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Towards a Hierarchical Definition of Life, the Organism, and Death

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Abstract Despite hundreds of definitions, no consensus exists on a definition of life or on the closely related and problematic definitions of the organism and death. These problems retard practical and theoretical development in, for example, exobiology, artificial life, biology and evolution. This paper suggests improving this situation by basing definitions on a theory of a generalized particle hierarchy. This theory uses the common denominator of the "operator" for a unified ranking of both particles and organisms, from elementary particles to animals with brains. Accordingly, this ranking is called "the operator hierarchy". This hierarchy allows life to be defined as: matter with the configuration of an operator, and that possesses a complexity equal to, or even higher than the cellular operator. Living is then synonymous with the dynamics of such operators and the word organism refers to a select group of operators that fit the definition of life. The minimum condition defining an organism is its existence as an operator, construction thus being more essential than metabolism, growth or reproduction. In the operator hierarchy, every organism is associated with a specific closure, for example, the nucleus in eukaryotes. This allows death to be defined as: the state in which an organism has lost its closure following irreversible deterioration of its organization. The generality of the operator hierarchy also offers a context to discuss "life as we do not know it". The paper ends with testing the definition's practical value with a range of examples.

Keywords Artificial life · Biology · Evolution · Exobiology · Natural sciences · Particle hierarchy · Philosophy · Big History · Astrobiology

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1 Introduction

In a chronological overview of developments, Popa (2003) presents about 100 definitions of life, meanwhile demonstrating that no consensus exists. Many classical definitions include long lists of properties, such as program, improvisation, compartmentalization, energy, regeneration, adaptability and seclusion (Koshland 2002) or adaptation, homeostasis, organization, growth, behavior and reproduction (Wikipedia: Life). Most properties in such lists are facultative; it is still possible to consider an organism a form of life when it does not grow, reproduce, show behavior, etc. The inclusion of facultative aspects is a source of lasting difficulty in reaching consensus on a definition of life. Because of the seeming hopelessness of the situation, certain scientists have adopted a pragmatic/pessimistic viewpoint. Emmeche (1997) christened this viewpoint the "standard view on the definition of life". He suggests that life cannot be defined, that its definition is not important for biology, that only living processes may be defined and that life is so complex that it cannot be reduced to physics. Others have warned that a comprehensive definition of life is too general and of little scientific use (e.g. van der Steen 1997).

In their search for a definition, other scientists have focused on properties that are absolutely necessary to consider an entity life. In this context Maturana and Varela (1980, p. 78) have proposed the concept of autopoiesis (which means "self making"). They use the following definition: "*An autopoietic machine is a machine organized (defined as a unity) as a network of processes of production (transformation and destruction) of components which: (1) through their interactions and transformations continuously regenerate and realize the network of processes (relations) that produced them; and (2) constitute it (the machine) as a concrete unity in space in which they (the components) exist by specifying the topological domain of its realization as such a network.*" Special about the autopoietic process is, that it is "*closed in the sense that it is entirely specified by itself* (Varela 1979 p. 25)".

The concept of autopoiesis has increasingly become a source of inspiration for discussions in the artificial life community about how to define life (Bullock et al. 2008). Reducing the number of obligatory traits defining life to just one, autopoiesis is a rather abstract concept. People have sought, therefore, to describe some of the processes that underlie autopoiesis more specifically. An example of such a description is a triad of properties defining cellular life: container (cell membrane), metabolism (autocatalysis) and genetic program (e.g. Bedau 2007).

These descriptions, however, have not resulted in a consensus definition of life. This has led Cleland and Chyba (2002, 2007) to suggest that a broader context, a "theory of life", is required. In line with a broader framework, life may be regarded as a special realization of the evolution of material complexity. According to Munson and York (2003), considering life in a general evolutionary context requires arranging "*all of the phenomena of nature in a more or less linear, continuous sequence of classes and then to describe events occurring in the class of more complex phenomena in terms of events in the classes of less complex phenomena.* "An important property of such a hierarchy would be that *"... an increase in complexity is coupled with the emergence of new characteristics ... suggesting that the hierarchical arrangement of nature and the sciences is correlated with the temporal order of evolution*". Similar views for integrating material complexity and the evolution of life can be found, for example, in the work of Teilhard de Chardin (1966, 1969), von Bertalanffy (1968), Pagels (1985), Maynard Smith and Szathmáry (1995, 1999), and Kurzweil (1999).

In contribution to these discussions, the present author has published an evolution hierarchy for all "particles". The latter hierarchy uses the generic word "operator" to address

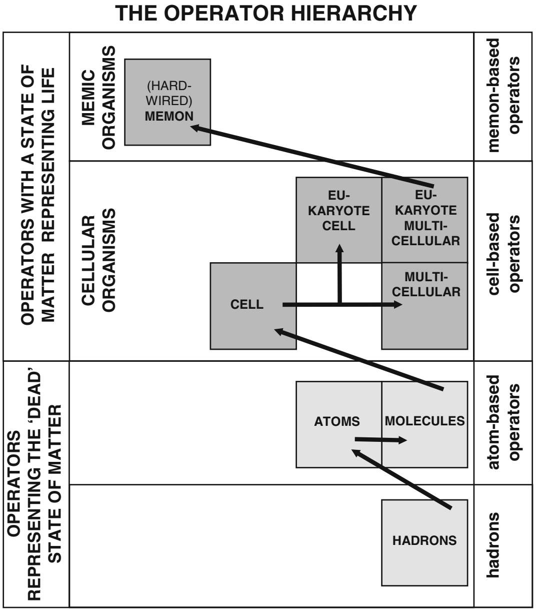

Fig. 1 Using the operator hierarchy to define life and organisms. *Arrows* indicate how closures create operators (more information can be found in Jagers op Akkerhuis (2008), and the author's website www.hypercycle.nl)

both physical (e.g. quark, atom, and molecule) and biological particles (e.g. prokaryote cell, eukaryote cell, and multicellular). The word operator emphasizes the autonomous activity of the entities involved, which "operate" in a given environment without losing their individual organization. The hierarchical ranking of all operators is called the "operator hierarchy" (see Fig. 1; Jagers op Akkerhuis and van Straalen 1999; Jagers op Akkerhuis 2001, 2008 and the author's website www.hypercycle.nl). Because the operator hierarchy is important for the definition of life proposed below, the outlines of this theory are summarized in the following lines.

The operator hierarchy ranks operators according to the occurrence of a circular pattern, such as that which connects the beginning and end of a process or structure. Circularity causes a closed organizational state, also referred to as "closure" (for discussions of closure see, for example, Heylighen 1990; Chandler and Van de Vijver 2000). Because closure causes a discrete "quantum" of organization (e.g. Turchin 1977, 1995; Heylighen 1991), the operator becomes an "individual entity", a "whole" or a "particle", while still retaining its construction of smaller elements. Closure thus defines the operator's complexity level and sequential closures imply a higher complexity level. An operator's closure is the cause of its existence and typical for its complexity. This implies that complexity is not measured in terms of the number of genes, functional traits or organs of an organism, but in a very abstract way, in terms of the number of closures. Upon losing its closure, the organization of the operator falls back to that of the preceding operator. The actual shape of a closure can differ. Biological examples of closure are the cell membrane and the circle of catalytic reactions allowing the cell to maintain its chemical machinery. It is essential for a strict ranking that a lower-level and a higher-level operator always differ by exactly one closure level. The single closure (eukaryotic cell) or a parallel pair of closures (autocatalysis plus membrane of the cell) that define the next level are referred to as "first-next possible closure(s)". A consequent use of first-next possible closures allows physical and biological operators to be ranked according to the "operator hierarchy" (Fig. 1). The operator hierarchy includes quarks, hadrons, atoms, molecules, prokaryotic cells, eukaryotic cells, multicellulars (e.g. plants, fungi) and "animals", the latter representing an example of the operators that possess a neural network with interface and that are called "memons" in the operator hierarchy.

Due to its focus on closure, the operator hierarchy represents an idealization because it excludes potential transition states in between two closures. For example, several hundreds of metal atoms may be required before a functional Fermi sea transforms a collection of single atoms into a metal grid. Also, the emergence of multicellularity (discussed in detail in §3 below) may require a colonial, multicellular state in between the single cell and the multicellular operator. The above shows that transition states form natural intermediate phases in the emergence of closures. The operator hierarchy does not include these transition states, however, because its hierarchical ranking is exclusively based on entities that already show first-next possible closure.

The main reason for writing this paper, and adding yet another definition of life to the listings, is that the operator hierarchy offers several advantages in solving definition problems. First, the definitions of the operators are generally applicable because they focus on the essences of organization. For example, demanding autocatalysis leaves open which specific catalysts will perform the process. Second, the use of first-next possible closures ensures a critical filtering of only obligatory properties from property lists. Finally, the use of the operator hierarchy makes it easy to develop a hierarchy-based definition of life. In other words, the operator hierarchy offers a novel path for structuring and simplifying discussions about which entities are life.

The following paragraphs discuss different aspects of existing definitions of life and examine new ways to define the organism, living and death. At the end, a test of the practical value of the present definitions for the solving of a range of classical problems, such as a virus, a flame, a car, a mule and a mitochondrion, will be presented.

2 Defining Life and the Organism

Before discussing the use of the operator hierarchy for defining life, living and the organism, it is important to note that when talking about definitions, care should be taken that "*a definition is a series of superimposed language filters and only the definiendum (the term to be defined) can penetrate it*" (Oliver and Perry 2006). Problems may arise when the words used for the definiendum and for the filter have a broad meaning or have different meanings in different contexts. It is thus useful to elaborate on the current context for "life" before continuing.

"Life" has different meanings in different contexts. For example, people refer to the period between birth and death as their life (this is the best day of my life) even though lifetime would be more correct. In addition, the experience of "being alive", or "living", also carries the label of life (to have a good life). Other uses of life holistically refer to the importance of selective interactions in ecosystems that over generations lead to better-adapted life forms (the evolution of life). Ruiz-Mirazo et al. (2004) have proposed a definition of the latter type. They state that life is "*a complex collective network made out of self-reproducing autonomous agents whose basic organization is instructed by material records generated through the evolutionary-historical process of that collective network*". In philosophy, life is sometimes considered a graded concept for being because all what is, is alive in the measure wherein it is (Jeuken 1975). Due to the contextual dependence of these and other interpretations, it is improbable that a general definition of life can be constructed. van der Steen (1997) indicates that even if such an overly general definition existed, it would probably be difficult to applie it to specific situations.

To avoid problems with generality and multiple interpretations of concepts, the present study adopts a limited viewpoint, presuming a one-to-one relationship between a definition of life and a specific material complexity. In this context, life is an abstract group property shared by certain configurations of matter.

The operator hierarchy offers a context for a general matter-based definition of life. Focusing on all operators showing a complexity that exceeds a certain minimum level, the hierarchy suggests a definition of life *sensu lato* as: matter with the configuration of an operator, and that possesses a complexity equal to or even higher than the cellular operator. Only the prokaryote cell, the eukaryote cell, the prokaryote and eukaryote multicellular, the hardwired memon and the potential higher-level operators fit this definition (Fig. 1). In addition to this general definition, various specific definitions are possible by focusing on operators that lay between a lower and an upper closure level. An example of a specific definition is one describing cellular life (e.g. algae, plants and fungi) as: matter showing the configuration of an operator, and that possesses a minimum complexity of the cellular operator and the maximum complexity of a multicellular operator. The latter includes only the cell, the eukaryotic cell, the prokaryotic and the eukaryotic multicellular. It is possible to choose any of these approaches for defining living as: the dynamics of an operator that satisfies the definition of life.

The above approach results in a strictly individual based definition of life as a group property of certain operators. This definition has the advantage, that it offers a solid basis for defining the creation of offspring. Subsequently, the evolution of life can be dealt with as an emergent process occurring in any system with interactions between individual living entities that lead to differential survival of variable offspring, produced either without or with recombination of parental information.

The organism is the key ontological unit of biology (Etxeberria 2004; Korzeniewski 2004) and is also referred to as a "living individual". Understanding the latter requires insight into what is "living", and what is an "individual". By defining "living" as the dynamics of those operators that satisfy the definition of life, the operator hierarchy uses operators instead of individuals because operators define a being or an individual more strictly than the Latin concept of *individuum*. The word individuum stands for an "indivisible physical unit representing a single entity". This definition leaves a great deal of room for choice of the elements that form the physical unit and for the rules that determine indivisibility. These indeterminacies may be the reason for the discussion about whether certain life forms are organisms. Townsend et al. (2008) use the phrase "unitary organism" to indicate the individual organism. However, certain jellyfish, for example, the Portuguese Man O" War (*Physalia physalis*), look like individuals, but consist of differentiated individuals, each with its proper neural network (e.g. Tinbergen 1946). In the operator hierarchy, the latter jellyfish are colonies, not organisms, because each contributing individual has its proper neural network as its highest emergent property, and the colony still lacks a recurrent interaction of the neural interfaces of the individuals.

The operator hierarchy now suggests a way to create congruency between the definition of life and the definition of the organism by accepting as organisms only entities that fit the operator-based definition of life. For example, using the general definition of life, only the cells, the eukaryotic cells, the prokaryotic and eukaryotic multicellulars and the memons are organisms.

3 Levels of Life

a. *The cell.* The most important properties of the cell are the autocatalytic set of enzymes and the membrane. The autocatalytic set shows reproduction as a set. Every molecule in the set catalyzes a reaction that produces some other molecule in the set until any last reaction product closes the cycle. In different ways, reproduction as a set is part of various theories about the origin of life (e.g. Rosen 1958, 1973, 1991; Eigen 1971; Gánti 1971; Eigen and Schuster 1979; Kauffman 1986, 1993; Bro 1997; Kunin 2000; Hazen 2001; Martin and Russel 2002; Hengeveld and Fedonkin 2007).

   Autocatalysis demands that a cell can potentially autonomously sustain its catalytic closure. Accordingly, if a cell allocates a part of its autocatalytic closure to another cell, the cell is no longer an operator. An example of the latter is the mitochondrion. It is generally accepted that mitochondria started the interaction with their host cells as autonomous endosymbiontic α-proteobacteria. Over many generations, these bacteria transferred more than 90% of their catalytic control to their host (Allen 1993; Berg and Kurland 2000; Searcy 2003; Capps et al. 2003; Lane 2005). The loss of the potential of autocatalysis implies that mitochondria have become a special kind of organelle.

   In addition to autocatalysis, the operator hierarchy demands an interface because a set of autocatalytic enzymes only gains the physical individuality that allows its maintenance when it functions in a limited space, the limits being part of the system. The integration of autocatalysis and the membrane is part of various important theories, for example, the theories of autopoiesis (Varela 1979) and of interactors (Hull 1981).

b. *The eukaryote cell.* A single cell has two dimensions for creating a next closure. One is to create cooperation between cells, which leads to multicellularity. The other is to create an additional closure mediating the hypercyclic functioning of the cell in the form of the nucleus. Interestingly, it is quite likely that the most important complexity boundary in cell biology, that between prokaryotic and eukaryotic cells, thanks its existence to the energy boost and genetic enrichment offered by endosymbionts. With respect to the emergence of eukaryotic cells, theories roughly divide along two major lines depending on whether the nucleus or the endosymbionts emerged first. In addition to other aspects, support for the nucleus-first hypothesis comes from allegedly primitive eukaryotes that show a nucleus without harboring endosymbionts. Genetic analyses (Rivera et al. 1998) and observations of endosymbiont traces (Clark and Roger 1995), however, suggest that the "primitive eukaryotes" are recent developments that lost their endosymbionts in a process of evolutionary specialization. The endosymbiont hypothesis advocates that a merger between a methanogenic bacterium that was member of the archaea and an α-proteobacterial endosymbiont created the eukaryotic cell (Martin and Russel 2002). Subsequent transmission of genes for membrane creation from the endosymbiont to the host allowed it to produce membranes that formed the basis for the engulfment of the nucleus. Whatever the actual path taken by evolution, the operator hierarchy focuses on the occurrence of closure involving both structural and functional aspects of the host cell, resulting in an internal interface for the autocatalytic set and the mediation of its functioning. Even though endosymbionts may become obligatorily integrated in the functioning of their host cell by the transfer of part of their genetic regulation to the host cell, they do not mediate the functioning of the autocatalytic set of the host nor form an interface for its functioning. For this reason the operator hierarchy does not regard endosymbiosis, but the nucleus as the relevant closure that defines the limit between prokaryotes and eukaryotes.

c. *The multicellular*. When does a group of cells become a multicellular operator and, according to the above definition, an organism? In the operator hierarchy, multicellularity involves a structural and a functional component represented by structural attachment of cells and an obligatory recurrent pattern of functional interactions between them. As such, it is possible to define a multicellular operator (a multicellular organism *sensu stricto*) as: a construction of mutually adhering cells showing obligatorily recurrent interactions based on the same interaction type, that has the potential of maintaining its functioning as a unit and that does not show memic structure.

Multicellularity has developed independently in many branches of the phylogenetic tree (reviews by, for example, Bonner 1998; Kaiser 2001; Grosberg and Strathmann 2007) presumably because it is associated with a range of evolutionary advantages. Multicellularity increases mobility and access to resources, and reduces predation, and finally yet importantly, the cells in genetically uniform multicellulars share the same genes and do not have to compete with each other for reproduction. Willensdorfer (2008) indicates that the alleviation of reproductive competition allows for a division of labor because "*cells can specialize on non-reproductive (somatic) tasks and peacefully die since their genes are passed on by genetically identical reproductive cells which benefited from the somatic functions*".

In some cases a multicellular organism results from the aggregation of individually dwelling unicellulars (for example, true slime molds, Ciliates and Myxobacteria). More generally, a multicellular organism develops when daughter cells cohere after cell division. A simple, temporary form of multicellular life is present in slime molds. Here, genetically-different, individually-dwelling cells aggregate and bind using membrane proteins to form a colonial state in which the cells intercellularly communicate by diffusion. At a certain moment, obligatory interactions between cells lead to the formation of irreversible cell differentiation producing a reproductive structure. During this state, the slime mold cells are temporarily a multicellular organism.

With the evolutionary development of plasma connections, advanced multicellular life became possible. Plasma connections allow efficient and rapid intercellular communication, involving electrical signals, chemical signals and nutrient transport (Mackie et al. 1984; Peracchia and Benos 2000; Nicholson 2003; Panchin 2005). Plasma connections have evolved in several lineages of multicellulars. Plasma connections between animal cells depend on gap junctions, between plant cells on plasmodesmata, in blue-green algae on microdesmata, and in certain fungi or in developing insect eggs on incomplete cell walls. The evolution of gap junctions some 700 million years ago coincided with an explosion of multicellular life forms.

Multicellular organisms may go through life stages that are not multicellular. For example, sexual reproduction involves single-celled egg and semen. Furthermore, during the two-, four- and early eight-cell stages most vertebrate embryos have loosely attached cells without obligatory dependency. Accordingly, they represent a colony. When separated from the colony, the cells show a normal development. Early separation of embryonic cells is the reason why identical twins exist. Embryo cells in the early stages can even mix with another embryo's cells of the same age and develop into a normally functioning organism, called a chimera, in which some organs and tissues belong to a different genotype than others. A definition of life should, therefore, respect that an organism's cells may differ in genotype. From the late eight-cell stage, the development of gap-junctions marks the emergence of regulation as a unit, which makes the cellular colony a multicellular.

The realization of a multicellular's potential for maintenance depends on prevailing conditions. For example, a tree twig that is stuck in the ground may become a tree again if the weather is not too warm, too cold, or too dry, etc. and if the twig has the genetic potential for regeneration and is large enough, in good condition, etc.. Whether the twig is an organism depends on its potential to show all dynamics required for being a multicellular operator. This potential is in principle gene-based, but it depends on the condition of the phenotype and the environment for its realization.

Sometimes two multicellular organisms show symbiosis, such as plants living in close association with mycorrhiza fungi in their roots. As the fungus and the plant already are multicellular on forehand, a plant with mycorrhiza represents an interaction between two multicellular organisms.

d. *The memon*. Attempts to define life frequently focus on the typical properties of the first cell. The underlying assumption may be that all organisms consist of cells and that, for this reason, the definition of the living properties of cells will automatically cover other, more complex organizations. According to the operator hierarchy, this reasoning is incomplete because, with respect to artificial intelligence, it unsatisfactorily excludes technical life *a priori*. The reason is that the fundamental construction of the brain is not principally different when built from cellular neurons, technical neurons (small hardware acting as a neuron) or programmed neurons (virtual devices modeled to act as neurons). Even though all organisms on earth currently consist of cells or show neural networks that consist of cells, the fact that technical memons may, one day, have a brain structure similar to cellular memons implies that a general definition of life must consider the possibility of technical memons.

Memons show a neuron network and a sensory interface. The basic neuron-units have been named categorizing and learning modules or CALMs and allow for a recurrent network of CALMs (Murre et al. 1992; Happel 1997). The interface includes sensors that allow the memon to perceive its body and environment, and effectors that allow it to move the cellular vehicle it resides in. The interface and vehicle co-evolved during the evolution of neural networks. In principle, it is possible to construct a functional memon from any kind of technical hardware that provides the required neural architecture. This is the reason that the study of neural networks in biology shows a fundamental overlap with research on technical artificial intelligence. The recognition that memons show a recurrent network of CALMs surrounded by an interface allows Siamese twins with separate brains to be classified as two memons sharing the same vehicle and showing in this vehicle a partial overlap of their interfaces.

4 No Life, no Reproduction

According to some authors (e.g. the von Neumann and Burks 1966) reproduction is a pre-requisite for life. Like the chicken and the egg problem, it can also be said that life is a pre-requisite for reproduction. Clearly, any decision on this matter critically depends on the context that is used to define life. If the operator hierarchy is used, the least complex life form is the prokaryotic cellular operator. Two arguments currently suggest that life is a pre-requisite for reproduction. The first states that even though all other organisms originate from the first cell by reproduction, the first cell itself had an inorganic origin. The emergence of the first cell thus shows that life does not obligatorily result from reproduction. The second argument posits that organisms do not need to show reproduction, i.e., producing offspring, to comply with the operator-based definition of life; The operator-based definition demands that organisms show two closures: autocatalysis and a membrane. Autocatalysis can be regarded as reproduction without creating offspring. As Jagers op Akkerhuis (2001) pointed out, autocatalysis implies that a cell autonomously creates a structural copy of its information, a process that is called "structural (auto-) copying of information". Before answering the question of whether the structural (auto-) copying of the cell's information means that it must reproduce, it is important to detail the concept of information. For the latter, I suggest applying Checkland and Scholes (1990) definition of information to the autocatalytic set. These authors have defined information as data with a meaning in a context. In line with this reasoning, Kauffman (1993) proposed that, by selecting the autocatalytic process as the context, every catalytic molecule becomes a data-unit with a catalytic meaning (the "purpose" mentioned by Kauffman 1993, p. 388) and represents a part of the information of the autocatalytic process. Following one round of autocatalysis, or more rounds to account for the loss of enzymes over time, the cell contains copies of all of its information. At that moment, it has autonomously performed structural copying of information and fulfills all the requirements of the operator hierarchy, even when it does not produce an offspring. Based on this reasoning, the capacity of autocatalytic maintenance is an obligatory requirement for cellular life and reproduction is a possible consequence.

The above implies that it is not relevant for a general definition of life to distinguish between life forms with or without replication, as Ruiz-Mirazo et al. (2004) has suggested. The latter authors distinguish "proto-life stages" that do not show a phenotype-genotype decoupling (soma with genes) from "real life" with genes. In line with the operator hierarchy based definitions, Morales (1998) warns that "*if reproduction is required: This is a troubling development, because it means that we could not tell whether something is alive unless we also know that it is the product of Darwinian evolution.*" The operator-based definition considers life as a prerequisite for reproduction instead of reproduction as a prerequisite for life. Consequently, worker bees, mules, infertile individuals and other non-reproducing organisms and/or phenotypes are life. This point of view also solves problems that may arise when demanding that memons be able to reproduce as a prerequisite for recognizing them as life forms. In fact, none of the cellular memons living today shows reproduction, at least not reproduction of their neural network structure determining their closure. The things they pass on during reproduction are the genes of their cells, allowing the development of a multicellular organism with a neural network, capable of learning but devoid of inherited neural information other than reflexes.

5 Life Holding its Breath

The above chapter shows that reproduction is not a prerequisite of life but a possible consequence of it. Going one step further, it can also be concluded that metabolism is not a prerequisite for life. Many taxa such as bacteria, protozoa, plants, invertebrates and vertebrates have developmental stages showing natural inactivity (seeds, spores) or reversible inactivation when submitted to desiccation, frost, oxygen depletion, etc. The inactive state carries the name of anabiosis, after the process of coming to life again (for a review of "viable lifelessness" concepts, see Keilin 1959). Another type of reversible inactivity showing marked similarity with anabiosis is the state of neural inactivity in memons following anesthesia. An anesthetic that blocks the transmission of signals between neurons while leaving the remaining metabolic activity of the neurons intact causes a reversible absence of neural activity that corresponds to an anabiotic state of the memon.

Even in the early days of the biological sciences, scholars discussed whether dried or frozen anabiotic stages are alive at a very slow pace, or whether they are truly static states of matter. In 1860, the famous Société de Biologie in Paris wrote a lengthy report on this subject (Broca 1860–1861). Quite importantly, this report concluded that the potential to revive an anabiotic stage is an inherent aspect of the organization of the material of which the object consists and that it is equally persistent as the molecular state of the matter forming the system. In short, the Société de Biologie found that "*la vie, c"est l"organisation en action*". Additional support for this conclusion came from Becquerel (1950, 1951) who subjected anabiotic stages to a temperature 0.01 degree above absolute zero, a temperature at which no chemical processes can occur, even not very slowly. Becquerel demonstrated that structure alone is enough to allow revival at normal temperatures. Anabiosis from absolute zero or complete desiccation has led to the conclusion that "*The concept of life as applied to an organism in the state of anabiosis (cryptobiosis) becomes synonymous with that of the structure, which supports all the components of its catalytic systems*" (Keilin 1959), or that "*life is a property of matter in a certain structure*" (Jeuken 1975). With respect to the question of: what certain structure?, the operator hierarchy suggests that all operators with a complexity similar to or higher than the cell answer this question.

6 Life as We do Not Know It

Considerations about "life as we do not know it" depend on assumptions. As a context for such assumptions, the operator hierarchy offers two advantages. First, the operator hierarchy has its basis in the general principle of first-next possible closure. Second, the rigid internal structure of the operator hierarchy offers a unique guide for assumptions about life that we do not yet know.

Based on the general principle of first-next possible closure, the operator hierarchy shows a strict sequential ranking of the operators. Assuming that closures act as an absolute constraint on all operator construction, the operator hierarchy then has universal validity. Support for the latter assumption comes from the observation that, as far as we know, all operators with a complexity that is equal to or lower than the molecules seem to have a universal existence. If this universality extends to the biotic operators, the material organization of higher-level operators, such as cells and memons, may then possibly be found in the entire universe. Such universality would significantly assist in the search for exobiotic life forms because alien life may show similar organization to the life we do know, at least with respect to the first-next possible closures involved. The demand of closure still leaves a good deal of freedom for the physical realization of operators. On other planets, different molecular processes may form the basis of the autocatalysis and interface of the first cells. Similarly, the operator hierarchy poses no limits to the actual shape, color, weight, etc. of exobiotic multicellular organisms. Furthermore, even though the presence of neural networks may be required for memic organization throughout the universe, the operator hierarchy does not restrict the kind of elements producing these networks, or the details of the neural network structure other than demanding hypercyclicity and interface.

The rigid internal structure of the operator hierarchy allows predictions about the construction of life forms that have not yet evolved on Earth. Of course, any discussion of this subject involves speculation, but the operator hierarchy may well offer a unique starting point for such a discussion. In an earlier publication (Jagers op Akkerhuis 2001), I have indicated various future operator types with a higher complexity than the cellular hardwired memon. To minimize the aspect of speculation, I would like to discuss here only the memon immediately above the cellular hardwired memon (see Fig. 1), the so-called "softwired memon". According to the operator hierarchy, this type of memon should be able to copy information structurally. This means that the organism should be able to copy all of its information by copying the structure of its neural network. At a lower level in the hierarchy, cells do this by copying their genetic molecules. Softwired memons can also do this. They are based on a virtual neural network that resides in computer memory arrays. During their operation softwired memons continuously track all their neurons, neural connections, connection strengths and interactions with the interface. It is therefore only a small step for softwired memons to read and reproduce all the knowledge in their neural network by copying these arrays. On these grounds, it may be deduced that softwired memons (or still higher complexity memons) form the easiest way to satisfy the demands of the operator hierarchy for the autonomous, structural copying of information. The operator hierarchy suggests therefore that life as we do not know it will take the shape of technical memons.

The above reasoning shows that the operator hierarchy offers clear criteria with respect to different forms of "artificial life". The acceptance of an artificial entity as life is only possible when it shows all of the required properties of an operator. Referring to the difference between strong artificial life and weak artificial life, which do and do not consider a-life entities as genuine life, respectively, it would be fully in line with the present reasoning to consider as genuine life all a-life entities that fulfill the requirements for being an operator.

7 On Life and Death

Given the present focus on states of matter, it is quite simple to define dead matter as: all operators that do not fit the general definition of life. It is more difficult, however, to define death.

Given the current point of view, death represents a state in which an organism has lost its closure. The use of closure in this definition helps prevent that "*.... the properties of an organism as a whole [would be confused] with the properties of the parts that constitute it*" (Morales 1998). However, organisms also loose their closure during transitions that are part of life cycles and that are not associated with the organism's death. For example, the closure of the organism is lost and a new closure gained when the zygote exchanges its unicellular organization for the multicellular state of the embryo and when the multicellular embryo develops to a memic state. Is it possible to specify the loss of closure during death in a way that excludes closure losses during life cycles?

With respect to the above question of how to exclude the loss of closure during transitions in life cycles when defining death, the general process of deterioration offers a solution. During their lives, organisms deteriorate because of injury and ageing. The loss of closure marking death is always associated with the organism's irreversible deterioration. Demanding irreversible deterioration, therefore, helps to prevent that one would be tempted to consider, for example, a caterpillar as having died, when its tissues are reorganized during the transition via the pupae to a butterfly. Accordingly, it is possible to describe death as: the state in which an organism has lost its closure following irreversible deterioration of its organization.

Using the above definition, death may occur in either an early or late phase of the deterioration process, and following the death of multicellulars, a short or long period may pass until the organism's body parts become dead matter. The latter has its cause in the hierarchical construction of multicellular organisms. Accordingly, the loss of the highest closure implies a classification of the remaining body as an operator showing the first-next lower closure.

Death depends on the loss of closure. To illustrate the contribution of this statement to the analysis of death, the death of a memon can be used. Due to the memon's strongly integrated organization, death may occur at various levels that affect other levels. For example, the multicellular regulation may be the first to collapse due to the loss of liver functions. After a certain period, this will cause failure of neural functioning, the latter marking the memon's death In another situation, the neural functions may be lost first, and the memon is the first to die, dragging its body with it in its fall. However, sometimes enough neural activity may remain for a vegetative functioning of the memon's body as a multicellular unit. The vegetative state cannot maintain itself autonomously (in principle, a requirement for a multicellular organism) but it may continue given the right medical care. If this care is withdrawn, the multicellular body will start deteriorating after which the cells in the organs and tissues will start dying at different rates. At a certain point, the multicellular closure is lost, and separately surviving cells have become the next level operators to die. Physiological differences between cells now determine the period during which they can survive in the increasingly hostile habitat of the dead memon, which is cooling below the normal operating temperature of cells and which shows many adverse chemical changes such as the lowering of oxygen levels, the release of decay products of dead cells, etc. Shortly after the memon's death, it is possible to take intact body-parts, organs and cells from its body and sustain their functioning following transplantation to a favorable environment. For example, the offspring of cells from the cervix of Henrietta Lane are still cultured as He La cells in many laboratories.

8 The Inutility of Property Lists

The above arguments and examples have explored the possibilities of using the operator hierarchy for creating coherent definitions of life, the organism, living and death. However, how should the outcome be evaluated? Have the present attempts led to definitions that could be generally accepted in the field? A way of evaluating this that has become rather popular is to check the results against lists of preset criteria. Those who want to evaluate the present approach in this way may want to examine the following lists of criteria.

Morales (1998) has published a list of properties for a definition of life that includes the following criteria: 1. Sufficiency (Does the definition separate living entities from non-living ones?), 2. Common usage (simple classification of easy examples), 3. Extensibility (Does the definition deal with difficult cases, such as viruses, mules, fire, Gaia, extraterrestrial life and robots?), 4. Simplicity (few ifs, buts, ands, etc.) and 5. Objectivity (Criteria are so simple that everyone applies them with the same result). Emmeche (1997) offers another criteria list for a definition of life that includes the following: 1. The definition should be general enough to encompass all possible life forms. (The definition should not only focus on life as we know it.), 2. It should be coherent with measured facts about life, (It should not oppose obvious facts.), 3. It should have a conceptual organizing elegance. (It can organize a large part of the field of knowledge within biology and crystallize our experience with living systems into a clear structure, a kind of schematic representation that summarizes and gives further structure to the field.), 4. The definition should be specific enough to distinguish life from obviously non-living systems. Emmeche (1997) furthermore states that a definition "should cover the fundamental, general properties of life in the scientific sense". Korzeniewski (2005) has also proposed a list of criteria for a cybernetic definition of life, and Poundstone (1984) has extracted further criteria for life from the work of von Neumann and Burks (1966). Oliver and

Perry (2006) have suggested a list more or less similar to that of Emmeche (1997) focusing specifically on properties of a good definition.

With respect to the use of criteria lists, I agree with other authors (Maturana and Varela 1980; van der Steen 1997) that it is not necessarily an advantage if a theory performs well or a disadvantage if a theory performs poorly according to a list of criteria; an approach's value does not necessarily correspond to its performance in these types of checklists. The match depends on the similarity in major goals and paradigms and the creator's influence on the selection and definition of criteria in a given list. In addition, the selection of "favorable" lists can lead to false positives.

For the above reasons, I am convinced that it is only possible to evaluate the currently proposed definitions "the hard way", i.e., by critically examining the internal consistency and transparency of their logic. In this respect, the present approach has the advantage of a fundamental bottom-up construction. It starts with defining elementary building blocks, the operators, and their hierarchical ranking in the operator hierarchy. To recognize and rank the operators, the operator hierarchy uses first-next possible closures. In the resulting hierarchy, the definition of every higher-level operator depends, in an iterative way, on a lower-level "ancestor" until a lowest-level ancestral system is reached, which is presumably the group of elementary particles that according to the superstring theory may have a common basic structure. The result is a strict, coherent and general framework that is open to falsification: the operator hierarchy. Subsequently, the operator hierarchy offers a fundament to define a range of secondary phenomena, such as life, the organism, living and death. Because of the reference to the operator hierarchy, the present definitions are short, logical statements that show a high specificity with respect to whether a certain entity satisfies the definition (list of examples in the following section).

9 Testing the Definition of Life

When using the operator hierarchy as a context for a definition, it is easy to conclude that viruses, prions, memes or replicating computer programs are not forms of live. Both a virus with a surrounding mantle and a viral strand of DNA or RNA are not operators, thus not life. Prions are molecules, thus not life. Memes, such as texts and melodies, are pieces of coding that memons can decode and replicate (Dawkins 1976). Accordingly, memes are not operators, thus not life. Ray (1991) has created computer programs that can replicate themselves onto free computer space, show mutation, and modify and compete for the available space in a virtual world called Tierra. Since its start, this virtual "ecosystem" has seen the evolution of a range of different computer programs. In the same way as molecular viruses depend on cells, the programs in Tierra depend on a computer to copy and track their structure. Accordingly, they are not operators, thus not life. Sims (1994) has used genetic algorithms for evolving virtual computer creatures with body parts and a neural network with interface. The simulation of these animal-models allows virtual movement such as finding and grasping virtual food items. Sims's programmed creatures may possess hypercyclic neural networks and on these grounds show similarity to softwired memons. According to the operator hierarchy, a softwired memon should autonomously be able to copy its information structurally. Although I am not an expert in this field, it seems to me that Sims's organisms do not *themselves* keep track of their arrays with information about their interface and neurons, neural connections, and connection strengths, and that they do not autonomously organize their maintenance. Assuming that the latter interpretations are correct, Sims's computer animals are not yet life.

The use of the present definition also allows the effortless rejection of other systems that are not operators and sometimes receive the predicate of "borderline situations", such as flames, whirlwinds, crystals, cars, etc. Technical, computer based memons, however, such as robots, can be operators when they show the required structure.

To summarize the practical applicability of the present definition of life, I include a list of the examples that were discussed in the text and supplement them with some additional cases. The examples in this list form three groups depending on whether the entities involved are operators or not, and whether they show a complexity that equals or exceeds that of the cellular operator. In the text below I use the concept of "interaction system" (e.g. Jagers op Akkerhuis 2008) for all systems that are not operators because the interactions of their parts do not create a first-next possible, new, closure type.

Group A. Systems that are not life because they are not an operator

1. An entire virus particle with external envelope (represents a simple interaction system)
2. A computer virus based on strings of computer code
3. A flame
4. A tornado
5. A crystal
6. A car
7. A bee colony (The colony is an interaction system, and the bees are organisms.)
8. A cellular colony not showing the requirements of multicellularity (The individual cells are organisms and thus represent life.)
9. A colony of physically connected cellular memons (As long as the individuals lack the required memic closure.)
10. A robot (As long as it is a non-memic technical machine.)
11. Computer simulations of organism (including memons) that depend on external "orchestration"
12. A cutting/slip of a plant that cannot potentially show autonomous maintenance given the right conditions (It lacks the closure required for multicellularity.)
13. A separate organ, such as a liver or leg (Not potentially capable of autonomous maintenance.)
14. Endobiontic bacteria having lost genes that are obligatory for autonomous maintenance. The transfer to the genome of the host of DNA coding for enzymes required in autonomous maintenance implies a partitioning of the aucatalytic closure between the endobiont and its host,. Because of this, the endobiont is no longer an autonomous organism but has become a special kind of organelle.

Group B. Systems that are operators but that are not life because their complexity is lower than that of the cellular operator

1. A prion
2. Self-replicating DNA/RNA particles (Catalyze their own copying in a solution containing the right building materials.)
3. A DNA or RNA string of a virus that is copied in a cell

Group C. Operators representing life

1. A cutting/slip or other plant part that can potentially maintain itself given favorable environmental conditions

2. Anabiotic organisms (The fact that they are dried, frozen, etc. does not take their required closure away.)
3. Fully anaesthetized animal supported in its functioning by a mechanical heart-lung support and showing no neural activity (This can be regarded as a form of memic anabiosis with the potency become active again.)
4. A computer memon or other technical memon (A memic robot.)
5. An artificial cellular operator constructed by humans
6. A exobiotic cellular operator with another chemistry than that found on earth
7. Sterile or otherwise non-reproducing organism (e.g. a mule, worker bee, sterile individuals)
8. Endoparasites or endosymbiontic unicellular organisms living in cells and still possessing the full potential of autocatalysis

10 In Conclusion

1. Overviews of the definitions of life from the last 150 years show that no consensus definition on life exists. In the light of the continuous failure to reach consensus on this subject, certain scientists have adopted a practical viewpoint, accepting, for example, the use of property checklists for identifying living systems. Others have advocated that the need for a generally accepted definition remains acute. Amongst the proposals for solving the problem is the suggestion to construct a broader context, a "theory of life" before continuing with attempts to define of life.
2. Inspired by the latter suggestion, the present paper invokes a classification of the generalized particle concept, called the operator hierarchy". This hierarchy has several advantages for defining life: first, it offers a general context for including and differentiating between life and non-life, and second, it offers the unique possibility to extrapolate existing trends in the evolution of material complexity and to use these as a guide for discussions about "life as we do not know it".
3. In close association with the reviewed literature, the use of the operator hierarchy allowed the following definitions to be suggested:

    A. From the viewpoint of the evolution of material complexity, life is: matter with the configuration of an operator, and that possesses a complexity equal to or even higher than the cellular operator.
    B. Living describes the dynamics of an operator that satisfies the definition of life.
    C. The definition of unitary organisms can take the form of: the operators that fit the definition of life.
    D. A multicellular organism (the cellular operator showing the multi-state) is: a construction of mutually adhering cells showing obligatorily recurrent interactions based on the same interaction type, that has the potential of maintaining its functioning as a unit and that does not show memic structure
    E. Dead matter applies to all operators that do not fit the definition of life.
    F. Death is: the state in which an organism has lost its closure following irreversible deterioration of its organization.

4. From the discussion of examples in the literature, it was concluded that the present set of definitions easily distinguishes life and non-life regardless of whether this is tested using the "obvious examples", the "borderline cases" or "life as we do not know it". This suggests that the present approach may well offer a practical step forward on the path towards a consensus definition for the states of matter representing "life".

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