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## **Open and closed systems: Styles of thinking explain controversies on the 'Negative Entropy' concept of Ludwig Boltzmann and Erwin Schrödinger**

'Now you see that the hope and the desire of returning to the first state of chaos is like the attraction of the moth to the light, and that the man who with constant longing awaits with joy each new springtime, each new summer, each new month and new year - deeming that the things he longs for are even too late in coming - does not perceive that he is longing for his own destruction. But this desire is the very quintessence, the spirit of the elements, which finding itself imprisoned with the soul is ever longing to return from the human body to its giver. And you must know that this same longing is that quintessence inseparable from nature, and that man is the image of the world.'

Leonardo da Vinci (Cod. Arund., fol. 156 v)

### **Abstract**

Erwin Schrödinger, expanding on the negative entropy concept of Ludwig Boltzmann [1], was attacked by Linus Pauling [2] and Max Perutz [3] in that his '*thermodynamics is vague and superficial to an extent that should not be tolerated even in a popular lecture*'. Difficulties of communicating fundamental thermodynamic principles even among Nobel laureates in chemistry and physics [4] reflect a dichotomy between terminology and styles of thinking in classical [5] and irreversible thermodynamics [6]. In the negentropy debate, paradigms of irreversible thermodynamics do not merge with the terminological framework of classical thermodynamics. The actual disparity is not specifically rooted in irreversibility, but in the complexity encountered when describing processes in open systems.

In the stationary-state analysis of Schrödinger, the living organism '*feeds upon negative entropy, attracting, as it were, a stream of negative entropy upon itself, to compensate the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level*' [1]. The entropy of the open system is constant ( $dS/dt = 0$ ), when entropy production by irreversible processes,  $d_{\text{int}}S$ , is compensated by external entropy flows across the system boundaries ( $d_{\text{int}}S = -d_{\text{ext}}S$ ). This perspective on (external) negative entropy differs from the biochemist's favourite thermodynamics of closed, isothermal systems (ci). The ci system's entropy change,  $T\Delta S(\text{ci})$ , equals the '*reversibly produced heat*' [3],  $\Delta_{\text{ext}}Q$ . In general, there is merely one restriction,  $\Delta_{\text{ext}}Q \leq T\Delta S(\text{ci})$ , the equality pertaining to reversible processes ( $d_{\text{int}}S = 0$ ). The static style of thinking relates entropy to a change of the ci system from an initial to a final state, whereas the dynamic style of thinking considers entropy flows across the open system boundaries, including exchanges of matter: '*How does the living organism avoid decay? The obvious answer is: By eating, drinking, breathing and (in the case of plants) assimilating*' [1]. This terminology could hardly be more precise.

### **1. On Entropy and Chaos**

Immediately after Erwin Schrödinger published his celebrated book '*What is Life?*' [1], a controversy on the meaning and meaningfulness of negative entropy started [7]. Half a century

later the debate is not settled. And the topic of the debate is not a minor one for science, entropy flow and entropy balance constituting one of the foundations of physical chemistry in general and biophysics in particular. *'What is negative entropy? Why the opposition? Apparently because here our comprehension of the foundations of this world is also called into question. It is fundamental for our understanding of life and remains essentially unclarified to this day'* [8]. Order and chaos, work and heat, information and dissipation are concepts intricately related to entropy as conceived by the statistical treatments of Boltzmann and Gibbs.

For the apparently impossible task to resolve this controversy we first have to clarify a remarkable phenomenon: A number of eminent scientists with a profound background in thermodynamics, physics and chemistry cannot reach agreement in a debate involving the most fundamental term in science - entropy. I can think of only three prepositions for such a controversy [4]: (1) There exists a *right or wrong* solution. Then we must conclude that one or the other side in the debate simply does not understand the concept of entropy. This is a ridiculous supposition, forcing us to choose a different perspective. (2) The topic itself is not a closed issue. A number of half-truths and half-wrongs might exist which have yet to be combined to a complete theory to resolve the disagreement - creating order from chaos. It would be an arrogation for classical thermodynamics to speculate that its fundamental entropy principle is incomplete. Walter Moore takes a scientifically unusual diplomatic position: *'Here Schrödinger fell into a partial error'* [9]. (3) Each side engaged in the controversy is fundamentally right and the topic is fundamentally settled. Nevertheless, if the conflicting parties do not use a common language they may debate about the same truth without agreement. Finding a common language would create order from order. To me this is the unpretentious interpretation of the 'negative entropy debate'.

Entropy is a simple and clear concept, whereas discussing about entropy is not simple and not always clear. I leave this to Wittgenstein for comment.

What are the contrasting positions in the negative entropy debate? They reflect a clash of new paradigms developed in irreversible thermodynamics, as pioneered by Schrödinger [1], with the terminological framework of classical thermodynamics to which Pauling [2] and Perutz [3] appear to adhere. The actual disparity is not specifically rooted in irreversibility, but in the complexity encountered when describing the dynamics of open systems. Schrödinger's dynamical world view is different from the static world of classical thermodynamics. Let us imagine a discussion on negative entropy. The original publication [4] is reproduced here with minor modifications and an extension of the last chapter.

## 2. Trialog of Schrödinger, Pauling and Perutz

### 2.1 Negative entropy versus 'free' energy

Schrödinger: *When is a piece of matter said to be alive? When it goes on 'doing something', moving, exchanging material with its environment, and so forth, and that for a much longer period than we would expect an inanimate piece of matter to 'keep going' under similar circumstances. When a system that is not alive is isolated or placed in a uniform environment, all motion usually comes to a standstill very soon as a result of various kinds of friction<sup>70</sup>. These ultimate slow approaches to equilibrium could never be mistaken for life, and we may disregard them here. I have referred to them in order to clear myself of a charge of inaccuracy.<sup>71</sup>*

Perutz: *Living systems do not come to thermodynamic equilibrium, defined as the state of maximum entropy,<sup>240</sup>*

Schrödinger: ... which is death. It can only keep aloof from it, i.e. alive, by continually drawing from its environment negative entropy - which is something very positive as we shall immediately see.<sup>72</sup>

Pauling: It was, and still is, my opinion that you made no contribution to our understanding of life ... or that perhaps, by your discussion of 'negative entropy' in relation to life, you made a negative contribution.<sup>229</sup>

Perutz: I suspect that you got that idea from a lecture by Boltzmann on the second law of thermodynamics, delivered before the Imperial Austrian Academy of Sciences in 1886. 'Hence the general battle for existence of living organisms is not one for the basic substances - these substances are abundant in the air, in water and on the ground - also not for energy that every body contains abundantly in the form of heat, though unfortunately in a non-available form, but for entropy which becomes available by the transition of energy from the hot sun to the cold earth.'<sup>241</sup>

Schrödinger: 'Entropy taken with a negative sign' is not my invention. It happens to be precisely the thing on which Boltzmann's original argument turned.<sup>79\*</sup>

Perutz: Franz (later Sir Francis) Simon .. pointed out to you that we do not live on  $-T\Delta S$  alone, but on free energy. ... You had regarded it as too difficult a term for your lay audience; to me this seems a strange argument, since the meaning of entropy is surely harder to grasp.<sup>241</sup>

Schrödinger: The remarks on **negative entropy** have met with doubt and opposition from physicist colleagues. Let me say first, that if I had been catering for them alone I should have let the discussion turn on **free** (Gibbs) **energy** instead. It is the more familiar notion in this context. But this highly technical term seemed linguistically too near to **energy** for making the average reader alive to the contrast between the two things. He is likely to take **free** as more or less an epitheton ornans without much relevance, while actually the concept is a rather intricate one, whose relation to Boltzmann's order-disorder principle is less easy to trace than for entropy.<sup>79\*</sup>

Pauling: You might have discussed a poikilothermic organism encapsulated in such a way as to be in thermal equilibrium with its environment but not able to effect a material transfer through its capsule. The organism will continue to live for some time, undergoing various spontaneous reactions. We know from the principles of thermodynamics that the free (Gibbs) energy of the organism necessarily decreases. One cannot say, without more information, whether there is an increase or a decrease in entropy of the organism.<sup>230</sup>

Schrödinger: After that the whole system fades away into a dead, inert lump of matter.<sup>70</sup>

## 2.2 A stream of negative entropy versus 'bound' energy

Perutz: Simon pointed out to you that 'The reactions in the living body are only partly reversible and consequently heat is developed of which we have to get rid to the surroundings. With this irreversibly produced heat also flow small amounts (either + or -) of reversibly produced heat ( $T\Delta S$ ), but they are quite insignificant and therefore cannot have the important effects on life processes which you assign to them.'<sup>241</sup>

Schrödinger: Indeed, Nernst's discovery was induced by the fact that even at room temperature entropy plays an astonishingly insignificant role in many chemical reactions.<sup>85</sup>

Perutz: The primary currency of chemical energy in living cells is ATP (adenosine triphosphate), and the free (Gibbs) energy stored in ATP is predominantly enthalpic. However, you did not remove this misleading chapter from later editions.<sup>241</sup>

Schrödinger: I will try to sketch the bearing of the entropy principle on the large-scale behaviour of a living organism<sup>70</sup>. ... We said before: 'It feeds upon negative entropy', attracting, as it were, a stream of negative entropy upon itself, to compensate the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level.<sup>74</sup> This

*stream of negative entropy* is entirely different from the (either + or -) entropy of a chemical reaction, including hydrolysis of ATP.

The proposal that the Gibbs energy for ATP hydrolysis is 'predominantly enthalpic' is quite true for the biochemist's standard molar Gibbs energy of reaction, at pH 7 and unit concentrations of reactants [10]. Yet at physiological ATP/ADP ratios up to 1000, the entropic term increases to 40%, rendering this Gibbs force partly enthalpic and partly entropic. Very well, this comment on a misleading chapter is besides the main point of our discussion.

The *stream of negative entropy* compensates for irreversible entropy production to keep the system at a steady state. But how does '*reversibly produced heat*' contribute to the entropy balance of a living system and to what is life? One may explain it in terms of the biochemist's favourite system of classical thermodynamics: closed, isothermal (ci).  $T\Delta S(\text{ci})$  is bound to change by an amount equal to the '*reversibly produced heat*'. This is true under reversible and irreversible conditions, entirely independent of the actually exchanged heat,  $\Delta_e Q$ . There is merely one restriction,  $\Delta_e Q \leq T\Delta S(\text{ci})$ , the equality pertaining to the reversible ci system, when there is zero entropy production (which does not mean that  $T\Delta S(\text{ci})$  is zero). This multitude of entropies is confusing to those not versed in irreversible thermodynamics. It might help to refer to the '*reversibly produced heat*' as 'bound energy',  $T\Delta S(\text{ci}) \equiv \Delta B$  [6]. The bound energy change is always **bound** to the ci system. In a reversible process, moreover, the bound energy change is **bound** to be exchanged as heat, it is never free to be transformed into work (contrast to Gibbs energy or Helmholtz energy changes [5]). The quantity  $\Delta B$  is thus linguistically separated from the entropy confusion. A clear distinction should be made between bound energy change, entropy exchange and entropy production [6].

Schrödinger: *Simon has very pertinently pointed out to me that my simple thermodynamical considerations cannot account for our having to feed on matter 'in the extremely well ordered state of more or less complicated organic compounds' rather than on charcoal or diamond pulp. He is right. But to the lay reader I must explain that a piece of un-burnt coal or diamond, together with the amount of oxygen needed for its combustion, is also in an extremely well ordered state. ... If you allow the reaction, the burning of the coal, to take place, a great amount of heat is produced. By giving it off to the surroundings, the system disposes of the very considerable entropy increase (the large Gibbs energy decrease) entailed by the reaction, and reaches a state in which it has, in point of fact, roughly the same entropy as before.*<sup>80\*</sup> Maintaining a state with roughly the same entropy is equivalent to saying that the bound energy change,  $T\Delta S(\text{ci}) \equiv \Delta B$ , is small. Unlike in the reversible case above, however, the entropy **exchange** (the great amount of heat given off) is very different from the bound energy change. And prepare yourself to take note of the following important point.

In *What if Life?* we are necessarily dealing with open feeding systems, and some of the classical thermodynamic constructs developed for ci systems break down. As a matter of fact, in a living system which exchanges energy and matter, the bound energy change due to reactions and all other transformations in the organism, is not equal to  $T\Delta S$ . Energy balances in open systems are not as trivial as they might appear to be [11]. *And so Simon is quite right in pointing out to me, as he did, that actually the energy content of our food does matter; so my mocking at the menu cards that indicate it was out of place. Energy is needed to replace not only the mechanical energy of our bodily exertions, but also the heat we continually give off to the environment. And that we give off heat is not accidental, but essential. For this is precisely the manner in which we dispose of the surplus entropy we continually produce in our physical life process* [7].<sup>80\*</sup>

### 2.3 Entropy balance in open systems

Pauling: Your *discussion of thermodynamics is vague and superficial to an extent that should not be tolerated even in a popular lecture. In the discussion of thermodynamic quantities it is important to define the system. You never define the system*<sup>229</sup>.

Schrödinger: *An isolated system or a system in a uniform environment (which for the present consideration we do best to include as a part of the system we contemplate) increases its entropy and more or less rapidly approaches the inert state of maximum entropy.*<sup>74</sup>

Pauling: *In this case it involves an increase in entropy of the organism plus its environment, with the entropy of the organism either increasing or decreasing.*<sup>230</sup>

Schrödinger: *Let us recall the central problem of explaining the stability of complex and ordered systems in the face of the tendency of things to approach the chaotic state.*<sup>74</sup> *Every process, event, happening - call it what you will; in a word, everything that is going on in Nature means an increase of the entropy of the part of the world where it is going on. ... What an organism feeds upon is negative entropy. Or, to put it less paradoxically, the essential thing in metabolism is that the organism succeeds in freeing itself from all the entropy it cannot help producing while alive.*<sup>72</sup>

Pauling: *In this case it involves an increase in the entropy of the universe.*<sup>230</sup>

Schrödinger: *We said before: 'It feeds upon negative entropy', attracting, as it were, a stream of negative entropy upon itself, to compensate the entropy increase it produces by living and thus to maintain itself on a stationary and fairly low entropy level.*<sup>74</sup> *I did not use the technical terms of irreversible thermodynamics, else I would not have attracted in a series of lectures an audience of about four hundred which did not substantially dwindle, though warned at the outset that the subject-matter could not be termed popular, even though the physicist's most dreaded weapon, mathematical deduction, would hardly be utilized.*<sup>1</sup>

Entropy appears in various guises, depending on the context. Even after eliminating one of the entropies by introducing the name 'bound energy' [6], three aspects of entropy must be distinguished [12]:

(1) *The stationary low entropy level of a living organism implies the equality  $dS/dt = 0$ , and the entropy of the system is constant at a stable state displaced from equilibrium. Maintenance of such a stationary dissipative state is the marvellous faculty of a living organism, by which it delays the decay into thermodynamical equilibrium (death) [1].*<sup>74</sup>

(2) *The entropy increase it produces by living is simply the rate of internal entropy production due to irreversible processes,  $d_i S/dt$ , leading in its local formulation to the dissipation function [12, 13].*

(3) *The stream of negative entropy corresponds to the external entropy flow,  $d_e S/dt$ , out of the system, the loss of entropy being expressed by the negative value of external entropy flow, between a living system and its environment. Much more important for us here is the bearing on the statistical concept of order and disorder, a connection that was revealed by the investigations of Boltzmann and Gibbs in statistical physics [1].*<sup>73</sup> *Hence the awkward expression 'negative entropy' can be replaced by a better one: entropy, taken with the negative sign, is itself a measure of order. Thus the device by which an organism maintains itself stationary at a fairly high level of orderliness (= fairly low level of entropy) really consists in continually sucking orderliness from its environment [1].*<sup>75</sup>

Taken together, these are the three components of the entropy balance equation of irreversible thermodynamics [12],

$$\frac{dS}{dt} = \frac{d_{\text{int}} S}{dt} + \frac{d_{\text{ext}} S}{dt} \quad (1)$$

considering (1) the entropy change of the system as a composite function of (2) the internal source term of entropy which is always positive as a consequence of the second law of thermodynamics, and (3) the external entropy change, which is *negative entropy* in a living organism *which maintains itself stationary at a fairly high level of orderliness*. ... *This conclusion is less paradoxical than it appears at first sight. Rather could it be blamed for triviality*. ... *Plants, of course, have their most powerful supply of 'negative entropy' in the sunlight* [1].<sup>75</sup>

#### 2.4 No problem from the thermodynamic point of view?

Pauling: *The real question about the nature of life, which you failed to recognize, is the question as to how biological specificity is achieved; that is, how the amino-acid residues are ordered into the well-defined sequence characteristic of the specific organism*.<sup>231</sup>

Schrödinger: *A single group of atoms existing only in one copy produces orderly events, marvellously tuned in with each other and with the environment according to most subtle laws. ... Since we know the power this tiny central office has in the isolated cell, do they not resemble stations of local government dispersed through the body, communicating with each other with great ease, thanks to the code that is common to all of them*<sup>79</sup>? *But the term code-script is, of course, too narrow. The chromosome structures are at the same time instrumental in bringing about the development they foreshadow. They are law-code and executive power - or, to use another simile, they are architect's plan and builder's craft - in one*.<sup>21</sup>

Perutz: *These statements reveal one vital misconception in your mind. ... In fact, biochemists had shown that the executive power resides in enzyme catalysts*.<sup>240</sup>

Pauling: *The gene has the power to reproduce itself, and also to direct the synthesis of the protein for which it has responsibility*.<sup>230</sup>

Schrödinger: *Well, this is a fantastic description, perhaps less becoming a scientist than a poet*.<sup>79</sup> 'Power of the gene' is a popular expression but vague when viewed from a thermodynamic perspective. Biologists have come to recognize the eminent role of metabolic power for the maintenance and growth of the orderly structures called living systems. In thermodynamics power is defined as the 'time rate at which work is done', or more generally in irreversible thermodynamics, power is the (Gibbs) energy change per unit of time [ $W=J\cdot s^{-1}$ ] [6]. The gene 'has' by no means the 'power to reproduce itself', but requires external power for duplication and protein synthesis.

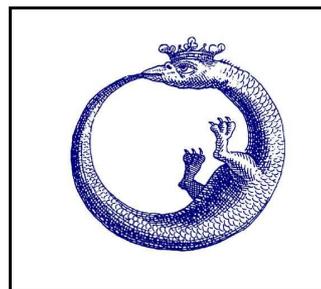
Pauling: *There is no problem from the thermodynamic point of view. Let us assume that there is in the cell a reservoir of the various amino acids, in a situation such that condensation into polypeptide chains is accompanied by a decrease in free energy (Gibbs energy), whether the sequence is ordered or not. ... It is not unreasonable that the gene might provide the information to permit a replica of itself to be synthesized and also to permit a particular polypeptide chain to be synthesized, with the specific reactions involved accelerated by a specific enzyme. The product, of course, has lower entropy than a similar product with a random sequence, it is accordingly something within the cell, rather than negative entropy from outside the cell, that is involved here*.<sup>231</sup>

Schrödinger: *It is by avoiding the rapid decay into the inert state of 'equilibrium', that an organism appears so enigmatic; so much so, that from the earliest times of human thought some special non-physical or supernatural force (vis viva, entelechy) was claimed to be operative in the organism, and in some quarters is still claimed. How does the living organism avoid decay? The obvious answer is: By eating, drinking, breathing and (in the case of plants) assimilating. The technical term is called metabolism*.<sup>71</sup> Ever increasing numbers of ATPs and GTPs are identified to provide the Gibbs energy necessary per peptide bond formation, for achieving the high specificity in biological processes such as translation and replication [14]. The over-all

products, of course, have a higher entropy, whence negative entropy flow is involved between the inside and outside of the cell. *The essential thing in metabolism is that the organism succeeds in freeing itself from all the entropy it cannot help producing while alive.*<sup>72</sup>

*An organism's astonishing gift of concentrating a 'stream of order' on itself and thus escaping the decay into atomic chaos - of 'drinking orderliness' from a suitable environment - seems to be connected with the presence of the 'aperiodic solids', the chromosome molecules, which doubtless represent the highest degree of well-ordered atomic association we know of - much higher than the ordinary periodic crystal - in virtue of the individual role every atom and every radical is playing here.*<sup>77</sup>

*To put it briefly, we witness the event that existing order displays the power of maintaining itself and of producing orderly events. That sounds plausible enough, though in finding it plausible we, no doubt, draw on experience concerning social organization and other events which involve the activity of organisms. And so it might seem that something like a vicious circle is implied<sup>77</sup> - a dragon biting its tail (the Oroboros; Fig. 1).*



### 3. Negative Entropy Equals Gibbs Energy Flow in a Steady State

Since Schrödinger wrote his book, the terminological and conceptual difficulties of thermodynamics have not diminished when the complexity of open systems has to be taken into account [11]. Convincing as Schrödinger's arguments in a confrontation with Pauling and Perutz may be, his readiness to turn from negative entropy to free (Gibbs) energy might appear paradoxical. Gibbs energy and entropy are contrasting terms in the classical thermodynamic equation,

$$dH = dG + TdS \quad (2)$$

Such apparent paradoxes are not uncommon owing to the fact that identical thermodynamic terms may adopt several meanings, depending on the precise context, frequently indicated just by an '*epitheton ornans*' as Schrödinger points out, or by a slightly different subscript, e.g.  $d_i S$  versus  $d_e S$  (Eq. 1).

A combination of Eq.(1) and (2) in a matrix (Table 1) provides the solution to the apparent paradox that entropy and Gibbs energy changes can be equal, yet only under specific conditions. At conditions of constant pressure, an expression of the first law of thermodynamics is  $d_{int}H = 0$  ( $dp=0$ ) [10]. The conservation law is restricted to energy and does not apply to Gibbs energy or entropy. In fact, the second law of thermodynamics can be stated as  $d_{int}S \geq 0$ ; entropy production can only be positive.

Analogous to Eq.(1), we can write the Gibbs energy balance [6],

$$dG = d_{int}D + d_{ext}G \quad (3)$$

Since temperature  $T$  can only be  $>0$ , the vertically written equation for internal changes (Table 1) yields, under conditions of constant pressure,

$$d_{int}D = -Td_{int}S \quad (4)$$

$d_{\text{int}}D$  is the 'dissipated energy' [6], which can only be negative (Gibbs energy can only be destroyed). We recognize a first level of identity between the approaches in terms of entropy and Gibbs energy.

**Table 1.** Thermodynamic balance equations for enthalpy, Gibbs energy and entropy, arranged according to the Gibbs equation. Column 1 indicates the changes of the system (Eq. 2), followed by the internal terms (sources, column 2). The external terms (column 3-5) are zero in isolated systems. Column 5 indicates the changes due to transfer of matter, which are zero in isolated and closed systems. The entropy balance (last row) is equivalent to Eq.(1).

System	=	internal	+	external				
Open	=	internal	+	heat	+	work	+	matter
closed	=	internal	+	heat	+	work		
isolated	=	internal						
$dH$	=	$d_{\text{int}}H$	+	$d_{\text{ext}}Q$	+	$d_{\text{ext}}W$	+	$d_{\text{mat}}H$
=	=	=	=	=	=	=	=	=
$dG$	=	$d_{\text{int}}D$	+	0	+	$d_{\text{ext}}W$	+	$d_{\text{mat}}G$
+	+	+					+	+
$T dS$	=	$T d_{\text{int}}S$	+	$d_{\text{ext}}Q$	+	0	+	$T d_{\text{mat}}S$

The flow of negative entropy,  $d_{\text{ext}}S/dt$  (Eq. 1), is the sum of heat flow and external entropy flow associated with the exchange of matter (Table 1). Schrödinger emphasizes the importance of external entropy for keeping systems at steady state, when  $dS/dt = 0$  (and all other system changes are zero). When considering only feeding and metabolism at steady state, in the absence of mechanical work performed on the system or on the environment, a particularly simple situation is obtained, quite typical for many adult organisms. The internal entropy production is compensated by the negative entropy exchange,  $d_{\text{int}}S = -d_{\text{ext}}S$ , and the energy dissipation is matched by the input of Gibbs energy in the form of matter,  $d_{\text{int}}D = -d_{\text{mat}}G$  (at  $d_{\text{ext}}W = 0$ ; Table 1). Combining these equalities with Eq.(4), we realize that under the specific condition of the steady state and zero performance of external work, the *feeding* on Gibbs energy equals the *stream of negative entropy*,

$$\frac{d_{\text{mat}}G}{dt} = -T \frac{d_{\text{ext}}S}{dt} \tag{5}$$

#### 4. Terminology and Ambiguity in Hard and Soft Science

The *negative entropy debate* of 'hard' science (physical chemistry) is only one side of the coin. It has a complementary side on the 'soft' science level, which I call the *negative entropy devotion*. Some advocates of Schrödinger's concept appear to be staggered by the term '*negative entropy*', as if mysteriously struck by the appearance of the holy grail or the philosopher's stone [8, 15-17]. The hard and soft sides are interrelated by language, not by mathematical equations. A formulation of the second law of thermodynamics '*The entropy of the universe always increases*' (Clausius) has the universal touch of fundamental truth which is not communicated by  $d_{\text{int}}S > 0$ .

To communicate scientific concepts, one has to cast them into common language which is inherently and repeatedly insufficient for resolving controversies or separating differences. The impact of different terminologies reflecting separate styles of thinking in terms of open versus closed systems has been apparently ignored in the historical discussion on Boltzmann's and Schrödinger's negative entropy in life [9, 18]. Without burdening himself and the reader with the terminological and algebraic jungle that characterizes less popular texts in biological thermodynamics, Schrödinger described the fundamental connections between the entropy principle embraced in the second law of classical thermodynamics, irreversibility, and '*order from disorder*' versus '*order from order*' mechanisms. He drew a picture of evolutionary optimization of dynamic (ordered, organized, organismic) living structures which are selected to keep a balance between the abyss of statistical decay into chaos and the void of static fixation into solid stability. Biologists are frequently worried about the applicability of the thermodynamic state functions to open irreversible systems [19]. This is in contrast to discussions prevalent in physics on the "*apparent paradox that natural processes are irreversible, always increasing the entropy of the universe, whereas molecular processes are essentially reversible*" [9]. The question of physics "*How do we introduce irreversibility into a 'reversible' world?*" [20] appears to be opposite to the problem of bioenergetics: How do we apply physicochemical concepts which are based on idealized reversible systems into the irreversible world of life?

The historical role of '*What if Life?*' was evaluated mainly and controversially in the context of the emerging science of molecular biology [18, 21, 22]. In the tradition of Boltzmann, Schrödinger pioneered biophysics by his unique transdisciplinary approach [23]. He made a distinctive contribution towards a general awareness for the position of thermodynamics in biology, and for the increasing role that molecular biology was to play in the expansion of the foundations of science. Coded in scientific poetry, Erwin Schrödinger's *aperiodic crystal* as a serial molecular form and '*regular array of repeating units in which the individual units are not all the same*' [9] introduced the concept of a 'genetic code': '*Schrödinger was the first to state the concept in clear physical terms*' [9]. On the other hand, differences in scientific opinion may have got entangled with rueful rivalry. "*I could not help being sympathetic to Pauling's somewhat egocentric contribution and in particular his view that Schrödinger's later work on biology, as recounted in What is Life?, was confused and misleading*" [24]; or Perutz: "*... the book does not appear to have had much impact on the people already in the field*" [25]. In contrast, the physicist Crick: "*On those who came into the subject just after the 1939-1945 war Schrödinger's little book ... seems to have been peculiarly influential ... conveyed in an exciting way the idea that, in biology, molecular explanations would not only be extremely important but also that they were just around the corner*" [26]. And the biologist Watson: "*I .. spotted the tiny book What is Life by the theoretical physicist Erwin Schrödinger. In that little gem, Schrödinger said the essence of life was the gene. ... then I thought, well, if the gene is the essence of life, I want to know more about it. And that was fateful because, otherwise, I would have spent my life studying birds ...*" [27].

Looking back at Schrödinger's account of the dynamic balance of living systems, we can only admire the combination of his sharp capture of basic concepts with an artistic style of his presentation. The dynamics of energy flow for dissipative systems at steady state are beautifully explained in his book. 500 years earlier, another pioneer of scientific and holistic thought captured the same idea: '*The body of anything whatever that takes nourishment constantly dies and is constantly renewed; because nourishment can enter only into places where the former nourishment has expired, and if it has expired it no longer has life. And if you do not supply nourishment equal to the nourishment which is gone, life will fail in vigour ... just as the flame of the candle is fed by the nourishment afforded by the liquid of this candle, which flame*

*continually with a rapid supply restores to it from below as much as is consumed in dying above'* (Leonardo da Vinci; Quad. Anat. II., fol. 43 b) [28].

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