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What Drives the Brain?
Organizational Changes, FEP and Anti-entropy

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Abstract

The free-energy principle (FEP) provides a computational, physical and teleological theory for understanding biological organization as cognitive agent minimizing their entropy in relation to their environment. Is minimizing entropy the first principle driving all dynamics of cognition? Is it enough to account for organizational changes in an open-ended way? After a general presentation of the literature on the FEP, we turn to the paradoxical case of the brain under the influence of psychedelics, where the FEP is challenged by an increased cerebral entropy, which induces organizational changes of the cognition. Building on this paradox, we identify some limits of the FEP, notably applying concepts of information, optimization and predefined phase space to biology that do not fit our criteria for a theory of biological organization. We also identify two aspects of entropy in physics and in the FEP: the local entropic trend that implies variations and the global entropic trend that leads to homogeneization and stability. Extending these concepts outside of their physicomathematical context, we contribute to an organicist theoretical alternative where living systems find a balance between these two trends, and, conceptually, a biological system's disorganization enable its "unprestatable" reorganization and so its open-ended evolution.

Keywords: free energy principle, anti-entropy, entropy, novelty, biological organization, organicism

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Introduction

Scientists often mobilize approaches from fields other than biology to understand living beings. However, it is not easy in biology to apply, for example, the principles of physics, which are based on conservation, optimization, and the pre-definition of the phase space. Indeed, as René Thom put it, "it is the lack of the definition [of the virtual possible] that affects – very seriously – the scientific nature of Darwin's Theory of Evolution" (Amsterdamski 1990). Similarly, since the discovery of the physicochemical structure of DNA as the material support of genes, principles derived from computer science have been widely applied to understand living organisms with a reductionist, genocentric viewpoint. They remain so today, even if their validity has been belied by numerous discoveries and analyses, such as the diversity of gene reading modes, alternative splicing, epigenetics, and developmental plasticity.

In this context, an interdisciplinary effort aims to rework the conceptual framework for understanding biological organisms by following an organicist approach that is neither physicalist nor "informationalist". This work has led to proposing three principles for a theory of organisms. The principle of variation posits the historicity of biological objects: the regularities of living beings playing a causal role, which we call constraints, are part of a history and can change over time. Biological objects cannot be defined based on invariants and symmetry as in physics; we say they are specific (Montévil *et al.* 2016a). The practical way of defining them is phylogenetics, sometimes also genealogy for laboratory strains, but in all cases, it is historical (Montévil 2019). If these objects are initially variable, the relative stability of their constraints needs to be explained. The principle of organization has this function: in an organism, a constraint canalizes a process that maintains another constraint, which canalizes a process, and so on, leading to circularity called the closure of constraints (Mossio, Montévil & Longo 2016; Montévil & Mossio 2015). This principle also allows us to speak of function in the sense of the relationship between a part and a whole, defined by the circularity of the closure. Finally, we posit that the default state of cells, i.e., their behavior when no particular cause acts upon them, is proliferation and motility, not quiescence (Soto, Longo, Montévil *et al.* 2016). In other words, living beings do not need stimulation to be active.

In line with this framework, anti-entropy has been introduced as an addition to entropy. The term anti-entropy stems from an analogy with anti-matter: anti-matter is symmetrical to matter, but has opposite properties in some respects. Anti-entropy was first introduced as a measure of phenotypic complexity and addressed through its metabolic consequences (Bailly & Longo 2009). The idea has since been refined based on biological variations interpreted as changes in symmetries, i.e., what was to become the principle of variation (Longo & Montévil 2012). Finally, the most recent concept defines the production of anti-entropy, by analogy with the production of entropy, as the production of a functional novelty, i.e., the production of a singular situation that contributes to the closure of an organization by this singularity (Montévil 2021). Indeed, entropy production provides the arrow of time of physics by the second principle of thermodynamics and the idea that a system spontaneously moves from being somewhat specific to the most generic configuration, given the constraints of that system. Biological historicity manifests a second time arrow, with objects that can produce increasingly functional specificity.

In this context, many questions remain. For example, closure of constraints does not imply that an organization remains unchanged. On the contrary, the principle of variation means that biological organizations can always change, but how do these changes take place? In particular, what is the relationship between organizational change and entropy? In the particular case where these changes correspond to functional novelties, i.e., correspond to a production of anti-entropy, what is their relationship to entropy?

These questions are met by an informational approach to biology defining the "free energy principle" (FEP). Schrödinger, in his book What is Life? (Schrödinger 1944), proposed that the primary characteristic of living systems is repelling entropy while maintaining their internal order. Similarly, the info-computational vision of the FEP understands the organization of living systems as the result of a computational process based on the minimization of entropy. The FEP aims to provide a mathematical framework for the temporal evolution of a living system and that of its model of "beliefs" in terms of Bayesian updates optimized to fit the statistics of the things to which the system is coupled (Ramstead *et al.* 2023). This theory states that living systems seek to minimize the variational free energy corresponding to the relative entropy of the system's generative model. This info-computational approach provides a self-organizing model of the living world, where organisms are made of layers of nested abstract representations generating probabilistic decisions (Kirchhoff *et al.* 2018).

The FEP is mainly used in neuroscience to formalize the leading theory in this field, namely the Bayesian brain theory. According to this theory, the brain actively infers the causes of its sensations and selects actions to minimize entropy relative to its subject. Thus, the Bayesian generative model of the brain updates and evolves by maximizing the evidence for its beliefs (Friston, Kilner & Harrison 2006). The FEP is a variational principle, posited as equivalent to the principle of least action, fundamental in physics, and the principle of maximum entropy, but applying to Bayesian mechanics as a "physics of and by beliefs" (Ramstead *et al.* 2023). This informational principle states that living systems tend to optimal maintenance and adaptation to their environment by organizing themselves against entropy. According to proponents of this theory, it applies to all living beings, even those without nervous systems, and even to all evolutionary phenomena, biological (Kuchling *et al.* 2020; Kirchhoff *et al.* 2018; Campbell 2016) and societal (Slijepcevic 2024). Thus, according to some of its advocates, it is a candidate for "a great unifying theory" (Sánchez-Cañizares 2021).

As argued in the first section, the FEP is incompatible *ex hypothesi* with the organicist framework we are helping to develop, as it develops an informational approach to living things and lean on optimization principles (Bailly & Longo 2011; Longo *et al.* 2012). Nevertheless, the FEP and its critique allow us to work on the relationship between entropy, organization and changes in organization (Chollat-Namy & Longo 2022). We begin with a general presentation of the literature on FEP as a principle of cognition and organization at all levels of living organisms. We then turn to the paradoxical and much-discussed case of the brain under the influence of psychedelics. This case is interesting since the FEP organizing principle is challenged by an increased cerebral entropy, which nonetheless seems to induce beneficial changes at both neurological and psychological levels.

Building on this paradox, we will criticize the FEP, first pointing out some general difficulties in applying information concepts in biology, then more specifically on the physicalist assumptions of the FEP, notably the existence of a predefined phase space. The aim will not be to reject all the ideas put forward by FEP theorists but to demonstrate some of their limits and contribute to overcoming them by proposing an organicist theoretical alternative based on current work in this field.

By analyzing entropy within living systems, we will add to the concept of anti-entropy, explaining how a biological system's disorganization can enable its reorganization and evolution towards new, viable, and not only unpredictable but also "unprestatable" configurations; that is, the changes are not just about a state among predefined possible states, but the possibilities themselves are unpredictable. This approach will lead us to rediscuss the default state of life and the notions of causality and finality in biology outside a physicalist paradigm.

1. Informational Theory of Cognition and Entropy Minimization as a Theoretical Principle

1.1. The Principle of Free Energy and its Application to Biological Organization

Many researchers have argued that algorithmic information processing by living systems is essential to their stability and survival (Walker & Davies 2013), and involves capturing information about their environment, then translating this information into exploitable and adaptive actions. It has been suggested that this process is the defining characteristic of living organisms and would be uniquely oriented towards maintaining organisms in their expected phenotypic and ontogenetic state (Kirchhoff *et al.* 2018).

This maintenance objective is achieved by the free energy principle, according to which living systems seek to minimize a theoretical quantity of information called "free energy," corresponding to the entropy relative to the system and its coupling to its environment. According to this theory, any biological organization, in particular the nervous system, creates statistical approximations, Bayesian generative models, corresponding to a hierarchical system of "beliefs" about the causes of its sensory data (Knill & Pouget 2004; Friston, Kilner & Harrison 2006; Friston & Kiebel 2009). A system minimizes its free energy when it implicitly optimizes its "belief" about what provokes sensory input. In other words, a living system actively infers and projects hypotheses about the causes of its sensations and selects actions to minimize the relative entropy about them. This free energy is also called "uncertainty," "surprise," or "prediction error," and minimizing it is equivalent to maximizing the evidence for the belief model (Kiverstein, Kirchhoff & Froese 2022). This localized control of entropy would act as a "driving force" for the adaptive reconciliation of living systems with their environment and thus towards their stability.

In this sense, the FEP implies that all living systems, considered to be endowed with cognition, can be modeled as visiting a limited set of states in order to continue to exist (Parr & Friston 2019). This modeling uses information geometry techniques that formally specify the boundary between a living system and its external environment, notably as a Markov blanket (Palacios *et al.* 2020). A Markov blanket is based on a statistical partitioning between internal states (systemic) and external (environmental) states. The Markov blanket includes a second partitioning between active and passive sensory states, mediating exchanges between internal and external states (Ramstead *et al.* 2021).

This info-computational and cognitivist vision of the living world, based on Bayesian model generation through FEP action, is applied beyond the brain (Kirchhoff *et al.* 2018; Slijepcevic 2024) and could be used to describe any type of biological evolutionary phenomenon, including morphological development (Kuchling *et al.* 2020), phylogenetic evolution, psychology and even the evolution of societies and scientific knowledge (Campbell 2016). In the case of phylogenetic evolution, for example, the set of "instructions" for growth and development that an organism inherits constitutes a kind of prediction about the organism's suitability for its environment. It is as if a phenotype were actively inferring the state of its ecosystemic niche under a generative model, whose parameters are learned through natural selection, seen as the optimization process of the Bayesian model (Friston *et al.* 2023; Czégel *et al.* 2022).

This theory considers that living organisms and their various forms are organized according to a generative computational model oriented towards their maintenance and adaptation to the environment by the FEP. It is mainly used in neuroscience to understand cognition's adaptive and learning capacities (Friston, Kilner & Harrison 2006).

1.2. The Principle of Free Energy Challenged by the Brain under Psychedelics

The FEP has been heavily discussed in the particular case of the brain under the influence of psychedelics. This case is interesting because it is challenging the FEP. The brain exhibits an increased entropy, which seems beneficial for inducing biologically novel and psychologically therapeutic changes. However, the FEP considers that cognitive systems must constantly minimize their entropy relative to their coupling to their environment, which correspond to "the long-term average of surprise", defined as "the difference between an organism's predictions about its sensory inputs (embodied in its models of the world) and the sensations it actually encounters." (Friston *et al.* 2012). This principle apparently contradicts the phenomena observed during the psychedelic experience. The theory of the entropic brain and its new version, REBUS (RElaxed Beliefs Under pSychedelics) (Carhart-Harris & Friston 2019), aims to overcome this paradox.

Psychedelics, including LSD, psilocybin, DMT, mescaline and many others, are natural or synthetic substances that act on the brain's serotonin network, producing intense psychological and physiological effects. Legal restrictions have limited their use in clinical research for several decades. However, in recent years, these substances have become the subject of active research, and numerous studies have revealed the therapeutic potential of these molecules to treat a variety of psychological problems, such as addiction (Zafar *et al.* 2023), end-of-life anxiety (Whinkin *et al.* 2023), post-traumatic syndromes (Fonseka & Woo 2023) and depression (Hristova & Pérez-Jover 2023; Rivera-García & Cruz 2023). Although their molecular mechanisms of action, through interaction with serotonin receptors, notably 5HT1A and 2A, are well known (Cameron *et al.* 2023), they are not sufficient to explain their effect on the dynamic organization of the brain and psyche, which requires a specific theoretical approach. The leading theory today is that of J. Carhart Harris, known as REBUS (Carhart-Harris & Friston 2019). It is based on the principle that thanks to their entropic effect on spontaneous cortical activity, psychedelics act to relax the precision of high-level hierarchical beliefs, freeing up activity at lower levels (note that this effect is especially visible at high doses of psychedelics, and that lower doses may induce the opposite effect, a strengthening of beliefs (Safron *et* *al.* 2020)). This theory mobilizes the principle of free energy. As mentioned above, the FEP describes brain behavior based on its inherent tendency to resist disorder and minimize uncertainty by optimizing, through Bayesian updating, its probabilistic representations and sampling of its environment. These representations, or *a priori* beliefs, constitute predictive processing organized in hierarchical levels (Friston 2010).

In the Bayesian vision of the brain, bottom-up sensory input is compared with inferred top-down predictions. The resulting prediction error is then passed on to higher hierarchies to update the representations, generating top-down predictions on lower levels (Badcock *et al.* 2019). Following the FEP, Neural dynamics attempts to minimize the amplitude of prediction errors at each hierarchy level. This process provides an optimized causal explanation of sensory input at several levels of hierarchical abstraction. The highest levels form compressive synthesis from the content of the lower levels they envelop, thus reducing their potential information content (Ruffini 2017).

The apex of this hierarchy of prior belief levels is instantiated by the DMN, the "default mode network" (Margulies *et al.* 2016; Carhart-Harris and Friston 2019) considered to be the seat of the sense of self, of identity as "internal narrative" (Menon 2023). The DMN, functionally positioned as far as possible from sensorimotor input (Smallwood *et al.* 2021), is associated with subjective states such as reflection, remembering, introspection, planning, social interaction, abstract thought... (Buckner, Andrews-Hanna & Schacter 2008; Menon 2023).

The theory's central idea is that psychedelics increase the entropy, the variational free energy, of brain activity and reduce the precision (inverse variance, felt confidence, rigidity) of higher-level prior beliefs, making them more sensitive to bottom-up prediction errors. This process would disrupt the DMN's directional function and relax prior beliefs, making them more plastic and susceptible to change into new configurations of meaning. Thus, at the psychological level, psychedelic intake can temporarily induce a feeling of uncertainty but also intuitive understandings and changes in perspective about oneself and the world (Timmermann *et al.* 2021). At the biological level, we observe that brain dynamics display increased complexity, the construction of new and diverse connectivities is promoted (Carhart-Harris 2018), and neurogenesis is stimulated (Calder & Hasler 2023).

In short, taking psychedelics in significant quantities "disorganizes" the cerebral hierarchy temporarily and seems to induce the creation of new configurations, sometimes functional at the physiological level and meaningful at the psychological level. Why?

Although psychedelics appear to "temporarily breach the free energy principle" (Carhart-Harris & Friston 2019), the authors point to a higher level at which free energy would be minimized, inducing a revision of beliefs about generative models themselves. This process would be achieved by selecting the best-performing model from a set of models (Bayesian Model Selection) or reducing complexity (Bayesian Model Reduction) by removing redundant model parameters. These mechanisms for simplifying and generalizing the model would produce "inferences used to fill an explanatory gap." This type of inference would underlie the experience of insight (also called "eureka" moment or intuitive understanding) (Friston *et al.* 2017) and explain the changes in point of view generated by the psychedelic experience (Carhart-Harris & Friston 2019).

These mechanisms would also be responsible for recalibrating the relevant beliefs to be better functionally harmonized with the other levels. As the cause of many psychological illnesses is the pathological weighting of certain prior beliefs, this process of recalibrating beliefs could explain the therapeutic effect of psychedelics on mental health over the long term (Carhart-Harris & Friston 2019).

On the informational level, the effect of psychedelics can be modeled as a reduction of the curvature of the energetic landscape that contains neuronal dynamics and a flattening of the local minima. This phenomenon allows neuronal dynamics to escape its attractor's basins and prior beliefs and explore the space of state with fewer constraints. The authors consider this flattening of the energy landscape of the brain by psychedelics as analogous to the method of annealing in computer science, a method of optimization to find new local minima. Inspired by metallurgy, this approach is performed in two steps. First, the system is "heated". It reaches a state of increased plasticity to discover "new" relatively stable low-energy states where the system can reside at lower temperatures (Wang & Smith 1998). This method is also similar to new approaches of complexity as emerging from transitions between an order and a disorder phase (Paperin *et al.* 2011).

In short, at the level of the brain, this exploration of the state space would correspond to a curious behavior of novelty exploration and openness to surprise, seeming to go against the FEP. However, K Friston and J Carhart Harris consider that this behavior, called "epistemic research" or "epistemic foraging", is induced by a learning objective, i.e., this behavior is allowed by the *a priori* that there is something to learn, a given expected uncertainty that must be reduced. Reducing this last level of uncertainty, and therefore learning, means choosing a policy that also maximizes the ability to predict through model selection (BMS and BMR) that makes the results less surprising (Friston *et al.* 2017; Carhart-Harris & Friston 2019). In this sense, a higher level of FEP, in the longer term, would generate exploratory behavior in the short term and be responsible for the experience of insight and intuitive understanding, whether during a psychedelic experience or not. Thus, in this perspective, the biological and human characteristics of curiosity, intuition and meaningful insight, essential to creativity, are always justified by the FEP.

The info-computational and cognitivist vision of life considers that any biological system is a computational process guided by the FEP, a principle of optimality oriented to preserving priors, homeostasis, and organization maintenance. If the entropic disorganization of living systems, by psychedelics in the case of the brain, allows the production of novelty, such a phenomenon is allowed only by a higher level following the FEP optimization.

However, we will see that the notions of information and optimization have shortcomings in life sciences. The FEP is based on assumptions (including the existence of a predefined phase space) that we think needs to be revised to understand living beings.

2. Criticisms and Limits of the Free Energy Principle Applied to the Living

2.1. Brief Philosophical Criticism of the Notion of Information

Information is at the core of many current technological developments, and it is tempting to go beyond this dimension and to think that the world is made of information and computations. Galileo followed a similar path when he stated that,

> Philosophy [i.e., natural philosophy] is written in this grand book — I mean the Universe — which stands continually open to our gaze, but it cannot be understood unless one first learns to comprehend the language and interpret the characters in which it is written. It is written in the language of mathematics [...] (Galilei 1623).

Instead, we think that it is necessary to distinguish our understanding from the things we aim to understand, that is, to distinguish physics (and biology) from metaphysics. The question we are addressing in this paper is theoretical: we seek to understand the world with conceptual tools, not to find its ultimate nature. From this perspective, the notions of information and computations are formal tools and concepts, not natural essences.

The info-computational paradigm is essentially based on the notion of Shannon information: in a given space of possibility, the possible signals to be transmitted, the amount of information, i.e., the informational richness, corresponds to the inverse of the probabilities of occurrence of a signal, in this sense, the rare is more informative than the frequent (Lesne 2014).

Boltzmann's entropy inspired this vision. However, Boltzmann's entropy has a coefficient – Boltzmann constant – that refers to a specific physical phenomenon requiring a physicomathematical interpretation, including units (Castiglione *et al.* 2008). Confusing information and entropy means forgetting this physical dimensionality. This misuse entails that information would be everywhere since entropy is produced wherever there is irreversible energy transformation. Brillouin's use is more interesting as it addresses information the experimenter can get from a system. He defines information as negentropy, that is, with the opposite sign w.r. to Shannon's information, and he argues that any measure that produces information requires a transformation of energy, therefore increasing entropy (Brillouin 1956). Information is physical in the sense that it requires physical transformations, but physics is not information; we do not think information is intrinsic to matter or that it has become a robust, fundamental concept of physics (Longo 2020). Notably, information is not associated with proper conservation principles.

The invariants of action constituted by a cognitive system, the belief structures from the perspective of the

FEP are the foundation of the notion of information, which creates a progressive detachment from the materiality of the phenomena that deepens with language, symbols, and even more by writing. Thus, cognition creates information from the contextual meaning, not vice versa. We distinguish information as the elaboration or transmission of signs and information as the production of meaning in active friction with reality.

In the informational approach, the production of meaning is the production of information. However, this approach eliminates intelligibility in favor of formal normativity by sets of instructions that would govern the living or by local optimization. This approach neglects the importance of interpretation and eliminates the biological singularity that comes from the historical formation of meaning by confusing salience and pregnancy. Salience has no meaningful depth; it is only a flat correlation, a regularity detection. It corresponds to what constitutes automatic learning algorithms, whose interpolative power finds regularities even in pure randomness (Calude & Longo 2017). By contrast, pregnancy already possesses elements of meaning, proto-semiotics embedded in the emotions and body (Sarti, Citti & Piotrowski 2022; Wildgen & Brandt 2010). In biology, pregnancy typically ultimately affects survival and the ability to reproduce.

Thus, in our view, constructing a hierarchy of meaning is not reducible to a formal question, to the results of computations constituting saliences in an optimized way. On the contrary, it is constituted by a practice of what is pregnant for the organism that acts for a purpose; it forces hierarchies of meaning on this basis. The brain is then a system of meaning production rather than information processing (Longo *et al.* 2012).

2.2. Criticism of the Principle of Optimality

The FEP can be understood as a physics of coupled systems (Ramstead 2023) and is based on two main physicalist assumptions, namely the optimization principle, grounded on the *a priori* of a pre-given phase space. There are relevant general criticisms that several authors have addressed (Longo, Montévil & Kauffman 2012; Montévil *et al.* 2016a; Sarti, Citti & Piotrowski 2019) included in (Colombo & Wright 2021; Guénin-Carlut 2023; Nave 2025). Here are the main points.

The principles of optimization presuppose the existence of an optimum locally or globally, in which case it serves as an attractor in the phase space and is determined *a priori*. This kind of reasoning is ubiquitous in physics to determine and predict dynamics. Even some dissipative systems far from equilibrium (e.g., clouds, hurricanes, or flames) are considered necessary and optimal geodesics in their phase space. Their forms are generic and not the result of a creative process, just like the configurations produced by algorithmic optimality methods. Accordingly, they can be generated de novo in practice. The phase space is predetermined, and all the possibilities are already there.

Thus, the main dynamics taking place are perpetuated and strengthened. The changes in configurations and the appearance of novelties take place only as a search for an optimum. This approach neglects the production of novelty in a strong sense, that is, involving a change of what is possible (Longo, Montévil & Kauffman 2012; Sarti, Citti & Piotrowski 2019; Montévil 2019). Similarly, assembly theory aims to understand how novelty can appear as a combination of the existing objects (Sharma *et al.* 2023). Thus, there is an opposition between creativity and mathematical optimality. This creativity, at the origin of the various survival strategies of an organism, does not pre-exist; there is no optimal way to discover it. Conversely, if we consider that the living produces new possibilities, optimization can have a meaning but is limited in its scope. When there are enough established and stable constraints to create a space with regular consequences, optimality can appear as an adjustment, primarily quantitative.

Let us unpack this concept of change of the possibility space. The way to model a change in physics is primarily a change of position in a predefined space, the state space. Some space changes exist, of course, in physics, from statistical mechanics fluctuations in the number of particles in the grand canonical ensemble to Fock's spaces in quantum mechanics; however, the condition for their use in modeling is that the new dimensions are theoretically identical to the old ones so that a single mathematical description can subsume them. By contrast, one of us has argued that biology requires addressing changes in possibilities that correspond more technically to situations whose organizational outcomes are not generic consequences of the causes established initially (Montévil 2019). In practice, it follows that what is possible cannot be prestated – even though we can, of course, prestate some possibilities.

This theoretical situation is the hallmark of historicity. The practical consequence is that the way to describe and manipulate theoretical living organisms is markedly distinct from physics, as exemplified by the names of systematics, which are defined by their historical origin and not by invariants of the causal determination (Montévil 2019). Without a proper account of this practical and theoretical consideration, there is a gap between the theoretical description and the empirical object of study.

The FEP also requires explicitly an assumption of ergodicity (Friston 2013), which has been criticized for biology (Longo, Montévil & Kauffman 2012). Ergodicity roughly means that the system will travel the possible states in a uniform way; and it is required to connect the microscopic and the macroscopic levels of description by means of entropy. The question of ergodicity is another way to look at the problem of predefined possibility spaces because ergodicity breaking corresponds to change in macroscopic possibilities.

On the other hand, within the FEP formalism, the result of a phenomenon depends on the path; one says pathway-dependent, a common approach in physics. Physics aims precisely to study what is generic and does not depend on context and history. In the case of pathway dependence, the past is integrated into the present, but only what has visible consequences on the path is taken into account. This approach does not retain what does not leave a visible trace in the final result; therefore, optimization levels down historicity. However, we understand biology only if we know evolutionary history, the past can re-emerge later in a contingent way and participate in generating new configurations (see Section 3).

Finally, the FEP needs to be revised in its relation to teleology. Indeed, variational principles, such as the principle of least action, can be interpreted teleologically, and this point is widely discussed (Glick 2023). In physics, there are counter-arguments to this teleological interpretation, but these counter-arguments are not relevant to the FEP. In physics, this principle can be seen as emerging; it is fundamental for FEP advocates. In physics, it corresponds to the stationarity of the action, so an extremum without specifying which, while it is a minimization for the FEP. Finally, the least action principle is about a trajectory, while the FEP explicitly sets the distal goal of a minimum of surprise. We do not think this assumption is necessary to biology, as we will see in Section 3.

Teleology raises different issues in physics and biology, and completely rejecting it in the latter is unnecessary. However, the teleology of the FEP considers a general purpose given by the FEP, which is problematic and constitutes, in our view, a conceptual regression concerning the historicity of the living coming from the theory of evolution. If there must be a biological teleology, it is very relevant to consider that living beings give themselves their own ends and that the latter can change over time. This point is precisely the proposal made by philosophers working with the closure of constraints: the organization can be interpreted as teleological because it self-determines through the circularity of the closure (Mossio & Bich 2017). The norms are then individual norms, which means that they can change. Moreover, the way closure changes also becomes historical and is not subsumed by an optimization principle.

2.3. The Cost of Optimality

According to the FEP, any living system is a nesting of Markov blanket, where each blanket defines a statistical partitioning between internal and external states. The internal generative model seeks to represent the external environment best in order to optimize its predictions and reduce the gap between what is perceived and what is expected. Thus, what is selected and observed preferentially is driven toward what can best validate the model's evidence and reduce its uncertainty. This situation amounts to an exploitative research behavior (Friston *et al.* 2017) consisting of being attracted only by what goes in the direction of the priors and denying or not paying attention to what is too distant from the expected, the things we do not know that we do not know. This optimization leads the sensory input to be similar to the output, thus the border between what is internal and external is transformed gradually in the impermeable border between the expected and the unexpected, i.e. the entropic alterity.

Moreover, more concrete actions on the world to reduce the uncertainty of the model also tend to reduce the unexpected and thus the possibility of learning genuinely new things. As a result, the priors are becoming stronger and less tolerant of uncertainty. In other words, the system becomes hyper-selective and only accepts what fits into the model and tends to stiffen it. This phenomenon is adequate to explain certain behaviors such as denial or confirmation bias, or even certain pathologies (depression, anxiety) where the world model takes over perceptions by conditioning them strongly (Badcock *et al.* 2017; McGovern *et al.* 2022).

Thus, the FEP alone necessarily induces self-referential confinement; Carhart Harris speaks of "conservation bias on adaptation" (Carhart-Harris 2018). This confinement can be compensated by a curious and exploratory behavior, requiring a certain acceptance of uncertainty, or by taking psychedelics, the two joining since psychedelics seem to encourage the exploratory behavior of the brain. According to REBUS theory, the increase in cerebral entropy by psychedelics "seems to breach the principle of free energy temporarily" (Carhart-Harris & Friston 2019), which appears beneficial to mental health and creativity (Mason *et al.* 2021). However, this breach is only apparent according to them. The authors evoke a new, higher level of application of the principle of free energy at the level of the models themselves (Bayesian Model Reduction and Bayesian Model Selection).

Thus, optimizing a higher level could explain the violation of the FEP at a certain level. The lower level, when it does not tend towards the optimum, would have an exploratory role because of the higher level. The latter would exercise the exploitative role necessary to speak of minimizing free energy and being causally responsible for curiosity. This induction of the local violation of the FEP would lead to new intuitive understandings. The upper layer would be responsible for this harmonious "recalibration" of beliefs, thanks to its operating FEP. Thus, the famous balance between exploration and exploitation, understanding and precision, or generalization and specification should be found in the interaction between two optimization layers.

However, the exploitation expected by the upper level induces and conditions the exploration of the lower level. The exploration is then remotely guided by the projection of what is helpful to discover and learn, which goes toward reducing uncertainty. This long-term orientation toward the optimal limits exploration, curiosity and will necessarily lead the system to shut itself from the unexpected.

Thus, a higher level of FEP does not, or only temporarily, counteract optimization excesses at the lower level unless it has an even higher level under the FEP and so on to infinity. These upper layers would be devoid of *a priori* in the form of belief except the intrinsic *a priori* of the FEP: a predetermined and, therefore, closed phase space and the pre-existence of optima imposing a finality.

Finally, in the FEP theory, exploration is an emerging phenomenon caused by its future optimality assumed by a higher level of FEP. Exploration is not a principle. There is no gratuitous curiosity; inferences act as motion-generating attractors, and the default state (without attractor) is immobility and conservation. Adaptation manifested as exploratory curiosity and learning, responds to a problem or a threat to survival, whether present or projected in the future as *a priori*. Necessity is the driving force of a transient contingency, just as invariance is the driving force of movement.

In Section 3, we will assume that exploration is a constituent of the default state of biological organizations and is revealed by suspending higher-level organizational constraints; therefore, the opening of a level does not require optimization at another level, the opening is constitutive. We propose to move from a computational Bayesian model to a more parsimonious theory of specific objects and constraints where we do not assume a general optimization principle.

3. For a New Biological Theory: Biological Organizations between Opposite Entropic Tendencies

In the continuity of Darwin's first principle, reproduction with variation, we elaborate a biology of the activity, motility, and changes in possibility that constitute the historicity of the living. We contribute to an alternative to the conservation and optimization principles inspired by the theories of inert objects, whose first assumption is the *a priori* definition of the phase space. Physics explains change on the basis of invariance; in biology, change is ubiquitous and we need to explain historicized invariances; see (Montévil & Mossio 2020). The relationships that constrain and enable the organization and evolution of life constitutes our theoretical starting point. In this section, we will analyze two aspects of entropy and use this analysis and the subsequent concepts to discuss biological situations where, we contend, entropy is not defined as a function in general.

3.1. Two Opposite but Complementary Entropic Trends

1) Physicists generally speak of entropy increase when there is a dispersion of energy. Entropy increase corresponds, at the local level, to an increase in the number of equivalent microscopic states, thus a form of randomness, and, at the global level, to homogenization. For example, when particles of a gas are concentrated at a given location, it tends towards a uniform distribution. The latter has a simpler macroscopic description than the former – we do not need to specify the location describing the heterogenous distribution –, and it corresponds to far more microscopic configurations, because all particles have the same chance to be anywhere. Entropy increase describes processes directed in a single direction, the most generic one, which amounts to tending towards a form of stability and predictability. In the structure of thermodynamics and statistical mechanics, entropy is used to specify the final state of a system tending to equilibrium, as the one with maximum entropy satisfying the constraints.

In a statistical physics system, in a sense, entropy and energy functions compete because they have opposite signs and thus effects. When the temperature is high, entropy, in the form of random agitation of particles, dominates, for example, in a gas. When the temperature is low, the energetic constraint dominates leading for example to a crystal. However, in both cases the above discussion still applies and entropy remains structuring. The system tends towards the most generic macroscopic state given the internal constraints, energy in particular, and the external constraints as the boundary conditions.

Then, local randomness gives stability at a larger scale; the homogenization of the local variation then justifies stability. The two trends described by entropy increase go together but they also have opposite meaning – increase of the predictability at the global level, and decrease at the local level, for example. While variation is generally associated with disorder, homogenization and stability are generally associated with "order." There is, therefore, a form of "ordering" described by entropy increase at the global level, as Schrödinger already envisaged in his notion of "order-from-disorder" (Schrödinger 1944), where order simply means macroscopic regularities.

2) We can find this double entropic trend in the FEP and its application to the Bayesian brain. Indeed, the FEP assumes that any living system, particularly the brain, follows a Bayesian generative model of world representation that evolves by maximizing its evidence and the validity of its representations, which amounts to minimizing its relative entropy. Here, the local entropic trend is described by the relative entropy, also called uncertainty, surprise, or prediction error. The FEP is a variational principle, like the least action principle and the maximum entropy principle, but applies to Bayesian mechanics as "physics of and by beliefs" (Ramstead *et al.* 2023). The FEP states that the generative belief model always evolves in the direction of the most probable, ultimately tending to a stationary state of maximum entropy that can be interpreted as the global entropic trend of the system under the constraint of the *a priori* of the model and external states. Thus, according to the FEP, living systems are teleologically oriented models, following a physics of beliefs toward their stability in their environments driven by the global entropic trend. They oppose the dissipative local entropic trend that is also a source of "information" on their environment. This modeling is organized as nested Markov blankets where the global level operates to optimize, notably simplifying and reducing the local level according to the regime of constraints made of *a priori* beliefs.

In the previous section, we pointed out some limitations of this vision. Firstly, the phase space is already predetermined, which means that the exploration of new possibilities is limited. Secondly, the process of optimization overrides historicity, which means that the context and history of the object are not properly taken into account. Finally, an exploration that is induced and determined by a higher layer of optimization does not compensate for the self-referential confinement. We propose an alternative perspective that shares some similarities with the FEP approach but has fundamental differences.

3) We extend the definition of these two entropic trends by their level of description. In physics, the global is derived mathematically from the local by a state or path integral, with the assumption of ergodicity. In biology, we introduce a concept of global entropic trend that would not derive mathematically from the local entropic trend, because we do not assume ergodicity and a fixed possibility space. Let us insist that in biology we do not assume that the global entropic trend corresponds to a state function; however, we import, in biology, part of the conceptual role played by entropy

in physics, specifically in the tension between the local and global aspects of entropy. The aim of this extension is to work out the articulation between local and global, variations and stability.

We will present briefly our perspective on biological organization to go further. The idea is not to give a fixed definition of biological entities, which are always transient and historical, but to think about the processes that give rise to their relative stability (Soto, Longo, Miquel *et al.* 2016). This involves considering their historicity and defining the organization of constraints within the living, according to a "closure of constraints" constituted historically and contextually (Montévil *et al.* 2016a; Mossio, Montévil & Longo 2016). This concept of closure differs from the concepts of convection cells or catalytic cycles. It also further specifies the autopoiesis of Maturana and Varela, since the latter does not specify the theoretical entities that are the subject of this self-production. The specificity of the closure of constraint is to define constraint dependency where the recursion in the constraint chain "folds and establishes a mutual dependence." Constraints maintain and compensate collectively for their dissipation through constrained processes (Montévil & Mossio 2015), generating and regenerating their interdependencies and leading to processes that would not occur without constraints. It is this mutual maintenance that enable biological organizations to last over time and diversify, by contrast with physical self-organization that is a spontenous self-organization of flows. The relevance of a given constraint remains limited in time and contingent; organization can change over time. Closure of constraint implements the coordination of interactions and relationships within living beings and with their environments. However, their environments do not fully determine them, and they resist them in a certain way. Thus, the network of constraints can collectively determine itself, that is, it self-maintains by self-constraint (Moreno & Mossio 2015). This framework also provides a concept of biological function (Mossio, Saborido & Moreno 2009).

Starting from this approach of organization, we define the global entropic trend as the "attractive" tendency of closure of constraints to shut itself from destabilizing influences and achieve a stationary equilibrium, i.e., a state less and less likely to evolve, neither under the influence of a (relatively small) external disturbance nor internal local fluctuations. This change is, therefore, a trend towards the most likely state related to the priors and the context. The constraint regime formed up to now is simplified by maintaining its link in the context and then, at the limit, maintaining itself identically. In this slow and gradual evolution towards stability, local entropic trend, fluctuations that can affect the closure of constraint, is minimized. The evolution of the closure of constraint following this tendency tends to behave as if it followed a trajectory in a state space co-determined by the relationship between its historicity and the context. Thus, the more a closure of constraints closes to the variation, the more the phase space and probabilities are definable. No entropy function is defined in the general associated case, but in this limit case, we may consider an associated function that could be that of the FEP. This limit case is also the reason we introduce the general terms of global and local entropic trends in a situation where there is no general corresponding state function.

Closure justifies at least in part the relative stability of the constraints involved, and as such, it participates in global entropic trend. However, once organized in closure, the global entropic trend also reinforces stability by self-simplifying (Umerez & Mossio 2013). This concept of global entropic trend can be used to talk about the invariances observable in the living, the tendency to maintain, reproduce, repeat, and homogenize. However, it is a trend and not a state reached in the living because any closure of constraint that would be too shut from the milieu becomes fragile, loses plasticity, and risks destroying itself abruptly with no possibility of resilience, which is encountered in second-order disruptions (Montévil 2022) (see Section 3.3). Let us also insist that this tendency to shut oneself differs from the thermodynamic sense of a closed system, an organization being always open from the latter point of view. It corresponds to the absence of change of organization by friction with the environment. Thus, the tick described by Von Uexküll reduces his world to a minimal number of relevant aspects and has mostly automatic responses to these aspects (Jakob von Uexküll 1965).

Let us emphasize that the global entropic trend should be analyzed at the level of the closure of constraints and that the latter always has a global dimension. It constitutes a higher level of organization compared to the constraints that constitute it, considered as local, multiple, diverse, and can be affected by local entropic trends.

In biology, we posit that local entropic trends corresponds to any variation affecting a closure of constraint that is not part of a pre-established possibility described by this closure and compatible with it. In this sense, the local entropic trend corresponds to unpredictable variations with respect to the knowledge of the initial situation (Longo, Montévil & Kauffman 2012). The local entropic trend is a source of closure of constraint's changes and manifests itself at different scales, such as "infidelities of the milieu" (Canguilhem 2013); these can be external, i.e., environmental or internal: DNA mutations, rare configurations and interactions of proteins (the stereo-specificity of the macromolecules being only partial), the random and asymmetric distribution of cellular components between two daughter cells, allelic rearrangements during meiosis, the recombination of ancestral phenotypes, new neural connections, neural spontaneous activity…

By contrast, already functionalized randomness is not a genuine contribution to the local entropic trend from the biological perspective. For example, stochastic resonance is a situation where adding randomness contributes to functionality by amplifying a signal by adding noise. Similarly, most molecule movements in a cell directly result from diffusion. In these examples, randomness does not destabilize the initial organization, it contributes to it.

The global entropic trend corresponds to maintaining the system and repeating at least some of its dynamics, allowing living organisms to maintain homeostasis and regulate their internal functions. On the other hand, local entropic trend leads to the divergence of the system and its disorganization. Therefore, we argue that living organisms exist in a tension between local and global entropic trends.

3.2. Anti-entropy as the Tension Between Global and Local Entropic Trends

In the living, global and local entropic trends are in tension between homogenization by the global, that is to say, by the organization at the larger scale, and heterogenization by the local, where one canalizes the other. For example, the ecosystem can exert a relatively stable environmental selection pressure relative to the life of an organism; at the same time, each new organism brings its contribution to variation, both in relation to other organisms of the same species and in relation to its viability in its ecosystem. This negative selective pressure is globally homogenizing; it stabilizes the local entropic trend in specific functional configurations. Thus, there is not a single optimal configuration, an organism stereotype, to select but a set with a common characteristic to be sufficiently viable in their ecosystemic context. This process of openness to variation and homogenization by excluding the incompatible is found at every scale of the living. This process creates the diversity of individualities and types of individuality (organism, cell, ecosystem, species), appearing homogeneous on a global scale but having an internal diversity that can manifest itself in a different, unusual context.

However, this tension is not in equilibrium or search of equilibrium; it is even less 'optimal' or 'perfect.' On the contrary, there is a discrepancy, a non-identity of oppositions, and a certain "relaxation" of constraints, which generates a continuously reorganized dynamic. This consists in changes of symmetry in cascade linking different levels of organization and allowing these levels of organization to exist. In our view, organization is more than near-critical, as describe in (Safron *et al.* 2022; Parerin *et al.* 2011), where organization emerges in "edge of chaos" inter-regimes balancing between disordered and ordered dynamics, in a pre-defined ''phase space'' containing the trajectories of the dynamic. Similarly, we argue that since the space of possibilities is constantly transforming (which is incompatible with formal optimality), we say that organizations are then in a state of extended critical transition (Longo & Montévil 2011).

In this context, we consider that the production of anti-entropy, that is to say the appearance of new functional possibilities, takes place between two opposite tendencies: to approach global entropic stability, a trend to "optimality," and to move away from it by local variation. It maintains its imbalance, a sort of back and forth between these two crucial but destructive tendencies in their limit case (see Section 3.3). Anti-entropy production would then be in the tension, never resolved, between local and global entropic trends.

This tension is found between the tendency to conservation, identical reproduction, and repetition by the stability of the global and the "open-ended" evolution, the divergence by the variability of the local. Each living system has a certain degree of stability for its maintenance. However, it also requires variation to maintain its internal diversity, which tends to disappear by homogenization (see Section 3.3). This idea is found in the concept of proliferation with variation, driving evolution and ontogenesis (Soto, Longo, Miquel *et al.* 2016). Even if the part of essentially similar reproduction is greater than the part that varies (some mutations in the case of meiosis, asymmetric distribution of some constituents in the case of mitosis), the combination of the two is necessary for life. In short, maximum homogenization and variation are like two entropic "attractors" but at different levels, respectively global and local.

From this perspective, the production of anti-entropy, as the appearance of functional novelty by integrating variation into an organization, still requires the local entropic trend in the form of variation. Consider, for example, one of the major evolutionary transitions: the formation of eukaryotic cells by the symbiosis of bacteria and archaea, particularly the formation of mitochondria (Martin, Garg & Zimorski 2015). The invagination of a bacterium in an archaeon, leading to the appearance of mitochondria, was a large entropic disturbance for the host archaeon or even for both. Then, by co-evolution, their relationship became symbiotic, a new viability situation among many failures of this evolutionary 'accident.' This case exemplifies diversity production through the entropic encounter of distinct evolutionary paths (Longo, Montévil & Kauffman 2012).

In general, of course, no variation is directly anti-entropic. Its effect in time and space on the existing biological organization causes successive symmetry changes, i.e., processes of disorganization requiring reorganizations. Think again of cell division: the entropic component of proteome distribution, of partial DNA repair, contributes to the anti-entropic production of the new organization, generating diversity. If the reorganizations make it possible to maintain this new organization, the entropic variation was then transformed into a functional anti-entropic novelty. It is then at the origin of evolutionary diversity at different levels of biological organization. However, it also contributes to tissue differentiation during embryogenesis – through strong sensitivity to contour conditions (pressures, biochemical flows, etc.). Thus, it is as if anti-entropy is "nourished" by the local entropic trend.

The notions of "flow of variety" and "stasis" in Nietzsche's philosophy could be associated, respectively, with that of local and global entropic trends. According to him, "the flow destroys inherently the means implemented by life to protect itself" (stasis). However, this flow feeds life by "incorporation," allowing it both to maintain itself and to evolve its stasis. The variability of the flow and the stability of the stasis are then in "tragic tension" (Stiegler 2021).

Entropic variability, which generates "defects" compared to the norm of a living system, is necessary for its evolution and, therefore, for evolution in all its forms, including learning.

Note that the new organization is not necessarily more complex than the one from which it comes; there is no teleology towards ever more complexity. However, complexity may allow for the invention of new ecosystemic niches, in which case it is more likely to survive (Cazzolla Gatti *et al.* 2018).

3.3. From the FEP to the Anti-Entropic Vision of Life

Let us now emphasize the fundamental differences between our proposal and the FEP.

The Toxicity of the Global Entropic Trend

Although the global entropic trend is an essential component of life, by limiting the local entropic trend, it also can have negative consequences. This trend does not end at the maintenance of the closure of constraints; it continues to strengthen by self-simplification of a closure. This tendency, when extreme, can lead to harmful consequences for living beings in two linked and mutually reinforcing ways: the reduction of the richness of historicity and the closure to the contingency of the real, understood as what resists, especially to representations. The real is nevertheless a source of historicity and, therefore, of anti-entropy production.

Indeed, reducing the entropy of the past, of the belief model itself in the FEP language, amounts to erasing its details, i.e., its internal diversity from history, by a semantic oversimplification. The excessive loss of the memory traces of the contextual elements in which the closures were built reduces the historical richness to a single trajectory and generic behavior devoid of tensions. This consolidates the oldest and most general traces by eliminating redundancies. The object becomes more and more predefined by an optimized pattern, able to predict in a fixed milieu and only open to the proximal, restricted future.

This trend results in intense selective pressure on the integration of the local variations. This closedness to the present diversity of reality reduces the integration of the local variations and the depth of integration. Thus, the global entropic trend tends to make the closure of constraint necessary, structural, rigid, automatic and ahistorical. It tends to abstract itself and become impermeable to the context by building a space of possibilities closed and in contraction. This phenomenon leads to a loss of function by loss of the frictional relationship with the contingent complexity of the context, leading, in short, to self-referential confinement.

In other words, we move from metastability to stability. The excess of constraint by the higher scale and the submission of the lower scale leads to eliminating its degrees of freedom supported by the various redundancies. There is a leveling down of levels into a synchronic unit exceedingly coherent with itself but detached from the real context and its improbable contingency. Diversity is reduced and canalized into hyper-specialization. These phenomena lead to a loss of the plastic resilience of the organization, i.e., its ability to produce anti-entropy by integrating local entropic variation. The result is a reduction in the space of possibilities that can go as far as second-order disruptions, that is, the loss or impairment of the ability to produce functional novelty (Montévil 2022).

The FEP, when considered the only fundamental law, entails the strengthening of a model by permanent research of validation of the model's proofs, leading to self-referential confinement. Concerning cognition, this is manifested by a rigidification of thoughts, which is found in several psychopathologies (e.g., physiological aging, end-of-life depression, Alzheimer's) where the activity of DMN is strengthened (Cieri & Esposito 2018). Additional levels of FEP do not eliminate these problems (see Section 2.3).

The rigidification and the reinforcement of the closure of constraint are limited by the local entropic trend, which tends to destabilize them by bringing variation and making them evolve. This idea is common to FEP and our approach. However, for us, the local entropic trend is not only external or "accidental," i.e., due to the organization's instability. Moreover, the living not only repels variation but also maintains an open relationship with the "unprestatable" (Longo, Montévil & Kauffman 2012). Local entropic trend cannot be modeled by injecting an amount of randomness into a model.

Organization and Local Entropic Trend

Local entropic trend not only includes disturbances coming from outside but also those of internal origin, i.e. brought by historicity. In the latter case, it corresponds to traces of history not fully functionalized to the system and can be reinterpreted into new functionalities according to the context. The traces of the past resist normalization; they constitute a form of internal diversity, of alterity within the system itself. Memory then constitutes a reserve of deviation and not only a united block conditioning the future towards ever more optimality. We can refer to the exaptation of vestigial structures as an example. A past structure reappears but not wholly; it is reinterpreted according to context and may result in a new organizational function (Rayner, Sturiale & Bailey 2022). Let us emphasize that its potentialities coming from traces of the past are not like hidden possibilities whose properties are actualized. Their reinterpretation in the present gives them a new biological meaning. Thus, what matters to the organization at a given moment only partially defines what it is for the next moment. The new organization cannot be formalized from the previous one because of this incompleteness resulting from historicity.

On the other hand, we argue that living beings maintain a fundamental openness to the local entropic trend that comes from the principle of variation (Montévil *et al.* 2016a). This openness also appears in what has been called propulsive constraints (Miquel & Hwang 2016; Montévil & Mossio 2015; Montévil & Mossio 2020). Their role is to actively open the system to variation, which goes against the FEP. For example, we can cite all the constrained processes (more or less dependent on the context) bringing novelty when generating a new organism: in bacteria, the modulations of genetic mutations according to the context, exchanges of genetic material; and in protozoa: crossing over, random phenomena during sexual reproduction.

Proponents of FEP could argue that evolution would have optimized its propulsive constraints. There is probably some optimization, but it occurs after the appearance of a novelty, including a second-order evolution novelty (Tenaillon *et al.* 2001), and does not explain its emergence. It requires a first opening to alteration, a relaxation of constraints not guided by a superior optimality.

These considerations lead us to discuss what activity and passivity mean in the living.

New Perspective on Activity and Passivity

From the perspective of the FEP, passivity is the reception of sensory input from outside; activity is active inference in two forms: transforming the environment or transforming the representation of the environment to make it less surprising in the future.

On the other hand, we propose that passivity corresponds to the mechanical, predictable functioning already included in the pre-established dynamics by the constraints of the organization. Thus, the "active" inference, made by the automatic projection and transformation of expectations according to the FEP, is then also passivity in the sense that its dynamic is pre-established towards the minimization of variation.

To explain this, let us return to FEP: it is not specific to the living and is considered as a "physics of beliefs" (Ramstead *et al*. 2023). Just as in physics, objects are passive with respect to the laws governing them; biological organization is passive with respect to the law described by the FEP. When the organization complies with the FEP, that is to say, when the closures of constraints constituting it are simplified without functional innovation, the evolution takes place "mechanically" within a space of possibilities predefined, thus in a kind of passivity. The case of the physicist's "active matter", as described in (Chvykov *et al*. 2021), corresponds to a statistical mechanics where the particles are out of equilibrium, but it also corresponds to passivity in our perspective because the particle follow fixed rules.

On the contrary, there is activity when there is a change in the organization in a strong sense. This implies an active opening to variation followed by a reorganization on several scales. The organization is actively involved in its transformation, outside a space of predefined possibilities, by integrating the local entropic variation that is not governed by a "law" (Tahar 2023).

3.4. The Question of the Default State of the Living

The question of the biological default state has been put forward by (Sonnenschein & Soto 1999), notably by analogy with the principle of inertia, a state at the basis of classical physics. Inertia is never exactly observable, but it structures the theory. The theoretical strategy is analogous for the default state in biology.

In the theoretical perspectives inspired by physics, the current paradigm of the default state of living systems is self-preservation (Bourgine & Stewart 2004), similarly a common assumption in biology is that the default state of cells is quiescence (Montévil *et al*. 2016b). Change appears as a means for maintenance; this hypothesis goes hand in hand with the search for balance, stability, and optimality, imposing a limit to the changes. For example, at the cellular level of multicellular organisms, this default state would manifest as quiescence, an inactive cell at rest waiting for a triggering stimulus.

Soto and Sonnenschein initiated a reversal of perspective by assuming that the default state of cells is proliferation and motility and not quiescence. It follows that there is no need for stimulation for cells to display this default state. Instead, quiescence requires an explanation in the form of a cause (Soto, Longo, Montévil *et al*. 2016).

In our approach, we suggest moving from the primacy of the teleological principle of entropy minimization to the notion of anti-entropy as a tension between local and global entropic trends. According to this notion, living beings are not intended to reduce entropy to the maximum but to maintain a degree of openness to feed on it, that is, to functionalize it and transform themselves. Living beings are not just fighting against the local entropic trend but, instead, grow from it.

We go from a default state of least action, passivity, to a default state of activity where the variation is not triggered in response to a disturbance from the outside but is intrinsically present, canalized, and more or less maintained. It is a state of exploration outside a predefined phase space without reward and not constrained by a superior organization. This exploration, requiring an intrinsic openness to variation, takes place not only through genetic variability but also at different levels of life; it appears as motility, mobility, or curiosity not motivated by a goal.

This exploratory impulse, most of the time repressed and constrained, does not stem from a superior commitment to optimization. Considering this as a default state has consequences on causality: if we assume that the activity is by default, then if it is not observed, it means that it is constrained, and we have to make these constraints explicit.

3.5. The Relationship to the Space of Possibilities

The principle of variation and the interplay between local and global entropic trends that we have just presented underlies a space of possibilities in continuous transformation by default and whose dynamics are not pre-definable (Montévil *et al.* 2016a). This is a fundamental difference between the living and inert, and also between biological and algorithmic creativity.

In algorithmic combinatorics, the elements are defined, distinct, and preexisting in a synchronic and complete co-presence. They are then combined according to pre-established rules with more or less randomness, which is itself predefined. The resulting "creativity" amounts to actualizing a part of a space of possibilities that is already defined, typically on the basis of a gigantic amount of data.

In biological generativity, there can be a combinatorics of elements and randomness. However, this process is diachronic because the "elements" are, in reality, a tissue of relationship, a set of constraints possessing a singular, meaningful historicity. They then have the possibility of being destroyed, mixed, entangled by the local entropic trend, and then "rewoven", allowing them to cross the barriers of the probable and thus open the space of possibilities. Of course, this view is a major epistemological challenge, which is why assembly theory assumes generic properties for selection that remain hypothetical and independent of the nature of the novelties appearing.

Let us take the example of a mutation on a DNA nucleotide. There seems to be a defined combinatorics, so a determined phase space. However, this space is not sufficient for the theoretical determination of the object. Its functional consequences will depend on the neighborhood of this nucleotide (if it is in a gene, if there are several modes of reading the gene), the epigenetic structure (e.g., accessibility of the gene, localization in the nucleus), the cellular context (e.g., cell type, cell neighborhood) and the context of the organism and its environment. All these layers of organization and their space of possibilities have a certain degree of determinism necessary to maintain them. However, the entanglement between the different levels opens the space of possibilities to the indeterminate, contributing to its expansion.

Conclusions

The question of a theoretical framework to understand organisms is an open debate. In this debate, one of us has contributed to developing three theoretical principles: the principle of variation, the principle of organization, and the default state (Soto, Longo, Miquel *et al.* 2016). These principles are sufficiently robust to be foundational in biology; nevertheless, they are also starting points, and much remains to be elucidated, notably concerning how biological organizations change.

In that regard, a parallel effort has been accomplished on the notion of a Free Energy Principle (FEP) stemming from cognitive sciences and based on an informational perspective. The FEP is a framework that explains how a system and its "belief" model evolve through Bayesian updating. This updating is guided by an optimization principle that involves adjusting the statistics of the things to which they are coupled. This info-computational approach provides a view of self-organization where organisms are layers of abstract representation that generate probabilistic decisions. These representations are created empirically by detecting common patterns, followed by a succession of reduction operations, leading to model changes. The temporal evolution of a system is considered as a combination of a deterministic component and a noise component, which must be minimized. Noise is considered a source of novelty, as in the case of the entropic brain, where entropic annealing is used to explore the phase space and update new configurations.

From the general perspective of the theory of organisms, we have argued that the FEP is not acceptable as is. It assumes a pre-given possibility space, which is the condition of possibility of an optimization principle. In contrast, the principle of variation posits that biological possibilities change over time and rejects general optimization principles. Moreover, the general informational perspective of the FEP is problematic and has been heavily criticized by others. Specifically, the FEP leads to systems that would strengthen their models in the context of their coupling with their environment by minimizing surprise and uncertainty. As a result, it struggles to address putative beneficial situations where the brain entropy increases, like in the model of the entropic brain under psychedelics. For FEP proponents, the way out is to propose a schema of nested optimization levels so that increased entropy at one level would be part of optimization at another level. This way out is problematic, though, since this higher level would also require a phase space and regularities to optimize entropy. In any case, it remains incompatible with the notion of changing phase space and historicity as we define it.

Nevertheless, the perspective of the FEP can be analyzed by concepts that we introduce here, namely the distinction between *global and local entropic trends*. In physics, the local entropic trend would be the tendency of the system towards the microscopic fluctuations, while the global entropic trend would be the tendency of the system towards the macrostate that is directly or indirectly determined and stable by the second principle of thermodynamics, that is to say, the most generic state. By generalizing these concepts in the context of the theory of organisms, the local entropic trend corresponds to changes that are not yet functionalized, irrespective of whether they are of intrinsic or extrinsic origin. Global entropic trend corresponds to a tendency toward homogenization provided by a given organization and its coupling with its milieu. Then, the FEP considers only the global entropic trend in a specific informational setting, while the theory of organisms includes a principle of variation that, in the terms of this article, posits the universality and ubiquity of the local entropic trend.

In the theory of organisms, the global entropic trend partly corresponds to the closure of constraints, understood as stabilizing constraints and the corresponding processes. However, the notion of global entropic trend is more general. It opens the perspective of the tendency to simplify a closure, preserving and stabilizing its main functions and couplings with its milieu, possibly by taking inspiration from the FEP. Now, local entropic trend, of course, is related to the principle of variation. However, the principle of variation is about functional variation, while the local entropic trend is about variations that may be functionalized. As such, for example, we have emphasized the traces of the past that are not functional for a given organization, and that would be leveled down by the global entropic trend, but that may also enable new functions.

In a nutshell, the core message of our work, in line with previous discussions (Montévil & Mossio 2020; Longo & Montévil 2012), is that biological organizations are not, and do not tend to, organizational fixed points. Instead, they are between two opposite tendencies: the global entropic trend of homogenization and the local entropic trend of destabilization.

As a perspective, from the analysis of the two approaches mentioned, FEP and organicist, we can conjecture that there are two modes of biological evolution:

- Passive: exploring the space of possibilities already defined by a set of constraints (previous belief, inclination, habitus). This mode of development, governed by the FEP, advances cautiously and incrementally by capitalizing on what already exists.
- Active: that is, creative in the strong sense. It involves the change of the set of constraint by the local entropic variations and is able to change the space of the possibilities. It is actively promoted by the propulsive constraints.

The conjunction of these two modes of evolution creates relevant organizational changes, i.e *anti-entropic* in that it induces *a virtuous circle of viability by allowing both stability of the organization and openness as a possibility of new changes*.

What are the Consequences for Cognition?

According to the current consensus, the brain's default state (when the DMN is activated) is linked to the ego as a medium of identity. This autobiographical self, supported by all the memories (representations), guarantees the stability of the sense of identity despite the perceptive changes (Damasio 2000) by minimizing free energy (Carhart-Harris & Friston 2010). It is, therefore, a state of constraint and self-maintenance.

Our perspective leads us to consider a different default state for the brain or, more generally, the cognition of living beings. In contrast to the DMN, which focuses on self-preservation, it would be a state of exploration activity and curiosity free from its constraints in the form of belief. At the biological level, it would be a state where neurons activate themselves and make spontaneous connections in a contingent way, as it is the case for unconstrained cryptic 'spontaneous electrical low-frequency oscillations' SELFO (Hanson 2021), and at the psychological level, a state of creativity. This default state, constrained and therefore repressed in everyday life, can possibly be experienced, among others, through the experience of ego death reached during psychedelic experiences or deep meditation. In this case, psychedelics and meditative practice would not act as triggers of this state but as a relaxation of constraints on this state, which corresponds to Carhart-Harris's thesis and his hypothesis of the entropic brain.

The question arises of the re-organization of constraints, which are preserved, destroyed, or created; how do they change in a relevant way, i.e., therapeutic? According to the FEP, these are the ones that minimize uncertainty the most. According to our anti-entropy approach, on the contrary, constraints are reorganized in order to generate a greater capacity for openness to uncertainty. This openness can involve the removal of the most restrictive constraints (beliefs related to depression, for example) but, above all, a greater capacity for acceptance of the contingency of oneself and the world, like in stoicism. This capacity corresponds to an increased ability to generate anti-entropy from local entropic variations. At the psychological level, it can manifest as greater confidence in the becoming, which precisely does not rest on beliefs because it comes before the constitution of beliefs itself.

The lifting of blocking constraints can be learned through different techniques, for example, meditation (Ho, Nakamura & Swain 2020) potentially complementary to the use of psychedelics. In a sense, philosophy or even sciences are also methods and attitudes that require such an openness. All these techniques of relaxation of constraints and openness to contingency require double attention to the sensitivity and suspension of judgment, a fundamental gesture in philosophy also called "epoché" (Guilielmo & Mudry 2021). This voluntary and active work can be considered as a propulsive constraint, since it is a question of organizing its disorganization in an undirected way. Thus, perhaps one of the main lessons of these practices is to realize that seeking to minimize uncertainty is a locking belief, while it is liberating to accept it.

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