

Autopoiesis, Autonomy, and Organizational Biology: Critical Remarks on “Life After Ashby”

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Abstract: In this paper we criticize the "Ashbyan interpretation" of autopoietic theory by showing that Ashby's framework and the autopoietic one are based on distinct, often incompatible, assumptions and they aim at addressing different issues. We also suggest that in order to better understand autopoiesis and its implications, a different and wider set of theoretical contributions, developed previously or at the time autopoiesis was formulated, needs to be taken into consideration: among the others, the works of Rosen, Weiss and Piaget. By analyzing the concepts of organization and closure, the idea of components and the role of materiality in the theory proposed by Maturana and Varela, we advocate the view that autopoiesis necessarily entails self-production and intrinsic instability and that can be realized only in domains characterized by the same transformative and processual properties exhibited by the molecular domain. From this theoretical standpoint it can be demonstrated that autopoietic theory does neither commit to a sharp dualism between organization and structure nor to a reflexive view of downward causation, thus avoiding the respective strong criticisms.

1. Introduction

The main appeal of the notion of autopoiesis consists in its internal coherence, its manifold domains of application, and also in its apparent self-sufficiency as an almost “standalone” theory, characterized by a considerable explanatory power and by what can be thought as some sort of theoretical completeness. Tom Froese and John Stewart in their paper¹ (Froese & Stewart, 2010) put into question the latter aspect, by pointing out some possible conceptual limits of the autopoietic theory, as well as the necessity to consider its genealogy. They also suggest the relevance of Ross Ashby as a possible contributor to the development of the systemic ideas orbiting around the theoretical notion of biological autonomy. In doing so they contributed to stimulate the process of clarification of Humberto Maturana’s own theoretical point of view and of his relations with Francisco Varela, already started around a decade ago (Maturana, 2002; Maturana, 2011; Maturana, 2012).

We find a basic agreement with Froese and Stewart in that autopoietic theory does not explain all that it aims at, that is too abstract and does not develop in depth or explicit enough

¹ Hereinafter we refer to it as ‘Life after Ashby’.

many crucial conceptual nodes - e.g. adaptive interaction, the role of thermodynamics processes, the intrinsic instability of living systems etc. Nevertheless we think, as we will show, that in most of the cases it is not necessarily incompatible with them².

Also, we agree with the importance of reconstructing the historical and the theoretical roots of autopoiesis. Yet, we consider this theory as part of a wider theoretical and epistemological tradition, a bundle of theories of the living and of cognition, gathered around the notion of biological autonomy, more or less directly connected, but sharing a specific approach to the problem of the characterization of the living. That is, they deal with biological systems primarily in terms of organization instead of focusing exclusively on the intrinsic properties of their components. It is an approach that today, is being particularly fertile of new ideas and developments in many disciplines.

Notwithstanding this basic agreement on the necessity of pointing out the limits of autopoiesis – and the difficulties in achieving this goal – and on the importance to study the theory in its historical and theoretical context, we contest the arguments proposed in “Life After Ashby” from both the methodological and theoretical points of view.

In the first place we contest the historical reconstruction attempted in the paper, for two main reasons. Firstly because it interprets autopoiesis exclusively in Ashbyan terms, so ignoring the rich and complex cultural context represented by systems sciences, 1st and 2nd-order cybernetics, embryology³ and sciences of self-organization etc. Even in the case Ashby’s influence had been deeper – something that we also contest – its historical reconstruction would result in something completely different than assuming the two frameworks to coincide, even in the early phase. In fact, if we consider the history of cybernetics alone, the theoretical approaches elaborated in those years had been varying and developing quite fast since Ashby’s pioneering works. This transformation is depicted in detail by Pickering in the case of British cybernetics (Pickering, 2010), but it is even more evident if we consider second order cybernetics: in particular von Foerster’s work and the influence exerted on him by Piaget’s line of research (von Foerster, 1982).

Secondly, the Ashbyan interpretation itself is attempted by ascribing to Maturana and Varela’s theory the whole of Ashby’s theoretical framework, together with its most fundamental basic assumptions, on the basis of a few terminological similarities - in a moment in which the Chilean authors were attempting to develop a new and increasingly precise language⁴ - and a couple of quotations of Ashby’s work in early essays on autopoiesis. If we ascribe to autopoietic theory the theoretical basis of another theory, focused on different issues than those of self-production and characterization of life, it is natural that contradictions follow, and that the former seems not to be able to deal anymore with its theoretical goal. Instead, by analyzing the main theoretical pillars of autopoietic theory we are forced to draw the opposite conclusion than that reached by Froese and Stewart. We argue, in fact, that the theoretical framework of autopoietic theory, although exhibiting some terminological similarities with Ashby’s work and referring to his notions (e.g. Ultrastability) in a few occasions in its early stage of development⁵, it is radically incompatible with Ashby’s approach from the theoretical point of view. The two frameworks, in fact, differ in the very basic theoretical foundations and in the main domains of application. Also, the reference to Ultrastability does not necessary make the autopoietic system

² For an overview of the core ideas, contributions and limits of the autopoietic theory see also Bich and Etxeberria (forthcoming).

³ Embryology is an important source of the idea of autonomy and of biological organicism. Weiss and Waddington were embryologists. Piaget himself was involved and was inspired by them.

⁴ This process is quite evident if we consider Varela and Maturana, 1972, where the terminology is in course of definition. What in the following papers will be called organization was then called structure or theory; what will be called structure was at the moment referred to as “instance” or materiality.

⁵ See for example Varela and Maturana, 1972 and Maturana, 1970: 25.

an ultrastable one, especially because the expression is not referred to autopoiesis itself but it is used in describing the nervous system rather than the organism as such (Maturana, 1970: 25).

An interpretation of autopoiesis in strict Ashbyan terms is therefore misleading and rather than being able to point out clearly the limits of the former in understanding life, shows that the latter is insufficient not only in order to better understand autopoietic theory but also, as we will show, the specificities of the biological domain. Furthermore, even in its initial development, the autopoietic theory progressively detaches itself from the framework of first order cybernetics, focuses the attention on the specificity of the living with respect to artifacts, and uses the notion of mechanism⁶ as a theoretical tool, strictly intertwined with the concept of organization, rather than as an attempt to apply a mechanical – let alone Newtonian - approach to biology.

It will be our content to emphasize that looking for different and more appropriate sources for interpreting the autopoietic theory is a necessary step in order to understand it, to point out its intrinsic limitations and attempt to solve them. We advocate the view according to which, even in the case a direct historical derivation cannot be identified, it is more useful and enlightening to analyze autopoietic theory in the light of authors and approaches which are closer to it from the theoretical point of view and address similar problems, like for example Robert Rosen's - and his precursor Nicolas Rashevsky's - relational biology (Bich & Damiano, 2008; Letelier et al., 2011), together with the works of Jean Piaget and Paul Weiss (Bich & Damiano, 2008). All together –the list is far from complete, and includes among the others Tibor Ganti, and many more –they represent a coherent group of theories of the living that constitute the historical and epistemological basis of the contemporary notion of biological autonomy. As such they are crucial for understanding and developing it.

Our main purpose will be theoretical, and it will consist in showing the deep differences between Ashby framework and the autopoietic one; the latter theory's crucial conceptual pillars rooted in a processual notion of organization and its target being the problem of the characterization of the living. In the next two sections we will analyze the main theoretical nodes where we disagree with the Ashbyan interpretation of autopoiesis and its implications, starting from the distinction between organization and structure, and addressing the issues of self-production, intrinsic instability and closure of autopoietic systems. Then we will take into consideration derived issues like those of downward causation and regulation, with regards to which we think a comparison with Ashby can be the occasion for a clarification of the concepts that could result ambiguous in the autopoietic literature.

2. Organization, structure and their role in the systemic characterization of biological systems

It is difficult to confront the main theoretical nodes around which the comparison between Ashby and autopoiesis is made. One reason is that the language and the concepts used by the two approaches - apart from the few cases of overlapping pointed out by Froese and Stewart - tend to diverge. Ashby's framework, in fact, is based on the language of dynamical systems theory, and it is articulated in terms of changes of states, behaviors and regularities. The language of autopoietic theory is much closer to biology. It refers to a domain of processes, relations and reciprocal modifications between processes; changes in terms of transformation of transient components rather than changes of states of fixed components: a terminology underlining a theoretical domain in which the distinctions between operators and states tend to collapse. It is a symptom of a radical difference.

⁶ See Varela and Maturana, 1972. See also Bechtel 2007 for an analysis of the role of the idea of mechanism in the tradition of biological autonomy.

2.1 Organization and materiality put into context

We start our theoretical analysis by addressing the general issue of organization, one of the main points on which is based the argument about “the autopoietic commitment to Ashby”: that in both theories materiality is “irrelevant”, an expression directly borrowed from Ashby (1956: 1), who in the early papers on autopoiesis (e. g. Varela & Maturana, 1972: 379) is cited together with Wiener (1948) and the tradition of self-organization. Interpreting the relation between organization and materiality only in relation to Ashby - and the latter being considered literally irrelevant - can be misleading and hide all the explanatory power of autopoietic theory. As already suggested in the paper of 1972, the interest in organization is shared by a wider group of researchers. This aspect needs to be contextualized even more. The focus on organization, in fact, is characteristic of several authors and lines of research from cybernetics, system theory, cognitive science, biology in general, embryology, mathematical biology, etc.: we are dealing with a whole tradition of research in organizational biology, or a general systemic approach to biology centered on the concept of ‘organization’.

Many authors can be gathered under this trend⁷, who besides the differences in the specific theoretical frameworks, share a common interest in characterizing systems, especially biological ones, in terms of relations and transformations⁸ instead on focusing on the intrinsic properties of their material components considered in isolation or in different configurations. It is a line of research developed in opposition to the approach of mainstream molecular biology (Jacob, 1970; Monod, 1970), and to the identification of life with the properties of a specific component, namely the nucleic acid (Bich and Etxeberría, forthcoming)⁹. It is a tradition that has deep roots that can be traced back at least to the work of Claude Bernard (1965), its interest in organization and its idea - deeply relational and processual - of conservation of the (self-produced) *internal milieu* of living system in spite of the turnover of components¹⁰.

An interpretation of the role of organization in autopoietic theory exclusively in terms of Ashby’s framework is therefore not justified. In addition, other authors share more similarities and a same domain of investigation – living organisms – with autopoietic theory. The main interest shared by this tradition in biology consists in the attempt to catch the common aspect to all the actual and possible manifestations of life, and to point out what differentiates living systems from other kinds of systems. And this, they sustain, cannot be found in the basic components of living systems but in the way they are related. The same components, in fact, can participate in other kinds of systems and, furthermore, in living systems they are subject to continuous transformations. These aspects are particularly evident in Rashevsky’s theoretical shift from a biophysics centered on structural models of energetic transformations¹¹ to a Relational Biology (Rashevsky, 1954):

⁷ The contributions from some of them are discussed in Bich & Damiano, 2008.

⁸ They are characterized by a common processual and transformative “ontology”, if this last term can be ascribed at all to a tradition deeply rooted in epistemology. However, it is the circular and self-referential nature of autopoiesis that allows for such ascriptions.

⁹ This focusing on the properties of a specific material component, to which almost all properties of the system are reduced, is also the target of the main autopoietic criticism against vitalism and molecular biology taken together: “*in a vitalistic explanation, the observer explicitly or implicitly assumes that the properties of the system, or the characteristics of the phenomenon to be explained, are to be found among the properties or among the characteristics of at least one of the components or processes that constitute the system or phenomenon. In a mechanistic explanation the relations between components are necessary; in a vitalistic explanation they are superfluous*” (Maturana, 1978: 30).

¹⁰ The heritage of Bernard is acknowledged by Maturana (1980: 52). The theoretical contribution of Bernard to the development of the tradition of biological autonomy is analyzed in Bechtel (2007).

¹¹ An approach criticized by Wiener (1948: 42).

“we must look for a principle which connects the different physical phenomena involved and express the biological unity of the organism and of the organic world as a whole” (Rashevsky, 1954: 321).

“all organisms can be mapped on each other in such a manner that certain basic relations are preserved in this mapping” (Rashevsky, 1960, v. II: 325)

These ideas will be then developed by Rosen into his well known relational model of the M/R-System: a model of the minimal metabolism of living systems (Rosen, 1972; 1991). This model is characterized by important aspects that are particularly relevant for the discussion presented here: (a) relational descriptions as radical alternatives to the description of living systems in dynamical terms as changes of states; (b) biological organization as a concatenation of processes of transformations of components that achieves global self-production through the continuous interaction with the environment in terms of assimilation of substrates¹²; (c) self-referentiality in models of living systems, expressed through the formalism of Category Theory, in which functions operate on other functions so that distinctions such as those between operators and states, hardware and software, collapse.

This attempt to find the relational topology common to all organisms is also characteristic of a cybernetician like Gregory Bateson, as it emerges from his famous quotation about “the structure that connects”:

What pattern connects the crab to the lobster and the orchid to the primrose and all the four of them to me? And me to you? And all the six of us to the amoeba in one direction and to the back-ward schizophrenic in another? [...] What is the pattern which connects all the living creatures? (Bateson, 1979: 8).

Paul Weiss is even more focused on the biological issue of the distinctive mechanisms at work in living systems, in particular in relation to the issues risen by embryology (Weiss, 1963; 1968). He points out the crucial importance of the organization, by stressing the insufficiency of considering only individual processes or components. Hence, he advocates an (organizational) approach based on the idea of a network of processes of transformation able to account for the interdependency of components and processes, and their intertwining in realizing the self-production of the whole system. By distinguishing between “maintenance” and “operation” he also introduces a theoretical specification that is extremely relevant in interpreting theories like the autopoietic one, and the behavior of components in living systems in general. In fact it opens the dimension of production, that is absent in Ashby’s framework focused on operations (on states).

For however familiar and expert one maybe with one particular feature of a cellular system, be it genic replication, contractility, respiration, selective permeability, impulse conduction, enzyme action, membrane formation, or what not, he misses the essence of the problem of cellular unity unless he takes into account of the indispensable *cooperative coexistence of all these features*; that is, that every single one must contribute to the maintenance and operation of all the others in such a way that collectively they achieve a relatively stable and durable group existence [...]

By the time we have laid out the pattern of the reproductive and functional performances of a cell in a total, rather than sectorial view, we recognize that the basic criterion of cell life lies in the intricate web of interactions and interdependences among all of its component activities (Weiss, 1963: 186).

¹² This is a form of complementarity between organization and materiality that in Rosen terminology is *Closure to efficient causation* and *Openness to material causation*, in Piaget, and in Maturana and Varela, is *organizational closure* and *structural openness*.

By applying a classical argument, he also stresses the importance of organization. He puts into evidence the difference - in the case in which the components are the same - between a “bag of compounds” and what he calls “highly coordinated chemical machinery”. This difference cannot be due to the intrinsic property of the constituents of the two systems, as they are the same, but to the way they are organized, thus appealing to a distinct logical order of description.

The standard affirmative answer, that after all proteins in the form of enzymes do hold the key to the synthesis of all other, non-protein, compounds in cell, begs the question; for it still leads only to a random bag of compounds, instead of a highly coordinated chemical machinery that is the cell.....Logically this ‘coordinating principle’ cannot be of the same categorical order as the individual reactions themselves – just one more of them. We must therefore acknowledge the problem of *coordinated unity* of the cell as a real one. (Weiss, 1963: 190).

In this way, Weiss anticipates the autopoietic idea of two complementary levels pertaining to the material structure and the organization of the living system. He further develops this idea in terms of global constraints on the components – contextual, not whole to parts - and of interplay between variance and invariance. This is another idea that is not far from the basic ones of autopoietic theory. It is coherent with a processual conception of living systems in which the individual parts are subjected to continuous alterations while the unity which they integrate and realize is conserved:

[...] the complex is a system if the variance of the features of the whole collective is significantly less than the sum of variances of its constituents; or written in a formula:

$$V_S \ll \sum (V_A + V_B + V_C + \dots + V_n)$$

In short, the basic characteristic of a system is its essential invariance beyond the much more variant flux and fluctuations of its elements or constituents (Weiss, 1969:12).

Furthermore, his idea of highly coordinated systemic organization characterized by interdependence and cooperativity, especially when considered in relation to development, leads to conceiving the system’s invariant side, that of organization, as a collective property that doesn’t involve any primary subsystem, or hierarchical control, and entailing an intrinsic activity of the system. The capability to maintain the organization of the system and to self-stabilize in face of material transformations or perturbations does not belong to the individual components of a biological system, but to their organizational and network-based transformative interaction. In other words it belongs to the totality. This idea of shared responsibility, non-decomposability of the system and absence of hierarchical cybernetic control is also shared by autopoietic theory (see section 3.2 below).

While the transformative-organizational theoretical perspective developed by Relational Biology and Weiss provides closer and more biologically oriented analogies with autopoiesis than Ashby’s framework, which is focused on machines and operations, the work that is more similar to the autopoietic one from the theoretical point of view is the one elaborated by Jean Piaget (Piaget, 1967; Bich & Damiano, 2008). Piaget’s approach also shares with autopoiesis the indissoluble intertwining between theory of the living and theory of cognition, that brings epistemology at the heart of biology and vice versa.

His initial concern regards the insufficiency of the thermodynamic notion of openness alone, as introduced by von Bertalanffy (1952) - and later developed by Prigogine (Nicolis & Prigogine, 1977) - in making sense of the distinctive character of living system. In line with the systemic tradition, he considers the latter to be organizational. He then combines the energetic and material requirement with a particular topology of relation between transformative processes inside the living system: an organization able to support self-production. This is one of the first explicit conceptual definitions of “organizational closure”.

He proposes organizational closure as a concept complementary to that of thermodynamic openness. The framework is the systemic one of transformative and processual unities.

The central ambiguity is that of the 'open system', for, if systems exist, then something like a closure intervenes, which has to be reconciled with the 'opening'. The opening is certainly justified and is founded on the basic idea that 'in biology there is not rigid organic form carrying out vital processes but a stream of processes which are revealed as forms of a seemingly persistent kind' (von Bertalanffy). The opening then is the system of exchanges with environment, but this in no way excludes a closure, in the sense of a cyclic rather than a linear order. This cyclic closure and the opening of exchanges are, therefore, not on the same plan, and they are reconciled in the following way, which may be entirely abstract but will suffice for a analysis of a very general kind.

$(AxA') \rightarrow (BxB') \rightarrow (CxC') \rightarrow \dots \rightarrow (ZxZ') \rightarrow (AxA') \rightarrow \text{ecc.}$

A,B,C ...: the material or dynamic elements of a structure with cyclical order A', B', C' ...: the material or dynamic elements necessary for their maintenance: the interaction of the terms of the first range with those of the second \rightarrow : the end points of these interactions. In a case like this we are confronted by a closed cycle, which expresses the permanent reconstitutions of the elements A,B,C ... Z, A, and which is characteristic of the organism; but each interaction (AxA'), (BxB'), etc., at the same time represents an opening into the environment as a source of aliment." (Piaget, 1967: 155-156).

Piaget's idea develops Weiss' appeal to coordination, cooperation, interdependence and gives it a precise and operational formulation in terms of organizational circularity and openness to the environment. The latter is an active one, as the organism, according to Piaget, is supposed to actively look for food. Piaget's theory is also particularly interesting as it inherits and integrates also other ideas from embryology – in particular Weiss' and Waddington's ideas - and applies them to the living organism tout court in order to describe the mechanisms underlining their ontogenetic adaptation. In particular he applies Waddington's ideas of assimilation and accommodation to the metabolic adaptive interaction of the organizationally closed organism to its environment: a process characterized by the interplay between structural openness and organizational closure, structural variability and organizational invariance. Structural variability allows internal adaptive restructuring through the continuous activity of regulation mechanisms, an aspect developed by Piaget and his school in many fields (Piaget, 1967b). This adaptive aspect of biological autonomy is, instead, less developed in the autopoietic theory, through not incompatible with it.

Coming back to the organizational framework and its relation with materiality, Piaget anticipates one of the main pillars of the autopoietic theory: the theoretical explicitation of the difference between organization and structure. He defines the relational scheme common to all the living systems, distinguishing it from - yet embedding it in - its effective materialization in specific and variable processes and components, and from the thermodynamic idea of openness and continuous dynamical flux. In such a way he is able to catch the peculiarity of the living systems in that their materialization keeps changing, while what persists are the transformative relations that integrate the components in the global unity¹³.

It is interesting to point out, in Piaget's formulation, the importance of organizational circularity, which corresponds to an intertwining of transformative processes that continuously re-constitute the components of the systems and the processes themselves and, in doing so, continuously realize the organism itself. This aspect is particularly relevant because, so formulated, the interplay between material and energetic openness and organizational closure

¹³ In Piaget, as well as in Rosen, the emphasis on the production of a physical boundary is missing, while, instead, it is an important feature of the notion of autopoiesis (Varela et al., 1974).

grounds the self-assertive character of living systems into the very theoretical heart of the organizational approach to biological autonomy¹⁴.

In the autopoietic theory the distinction and complementarity between organization and structure is a key concept. It allows for any kind of dynamicity in the system, without necessarily committing to a reactive framework like that entailed by Ashby's notion of Ultrastability. The Autopoietic system, in fact, can be at the same time stable in terms of organization and intrinsically instable at the level of structure. Thus, it is not necessary to assume it as a fixed and stable unity by default, and its dynamics triggered only by external perturbations, like asserted by Froese and Stewart. But let us proceed with order.

The distinction between the two aspects is at the core of the theory since its early formulations, when the terminology is not yet fixed.

Any explanation of a biological system must at least contain two complementary aspects one referring to its structure [later called "organization"] and the other referring to it as an instance [later called "structure"]. The first must account for the specific dynamic configuration of components that define it; the second must account for how its particular components enter in the given interrelations that constitute it. (Varela & Maturana, 1972: 380)

And then:

The structure of living systems and their actual (material) components are complementary yet distinct aspects of any biological explanation: they complement each other reciprocally but cannot be reduced to one another. (Varela & Maturana, 1972: 382).

Organization, then, is defined as the topology of relation that constitute a unity of a certain class. Its structure, instead, consists in its material realization. Structure can vary in time, or can vary among different unities of the same class. The possibility of different structural realizations of living systems can also justify in principle multiple realizability.

The significance of the term "irrelevant" in reference to materiality, that Maturana and Varela (Varela and Maturana, 1972: 379) borrow from Ashby (1956:1) - on which Froese and Stewart build part of their argument - needs to be contextualized not only historically in the wider tradition of biological autonomy, but also in the autopoietic theory itself. It is a radical expression, used in the early autopoietic texts in order to emphasize the primacy of organization over the intrinsic properties of the components for understanding the distinctive character of a system. This is especially important in the case of living systems, where components are transient while the system as a whole is not: a position shared with the tradition mentioned above. At the same time it points out some limits of the approaches to the study of

¹⁴ This brief survey of a possible genealogy of the notion of biological autonomy is far from exhaustive. Its purpose is only to show that the context in which autopoietic theory was born was a lot richer and complex than can be thought if autopoiesis is compared with one of few instances of 1st-order cybernetics. It also aims at showing that other theories of the time are more useful and insightful in order to interpret the main conceptual pillars of autopoiesis, especially if the ultimate target is to understand and develop the contemporary notion of biological autonomy. Other authors can be added to the list. Of course, among the others, Ganti (2003) needs to be quoted, even if his influence at the time is to be verified. Prigogine is surely a point of reference for his development of the ideas of dynamical stability, and of molecular aggregates exhibiting dynamical pattern (Nicolis and Prigogine, 2007), even if the autopoietic theory points out the need to go beyond the idea of pattern and structural stability (see for example, Varela, 1979; for an analysis of the distinction between pattern generation and autopoiesis in an epistemological context, see Bich, 2012). From a more philosophical point of view Georges Canguilhem (1965), who probably first coined the term autopoiesis (we thank Arantza Etxeberria for this reference), Hans Jonas (1966; see also Weber and Varela, 2002) and many other authors, we are sure, need to be added to the list (see also Bich and Etxeberria, forthcoming).

living systems based on energetic or material considerations only¹⁵. Yet, it does not imply that materiality is to be ignored, but only that the relevant properties of components are those relational properties that they exhibit in integrating the system they realize:

What is not so apparent is that the actual nature of the components, and the particular properties that they possess other than those participating in the interactions and transformations which constitute the system are irrelevant and can be any. In fact, the significant properties of the components must be taken in terms of relations, as the network of interactions and transformations into which they can enter in the working of the machine which they integrate and constitute as a unity. (Maturana & Varela, 1973: 77)

What is “irrelevant”, then, is not all that concerns materiality, but those properties of components that do not participate “in the interactions and transformations” which constitute the system. Therefore autopoiesis does not exclude in principle the problem of materiality. Indeed, the latter is deemed as extremely relevant when a definition of the organization of living systems is to be elaborated, as structure and organization are mutually specified and materiality needs to satisfy the conditions of realization of the organization it integrates. Nonetheless it is true that the autopoietic theory remains on a high level of abstractness and does not develop an analysis of the structural properties of possible effective realizations of a system of this class¹⁶.

The distinction between organization and structure, rather than excluding the latter, opens a large range of possible materializations of the autopoietic organization. The autopoietic theory, in fact, identifies the crucial aspect of components not in their intrinsic properties, but in their interactive specificity that emerges in the particular context in which the components are involved. What is central, then, are those relational properties that define the forms of interaction that the elements can establish. As a consequence, the constitution of the elementary level is allowed to change, although in a well defined range of variability: the space of all the elementary compositions able to generate a recursive chain of functional relations of reciprocal production. In such a way the autopoietic theory provides a theoretical framework for expressing the idea that in living systems the conservation of organization is obtained through the continuous structural variation.

Furthermore, the variability allowed to the structure points out the possibility of multiple realizability, that is the possibility in principle, that a same system could be realized by different components, yet not any components! It can be realized by different kinds of components under the condition that they satisfy the relation that characterize the organization of that system. In such a way Maturana and Varela provide a framework compatible with the claims of Artificial Life, Synthetic Biology and Astrobiology.

With respect to the comparison with Ashby’s framework, it has to be established whether Ashby’s machines can enter into relations such as those required by the autopoietic organization. Before entering this issue it is worth pointing out that, from the methodological point of view, the structural variability allowed by the distinction between organization and structure, does not mean, as instead is asserted in Froese and Stewart (2010:22), that autopoiesis commits to a synthetic method analogous to Ashby’s one. The idea of generative mechanism has different meanings in the two frameworks. Ashby, who is focused on regularities

¹⁵ The limits of thermodynamics of dissipative structures and its formalism to model even the energetic dynamics of living systems has been pointed out by many authors (see, among the others: Morowitz, 1992; Mikulecky, 2001). See also Kauffman, 2000, for the search for new principles of thermodynamics in order to make sense of living systems and their origins.

¹⁶ A connection between the idea of autonomy and thermodynamics in order to establish the requirements for its effective realization in the material domain has been attempted only recently by Kauffman (2000) and by Ruiz-Mirazo & Moreno (2004).

of behavior, implements mechanisms that are closer to what Rosen in his analysis of the modeling relation would define as simulative ones (Rosen, 1991). The synthesis of the model system aims at reproducing the same behavior or sequence of states. In the case of Maturana and Varela, the mechanism is a properly generative one, aimed at reproducing the same mechanism that produces a certain unity, which then produces a certain behavior: the isomorphism concerns primarily processes that realize the system under study, instead of the behaviors that it generates. The latter, in fact, can be shared by systems with quite different internal mechanisms.

The main difference between Ashby and autopoiesis is due to a more basic difference, that concerns the same definition of organization. Surely, differing in the notion of organization implies a theoretical divergence also in what is meant by conservation of organization. In Ashby's case the notion of organization is more related to a description belonging to dynamical systems thinking. As quoted already by Froese and Stewart (2010: 16), according to Ashby:

[...] any calculating machine shows that what matters is the *regularity* of the behavior (Ashby, 1962: 261)

And also:

A Machine is that which behaves in a machine-like way, namely, that its internal state, and the state of its surroundings, defines uniquely the next state it will go. (Ashby 1962: 609).

[Organization] demands only that there be conditionality between parts and regularity of behavior (Ashby 1962: 610).

Define the set S of states so as to specify which machine we are talking about. The "organization" must then, as I said above, be identified with f , the mapping of S into S , that the basic drive of the machine (whatever it may be) imposes. (Ashby, 1962: 613).

In Ashby's framework organization has a wide meaning. It entails some coupling between parts in terms of mutual conditionality, and it concerns the regularity of behavior of the system, given the possible states as a fixed domain. It can be identified with the function that drives the system from a pre-defined state to the other.

In the Autopoietic theory, as well as in the tradition we briefly surveyed, organization has a different meaning. For example the function f of Ashby is only one possible process in what Rosen considers as an organized system. What is meant by organization in autopoiesis and in other instances of biological autonomy like Rosen's and Piaget's theories, is not defined in terms of succession of states in time, but is characterized in terms of how the components interact and transform each other and in doing so generate the system and its behaviors. It is an idea more related to the contemporary notion of mechanism (Bechtel, 2007). In Maturana (1970) the organization concerns the general configuration of a system - what specifies its identity - that is, how parts and processes are related in a higher order unity, rather than just particular connectivities. Also, components are not necessarily fixed elements, nor are they easily isolable, but are characterized in processual terms as nodes of a reticular process or patterns of activities between anatomical constituents of the system (Maturana, 1970: 47).

In the autopoietic theory, thus, the general configuration called 'organization' is characterized in terms of connections between processes of transformation of components. The autopoietic organization, in particular, is the relational scheme able to account for the basic property of self-production characteristic of living systems. The framework based on succession of pre-given states and fixed components is therefore abandoned as well as the Ashbyan domain of artifacts in which it is implemented.

What is implied exactly by processes of production of components that is not accounted for in the Ashbyan framework? As already pointed out with respect to Piaget, in an organizational framework living systems are characterized by both closure and openness, even though these two properties pertain to two different logical orders. Organization is the relation between

those processes in which components are created and destroyed in the realization and maintenance of the unity through a continuous flux of exchange of energy and matter with the environment (structural openness). Transformative relations between processes means that the components produced in one phase are necessary as substrates or as operators for a subsequent phase. They are not stable or fixed like in a machine. Processes do not stop, and the components neither become static like in a crystal after its formation, nor can be considered as only in movement, captured in a pattern like in dissipative structure. Rather, they are produced by the system processes and used (transformed, broken down, degraded) by them in realizing its maintenance as a unity.

As a consequence, the idea of maintenance of organization is quite different in the two approaches. In Ashby it concerns the maintenance of patterns or regularity of behavior of a system with fixed components put into network. In the autopoietic theory it is placed on a radically different domain and concerns the maintenance of the general topology of the connections between processes of production of components. In mathematical terms one aspect of this difference can be expressed by pointing out that in one case the maintenance of organization concerns relations between states, in the other relations between operators¹⁷.

The intrinsic transformativity of the autopoietic organization also overcomes what Pickering (2010: 154) considers as one of the main limits of the early Ashbyan cybernetics: the incapability to create novelty, as the system just selects states or behaviors in a given space of possibilities. Autopoietic systems, instead, by producing their own components continually redefine their internal structure, and by realizing their organization continually generate their own space of internal and external viability: the autopoietic space, “whose dimensions are the relations of production of the components that realize it” (Maturana and Varela, 1973: 88).

One of the main problems in Froese’s and Stewart’s argument is that they interpret autopoiesis by focusing on Maturana’s characterization of the nervous system. In such a way they miss his main conceptual arguments about living systems in terms of self-production instead of operations only. In doing so, they merge concepts referring to different domains, that is: (a) the organization and realization of the living system with the organization and operations of the nervous subsystem described as something already established, not as generated in the more comprehensive system that is the organism itself; (b) the internal production of the system with its behavior in the external environment. Maturana’s reference to Ashby’s Ultrastability (Maturana, 1970: 25), in fact, pertains to the discussion of certain properties of the operations of the nervous system, not of the autopoietic system itself. In fact, the interactions between neurons considered in the Maturana’s quotation are not relations of transformation of components. The significance of this conceptual mistake will become even more decisive and clear in the course of our analysis.

2.2 The autopoietic organization: self-production and intrinsic instability in the molecular domain

The idea of self-production is already present in explicit form in the early formulation of Maturana’s theory of living systems in *Biology of Cognition* (1970). It is on this theoretical foundation of the basic activity of the organism that the analysis of the nervous system is then grounded and can be understood, and not vice-versa. This means that we cannot characterize

¹⁷ Of course at the light of this distinction it is problematic to ascribe to Ashby’s model any form of self-maintenance, a property usually ascribed to dissipative structures or living systems in which entities are processual, not fixed (Collier & Hooker, 1999; Bickhard & Campbell, 2000; Campbell & Bickhard, 2011). See Mossio & Moreno, 2010, for a discussion of differences in the realization of self-maintenance in dissipative structures and living systems).

the organism from an analysis of Maturana's model of the nervous system as a standalone unit. The living system, instead, is defined as follows:

The living organization is a circular organization which secures the production and maintenance of the components that specify it in such a manner that the product of their functioning is the very same organization that produces them (Maturana, 1970: 48).

Here the idea of organizational closure is already clearly stated. It consists in a circularity of processes of production and also maintenance of components, which implies a continuous processual dynamics. This idea of self-maintenance and self-production of the whole system is compatible with and suggests a self-assertive rather than reactive conception of the living system, theoretically distinct from Ashby's Ultrastability.

This proto-formulation of the notion of autopoiesis already overcomes Ashby's framework and his perspective on biology. If Ashby, when reflecting upon the living, considers it in terms of parameters or "essential variables" to be kept constant (e.g. pH, temperature etc., Pickering, 2010: 98), in Maturana's framework there is a crucial theoretical shift. The structure is left free to continuously vary in realizing self-production and self-maintenance: within certain limits, of course. What is kept invariant pertains to a higher order, that is, the general relational scheme.

This circular organization constitutes a homeostatic system whose function is to produce and maintain this very circular organization by determining that the *components* that specify it be those whose synthesis or maintenance it secures. [...] the circular organization in which the *components* that specify it are those whose synthesis or maintenance it secures in a manner such that the product of their functioning is the same organization that produces them, is the living organization (Maturana, 1970:9).

And also:

[...] a living system is an homeostatic system whose homeostatic organization has its own organization as the variable that it maintains constant through the production and functioning of the *components* that specify it (Maturana, 1970:48).

In such a way this framework, thanks to the distinction between organization and structure, - despite the unfortunate choice of the term homeostatic, which seems not perfectly appropriated if compared to similar ones like homeorhetic, etc... - can account for the distinctive features of living systems: their invariance as a unity in face of the continuous variance of their components. This is one argument that justifies a distinction between the two frameworks in terms of self-assertiveness versus reactivity. In fact, while Ashby's model is by default static, and seems to be activated only in reaction to perturbations in order to bring some parameters back to the equilibrium state, the autopoietic system, since its early formulation as a model of the living, is self-assertive and never static from the structural point of view. The "variable" that is kept invariant, in fact, belongs to a different, yet complementary, logical order: that of the overall connectivity. Thus, the internal processes of the system do not need to be static in absence of perturbations. What is called perturbation here does not consist in just one or a series of isolated events. On the contrary it is a continuous flow that affects the open structure of the system.

This argument is also supported by the fact that already in Biology of Cognition there is an explicit reference to the molecular domain as the domain of realization of the living and that energetic aspects are considered: a theoretical stance that is coherent with the idea of structural openness already emphasized by Piaget. It is also true that the structural analysis of the material and energetic conditions to be satisfied to realize an autopoietic organization, then, is not pursued.

Living systems as they exist on earth today are characterized by exergonic metabolism, growth and molecular replication, all organized in a causal circular process that allows for evolutionary change in the way the circularity is maintained, but not for the loss of the circularity itself. Exergonic metabolism is required to provide energy for the endergonic

synthesis of specific polymers (proteins, nucleic acids, polysaccharides) from the corresponding monomers [...] (Maturana, 1970: 9).

What follows on a general theoretical level is that in order to satisfy the autopoietic specifications the domain of components needs to exhibit the same subset of properties that allow to the molecular domain to realize self-production and self-maintenance¹⁸. What is also important in view of a discussion of the genealogy of the autopoietic theory is that the reference to the molecular domain is not just an aspect introduced in late Maturana's work, but is part of his framework since the beginning: it distinguishes it from Ashby's one, while it constitutes part of a common ground with the other lines of research cited above.

The processual idea of the organization and of the relations between components characteristic of the autopoietic systems is made explicit in Maturana and Varela, (1973) in contrast with the properties of other classes of systems, for example artifacts. This constitutes another crucial difference between their framework and the one of Ashby's.

An organization may remain constant by being static, by maintaining its components constants, or by maintaining constant certain relations between components otherwise in continuous flux or change. Autopoietic machines are organizations of the latter kind: they maintain constant the relations that define them as autopoietic (Maturana & Varela, 1973: 81).

This quotation is not contradictory in light of some autopoietic commitment to Ashby's framework, as claimed instead in Froese and Stewart (2010: 38). Maintenance, in fact, is already entailed by the specific nature of the autopoietic components: that are in continuous turnover, unlike Ashby's vibrating cubes facing perturbations. Indeed, as stated above, the components of an autopoietic system are: (a) generated and regenerated inside the system, which does not only self-maintains but also self-produces; (b) they are molecular in a molecular domain (or at least have the same relational properties of molecular components). As a consequence they are constantly subject to degradation; (c) autopoiesis is a network of processes of transformation: the components produced in a process are used in other process of production and transformation of other components and so on.

Therefore, the example of the robot that repairs its damages when it is perturbed (Froese & Stewart, 2010: 38) as a case of a purely reactive otherwise stable autopoietic system, is not pertinent. The robot, in fact, is not autopoietic. And the damage it receives from the environment, as well as in the case of Ashby's vibrating cube, is of a different kind than the intrinsic degrading and transforming of components that takes place in the autopoietic system. Obviously, this difference cannot be caught if the theoretical basic framework of the autopoietic theory is replaced with that of belonging to a different theory.

The autopoietic commitment to a transformative and biology-oriented framework is clear in the definition of autopoiesis as self-production under invariant self-realized circular organization:

An autopoietic machine is a machine organized (defined as a unity) as a network of processes of production (transformation and destruction) of components that produces the components which: (i) through the interactions and transformations continuously regenerate and realize the network of processes (relations) that produces them; and (ii) constitute it (the machine) as a concrete unity in the space in which they (the components) exist by specifying the topological domain of its realization as such a network (Maturana & Varela, 1973: 78-79).

The processes of production in which the components are involved, in fact, do not concern only reparation or even replacement but, production itself, transformation – for example the

¹⁸ This aspect is made explicit in the late work of Robert Rosen (1991), where it acquires a central significance in his attempt to catch the distinctive character of living systems and to address the issue of their possible artificial fabrications.

use of components to build other components – and degradation – i.e. decay or decomposition in order to release energy useful for other processes. This aspect of the theory is even clearer if we keep in mind the distinction between invariant closed organization, and open variant structure: the heritage of von Bertalanffy's notion of thermodynamically open system, that underlies the idea of continuous flux of matter and energy through the system. The emphasis placed on the idea of conservation of organization should not imply forgetting the intrinsically processual framework embedded in the autopoietic theory since its early formulations.

In this processual framework one can also identify what Pickering says of Kauffman's networks while contrasting them with Ashby's homeostat:

On the one hand these networks [Kauffman's binary network] are livelier than, especially, Ashby's machines. Walter sometimes referred to the homeostat as *Machina sopora* – the sleeping machine. Its goal was to become quiescent; it changed state only when disturbed from outside. Kauffman's nets, in contrast, had their own endogenous dynamics, continually running through their cycles whether perturbed from the outside or not. (Pickering, 2010: 164).

But in the case of autopoietic systems, this argument is even stronger because also the components themselves are subject to transformation, in a way that is more similar to the dynamics of an auto-catalytic network than to a boolean one.

Being stable is a property that pertains only to the autopoietic organization, and not to its effective physical realization. The structure of the autopoietic system is in principle in continuous variation, intrinsically unstable, whether or not perturbed by the environment. This thesis is explicit in Piaget's school:

C'est cette phénoménologie très particulière qui rend peu significative l'application au système organisé de concept d'équilibre. L'invariance résultante n'est point, come dans un système mécanique ou physico-chimique banal, l'effet de forces antagonistes qui se font finalement équilibre dans l'inertie, mais la résultante d'une multitude de processus toujours en action. On peut exprimer cette situation par la mot de métabolisme, en soulignant les sens étymologique: changement. Plutôt que d'équilibre il s'agit d'un «état stationnaire entretenu» ou d'un «métabolisme stationnaire» (L. von Bertalanffy). Le pseudo-équilibre du système vivant est l'effet dynamique d'une multitude de déséquilibres mutuellement compensés. C'est même cette instabilité par le nombre extrêmement grand de ses degrés de liberté, qui permet au système des rétablissements d'équilibre dans des situations extrêmement variées. (Meyer, 1967: 788).

From this standpoint, the implication of the complementarity between closed invariant organization and open variant structure in self-producing systems are at least two.

(a) In the first place, frameworks like the Piagetian and the autopoietic one, unlike the case of Ashby's homeostats, are able to harbor intrinsic or constitutive instability: at least in principle. The definition of living systems as organizationally closed autopoietic ones, therefore, includes, for example, Di Paolo's reformulation of it in terms of 'operational closure under precarious conditions'.

Precairous circumstances are those in which isolated constituent processes will tend to run down or extinguish in the absence of the organization of the system in an otherwise equivalent physical situation. In other words, individual constituent processes are not simply conditioned (e.g., modulated, adjusted, modified, or coupled to other processes) but they also depend for their continuation on the organizational network they sustain; they are enabled by it and would not be able to run isolated (Di Paolo, 2009: 16).

Even if the mechanism has not been described in detail yet, the autopoietic system, as well as other theoretical models of biological autonomy like Piaget's, is intrinsically characterized by continuous dynamics of production of components and by the capability to interact continuously and constitutively with the environment.

(b) Therein lies the second implication of the autopoietic framework. In the same way as it is made explicit in the work of Piaget and his school, autopoietic systems can in principle harbor an internal mechanism capable of active interaction with the environment, that is, without being static and stable by default. The reason resided in the intrinsic instability of the self-production dynamics and its openness to the environment, so that the interaction is constitutive of the structure of the system.

Nevertheless, apart from Piaget's models themselves (e.g. adaptation as assimilation and accommodation) these mechanisms have not been investigated in detail yet from the point of view of autopoietic theory, except for its concept of structural coupling¹⁹. Recently, the need of a development of the autopoietic theory in this direction has been pointed out by several authors (see e.g. Bourguine & Stewart, 2004; Bitbol & Luisi, 2004; Di Paolo, 2005). Furthermore, there has been a considerable line of research by several authors (e.g. Bickhard 1993, 2000, 2001; Brier 1995; Ruiz-Mirazo and Moreno 1998, 2000; Collier and Hooker 1999; Collier 2000, 2002), that although they take autopoiesis as their implicit or explicit epistemological basis, they then stress its lack of internal functionality and attempt to introduce models that compensate for its 'all-or-nothing' nature. These works have provided significantly more detailed frameworks than the autopoietic one with respect to the naturalized functionality of an autonomous system, and in addition, they haven't only emphasized the need to explain the emergence of norms in such systems but they have also suggested relevant models. One of the common aspects of those models is that autonomy, and especially the organization of living (biological) autonomous agents cannot deal without a naturalized notion of organizational closure and of systemic (non-reflexive downward) causation (Arnellos, Spyrou and Darzentas, 2008; 2010), which as we explain further below, appear to have their epistemological basis on the roots of the autopoietic framework or /and being compatible with it.

2.3 Closure

A last theoretical pillar, crucial in order to understand autopoiesis, is constituted by the notion of "closure". It has already been cited in the previous section, inasmuch as it is involved in most of the ideas that characterize the autopoietic framework: organization, self-production, circularity. It requires a separate section as it is often a source of confusion, because the same name can convey different theoretical ideas when combined with different adjectives (operational, organizational, etc.). For instance, in the Ashbyan interpretation of autopoiesis, among the other cases, the closure of the nervous system is confused with the closure of the processes of production of the organism,

As pointed out by Mossio (forthcoming), despite the increasing contemporary interest in this notion as a crucial one in order to understand the distinctiveness of biological systems - together with natural selection - there is still no agreement on a common definition. The panorama is indeed quite complex. Already in the wide pioneering literature about biological autonomy there are many different ideas and definitions of closure: from Rosen's closure to efficient causation (Rosen, 1972; 1991) to Piaget's cyclic metabolic closure (1967a); from the autopoietic notion of operational closure to that of organizational closure; from Kauffman's concepts of catalytic closure and work cycle (Kauffman, 2000; Letelier et al., 2011) to Pattee's semantic closure (Pattee, 1982) and to instances of semiotic closure (Hoffmeyer, 2000; 2001; El-Hani, Arnellos and Queiroz, 2007) not considering also related concepts like Weiss' interdependence and coordination. Recently, a reformulation of these ideas has been provided in Mossio and

¹⁹ The notion of structural coupling, nevertheless, is not as weak as a theoretical tool as it is usually depicted, in spite of its generality. In fact it is capable of accounting for the viable evolutionary interaction between organism and environment, the construction of higher levels of systemic organization as that of the niche, and open-ended evolution in the neutralist framework of natural drift. (Maturana & Varela, 1987; Maturana & Mpodozis; 2000).

Moreno (2010) and Mossio et al. (forthcoming), by redefining closure in terms of mutual (generative) dependence of self-produced constraints, starting from a conceptual reformulation of Rosen's model of M/R-System (Rosen, 1972; 1991).

In the autopoietic framework at least two different concepts of closure are at work, which are often source of confusion. One is operational closure and the other is the closure related to the organization that enables the self-production of the autopoietic biologic system. We will call the second simply organizational closure, coherently with the tradition to which it belongs. One problem in the Ashbyan interpretation of autopoiesis, and in a great part of the general debate about autopoiesis, is that circularity is often intended in the sense of operational closure. This is also due to Varela's general use of the notion in his attempt to elaborate a general framework of autonomy at different levels of organization, not limited to autopoietic systems only. His generic definition of closure in operational terms is the following:

A domain K has closure if all operations defined in it remain within the same domain. The operation of a system has therefore closure, if the results of its action remain within the system (Bourgine and Varela, 1992: xii).

Depending on the meaning ascribed to the terms operations and actions we can obtain different concepts. Operational closure as generally intended – e.g. as used in Froese and Stewart, 2010 or, in its early version, in Maturana's analysis of the nervous system as a "functionally closed one" (Maturana, 1970) – means a recursion between the operations of the components of a system: all the actions of the components have an effect inside the system. It is compatible with a model of the dynamics of the system in terms of sequences of states, and with Ashby's networked homeostatic machines. Mathematically it can be expressed in a minimal form through recursive functions. This is the concept that is used in comparing Maturana's framework to Ashby's. Yet, Maturana uses this or a similar notion, only in describing the nervous system and not the organization of the autopoietic system as a biological one.

On the contrary, he starts his discussion of the organism by providing a different notion of closure, organizational closure, that has very strong analogies with Rosen's and Piaget's ones. The idea of self-production and the characterization of the type organization that enables it constitute the core of Maturana's and Varela's frameworks for living systems. As acknowledged also in Froese and Stewart (2010: 37), it has no equivalent in Ashby, but it is neither a collateral aspect of the autopoietic theory, nor an unjustified one.

Organizational closure, unlike operational one, involves not just a circular recursion or closed network of operations, but also a 'generative' dependence between components realized through a closed topology of transformation processes. Varela tried to develop formally this idea by overcoming recursivity and moving into the domain of self-referential functions (Varela, 1975; 1979; Soto-Andrade & Varela, 1984)²⁰, that is, functions that operate on themselves or on other functions, in a way analogous to what happens for processes of transformation of components. In other words, it is a closure at the level of operators rather than states.

The emphasis is reversed with respect to operational closure: what is important is not only that the result of the action remains within the system, but that for any component its production process can be traced within the system. In such a way, what is entailed by this notion is not just the activity of the components but their conditions of existence, provided by their participation in the organized system they continuously realize. While operational closure does say nothing on the origin of the components, organizational closure points to their internal generation as well as to the properties they have to satisfy in order to contribute to self-production, that is: to be able to participate in processes of production – transformation and degradation – of components. In other words the components are required to exhibit the same

²⁰ This idea is more rigorously expressed by Rosen in his model in the formalism of category theory: the M/R-System (Rosen, 1972; 1991). Unlike Varela's formalisms, the M/R-System is able to express not only organizational invariance but the whole idea of closed concatenation of processes

relational properties that make the molecular domain able to generate living system and that make the whole structure open to the environment, intrinsically instable: hence, continuously self-generated.

3. Other theoretical nodes

"Life after Ashby" (Froese and Stewart, 2010) raises many more interesting theoretical questions that, even though the association between Ashbyan and autopoietic frameworks has been shown to be problematic, it anyway, provides the opportunity to attempt to clarify some important implications of the autopoietic theory. We will briefly focus on two of them. One, directly raised in Life after Ashby, concerns the part-whole relation and the possibility or not of downward causation. The other concerns some remarks generally related to the issue of regulation. It is the issue of the capability of internal modification and of plastic interaction with the environment, with respect to which the autopoietic and Ashbyan perspectives once again provide divergent answers.

3.1 Downward Causation into question

Froese and Stewart raise the point whether in Maturana's framework there is place for a "reciprocal relation between the local and the global levels of description, namely a circular relationship between components (the processes of production) and the whole (the organization)" (Froese and Stewart, 2010: 26).

They advocate the view according to which Varela's interpretation of autopoiesis is coherent with an idea of reciprocal causation between whole and parts, expressed by the notion for reflexive downward causation. They quote, as paradigmatic example of reciprocal whole-part causation in living systems, the crucial passage from Kant's Critique of Judgment about the characterization of organisms in terms of natural purposes (Kant, [1781]1987), in which the proto-idea of biological autonomy as self-production and circular organization is formulated²¹. Kant's idea that the existence of the constituents depends on the whole seems to imply downward causation from the whole to the parts.

The parts of it produce themselves together, one from the other, in their form as much as in their binding, reciprocally, and from this causation on, produce a whole. In such a product of nature each part, at the same time as it exists throughout all the others, is thought as existing with respect to the other parts and the whole, namely as instrument (organ). It is then - and for this sole reason - that such a product, as organized and organizing itself, can be called a natural purpose (Kant, 1987, §65, p. 287).

It has to be pointed out, though, that reflexive downward causation is not a widely accepted concept but, on the contrary, it is an extremely controversial issue.

In order to discuss Maturana's, and in general, the autopoietic stance with respect to downward causation it is necessary to clarify which are the different levels involved. One is the components, let them be processes or constituents, the other is the whole system. The term whole, though, can have different meanings. (a) It can be considered as the system as a unity in his environment – what Maturana calls "simple unity". Or (b) it can be considered as the global organization. It consists in the whole configuration of components (processes of production) – the "composite unity" according to the autopoietic terminology. In this case the components are as such qua part of that specific configuration, that is, by exhibiting their relational

²¹ With regards to the Kantian idea of natural purpose in explaining autonomy, see also Kauffman (2000) and Weber & Varela (2002).

properties. They are not the potential constituents considered in isolation²². In this second case it is more difficult to identify a causal role of the whole on the parts, since the configuration and the parts that realize it are not distinct entities (Craver & Bechtel, 2007).

The question that emerges here is to what extent the autopoietic subordination of components to the maintenance of the autopoietic organization implies direct whole-to-part causation or reflexive downward causation. According to Maturana, the crucial problem with whole-to-part relations as direct reflexive downward causation is how the whole can directly interact at the same level with the components. It is a possibility that Maturana denies in his framework. Yet, this does not imply that his theory is contradictory or loses explanatory power.

The unity of an autopoietic system is the result of the neighborhood relations and interactions (interlay of properties) of its components, and in no way the result of relations or interactions that imply the whole that they produce. In other words, nothing takes place in the operation of the autopoietic network with reference to the unity of the network. (Maturana, 1981: 23).

The relation between Maturana's stance on downward causation and the previous Kantian passage, considered as the historical root of the idea of biological autonomy and which seems to entail a form of downward causation, is complex. According to Maturana, the Kantian expressions "throughout the others" and "with respect to the other parts and the whole" mean that the "parts exist for the whole and the whole for the parts" (Maturana, 2002: 9) thus implying reciprocal causation in the Kantian framework²³. However, does Kant imply some reciprocal causality at all, in the sense of reflexive downward causation? We propose a possible response to this issue by arguing that both the autopoietic theory - in Maturana's and in Varela's interpretations - and the passage by Kant are compatible with a relation between wholes and parts that does not assume the problematic form of direct reflexive downward causation. The explanatory power of the theories is maintained without incurring in possible criticism due to a commitment to a notion usually subject to strong criticism (e.g. Kim, 1998, 2000, 2006; Craver & Bechtel, 2007).

In the first case mentioned above, which relates the components with the "simple unity", downward causation is easily excluded: it is a case of two distinct descriptive domains like, for example, an emergent system exhibiting global properties non-deducible to those of its parts. From the epistemological point of view, in fact, a direct causal relation between the whole as a "simple unity" and its components implies a category mistake, as making the whole to interact at the level of its part would mean to put on the same domain two classes of entities belonging to two distinct and irreducible domains of description.²⁴

If we take into consideration the second case we deal with the relation between the components of the "composite unity" and the configuration they realize and integrate - i.e. the "composite unity" itself. Considering the components of the "composite unity" as directly affected by the configuration they realize is unnecessary or even redundant, because being part of a system already means exhibiting relational properties. They are distinct from the potential constituents in isolation.²⁵ Therefore the two levels - relational components and the

²² It is important to remind in this context the distinction proposed by Maturana between the anatomical components of the nervous system as isolated elements, and its structural components, whose relational properties are at work as part of an organized system.

²³ It can also refer to the problems of purpose or normativity, but we decide to focus on the issue of downward causation.

²⁴ See Bich 2012 for an epistemological analysis of emergence where a criticism of downward causation is provided in line with the autopoietic framework.

²⁵ In the epistemological framework of the autopoietic theory they are already distinguished as components of the system with respect to their contribution to the organization they realize. In other words, they are already distinguished according to their relational properties they express in the "composite unity".

configuration - coincide²⁶. As a consequence there is no need to appeal to an action of the system - that is, the whole set of constituents and their relations - in order to explain the behaviour of each component, whose characterization already includes its relational properties as part of the configuration (Mossio et al., forthcoming). What can be interpreted as causal action of the whole on the parts, instead, can be explained in terms of mutual influences on the relational components of the system (Craver & Bechtel, 2007). The behavior of the components seems to be directly influenced by the action of the system only if they are considered from the point of view of their intrinsic properties in isolation (out of that system) without taking into consideration their relational ones.

Direct downward causation is therefore at the same time problematic and dispensable, without necessarily implying any contradiction in the framework of autopoietic theory. It is also relevant to point out that Varela himself, when referring to downward causation, is not really committing to a reflexive one. On the contrary, he uses the notion of downward causation in describing the reciprocal relation between the membrane of the system and the processes that produce it²⁷. This constitutes an attempt to achieve closure, not to establish a direct whole-to-part relation:

In the simple example of the cellular automaton illustrated above, it is precisely the reciprocal causality between the local rules of interactions (i.e., the components rules, which are akin to chemical interactions) and the global properties of the entity (i.e., its topological demarcation affecting diffusion and creating local conditions for reaction) which is in evidence. It appears to me that this reciprocal causality does much to evacuate the mechanist/vitalist opposition and allows us to move into a more productive phase of identifying various modes of self-organization where the local and the global are braided together explicitly through this reciprocal causality. Autopoiesis is a prime example of such dialectics between the local component levels and the global whole, linked together in reciprocal relation through the requirement of constitution of an entity that self-separates from its background (Varela, 1997: 78)²⁸.

By local and global Varela means the processes of production of components and the physical pattern, or boundary. There can be a case of inter-level causation in this case if we consider the boundary as a configuration interacting with the individual components of the metabolism (e.g. as a constraint). Yet, it is not a case of reflexive downward causation because the components affected by the membrane are not part of it, but belong to the surroundings of that configuration (Mossio et al. forthcoming).

Of course downward causation becomes unproblematic in itself and compatible to autopoiesis if we interpret it in the sense that the components for their existence are dependent on their involvement in the dynamics of the system as a whole. This means that there is, indeed, a mutual dependence between the components and the network of processes of production, but this relation does not imply direct causation between its two poles. This can be an interpretation of the Kantian “throughout the parts” and “with respect to the parts and the whole”. ‘Depending on the whole’ would then mean only depending on the whole network of interactions without appealing to the whole as a causal participant in the dynamic of the components. It is a contextual relation, coherent with ideas like Bernard’s specificity of the internal milieu (1965). The existence and the activity and of the components qua components – that is, exhibiting relational properties - depends on their being parts of a wider system which produces them and provides a certain context of interactions and constraints.

²⁶ Under the hypothesis of the inclusivity of levels.

²⁷ With an eye to its modeling implications that consist in trying to express how a pattern, like the one emergent in the computational model of the 1974 (Varela et al. 1974), can have an effective level on the internal dynamics of the system.

²⁸ See also Varela, 1979, 1984.

3.2 Regulation

Another aspect with respect to which autopoiesis and Ashby diverge concerns the properties usually related to regulation and control. In particular, we mean those mechanisms or processes that allow change in the dynamics, properties and specific interconnectivity of components without the system losing its general organization when it is affected by perturbations (external or also internal in the case of autopoiesis). It is important to mention, however, that in the autopoietic framework the appeal to concepts like regulation and control is refused in operational descriptions, because of their relation to teleology. Nevertheless this does not mean that the autopoietic system is fixed and that there are no mechanisms or processes of internal change without loss of organization in the continuous interaction with the environment and the continuous flux of internal transformations.

Ashby's framework is characterized by an idea of regulation and control based on internally differentiated hierarchical mechanisms, with the presence of control subsystems that account for regulative behavior. According to Ashby, the regulator component (or subsystem) needs to have at least as many possible states as the environment or the other subsystems with which it is going to interact: Ashby's principle of "requisite variety" (Ashby, 1958). The reason resides in the fact that the regulator is required to act as a blocker of perturbations. The system, in fact, is by default stable and after perturbations occur, it needs to be brought back to stability (e.g. some variable has to be restored in its required value). Since it has to act as a blocker it makes sense that the regulating subsystem needs to have as many states as the possible perturbations. In fact, the system is considered to be in its required state by default, at rest. It does not have a constitutive openness to its environment, required by its self-production. Hence the perturbation is only a disturbance.

Then, analyzing regulators and their efficiency, Ashby proposes a further property for the efficient regulator, related to cause-control instead of error-control (Conant & Ashby, 1970). The latter mechanism, like the one instantiated by the thermostat, is imperfect since it responds to variations in the variable to be controlled. The values of the regulated variable, therefore, are always fluctuating. Cause control, instead, can reach perfection by blocking the causes of variation. In order to do so it is required to have a model of the system, of its own role in it, of the behavior of other components, of the features of the external environment and of what can disturb the system and bring it out of its space of viability.

The assumptions at the basis of Ashby's principle of requisite variety and of the mechanism of cause control are quite strong, and presuppose an essential control subsystem. In the second case an absolute knowledge is also required. The possibilities of shared control, and of complex subsystems being regulated in whatever way by less complex subsystems, are excluded. Furthermore, this theoretical scheme is rigid. Goals and required values of variables are pre-given. The system is static with respect to regulation, rather than plastic, and presupposes a fixed environment. A new type of perturbation, in fact, would affect and destabilize the system.

The general idea of central or hierarchical²⁹ regulation is common to other cybernetic frameworks. For instance it can also be found in some of the ideas by Stafford Beer: for example in his system of centralized control of the Chilean Economy (CyberSyn, see Beer, 1972). In Systems Theory too, Miller's framework of living systems theory (Miller, 1978) presupposes an essential critical subsystem, the "decider", which controls the entire system.

In the autopoietic framework, instead, internal change is not prevented. On the contrary, it is required in order to cope with the continuous changes taking place in the production processes, due to structural openness and the consequent intrinsic variability. Being realized in a molecular or similar domain, the system is plastic and does not require the precision of Ashby

²⁹ In the sense of control or command hierarchies, expressed by trees and hierarchic organizational charts in general.

control mechanisms. The response to perturbations, in fact, can be transformative at the level of structure without loss of organization: this aspect is made explicit in Piaget's idea of accommodation. Also, the response is mediated through the network by means of modifications of the components or of their behaviors. It does not mean that the contribution is the same – it can be differential - but that it is shared. Indeed, with respect to regulative behavior the autopoietic framework can be considered heterarchical, unlike the Ashbyan, which is hierarchical (Heij, 1990).³⁰ In heterarchical systems the organization is such that in principle no component is excluded from the contribution to the systemic response, even if temporary dynamical hierarchies can emerge. In autopoietic systems there is no command or control center, be it the nucleus of the cell or the brain. There is neither a sharp decomposability into distinct fixed submodules to which can be ascribed a specific function.

As such, also in the domain related to regulative processes, the autopoietic framework abandons some of the features characteristics of Ashby's and other cybernetic approaches, namely, blocking response, fixed hierarchy, control subsystems, and centralized control.

4. Conclusions

The main claim of this paper is that autopoietic theory, even in its early formulations, is not committed to Ashby's framework neither in the basic theoretical assumptions - a processual transformative framework rooted in the molecular domain as opposed to a static one, focused on changes of states - nor in the target, the former being primarily focused on life, the latter on machines. As we have shown, the two frameworks entail different notions of organization and of process, and while Ashby's theory is centered on the notion of stability, the autopoietic one is focused on self-production and entails an idea of intrinsic instability. In addition, the distinction between organization and structure proposed by Maturana and Varela, as well as by other authors like Piaget in the same years, allows for an internal variability and an assertiveness that are impossible in Ashbyan systems. Also a brief analysis of what are usually called "regulative" mechanism, shows a deep divergence between the two frameworks.

Rejecting the thesis of an early commitment of autopoiesis to Ashby's framework implies also abandoning the distinction between two opposing interpretations, an Ashbyan versus a Kantian one. We have furthermore argued that the original formulation of autopoiesis is not necessarily incompatible with a Kantian interpretation if we drop the theoretically problematic idea of reflexive downward causation.

Of course it does not amount to sustaining that autopoietic theory is somehow complete, and to ignoring its limitations. As a matter of fact, its conceptual and applicative limits are several, starting from its abstractness, and from the fact that many aspects are left almost implicit. But, on the other hand, it is also worth mentioning that many of the criticisms directed to the autopoietic theory concern aspects which are not in principle incompatible with it or, like in the case of the "ashbyan interpretation" criticisms based on the thesis of ultrastability and lack of variability, are just left undeveloped in their implications: it is the case of intrinsic instability and its rooting in thermodynamics. Also, it has to be emphasized that the autopoietic theory itself and its significance have to be considered in a wider perspective in relation to what is now one of the main goals in its field of investigation, that is, with respect to the development of the contemporary idea of biological autonomy.

On these bases we have argued that different theories are to be taken into consideration as sources or as sharing common theoretical roots with autopoiesis. As such, they are more pertinent as tools for an interpretation and a development of this theory in the wider context of the research line of biological autonomy. Examples are those systemic theories that tried to

³⁰ According to the meaning explained in the footnote above. Autopoietic theory in fact, in line with the systemic approach, does not exclude other kinds of hierarchies, like nested ones: for example entities of second and third order (see Maturana and Varela, 1987; Maturana and Mpodozis, 2000).

make sense of the specificity of the living in the physical world and of its differences with artifacts, like for example Rashevsky's, Rosen's, Bateson's, Weiss' and Piaget's works. We therefore advocate a more integrative approach to the origin of the idea of autopoiesis and, especially, of biological autonomy, of which Maturana's and Varela's theory is only one - though very important - among many other sources. As demonstrated by the boost in the studies related to Rosen's M/R-System model in the last decade, the insights it provided and the discussions it triggered, rediscovering the roots of a theory and of a whole tradition of investigation can only contribute to provide it further impetus and theoretical depth.

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References

1. Arnellos, A., Spyrou, T., Darzentas, J. (2008). Emergence and Downward Causation in Contemporary Artificial Agents: Implications for their Autonomy and Some Design Guidelines *Cybernetics and Human Knowing*, 15(3-4): 15-41.
2. Arnellos, A., Spyrou, T., Darzentas, J. (2010). Towards the Naturalization of Agency based on an Interactivist Account of Autonomy, *New Ideas in Psychology*, 28(3), 296-311.
3. Ashby, W. R. (1956). *An Introduction to Cybernetics*. London: Chapman & Hall.
4. Ashby, W. R. (1958). Requisite Variety and its Implications for the Control of Complex Systems. *Cybernetica*, 1, 83-99.
5. Ashby, W. R. (1962). Principles of the self-organizing system. In H. von Foerster & G. W. Zopf (eds.), *Principles of self-organization* (pp. 255-278). London: Pergamon Press (quotations from G. J. Klir (1991) *Facets of Systems Science* (605-620), New York: Kluwer.
6. Bateson, G. (1979). *Mind and Nature. A Necessary Unity*, New York: E. P. Dutton.
7. Bechtel, W. (2007). Biological mechanisms: Organized to maintain autonomy. In F. Boogerd, F. Bruggeman, J. H. Hofmeyr, H. V. Westerhoff (eds.). *Systems Biology. Philosophical Foundations*. Amsterdam: Elsevier, 269-302.
8. Beer, S. (1972). *Brain of the Firm*. London: Penguin.
9. Bernard, C. (1865). *Introduction à l'étude de la médecine expérimentale*. Paris: Baillière.
10. Bich, L. (2012). Complex Emergence and the Living Organization: An epistemological framework for biology. *Synthese*, 185(2), 215-232.
11. Bich, L. & Damiano, L. (2008). Order in the Nothing: Autopoiesis and the Organizational Characterization of the Living. *Electronic Journal of Theoretical Physics*, 4(16), 343-373.
12. Bich L. & Etxeberria A. (forthcoming). Systems, Autopoietic. In W. Dubitzky, O. Wolkenhauer, K.-H Cho, & H. Yokota (eds.), *Encyclopedia of Systems Biology*. New York: Springer (in press).
13. Bickhard, M. H. & Campbell, D. T. (2000). Emergence. In P. B. Andersen, C. Emmeche, N. O. Finnemann, & P. V. Christensen (eds.), *Downward Causation* (pp. 322-348). Aarhus: Aarhus University Press.
14. Bitbol, M. & Luisi, P. L. (2004). Autopoiesis with or without cognition: defining life at its edge. *Journal of the Royal Society Interface*, 1(1), 99-107.
15. Bourguin, P. & Varela, F. J. (1992) *Toward a Practice of Autonomous Systems*. Cambridge MA: MIT Press/Bradford Books.
16. Bourguin, P., & Stewart, J. (2004). Autopoiesis and cognition. *Artificial Life*, 10(3), 327-345.
17. Brier, S. (1995). Cyber-Semiotics: On autopoiesis, code-duality and sign games in bio-semiotics. *Cybernetics & Human Knowing*. 3(1): 3-25

18. Campbell, R. J., & Bickhard, M. H. (2011). Physicalism, Emergence and Downward Causation. *Axiomathes*, 21(1), 33-56.
19. Canguilhem G. (1965), *La connaissance de la vie*, Paris: Librairie Philosophique J. Vrin.
20. Collier, J. D. & Hooker, C. A. (1999). Complexity Organized Dynamical Systems. *Open Systems and Information Dynamics*, 6, 241-302.
21. Conant, R. G. & Ashby, W. R. (1970). Every Good Regulator of a System Must be a Model of that System. *International Journal of Systems Science*, 1(2), 89-97.
22. Craver, C. F., & Bechtel, W. (2007). Top-down causation without top-down causes. *Biology and Philosophy*, 22, 547-563
23. Di Paolo, E. A. (2005). Autopoiesis, adaptivity, teleology, agency. *Phenomenology and the Cognitive Sciences* 4(4), 429-452.
24. Di Paolo, E. A. (2009). Extended Life. *Topoi*, 28, 9-21.
25. El-Hani C. N., Arnellos, A., & Queiroz, J. (2007). Modelling a Semiotic Process in the Immune System: Signal Transduction in B-Cell Activation. *Triple-C Cognition, Communication, Cooperation*, 5(2): 24-36.
26. Froese, T. & Stewart, J. (2010). Life After Ashby: Ultrastability and the Autopoietic Foundations of Biological Autonomy. *Cybernetics and Human Knowing*, 17(4), 7-50.
27. Ganti, T. (2003). *The Principles of Life*. Oxford: Oxford University Press.
28. Hejl, P. M. (1990). Self-regulation in Social Systems. In W. Krohn, G. Küppers & H. Nowotny (eds.), *Selforganization: Portrait of a Scientific Revolution* (pp. 114-127). Dordrecht: Kluwer Academic Publishers.
29. Hoffmeyer, J., (2000). Code-Duality and the Epistemic Cut. In J. Chandler and G. Van de Vijver (Eds.) *Closure. Emergent Organizations and their Dynamics*. Annales of the New York Academy of Sciences, 901. 175-186.
30. Hoffmeyer, J., (2001). Life and Reference. In L. M.s Rocha (guest editor) *The Physics and Evolution of Symbols and Codes: Reflections on the Work of Howard Pattee Special Issue of BioSystems*, 60(1-3). 123-130.
31. Jacob, F. (1970). *La logique du vivant. Une histoire de l'hérédité*. Paris: Gallimard.
32. Jonas, H. (1966), *The Phenomenon of Life. Towards a Philosophical Biology*, New York: Harper and Row.
33. Kant, E. [1781] (1987). *Kritik der Urteilskraft* (Critique of Judgment. Indianapolis: Hackett Publishing)
34. Kauffmann, S. (2000). *Investigations*. New York: Oxford University Press.
35. Kim, J. (1998). *Mind in a Physical World*. Cambridge MA: MIT Press.
36. Kim, J. (2000). Making Sense of Downward Causation. In P. B. Andersen, C. Emmeche, N. O. Finnemann, P. V. Christiansen (Eds.), *Downward Causation. Minds, Bodies and Matter* (pp. 305-321), Aarhus: Aarhus University Press.
37. Kim, J. (2006). Emergence: Core Ideas and Issues. *Synthese*, 151(3), 547-559
38. Letelier, J.-C., Cardenas, M. L., Cornish-Bowden, A. (2011). From L'Homme Machine to metabolic closure: Steps towards understanding life, *Journal of Theoretical Biology*, 286, 100-113.
39. Maturana, H. (1970). Biology of Cognition. In H. Maturana & F. J. Varela (1980), *Autopoiesis and Cognition: The realization of the living* (pp. 1-58). Dordrecht: Reidel Publishing.
40. Maturana, H. (1978). Biology of Language. In G.A. Miller & E. Lenneberg (Eds.), *Psychology and Biology of Language and Thought: Essays in Honour of Eric Lenneberg* (pp. 27-63), New York: Academic Press.
41. Maturana, H. (1980). Autopoiesis: Reproduction, Heredity, and Evolution. In M. Zeleny (Ed.), *Autopoiesis, Dissipative Structures, and Spontaneous Social Orders* (pp. 45-79), Boulder: Westview.
42. Maturana, H. (1981). Autopoiesis. In M. Zeleny, (Ed.) *Autopoiesis: A Theory of Living Organization* (pp. 21-33). New York: North Holland
43. Maturana, H. (2002). Autopoiesis, structural coupling and cognition: A history of these and other notions in the biology of cognition. *Cybernetics & Human Knowing*, 9 (3-4), 5-34.

44. Maturana, H. (2011). Ultrastability...Autopoiesis? Reflective Response to Tom Froese and John Stewart. *Cybernetics and Human Knowing*, 18(1-2), 143-152.
45. Maturana, H. (2012). Reflections on My Collaboration with Francisco Varela. *Constructivist Foundations*, 7(3), 155-164.
46. Maturana, H., & Mpodozis, J. (2000). The origin of species by means of natural drift, *Revista chilena de historia natural*, 73(2), 261-310.
47. Maturana H. & Varela F. J. (1973), *De Máquinas y Seres Vivos: Una teoría sobre la organización biológica*, Santiago: Editorial Universitaria. References from the english version Autopoiesis: The realization of the living, In H. Maturana & F. J. Varela (1980), *Autopoiesis and Cognition: The realization of the living* (pp. 59-140). Dordrecht: Reidel Publishing.
48. Maturana, H. & Varela, F. (1980). *Autopoiesis and Cognition. The Realization of the Living*. Dordrecht: Reidel Publishing.
49. Maturana H. & Varela F. (1987). *The Three of Knowledge*, Shimbhala, Boston.
50. Meyer, F. (1967). Situation Épistémologique de la Biologie. In J. Piaget (ed.), *Logique et Connaissance Scientifique. Encyclopédie de la Pléyade* (pp. 781-821). Paris: Gallimard.
51. Mikulecky, D. C. (2001). Network Thermodynamics and Complexity: a transition to relational system theory. *Computers & Chemistry*, 25, 369-391.
52. Miller, J. G. (1978). *The Living System*. New York: Mc Grow-Hill.
53. Monod, J. (1970). *Les hasard et la nécessité*. Paris:Seuil.
54. Morowitz, H. J. (1992). *Beginnings of Cellular Life: Metabolism Recapitulated Biogenesis*. New Haven: Yale University Press.
55. Mossio, M. (forthcoming). Closure. In W. Dubitzky, O. Wolkenhauer, K.-H. Cho & H. Yokota (Eds.), *Encyclopedia of Systems Biology*. New York: Springer (in press).
56. Mossio, M., Bich, L. & Moreno, A. (forthcoming). Emergence, Closure and Inter-level Causation in Biological Systems. *Erkenntnis* (in press).
57. Mossio, M. & Moreno, A. (2010). Organizational closure in biological organisms. *History and Philosophy of the Life Sciences*, 32(2), pp. 269-288.
58. Nicolis, G., & Prigogine, I. (1977). *Self-organization in Nonequilibrium Systems: From Dissipative Structures to Order Through Fluctuations*. New York: Wiley & Sons.
59. Pattee H.H. (1982). Cell psychology: an evolutionary approach to the symbol–matter problem. *Cognition and Brain Theory*, 5 (4), 325–334.
60. Piaget, J. (1967a). *Biologie et connaissance*. Paris: Gallimard (quotations from the English translation, (1971) *Biology and Knowledge. An Essay on the Relations Between Organic Regulations and Cognitive Processes*. Edinburgh: Edinburgh University Press).
61. Piaget, J. (ed.) (1967b). *Logique et Connaissance Scientifique. Encyclopédie de la Pléyade*. Paris: Gallimard.
62. Pickering, A. (2010). *The Cybernetic Brain. Sketches of Another Future*. Chicago: The University of Chicago Press.
63. Rashevsky N. (1954). Topology and Life: in Search of General Mathematical Principles in Biology and Sociology, *Bulletin of Mathematical Biophysics*, 13, 317-348.
64. Rashevsky N. (1960) *Mathematical Biophysics. Physico-Mathematical Foundations of Biology*. New York: Dover.
65. Rosen, R. (1972). Some relational cell models: the metabolism-repair systems. In R. Rosen (ed.), *Foundations of Mathematical Biology*, vol. II, New York: Academic Press, 217-253.
66. Rosen, R. (1991). *Life Itself. A Comprehensive Inquiry into the Nature, Origin, and Fabrication of Life*. New York: Columbia University Press.
67. Ruiz-Mirazo, K., & Moreno, A. (1998). Autonomy and emergence: How systems become agents through the generation of functional constraints. *Acta Polytechnica Scandinavica*, 91, 273–282.
68. Ruiz-Mirazo, K., & Moreno, A. (2000). Searching for the roots of autonomy: The natural and artificial paradigms revisited. *Communication and Cognition—Artificial Intelligence*, 17(3–4), 209–228.

69. Soto-Andrade, J. & Varela, F. J. (1984). Self-Reference and Fixed Points: A Discussion and an Extension of Lawvere's Theorem. *Acta Applicandae Mathematicae*, 2, 1-19.
70. Varela, F. J. (1975). A Calculus for Self-Reference. *International Journal of General Systems*, 2, 5-24.
71. Varela, F. J. (1979). *Principles of Biological Autonomy*, New York: North-Holland.
72. Varela, F. J. (1984). The Creative Circle. Sketches of the Natural History of Circularity. In P. Watzlawick (ed.), *The Invented Reality* (pp. 303-323). New York: Norton Publishing.
73. Varela, F. J. (1997). Patterns of Life: Intertwining Identity and Cognition. *Brain and Cognition*, 34, 72-87.
74. Varela, F. J. & Maturana, H., (1972). Mechanism and Biological Explanation, *Philosophy of Science*, 39(3), 378-382.
75. Varela F. J., Maturana H. & Uribe R. (1974). Autopoiesis: the Organization of Living Systems. Its Characterization and a Model, *Biosystems*, 5, 187-196
76. Von Bertalanffy, L. (1952). *Problems of Life: An Evaluation of Modern Biological Thought*, London: Watts & Co.
77. Von Foerster H., 1980, *Observing Systems, Selected Papers of Heinz von Foerster*, Seaside: Intersystems.
78. Weber A. & Varela F. J. (2002) Life after Kant: natural purposes and the autopoietic foundations of biological individuality. *Phenomenology and the Cognitive Sciences* 1(2), 97–125.
79. Weiss, P. (1963). The Cell As Unit. *ICSU REVIEW*, 5, 185-193.
80. Weiss, P. (1968). *Dynamics of Development. Experiments and Inferences*, New York: Academic Press.
81. Weiss, P. (1969). The Living System: Determinism Stratified. In A. Koestler & J. R. Smythies (Eds.) *Beyond Reductionism: The Alpbach Symposium* (pp. 3-55). London: Hutchinson & Co.
82. Wiener N, 1948, *Cybernetics, or Control and Communication in the Animal and in the Machine*, Cambridge MA: MIT Press (second edition, 1961).