OPINION ARTICLE
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How to deduce and teach the logical and unambiguous answer, namely $L = \sum C$, to "What is Life?" using the principles of communication?

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Is it possible to understand the very nature of 'Life' and 'Death' based on contemporary biology? The usual spontaneous reaction is: "No way. Life is far too complicated. It involves both material- and an immaterial dimensions, and this combination exceeds the capacities of the human brain." In this paper, a fully contrarian stand is taken. Indeed it will be shown that without invoking any unknown principle(s) unambiguous definitions can be logically deduced. The key? First ask the right questions. Next, thoroughly imbue contemporary biology with the principles of communication, including both its 'hardware' and its 'software' aspects. An integrative yet simple principle emerges saying that: 1. All living matter is invariably organized as sender-receiver compartments that incessantly handle and transfer information (= communicate); 2. The 'communicating compartment' is better suited to serve as universal unit of structure, function and evolution than 'the (prokaryotic) cell', the smallest such unit; 3. 'Living matter' versus 'non-living' are false opposites while 'still alive' and 'just not alive anymore' are true opposites; 4. 'Death' ensues when a given sender-receiver compartment irreversibly loses its ability to handle information at its highest level of compartmental organization; 5. The verb 'Life' (L) denotes nothing else than the total sum ($\sum$) of all acts of communication (C) executed by a sender-receiver at all its levels of compartmental organization: $L = \sum C$; 6. Any act of communication is a problem-solving act; 6. Any Extended Evolutionary Synthesis (EES) should have the definition of Life at its core.

Keywords: coma, definition of life, definition of death, extended evolutionary synthesis, EES, Mega-evolution, neo-Darwinism, philosophy of life, problem-solving

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Introduction

Despite the enormous increase in knowledge about the way living systems function, biology's most fundamental question, namely "What is Life?" remains largely unanswered. No wonder, if one realizes what conditions an adequate definition of 'life' should meet, at least according to Schejter and Agassi: [1] "*Apart from its not being trite and uninformative (circular, to use a traditional term), it should be neither too wide nor too narrow; it should not exclude living things and it should not include dead ones. Furthermore, it should not make biology part-and-parcel of chemistry and physics* (meaning that there should be room for an immaterial dimension)." I add: "*and it should organize all known dimensions and properties of living matter in a logical order and context, and it should pave the way for defining what exactly happens at the very moment of Death.*"

Over the years at least a hundred definitions of life have been published. Erwin Schrödinger [2] pioneered with an approach from thermodynamics, in particular its second law that says that when a system performs work it runs down, not only because the free energy decreases but also because the entropy, its state of disorganization increases. According to Schrödinger, "Living organisms stay alive by virtue of their ability to get rid of the entropy that is created by the processes by which the organisms live." Schejter and Agassi (1994) attempted to correct some of the limitations of this approach. Robert Rosen [3] addressed the validity of the popular "Life is a machine" metaphor. Using good arguments he concluded that this metaphor is entirely wrong. He used a mathematical approach for his definition:

"Life is the manifestation of a certain kind of (relational) model. A particular system is living if it realizes this model." I will argue that indeed Life is not a machine, but *the activity* of a special type of machine, namely of a sender-receiver. Only after the constituting parts of a given entity start *interacting* and perform an activity, the 'total sum of the parts' deserves the description 'machine'. For a few lists with additional definitions that are often centered on a particular property of living matter, see refs.[4-5]

Yet, despite so many trials, the feeling persists that the definition on which a large majority can agree still needs to be formulated. As a surrogate for a clear definition of life, introductory textbooks of biology often tend to content themselves with enumerating a number of properties in which living systems differ from non-living or inanimate ones. Such an approach was also used by Koshland Jr, who at that time was the Editor-in-Chief of the prestigious journal Science.[6] The figure in his 2002 paper (page 2215) featured the Temple of the goddess of Life or PICERAS with its 7 pillars, namely Program, Improvisation, Compartmentalization, Energy, Regeneration, Adaptability, Seclusion (**Fig. 1**). The combination of these properties enables living systems to maintain themselves in a state far from thermodynamic equilibrium (steady state) and enables reproduction and autopoiesis (self production or making itself.)[7] Such a reductionistic approach strengthens the feeling that the human brain is still too underdeveloped to truly understand Life's very nature.

In this paper, I will show that another approach, a truly integrative one, is possible on the condition that one starts by asking the right questions.

It matters how some key questions are formulated

One approach in trying to get the answer to "What is Life?" starts from asking the question: "Can we deduce the very nature of Life by opposing 'living matter' to 'non-living- or inanimate matter as is common practice in textbooks on Introductory Biology?" Another approach starts from the question: "What exactly changes at the very moment of death, when a given compartment undergoes the change from 'still alive' to 'not alive anymore'?"

Both approaches seem plausible. Intuitively, most people may agree that the first one should be the most appropriate one. Yet, hitherto for one reason or another, it failed to yield an unambiguous answer. The second approach, in my opinion the right one (see later) never attracted much interest from researchers. The first reason for the lack of success of the first approach, although a logical one at first glance, is that the first question hides an understandable, but nonetheless fatal thinking error that prohibited plausibly defining 'Life' for many decades. The second reason is that it took until the introduction of the digital-era vocabulary (hardware, software, information etc.) that one could engage in wording some key properties and activities of living matter. Indeed, if the right wording is missing, one cannot make descriptions or explanations.

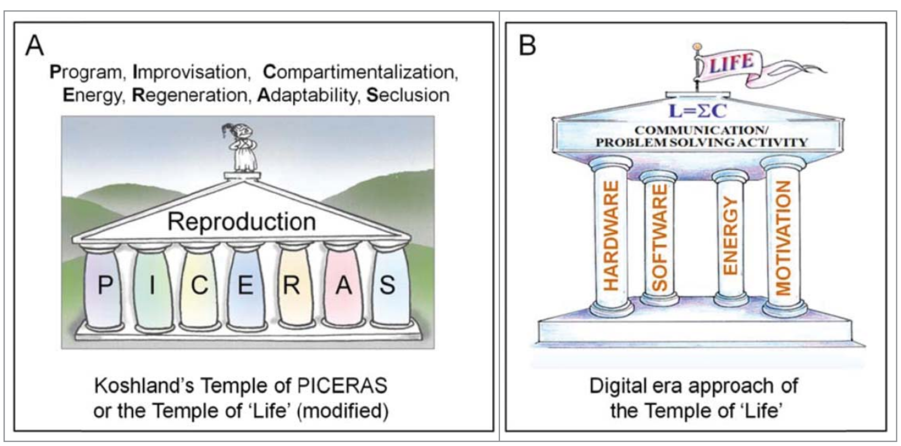

Figure 1. Two major approaches used in trials to uncover the very nature of 'Life'. (**A**) Koshland Jr. tried to list the major features of living matter in the form of a temple. [6] In this classical approach reproduction features as the major outcome of the interactions among all 7 pillars. According to Koshland Jr. himself, 'Life' cannot be defined this way. Modified after Koshland Jr. [6] (**B**) A digital-era approach for visualizing the essence of 'Life' (as an activity). Here the temple has only 4 'pillars'.[5] They are all subject to change and therefore possible sources of variability. Their interactions enable communication/problem-solving activity. The 'Life as a temple' idea was borrowed from Koshland Jr.[6]

The nature of the thinking error: Rationale

1. The term 'Life' has many different meanings as apparent from good dictionaries. Thus when trying to define 'Life', one should first make clear what meaning one is going to define. In this paper, the meaning is the state in which an organism is before the moment of death.
2. Life sounds like a noun. However, is it correct to define it as a noun if some of its typical features refer to activities which are denoted by verbs? Could it be that 'Life' in its totality is not a noun, but a verb?
3. Numerous authors who formulated a definition of 'Life' focused on one or a few properties in which living matter differs from non-living or inanimate matter (**Fig. 1**), assuming that from such comparison the true nature of 'Life' will emerge. The underlying idea stems from the ancient Greek philosophers (Empedocles, Aristoteles etc.) who stated that a given property of something, e.g. the quality 'warm' can only be defined if there is the quality 'cold', the quantitative property 'light' if there is 'heavy', 'high' if there is 'low', etc., thus if a *true* opposite exists. Are 'living matter' and 'non living matter' each other's true opposites? No, they are not, the terms only sound so. They are *false* opposites. Why? Genuine opposites can only have one opposite: 'warm' opposes 'cold' but not 'low' or 'dark'. In contrast, 'living

matter' can be opposed to an endless number of examples of 'non-living matter'. A giraffe can be opposed to a pebble, a bottle, a pencil etc. This makes that 'living matter' and 'non-living matter' are not genuine but *false* opposites. Hence the ancient Greek philosopher's method does not work properly in this comparison.
4. In philosophy, the quality of questions changed fundamentally in the 20th-early 21th centuries with much emphasis on communication.[8] Major novelties were the introduction of 'linguistic turn'[9,10] and 'pragmatic turn'[11]. This increase in interest in communication was particularly important for sociology.[8] It did not (yet) yield an unambiguous answer to "What is Life?".

The 'right' question

The second cited question reading: "What is the difference between the situation 'Still alive' vs. 'Just not alive anymore"? is correct according to the ancient Greek method because there are no other alternatives to 'still alive', than 'just dead'. It prompts the next questions: "What exactly changes at the very moment of Death?" and: "How to define 'Death'?" The answer "Death is the end of Life" or that "Life is what precedes Death" are circular definitions. They do not have any informative value and are therefore useless. Indeed they do not provide any opportunity to engage in unravelling the properties of Life or Death in an experimental and falsifiable way.

A logically deduced unambiguous definition of 'Death'

As I experienced myself, defining 'Death' is less simple than one might think. Medical doctors, in particular when confronted with situations of deep coma will certainly agree. The following thought-experiments will illustrate the duality of death problem. For the first illustration, sensitive souls should assume that the poor experimental animal had been anaesthetized before the sequence of events. Is a chicken dead when one leg is amputated? No. Two legs? No. Two legs and 2 wings? No. Thus, 'Death' is not primarily a matter of loss of mass. Is a chicken dead at the very moment of decapitation? Some will say yes, other will say no because the headless body can still move around for a while, be it an uncoordinated way. Who is right? Is just cutting through the central nervous system in the neck region without removing any tissue sufficient to instantly kill the animal? Yes. One additional experiment: Imagine that a chicken is decapitated in a laboratory and that immediately upon decapitation, all tissues are dissected and brought into tissue culture, where they continue to exhibit a number of so called 'typical properties' of living matter as outlined in the PICERAS approach. Some cells will even multiply. The chicken does not exist anymore, but its parts are still alive: this I call 'the duality of death'. Is it allowed to say that the chicken is fully dead? Yes, even if all its constituent cells are still alive for a while. Thus, 'Death' refers to a particular level of compartmental and communicational organization, namely the highest one, the brain in this example.

A second, less bloody example with a small population of a dozen deer in a prairie. Imagine that something scares the deer so much that each of them runs away in opposite directions, so far and so long that they do not see or smell each other, and that they do not find each other anymore. No doubt, the population does not exist anymore but its original constituent parts are still alive, they metabolize, carrying females will give birth, etc. Again the same duality: the higher order compartment, the population in this example, is dead while its constituent parts are still alive.

A third example: At which moment does an eukaryotic cell die? At the moment that it irreversibly loses its voltage gradient over its plasma membrane. At that moment, the mitochondria or chloroplasts (if present) which are modified prokaryotes in origin can continue to live for a while.

The fourth example: a prokaryotic cell, the least complex level of compartmental organization. When such cell loses its transmembrane electrical gradient the cell is dead. Because such cell has no internal membrane-limited organelles nothing 'alive' remains after the collapse of the membrane potential.

What is the common denominator in these examples and in all other ones with other types of compartments (tissue, organ, aggregate, community etc: (see later in this paper) that pass from 'still alive' to 'no longer alive'? The common denominator is an activity not mentioned as such in the Seven Pillars approach, namely: "Death ensues when a given sender-receiver compartment irreversibly (to exclude regeneration) loses its ability to communicate at its *highest* level of compartmental organization." What happens with the lower levels, e.g., the organs, tissues, cells etc. in the chicken example, or the individual deer in the population example (stay alive or are killed), is irrelevant for the status 'living' or 'not living anymore' of the highest compartmental level. In the case of the chicken, irreversibly damaging the central nervous system, the highest level of coordinated communication in this multicellular organism, causes death. The communication between individual deer, the highest level of communication in a population (as a communicating compartment), is lost in the second example. In an individual cell, the plasma membrane harbors the highest level of communication. If that is killed, the cell is dead.

The conclusion is that *the* difference making property between 'still alive' and 'no longer alive' is none of the PICERAS-temple properties as such, but simply communication activity executed by entities organized in the form of sender-receiver or communicating compartments. It is not any individual pillar that enables communication, but *the interplay-interaction* between all 7 pillars. Thus 'Life' is a *verb* and its very essence refers to communication.

The Nature of Communication and The Architecture of a Communicating Compartment. Gradients. No Life Without Self-Generated Electricity

How to define 'communication'?

Textbooks of General Biology frequently use the term 'communication' but they fall short in explaining what it means, probably because "everybody knows." It is a big mistake to assume that everybody knows what something as self-evident as communication is. Years ago, at the beginning of my thinking on Life's nature, I did not manage to come up with a plausible definition of communication by myself, an embarrassing experience indeed. I had to cross the border to the humanities, which is not always evident in the exact sciences in which I have been active, and invoke the help from specialists in the communication sciences. To my relief, I learned that even specialists in the field find defining 'communication' difficult, at least if they have to reach unanimity on a definition that is acceptable to all, thus to both the exact sciences and the humanities. The same holds true for 'information', 'problem-solving' etc.

The simplest yet workable definition of communication reads: Communication is transfer of information, and such a transfer is only possible in what is called 'a communicating compartment'. This definition requires that information is also plausibly defined. This will be done later in one of the next sections. Communication and interaction are not synonyms. Interaction does not necessarily involve the decoding of a message, while communication does. Thus, communication is a special form of interaction.

Another commonly shared definition, particularly valid when dealing with the various aspects of spoken and written (human) languages and in which 'information' is not mentioned was recently suggested to me: "Communication is sign-mediated interaction (in contrast to non-sign-mediated interactions) whereas the signs that are used underly 3 levels of rules (syntax, semantics, pragmatics).

Communication activity is based upon 4 pillars

The Temple of PICERAS was constructed with concepts mainly from for classical (pre-digital era) biology (**Fig. 1A**).[6] In analogy I have proposed a Temple of Life with concepts formulated in the language of the digital era. Its pillars (**Fig. 1B**) are: hardware (= the body of organisms), software (the coding- and decoding programs, in particular those used in the cognitive memory system), energy (in particular self-generated electricity carried by inorganic ions) and motivation (why do organisms engage in communication and problem-solving at all?). This is the 'innate' language of contemporary students. For them it is self-evident that the engineering rules and methods for constructing the hardware are very different from those for writing software programs. They do not have any problem in accepting that, just like computers, living problem-solving compartments are constructed as sender-receiver entities and that they need 2 different memory systems. The hardware-software-information wording is attractive because of its simplicity and modernity. It is certainly somewhat simplistic, and one should always keep in mind that Life is more than a computer running DNA software.[12,13]

The architecture of a communicating compartment

A communication system invariably consists of a sender that emits information-carrying messages that are always written in *coded form* [14] as already repeatedly outlined before.[5,15] Upon release, the message is transported through a communication channel (air, blood, axon etc.). Finally, a competent (= with appropriate receptors) receiver has to decode, amplify and respond to the message by doing some sort of work (movement, release of another message, generate order etc.) sooner or later (**Fig. 2A**). Gradients, being higher-lower situations, are essential in communication: the message has to move from the sender to the receiver. Maintaining gradients and responding to messages requires energy, this being the major reason why organisms need food. This energy has to be stockpiled in the system before communication activity can start. One could compare it to a mouse trap in which the spring has to be stretched to become functional. All this means that communicating compartments are systems far from their thermodynamic equilibrium: they are in what is called 'a steady-state'. Upon being used, part of the chemical energy gets lost as heat; the dissipative (heat producing) nature of living systems represents another difference between living and non-living systems.

Energy: No Life without self-generated electricity

Communication requires energy, both chemical (ATP e.g.) and electrical. For medical doctors, neurobiologists and electrophysiologists in particular the 'electrical dimension of cells' is self-evident. The general public is more or less familiar with the terms electrocardiogram and electroencephalogram. For disciplines that do not employ biochemical methods, the self-generated-electricity, however the distinguishing property between 'still alive' and 'no longer alive' at the cellular level, the importance of biological electricity may not be so evident. In school we learn the principles of the 'electricity from the socket' as we use it in daily life. Electricity is the movement of charges at very high speed through a conducting medium, e.g., metal wires, water etc. However, although the same electricity-laws (e.g. Ohm's law) apply, most of the electrical phenomena in biological systems have nothing to do with the transport of electrons, but rather with the much slower transport of simple *inorganic* ions such as Na^+, K^+, H^+, Ca^{2+}, Mg^{2+}, Cl^- and HCO_3^-.

Why ions and not electrons? Electrons cannot be stored in the watery environment of the cytoplasm and they cannot be confined in membrane-limited compartments in the cell's interior. Electrons would instantly dissipate into the aquatic environment. In contrast, the much larger inorganic ions do not readily diffuse through the lipidic membranes of cells, unless they can pass through channels that are gated in various ways. Depending on the prevailing conditions ions can be pumped in or out the cells, in particular by energy requiring ion pumps (Na^++K^+-ATPase(s), H^+-ATPases etc). This means that the electrical dimension of cells is based upon the use of a few simple inorganic ions. It also means that if channels and pumps are non-spherically distributed in the plasma membranes (= the usual situation), cells are, in principle, able to drive a self-generated electric current through themselves, at least in some stage(s) of development. This property has given birth to the (undervalued) 'cell as a miniature electrophoresis concept).[16]

The key gradient in living systems is the ionic/voltage gradient over the plasma membrane of all cell types.[16] A potential difference of 50 mV over a membrane 100 nanometres thick, which is an average in animal cells, corresponds to 50,000

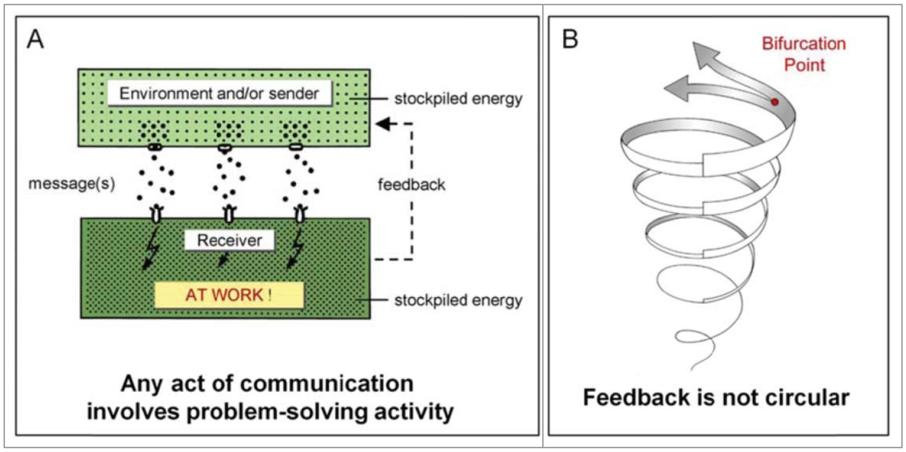

Figure 2. (**A**) Schematic representation of the architecture of a simple communication system. The sender releases a coded message that next is transported through a communication channel (e.g., air, blood, axon etc.) to a competent receiver, meaning that the receptor must have appropriate receptors to catch the message as well sufficient stockpiled energy. If message and receptor match, a signaling cascade is induced involving decoding, amplifying, mobilizing part of the stockpiled energy, and doing some sort of 'work' sooner or later. In case of feedback, the receiver becomes a sender. (**B**) In case of feedback, communication is a unidirectional spiral-like (helical) process. Bifurcation point: more than one solution for a given problem becomes possible.[5]

Volts per cm. Such a huge gradient can be maintained because biological membranes (plasma membrane and intracellular membranes) are very rich in lipids. That turns them into efficient insulators for electricity carried by inorganic ions, but not for electron-carried currents. The lipid membranes are also essential for maintaining Ca^{2+}-homeostasis.[17,18] It means that the main reason why we need lipids in our food is not so much for providing energy, but for ensuring that cells can be surrounded by a membrane with a very low permeability for ions so that cells can build up ionic/voltage gradients. Self-generated electricity is only possible and useful in an aquatic environment.

The problem of communication in a terrestrial environment

It is superfluous to say that a wide canyon in the wording with respect to communication activity and 'Life' separates the exact (biological) sciences and the humanities. This is clearly visible in their respective definitions of communication and of 'Life'. In my opinion, the main reason for this divergence resides in the novel types of communication activity that became needed after the evolutionary ancient ancestors of animals, plants and Fungi left the aquatic environment in which they used to live. It forced them to adapt to transmitting and receiving messages in a gaseous environment instead of in water. Indeed, terrestrial organisms live on the bottom of an ocean of gas, namely air. Yet, their body keeps using the biochemical pathways adapted to communication in an aquatic environment. Its typical wording[19] comprising terms such as membrane potential, action potentials, depolarization, hyperpolarization, ligand-receptor interactions, secondary messengers, Ca^{2+} signaling, cAMP etc. is not suited for describing communication in a gaseous environment. Here a novel vocabulary is needed for analyzing and describing spoken, written-, olfactory etc. languages to complement the 'aquatic vocabulary' of the cellular level. The saying that 'each bird sings its (own, personalized) song', illustrates that the number of causal factors that enable such an endless degree of variability and complexity is at least as high as the ones that govern the variability in cellular communication in an aquatic environment. Just a few examples: semiotics,[14] signs, signals, frequency, messages (form and content), language, word, sentence, intonation, click, grammar, culture, gestures, rituals, mimicking, coding and decoding programs, teaching, mimicking etc.

Engineers have managed to employ the principles of communication in both the aquatic- and terrestrial biological environment in mechanical tools, mainly for increasing the distance over which a message can be propagated and for increasing the speed of transfer or messages. An additional third vocabulary emerged: telephone, radio, TV, computer, internet, cable networks (metal, glass fiber), satellites, with new wording or wording derived from some disciplines of physics and mathematics (waves, electricity, electronics, digitalization, bytes, algorithm etc.).

This concise overview shows that different levels of organization of biological systems as well as the environments in which they operate may require a specific wording to describe their communication activities. In essence: biologists/biochemists focus on Mono-organismal compartments (see next sections). The humanities take the biochemical signaling pathways operating at levels 1–8 of the Monorganismal compartments for granted, and concentrate mainly on Polyorganismal-monospecies compartments. Ecologists are particularly interested in the population level and in Polyorganismal-heterospecies compartments. In a next section a system will be advanced to bring some order in the tangle of communicating systems/compartments.

Definition of 'Compartment'

A major goal of this paper is to outline that all these levels of organization as well as the fact that "each bird sings its song" are, despite all differences, only variants of the following universal unit. A biological compartment – or simply 'compartment' – is a unit based on carbon chemistry and on electricity carried by inorganic ions. This unit is limited by a moderately 'leaky' boundary with appropriate 'holes'; it can stockpile the right form(s) and amounts of energy; and it can generate gradients that can be used for communication to enable the compartment to function from its lowest to its highest levels of compartmental organization (see later). Feedback is very common in communicating compartments. It is the basis for the social and gregarious behavior of living matter: all living systems are interconnected one way or the other by communication. Feedback is not circular but spiral-like (**Fig. 2B**). Retrogression is not possible in communication. As will be mentioned later, this means that retrograde evolution involving the principles of communication is not possible either.

Finally, some types of languages, e.g., spoken ones, can occur in a variety of variants, dialects, and contribute to reproductive isolation, without any mutation being involved. This form of variability is often overlooked in biology in general, and in evolutionary theory in particular.

Bringing order in the multitude of communicating compartments

For fully understanding my definition of life, it is absolutely necessary to have an idea of the variability in the numerous (at least 16) levels of compartmentalization. It matters which level of compartmental organization one is studying. This is also of primordial importance for understanding evolution of biological systems/compartments as well as evo-devo. When analyzing 'Death', the conclusion was reached that Death is linked to the highest level of compartmental organization, and that the fate of the lower levels is unimportant for the definition of Death. This raises the question what the different levels of compartmentalization as related to communicating compartments are. Textbooks usually list 5 levels: the cell organelle, the cell, the multicellular organism, the population and the community, usually without elaborating on what links these levels.

It took me quite a while to find out how nature became organized the way it is, using the communicating compartment as the basic unit of structure and functioning. The invention of ever novel 'languages', allowing solving ever novel problems, turned out to be the thread through the system. My system [5] for classification criss-crosses the borders of the present day classification systems that are based on genetic relatedness. Rather, it is based on sets of genes that allowed the coming into existence of communicational connections, or – in scientific terms- of novel signal transduction pathways. Such sets of genes will likely differ from level to level and from species to species. The biochemistry of major pathways is well documented (see modern textbooks of Biochemistry), and continues to be better and better understood as more and more receptor-ligand pairs are identified.

My classification system has been dealt with before in sufficient detail in other publications.[5,15,20] Here I only outline the 3 main categories.

1. **Mono-organismal compartments**: compartments restricted to one and the same organism:

- the prokaryotic cell and the cell organelles in the eukaryotic cell of prokaryotic origin, e.g. mitochondria and chloroplasts
- the eukaryotic cell
- the cell aggregate
- the syncytium
- the mono-epithelium
- the polyepithelium
- the segmented organism
- the tool-utilizing compartment

2. **Polyorganismal-monospecies compartments**: compartments consisting of more than one individual of the same species:

- the colony
- the heterosexual compartment
- the social compartment
- the baby-inside mother compartment
- the population
- the electrosphere compartment (e.g., humans linked by telephone, radio etc.)

3. **Polyorganismal-heterospecies compartments**: compartments consisting of individuals belonging to different species (communities):

- nutritive and protective compartments (e.g. food chains; host-parasite)
- the planetary compartment: the Gaia-level.[21]

Some of these levels can be further subdivided but it would take me too far also list the subdivisions. Details, description of which type of problems can be solved by the different levels, as well as illustrations can be found elsewhere.[5] All levels correspond to major innovations/revolutions in Mega-Evolution.[5]

Information and the immaterial aspect of Life

Nowadays the terms 'information' and 'information processing' are omnipresent in daily life and in almost all scientific disciplines suggesting that everybody knows what 'information' is.[22] Again, biology textbooks and dictionaries seldom engage in explaining its nature. Upon consulting specialists in the field of informatics and communication sciences, I learned that there are nearly as many definitions as specialists. In other words, there seems to be no definition that everybody agrees upon. One such definition that was communicated to me by a colleague says: "A message contains information if, upon decoding, it decreases the degree of uncertainty in the system." This can be a workable definition in physics but it is not practical in biology, because it is not evident how to quantify the degree of uncertainty. A workable definition for biology could be: A message contains '*information*', when upon decoding the receiver starts to mobilize sooner or later part of its stockpiled energy to engage in some sort of 'work'.[5]

In my view, information is immaterial, but it usually requires a material carrier for its transport. I have met colleagues who do not accept that information is immaterial, with the argument that something that has no mass cannot exist. But how to respond to the following arguments? Absence of something can be information in some circumstances. The information present in e.g., a computer program remains unchanged if it is used 2, 100 or even a billion times. A hormone molecule can be a carrier of information if the conditions are right. E.g. a testosterone molecule in a bottle on the shelf in a laboratory does not carry any information. Yet, it acquires information at the moment that it binds to a membrane receptor in a living cell. By binding, the testosterone molecule does not undergo a change in mass. It is the ligand-receptor interaction that sets off a signaling cascade that is experienced by the target cell as receiving information. Binding of testosterone to the same receptor but present in a membrane preparation or in purified form does not trigger a signaling cascade. It is nothing more than an interaction, illustrating the already cited difference between communication and interaction.

If my view is correct, in addition to the 3 dimensions of space, their dimension in time, and their electric dimension (cells produce their own electricity), living systems also have an immaterial dimension, inherent to the nature of information.

The Meaning of "AT WORK!." The Spring in the Mousetrap. The Purpose of Communication?

In the analogy with the stretched spring in the mouse trap: a hormonal ligand that touches its matching membrane receptor is like a mouse that touches the piece of cheese in the trap. All of a sudden some of the stockpiled energy in the spring is released. To illustrate that this principle also applies to our daily conversations, I did the following experiment in the class room. First I asked one student to raise his right arm for 5 seconds. He did. Next I asked the whole classroom to do the same. Next I reminded them of the conservation of energy law in physics that says that energy cannot be lost or created out of nothing. Then I confronted them with the following conclusion: because of this law in physics, the energy in my command "Raise your arm for 5 seconds!" must equal the energy that all of you have put in raising your arm. Everybody feels that something is wrong, but what? One more step: "You all raise your right arm after you observed that I kept silent for 5 seconds." After some hesitation, the arms start rising. My next challenge was: "Absence of something created the energy for raising your arms." Finally, I asked: "Did I provide the energy for raising your arm, or did my command simply put you at work and make you use part of the stockpiled energy in your body to exert a certain task?" This way, the students become aware of the fact of the 'goal' of communication, usually unintentional and automated, is that the sender emits messages that will put a receiver that has the matching receptors at work sooner or later. This only happens if several conditions are met, e.g. that the message is perceived and that it does not result in a dead-end signal transduction cascade. This aspect of communication is undoubtedly counterintuitive, but nonetheless conceptually and physiologically correct.

Two memory systems and 2 types of progeny, children and pupils. Life as 'A Double Continuum'

The continuation of the machinery required for communication (our body, or with a modern term, our hardware) uses DNA as the carrier of the genetic memory. Nowadays, thanks to the tremendous progress in molecular biology and genetics, the (first) central dogma of biology, (a term not liked by everybody) DNA $\rightarrow$ RNA $\rightarrow$ Protein(s) is well understood.[23] In the course of time it underwent some minor adaptations which are not relevant in the context of this paper.

Currently we are almost as ignorant about the nature of 'the second central dogma, the one that governs the cognitive memory', as Darwin was about the principles of genetics when he published On the Origin of Species.[24] Sooner or later this second dogma will be unveiled. The principles enabling the cognitive memory activity in brain cells are evolutionarily very old.[25] They may date back to the very first cell on earth.[26] Despite their organismal simplicity, bacteria perform complex communications allowing them to deal with a complex environment. They anticipate predictable changes in their environment with a clear sense of both time and space and their immediate neighbors.[25] Quorum sensing is a bacterial language. Bacteria can learn according to Shapiro.[28] I think that a neuronal-type cognitive memory system is not only present in neuronal cells of free-living organisms, but in any cell on earth, possibly in a different gradation. My major argument is that any cell faces the problem as to how to decode an incoming message. A cell can only do so if an appropriate decoding program had been installed in the decoder's memory system *beforehand*. Another argument comes from stem cell research. Neuronal cells do not acquire their specific properties completely *de novo*, but develop them from the information they inherited from stem cells. Stem cells are usually pluripotent; depending upon the conditions they can differentiate into different cell types.

I have explained elsewhere why I think that the seat of the cellular cognitive system resides either in DNA or in a proteinaceous system that is associated with DNA.[5] In case of the second option, my prime candidate is the plasma membrane (with its electrical properties) – cytoskeletal complex (in particular its actin-like molecule part, also with its special electricity conducting properties). DNA and actin present in the chromosomal skeleton of eukaryotes are lifelong present and therefore preferential candidates for memory systems.

It is not because the mechanisms of the functioning of the cognitive memory system are only very partially understood, that one should neglect its importance for e.g., evolution. For example, the consequence of the existence of 2 memory systems, each with their own set of rules, is that, with respect to reproduction, one should think in terms of 2 types of progeny. Reproduction 'the hardware way' yields children, reproduction 'the software way' through teaching-learning yields pupils. When present, the second type of reproduction is much faster, more versatile and more efficient than the first one. The theory of Evolution should take into account this *double continuum* in a better way than neo-Darwinism momentarily does.[15]

The overlooked relationship between communication and problem-solving

Living matter can solve problems, nonliving matter never can. Why? Because only living systems have genes? Because of the central dogma? Or because only living systems are organized in the form of sender-receiver compartments?

If one analyzes the functioning of a communication system, one willy-nilly reaches the unexpected and counterintuitive conclusion that each act of communication is, *at the cellular level* in fact a *problem-solving act*. This follows from the fact that any message (e.g., a hormone molecule binding to a receptor), whatever its nature, is written in *coded form*. The receiver of a message invariably faces the problem as to how to subtract the information present in a message. All incoming messages in organisms (sounds, visual stimuli etc) have, in the end to pass the organizational levels 1 and 2 (= the (sub) cellular level) in my system. Subtracting information from a message does not mean that at higher levels of compartmental organization, e.g., at the level of a conversation by humans, any sentence should invariably solve a problem. Such a conversation can evidently be simply narrative, not requiring any action at the organismal level.

This conclusion is indeed counterintuitive because in daily life, we do not experience our conversations as a problem-solving activity, but as automated. We understand our mother tongue, but no other languages, because as a child our parents, family etc. helped to install in our brain, by teaching and gestures, the decoding program for the sounds they produce. The second aspect is mimicry of behavior that interconnects use of language terms with actions. The automaton aspect of living systems follows from the fact that 99,999. . .% of all communication acts are executed in an automated way because of the pre-installation in our brain of decoding programs. Conscious problem-solving is the exception, not the rule.

The more communication acts a given compartment can execute at a given moment, the more complex the problem(s) that can be solved. When two solutions for a given problem become possible, decision-making, both unconscious and conscious, comes into play. Decision-making happens at 'bifurcation points' (**Fig. 2B**), the overlooked companions of mutations with respect to evolution. In my opinion, this is the basic principle underlying 'free will'.

Motivation

Why do we solve problems? Although problem solving requires an input of energy and is seldom pleasant, we nevertheless engage in it. Why? In order to be rewarded with something, most of the time unconsciously. In my opinion, Life's basic drive (or impulse) is: "Solve problems if you want to enjoy comfort and feel contented!." [5]

Definition of 'Life': 'Life' is an Activity, thus not a Noun but a Verb

The following definition is compatible with all properties of 'the living state', the immaterial one inclusive, that have been published over the years. In my opinion, *what we call "Life" is an activity, thus a verb, executed by carbon chemistry-based entities that generate their own electricity carried by inorganic ions. This activity is nothing else than the total sum of all communication/problem solving acts that are executed in a given compartment at moment t, at all its levels of compartmental organization (cell organelle, cell, tissue, organ, etc.)*. There are at least 16 possible levels of compartmental organization as mentioned before, each of them with a specific language(s).

Symbolic notations of 'Life'

In its simplest formulation, the general symbolic notation of 'Life' (as an activity) reads:

$$L = \Sigma C$$

L = life; **Σ**= total sum; **C** = Communication/problem-solving acts

More detailed:

$$\mathbf{L}\left(\mathbf{S}_{(\mathbf{TC},\mathbf{TE})},\, \mathbf{t}\right) = \sum_{\mathbf{1}}^{\mathbf{j}} \mathbf{C}\left(\mathbf{S}_{(\mathbf{TC},\mathbf{TE})},\mathbf{t}\right)$$

S= type of compartment; **t** = moment at which the communication acts are executed; **1** = lowest level of compartmental organization (1 = prokaryotic cell or cell organelle in a eukaryotic cell); **j** = highest level of compartmental organization (cell, tissue, organ, organism, . . ., aggregate, . . ., population, community, the Gaia-level); **TC** = Type of Chemistry; **TE** = Type of Energy.

This definition says that the 'Life' of all existing compartments is different, both quantitatively (= number of communication acts) and qualitatively (= type of communication acts). Furthermore, it follows from the nature of communication that life cannot remain constant, that it changes continuously, and that it cannot retrograde (**Fig. 2B**).

Is a Computer Alive? Mechanical Life

In the past computers have occasionally been denoted as human exosomatic organs.[22] Nowadays we rather say that they are mechanical extensions of the human brain. Therefore by themselves they do not form one of the possible levels of compartmental organization, but they are inherent to the level 'Tool utilizing compartment' (level 8 in my classification system). Computers are not alive, even if they can perform some problem-solving activities and generate their own electricity (e.g. by means of a solar panel) because they miss the fourth pillar, namely 'motivation' (**Fig. 1B**). Maybe someday the boundary between organic-chemistry-based computers using inorganic ions as carrier for their self-generated electricity (= living organisms) and mechanical computers based on metal-silica chemistry that use electrons as carrier for their electricity will become very thin.[20]

To distinguish between 'truly biological' and 'artificial computer or electronic life', the symbolic notation of life cited before can be made more specific:

'Biological life':

$$\mathbf{L}(\mathbf{S})_{(\text{Carbon chemistry} - \text{based, ion} - \text{borne electric current})}.\mathbf{t)} = \sum_{\mathbf{1}}^{\mathbf{j}} \mathbf{C}\ (\mathbf{S},\ \mathbf{t})$$

'Man-made communication machines such as computers:

$$\mathbf{L}(\mathbf{S})_{(\text{Silicon} + \text{metal chemistry} - \text{based, electron} - \text{borne electric current})}.\mathbf{t)} = \sum_{\mathbf{1}}^{\mathbf{j}} \mathbf{C}\ (\mathbf{S},\ \mathbf{t})$$

The general symbolic notation finally becomes:

$$\mathbf{L}\left(\mathbf{S}_{(\mathbf{TC},\mathbf{TE})},\, \mathbf{t}\right) = \sum_{\mathbf{1}}^{\mathbf{j}} \mathbf{C}\left(\mathbf{S}_{(\mathbf{TC},\mathbf{TE})},\mathbf{t}\right)$$

Where **L** = 'Life activity', **S** = a given system or compartment which uses a given **T**ype of **C**hemistry, and a given type of **E**nergy, **TE**, to produce its communication actions **C**. The condition is that $\Sigma^j C > 0$ and that actions of communication are only 'added up' once.

'Life' is an activity at a given moment **t**. This makes that to make the symbolic notation complete, 'time' too should be defined, not a simple task. The definition of 'time' that I tried to formulate reads: "Time as experienced in daily life (to distinguish it from Newton's absolute time) could, perhaps, be defined as the inertia by which in a given energy-converting system, one form (s) of energy is converted into one or more other form(s) plus change in entropy."[5]

Is a Virus or a Prion Alive?

Certainly not. Because it has no membrane with ion pumps and channels, a virus cannot generate electricity carried by inorganic ions. Furthermore, it has no 'motivation'. Viruses are complexes of proteins and nucleic acids that function as messengers. Prions, well known as causal agents of the mad cow disease almost 20 y ago, are proteins, thus chains of amino acids, that can undergo an abnormal folding and transmit this abnormality to other prion protein molecules in a sort of domino effect without using the complete normal DNA-RNA-Protein synthesis pathway.

Consequences of 'Life' as a double continuum for the theory of evolution: Mega-evolution

My definition, if correct, has important implications for the theory of Evolution because it allows to broaden its scope from "On the Origin of Species by Means of Natural Selection," [24] to "How does 'Life' evolve?," or "How can transfer of information by sender-receiver compartments change in the course of time?." To date, for lack of a plausible definition of 'Life', it is silently assumed in classical neo-Darwinism that the combined principles of micro- and macroevolution, not even always complemented with 'cultural evolution' for *Homo sapiens*, suffice for a (nearly) complete theory of evolution.[29,30] However, the number of authors contesting this view (with solid arguments) is increasing rapidly.[17,18],[31-39]

In a recent paper I have shown that the principles of communication open new avenues not only for the seamless integration of organic- and cultural evolution but also for constructing a much needed Extended Evolutionary Synthesis (EES).[15] The difference in 'Pillars of the temple of Life' in **Fig. 1A** versus in **Fig. 1B** illustrates that by replacing the 'cell' by the 'communicating compartment' as the universal unit of structure, function and evolution, a truly novel paradigm in biology and in evolutionary theory is emerging. The novelty in the communication- and problem-solving approach of evolution theory is that 'Life' is not a single, genetic continuum but a double hardware-software continuum with 2 possible modes for the (transgenerational) continuation of information: the one with reproduction the hardware way (yielding children), and the other with reproduction the software way (teaching-learning where relevant), yielding pupils.

This approach also questions the commonly held view that Selection is the (nearly) universally accepted driving force of evolution. Indeed, selection *is itself a result* from prior problem-solving activity.[30] It mimics doing an exam: not the teacher does the selection but by answering the questions (right or wrong) the students themselves. The teacher only builds up the 'gradients' (exam questions) and he/she only verifies which students succeed in problem-solving. Thus not the posing of the questions but solving them is the driving force in generating success.

This conclusion leads to an at first glance unacceptable conclusion, namely that if problem-solving is the driving force of evolution, that this also means that Life itself is the universal driving force of its own evolution:

The communication act is the basic unit of Life (as an activity)
Any act of Communication is a Problem-solving act, instrumental to adaptation

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Communication/Problem-solving activity, thus Life itself drives its own evolution

This looks like a circular conclusion, thus absolutely worthless. However, it is not circular but spiral-like as depicted in Fig. 2B. Thus Life cannot other than constantly develop in the short run and evolve in the long run in a unidirectional way, because communication is always unidirectional.

One should admire the ingenuity of this principle.

Concluding Remarks

The definition I forwarded in this paper meets all essential criteria of a plausible definition of Life, as outlined by Schejter and Agassi.[1] It does not invoke any not yet known property of living matter. It offers a novel approach, simply by rearranging in a logical order known data from both the exact sciences and the humanities. As a result, the forest (Life's nature) becomes visible for the trees (the various properties/pillars of living matter). Because my expertise is mainly in the exact sciences, in particular in the biochemistry of signaling pathways in neurobiology and endocrinology, my approach focuses more on the biochemical/biophysical and evolutionary ancient aspects of 'Life' that are present in Mono-organismal compartments than on linguistic- or philosophical ones relevant to Poly-organismal compartments. For me 'Life' is mainly written in the language of chemistry that enabled the coming into existence of the cell that became the common ancestor of all contemporary cells. This language is well conserved in evolution up to the present day. When some organisms became terrestrial, superstructures in signaling became necessary. One should keep in mind that the superstructure of human language is probably less than 10 million years old. Communication by the internet dates from a couple of decades ago.

It is hard to believe that 2 truly difference-making properties of living matter as compared to non-living matter, both being practised by ourselves continuously in daily life, namely communication and problem-solving, remained unnoticed for so long. My analysis of the cause of this blindness, from which I also suffered for quite some years, is that only very few people do an effort to analyze the principles of something that is experienced as self-evident, like communication, because one thinks that "everybody knows." Yet, self-evident phenomena are seldom simple. It is self-evident that an apple will always fall downwards and not upwards. It took the great mind of Isaac Newton to formulate the laws of gravity. To date, we still don't fully understand the physical principles underlying gravity as a force. A similar situation prevails for the cognitive memory: everybody uses it, but nobody understands how it really works.

Clear definitions of 'Life' and 'Death' are relevant for medicine, in particular with respect to some ethical questions, e.g., with respect to the status of coma patients and fetuses. A good definition of 'Life' is also relevant for the humanities. I can imagine that students in philosophy, psychology, sociology, the communication sciences and economy to name a few disciplines, might gain more insight in their specific fields of interest by becoming aware of the causal relationship between communication and problem solving activities, based on 4 pillars.

Biology as a discipline, despite its enormous successes in recent decades and proof of the contrary, continues to be perceived as a less hardcore science than physics, chemistry or mathematics. In the minds of many, biology is rather a compilation of interesting facts than a truly fundamental science because it has (as yet) no unifying principle like $E = mC^2$ in physics or the atomic theory in chemistry. With my approach this can change drastically as it unveils a candidate unifying principle that reads: "Living matter, being invariably organized in the form of sender-receiver compartments, incessantly talks/transfers information, thereby solving problems and changing continuously, both in the short run (development) and the long run (evolution)." In very concise form: "While talking, Living matter solves problems" and $L = \sum C$.

Replacing 'the cell' by 'the sender-receiver (communicating) compartment' as the universal functional unit in biological systems, the prokaryotic cell being the smallest such unit, offers many advantages for teaching. Textbooks of general biology should (urgently) incorporate chapters on the most important activities of all living beings, namely communication and problem solving. They should also list clear definitions of 'Death', 'Life', 'communication', 'information', 'gradients', 'dissipative systems', etc. and stimulate the use of the terms 'hardware' and 'software' in biology.

With respect to the ongoing discussion whether or not neo-Darwinism needs an upgrade,[31] the theory of evolution – the very heart of biology – in its present form could shed many of its shortcoming if the principles of communication were better incorporated into it. In particular, such an integrative advance could render superfluous the Cartesian mind-body distinction and the dichotomy between cultural and genetic/organic evolution that grew out of it. In my approach there is ample room for feelings, emotions, decision making, problem-solving, ethical principles as well as for optimism in life's basic drive.[5,15]

Paraphrasing Theodosius Dobzhansky, my final message to students is: Keep always in mind that nothing in biology and evolutionary theory makes sense except in the light of communication and problem solving."[38,40]

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No potential conflicts of interest were disclosed.

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