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# Systems, Self-Organization and Information: An Interdisciplinary Perspective

Complex system studies are a growing area of central importance to a wide range of disciplines, ranging from physics to politics and beyond. Adopting this interdisciplinary approach, Systems, Self-Organization and Information presents and discusses a range of ground-breaking research in complex systems theory. Building upon foundational concepts, the volume introduces a theory of Self-Organization, providing definitions of concepts including system, structure, organization, functionality, and boundary. Biophysical and cognitive approaches to Self-Organization are also covered, discussing the complex dynamics of living beings and the brain, and self-organized adaptation and learning in computational systems. The convergence of Peircean philosophy with the study of Self-Organization also provides an original pathway of research, which contributes to a dialogue between pragmatism, semeiotics, complexity theory, and self-organizing systems.

As one of the few interdisciplinary works on systems theory, relating Self-Organization and Information Theory, Systems, Self-Organization and Information is an invaluable resource for researchers and postgraduate students interested in complex systems theory from related disciplines including philosophy, physics, and engineering.

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Systems, Self-Organization and Information

An Interdisciplinary Perspective

Edited by Alfredo Pereira Jr., William Alfred Pickering and Ricardo Ribeiro Gudwin



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Presentation of Chapter 6, not included in the published version. Vital Flow – The Self-Organization Stage *Romeu Cardoso Guimarães* 

Technical aspects of the formation of the genetic code (the code of biological 'letters') are hyper-condensed. I apologize for possible difficulties with this topic. The space is dedicated mostly to aspects that make contact with other disciplines, from physics to the humanities.

One aspect of the model for the origin of the genetic code finds an analogy with a rationale belonging to quantum mechanics. This is not to say that we advocate specific quantum processes in the realm of biomolecules at formation of the genetic code, beyond the generality of quantum mechanisms being subsumed in all molecular processes.

The starting entities, in both the biological and in the quantum realms, are singular – the 'prototRNA dimer' and the 'wave-particle' – and both show aspects of complementary composition with undecided identity of the components. Identity is obtained in later stages of the process – decoherence, springing from interactions with additional entities (the 'other' in social contexts). It is possible to advance the rationale further, saying that the differentiation of entities accompanies the formation of systems made by all those entities interacting in mutuality.

A similar process is seen in the character of the first set of amino acids that are incorporated into the coding system, of forming preferentially Intrinsically Disordered Regions of proteins. The message is recalled that identity ('order, organization') is revealed at the interaction that this sequence establishes with a ligand, that is: the functional specificity, that can be called a piece of information (a specific pattern), arises at an interaction. Later aspects of organization in protein sequences include the traditional secondary structures, e. g. the  $\alpha$ -helices and  $\beta$ -strands.

The chronology of the encodings that this Self-Referential Model (SRM) proposes (start with Gly and Ser) does not coincide with the list of the most abundant amino acids in abiotic syntheses (Gly and Ala). The SRM is apparently validated by the identification of the two first encodings with the core section of the Glycine-Serine Cycle of assimilation of C1-units. This is also the simplest among the central metabolic pathways, coincides with the origins of the autotrophic routes (Braakman and Smith, 2012), and with the C2 pathway of the origins of bioenergetics (William Martin).

Genomic signatures of the first encodings were looked for among Low Complexity Regions of proteins. The SRM proposition was found apparently consistent with the composition of the RNP Granules (also called Phase-Separated Droplets or Condensates, Stress Granules, P-bodies, Cajal Bodies etc.), which include, most interestingly the nucleoli. It is constant among the majority of this class of 'membraneless organelles' that the protein component of the RNPs are very Glycine and Serine-rich.

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Introduction Alfredo Pereira Jr., William A. Pickering, and Ricardo Ribeiro Gudwin

Complex system studies are a growing area of central importance to a wide range of disciplines. Here, we publish the research from members of the *Interdisciplinary Self-Organization Group* of the Center for Logic, Epistemology, and the History of Science at the State University of Campinas (Campinas, São Paulo State, Brazil). This research group was formed in order to foster the theoretical and applied study of complex systems, and has operated continuously since its foundation. The chapter authors, representing a variety of disciplines, are all members of this group, as well as professors and academic researchers at Brazilian universities. The chapters are structured logically and integrated around the theme of Self-Organization in complex systems, forming a mosaic of different perspectives held together by this central idea. By publishing this collection in English1, we make these works accessible to an international audience interested in complex systems theory and the related areas of Self-Organization and Information Theory.

The history of this book begins in the 1980s, when French philosopher Dr. Michel Debrun organized a series of seminars to study self-organizing systems. At the same time, two researchers of the Department of Philosophy of the State University of São Paulo (UNESP), located in the city of Marília, São Paulo State, Brazil, went to England to study information theory and cognitive science. Another series of seminars focused on self-organizing systems, organized by Dr. Célio Garcia, was taking place almost 400 miles away in the graduate philosophy program at the Federal University of Minas Gerais (UFMG), located in the city of Belo Horizonte in Minas Gerais State. Members of the three groups joined forces at the end of the 1980s under the leadership of Dr. Debrun. After his death in 1996, Dr. Itala Loffredo D'Ottaviano took his place in the organization of seminars and the coordination of research, tasks that she has continued to perform up to the present time.

## 2 Alfredo Pereira Jr. et al.

The works by Debrun that compose the first two chapters of this book were originally published in Portuguese 1996, but were only recently translated into English. Debrun constructed an original approach to the concept of Self-Organization, using relevant ideas from his predecessors, among them Auguste Cournot, Heinz von Foerster, Hal Ashby, Henri Atlan, Humberto Maturana, Francisco Varela, Ilya Prigogine, and Jean-Pierre Dupuy.

## A self-organizing system

is conceived as an open system that builds its organization and functionality from the patterns of interaction of its components. Self-Organization can coexist with hetero-organization, understood as the case when the organization and functionalities of a system do not derive from the free interaction of the system's components. In consonance with his previous studies on Antonio Gramsci, Debrun argues that a linear hierarchy – as in the case of dictatorial political organizations – is not an instance of Self-Organization, even when the center of power is located inside the system. His concept of Self-Organization requires that the dynamics of a system arise from the free interaction of the components.

The concepts of systems theory used in Debrun's approach to Self-Organization were further developed by D'Ottaviano, a skilled logician, mathematician, and philosopher, with Ettore Bresciani Filho collaborating with his strong background in engineering and administration. They provide apt definitions of concepts such as "system", "structure", "organization", "functionality", and "boundary". The dynamics of self-organizing systems is heavily dependent on the information that is available to and processed by their sub-systems. A cognitive scientist and a philosopher, Maria Eunice Quilici Gonzalez, from the UNESP-Marília group, has joined forces with Alfredo Pereira Jr., a philosopher of science, who participated in the UFMG group to discuss the role of information in Self-Organization. This chapter was originally published in 2008, building on a previous work published in 1996. The authors distinguish informational processes from the properly causal physical processes present in cognitive agents, and attempt to categorize the kinds of information that contribute to self-organizing processes.

Extending this framework, we have chosen the remaining chapters from the collections of articles previously published in Portuguese by our group, and have also included other articles by group members that deserve to be presented to an international interdisciplinary community.

The book is divided into four sections. The first section is on foundational concepts, and the second section focuses on biophysical and cognitive approaches to Self-Organization, containing chapters on the complex dynamics of living systems, self-organized adaptation, and learning in computational systems. The third section discusses practical issues of information technology and related ethical questions, all dealt with in the social context of community Self-Organization and technology. The chapters in the final section take a semiotic perspective, investigating the convergence of Peircean philosophy with

### Introduction 3

the study of Self-Organization, an original pathway of research contributing to a dialogue between pragmatism, semeiotics, complexity theory, and self-organizing systems.

The editors are grateful to Itala Maria Loffredo D'Ottaviano, not only for her leadership of the group but also for her help with the book project. We also give our thanks to all chapter authors and other members of the research group for their collaboration in the evolution of the group and contribution to the quality of the results. This is surely an example of a successful collective self-organized process!

The editors hope that this book will not only communicate our group's research to an audience beyond the borders of Brazil, but that it will also demonstrate the wide range of applications of complex systems theory. Above all, we hope that the fruitfulness of the results will inspire readers to further investigations and discoveries in this profound subject of study.

### Note

Several of the chapters are English translations of previous publications in Portuguese: Chapters 1 and 2: Michel Debrun – A Idéia de Auto-Organização and A Dinâmica da Auto-Organização Primária, in Debrun, M., Gonzalez, M.E.Q., and Pessoa Jr., O. (Orgs.) Auto Organização-Estudos Interdisciplinares, Coleção CLE 18, CLEUNICAMP, 1996; *Chapter 3*: Ettiore Bresciani Filho and Ítala Maria Loffredo D'Ottaviano - Conceitos Básicos de Sistêmica, in D'Ottaviano, I.M.L. and Gonzalez, M.E.Q. (Orgs.) Auto-Organização; Estudos Interdisciplinares Coleção CLE 30, CLE-UNICAMP, 2000; Chapter 4: Alfredo Pereira Jr. and Maria Eunice Quilici Gonzalez – O Papel das Relações Informacionais na Auto-Organização Secundária, in Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.Q. and Souza, G.M. (Orgs.) Auto-Organização; Estudos Interdisciplinares Coleção CLE 52, CLE-UNICAMP, 2008; Chapter 5: Ricardo Pereira Tassinari – Sobre a Realidade-Totalidade como Saber Vivo e a Auto-Organização do Espaço Físico, in Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.Q., and Souza, G.M. (Orgs.) Auto-Organização; Estudos Interdisciplinares Coleção CLE 52, CLE-UNICAMP, 2008; Chapter 6: (revised and updated) Romeu Cardoso Guimarães – Dinâmica Vital, em Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.Q., Pellegrini, A.M., and Andrade, R.S.C. -Auto-Organização; Estudos Interdisciplinares Coleção CLE 66, CLE-UNICAMP, 2014; Chapter 9: Mariana Cláudia Broens – Auto-Organização e Ação: uma abordagem sistêmica da ação comum, in Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.O., and Souza, G.M. (Orgs.) Auto-Organização; Estudos Interdisciplinares Coleção CLE 52, CLE-UNICAMP, 2008; Chapter 11: Renata Cristina Geromel Meneghetti -Uma Compreensão da Economia Solidária à luz da Teoria da Auto-Organização, in Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.O., Pellegrini, A.M., and Andrade, R.S.C. – Auto-Organização; Estudos Interdisciplinares Coleção CLE 66, CLE-UNICAMP, 2014; Chapter 13: Vinícius Romanini – Prolegômenos para uma teoria semiótica da Auto-Organização, in Bresciani Filho, E., D'Ottaviano, I.M.L., Gonzalez, M.E.Q., Pellegrini, A.M., and Andrade, R.S.C. - Auto-Organização; Estudos Interdisciplinares Coleção CLE 66, CLE-UNICAMP, 2014; Chapter 15: Lauro Frederico Barbosa da Silveira - Pragmatismo e o Princípio da Continuidade no Cosmos Auto-Organizado, in Souza, G.M., D'Ottaviano, I.M.L. and Gonzalez, M.E.Q. (Orgs.) Auto-Organização: Estudos Interdisciplinares Coleção CLE 38, CLE-UNICAMP, 2004.

## Chapter 6

## Vital flow The Self-Organization stage

## Romeu Cardoso Guimarães

## Introduction

Living beings and the life process are difficult to define. Both entities are complex, as are the observers of these phenomena. There are many aspects to their components, and their multi-faceted interactions involve them in mutuality. In this chapter, we approach the problem from an evolutionary perspective.

Our origins-of-life model sprang from studies on the formation of the genetic code, specifically, the origins of the association between genes and proteins. These researches focused on the singular ("digital") "letter-by-letter" correspondences (Butterfield et al., 2017) between the triplets of bases in the genetic material which are the codons of messenger mRNAs or the complementary anticodons of the transfer tRNAs, and (Froese et al., 2018) the amino acids that the latter carry with specificity (cognitively) and transfer to a nascent protein chain. The formation of a system of correspondences describes the encoding process.

Decoding is accomplished inside cellular ribosomes. This process, called the translation of a sequence of codes into that of proteins, would be better named transliteration, since it involves no interpretation. These correspondences are the first instance of the specificity that characterizes life, allowing the construction of structures and functions via the organization of the sequences. Most studies in code formation take for granted the origins of encoding (Froese et al., 2018), and do not address the question of whether the enzymatic aminoacyl-tRNA synthetase activity was or was not preceded by a ribozyme.

## Leading concepts

*"Living beings* are metabolic flow systems that self-construct on the basis of memories and adapt/evolve on the basis of constitutive plasticity. *Life* is the ontogenetic and evolutionary process instantiated by living beings" (Guimarães, 2017). Flow dynamics is a scientific substitute for the old mystical "vital force". Viruses are mobile elements.

In Guimarães (2017), there is a technical exposition of the Self-Referential Model (SRM) for the formation of the genetic code; Guimarães and Santos (forthcoming) is a discussion intended for the general reader.

These concepts mean that the nucleoprotein system is sustained by metabolism. The system is internal to the cell but is fed from environmental substrates, which indicates that the living is an integral part of geochemical systems. Therefore, the evolutionary flow is universal and includes the biologic or metabolic. This chapter identifies the series of cellular structures and functions that construct the metabolic flow and guarantee its nonstop activity. These serial mechanisms configure a suite of molecular sinks that are also the activities of the living.

Our description ends with the development of cellular reproduction, which is the last component of the sink system. It is also the initiator of the next stage, where Darwinian processes are added to Self-Organization. It is considered that other aspects of living activities and life processes are evolutionary additions to the cellular basics. Most prominent is the development of sexual mechanisms, from meiosis, and of aggregative abilities. These start with multicellularity and open the routes to other elaborations, including the social and psychic. It is suggested that all these aspects should be at the least compliant with, if not promoters of, the flow. Accordingly, the classification of diseases should also benefit from an examination of their impacts on the metabolic flow. The final section of the chapter examines an apparent convergence between models attempting to describe the origins of the three large realms: the quantum, the cosmic, and life.

### Construction of the cellular flow system

Proteins are the main cellular components. The system that accomplished their synthesis includes the nucleic acids and is the center of the sink mechanisms. This central sink, the protein synthesis system, has to be maintained as healthy. If not continually or perennially active, it must at least be fully capable of resuming activity as soon as environmental conditions are adequate, in case it has to be temporarily suppressed due to harmful intercurrences.

The first necessity during the period of evolutionary origins was for diversification of protein structures and functions, so as to guarantee energy and amino acid sources in the upstream (nutrition) direction and safe transport of products away from synthesis sites in the downstream direction.

There must be no clogging, blockades, or accumulations along the flow routes. The protein synthesis system works as a substrate-stimulated ratchet, and does not function as a drive-forward mechanism in itself. Diversification of proteins depends mainly on gene duplication, genetic mobility, and horizontal gene transfers, and incorporates epigenetic influences. All these mechanisms are grouped under the concept of plasticity, both phenotypic and genomic.

The living mechanism incorporates reversal of the direction of polymerization (that is, degradation via hydrolysis) only for generating monomers at nutritional salvage. Sensitivity to saturation is one of the regulatory processes of polymerization activity. Mechanical saturation is avoided through control of cell volumes and shapes, avoiding the effects of overcrowding through skeletal features such as the microtubules and filaments of eukaryotes, and the cell walls of plants, fungi, and prokaryotes. If saturation does not work by itself, it triggers the activation of repressors. Saturation may not need to be general but may be restricted to some specific kinds of processes that developed the role of critical sensors for control. One of the main metabolic sensors, the mechanistic target of rapamycin (mTOR), is directed precisely to amino acid availability in cellular pools, especially to leucine, which is very abundant in protein compositions.

## The flow sectors

### The central sink

Vital dynamics are configured as a metabolic flow system. The flow starts at nutrition but is centered on the protein synthesis sink of amino acids and energy, which is kept constantly active and healthy. Nucleic acids, aside from their possibly original role as protein-producing machinery (Figures 6.1 and 6.2), develop the ligation of codes into long polymer strings that work as replicative memories (genes) for protein sequences (Figure 6.3).

The SRM data indicate that elements taken up from the environment in the era of the formation of the code and of the metabolic system were very simple, being of the C1–C2 realm (e.g., methanol, CO2, acetate) from which more complex internal materials were constructed. The search for the prebiotic equivalents of the present-day compounds that carried the C1 compounds should, thus, focus on the pterin- and folate-like functions. All kinds of amino acids that would have been formed in abiotic contexts might have participated as substrates or ligands for dimer-directed-proteinsynthesis (DDPS) (Figure 6.1), but the quantitative availability of most of them would have been subjected to fluctuations that impeded the construction of codes on their bases. The only firm connection that is supported by the SRM is glycine: it is abundant prebiotically and the first in biosynthesis. Pg 92

*Figure 6.1* Dimer-directed-protein-synthesis (DDPS). The proto-tRNAs in the dimer are shown with structure and direction, indicated by the numbering of the bases, to mimic present-day tRNAs' anticodon stemloop and acceptor stem. Members of the dimers are exchangeable with others in the pool since base pairs are weak and thermally dynamic hydrogen bonds. According to the "singularity" (monomers paired, coherent or superposed) of the state of the pair, there are no definitions in the direction of the transferase reaction, that may be bi-directional, or in the codon *versus* anticodon exchangeable identity. The structure is considered a proto-ribosome: it holds two tRNAs together and facilitates the transferase reaction (double arrow).



Pair 8:8 at center of anticodons is strict A:U or G:C. Pairs 7:9 at laterals of anticodons: base 9 accepts wobbling with base 7 (A,G) R:Y (U,C). Pairs 6:10 and 5:11, presently in the anticodon loops. Pairs 4:12, presently in the stem of the hairpin together with 1:15, 2:14, 3:13. Bases 16-18 presently the constant CCA ends. The size 18 of the proto-tRNA sequence is one quarter of present day tRNAs.

*Figure 6.2* Decoherence by protein binding and encoding. Association of a productfrom the DDPS with a proto-tRNA. This is the self-referential aspect in the process and also the mechanism of decoherence produced by proteins. At the ribonucleoprotein (RNP) association, precursor and product bind to each other. The ensemble forms a production system when the protein is stable, and confers stability to the RNP that maintains the protein synthesis activity. The protein has more affinity to one of the proto-tRNAs. The RNP is precursor to a synthetase-tRNA encoding reaction with specificity. Other early associations may be precursors to, e.g., the ribosomal RNPs. A designed viral version of a similar process is in Butterfield et al. (2017).



### Specificity

Encoding of "letters" is the first instance of biological specificity, which makes possible the construction of genetic sequences that specify structures and functional attributes. Encoding is the result of a long evolutionary development of an association between a protein – a (proto)synthetase – and its substrate (proto) tRNA (Figure 6.2).

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*Figure 6.3* Decoherence by intromission of mRNA and decoding at ribosomal protein synthesis. The mRNA is a chain of contiguous triplet codes (codons) that are decoded by the anticodons of tRNAs, inside ribosomes. The synthetase reaction and the movement of the ribosome along the mRNA are unidirectional. Evolution of codon contiguity required various torsions and curvatures in the components to reach adequate topological fitting.



The iterative cycles of association reach specificity at some dynamic plateau of the process that is called "cognitive"; the members in the association become cognate to each other. The protein activity is initially (proto)tRNA binding that evolves into an enzyme that attaches its other substrate, an amino acid, to the (proto)tRNA. In the aminoacyl-tRNA that is formed, the tRNA becomes a carrier of the amino acid that can be transferred to a growing (nascent) peptide or protein. Only after "knowing" how to work with the "letters" (tRNAs and amino acids) could cells start the process of enchaining them into organized sequences that can be decoded (Figure 6.3). A designed version of a similar but viral-like associative process has already been proposed (Butterfield et al., 2017). Our proposal is to start with proto-tRNAs that make proteins, which, in turn, coat the proto-tRNA, thereby building a ribonucleoprotein (RNP) system. This evolves into a cognate functional ensemble. The object envisioned as being at the early state of the process – an RNP globule – may be similar to RNP granules, stress granules, and P-bodies (Hughes et al., 2018; Treeck et al., 2018). A generic demonstration of specificity is the homochirality in biopolymers. It is required that amino acids in proteins are homogeneous with respect to the "handedness" (hand, in Greek: keir) of their structures, in the sense that our hands match one against the other but do not match when superposed. Another analogy is with the movements of clock hands: clockwise means right-handed, counter-clockwise left-handed. The chiral property of amino acids is related to the complexity of the alpha-carbon (the central lower case **c** in the oval amino acid symbol in Figures 6.1 and 6.2). This carbon is simple in glycine, which is non-chiral, but complex in serine, which is left-handed like all other protein amino acids. Conversely, all nucleic acid sugars are right-handed. This property reflects the strict enzymatic requirement for precise and specific 3D-fitting between catalytic pockets and substrate shapes. This homogeneity would be better than mixtures of different 3D structures, possibly guaranteeing speed, smoothness, and repetitiveness in all steps of molecular interactions, thereby being an adequate and necessary participant in the flow dynamics. A useful image is that of the common toboggan-like helical structures of biopolymers; these would be kinky and stepladder-like if built from left-handed and righthanded mixtures.

### Protein diversification

A large diversity of cellular structures are directed to guarantee the flow. This starts with an uptake of substrates from the environment and ends with the extrusion of waste into the environment, which is degraded due to both kinds of interference. Environmental modifications are only one among a variety of challenges and stressful conditions that organisms confront from external and internal sources, and which take part in forcing the evolution of the flow

system. The cells can only answer with further diversification. Their resources for this reside in the *plasticity* of their components (less extensive in RNA than in proteins, and even less extensive in DNA than in RNA) and of the network organization. The model for the protocell is that of a spongy RNP granule or globule imbibed in water. The internal/external distinction is maintained in the globule through spontaneous protein motility and binding activities.

## Crowding without saturation

The aggregating forces among components of the "spongy globule" and in development of surface structures (the membrane function) are rudimentary at the start, and only later guarantee resistance to fragmentation and invasion by water. Under such fragile conditions, the globule cannot grow beyond a certain limit, at which point aggregation and surface tension forces are overcome, resulting in chunks being split from the main body and lost. Otherwise, however, these conditions introduce a stimulatory effect on the flow system, based on reduction of the crowding intensity in the globule.

The process is spontaneous, but functions as though the system itself were avoiding saturation from overcrowding and guaranteeing that the protein synthesis activity keeps a steady pace. This spontaneity, in the case of non-living physicochemical events, is documented by Sydney Fox's microspheres and Alexander Oparin's coacervates. Their gemmulation or budding is similar to the oocyte-polar body or the mother-daughter cell associations of budding yeast. This mechanism of losing chunks of protoplasm, now called the shedding of vesicles or exosomes, became regulated in fully developed cells but has the same stimulatory effect.

## Waste

Such spontaneous stimulatory benefit is afterwards combined with the solution of the problem of extrusion of waste so that the chunk-shedding mechanism acquired enriched functionality. Metabolic waste is problematic mostly with respect to nitrogenous compounds. These cannot be transformed into gases and vapor, as happens with hydrocarbon and carbohydrate waste. Nitrogenous derivatives are toxic (ammonia), insoluble (urate), or water-requiring and pollutant (urea). Some amino acids and some proteins are not well reabsorbed by the kidneys and are disposed of.

The problem is greater with some proteins that are most difficult to degrade and cannot be recycled through catabolic processes such as the proteasomal and the lysosomal-autophagic. Degradation intermediates may include indigestible remnants that form entangled aggregates. These may be toxic to cellular organization, especially via the exposition of the unprotected internal hydrophobic protein cores, finally forming amyloid grains and plaques. The solution was

their shedding as chunks accommodated in vesicles. These associated benefits are at the origin of the ubiquitous cellular character of shedding vesicles and exosomes.

Exosome multifunctionality includes, through the loss of biomass, the beneficial effect of the protein synthesis sink stimulation, regeneration, and replacement of lost aged material by renovated materials, and the corresponding structures and functions. The stimulatory mechanism is analogous to that obtained from tree pruning.

Extracellular vesicles and exosomes are also seen as communication vehicles that cells utilize for transport of macromolecules inside multicellular bodies, and can be utilized in medical "liquid biopsies" for diagnosis. Intracellular accumulation of protein tangles is seen as a possible causative agent of various diseases, including Alzheimer's and other (mainly neurological) conditions. The SRM is the first model of the code to consider 3D protein construction pathways - the 3D folding rules - among the tests and components of its structure. Correct folding is important not only for the construction of the native or functional architectures but also for guaranteeing the proper degradation of the proteins without accumulation of toxic intermediates. Empirical data - the N-end Rule – describes which amino acids contribute to protein resistance to degradation, that is, those with the correct folding when placed at their amine-ends. Nascent peptides without the adequate conformation, bearing destabilizing amino acids at the N-ends, are directed to quick degradation. This property shows that the code has a circular structure: initiation and termination codes are the last to form and are dictated one by the other, producing an "informational closure" that is also material.

## Reproduction

The cost associated with such losses of protoplasm were partially circumvented when some of the shed chunks received portions of the genetic memories and became daughter cells. This marks the beginning of the evolution of reproductive cycling: losses turned into regulated protoplasmic fission with an inclusion of genomes. Cells acquired the properties of (1) potentially perennial activity of the protein synthesis sink and (2) the installation of the Darwinian process. Reproduction accomplishes various functions: it avoids wasting some of the extruded pieces, such as the vesicles; it guarantees continuity of the individual self-maintenance flow; it is generic-nonspecific, driving the whole individual chain of flow, and installs the population-evolutionary open-ended flow. Cells that reach large sizes (such as in the G2 stage of the eukaryotic cell cycle) run the risk of having protein synthesis reduced/inhibited due to mass-action or saturation-induced repression. In consequence of the benefits of releasing them from the inhibition and maintenance of activities that contribute to health and productivity, exosome extrusion became regular and obligatory.

This is equivalent to the cytoplasmic fission in cell reproduction. This stage was reached when sets of genetic memories – genomes – were added to the chunks of cytoplasm being eliminated, these becoming daughter cells. The original function of the first phase in the reproduction process – cytoplasm fission – is that of regenerating protein synthesis activity, while the second function was that of rescuing the cytoplasm portions from loss by becoming daughter cells. Bacteria that have had the walls peeled off, L-forms, bear an exposed fragile membrane, and the formation of exosomes is easily observed. In some of these, genome inclusion is found, showing that this is a primitive form of reproduction. Furthermore, it was seen that cell reproduction may be asymmetric with respect to the inclusion in only one of the daughter cells of an "inclusion body", which contains the tangles of damaged and undigested proteins clumped together. This is a simple way of producing healthier lineages, free from the tangles (germ-line analogs) and separated from the less healthy lineages (somatic line analogs).

## Behaviors focus on the extremities of the flow system

Understanding cell reproduction as a beneficial by-product of protoplasm loss is another instance of "informational closure". Evolutionary populations are formed when the Darwinian open-ended process is installed; whenever reproduction is active, the protein synthesis activity may be never-ending. The main environmentally open behaviors, the most evident "vital force" manifestations, are at the extremes of the flow process: nutrition, which feeds the protein synthesis sink, and reproduction, which pulls the sink downstream and keeps it active nonstop. Intermediate mechanisms are internal and organic and may go unnoticed by organisms or external observers, as they are mostly hidden to the organic senses and to the conscious feelings of individuals. The work presented here is dedicated to clarifying these internal and not readily accessible drives.

#### **Realms of the flow**

The general idea of the flow is not new, but we add a plausible rational explanation for it, spanning from the entropic universe to the origins of life and to reproduction. The internal drive mechanisms, often not apparent to most observers, are clarified. In medical genetics, the idea of flow is essential to the concept of the inborn errors of metabolism, and we propose that medical science attempt to verify how the flow concept can be applied interestingly to all disease categories and classifications. In the Darwinian account, the reproductive flow is measured as adaptive fitness. We will now pinpoint its centrality to protein synthesis at the cellular-unit level, and generalize the flow concept for all realms of biology.

#### Cognitive convergence

As previously mentioned, the most salient aspects of the organismal flow dynamics, with stronger appeal to the general observer, are (1) the relational and interactive behaviors, at the openings of the metabolic mechanisms to the environments, mostly at the uptake domains, that is, nutrition and feeding, and (2) the reproductive drive. The psychological counterparts are the obvious ones - desires, impulses, and drives for food and sex - that are consistently accommodated together with the cellular basis. Such convergence may mean more than just coincidental final results of investigations. The mutual fit indicates that our minds should follow tendencies or biases in favor of repetitions of mechanisms, that is, of the application of the same or similar explanations in a diversity of realms. According to the view presented here, the background to this constancy is engrained in the natural selection mechanisms, which are continually forcing the adjustments and adaptations between organisms/observers and environments/objects of interest. Our minds are biased in this unidirectionality; in the ethological and psychological realms, this would be reflected in certain "cognitive architectures" of minds, configured like some kind of the Jungian archetypes, that is, as modes of apprehension of experiences. Evidence for these converging routes have arisen repeatedly during our studies, intriguingly enough to raise suspicions of some kind of constraints or directedness/limitations to reasonings or creativity. The initial protein conformations indicated by the SRM were the intrinsically disordered segments. This is consistent with the quantum mechanical rationale that their primal objects - wave packets - are also disordered. In both cases, the order, reflected in informational patterns, would arise at the interaction of entities. The same mechanism shows up in very different realms of study, and different approaches often find a way of fitting together. It seems that our minds can only be relaxed, pleased, and happy, when some kind of "informational closure" is reached; the alternative would allow for sustaining instabilities and loose ends in the lines of reasoning that would create or maintain intellectual tension. Another closure was reached at the formation of the initiation and termination mechanisms at translation of mRNA. The entire set of elongation codes was formed utilizing a "primitive punctuation system" based on the higher metabolic stability of the protein head segments and the lower stability of the tail segments. The last codes were the specific punctuation: adding one specific anticodon for initiation made the system immediately delete the anticodons that were in conflict with the initiation, whose codon complements became the terminators. In favor of this convergence, there is also the highly prevalent (and justifiable,

within the scientific community) principle of parsimony, which states that multiplicity in the composition of explanations is acceptable only when there is compelling evidence. In situations where evidence is lacking, the

principle of simplicity becomes a methodological must. Parsimony reigns, but the propositions based solely on this principle are challenges for the attempts of experimentalists.

## Coherence-decoherence

The DDPS process (Figure 6.1) has some peculiarities that are worth being analyzed in themselves and compared with the ribosome- and mRNA-directed processes (Figure 6.3). The (proto)tRNA associations are dynamic, via hydrogen bonding, and may generate different states:

a States complementary to other (proto)tRNAs, forming the dimers and opening the route to the DDPS (Figure 6.1);

b States complementary to other RNAs, which may open the route toward translation of mRNA;

c States with binding to proteins, which inaugurates the RNP associations such as the ribosomal associations and the evolution of the aminoacyl-tRNA synthetases for encoding (Figure 6.2).

The state in Figure 6.1 is called *coherent* or *superposed*, following the terminology of quantum mechanics. The proto-tRNA components are simple, singular, and of the same kind – that is, mutually equivalent – and, therefore, presenting undecided identities and functions: (1) the transferase activity is adirectional or bidirectional, the donor or acceptor functions are interchangeable. Any of the partners may serve the aminoacyl- or peptidyl-carrier functions, and may exchange the functions in each round of the realization of the transferase function, which is a job of the joint pair; (2) the codon and anticodon functions are also interchangeable, coding and decoding being the same. This would have been the only state present at the initial encoding, during the primordia of the formation of early protocell populations.

In the quantum realm, the components of wave packets in a coherent or undecided state may probabilistically produce the classical wave or the particle states (and associated properties) after going through the interactions that lead to decoherence, including those that are part of the detection or measurement processes. States (b) and (c) (see Figures 6.2 and 6.3) are decohered, and each (proto)tRNA may acquire individuality as "classical" components of the cellular translation machinery. The transition from the DDPS to the ribosome- and the mRNA-directed state would involve the intromission of two decohering interactions: one with state (c), the peptide products of the DDPS that may be heterogeneous and able to bind differentially to the oligomers (Figure 6.2); and another with state (b), the entry of another (proto)RNA in the place of one of the members of the dimer, which would be taking the role of the classical mRNA (Figure 6.3).

## Three singularities

The explanatory similarity may be extended even more, to reach the third great division of the knowledge of nature, cosmology, which utilizes the same terminology of singularity. Life and quantum mechanics have already been commented upon. All are described by us, the observers – reflexively, in a fourth realm. In the micro-world, the quantum objects – wave packets – are difficult to describe, almost intangible, and are said to be of undecided (superposed) identity. The interactive events that gave origin to the conversion into the classic wave or particle – with probabilistic distribution – are said to produce decoherence or to detach one from the other component(s) that are no longer superposed.

In the macro-world, there would have been a primeval singularity. A very dense and hot object became unstable by itself – of course, there was nothing else with which it could interact – and entered a process of expansion, the Big Bang. Space was extended in between the wavicles, particles and waves. It started a trajectory of progressive cooling, with degradation of different kinds of energy – from the highly dense, e.g., photons, to the less dense, e.g., heat. At some intermediate point in this evolution, living beings appeared. It is tempting to suppose that the two primeval singularities, the micro and macro cases, would share some characters. There are other names to describe the idea whose basic character is that of some kind of primeval association between distinct states which, submitted to some not well-defined interference, dissociate into our good old classic states. In our cultural traditions, these are the oriental yin-yang complementarity, and the original symmetry plus symmetry-breaking events in physics.

Then enters the third singularity: the proto-tRNA dimer that is supposedly a proto-ribosome and the initiator of the primeval cellular entity. Its dynamics shares various similarities with the singular states of the entities in both of the preceding physical realms. It took us almost a decade to realize how similar the proto-ribosome model was to both of the physical models.

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