On the role of semiotic bordering in the hierarchical structures of biological systems

Franco Giorgi[1]

Abstract

In this paper, I examine the variety of hierarchical structures that biological systems have been able to construe by changing the extension of their borders. By acting as a space/time structure separating the inside from the outside, a border allows one to be distinguished from otherness and to perceive as meaningful any difference from the external environment. Based on these premises, I then discuss the role these borders have played in the course of evolution for allowing both eukaryotic cells to become functionally differentiated and multi-cellular organisms be equipped with a bodily basis for cognition.

Keywords: *border; hierarchical structures of biological systems; membrane; biosemiotics, cognition*.

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[1] University of Pisa, Italy

Email: francogiorgi7@gmail.com

Introduction

Life is a historical process of becoming (Weisblat, 1998; Flatt & Heyland, 2011). As such, it is substantially different from the physical world governed by invariant laws. While the properties expressed by physical systems can be verified experimentally by tracing back their cause-and-effect relations (Woodward, 2003), the same experimental procedures cannot be used to reconstruct the evolutionary history of the living world (Ramsey, 2015). Unlike the physical objects that are exclusively determined by causal interactions, the living world is comprised of subjects capable of choosing between different adaptive strategies (Kull, 2007). This ground level composition, as based on the biological individualities of autonomous agents, has allowed life to emerge in the form a network of relational processes and explore new environments ever since its origin on this planet.

It is worth recalling here that what distinguishes the subjective experience of the biological world from the objective and experimentally accessible world of things is the subject’s capacity to perceive differences and act accordingly (Bateson, 1979). The essential requirement for expressing this capacity is the separation from the surrounding space through the interposition of a border (De Luca Picione & Valsiner, 2017). This latter acts as a space/time structure separating the inside from the outside, distinguishing oneself from otherness and, not least, defining the context of the enclosed individuality (De Luca Picione & Freda, 2014). However, the outside is not only a space to be separated from, but also a space for extracting energy and material resources. This is a crucial point to understand how the autonomy of living organisms correlates with the constraints imposed by the environment. We refer to this condition as *topological closure* (Giorgi, 2021). The biological structure that has allowed life to express this function in the course of evolution is the plasma membrane. The most accredited model for interpreting the structure of the plasma membrane is the *fluid mosaic* proposed by Singer and Nicolson (1972). It is by virtue of this topological cell closure that living systems have gained access to new relational domains and built multi-cellular hierarchies. However, besides creating a spatial discontinuity, closure is also forcing the living system to deal with its own entropic decay. Upon reaching a thermodynamic equilibrium, any physical system tends to reduce its energy availability to a minimum and express the maximum possible disorder. Prigogine (1989) defined *dissipative structures* the physical systems that are open to the outside and operate far from the thermodynamic equilibrium. Under these conditions, they extract enough energy from the environment to decrease their internal entropy and maintain their inside/outside closure unaltered.

By their very nature, all living things are organized in the form of multi-level hierarchical systems (Zylstra, 1992). Organisms are made of cells and cells are, in turn, made of aggregates of myriads of different macromolecules. Needless to say that many of these relational properties are made possible through the insertion of boundaries controlling selectively the extent of metabolic exchanges. Borders impose themselves not as limits, but as constraints that restrict the range of available alternatives only to those that are phenotypically compatible with the hierarchy’s internal cohesion (Atmanspacher, 1998). The transition to relational entities marks the entry into a domain in which each living system can no longer perceive itself as single individuality, but as embedded in a set of relationships governed by the whole they are part of (Frauen, 2021). The emerging relationships are thus explored in terms of either competition or cooperation and evaluated in relation to the whole's capacity to persist (Fantasia et al., 2014). It is in this dynamic interplay that the living system acquires the capacity to perceive *identity* and *difference* along their border interfaces and set the structural conditions for reducing entropy and enhance the system stability (Kotov & Kull, 2011; De Luca Picione & Valsiner, 2017).

On the nature of semiotic borders

Fixing a border is therefore an act of semiotic mediation that depends on the system's capacity to grasp the significance of a choice (Kull, 2018). As such, the choice opens the factual and allows one to perceive the possible as a sign of relevance (Favareau, 2010). The boundary can thus be expanded along the hierarchy and create new levels of greater complexity. If expansion occurs both in the temporal and spatial domains, fixing new borders entails breaking the continuity of a space and entering a time of irreversible duration (Kull, 2017). With the beginning of a historical journey, each choice is revealed in the form of apparently contradictory alternatives by either maintaining an openness to the possible or being confined to the certainty of a safely acquired memory. It is in the nature of any choice to deal with intrinsically incompatible options, so that the system can only grow in complexity if proves capable of resolving them (Kull & Favareau, 2022).

Choosing means building paths and benefitting of their positive outcomes. If there is a meaning in the ability to choose autonomously, this lies precisely in the comparison between what is taken and what is lost, between what *is* and what *could have been* (Alquist et al. 2015). Overall, the sequence in which choices can be articulated provides clear evidence of how nothing of what is available in nature is offered in a predetermined manner. The transition from the available to the factual always takes place in the course of the eternal dialectic between constraints and opportunities in such a way that the final goal can only be defined along the path. It follows then that, if there is a final goal to be achieved in evolution, this is revealed only along the way and by means of a progressive construction of stages made mutually compatible by the very sustainability of their incompleteness (Pattee & Kull, 2009; Jansen, 2020).

Given this understanding of bordering processes, how are new boundaries defined in a developing hierarchy? For example, during embryonic development, cells increase progressively in number and merge into larger aggregates. In this context, morphogenetic movements are not exclusively due to individual cell boundaries, depending also on how information is distributed and integrated in the embryo as a whole (Banavar et al., 2021). The difficulty is thus to understand how individual and collective cell behaviors are causally related and whether we need to explain them experimentally or interpret their significance semiotically. The two alternatives are related in much the same way as *how* and *why* questions in every type of search activity. It should be clear that *how* questions lead to the discovery of *mechanisms*, while *why* questions lead ultimately to the appreciation of meaning (Vale, 2013).

The Biosemiotic perspective

In Biosemiotics, many cellular processes are interpreted by referring to the role played by signs. This attitude contrasts strongly with the current use of scientific terms that primarily refer to signals rather than signs. While signals are dyadic relationships between temporally related events, signs are triadic relationships perceived as significant by an *interpretant* (Kalaga, 1986; Bergman, 2003). In any causal relationship, effects produced by signals are necessarily determined by the physico-chemical properties of the bearing molecule. On the contrary, signs are arbitrarily associated with an object, for the effects they produce are not determined, but mediated by interpretation. Given the conventionality of this relationship, effects could have been realized otherwise and possibly carried out by different mechanisms (Deacon, 2021).

This be the case, how should a boundary be construed for living creatures to gain access to the possible? In semiotic terms, this is equal to ask how a system may evolve from a condition of *firstness* to *secondness* and how eventually reaches the highest level of *thirdness* (Andrade, 2007). These are the terms Peirce himself used to describe the dynamics by which relationships may gradually transform the possible into the actual, until it reaches the conditions of being exclusively constrained by rules and habits. Today, we would describe the same progression by saying that the order construed by a living system has gradually emerged from conditions initially chaotic. In Deacon's terminology, the same Peircian transition can be referred to the categories of *potential*, *instantaneous* and *systemic* (Deacon, 2013).

Examining the living world from a biosemiotic perspective implies questioning the very nature of *explanation* and, at the same time, proposing *meaning* as the driving force for all vital processes propelling evolution on this planet. However, the real trend of the physical world is not evolution but entropy (Tributsch, 2018), for living systems have been able to create new order only by subtracting energy from the environment and by taking advantage of the topological closure made possible by semiotic borders (De Luca Picione, 2020). This paper provides a testimony of how transformation of cell boundaries from spatially to temporally differentiated barriers has allowed life to evolve an amazing variety of living forms. Justifying evolution in semiotic terms does not imply denying the role played by mechanisms, but simply defending the primacy of relationships and place the choice at the foundation of the evolutionary potential unfolded over time. Every choice presupposes the existence of a boundary defined not by the limits, but by the constraints that allow space and time to be perceived as opportunities and resources to be exploited (Soto et al., 2016). The examples discussed here are presented in a sequence that reflects the bottom up direction of every living hierarchical structure: from the molecular domain to the cognitive dimension.

The molecular domain

The significance of the molecular domain must be sought in the relationship between the potentially existing molecules and those present in the biomass. It is a question of comparing the space of what could exist by virtue of the sole rules dictated by valence electrons and what has been selected for the biosynthesis of life processes. The gap between the two categories should give us an idea of the choices that have been made in the initial phase of life. For instance, proteins perform an impressive variety of functions by folding a precise sequence of amino acids in particular three-dimensional shapes. Although there are more than 500 types of amino acids nature, those that have actually entered protein metabolism are only twenty, called proteinogenic (Wagner & Musso, 1983). In addition, since all amino acids are optical isomers, those employed for protein synthesis are exclusively of the left-handed (L) type (De Poli et al. 2013). Once properly folded, proteins expose their outer surface to the water environment and hide the non-polar side chains internally. Ultimately, the acquisition of the three-dimensional conformation allows proteins to remain functionally active by counteracting their entropic decay for a limited time (Dill et al., 2008). By comparison, the DNA double-helix is a highly stable molecule, as demonstrated by the recovery of fossil skeletons from the permafrost. The surprising stability of DNA is due to the complementary base pairing by hydrogen bonds that impedes water molecules from entering the double helix. In the absence of any water interference, DNA is practically impeded to express any functional activity so as to avoid the entropic decay (Privalov & Crane-Robinson, 2020). The ultimate outcome is the possibility for DNA information to be handed down unchanged from generation to generation. In conclusion, while proteins become functionally active by interacting with the water environment, it is the physical separation from water that allows the DNA to become stable and work as a sort of digital memory for all life processes (Feng et al., 2019).

Cellular Domain

The cellular domain began with the appearance of the first plasma membrane. This occurred when such molecules as phospholipids started forming double layered structures in an aqueous environment (Adams, 2010). In this section, I will argue that the plasma membrane has played a major role in making the world of multi-cellularity increasingly complex. However, the exploration of new cell-to-cell interactions will not be justified in mechanistic terms, but for the capacity that any living system has to choose between levels of different complexity. Lemke (2009) speaks of *opening up closure* as a way to overcome the boundaries of one's own identity as a precondition for acceding to higher hierarchical levels. Let's start by comparing prokaryotic with eukaryotic cells. The difference that stands out more than any other is the extension of the internal membranes in eukaryotic cells. While prokaryotic cells comprise a single compartment bound by the sole plasma membrane, eukaryotic cells have numerous intracellular compartments (Diekmann & Pereira-Leal, 2013), each delimited by a proper membrane. Hoffmeyer (1998) refers to this process as *surfaces inside surfaces*, suggesting that the resulting boundary asymmetry is equivalent to the internalization of an external space. This separation is not only spatial, but also and above all, temporal, since membrane extension allows protein synthesis to be temporally delayed from gene transcription (Lashkevicha & Dmitrieva, 2021). In addition, many compartmental activities are no longer regulated by one-to-one relations, but by complex one-to-many interactions, as indicated by the observation that their metabolic fates are controlled by selective receptor interactions

(Johnstone et al., 2018). One of the main constraint dictated by the mosaic fluid model is the need for the lipid bilayer to maintain its structural integrity during selective uptake, implying that no macromolecule, regardless of its size, can actually cross the plasma membrane. In line with this expectation, eukaryotic cells have overcome this impediment by sustaining trans-membrane protein permeation only in the linear form i.e., when proteins are still in their nascent form prior to acquiring the three-dimensional conformation (Simon, 1995).

Intracellular membranes are sufficiently plastic to merge with one another, and sustain a dynamic vesicular flow from the nuclear envelope to the plasma membrane. The role played by the vesicular traffic is so important to be practically expressed by all differentiated cells and be involved in processes as diverse as cell movement, membrane turnover, secretion and intracellular digestion (Mehrani & Stagg, 2022). In spite of the diversity of the mechanisms lying behind each of these processes, their overall significance is clearly related to the extension of the intracellular membranes. The dramatic morphological change induced by the internalization of the external boundary has provided eukaryotic cells with the possibility of transforming their spatial separation into temporal distinctions, with the ultimate result of entering a historical journey of differentiation (De Luca Picione & Freda, 2016). Comparison with prokaryotic cells shows that all of this could not happen in the absence of any membrane extension.

Intercellular Domain

Maturana and Varela (1980) defined *autopoiesis* as the ability of living systems to produce the elements that recursively participate in the construction of those processes that elaborate them. The circularity of this definition suggests that living systems behave as self-referential and operationally closed entities, thus indicating that autopoietic systems are structurally autonomous. For instance, two eukaryotic cells behave as autopoietic systems when interact without one determining the metabolic fate of the other. Maturana and Varela (1988) refer to this process as *structural coupling*. Two systems are coupled when capable of becoming structurally congruent in the absence of any message exchange. Let us see how this principle works by comparing *autocrine* and *paracrine* cells (Krey et al., 1989). Autocriny is a type of cell signaling by which a chemical messenger released in the external environment can be captured again by the same cell through an adequate receptor system. By perceiving their own message, these cells define a relational interface with the surrounding medium and assess the extension of their feedback loop. By comparison, paracrine cells can only receive molecules that are released by nearby cells. This so called paracriny can be proved experimentally by simply testing the specificity of the mechanism that accounts for their ligand/receptor relationship. However, the discovery of a mechanism does not entirely justify the origin and meaning of the paracrine interaction. From a semiotic standpoint, the existence of paracriny is better accounted for by assuming an accidental insertion of a new cell into an autocrine circuit (Giorgi & Auletta, 2016). The adoption of this interpretative paradigm exempts us from assuming the pre-existence of the secretory and signaling apparatuses as necessary and sufficient conditions for the establishment of the intercellular relationship. In conclusion, neighbor cells prove capable of perceiving each other's presence by reciprocally adapting their boundary interfaces. For instance, a local phenomenon can be transformed in a systemic interaction if the hormone released by a cell spreads throughout the space available and interact with any cell type, regardless of the intervening distance. Under these conditions, endocrine hormones may diffuse uniformly into the entire system at concentrations as low as 10^{-12} M (Hiller-Sturmhöfel & Bartke, 1998). Conversely, they would be exclusively conditioned by local gradients if restricted to the self-referential circuits of nearby cells. However, in addition to long range cell-to-cell interactions, cells may also extend their cytoplasmic contour up to the point of contacting nearby cells and realize what is referred to as synaptic interaction. If the intervening distance is less than 20-30 nm, signaling by neurotransmitters can occur more efficiently and be resolved just as quickly (de Wit & Ghosh, 2016). This makes synaptic relationships particularly suited for supporting such complex biological functions as muscle contraction and cognitive processing. The opposite strategy has been adopted by epithelia whose plasma membranes are tightly anchored to each other by means of *adhesive junctions* and highly connected by *gaps junctions*. Both these conditions enable epithelial cells to behave as well coordinated cell clusters during a variety of morphogenetic movements (Hervé & Derangeon, 2013). These few notions of cell biology testify the variety of morphologies that can be realized by simply modifying cell boundaries. The significance of these types of interactions should not be searched in the diversity of the signaling mechanisms *per se*, but in every new function(s) that has been gained by matching cell signaling and cell distances so as to guarantee the persistence and evolution of cell coupling in a selectively advantageous manner.

Developmental Domain

The developmental domain does not concern cells as singularities, but as clusters governed by flexible cell boundaries. As such they are required to renounce to any self-reference and converge into larger and cohesive wholes (Giorgi & Bruni, 2015). In other words, when more cells converge in larger groups they come to constitute new interacting unities sustaining a variety of morphogenetic movements. It is clear that the diversity of these behaviors reflects a cellular heterogeneity, but it is equally clear that the capacity to join, extend and communicate depends on the type of junction that connects the embryonic cells. For instance, all cells connected by gap junctions are isopotential, have the same pH and share the same ATP and Ca^{2+} concentrations. In conclusion, thanks to the ability of intercellular boundaries to change during embryonic development different cells can orchestrate their interaction and, together, form increasingly complex three-dimensional structures (Levin, 2007).

Cognitive Domain

Most likely the cognitive domain is reached when a living hierarchy has become so complex to act autonomously in its own environment. The complexity is such as to guarantee a total internal cohesion and a high degree of external semiotic freedom. We talk about autonomy as an exclusive prerogative of individuals capable of behaving as agentive subjects in the world of objects (Sharov & Tønnessen, 2021). It is in the subject/object relationship that such cognitively elevated functions as perception, memory and knowledge can actually be expressed. However, cognition does not refer only to the mental faculties of attention, learning and information processing, but to the basal cognition typical of all forms of life, starting from the simplest cells (Lyon, 2006). To appreciate the nature of this *biogenic* approach let us compare embryonic morphogenesis and perceptual categorization. In both cases there is a cross-border exploration of relationships to make cells coordinated within the whole they are part of. The ultimate result is the evolutionary acquaintance of a correspondence between analogical and digital codes as between information and meaning. In this perspective, cognition may be accounted for by looking at how cells construct such complex three-dimensional structures as embryos and brains (Chang-Gonzalez et al., 2021).

According to the *free energy principle*, cells attain a final morphology by deducing their position from all chemotactic signals expressed in the surrounding (Kirchhoff et al., 2018). Since cells possess a model for predicting which signal may be expected before reaching their final target, they are initially equipped with the same information and potentially prone to assume any position. The target will be eventually reached when the free energy perceived by all cells is reduced to a minimum value. In strictly physical terms, it can be imagined that the model is genetically encoded, and that cells learn how to be properly positioned by deducing the adequacy of their response from nearby cell signaling (Friston et al., 2015). By doing so, any subject can actually learn how to act in response to a discrepancy between the *predictable* and the *verifiable* (Badcock et al., 2022). Regardless of the physical nature - whether cells or organisms - every subject will therefore try to respond (1) by modifying the *perceptive threshold* to reduce the effectiveness of the signal or (2) by acting in the environment to reduce the signal intensity (Seth & Friston, 2016). In developing embryos, positional information is perceived as a complex interplay between morphogen gradients and genetic heritage. In this context, cell borders define the limits with which both position and discrepancy can be perceived (Kerszberg & Wolpert, 2007). The system finds its stability when no cell has enough energy to escape from nearby interactions, so as to reduce its phenotypic surprise and quiet any propensity for new interactions. In semiotic terms, one could say that cells interpret the acquisition of this new energy balance as a sign of their own stability and, in so doing, learn how define new topological closures.

Embodied Cognition Domain

The acquisition of a multi-cellularity has equipped organisms with a body capable of moving freely in the environment (Varela et al., 1991). This has marked a fundamental transition in the evolutionary process toward complexity: *the origin of individuality* (Buss, 1987). Individuals are embodied organisms which play agentive roles by their ability to aim autonomously for pre-established targets. However, unlike physical systems for which predictability can be expressed computationally, individual subjects cannot be explained by computational models, nor can their behavior be reduced to mere representations. Cognition therefore does not coincide with a disembodied representation of the external world, nor with the simple manipulation of neural symbols or algorithms, but with a real *ecological reality* that living systems make use of by *embodiment* (Fuchs, 2020). Somehow embodiment allows living beings to experience the interaction between *touching* and *being touched* (Brandstetter et al., 2013) in much the same way as *intentional* subjects are related to *manipulable* objects (Kirchhoff, 2017). Ultimately, it is precisely the relational coincidence between *lived* and *living* that may lead to the emergence of a self-referential individuality (Zlatev, 2009). In an attempt to give a topological representation to this type of self-reference, Van Foester suggested to compare it metaphorically with the famous *Möbius strip* (Vijver, 1997). This is a topological figure obtained by joining both ends of a half-twisted ribbon. The final result is the construction of a non-orientable surface in which internal and external sides converge to form an infinite ring with no borders. The metaphor of the *Möbius strip* suggests that a self-referential individuality may emerge whenever a boundary is challenged by the formation of an *externalized internal space* (Hoffmeyer, 1993). However, there is a substantial difference between *basal cognition* and *embodied cognition* in relation to the role played by borders. In the first case, it is a cell individuality that embodies a form of evolutionary memory, while in the second it is an organismic memory that has accumulated in the course of one’s life. This is the underlying reason that has enabled embodied cognition to interact imaginatively with the environment in a forward-looking manner, rather than being simply predictive of predetermined objectives (Parn, 2021).

However, in spite of these limitations, the transition to embodied cognition has enabled living beings to explore the *domain of temporality* (Valsiner, 2018). The extension of a boundary to the temporal dimension has brought the individual self-referential circuit beyond the immediately available, enabling him to perceive it as possible. Gibson (1986) speaks in this regard of *affordances*, as actions considered achievable in relation to present objectives or future propensities. Affordances are thus opportunities for action that may emerge from all those contingencies that the agentive subject perceives as accessible (Greeno, 2008). However, to be recognized as opportunities, affordances must be identified as *something that stands for something else*, that is to say, they must act as signs (Pickering, 2007). The relationship between availability and opportunity is therefore not predetermined in any environmental way, nor preconstituted in a sensorial way, but learned by choosing. Ultimately, every living being creates anticipatory projections beyond his own self-reflexive boundary by including his own acting as a necessary condition for perception. The possible is thus offered as a space where to explore the creative potential and the capacity to reinvent oneself. The primary goal of a living being is not to interact with a hypothetical physical world, but to learn how to act in a perceptually guided way. Meaning therefore cannot be represented cognitively, but only revealed through the experience of embodied actions (Hoffmeyer, 1993; Juarrero, 2002).

Conclusions

In conclusion, cognition is not only embodied, but also extended, in the sense of emerging from a mental domain wider than the sole brain’s neuronal activity (Borghi et al., 2013). Cognition cannot therefore be justified exclusively in terms of mechanistic coupling between acting and neural coding and reduced to the sole role played by computational operations. The necessity for a complementary approach stems directly from the recognition that the body does not act as an external machine for information processing, but as an active participant of cognitive processes (Konderak, 2018). When considered in this semiotic perspective, cognition can no longer be described via non-contradictory *laws*, but more appropriately considered as a faculty emerging from a life-long experience of solving the semantic incompatibility between incongruent operations (Kull, 2015). Since alternatives are offered simultaneously, the outcome of any choice can only be evaluated retrospectively. It thus follows that simultaneous options may be interpreted as meaningful only if perceived as *timeless signs* and experienced in the temporality of a *subjective present* (Kull & Favareau, 2022). The link created by connecting conventions, habits and codes in the experience transforms the initial choices in habits and restricts any effective goal-setting to the sole accessible objectives.

Starting from the plasma membrane up to the perceptual interface of cognitive processes, we have identified the border as a key factor separating domains of different hierarchical complexity. The co-determination of perceptual and sensorimotor processes along this border does, ultimately, result in the distinction between an enclosed *self* and the outside world. In semiotic terms, this is equivalent to perceiving the difference as *a sign* that may eventually lead to the emergence of an *interpretant*. It is in the very nature of any semiotic process, as based on the triadic relationship between *sign, object* and *interpretant*, to be consolidated in the form of habits or mental categories. The emergence of an interpretant is thus the acquisition of a competence to interpret the environmental availability as *affordances*. The meaning of the entire process is to be found in the possibility for the agentive subject to explore the boundary between what is revealed to him as possible and what is really feasible: between the *adjacent possible* and the *factual* (Kauffman & Gare, 2015).

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