2013; 2014; Grandpierre and Kafatos, 2012; 2013; Voeikov and Del Giudice, 2009; Elek and Müller, 2013).

Bauer sought to prove that all basic life phenomena are the consequence of the same underlying universal principle that characterizes only living matter (Bauer, 1967; p.18). He had worked out a systematic approach starting from the most elementary to the most complex requirements of life.

2.1. The first requirement of life

Bauer found three basic requirements of life: "First, it is characteristic for all living organisms that spontaneous changes occur in their states, changes not arising from external causes outer to the body of the organism" (Bauer, 1967; p.32). No one calls a body or system living unless 'active' changes occur within it due to the contribution of the system itself. In other words, a system cannot be living if all its changes are a direct consequence of external physico-chemical laws alone.

The first requirement thus states that all living organisms must manifest spontaneous changes even in the absence of outer influences, meaning a constant environment. An example might be a paramecium swimming at will in a perfectly still drop of water. Of course, in such an organism a certain amount of free energy must still be available. Bauer notes that potential differences must be present inside a living system, which can equilibrate them in the absence of any external influence. He argues that such a requirement is not enough to distinguish living from non-living forms, however, since all "powered" or "charged" machines when switched on satisfy it. A toy robot running on batteries is capable of doing work in the absence of actions from its external environment.

Switched-on machines are not to be regarded as living. Yet today many biologists and natural scientists are inclined to consider living organisms precisely as switched-on machines, which, similarly to all other machines, obey physico-chemical laws according to their given conditions. They reject ab ovo the possibility of genuine biological laws and factors, assuming that physical laws suffice. Bauer thought that such a position cannot be accepted without a closer study of the scientific problem itself. Therefore, in his eyes the task is to elucidate whether living systems show *sui generis* properties that differentiate them from other systems (Bauer, 1967; p.33).

2.2 The second requirement of life

The second requirement of life (Bauer, 1967; p.34) states that living organisms in a changing environment must manifest changes that are different from those manifested by inanimate systems. For example, consider the difference between pushing a cat across the floor and pushing a shoe. Acting on the cat with a force 'F' practically never corresponds to the inertial trajectory plus the drag force. Indeed, other forces inevitably come into play (as the cat hisses, squirms, and claws), which are not taken into account in the purely physical picture. A living cat exerts internal biological forces that change its (highly unpredictable) potential trajectory (*ibid.*, 35).

Bauer adds that living systems modify the initial conditions within which the physical forces act (*ibid.*, 36). In order that such modifying processes occur, the system must possess potential energies that it can apply to change the effect of external changes upon itself. A shoe being pushed across the floor can't fight back; a cat can. Although the second requirement may be satisfied occasionally by suitably constructed inanimate machines (e.g., a shoe that explodes if you try to push it across the floor), living organisms satisfy this requirement regularly.

Bauer notes that this ability has often been regarded as responsiveness. Living things are characterized by complex, unpredictable responses (as well as deterministic ones innate to their species, like a duck taking to water). However, he adds that responsiveness is conventionally conceived to be essentially a "discharge" phenomenon, i.e., as a physical process only. He points out that even if responsiveness is a discharge phenomenon; this fails to explain the peculiar way in which such discharges occur in living organisms. The discharge phase is regularly followed by a new recharge (e.g., after a synapse fires between two neurons, the depleted chemical charge is almost instantly replaced by a new charge). This means that responsiveness contains a lawful element in relation to recharge processes which is missing from purely physico-chemical explanations (a battery that loses its charge is called dead for good reason).

Bauer presents detailed arguments showing that living systems are not chemical machines and are fundamentally different from dynamical systems like a waterfall or a whirlwind, since these latter ones do not contribute to generate the conditions of their specific activities. Waterfalls do not generate the height differences which drives them, whirlwinds do not generate pressure differences; both of them behave passively; their gross behavior is governed by physical laws.

Bauer radically challenged an unquestioned assumption that life can be accounted for by physics and chemistry. He offered a subtle qualifier: physico-chemical conditions can be such that they allow the behavior of biological phenomena to exist in a way that qualifies as life. Most biologists still want to determine only the precise conditions impinging on living phenomena, because they accept that the laws beyond them (defined by physics and chemistry) are already known. Yet that knowledge isn't sufficient - as Bauer argues, science can explain living phenomena only if it explores the corresponding laws associated with life as such. It is futile to reject their existence without close, systematic study.

2.3. The third requirement of life

In summary, the first two requirements of living systems call for spontaneous changes independent of outside forces and the ability to modify their behavior in a way foreign to inanimate objects. The third requirement takes another step forward; it corresponds to the direction of change relative to the physico-chemical pathway. This is formulated as follows: *We regard any system as living only if it utilizes its free energy to increase its ability to do work.* There must be internal machineries, then, making it possible to increase the organism's capacity for work even if the environment remains unchanged. In short: the organism uses its capacity for work to increase that capacity. Bauer writes;

> "The work of living systems, independently from outer conditions, is directed against the equilibrium that should be reached within the given environment and initial conditions." (Bauer, 1967; p.44).

Without the third requirement, living things wouldn't be able to maintain themselves, to regulate their activities, and to act accordingly to the requirements of life on longer timescales. Certainly living organisms wouldn't be able to invest work without the ability to act spontaneously. Moreover, they wouldn't be able to invest work systematically without the ability to recharge themselves regularly. The third requirement of life includes the first two.

In principle, Bauer adds (*ibid.,* 51), it may be possible to imagine systems that conceivably fulfill the third requirement of life, yet they would still not count as living organisms. Yet it is plausible to accept that the existence of such inanimate systems is in principle impossible. We can regard the third requirement as not only a necessary but also a sufficient criterion of life: it stands as the universal principle of biology.

Bauer's principle states that,

> "The living and only the living systems are never in equilibrium; they permanently invest work on the debit of their free energy budget against that equilibration which should occur for the given the initial conditions of the system on the basis of the physical and chemical laws" (Bauer 1967, 51).

Bauer's principle qualifies as the basic principle in biology under the following conditions: If it can be confirmed in each and every living organism; if it leads to correct conjectures and isn't found to conflict with the facts; and finally, if it is suitable as the basis of all biological investigations. We consider Bauer's principle as the definition of life that is suitable to serve as a foundation for an exact biology.

We contend that Bauer's principle is highly likely to meet these conditions. He has shown that it is possible to derive all the fundamental phenomena of life from one basic principle (Bauer, 1967; pp.113-198). For example, he was able to derive the fundamental law of metabolism in a mathematical form and to thus determine the limits of growth.

Bauer points out that his basic principle will have to be completed, since in its current form it does not say anything about the quantitative aspect of energy use. He conjectures in general that living organisms transform all of their free energy into work against decay, against thermodynamic equilibration dictated by physico-chemical laws. Since energy dissipation from the living body is continuous, the maintenance of life requires continuous activity to maintain a distance from equilibrium. This makes it plausible to assume that all the free energy of the organism is guided into a phase in which it makes biologically useful work. With this additional thesis, if proved, the basic principle of biology can be formulated mathematically and can be confronted with empirical data.

2.4. The mathematical formulation of Bauer's principle

Let us consider a closed isothermal room, the walls of which allows heat to be transmitted, and in which we can take the temperature as approximately constant. The Second Law of Thermodynamics states that if we make a thought experiment and put a system into this room, it cannot work indefinitely but must equilibrate within a finite time. The free energy of the system can be expressed as the maximal useful work of the system within those conditions. The equilibrium will occur when the free energy content of the system cannot decrease anymore, reaching its minimum. Bauer's thesis states that an isothermally closed living system will transform all its free energy into work that modifies the conditions within the organism in a way that the minimum achieved will be not only a relative, but an absolute one, in order to reach its lowest minimum value. Therefore, if the same experiment is repeated with another, now inanimate system having an initial state in which the sum of all potential differences, measured in absolute units, is equal with that of the living organism, then, within such conditions, after equilibration occurs for both systems, the final free energy content of the organism F will be smaller than that of the inanimate one, F', by an amount equal to the work invested by the organism against the equilibration process. Now if the terms of work – differences in pressure, concentration, electric voltage etc. – are denoted by X (X'), and the changes driven by them in a time dt are dx (dx'), then we obtain the universal law of biology in the following form (1):

$$F' - F = \left| \int X dx/dt \, dt - X' dx'/dt \, dt \right| \qquad (1)$$

We can add to (1) the additional thesis expressed by Bauer, namely, that this difference for living systems F' (F represent inanimate, physical systems) achieves the maximal possible value,

$$(F'-F) \Big| \text{(living systems)} = \max. \qquad (2)$$

The difference between F' and F arises from the fact that the terms in living organisms F' the quantities X' and x' in (1) vary in time differently than in inanimate systems F. The difference between the physical and biological system acts always against or compensates the effect of physical equilibration processes, and the organism always uses all its free energy content against equilibration.

3. An attempt to clarify Bauer's requirements in the context of modern science

In the formulation of Bauer's first requirement of life there are, as we found, two terms having crucial importance: 'spontaneity' and 'active'. We are impelled to consider the relevant meaning of these terms in order to grasp Bauer's theory more fully. In effect, the spontaneity of living things seems to be at odds with basic physics, which poses both a problem and an opening for new thinking.

Spontaneity in physics is of two basic types, deterministic and indeterministic. The first corresponds to physically determined processes, as in the spontaneous equilibration of temperatures between a system and its environment. This type of spontaneity is present in thermodynamics. (Hence, ice cubes spontaneously melt at room temperature.) It characterizes classical Newtonian physics as a whole, where physical determinism is complete. As we have seen, biological activity would be impossible under such conditions.

The second type of spontaneity, unknown to classical physics, corresponds to physically indetermined processes in the quantum domain, like the spontaneous creation of particle-antiparticle pairs of virtual particles (Kane, 2007). This type of spontaneity presents a significant conceptual difficulty for two reasons, both applicable to biology: One is that physically indetermined spontaneous processes apparently violate the law of energy conservation. As Paul Davies (1983; p.162) expresses it;

> "In the everyday world, energy is always unalterably fixed; the law of energy conservation is a cornerstone of classical physics. But in the quantum microworld, energy can appear and disappear out of nowhere in a spontaneous and unpredictable fashion."

The second difficulty with physically indetermined spontaneity is the violation of causality. According to one popular view among quantum theorists (e.g., Bohr, 1999; p.17), the spontaneous creation of particle pairs occurs acausally. But accepting such an assumption is equivalent to giving up the principle of causality. According to physicalist views, only physical causes are possible in Nature (Kim, 1993; p.280). Accepting this restricting view has the consequence that if a phenomenon does not have a physical cause, it must be acausal.

So within a single process, the spontaneous generation of virtual particle pairs meant that loopholes had to be created regarding two cornerstones of classical physics. We think, however, that the universal validity of the conservation of energy and the principle of causality deserves more attention. There's an indication, in the light of Bauer's principle, that their violation isn't necessary.

In other words, we propose a wider horizon that takes in biology as being just as fundamental as physics in offering explanatory models. One can conjecture that physically indetermined spontaneous processes in living organisms may be determined by biological factors. If so, *biological activities can be responsible for the creation of virtual particles, and biological causes can be responsible for physically "acausal" processes*. We call this new type of spontaneity, initiated by biological causes, biological spontaneity.

Bauer writes that the chemical energy in food is not used directly but is transformed first to a biologically usable energy form. This biologically governable form of energy must be utilized for the sake of biological purposes. The fact that biologically governable energy is mobilized must be related to a motivational power like desire or will. For example, voluntary motion seems to be due to an act of will, representing a certain kind of energy (when someone runs after a train hoping to hop on). If creatures are able to move their legs according to their willpower, than physical energy is being transformed into a biologically governable mode. The will to run after a train, or to move at all, is the real cause of the resultant motion (Baumeister, 2012). In our view, this leads to the possibility that the energy underlying the will to move can cover the energy cost of creating virtual particles from the vacuum. Our proposal would shed light on how willpower acts on living matter by acting on the quantum vacuum level to create virtual particle pairs, offering a scientific approach to solve the mind-body problem. At the same time, without any additional input, it resolves two basic insufficiencies of physics by restoring the universal validity of energy conservation and causality.

In formulating the first requirement of life Bauer does not make explicit which kind of spontaneity he has in mind. He presents examples of the physically determined type only. A plausible reason is that quantum physics, the source of the second type of spontaneity, was relatively new in the 1930s, and the link between biology and physically indetermined spontaneous processes had not been explicitly made. As far as we know, our attempt is the first.

The second term we wanted to expand on is "active," because it poses a closely related conceptual difficulty. A switched-on machine can be regarded as active in comparison to its switched-off, passive state. As discussed earlier, Bauer considered that specially designed machines may seem to work in a way that deviates from what would be expected given physical conditions and laws. Yet such deviations are due to hidden internal workings; in reality, the machine's activities are physically determined. It does nothing spontaneously, either through willpower or decision-making.

In contrast, physically indetermined activity of living organisms can be traced to biological causes, which support and determine all manner of living behavior, as in the process of lifting your arm. This physically indetermined but biologically determined type of activity we would term biological activity. It is not easy to figure out which version of the term 'active' Bauer had in mind. Notwithstanding, we think that in presenting the three requirements of life, he proceeded to postulate the concepts of biological spontaneity and biological activity as we have defined them. These considerations play the most pronounced role in the detailed interpretation of the basic principle of life, namely, Bauer's principle.

What's taking place here is a conceptual shift from simpler physical activity to its more difficult biological aspects. As an illustration, when Bauer discusses responsiveness in his treatment of the second requirement of life, he writes, "In living systems the discharge is followed generally by recharge. And this latter general law, and not the unknown character of the reaction chain, is what led to the creation of the concept of responsiveness." (ibid. p.40) Muscles and springs both move back to their original state after being stretched. The difference is that in a living organism the regeneration of energy supply with potential differences after the contraction of the muscle occurs as a law.

As we see it, since biological regeneration in general is extremely flexible, it may be impossible to model it by pre-fixed genetic information patterns and machine-like behavior. For one thing, regeneration would require too many genetic patterns. More importantly, these patterns would have to be flexible, renewable, creating new elements even at the level of algorithmic complexity (Grandpierre, 2008b).

Even if recharge occasionally occurs on a physico-chemical-genetic basis, its regular, constant recurrence transcends randomness and replaces it by a law (of the biological kind that Bauer attempts to formulate). It is this undeniably lawful character and the existence of a deeper, more general biological law that is ignored and denied in the physicalist approach.

In his third requirement, Bauer holds that a living system "always" uses its energy to modify the environment in such a way that it can do more work. The qualifier "always" indicates an emphasis once again on the lawful aspect of life. In our understanding, the term "always" may refer to all elementary or quantum time-steps of the given biological process. The Bauer principle requires biologically initiated modifications of physical pathways. Following biological pathways, these modifications reach significant amplitudes. Since the chain of physical causes is almost closed, and the only holes in it are the ones offered by the Heisenberg Uncertainty Principle, the macroscopic amplitude biological changes should develop from much small amplitude, elementary biological interventions all compatible with the uncertainty relation. Elementary biological interventions act on the inputs of physical laws applied at every time step, changing these inputs so that at the endpoint the arising biological behavior deviates significantly from the one expectable on merely physical grounds. We propose that the length of these elementary temporal units are determined from the Heisenberg principle between time and energy - the duration of an elementary process generating a virtual particle pair with a certain energy. If this is the case, the third requirement demands the modification of biological structures, including their physical conditions, from one time step to the next at the quantum- or nano-level of elementary biological processes. This means that the length of the elementary time step is limited by the relevant energies of virtual processes, constrained by the Heisenberg uncertainty principle. Moreover, the biologically initiated modification is not random but directed against equilibration, increasing the ability of the organism to do work.

4. Conclusions

We note that the proper understanding of Bauer's principle, as history shows, proved to be unusually demanding, especially regarding fields of scholarship where the influence of physicalism is dominant. As an already wide literature indicates, its oversimplification and misinterpretation are not rare; Bauer's principle is even thought to be simply a subordinate physical principle (see e.g., Elek and Müller, 2013). Yet we note that if a system works in a way that its gross behavior deviates from physically expectable behavior (governed by the least action principle) in its most fundamental aspects in almost all its manifestations, than it differs fundamentally from every machines as well as from dynamical and open systems with which nowadays living organisms are frequently confused. Since these aspects are beyond the scope of our paper, we only mention that the basic difference of living organisms from physical systems are more and more recognized (Toepfer, 2012; Nicholson, 2013).

Bauer's principle fulfills the pressing need in biology for a theoretical foundation. In contrast to all other biological theories approaching life from "fundamental" phenomena like metabolism and reproduction, Bauer's theory shows a remarkable, as yet unexplored similarity to the conceptual structure of modern physics and its highest achievement, the least action principle.

To wit, modern physics has grasped three levels of Nature: the level of observable phenomena, the level of fundamental physical laws, and the level of the least action principle. Observable phenomena (*first level*) correspond to the physical conditions that are input elements to the equations of physics. Fundamental physical laws (*second level*) are approximated by differential equations describing physical behaviors. The least action principle (*third level*) is an integral principle; it grasps physical processes holistically, between their initial point and endpoint.

The action principle usually corresponds to least action, expressing one of the most basic facts of Nature, that inanimate objects do not contribute to changing their paths but simply follow the trajectory of the least action, namely an inertial trajectory.

If living organisms contribute, through the spontaneous generation of virtual particles, to changing their behavior from an inertial trajectory to one following Bauer's principle, this means that biology begins at the deepest level of Nature. Life begins beyond the quantum level.

Living behavior systematically deviates from the least action principle and follows the greatest action principle instead in their gross behavior (Grandpierre, 2007). Here we have portrayed a biological principle governing the creation of virtual particles to modify the input conditions of the least action principle in a systematic, lawful, principal manner.

There is a close parallel here with control theory. Control theory is an interdisciplinary branch of engineering and mathematics that deals with the behavior of dynamical systems that have inputs. The external input of a system is called the reference. When one or more output variables of a system need to follow a certain reference over time, a controller exists to manipulate the inputs in order to obtain a desired effect on the output end. A new class of phenomena, laws, and principles appear before us, leading to a new theoretical biology as a stronger sibling of theoretical physics. Bauer has pointed us to the principal level underlying the quantum level of Nature.

We have argued that biological spontaneity and biological activity are physically allowed by the existence of already established, physically indetermined processes. This means that there exists a foundation that is suitable to develop into a mature theory as its tenets are expanded and tested in detail. Ervin Bauer's work opens a natural way to explore the fundamental connection between quantum physics and biology. We think that only his theory allows biology to develop into the next exact natural science.

Finally, we propose that Bauer's principle and quantum physics are related at a fundamental level of the universe. His theoretical biology continues where quantum physics arrived at with the measurement problem: to a general theory, not just of the observer whose indeterminacy revolutionized physics, but of every living organism.

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