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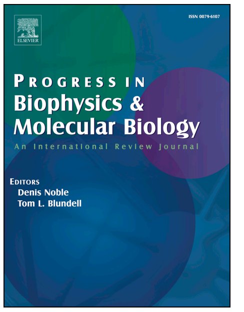

Towards a heterarchical approach to biology and cognition

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Towards a heterarchical approach to biology and cognition[1]

Luis Emilio Bruni and Franco Giorgi

Abstract

In this article we challenge the pervasive notion of *hierarchy* in biological and cognitive systems and delineate the basis for a complementary *heterarchical* approach starting from the seminal ideas of Warren McCullock and Gregory Bateson. We intend these considerations as a contribution to the different scientific disciplines working towards a multilevel integrative perspective of biological and cognitive processes, such as systems and integrative biology and neuroscience, social and cultural neuroscience, social signal transduction and psychoneuroimmunology, for instance. We argue that structures and substrates are by necessity organized hierarchically, while communication processes – and their embeddedness – are rather organized heterarchically. Before getting into the implications of the heterarchical approach and its congeniality with the semiotic scaffolding perspective to biology and cognition, we introduce a set of notions and concepts in order to advance a framework that considers the *heterarchical embeddedness* of different layers of physiological, behavioral, affective, cognitive, technological and socio-cultural levels implicit in networks of interacting minds, considering the dynamic complementarity of bottom-up and top-down causal links. This should contribute to account for the integration, interpretation and response to complex aggregates of information at different levels of organization in a developmental context. We illustrate the dialectical nature of embedded heterarchical processes by addressing the simultaneity and circularity of cognition and volition, and how such dialectics can be present in primitive instances of proto-cognition and proto-volition, giving rise to our claim that subjectivity and semiotic freedom are scalar properties. We collate the framework with recent empirical systemic approaches to biology and integrative neuroscience, and conclude with a reflection on its implications to the understanding of the emergence of pathological conditions in multi-level semiotic systems.

Keywords: Heterarchy; Hierarchy; second-order emergence; embeddedness; cognition/volition; dialectic; proto-subjectivity, semiotic freedom, systems biology, integrative neuroscience.

1) Introduction

Contemporary science has become "big data" science. This is true for all the disciplines that have to do with living systems, whether at biological, cognitive or social levels. This can be appreciated in the similitude and interrelations between the research agendas that propel the emerging bio- and neuro-technologies. Both fields are involved in grand mapping schemes of their objects of research, both are suffering from an overflow of data with great difficulties for its integration, and there are complaints about the lack of suitable theoretical frameworks to achieve such integration (e.g.: Schadt & Björkegren 2012; Akil et al.2011; Barabási 2011; Kriegeskorte et al. 2008; Insel et al. 2004). One of the conceptual limitations for the big data 'integrative' disciplines, in their jump from biology to cognition, is the "embodiment issue". As part of the reductionist strategy, this issue has customarily been approached in life and cognitive sciences by the tendency to map data and processes into hierarchical models of interrelated levels of organization[2]. As we

[1] We would like to express our sincere gratitude to Peter Harries-Jones for having introduced us to the notion of heterarchy and for the stimulating discussions through many years when it became clear to us that a Batesonean approach to multi-level semiosis would be incomplete without this important concept. For his discussion on Bateson and the notion of heterarchy we refer to Harries-Jones (2005, 1995).

[2] Given that hierarchies are but a specific case of heterarchies, we avoid here to refer to hierarchical levels in living systems and recourse rather to the more general expression "levels of organization" or "scalar levels".

will argue, organization in terms of hierarchies characterizes well physical structures and substrates, but it fails to give an accurate picture of the living processes embedded in such structures.

Although the notion of "heterarchy" was introduced into science by Warren S. McCulloch almost 70 years ago, the implications of this notion "…and its epistemological consequences have not yet been reflected by the mainstream of the scientific community" (von Goldammer et. Al. 2003: 1). Surprisingly, not even in cybernetic and complex systems circles. As we will show, a heterarchical approach to biology and cognition is actually concomitant to a biosemiotic perspective and it shares many of its premises and concepts.

In this article, we first introduce the concept of heterarchy followed by a set of necessary related notions and ideas. We start with McCulloch's concept of "diallel" and "value anomaly" (McCullock, 1945). From there we proceed to discuss the importance of non-transitive relations in semiotic systems and the implications to self-referentiality. We present Günther's notions of "contexture" and "poly-contexture" (Günther, 1973), and how they relate to the semiotic notion of "emerging interpretant" (see box). The distinction between complicated and complex systems in terms of determinacy and indeterminacy leads us to postulate two different ways of understanding the idea of "emergence" in biological and cognitive processes: first- and second-order-emergence (see box). We illustrate the dialectical nature of embedded heterarchical processes by addressing the simultaneity and circularity of cognition and volition, and how such dialectics can be present in primitive instances of proto-cognition and proto-volition, giving rise to our claim of subjectivity and semiotic freedom being a scalar property. In order to model such dialectical relation between proto-cognition and proto-volition we propose the notion of "digital-analogical consensus" (see box) as a logical operator for coincidence detection and coordination of multiple irreducible domains (i.e. the emergence of an interpretant) in a poly-contextural heterarchical organization. Based on this, we then proceed to collate the framework with recent empirical systemic approaches to biology and cognitive neuroscience, and conclude with a reflection on the implications of this approach for the understanding of how pathological conditions emerge in multi-level semiotic systems.

2) On the concept of "heterarchy"

Hierarchies are usually defined in terms of sub- or super-ordination (such as in bureaucracy, armed forces, political organizations, etc.). In a heterarchy, on the other hand, there can be relations of complementarity and subordination between categories of different logical levels, giving place to a more network-like nature of emerging processes than a strict relation of vertical subordination, where "horizontal" relations between different levels of organization, or different logical standpoints, are as important (von Goldammer et. al. 2003: 2). Physical structures and substrates are by necessity organized hierarchically, while communication processes – and their embeddedness – are rather organized heterarchically. Thinking exclusively in terms of spatial hierarchies ignores the role that higher-scale levels may play in sustaining interlevel relationships. Levels are not stable entities, for their persistence is not due to the properties of their material constituents. If the dynamics of their relationships is to be taken into account, the apparent stability of their material structures depends solely on the timescales through which they organize the constitutive-disintegrative processes relative to each other (Lemke, 2000a). However, the structures (hierarchically organized) can underpin, i.e.: scaffold, a process which is heterarchically organized. It is a logical organization, not a physical one. There is though a heterarchy/hierarchy complementarity, and therefore the issue is not that there cannot be biological, cognitive or logical processes that are hierarchically organized, but it means that the picture is incomplete if one does not include heterarchical processuality. Salthe (2012, 2013) distinguishes between two complimentary logical forms of hierarchy: 1) the compositional or scale hierarchy (which can be a synchronic map of the command “tree” hierarchy, or a hierarchy of nested entities), being a modular form “suited to the synchronic modeling of systems as they are at any given moment, focusing on dynamic energy transactions and ongoing processes”, and 2) the subsumption or ‘specification’ hierarchy (including a diachronic model of the trajectory of a given command), claimed by Salthe to be suitable for modeling the diachronic emergence of forms as stages in a developmental process of acquisition of new informational constraints. Whereas the former may find a suitable placement in the heterarchical approach (since structures do conform to hierarchies), we see the latter more problematic. Salthe (2012) presents embryological development as an example of the subsumptive hierarchy, implying that important information about the system can be found in antecedent conditions of the development that can be “cut up into discrete stages, or series of ancestral kinds”. In this sense, prior stages or phases of the development are considered to be lower levels of the hierarchy providing a model that represents “emergent” changes in the world. Allegedly, the developmental *process* would be hierarchically because previous (historical) stages or phases are material causes for present and future stages, which is a truism, and we see no reasons why being historically “prior” should represent a lower hierarchical level. Phases cannot be conflated with levels, and different phases may manifest similar arrangements of levels. By considering stages as different hierarchical entities, “emergent” processes and processes of becoming are also conflated. Salthe (2012) refers very briefly that sometimes the term ‘heterarchy’ is posed in opposition to the compositional hierarchy model because of *supposed failures* of actual systems to conform to hierarchical constraints. However he does not address what these supposed failures may be (e.g.: intransitivity, reflexivity, re-entrance, paradoxes, etc.) limiting himself to state that often “the ‘hetero’ opposition to hierarchy is based merely on faulty understanding (sometimes politically motivated!)”. In his discussion, the implications of the heterarchical approach are also underestimated by the fact that his examples for dismissing its pertinence are all from physical systems at different micro or macro scales. Therefore it makes no sense to introduce notions of intransitivity, self-reflexivity or semiotic processes, unless one is ontologically under the assumption of some sort of pan-semiotism. Furthermore, Salthe claims that the heterarchy dissent needs to focus upon what some take to be the true basis of material applications of the scale hierarchy – the order of magnitude separation of rates of change among levels separated by scale. Being entity oriented Salthe’s approach proposes in addition that boundaries must be taken into consideration if we are to make sense of the world: “Boundaries allow us to separate processes and *localize them in the world*, and this localization generates both behavior and events” (Salthe 2013, our italics). It is this emphasis on *localizable entities* in the “world” that makes this approach problematic when considering informational, semiotic or sign processes (Bateson, 1972). Salthe’s theory is compatible with the heterarchical approach as long as two things are made clear: 1) that hierarchies can map the organization of (material) *structures* (i.e. entities), while heterarchies are more suitable for describing semiotic *processes* which cannot be physically localized, 2) that a heterarchical organization does not exclude “internal” hierarchies within its organization, neither the hierarchical organization of its substrate. Whereas Salthe’s theory of hierarchies offers numerous opportunities for discussion and clarifications about the hierarchy/heterarchy relation, developing them systematically would be out of the reach of the present article.

Before we make explicit the main defining characteristics of heterarchical processuality, let's anticipate the picture with an oversimplified account: physical processes don't deal with options or choices. Only living organisms that *sense differences* develop and act upon response-repertoires that involve two or more potential options. The nature and degree of semiotic freedom of the response-repertoire – i.e., the kind of options that it affords – and the way cells and organisms enact the selected option in response to interpretation of contextual cues (i.e., aggregates of sensed differences), varies widely depending of the level of organization in question.

The difference between "mere" circular causality (e.g.: a self-regulated toilet that embodies only the purpose of its designer) and purposeful behavior is not a matter of *either or*, but rather of *more or less*. The feedback loops present in neural networks, or in systems of cellular signal transduction, for instance, are a sort of relatively "low level" purposiveness, or proto-subjectivity. In fact, they are instances of elemental *triadic causality* (see Box 1), which supersedes circular causality as soon as the "purpose", informed by the feedback, is taken into account in a decision-making process. Otherwise the circular causality of feedback mechanisms could also be described dyadically. The differences are in the degree of semiotic freedom, which means that semiotic freedom is a scalar property. As noted by McCulloch, from the empirical point of view, the systems must exhibit the possibility for choice and "… choice implies that two or more potential acts are incompatible. The observation requires some overt act with inhibition of incompatibilities" (McCulloch, 1945: 90). It is precisely " … the 'process of decision' itself that has to be analyzed to understand what distinguishes a 'heterarchy of values' from a 'hierarchy of values' from a logical point of view …" (von Goldammer et. al. 2003: 2). At whatever level of the scale of semiotic freedom in living systems in which choices – based on assessment of the context – are enacted by the system, there is the possibility of a *value anomaly* between the options of the repertoire. This means that the options are not necessarily ranked hierarchically, and therefore the transitivity law is not valid (see below). Moreover this *heterarchy* of values can be highly context-dependent and vary from one situation to the other (von Goldammer et. al. 2003).

3) Diallel and value anomalies

McCulloch (1945) introduced the notion of "diallel" to refer to a logical circle or a logical contradiction. The term can be related to similar notions such as paradox, tautology, antinomy, contradiction, dissonance, semantic incongruence, and to Bateson's notion of double bind. Moreover, such antinomies and *value anomalies* occur only in semiotic processes of interpretation, and they are never part of the description of physical systems or of physical states (von Goldammer et. al. 2003). They occur only within systems endowed with discrimination and/or interpretation capacity, where, based on such interpretations (i.e., cognition or proto-cognition) the system chooses (i.e., volition or proto-volition) between two or more available acts or behaviors. However, as we will see, these two aspects are not sequential but rather simultaneous. In normal healthy circumstances, diallels and vicious circles usually are resolved *heterarchically* by the organization, that is, within a wider gestalt (or contexture) that may involve or coordinate qualitatively different and irreducible domains. One can suspect that the condition becomes pathological when, from one or another reason, the system has no access to the larger gestalt and communication is disrupted. This can involve problems with self-referentiality and/or with the irresolution of conflicting values, which can only be dealt with in a heterarchical organization at a meta-context of communication.

4) **Non-transitivity**

In a value system (or scale) the transitivity law would take the following form: "if A is preferred to B and B to C that means that A is preferred to C". This is usually expressed in logic as:

$$(A \rightarrow B) \land (B \rightarrow C) \rightarrow (A \rightarrow C)$$

As stated by von Goldammer et. al. (2003: 6), transitive logical statements can always be constructed for physical attributes, or physical quantities, or more generally for quantities which can be measured. Actually, from a logical point of view every physical process of measurement or determination can be considered an application of the transitivity law, e.g. comparative statements on weight, distance, temperature, concentration, etc.

Normally, it is assumed that hierarchical systems reflect the validity of the transitivity law of the classic-logical implication postulated for a hierarchy of values or processes which only admit a notion of super- or sub-ordination but not co-ordination (like for instance Russell's theory of types or implication hierarchies). This is why biological models based on (physical) states and transitions between (physical) states conform to the transitivity law and therefore tend to be described as being *modularly hierarchical*. This is evident for example in biochemically kinetic reaction networks that consider sets of hundreds of thousands of reactions described by nonlinear ordinary or partial differential equations (Resat et al. 2009: 311). The dynamics of how the constituent components of biological processes interact in spatio-temporal responses to environmental stimuli are postulated to be of a multi-scale nature. However, independently of whether the systems are considered to be deterministic or stochastic, the multi-scale aspect is invariable postulated to be hierarchical. Therefore these models or explanations exclude recursiveness and self-referentiality in a fundamental logical sense. "Their data and algorithmic structures are reducible to one and only one comprehensive logical fundament as and operational 'universe of discourse' " (Kaehr and von Goldammer, 1988: 2), i.e.: a single "contexture" (see below).

This logic is then extrapolated to the higher levels of the *hierarchy* (e.g. perception, cognition, behavior) that are often considered to be epiphenomenological with respect to the complex dynamics of the substrate. This is the case for systems that are modeled or understood under the assumption that the *emergent* biological or cognitive property is the result of a highly complicated (and therefore probabilistic, or seemingly possibilistic) Laplacean system. This assumption does not take into consideration the possibility of "second (or higher) order" emergence (see Box 1), i.e. the possibility of emergent properties that are the result of combinations and coordination of many other emergent properties, which represent different "contextures" or "standpoints" within the system. Second-order-emergence results in true complexity as opposed to simply "higher complication", and entails an increase in semiotic freedom, non-linearity, and irreducibility of multiple scales and domains (i.e., the interplay and coupling between factors across different levels and layers). For instance, while prokaryotes control gene expression primarily at the transcription level, eukaryotes have evolved more sophisticated control mechanisms at the epigenetic, post-transcriptional and translational levels (Huang et al, 1999). This entails that organisms have gradually evolved from an original simple and reversible gene-to-enzyme hierarchy to a more complex organization in which gene-to-gene relationships are irreversibly regulated with a higher degree of freedom, i.e. with a wider range of options in regard to different control levels.

Such hierarchical structural and spatial organization is acknowledged to have a great importance for the rates of biochemical activities and for "information transfer". Spatial organization becomes particularly important when the kinetics of the interaction networks "depend on local conditions and the environment or when *material transport is required to convey the information*". (Resat et al. 2009: 313, our italics). These processes are though characterized as a combination of highly localized molecular events and macroscopic transport of products over a much larger spatial scale. The resulting picture is a hierarchy of compartmentalized activity through drastically different spatial scales and locations, posing a great challenge to modeling efforts (Resat et al. 2009: 313-14). There are several problems with this metabolic view of biological processes. When seen exclusively in this fashion only the transitivity laws of the physical world can be applied. Therefore in these models, "information processes" are treated as kinetic reactions and as "transport of materials", as the only way in which they can be included in the model. That is, under these assumptions, biochemical processes and informational processes are lumped into the same contexture, and are dealt with the same logical operators, and from the same standpoint. Furthermore, this view results in a hierarchical portrait of multi-scalar systems and processes. Thus the additional degree of complexity provided by the spatial organization and the structural hierarchies in biological systems is treated under a perspective of first-order-emergence (see Box 1) with deterministic, quasi-deterministic or stochastic assumptions. The "system's volume" may be subdivided into sub-volumes "that are small enough for each to be considered spatially homogeneous. Each subvolume forms a reactor compartment, and the compartments are linked at the higher whole-system scale" (Resat et al. 2009: 315), which results into an additive hierarchical-transitive integration of the whole.

In any biological process, no single factor can account for the complexity of a casual chain. Thus, it makes no sense to disentangle a multi-causal chain, if every contributing factor may be equally relevant for triggering its activation. Synchronicity is thus the contextual condition that makes the coincidence of this co-factor relationship highly significant in causal terms. On the other hand, one of the implications of the transitivity law is that it cannot deal with synchronicity, i.e. with the possibility of pondering two or more values in simultaneity. This is a crucial point to understand heterarchical processuality because, as mentioned before, we need to consider the "process of decision" which entails a synchronous dialectics between proto-cognition and proto-volition in deciding among values that are not presented or compared one after the other but simultaneously. The unquestioned sequentiality of state transitions is what makes us get the impression that our descriptions of biological and cognitive processes fulfill the transitivity law as far as their time dependence goes, and therefore we see them as hierarchically structured (von Goldammer et. Al. 2003: 6). The increasing importance given to synchronicity, coordination, coincidence, binding and integration in biology and cognitive neurosciences (Goldfarb & Treisman 2013; Fell & Axmacher 2011; Kelso 2009; Singer 2007; Canales et al. 2007) poses a great challenge to the hierarchical perspective. This is the case because simultaneity in physical systems is not linked to choices or decisions. Three simultaneous physical events may be in relation to each other, or together determine a particular outcome, but that outcome will be the only possible one. There is no possibility for error. On the other hand, under triadic causality, in biological and cognitive processes, coincidence detection is an important informational process that implies choices between two or more potential acts which are mutually exclusive, i.e. there must be an act with inhibition of incompatibilities. Several examples testify how incompatible alternatives are solved in nature. For instance, to prevent inbreeding, many angiosperm plants are endowed with the capacity to reject incompatible pollen and avoid self-fertilization. This decision-making process is made naturally irreversible through the inhibition exerted by programmed cell death (Thomas & Franklin-Tong, 2004). On a more cognitive ground, the dilemma presented by double bind constitutes another example of how incompatible messages can lead to failure to accept or solve certain contextual situations. And, at the same time, it indicates that the dilemma cannot be solved by rejecting one or the other of the messages, but more wisely by embracing a larger contextual perspective outside of the paradoxical situation.

If attributes are involved that belong to any category of subjectivity, or proto-subjectivity, from a particular standpoint of a "stakeholder" in a given process, the situation reverses and it becomes difficult to construct logically meaningful descriptions where the transitivity law can be applied (von Goldammer et. Al. 2003: 8). Similar properties of subjective attributes are extrapolable to lower levels of proto-subjectivity (i.e. lower degrees of semiotic freedom) in biological and cognitive processes. Our use of the "proto" prefix – as in "proto-subjectivity", "proto-cognition" and "proto-volition" – deserves some qualification. Jonas (1984) points out that "mind" serves as a blanket title for many different kinds and degrees of subjectivity, and that it appears only in conjunction with certain organizations of matter. If we are not able to consider different degrees and kinds of subjectivity with low levels of semiotic freedom, then subjectivity, as an emergent property, would be a radical evolutionary leap hard to justify. It would be "… awkward, not to say grotesque, to carry dualism, and with it a share in transcendence, into the amoeba or wherever else 'feeling' [i.e., sensing] begins." (Jonas 1984: 67-68). Thus subjectivity, as an emerging novelty, must be preceded by different degrees of proto-subjectivity (and its cognates: cognition, volition, semiotic freedom, purposeful-behavior and in general triadic causality). As mentioned before, this yields a scalar perspective of semiotic freedom and a substantive continuity from proto-subjectivity to full-blown kinds of subjectivity and *vice versa*. This requires a variability of the "representational" capacity and richness manifested with the different shades and degrees of subjectivity and proto-subjectivity, perhaps gradually, somewhere, erasing the traces of a real subject (Jonas 1984: 73), and affording just minimal degrees of semiotic freedom, as for example a cell reacting to a signal.

Subjectivity in its most elemental meaning entails the possibility of selecting alternatives evaluated from a particular standpoint. Objectivity, on the other hand, is brute force, nothing to select, nothing to decide, no mistakes to be made; the only possible standpoint is that of a potential subjective observer. As soon as we encounter the degrees of subjectivity or proto-subjectivity inherent in processes of contextual interpretation where an outcome can be selected from a response, the transitivity law, so universal in the quantitative attributes of the physical world, does not apply with the same consistency. It is of course a matter of degree, of more or less, according to how primitive or complex the level of subjectivity, or interpretation capacity, the system exhibits. But what is clear is that the more complex and variable the context gets and the larger the response-repertoire and the freedom of choices and creativity of responses (a function of semiotic freedom), the more we will be dealing with "anomalies" or heterarchies of values and non-transitive operations.

As opposed to a hierarchy, there is therefore an inherent difficulty in representing graphically (that is, physically) the organization of heterarchical processes. This is particularly so because the process' "units", "modules" or "parts" which are heterarchically organized – information, patterns, representations or logical products (i.e. the subject matter of an interpretation system) – are not only a function of dynamic spatial configurations of the underpinning substrate (which serve as sign-vehicles), but also a function of temporal configurations involving the processual interplay of synchronicity and diachronicity. Furthermore, the spatial configurations of constitutive elements of the particular sign-vehicles involved do not give rise to logical products which emerge exclusively in the horizontal kind of first-order emerging processes but involve in most cases a sort of second-order emergence, in which the logical products of a first layer of emergence (from different standpoints of the process) may be combined heterarchically to form more complex logical products which in turn get in synergy with many other first or second order logical products in non-hierarchical ways (what we have conceptualized with the logic of digital-analogical consensus, see Box 1).

So the physical picture of the substrate underlying such a process gives only a "horizontal cut" which cannot be interpreted as a mere complicated configuration (i.e. not truly complex) with a one-to-one mapping to the observed "epiphenomenon", because the dynamic "horizontal" first-order configuration is actually scaffolding many layers of heterarchically organized combinations of logical products attained by the diachronic/synchronic combinations of distributed physical configurations. Seen in this way there cannot be a deterministic relation between the horizontal configuration (or state) of the substrate on the one hand and the biological, behavioral or cognitive manifestation on the other. Different complex combinations of "middle layers" of second order emerging logical products may give rise to similar manifestations (e.g. pleitropy, epistasis, redundancy, neuroplasticity, polymorphism, modularity, and similar attributes).

McCulloch's concept of logical diallel combines the property of non-transitivity, self-referentiality and heterarchical organization, which as stated by Kaehr and von Goldammer (1988: 3) allows for "the coordination of domains or values which cannot be submitted to a *summum bonum*", that is, an optimal and unique value or choice, that can be selected or realized from a set of options that have been hierarchized or ranked in a scale from worst to best. A heterarchical organization provides the possibility of coordination across scales, sub-levels and supra-levels of many different kinds of networks – as e.g. the concomitance co-ordination of cellular signal transduction and neural networks with other physiological and cognitive levels.

5) Contexture, poly-contexture and emerging interpretants

A mechanical deterministic world view is "mono-contextural". Logically speaking everything that belongs to this "contexture" is objective and universal, and what does not belong to it is just nothingness (Günther 1973). Every logical operation that can be performed is confined to the contexture in which it originates. In this regard, a contexture comes to resemble a "tautology" in the sense Gregory Bateson (1979) was giving to the term. As explained by Günther (1973), it became very soon evident in the history of logic and of epistemology that the classic pattern of thinking with its mono-contextural ontology offered no place for the subjective cognizer. Thus a single contexture implies a single standpoint. While the notion of human inter-subjectivity have made clear the "poly-contextural" nature of human relations, with its myriad of "standpoints", the notion has been more problematic in the rest of the natural world, i.e. accepting the distribution of subjectivity and the constant negotiation of indefinite standpoints in nature, not only in the phenomenological worlds of organism (umwelt) but also in their biological processes.

Therefore, different logical levels, or qualitative domains, imply different contextures, which need to be mediated by "special logical operators" or "operations". In biosemiotic terms this corresponds to an *emergent interpretant*: a point of view where an aggregate of differences that has been sensed makes a difference at a given level of integration (see Box 1, and Bruni, 2003, 2007). By this convergence of synergic factors a locus for selection or decision is constituted. The emerging system manifests therefore a qualitative domain of a different logical type from the contextures that have been mediated. Seen in this way, one new level of subjectivity may be constituted by the synchronous consensus of many local proto-subjectivities, in Gunther's terms, a "poly-contexture". According to this view, the subjectivity of the biological-cognitive world has indefinite standpoints or logical locations. These locations are representable by a two-valued system of logic when viewed in isolation. However the heterarchical coexistence and relations of such qualitatively different standpoints can only be described in a polycontextural logical system, which cannot be described with classic two-valued or even multivalued logical systems that are confined to a single contexture (Kaehr and von Goldammer, 1988). In this way the circularities, diallels and instances of self-referentiality that appear in the descriptions of biological and cognitive systems can be modeled, allowing for the mediation of the different qualitative domains in a heterarchical processuality. Contrary to the hierarchical nature of Russellian logical types, in a heterarchy there can be categories disseminated or distributed *polycontexturally*, i.e.: a set in one contexture can be a class in another, depending on the particular standpoint of a given selection locus. Therefore the local paradoxes of a given contexture can be resolved at a parallel or a more global level.

6) The dialectics of cognition and volition and the response-repertoire

"Decision processes" in a given system are by definition open, not determined a priori, and standpoint-dependent (McCulloch, 1945, von Goldammer et. Al. 2003). Each potential choice in the response-repertoire represents a different standpoint. These potential choices cannot be considered sequentially one after the other because this already produces a hierarchical ordered-sequence between the different standpoints, in which a decision has already been made. This is why the consideration of synchronicity and simultaneity is so important in systems under the regime of triadic causality (i.e., biological and cognitive systems). It becomes a necessity that the description of the decision process maintains the simultaneous consideration of the different standpoints implied by each potential choice of the response-repertoire.

The parallel and simultaneous logical places of each standpoint have to be mediated by some adequate logical operators that consider the synchronicity of all the factors, perspectives and potential scenarios of each of the standpoints that are part of the process, until the dialectical contradiction is reconciled in a new synthesis and a decision has been reached (von Goldammer et. Al. 2003:13). If there is only one standpoint then it is not a decision process what we are dealing with, and the sequence can be resolved within the single contexture of that standpoint.

These processes in living systems are enacted in the continuous dialectics between cognition and volition, (and their more primitive proto-manifestations), which as explained by Günther (1979) are complimentary (dialectical) aspects of subjectivity, inseparable and simultaneous. This is eloquently stated by Kaehr and von Goldammer (2003:4) in the following circularity:

> "(a) … a volitive (decision making) process structuring the environment by a determination of relevances and a corresponding context of significance within the semantical domain produced by (b) …

> (b) … a classification and abstraction of the data by cognitive processes producing a representational structure of content and meaning within the context in (a) …"

It is precisely this kind of complementarity that is conceptualized in a more abstract form in the logic of digital-analogical consensus (DAC)(Box 1), which we exemplified in the context of cellular semiotics (Bruni, 2003, 2007). One of the simplest examples of this logic can be found in the process of protein folding. If considered in their primary structure, proteins can be said to be *digitized* in their discrete amino acid sequence. However, when this sequence is properly folded it may emerge into secondary and tertiary structures that relate to the external milieu by surface-to-surface *analogical* interactions. But whenever this 3D structures come to interact with compatible ligands or receptors, the specificity of their relations is once again fixed by one-to-one *digital* interactions (Carbonaro et al., 2006). The reason for abstracting this logic is to be able to apply it at different levels of organization where we can observe different degrees of proto-volition and proto-cognition in such dialectical relation. What triggers a selection from the response-repertoire (volition) is an informed assessment of the context by a digital-analogical consensus (cognition): a continuous process of coincidence detection in which an indefinite set of digital messages (presence/absence, activation/deactivation) from different domains and levels of the heterarchy (being manifested in simultaneity), form an analogical message that binds the most comprehensive interpretation of the context to an appropriate response, i.e., the formation of an *emergent interpretant* – a standpoint for the decision. These processes relate different qualitative domains in a heterarchy because such analogical integrated representation may in turn be a digital representation or piece of information to a different level of aggregation (by being or not being present or activated), which combines with other analogical signs into a higher order logical product. In this way the new analogical sign can also be a digital representation interfacing another domain in a still more complex analogical sign. The emerging analogical mode may also constraint, or influence, the informational processes in the constitutive domains by a process of re-entrance and self-referentiality. It is in this sense that we claim that the DAC-logic could mediate different (logical) non-hierarchical domains maintaining the parallel simultaneity of processes that lead to a choice or decision (triadic causality). We have previously argued that G protein-coupled receptors can potentially discriminate a wide variety of intercellular signals by self-assembling in the form dimeric/oligomeric complexes along the plasma membrane. By doing so, the plasma membrane comes to act as the first hierarchical cell structure involved in a heterarchical process of selective categorical sensing (Giorgi et al., 2010). This allows several contextual cues to be integrated and eventually to be selected for their capacity to entertain relations of correspondence with other cell molecular partners that share the same spatial compartment or the same timeframe (Giorgi et al., 2013).

7) Heterarchies at the biological level

Contrary to "classical" complex systems science, network theory approaches ally with "discovery science" and rely on the massive datasets that pour out of high-throughput technologies. The similar treatment of huge data sets in very different kinds of systems, is paradoxically transforming biology and cognitive neuroscience from their heavily inductive roots into disciplines that see cellular, metabolic and neural networks as governed by specific laws and principles (Vidal et al. 2011: 986). These new perspectives somehow question the genetic-deterministic assumptions of genome science opening the doors to more probabilistic approaches that consider epigenetic, environmental, relational and contextual factors, however for the most part within a deterministic ontological assumption that nonetheless allows for, or has to deal with, epistemological indeterminism, with the collateral normative assumption that complexity can be tackled with ever more powerful algorithms, (Barabási, 2012: 15-16). In this vein, Vidal et al. (2011) discuss the link between network properties and phenotypes and the possibility that perturbations of the properties of cellular networks have an important influence on phenotypes. From a systems and network biology perspective, cells are now seen as a complex web of macromolecular interactions that constitute different types of "interactome networks". Some of them map actual physical relations, such as the interactions between transcription factors and putative DNA regulatory elements in transcriptional regulatory networks, or protein to protein interactions in whole cells. Others can map multivariate correlations, such as disease networks in which nodes represent diseases and edges represent gene mutations, which are associated with the linked diseases. Highlighting such interactional features supports the biosemiotic view that the evolving and developmental "units" are actually "systems of correspondences" (Bruni, 2007, 2003). Emblematic is the case of symbiotic relations, which evidences how the symbiont's proteins and the host's proteins interact in complex lock-and-key systems. Therefore, coincidence detection and synchronicity is a salient semiotic feature in the workings of such systems of correspondences (Bruni, 2003, 2007).The semiotic aspect of a given digital-analogical consensus lies in the fact that once a consensus (which can be a particular threshold, or the simultaneity of many different cofactors) has been reached, the system enacts the selection of an appropriate response that correlates to the complexity of the context, this latter being mapped or represented in the variety of cofactors necessary for that particular "consensus" (Bruni, 2007, 2003). The difference between the semiotic approach to this kind of coincidence detection in systems of correspondences and the version emerging in systems biology and network theory is that the latter postulate systems and meta-systems in a modular-hierarchical architecture that treats complexity as a first-order-emerging process, whereas the semiotic approach advanced here insists on a heterarchical architecture that allows for the interrelation of qualitatively different domains and levels of organization in a second-order-emerging process (see Box 1) – which entails an increase in semiotic freedom as the system grows in complexity, therefore assuming indeterminism not only epistemologically and probabilistically, but also ontologically.

The synchronicity of factors is emerging as a clear motif in biological and neurocognitive systems. Gerstein et al. (2012) analyze the co-association patterns between different transcription factors in proximal and distal regulatory regions which constitute the regulatory network for a cell. They organize the binding patterns into a stratified hierarchy representing the overall systems-level regulatory wiring. Several of their key findings point to the centrality of the digital-analogical consensus logic in complex biological systems, and are worth mentioning here. In particular that the combinatorial co-association patterns of transcription factors are highly context specific: distinct combinations of factors bind at specific genomic locations. From the biosemiotic perspective, the main point of digital-analogical consensus was to take into consideration the context-specific nature of biological processes and how the combinatorial "habits" (the analogical signs) codified or mirrored specific context situations that were then bound to a specific response that meets the contextual demands (and hence the necessity for invoking triadic or semiotic causality). For example, in cellular signal transduction we hypothesized that what assures the signal specificity and avoids undesired cross-talk in a complex network – where there is the presence and mediation of ubiquitous non-specific second-messengers – is precisely an aggregate of indefinite digital bindings that constitute a specific complex (i.e., an analogical sign) which characterizes the actual context, and therefore the appropriate specific response gets selected (Bruni 2003, 2007).

Gerstein et al. (2012) present a variability map of factors' co-presence that has semiotic relevance. This map shows the degree of variability in the partners of a given transcription factor over the different contexts. Some factors show mostly the same partners in many contexts, a few partners are present in only some contexts, while some factors completely change its partners in different contexts. In other words, some factors are more "meaningful" in the characterization of the particular context, guaranteeing specificity. The way Gerstein et al. (2012) organize their hierarchy does not depend exclusively on physical contact but also on indirect regulatory relations, so it can be said to be a functional hierarchy. This may not pose the problem of not considering non-transitivity (as if it was a physical hierarchy), but may present problems to address the paradoxes of re-entrance and self-referentiality, for which a heterarchical processuality would be better suited given that regulation across levels of organization is highly self-referential. After identifying all primary and local partners for each focus-factor context, Gerstein et al. (2012) use multivariate rules to identify pairs and higher-order clusters of significantly co-associated transcription factors, which is what allows them to organize the network hierarchically. However, in complex networks, be that signal transduction networks, genetic regulatory networks or neural networks, all the pathways involved in "control" or "regulation" processes are themselves opportunities for further regulation and control (Bruni, 2007). This is why regulation cannot be found on a single element within the same contexture since the process would fall into an infinite regress of regulatory elements. If regulation is seen dyadically as a first-order-emergent hierarchical process it would result into a paradox such as: "The coordinate regulation of stimulatory and inhibitory pathways provides an efficient mechanism for operating switches and is a common phenomenon in regulatory biology" (Lodish et. al., 2000: 886); in other words, the coordinate regulation of many factors provide the mechanism for regulation, a circular statement. In semiotic terms, such perspective would not consider the formation of different local interpretants that combine into higher order interpretants (i.e., second-order-emergence), but admits only the formation of one global interpretant for the whole process (i.e., first-order-emergence). If seen exclusively from a quantitative-hierarchical point of view then the "more 'influential' transcription factors tend to be better connected and higher in the hierarchy" (Gerstein et al., 2012: 96). But if seen from a semiotic – heterarchical point of view, absences and few "elitists" connections can manifest a very high level of significance. Thus, it appears surprising for Gerstein et al. (2012: 96) that "a model integrating the binding–expression relationships of all the highly connected transcription factors has about the same predictive power for expression as a model integrating all the less connected ones, indicating that the weak binding–expression relationships of the less influential factors are collectively quite influential".

8) Heterarchical processuality in cognition

There is a growing area of research that considers healthy and pathological brain activity in terms of complex networks with the use of graph-theoretic approaches similar to those of systems biology (Power et al. 2011; Thompson & Swanson 2010; Bassett and Bullmore 2009). Considering the brain as a complex network, the attempt is to identify hubs and critical nodes, traffic flows at different scales, efficiency of information transfer, modularity, feedbacks and controls of the system in order to quantify the hierarchy and its substructures at the level of the entire graph, sub-graphs, or individual nodes (Power et al., 2011: 665). In other words, the functional correlations are mapped onto a hierarchical spatial and functional organization (in the cortex) at the level of neurons, local circuits, columns, functional areas, and functional systems (Power et al., 2011: 666). The contention of the heterarchical approach advanced here is that the hierarchical spatial-structural organization scaffolds a functional organization that cannot be exclusively hierarchical, and much less symmetrical or isomorphic to the structural hierarchy. This is hinted by the observation that certain differential correlations (of brain regions) are unlikely to reflect only anatomical connectivity, but instead might be related to the history of *coactivation* that these regions surely share (Power et al. 2011: 669). Some approaches establish analogies to the "small-world phenomenon" observed in sociological network theory in order to address the dichotomy between localized and distributed models of brain organization. It is claimed that, in principle, a small-world structural network can provide the scaffolding for both locally specialized functions in segregated areas and globally distributed or integrated processing with efficient communication and coordination (Bassett and Bullmore 2009). Usually these models entail some sort of non-overlapping modules or communities that can be identified. On the other hand, Ferrarini et al. (2009: 2222) point out that brain modularity should not be restricted to a non-overlapping partition of the functional connectivity map. They emphasize that different local or regional modules can cluster together in larger modules, which in turn cluster again in overlapping and inclusive relationships (similar to the logic of digital-analogical consensus to which we have referred before). However, they see this overlapping of meta-clusters as climbing up through a hierarchical organization.

Seen in such hierarchical way the functional synchronicity and coincidence of non-contiguous structures demand a direct structural, i.e. physical (hard-wired), connection in order for the "coincidence" to be detected or activated. Therefore there is somehow a one to one mapping of function and structure (i.e., no semiotic freedom). A relative increase in (physical) distance between connected nodes may be considered as inefficient wiring and abnormal neurodevelopment, which results in an attenuated hierarchical organization, that in turn may be correlated to some pathologies as e.g.: schizophrenia (Bassett and Bullmore 2009). Whereas in a heterarchical organization, the coincidence of events in non-physically connected (brain) structures could be detected (i.e., "connected") at a different qualitative level, standpoint or contexture, i.e. sensed at a second-order-emergent interpretant (for example in relation to the immune or the endocrine systems).

In networks' metrics, hierarchy is a quantifiable parameter. Even though there seems to be lack of consensus of how to quantify it, the parameter always implies a ranking of values of other parameters, as for example the "clustering coefficient" (i.e. local connectivity) and the "degree distribution" (i.e. global connectivity), precluding, at the functional level, the possibility of considering heterarchies of non-transitive values, and therefore the processual possibility of self-referentiality, reentrance, co-ordination of qualitatively different domains, second-order-emergence, etc.

The notions of "reentry" in nervous systems (sometimes call "recurrent" or "recursive" processes) and of "binding by synchrony" are acquiring increasing importance in integrative neuroscience. As pointed out by Harries-Jones (2005: 169), "Questions about electrical circuits that re-entered themselves were perplexities for engineers with Ph.D's in 1973 …" and computer programmers were struggling with interactive loops that were not only challenging their logic but also crashing their systems. These notions are very relevant for the heterarchical perspective. Reentrant signaling is hypothesized to functionally coordinate multiple dispersed neuronal populations and areas of the cerebral cortex and to be one of the most important integrative mechanisms in vertebrate brains (Edelman and Gally, 2013).

What distinguishes reentry from the canonical notion of feedback warrants the speculation of the existence of reentering signaling instances in proto-cognitive/volitive processes when seen from a heterarchical and biosemiotic perspective. As opposed to feedback, neural reentry does not utilize fixed error-correcting functions or paths, but involves *selectional* systems across multiple reciprocal paths that are not pre-specified or determined *a priori*, but rather acquired through experience (Edelman and Gally, 2013). This is what prefigures reentry as an important and plausible feature in proto-purposive and proto-subjective systems, especially considering the fact that these reentrant processes are scaffolded by intrinsic properties of neural anatomy and physiology. Therefore it is not surprising to see similar signaling processes based on coincidence detection of different variables (i.e. signals) that fluctuate or oscillate between “meaningful” synchronous thresholds – from cellular signal transduction, to synaptic synchronization of local neural populations, to the large scale synchronization of global electrical brain signals, to coordination of neurocognitive activity with endocrine and immunological responses, for instance. Moreover, many physiologically different signaling systems may be embedded and synchronized in the same heterarchy. One thing which they have in common is the use of oscillations and synchrony in the temporal domain as a highly context-sensible coding feature (Singer 1999, see also Bruni 2007).

Reentry makes a lot of sense if seen in the light of the heterarchical embeddedness of different contextural domains that have to be coordinated and integrated, as for example the binding of cross-modal sensory features through the synchronizing and integrating patterns of neural activity in different brain regions and the binding of the elaborated percept to the significance (and emotional) systems embedded in memory, which may result in a volitional enactive response. Reentrance is one instantiation of *coincidence detection* (or digital-analogical-consensus) in the temporal integration and coordination of multi-level (local/global) domains in a heterarchical process. Such complex reentrant architectures correspond to what McCulloch was calling diallels, and therefore it would not be possible to represent them as a hierarchy. The distributed pattern of reentrant activity in which the brain is engaged at any one instant can act to inhibit, suppress, or compete with conflicting alternative response patterns, which have to exist as alternatives. In turn, alternative response patterns are the prerequisite for “decisions” or selections, and therefore for potential conflicting heterarchical values. If thought hierarchically, the unified conscious scene would be the direct emergent result of a myriad of low level physiological transactions, i.e.: first-order-emergence. Whereas if seen heterarchically it would be the top-down/bottom-up dialectical coordination of “middle layer” emergents or domains, i.e.: second-order-emergence, including not only the horizontal (same level) reentrance but also loops of self-referentiality across qualitatively different domains.

9) Pathologies in heterarchies

The Impossibility to enact a choice, when needed, leads to phenomena akin to double bind, paradox, cognitive dissonance, ambiguity, incongruence, antinomies and many pathological conditions, as perhaps the case of cancer – all kinds of phenomena which Bateson acutely associated with either creativity or pathology. In Bateson’s double bind theory, at the root of schizophrenia there is “a logical incongruence, a disruption in thought and communication” caused or exacerbated by patterns of relationships in the subject’s family (Bateson, MC, 2005). However as pointed out by Gregory Bateson himself and emphasized later by Mary-Catherine Bateson (2005), the issues related to double bind can be generalized to other biological processes and entities in a communicational relation, bringing the notion of double bind close to McCulloch’s diallels. “In this pattern there is a contradiction between messages at different logical levels: a primary injunction and a second conflicting injunction at another level affecting the interpretation of the first” (Bateson, MC, 2005: 13). In addition, there is a contextual or environmental constraint that makes it impossible to escape the contradiction between two different domains, creating an oscillation, which does not allow the system to finalize a choice or the selection of a value. "The confusion of logical levels that create the double bind would seem to occur most easily where one system is embedded in another" (Bateson, MC, 2005: 16). This embeddedness does not necessarily have to be physical or structural; it can also be logical or functional.

It has been often assumed that Bateson's approach to recursiveness in general, and in relation to double bind and dialles in particular, was conceptualized within a hierarchical perspective due to his extensive use of Russell's theory of logical types. Peter Harries-Jones (2005) convincingly shows that Bateson's logic was actually more prone to the heterarchical perspective. According to Harries-Jones (2005: 169), Bateson recognized in letters to his critics that the Russellian "ladder of types" had slippery edges, and that the hierarchies that he was postulating in context and meta-contexts of communication were not the canonical mathematical hierarchies, nor of any organization of control, nor of power hierarchies. Thus:

> "Bateson's hierarchy of types focused upon relations that exist between levels of a hierarchy. So while Russell's logical typing imposed a higher, more inclusive meta-level, on a lower level, Bateson's "meta-context" gives rise to a logic in-between. It also embraces meaning. The recursive logic of in-between requires oscillation between two dimensions [or qualitatively different domains], context and meta-context, and the meaning of an event emerges from this oscillation" Harries-Jones (2005: 169).

This interpretation is congruent with a heterarchical perspective that can better account for the circularities, reentry, and oscillatory phenomena that is usually found in biological and cognitive systems. By stressing the importance of dialectic relations, Bateson's perspective claims that in the emergence of meaning both digital and analogical codes had to be present, but one cannot be reduced to the other. This dialectics is what we attempted to describe with the digital-analogical-consensus logic as a starting point for the formalization of a "logic in-between" that puts different qualitative domains in heterarchical relations of contexts and meta-contexts. The heterarchical framework allows a more comprehensive conceptualization of the emergence of higher levels of organization. To understand how a multilevel scaffold may actually grow in complexity one has to consider how levels are interfaced with one another and, above all, how their closures may be re-opened and under which circumstances. In a topologically stable hierarchy levels are semiotically related such that each level is constrained by the ones lying above and sustained by the narrowed variations nested below. This entails that of the many possible realizations that each level may potentially express only a few will be filtered out and made compatible with the constraints that higher levels impose on them. This allows the hierarchy to attain an interlevel compatibility that renders each level self-referentially encoded and contextualized in a larger system of interpretance. Hierachical self-referential processing is thus related to the levels' capacity to fix their structural and functional identity and maintain it invariant through stable feedbacks. However, hierarchical stability is threatened whenever this self-referential processing is no longer restrained within the many-to-one mapping with which higher levels classify and filter (interpret) variations in lower levels. Lemke (2000b) refers to this situation as conceptually equivalent to an opening of the closure, i.e. the possibility of exploring wider ranges of buffering conditions that may include new typologies and more elaborate taxonomy criteria. On a similar ground, Cariani (2009) interprets inter level communication as conceptually equivalent to the observed/observer relationship. In this logical framework, creative emergence rises whenever a higher level proves no longer capable of knowing (interpreting) the full range of properties expressed by the lower levels. This failure prompts a transition from a topological type of semiosis to a more typologically grounded semiosis whereby meaning is no longer assigned by degrees but through an extended range of distinctive qualities. Emergence can thus become creative and grow in novelty if, and only if, interlevel relationships are mediated by a contextualized system of correspondence. Because of the semiotic nature of these relationships, properties expressed by each level within the hierarchy cannot be deduced from those of lower levels nor can they determine the properties of the ones lying above. The contextual and historical nature of this part-whole relationship makes the hierarchical organization essentially heterarchical because no longer determined by the sole upward or downward causality. On the contrary, by embodying context-sensitive constraints interlevel relationships may become susceptible to past experiences and more prone to adopt open-seeking behaviours (Juarrero, 2000).

Many, if not most, or even all, pathologies in the realm of biology and cognition, consist of, or involve, a sort of communication problem at some level of organization. A certain degree of semiotic freedom and plasticity is therefore necessary in order to deal with ambiguity, paradox, incongruence, double-binds, dissonance, logical contradictions, conflicting values, tautological propositions, vicious circles, antinomies or “value anomalies”, which are implicit in non-transitive processes. All such paradoxical propositions, be that at the level of cellular misinformation which may lead to cancer or at the individual’s socio-cognitive level where continuous double-bind patterns may lead to schizophrenia, occur only within systems endowed with more or less interpretation capacity at any level, from pattern recognition in signal transduction to autobiographic narrative intelligibility in human cognition.

In fact, cancer is being increasingly recognized as a “miscommunication disease”, in which intercellular signals are aberrantly sent and/or received, resulting in the uncontrolled proliferation, survival and invasiveness of the cancer cells (Milella et al., 2010). There is an increasing body of evidence that document a variety of miscommunication instances in these processes. However, since cancer has traditionally been interpreted as a clonal process, the majority of the documented cases have to do with miscommunication occurring in the tumor mass at the level of cell-to-cell relationships and with the way signals are interpreted by the communicating cells. This means that the sole causal level under consideration is the cellular level, which determines the fate of higher levels of the hierarchy, such as the tissue level, organ level and even adjacent organs in the process of metastasis (Greaves & Maley, 2012).

In recent years, however, cancer has been more realistically considered as a tissue-based phenomenon rather than as a simple cellular process (Soto & Sonnenschein, 2011). The ascription of oncogenesis to abnormal interactions between a mesenchymal type of cells and the surrounding parenchyma allows a more realistic comprehension of its developmental progression. If oncogenesis is a tissue-based process, miscommunication should in fact involve wider regional districts and tumour expansion should not depend solely on cell proliferation, but rely on factors that extend the relationship between stromal cells and the tumour environment on longer distances. In other words the miscommunication would not be exclusively intra-level but also inter-level. In fact, in recent years it has become evident that cancer cells may also communicate over longer distances by diffusing into the surrounding milieu, including blood and body fluids, and by releasing their specific contents of proteins and nucleic acids (mRNA and miRNA) onto target cells, inducing oncogenic transformation in many adjacent tissues (Lee et al., 2011), and the metastatic dissemination of cancer cells (Deryugina & Quigley, 2006; D’Asti et al., 2012).

A multilevel heterarchical approach to the study of cancer would consider the causal value of the context where cancer cells emerge, proliferate and eventually interact with adjacent healthy tissues to exert their malignant properties. It would need to consider the heterarchical relations and communication between different levels of proto-subjectivity from the standpoint of the cells, tissues, organs and even the full-blown subjectivity of whole organisms with their history and context – taking into consideration the alteration of heterarchical self-referential properties produced by the impossibility of resolving communicational incongruences at the appropriate domain.

Genomic science and systems biology are willy nilly opening the doors to notions and fields of research that for a long time have been excluded and sometimes even ridiculed by mechanistic science, as for example the notion of "downward causality" or the field of "psychosomatic medicine". The latter has morphed into the more respected fields of behavioral medicine and psychoneuroimmunology. Striking examples of the new acceptance of downward causality are the emerging fields of "social signal transduction" (Cole, 2009; Slavich and Irwin, 2014) and "social human genomics" (Slavich and Cole, 2013) which are beginning to provide "mechanistic" evidence of the very psychosomatic effects that for decades have been negated by mainstream science. However, even though these lines of research are questioning the genetic stability of organisms and try to empirically assess how our *subjective perceptions* of external environmental and social conditions can influence our most basic internal biological processes (i.e., gene expression), the framework remains deterministic and for the most part mechanistic. This represents a big challenge, given that the notion of *subjectivity* is being incorporated without careful consideration of what it means in terms of causality.

There is "increasing evidence that changes in the expression of hundreds of genes can occur as a function of the physical and social environments we inhabit", but these effects are considered to be "often more strongly tied to peoples' subjective perceptions of their surrounding social environment than to 'objective' features of those environments" (Slavich and Cole, 2013: 331), and "even [to] purely imagined or symbolic cognitive representations of such conditions" (Slavich and Cole, 2013: 333). This perspective still remains genetic-deterministic because even though the genome is not seen as a static blueprint for human potential, it is still seen as encoding a wide variety of "potential biological selves". It will be the particular constellation of our *experienced* social conditions which will determine which one will get realized. Moreover, the genetic determinism bounces back as "the external social world gets … 'onto the genome' to shape complex behavioral phenotypes and susceptibility to disease". Furthermore, genetic factors "have been found to moderate individual differences in genomic sensitivity to social context" (Slavich and Cole, 2013: 332). Causality gets blurred as the social condition (actually our subjective perception of it) determines a gene profile which then interacts to shape a complex behavioral phenotype (through proteins that mediate moods, cognition, behavior and health) – not a subjective social response!

The central targets of these new lines of research are, first the identification of the gene profiles that are sensitive to external social conditions, and second *the neural and molecular mechanisms that mediate the effects of the external social conditions* on gene expressions (through hormones and neurotransmitters). The step forward in this perspective is that now it is not just an aggregate of environmental factors that activate entire gene profiles, but also our *subjective experience* of that environment. However, the key question would be how does subjectivity emerge in such deterministic framework and how does it mediate the "external" socio-environmental conditions. In other words, how is the subjective experience formed and how is it disaggregated into neural and molecular mechanisms. Before being translated into signals for the endocrine and sympathetic nervous systems, how is subjective meaning recognized? What kind of interfaces are operating here? If, as stated by Jonas (1984: 211), "Epiphenomenalism makes matter the cause of mind and mind the cause of nothing", and, the materialist is bound to determinism (as only an indeterminist can admit semiotic freedom), how are we going to account for the subjective perception that determines a gene profile which actualizes one of the "potential biological selves" encoded in the genome?

By introducing "subjectivity" in such deterministic-mechanical and hierarchical framework the "causal bookkeeping" will run into trouble. Jonas (1984) remarkably described the problematic kind of interface that is at work here:

> "... between input and output there is interposed a process of an entirely different order from the physical one. Short or long as may be the loop of the circle that passes through the mental field on the other side of the wall, it does not move by the rules of quantitative causality but by those of mental significance. 'Determined' it is too of course, but by meaning, understanding, interest, and value – in brief, according to laws of 'intentionality', and this is what we mean by freedom." (Jonas, 1984: 220)

Even though such investigations are making great progress in revealing and correlating the effects of acute social stressors on immune response, resistance, resilience and morbidity, it becomes obvious that a modular-hierarchical characterization of the system will not suffice if causality is admitted to be codetermined by meaning, understanding, interest, and *value* at the psycho-neuro-immunological interfaces. Usually the modular-hierarchy includes the central nervous system, which transduces "social information" into changes in hormone and neurotransmitter dynamics that in turn modulate gene expression changes throughout the body and in the brain. From a heterarchical perspective this is an interesting case of "re-entry", circularity and downward causality (i.e., diallels) in the mediation of irreducible domains: how the subjective phenomenological representation of a situation, mediated by multimodal perceptual integration, and elaborated within the cognitive history of the individual (including value anomalies), impinges on the biological substrate that has *mediated* the subjective experience. In such a perspective there would not be a one to one mapping, first between perception and subjective appraisal, and then between subjective appraisal and biological and/or behavioral response. There must be in the middle second-order emerging layers that mediate irreducible domains in the increasing semiotic freedom that forms the subjective interpretant with its downwards effects. However, what is being hypothesized is that particular genetic pathways could be "effectively 'disconnected' from social environmental regulation, thus preventing social adversity from 'penetrating' the genome to impact health." (Slavich and Cole, 2013: 339). In this view the farther that we get in unpacking the black box of subjectivity (as an interface), is by defining it in terms of "subjective neurocognitive appraisals". What sorts of interfaces are implied between the neuronal, the cognitive and the "subjective appraisal"? The answer is: complex cascades of signal transduction and transcription factors that in turn determine complex behavioral phenotypes. The neurocognitive part adds neural/brain-region determinism to the picture, i.e., which neural correlates and brain regions are implicated in subjective appraisals and therefore considered pathways to gene expression. By reducing subjectivity to neurocognitive biochemistry without considering the (physically) indeterminate world of semiotic freedom and subjectivity, these approaches are missing the necessary interfaces that could eventually interconnect genomes socially.

10) Conclusion

We intend the considerations of this article as a stimulus to the different scientific disciplines working in such kinds of "horizontal" integration or "expansions" of biological and cognitive processes, e.g.: social and cultural neuroscience, social signal transduction, systems biology at ecosystem level, psychoneuroimmunology, etc. In order to overcome the limits of a perspective that considers the kind of first-order emergence implied by transitivity and hierarchical modular levels, we advocate for a heterarchical semiotic perspective which offers a continuity between logical levels, including or postulating the necessity of relating different qualitative domains or contextures, and accounting for the scalar increase in semiotic freedom. Kaehr, von Goldammer and their colleagues (Kaehr & von Goldammer 1988, 1989; von Goldammer, Eberhard et al. 2003; von Goldammer & Paul 2007) have developed rigorous logical strategies for the formalization of polycontextural semiotics that could be a starting point for the integrative modeling efforts necessary in systems biology and integrative neuroscience.

In the heterarchical perspective advanced here, we have stressed the scalar nature and the embeddedness of subjectivity. This has to be considered in relation to the dialectics between proto-cognition and proto-volition. We have suggested that the most primitive instances of proto-cognition are the most basic types of sensing in living beings such as cellular signal transduction systems, which result always in some sort of response (triadic causality), starting therefore the dialectics of proto-cognition and proto-volition. In a sense, these responses are, as we have explained, decisions, and decisions are subject to heterarchies of values, that is, value anomalies. This entails the possibility for, creativity, resilience and semiotic freedom on the one hand, or for error and pathology on the other. We also highlighted that biological and cognitive systems are always embedded. However, this embeddedness cannot be considered hierarchically. A hierarchical view would yield a topology of embedded concentric spheres. On the contrary, a heterarchical organization can place different logical levels or domains in communication with each other. The picture of hierarchical embeddedness, as in concentric spheres, or hierarchical modularity, is the one we can see for example in the emerging research field of “social signal transduction” seem as the horizontal enlargement of the endo- and exo-semiotic relations of cellular signals in living systems, which then give rise to higher level logics that organize hierarchical emerging systems and processes as for example neural networks, physiological organs, perception processes and so on, until we can eventually expand these hierarchical embedded spheres into what then becomes culture. This strategy would result in a horizontal characterization of culture in terms of massive sensing. In our opinion, this is a misplaced sense of anti-reductionism, which is searched through the integration of big-data approaches from “lower” to “higher” levels.

A system that is heterarchically embedded puts into relation different contextures from different logical levels or standpoints that are synchronically considered, interrelating irreducible qualitative domains. This is why in logics it is postulated that what it is needed are special operators that link particular domains (“the logic in-between”). Some of these domains or standpoints may be described by the means of classical logic and mathematical models, where the law of transitivity may hold, and therefore may be organized in a hierarchical fashion. However, there is a fundamental change in causality when dyadic causal links are “filtered” through the embedded networks of an organism (Jonas 1984; Günther 1979). This is what we mean by triadic or semiotic causality. In such heterarchically embedded networks we need to consider the different logical levels that are implied in diallels, in paradoxes, or in communication anomalies like cancer and double binds. Therefore in our opinion, thinking in terms of dyadic causality in hierarchical concentric systems and expanding the methods of systems biology to ecosystem level; or the extension of signal transduction to “social signal transduction”; or the “horizontal expansion” of neural networks and neural correlates implied in social and cultural neuroscience – in general the kind of integration that is implied or implemented by hierarchical modules and first-order emergence, as opposed to some sort of embedded heterarchy – may be leading to the possibility of reproducing mistakes in scientific tautologies that are based on a single mono-contexture for mapping these complex processes (Dougherty & Dalton 2013; Kriegeskorte et al. 2009; Dougherty 2008), neglecting the scalar increase of semiotic freedom, subjectivity, cognition/volition and consciousness.

Box 1. Glossary of terms

First order emergence – considers only one level of freedom between the level of the compound array of the myriad of dyadic relations of a complex substrate and the putative emerging property. Therefore, material-mechanical causality can be invoked at the ontological level but since the elucidation of its complexity escapes our natural epistemological limits, we treat such gaps epistemologically as if they were emergent properties. Usually it is taken for granted that first-order-emergence occurs from a complex combination of material-mechanic (dyadic) causal events giving rise to the emergent level.

Second order emergence – originates from a complex combination of causal factors that are themselves emergent properties of a first order. The higher the emergence orders of the factors involved, the more divorced these causal links are from the kind of material-mechanic causality which determined the first order emergent property at the molecular level. It allows for emerging levels (or thresholds) of freedom by the formation of more complex logical products formed by the combinations of lower-level logical products. Such higher order logical products give rise to an accumulated divorce from deterministic causality when complex logical combinations taking place not on the physical plane – but on the informational or logical plane – give rise to levels of semiotic freedom that are characteristic of higher cognition, consciousness, imagination, symbolic reasoning, and so on (Bruni 2008).

Dyadic causality – corresponds to the material, energetic and mechanical regularities described in the physical sciences, where forces, impacts and energy exchanges are the “causes” of events (Bateson’s “pleroma” and Peirce’s “dyadic action”).

In **triadic (or semiotic) causality** a “*sensed difference*” can be a cause, which leads to an event that is not proportional to the material-energetic exchange of the process. Usually the resulting event entails a choice (or decision) from a response-repertoire (Bateson’s “creatura” and Peirce’s “triadic action”).

Digital-analogical consensus (DAC) – A continuous process of coincidence detection in which an indefinite set of digital messages (presence/absence, activation/deactivation) from different domains and levels of the heterarchy (being manifested in simultaneity), form an analogical message that binds the most comprehensive interpretation of the context to an appropriate response (triadic causality). These processes relate different qualitative domains in a heterarchy because such analogical integrated representation may in turn be a digital representation or piece of information to a different level of aggregation (by being or not being present or activated), which combines with other analogical signs into a higher order logical product. In this way the new analogical sign can also be a digital representation interfacing another domain in a still more complex analogical sign. The emerging analogical mode may also constraint the informational processes in the constitutive domains by a process of re-entrance and self-referentiality.

Emergent interpretant – a standpoint within a heterarchically organized system from which the system, or part of it, enacts a choice or selection based on the most comprehensive available interpretation of the context and in relation to its internal coherence. At this locus, the emerging system reaches a qualitatively different logical type of manifestation with respect to the dynamics that underpins it. A point of view where an aggregate of differences that has been sensed makes a difference at a given level of integration. By this convergence of synergic factors a locus for selection or decision is constituted at a threshold level where semiotic integration occurs.

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