The IdEP-IdLA model and the biochemistry of aggregative processes: the Arianna's conjecture

Le modèle IdEP-IdLA et la biochimie des processus agrégatifs : la conjecture d'Ariane

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ABSTRACT. In previous works an exhaustive description has been obtained of the aggregative processes to which the ideal system described by the so called IdEP-IdLA model can be subject both in closed conditions (at equilibrium) and in open conditions (far from equilibrium). The model has shown such a thermodynamic coherence that it can be used for a theoretical study of real processes. The aim of this work is therefore to try to transfer the results obtained to the biochemical field: in particular, we here propose to investigate whether the model is able to contribute to define probabilistic requirements to which biogenesis must be subject. The reasoning leads to conclusions largely in line with the state of the art on this topic but, at the same time, opens the way to a completely innovative conjecture: the possibility that some phenomena can be supported by an information flow that proceeds according to an inverted time arrow. This is the Arianna's conjecture.[1]

RÉSUMÉ. Dans des travaux antérieurs, une description exhaustive a été obtenue des processus d'agrégation auxquels le système idéal décrit par le modèle dit IdEP-IdLA peut être soumis à la fois dans des conditions fermées (à l'équilibre) et dans des conditions ouvertes (loin de l'équilibre). Le modèle a montré une cohérence thermodynamique telle qu'il peut être utilisé pour une étude théorique de processus réels. L'objectif de ce travail est donc d'essayer de transférer les résultats obtenus dans le domaine biochimique: en particulier, nous proposons ici d'étudier si le modèle est capable de contribuer à définir les exigences probabilistes auxquelles doit être soumise la biogenèse. Le raisonnement conduit à des conclusions largement en phase avec l'état de l'art sur ce sujet mais ouvre en même temps la voie à une conjecture tout à fait innovante: la possibilité que certains phénomènes puissent être soutenus par un flux d'informations qui procède selon une flèche inversée du temps. C'est la conjecture d'Ariane.[1]

KEYWORDS. Entropy, Mathematical modeling, Aggregative processes, Markov sources, Chance and necessity, Open systems, Dissipative structures, Biogenesis.

MOTS-CLÉS. Entropie, Modélisation mathématique, Processus agrégatifs, Sources de Markov**,** Hasard et nécessité, Systèmes ouverts, Structures dissipatives, Biogenèse.

1. Introduction

The results obtained in previous papers [Ref.1, Ref.2, Ref.3] encourage us to try to use the IdEP-IdLA[2] mathematical model in the biochemical field. In particular, we intend to investigate the relationship between the various aggregative dynamics studied by the model and the formation of the first molecules, useful for life. This is still an open topic and it seems appropriate to investigate whether and to what extent the use of the model can suggest some answer to this fundamental question or, at least, address speculation in some way.

The initial appearance of life on Earth still does not have a sure explanation: many hypotheses are available, but fewer experimental findings and no organic picture which is shared by the scientific

[1] In Greek mythology, when Theseus entered the labyrinth to kill the Minotaur, Arianna, daughter of King Minos, gave him a ball of wool with which he marked his path and he could thus retrace his steps from that place from which no one had ever safely returned.

[2] IdEP stands for *Ideal Elementary Particle*; IdLA stands for *Ideal Linear Aggregate.*

community. Science has been able to reconstruct in a precise and reliable way the first moments of the universe, which no one attended while, on the contrary the appearance of life, which affects so closely our world and ourselves, is not yet explained in any convincing way. The same is true for biological evolution, whose dynamics is only partly explained by the Darwinian paradigm that, at least in its most orthodox form, is considered unsatisfactory by a large number of scientists.

The aim of this work is therefore to analyze the exportability of the results obtained in the aforementioned publications to the world of biochemical aggregations and to study which aggregative mode, among those explored, are best suited to describe the first emergence of life; if any.

For this purpose, it will be useful to briefly summarize the structure of the model and the general results obtained.

1. References to the IdEP-IdLA model

The IdEP-IdLA model is based on the following reaction whereby one mole of reactants produces one mole of products:

$$\alpha XO^* + (1-\alpha)O \leftrightarrow \sum_{\lambda=1}^{\Lambda} \nu_{O\lambda}\, O^*_{\lambda-1}O + \alpha X \qquad [1]$$

where:
- α is the molar fraction of the *giver compounds*
- XO^* are the giver compounds consisting of one IdEP X, called the *grey particle*, and one IdEP O^* of ζ_{O^*} different colors, called the *active primary particle*
- O are the free IdEPs, called *passive primary particles*, of ζ_O different colors
- $O^*_{\lambda-1}O$ represents the generic IdLA of *length* λ (with Λ = maximum value of λ) variously composed of $\lambda - 1$ active primary particles and a single passive primary particle at the end of the sequence
- $\nu_{O\lambda}$ is the molar fraction of IdLAs of length λ.

All IdEPs (O, O^* and X) are also assumed to have the same inertial characteristics even if of different colors. The aggregative process is driven by a coupling code between primary particles that affects entropy through a single parameter: the *coding factor* η, ranging from 0 to 1 so that

- when $\eta = 0$, the coupling between primary particles is completely *random*
- when $\eta = 1$, the coupling sequence is *mandatory* (reaction products are fully determined)
- when $0 < \eta < 1$, the coupling sequence suffers probabilistic conditioning.

If the aggregation develops as a consequence of binding energies (described by a specific matrix) between IdEPs, the process is called *autopoietic*: in particular the random aggregation can only be autopoietic, with the matrix of binding energies formed by identical elements. Instead, we speak of *heteropoietic* aggregation when the coupling between primary particles is guided by *ordering agents* external to the system. These entities are able to impose their own coupling code, in spite of the natural autopoietic inclination dictated by the matrix of binding energies.

In any case, the breaking of bonds holding together a mole of giver compounds implies the absorption of energy E_b from the environment. At the same time, the formation of bonds in a mole of newly aggregated IdLAs involves the transfer of energy E_f to the environment. Evidently if the *molar energy balance* $\Delta E = \Delta E_b - \Delta E_f$ is negative the reaction is exothermic while it is endothermic if the balance is positive.

Thus defined the chemical-physical context in which reaction [1] takes place, if the reaction environment is closed (but not insulated), the imposition of constant temperature and pressure conditions allows us to calculate the fundamental thermodynamic functions depending on the extent of reaction ξ. Therefore, the aggregative process can be characterized in terms of reaction entropy ΔS_R, reaction enthalpy ΔH_R and reaction free energy ΔG_R. The results obtained show that:

- the extent of reaction at the equilibrium ξ_0 is the higher the more *energetic* the reaction is (i.e. ΔE more negative and α higher).[3]
- entropy $S(\xi)$
  - does not depend on ΔE
  - is the higher, the higher the IdEP inertial characteristics (summarized by *allocation inertia* ρ)[4]
  - decreases when η increases[5]
  - always has a maximum[6]
- free energy $G(\xi)$
  - depends on ΔE, because $H(\xi)$ depends on ΔE. In particular its values are lower the more exothermic the reaction is
  - is the lower the more *energetic* the reaction (i.e. ΔE more negative and α higher)[7]
  - increases when η increases[8]
  - presents a minimum for low-energy reactions (ΔE small negative and low value of α)[9]
- reaction entropy ΔS_R
  - depends on ΔE to the extent that this affects the extent of reaction at the equilibrium ξ_0. It no longer depends on it when the reaction is so energetic to be complete[10]
  - does not depend on the IdEP inertial characteristics
  - decreases when α increases in exothermic reactions[11]
  - decreases when η increases[12]
- reaction free energy ΔG_R
  - depends on ΔE. In particular, it is the lower the more exothermic the reaction is[13]
  - does not depend on the IdEP inertial characteristics
  - increases (in absolute value) when α increases in exothermic reactions[14]
  - decreases when η increases[15].

[3] See Figs.7 and 13 in Ref.2.

[4] See Fig.5 in Ref.2.

[5] See Fig.12 in Ref.2.

[6] See figures mentioned in notes 3 and 4.

[7] See Figs.10 and 13 in Ref.2.

[8] See Fig.13 in Ref.2.

[9] See Figs.7 and 13 in Ref.2

[10] See Figs.9 in Ref.2

[11] See Fig.9 in Ref.2.

[12] See Fig.17 in Ref.2.

[13] See Fig.10 in Ref.2.

[14] See Fig.10 in Ref.2.

The results also show that in the case of heteropoietic aggregation, the ordering agents must necessarily be the seat not only of the code guiding IdEP combinations, but also of a *compensatory heat dissipation*, that is the dispersion into the environment of an additional amount of heat δH is necessary in order to counterbalance the entropic gap σ (*addressing entropy*) due to the higher level of order in the reaction products. Fig.1 proposes the comparison between the energy development of a system that evolves along an autopoietic aggregative path and the energy development of the same system to which external ordering agents impose a heteropoietic aggregative process with a higher coding factor. It is evident that, in the case of heteropoietic aggregation, only the so-defined *enlarged system* (reactants + ordering agents) offers the possibility of producing the necessary addressing entropy through the compensatory dissipation of a heat quantity at least equal to δH:

$$\sigma = -\frac{\delta H}{T} > 0 \qquad [2]$$

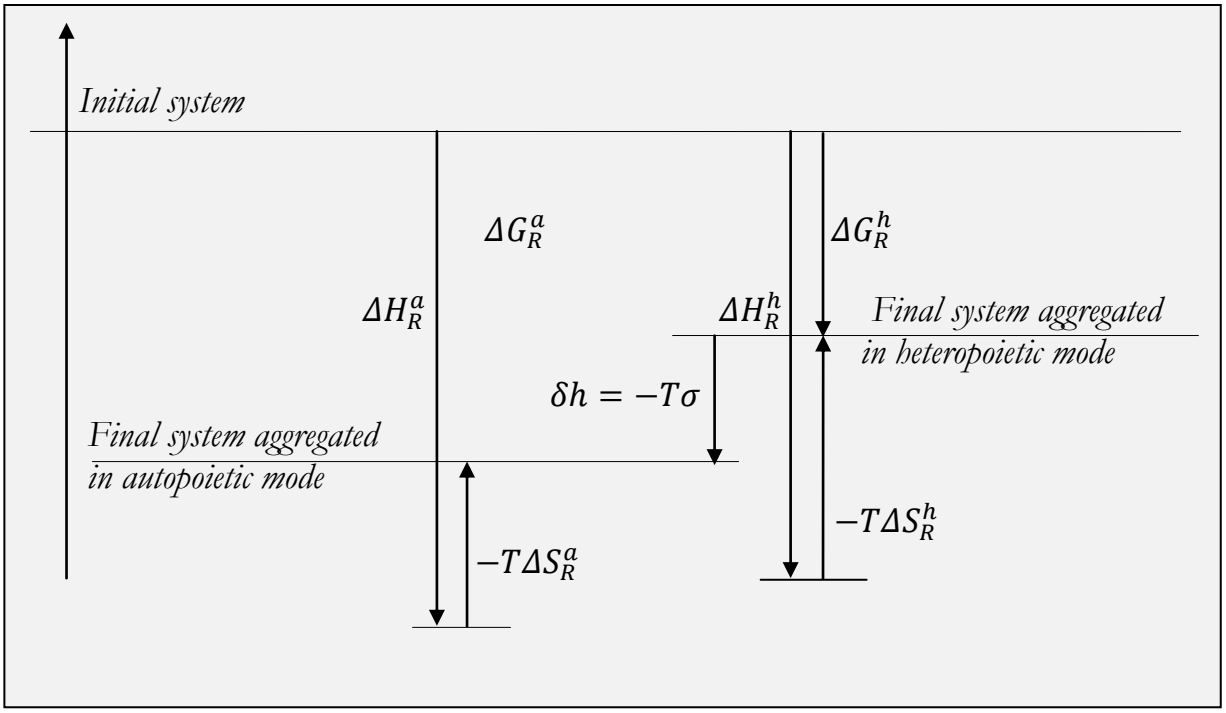

Figure 1. *Qualitative comparison between the energy development of the same system following autopoietic and heteropoietic aggregative processes.*

This is actually the only way to make the entropic balance consistent with the second principle of thermodynamics.

If the system is open and exchanges energy and matter with the environment at constant temperature and pressure, the model allows us to calculate entropy production $d_i S/dt$ far from equilibrium as a function of material flow φ and rate constant k.

[15] See Fig.13 in Ref.2.

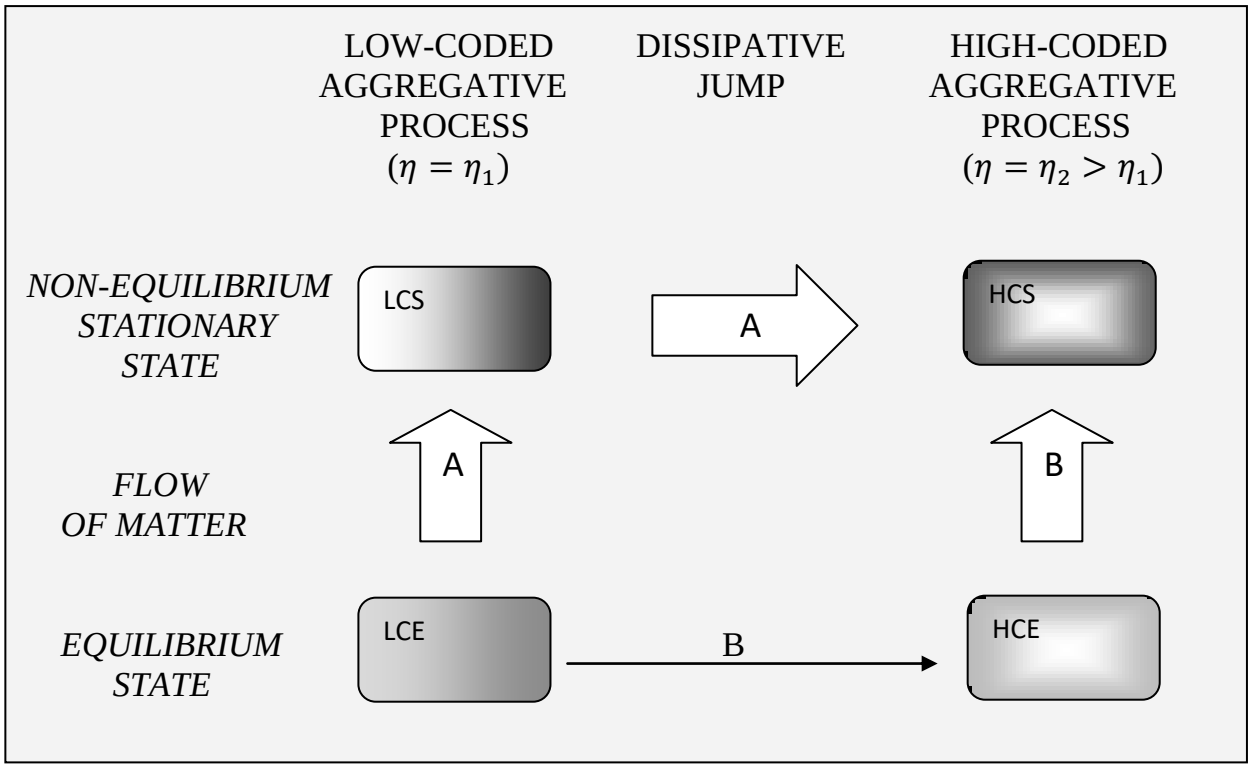

Figure 2. *Transition between contiguous states.*

The results show that:

- in stationary conditions close to equilibrium[16]
  - entropy production d_iS/dt due to irreversible internal processes equals entropy variation d_eS/dt due to thermal and material flows
  - the aggregative process develops according to a succession of internal states such as to minimize entropy production d_iS/dt
  - the extent of reaction ξ_τ of reactants and products mixture that continuously comes out of the reference volume V is all the lower with respect to the extent of reaction at equilibrium ξ_0 the smaller the product $k\tau$, where k is the already mentioned rate constant and $\tau = 1/\varphi$ is the average time of permanence of reactants in V. Moreover, when ξ_τ gradually decreases, the value of A/RT (A=affinity; R=gas constant; T=absolute temperature) gradually increases to indicate that stationary conditions are less and less stable
- far from equilibrium[17]
  - when instability conditions are reached and thanks to a possible *dissipative jump*, the system can find a new stationary state characterized by a higher level of order and, at the same time, by a higher entropy production
  - for this to happen, when (and if) the dissipative jump occurs the material flow must increase a lot. At the same time it is necessary that the molar energy balance does not change (or decrease only a little in absolute value) and that the rate constant increases appreciably
  - before the dissipative jump, the aggregative process must be of the random or quasi-random autopoietic type. Afterwards it can only be of the heteropoietic type, thanks to the action of external ordering agents, only activated on occasion of the jump and also performing a catalytic function.

[16] See Ref.3, paragraphs 1 and 2.

[17] See Ref.3, paragraph 3.

Related calculations have been developed using the *principle of retro-equivalence*. With reference to the scheme in Fig.2, the retro-equivalence principle assumes that the dissipative jump, leading a system from the stationary state of a low-coded aggregative process (LCS state) to the stationary state of a high-coded aggregative process (HCS state), can be simulated by moving an appropriate system characterized by high-coded aggregative process (HCE state) from equilibrium. That is, path B is equivalent to path A.

2. The model's dependability

In view of the use of the IdEP-IdLA model in the biochemical field, it is appropriate to recall the assumptions on which the theoretical pattern is based and assess whether and to what extent such assumptions may be limiting the usability of the results.

1) The model has been developed using formulas that describe the thermodynamic behavior of matter in the gaseous state. In reality, the processes of biological interest take place mainly in the liquid phase, even if important reactions in the gaseous phase are far from negligible[18]. In any case, the assumption reinforces the role of entropy in thermodynamic transformations and accentuates its contribution to Gibbs free energy without compromising the quality of results.
2) The Markovian expression of entropy[19] is based on the hypothesis that the number of allocation cells is much greater than the number of particles examined. In fact, the calculations were carried out assuming values of IdEP allocation inertia ρ ranging from 10^{-83} to 10^{-81} $\mathrm{Kg}^{5/2}\mathrm{m}^2$. The consequent space splitting, under standard temperature and pressure conditions, provides a number of allocation cells that exceeds the number of particles by a minimum of 1.400 to a maximum of 140.000 times. Most of the calculations were carried out with $\rho = 10^{-82}$ $\mathrm{Kg}^{5/2}\mathrm{m}^2$. Such a value ensures a ratio between particles and allocation cells of 1/14.000. With more reason, the condition of validity of the Markovian expression of entropy is respected for IdLAs, which are characterized by values of ρ getting bigger and bigger as the length of the aggregates increases.
3) Ideal elementary particles (IdEPs) are supposed to be linear and homogeneous: it is therefore assumed that, with respect to the three directions of space, they have two equal barycentric moments of inertia while the third is null: hence, they are much more than a simple material point even if much less than a generic three-dimensional particle. However, with a minimum of parameters involved, they allow both to take into account a rotational contribution to entropy (totally absent in dimensionless particles) and to produce the precondition for creating geometrically defined aggregates. The extreme values of allocation inertia ρ used in the calculations (10^{-83} and 10^{-81}) are matched by particles ranging from $\mu \approx 0{,}5\ 10^{-25}$ Kg (nearly 30 atomic units) to $\mu \approx 2{,}0\ 10^{-25}$ Kg (nearly 120 atomic units) and from $\delta \approx 10^{-10}$ m (typical distance between two contiguous atoms) to $\delta \approx 5\ 10^{-10}$ m (order of magnitude of a medium sized aggregate)[20].
4) IdEPs are supposed to have a rigid frame. This implies that they cannot be affected by vibrations: therefore, the contribution to entropy due to different modes of internal vibration is null.

[18] Among these, reactions that are supposed to be at the basis of the formation of molecules of biochemical interest, in accordance with the reconstruction of primordial scenarios.

[19] $S = \frac{5}{2}RlnT + R\left[ln\frac{V}{n_A} - lnv^* + 1 + h\right]$ where R is the Boltzmann constant, T is the absolute temperature, V is the volume, n_A is the Avogadro number, v^* is the volume of the *allocation cell*, h is the entropy of the *population descriptor*. This formula expresses the entropy of a gaseous mixture whose composition is described by a Markov no-memory information source (See Ref.1).

[20] In terms of composites, such intervals cover objects ranging from diatomic molecules to organic molecular groups such as amino acids.

But at the temperature level taken into account (standard temperature of 25°C) the hypothesis does not introduce appreciable errors.

5) IdLAs also have a linear, homogeneous and rigid structure. Such a schematization is significantly different from any real aggregate but it allows an algorithm able to calculate univocally their inertial characteristics for any length and allows the generalized use of the Markovian expression of entropy.
6) The number of different colors of primary particles (passive as well as active) varies quite widely in calculations. Entropy of the descriptors ranges from 1 to 2: most of the calculations have been carried out with entropies equal to 1,5 which means 5 colors with $\gamma = 1$ (i.e. equal probability of colors), 7 colors with $\gamma = 0{,}8$, 12 colors with $\gamma = 0{,}6$, 42 colors with $\gamma = 0{,}4$. These values have the same order of magnitude of the different types of elements that form remarkable organic chains.[21]
7) The specific heat at constant pressure of both reactants and products is calculated on the basis of the hypothesis of energy iso-distribution on 5 degrees of freedom ($c_p = 7/2R$). The validity of this assumption is experimentally confirmed only for linear molecules with a mass comparable to that of the smallest IdLAs but there is no reason not to consider it applicable also to most massive IdLAs.
8) Values of molar energy balance taken into consideration range from -60 KJoule/mole to $+20$ KJoule/mole. Most of the calculations were carried out with $\Delta E = -20$ KJoule/mole, mainly in order to make the model's response evident in the case of incomplete reactions. It must be considered that, in general, binding energies range from approximately 0,04 eV (i.e. 4 KJoule/mole) for Van der Waals forces, to 0,2–0,5 eV (i.e. 20–50 KJoule/mole) for hydrogen bonds, to 1,5–9,4 eV (i.e. 150–940 KJoule/mole) for covalent bonds. Among the latter, binding energies of single bonds range from 155 KJoule/mole for the F–F bond to 459 KJoule/mole for the O–H bond, while bonds such as Cl–Cl, C–N, C–C, C–H, H–Cl, H–H, have intermediate molar formation energies. Therefore, as far as covalent bonds are taken into consideration, the value of -20 KJoule/mole assumed for molar energy balance in calculations means that the binding energies in giver compounds are supposed not to be much lower than binding energies holding primary particles together in IdLAs[22].
9) From a kinetic point of view it is assumed that reaction [1] is of the first order: that is, the velocity of reaction is proportional to the concentration of giver compounds. Apart from the fact that this is one of the most common kinetic schemes, it must be remarked that the aim of the model is to attribute a value to the extent of reaction ξ_τ of the mixture coming out from volume V (always lower than ξ_0) in order to obtain numerical results. Any different relationship between the concentration of reactants and rate of reaction would in any case lead to quantitatively different but qualitatively similar results. In particular, the scheme in Fig.1 would not be substantially different.

In the light of the above considerations, the results obtained in Ref.1, Ref.2 and Ref.3 can be considered fit for biochemistry. Furthermore, these results are in line with what is expected from the thermodynamics of both equilibrium and non-equilibrium states for a reaction such as the one represented in [1]. The model in fact:

- at the equilibrium, gives reason for the incompleteness of some reactions, indicates the causes and responds correctly to the sensitivity analysis

[21] For example, 4 for nucleotides forming nucleic acids or 20 for amino acids polymerizing in proteins.

[22] Actually, this is the order of magnitude of the energies involved in the formation of bonds necessary for building important organic compounds such as proteins (peptide bond), nucleotides (ester bond) and nucleic acids (phosphodiester bond).

- in stationary non-equilibrium conditions, presents an entropy production, due to internal aggregative processes, that always balances the variation of entropy due to thermal and material flows. It also matches the principle of minimum entropy production
- far from equilibrium, convincingly describes dissipative structures.

In conclusion, the model, in its simplicity, can be taken as emblematic of the way in which, starting from poorly organized material and by virtue of the laws of physics, biocomplexity arises. In particular it seems possible to use it as a tool for theoretical investigation of the most unclear aspect of biocomplexity: its first emergence, that is *biogenesis*. This is what we intend to do, but not before having measured, in probabilistic terms, the ability of an aggregative code to give rise to fruitful results.

3. The ordering power of coding

Let us suppose that a given IdLA has a special importance for the origin of life. We assume, for example, that a particular sequence of IdEPs represents one of the fundamental prebiotic structures, leading to self-replication. We call such a special IdLA a *target structure* and we indicate with P_η the probability of finding target structures among the IdLAs that are formed as a consequence of a generic aggregative process, characterized by the coding factor η. The number N_η of such an IdLA produced by one mole of reactants is therefore

$$N_\eta = P_\eta(1-\alpha)n_A \qquad [3]$$

Let us also suppose that the target structure is an aggregate of length L consisting of a succession of $(L-1)$ O^*-type IdEPs of ζ_{O^*} different colors (with $\zeta_{O^*} \leq L-1$) closed by one O-type IdEP of a single color ($\zeta_O = 1$). Values of P_η and N_η can be easily calculated in the limit cases of mandatory aggregation ($\eta = 1$) and of random aggregation ($\eta = 0$). If $\eta = 1$ and only a single type of aggregate is systematically produced, we have

$$P_1 = 1 \qquad [4/a]$$
$$N_1 = P_1(1-\alpha)n_A = n_A(1-\alpha) \qquad [4/b]$$

where the length L of the unique target structure is necessarily linked to α by the following relationship[23]:

$$L = \frac{1}{1-\alpha} \qquad [5]$$

In the opposite limit case, in which a system defined by the same population descriptors (supposed to be iso-probable for ease of calculation) produces aggregates in a random mode, the probability of finding target structures and the total number of them is, for [5]:

[23] See [21] in Ref.1. Actually, the sequencer could also impose an aggregation rule not coherent with this relationship and therefore produce target structures of different lengths from L. In this case, however, at the end of the reaction an excess of giver compounds or an excess of inactive primary particles would occur. In both cases we can easily restore compliance with [5], by considering the residual fraction not taking part in the reaction as virtually inert: this fraction is actually forced into inertia by the power of the sequencer. The system thus reduced is formed by a number of reactive particles necessarily lower than n_A but characterized by a new value of α fully consistent with [5]. The calculation based on a mole of reactants where α and L are linked by [5] is therefore not lacking in generality.

$$P_0 = \left(\frac{\alpha}{\zeta_{O^*}}\right)^{L-1}(1-\alpha) = \left(\frac{\alpha}{\zeta_{O^*}}\right)^{\frac{\alpha}{1-\alpha}}(1-\alpha) \quad [6/a]$$

$$N_0 = n_A\left(\frac{\alpha}{\zeta_{O^*}}\right)^{\frac{\alpha}{1-\alpha}}(1-\alpha)^2 \quad [6/b]$$

If we are interested, as we are in fact, in the production of long chains, then α concentration of giver compounds must be very high. The table in Fig.3 shows the values of N_1 and N_0 for different values of α (and therefore of L) and for different values of ζ_{O^*}[24].

Although a very wide range of possible intermediate scenarios can exist between the two extreme cases, we can assume the following statement as valid: starting from the same initial system and all other conditions remaining unmodified, the aggregative process with a higher coding factor not only generates a more ordered IdLA population (i.e. with lower entropy) but can also produce a larger number of target structures. This is all the truer the longer (and therefore more complex) the target structure is. On the other hand, as already pointed out, it is precisely these structures that we are interested in, as possible promoters of life. The table in Fig.3 therefore demonstrates that we must necessarily resort to some form of coding in order to obtain target structures of fruitful length (from a prebiotic point of view) and in non-negligible quantity. The sequencer must consequently operate with a very high coding factor η (as close as possible to 1) and produce limited types of aggregates (better if a single one).

α	L	ζ_{O^*}	N_1	N_0
0,909	11,0	2	5,47E+22	1,87E+18
		5		1,96E+14
		10		1,91E+11
0,952	21,0	2	2,87E+22	4,88E+14
		4		4,62E+08
		5		5,32E+06
		10		5,04E+00
		20		4,78E-06
0,968	31,0	2	1,95E+22	2,25E+11
		5		2,69E-01
		6		1,14E-03
		10		2,58E-10
		15		1,37E-15
		30		1,31E-24
0,980	51,0	2	1,18E+22	7,53E+04
		5		9,36E-16
		10		8,20E-31
		25		1,02E-50
		50		8,93E-66
0,990	101,0	2	5,96E+21	1,71E-11
		4		1,34E-41
		5		2,72E-51
		10		2,13E-81
		20		1,67E-111
		50		2,66E-151
		100		2,08E-181

Figure 3. *Comparison between the number of target structures produced by mandatory and random modes of aggregation.*

[24] Values of ζ_{O^*} taken into consideration are submultiples of $L-1$ so that the mandatory formation of a single IdLA of length L from a homogeneous mixture of giver compounds is likely.

4. The model and the biogenesis

In the light of the above conclusion, let us go back to the end of paragraph 3 and try to analyze what kind of information we can deduce from IdEP-IdLA model about biogenesis. The question to arise is: which mode of aggregation, among those examined, can be considered the most promising mechanism for the birth of life?

The initial appearance of life on earth is, as mentioned in the introduction, still a subject of discussion: different branches of science deal with it without reaching satisfactory conclusions. Anyway, overlooking the paths followed by various fronts of research, some fixed elements seem to be sharable:

1) all evidence suggests that the birth of life on Earth was made possible by a natural tendency to the aggregation of elementary entities into more articulated structures
2) after its first emergence, the evolutionary development of life has followed (and still follows) tortuous paths, not without errors and failures: but all of them share the same tension towards a growing complexity of organisms
3) the prebiotic material must have been abundant enough to make possible a great variety of combinations before consolidating fruitful structures by means of self-replication
4) since the molecules that self-replicate or guide aggregative processes, are very evolved, the initial aggregation of inorganic matter can only have occurred spontaneously without the help of external ordering agents.

The first two points express a sort of *law of gradualness* in increasing complexity for which the model is certainly suitable. On the other hand, the model seems to have difficulty in processing the third and the fourth conditions: none of the aggregative modes taken into account is apparently in compliance with them. Let us examine the reason.

First of all, the possibility of entrusting pure chance[25] with the task of promoting life is not acceptable. Results shown in Fig.3 demonstrate that the use of chance can hardly match the third condition: as soon as the target structure is a little more complex (longer and with more differentiated components) the probability of getting it randomly, drops dramatically. Secondly, among the codified aggregative processes, the heteropoietic mode[26], even if able to produce a large number of target structures, is obviously not compatible with the fourth condition. Consequently, only the autopoietic mode remains to be taken into consideration: but even this type of aggregative process does not seem completely persuasive.

[25] Random autopoietic aggregation, as it was defined in Ref.1, represents a practically non-existent scenario in chemistry. It describes a system of reactants in which binding energies are all the same regardless of colors of different species; at the same time, also products are characterized by a unique value of binding energy even if very variously formed. In such conditions all possible couplings between particles have the same probability of occuring. It is certainly a very unlikely scenario, but useful to limit (in terms of maximum possible disorder) the probabilistic range within which the aggregation processes can develop. In any case, it is evident that the production of target structures through random (or at high randomness rate) processes is of very little effect.

[26] Heteropoietic aggregation is much more representative of real processes. In fact, this particular mode of building reaction products can, for example, describe (in a quite appropriate way although very simplified), the formation of nucleic acids whose nucleotides are combined in succession by covalent bonds of phosphodiesteric type. The external agents involved with the model, then, represent the specific enzymes (DNA polymerase, RNA polymerase, DNA ligase) that allow the polymerization and provide the sequencing of nucleotides as carriers of the assembly code. And it is precisely from the chemical interaction between enzymes and substrate (ionic bonds, hydrogen bonds, hydrophobic interactions, Van der Waals forces) that the additional heat dissipation necessary to adjust the entropic balance required by the scheme in Fig.1 emerges. And since enzymes, in addition to sequencing the construction of organic macromolecules, also perform the function of catalysts, the model seems to be able to describe appropriately also the dynamic aggregation in open systems, including dissipative structures.

In fact, attributing the merit of the whole construction of biological complexity to this aggregative mode confronts the arguments against any form of strict determinism. The strong causality underlying this hypothesis implies that matter, starting from its most elementary constituents, contains in itself a long chain of finely differentiated attitudes promoting complexity. Only in this way would it be possible to follow a path that could produce a sufficiently large number of targets (as required by condition 3), regardless of any external help (as required by condition 4). The attitude of privileging the formation of given compounds at the expense of the others should therefore constitute a sort of grammar written in the natural elements themselves. But if this is, in some way, admissible for the formation of basic, organic compounds, it is less and less acceptable as we proceed in biocomplexity; otherwise, we should admit that in the conformation of atoms and in the elementary interactions between them (and between the subatomic particles themselves) a code of exceptional power is already implicit by virtue of which, step by step, life can only thrive as a matter of necessity. A code not only powerful, not only pervasive but also exceptionally targeted because among all the possible codes, matter would be aggregated by following singularly fruitful paths. Let's not forget that among all the possible amino acid sequences very few of them go to form useful proteins. The same is true for the assembly of nucleotides: it is practically impossible to obtain a working nucleic acid if not assembling the base material according to very precise sequences.

It is fundamentally implausible that the enormous variety and even greater complexity of everything living around us, including ourselves, is the result of extraordinarily happy events promoted by a combination of codes that has guided nature for billions of years along paths as creative as complex. In conclusion, autopoiesis is too critical a mechanism to be credible. Even if this aggregative mode correctly represents small scale processes, it cannot alone justify the biocomplexity we observe. On the other hand, the alternative to admitting the extraordinary uniqueness of our physical world is that there are an infinite number of worlds and that we happen to live in the one which, among all possible configurations, has randomly assumed the very one that generated us, thinking beings, capable of reflecting on its nature. It is the theory of the multiverse, which postulates the existence of other universes in dimensions parallel to our own space-time. It is an idea proposed for the first time at the end of the 1950s, that finds some foundation in quantum mechanics and that is a possible consequence of unifying theories such as string theory. However, since such a hypothesis cannot be falsified, it is today rejected by most scientists, relegated among pseudo sciences and even considered as a deleterious suggestion for the achievement of a rational knowledge of the material world.

But if the aggregative dynamic at the basis of biogenesis rests neither on chance, nor on a code implicit in the matter (or a sort of collaboration between these two possible driving forces), then biogenesis itself and with it the entire subsequent evolution remain an enigma. And in fact, the phenomenology of life still presents itself as an arcane, impregnable fortress around whose walls one continues to turn in vain. The question now is: have we really acquired all possible information from the IdEP-IdLA model, or would a more audacious use of it permit us to glimpse a breach through the wall surrounding the mystery?

Then, let's try to admit that, even in the absence of ordering agents, a coded aggregation of the heteropoietic type may exist: a mode of aggregation according to which autopoietic couplings are overcome by a code somehow imposed from outside. Then the question is: can such an aggregative mode find room within the model in a way that is fully in compliance with the physical laws we know and without digressing into metaphysics? Well, perhaps it can.

5. Entropy and the arrow of time

The equations of classical mechanics are all symmetrical with respect to time: in fact they describe phenomena that can indifferently develop both in a temporal direction and in the opposite one. It is not so for the physical phenomena that involve heat exchange: it is generally recognized that the second law of thermodynamics, which postulates the continuous and inexorable increase of entropy in the universe, is the only physical law that implies a precise directionality of time flow. It can even be said that it is precisely the temporal direction according to which the degree of disorder of any isolated system increases irreversibly that establishes the arrow of time. What is less ordered necessarily comes later than that which is more ordered. In an even more radical way, we can argue that when our mind compares two states of the same system it disposes them precisely according to the degree of order that it recognizes by calling *first* the most ordered state and *then* the least ordered one. It is that creation of the mind that somebody calls *psychological arrow of time*.

But an ordered system (low entropy) is a system that needs a lot of information to be described: in other words, it is ordered because a great amount of information is directed towards it. It is exactly the opposite for a disordered system (high entropy) whose poorly specified configuration denotes a low information content. It can then also be said that our perception of time is determined by how we can appreciate the quantity of information contained in the systems in progress. In fact the inequality

$$\Delta S > 0$$

which is at the basis of the definition of time as we perceive it, describes a statistical truth and as such is the expression of our foggy way of reading reality from a macroscopic point of view. At a microscopic level, in fact, all states are comparable and physical processes return to be symmetrical with respect to time or to be described by equations that have the same form whatever the chosen direction of time.

If so, then a process such a heteropoietic aggregation in the absence of ordering agents, which appears to us to be characterized by an uncompensated deficit of entropy, could be interpreted as a phenomenon that takes place in an inverted direction of what we call *time* and therefore, instead of dissipating information, concentrates it: a phenomenon in which, according to our notion of time, effects precede causes.

It would not be the first physical phenomenon for which such an enterprising hypothesis is proposed. Dirac's relativistic wave equation admits two solutions: the first one, defined as *delayed potentials*, proceeds in the direction of the arrow of time and describes ordinary physics and the second one, defined as *anticipated potentials*, goes backwards and describes a phenomenology of syntropic[27] type based on a temporally inverted causal nexus. Richard Feynman also proposed interpreting antimatter as matter that travels backwards in time.

[27] The concept of *syntropy* was proposed in 1942 by the Italian mathematician Luigi Fantappié in his "Unitary Theory of the physical and biological world" [Ref.4] and recovered in 1974 by the Hungarian physiologist Albert Szent-Gyorgyi. In particular Luigi Fantappié (1901-1956) was the author of a theory based on the idea that progressive and regressive solutions of the wave equation represent processes simultaneously present in physical phenomenology: solutions that proceed forward in time would give rise to common physical phenomena (entropic) in which entropy increases, while solutions that proceed backwards in time would give rise to organized forms that oppose the increase of disorder (syntropic phenomena). The similar concept of *negative entropy* was also used by Erwin Schrodinger in 1943 in the popular book "What is life?". The synthetic term *negentropy* was later coined by the French physicist Léon Brillouin to indicate the accumulation of negative entropy in living beings.

In our case, contrary to these precedents, the suggestion of a local inversion of the arrow of time would come from considerations that pertain to the world of statistical mechanics and from results that concern macroscopic phenomena. It must be admitted that there would be no need to compensate the *addressing entropy* if we accepted the idea that the information necessary for aggregation can flow backwards in time: everything would be fine. It would also justify not only the entropic balance but also the strong teleonomic character that aggregation modalities necessarily must have if they are required to be fertile in an evolutionary perspective. So much so that we could define as *telepoiesis* this particular aggregative mode.

6. Telepoiesis

The concept of *telepoiesis* is at least unconventional. Indeed, official science has decisively excluded from the perimeter of orthodoxy any finalistic approach to the comprehension of nature. Without dwelling on the epistemological implications of such an ostracism, however, it must be admitted that, until today, official science has succeeded very well, even without telepoiesis. Also in the light of this consideration, the indications provided by the IdEP-IdLA model suggest that, if it exists, telepoiesis

- must take place when very special boundary conditions occur that are difficult to reproduce
- must produce an outcome univocally defined by the physical conditions of the system itself and by its boundary, so as to follow a process that is fundamentally causal and therefore highly deterministic
- must have a trigger, albeit accidental
- must be a phenomenon not necessarily rare but certainly difficult to identify by measurement of the physical quantities involved. In particular, entropic deviations must be so marginal as to be imperceptible
- must produce an outcome directed not only to the production of more ordered states (i.e. with a higher information content) but also to the development of structures that are fruitful from a biogenetic point of view (i.e. profitably inserted in a chain of events successful for life).

In short, telepoiesis fundamentally must be a subtle, deterministic phenomenon, detectable only in the context of a finalized reading of the complexity.

In light of all this, it seems very doubtful that telepoietic dynamics can take place in closed systems whose composition is well defined and on whose evolution accidental factors such as impurities or internal fluctuations, can have little influence. It is hard to imagine what and how, in the absence of ordering agents, could activate an aggregative process more orderly than that allowed by the autopoietic tendency of reactants. In addition, chemical reactions in closed systems are easily replicable in the laboratory and allow very precise measurements, while no trace of phenomena has ever been found in closed systems which need telepoietic models in order to be explained.

Things are certainly different in open systems far from equilibrium: dissipative structures certify the existence of natural processes capable of spontaneously channeling material and energy flows along aggregative paths more ordered than others, while degrading a greater amount of energy. There are even those who support this class of phenomenon as the cradle of life [Ref.5 and Ref.6]. Are they examples of telepoiesis? Actually, with reference to the characteristics of telepoiesis listed above, dissipative structures:

- do not give rise to resounding events
- as dynamic and complex phenomena, hide possible inconsistency of internal energy parameters due to a higher difficulty in measurements
- are not easy to reproduce in the laboratory and therefore to study experimentally and are even more difficult to simulate theoretically

- acquire, far from equilibrium, a strong instability that makes them vulnerable to small irregularities that can easily act as a trigger for the dissipative jump; a trigger that, however, in the absence of external ordering agents can be favoured by the activation of an autocatalytic effect when critical conditions are reached
- normally reach new stationary states in a univocal way. After the dissipative jump the system configuration is often the same, even starting from previous conditions very different from each other.

Dissipative structures therefore present many elements validating the assumption that they are the places where telepoiesis arises. Let's focus then on the scheme of Fig.2 that synthesizes how the IdEP-IdLA model interprets the dissipative jump. The HCS state (as a result of the highly ordered self-organization in dynamic conditions) is also theoretically obtainable by pushing the system in HCE state (necessarily lacking ordering agents in the case of telepoiesis) far from the equilibrium. Here then the only way to justify the existence of the addressing entropy σ defined by [2] can be the temporal inversion of the information flow.

7. Arianna's conjecture

The acceptance that the uncompensated addressing entropy in the heteropoietic aggregative phenomena in the absence of ordering agents may be the sign of a flow of information that proceeds backwards in time (Fig.4), would make a new contribution to the epistemology of complexity.

It would result, in fact, in a reading of aggregative phenomena that contemplates the existence of two orders of causes as well as two information flows. These, coming from different regions of space-time, interact with each other giving rise to structures that can then appear to us partly causal (in the traditional sense) and partly teleonomic. In particular the biological complexity would be governed on one hand by well-known interactions constituting a dense warp of causal links (where causes are firmly placed in the past) and on the other hand by forces (the *telecauses*) that, according to our perception of time and to the reading of natural phenomena that comes from it, seem to push the events toward the future, toward what *shall* be.

A process, therefore, that would remain largely controlled by dynamics whose knowledge is grounded on what science has investigated so far. But on this strong basis, where chance plays a large part in determining microstates and necessity of physical laws is expressed by experimentally reproducible interactions, a *telecausal mechanism* would overlap: a kind of hidden force that would accomplish the task of guiding the evolution (in our model, the combinations between particles) thanks to information (in our model, the sequencing code) coming from that region of the space-time that we usually call *future*.

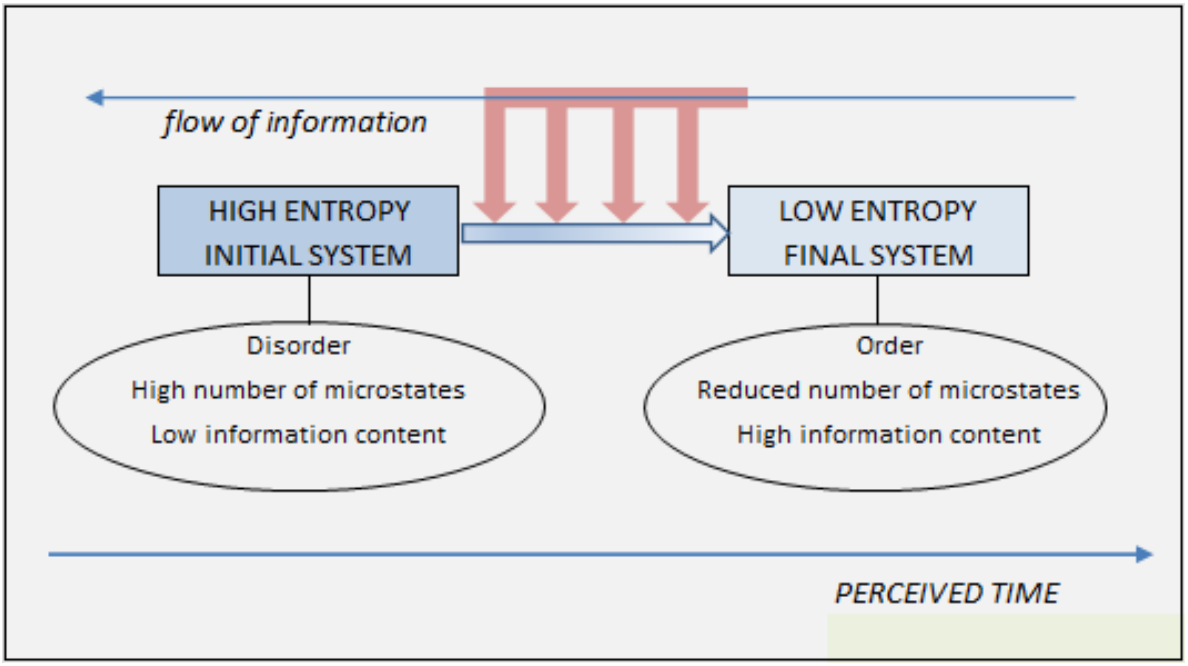

Figure 4. *Telepoiesis*

If we admit the existence of an aggregative dynamic similar to the one just hypothesized to justify the first emergence of biological complexity, it would be difficult to think that such a mechanism is limited only to the formation of elementary structures related to biogenesis. Perhaps, then, the dialectical relationship between causes and telecauses innervates the entire biological phenomenology. This, in reality, appears acceptable if, approaching the reasoning from the opposite point of view, we ask ourselves what characteristics should have those natural phenomena that were also determined by a telecausal dynamic, if this exists. We must admit that for such phenomena we would expect

- a gradual abandonment of the initial homogeneity and uniformity with an evident tension towards differentiation
- a progressive concentration of orderly structures with a high energy content in ever smaller spaces
- a clear evolution in the direction of ever greater structural complexity
- the impossibility of any experimental reproduction
- the possibility that they are delayed or variously diverted by causal interference but never blocked
- a strong sensitivity to environmental conditions that can alter the course of events, without substantially failing to achieve an identifiable final objective.

It is quite evident that vital phenomena fully respect all these conditions, so that even evolution could be permeated by telecausality. Does this make sense? It is difficult to say, even if one cannot hide the fact that such a hypothesis would rectify in a convincing way the deficiencies of the Darwinian orthodoxy that, although forcefully defended by many, is considered insufficient by many others. There is no doubt that admitting the presence of a telecausal watermark in the evolutionary phenomenology as we observe it, would contribute greatly to make understandable that "tortuously ordered" flow of events that characterizes the evolutionary history of living species. We would like to refer to the supposed presence of such thin weft threads of telecausality crossing the warp of ordinary phenomenology as the *Arianna's conjecture*: as in the myth of Arianna, following the threads of telecausality could help us to get out of the labyrinth of appearances.

Conclusions

Thanks to the Markovian formulation of entropy and the consequent possibility of characterizing processes in a simple way using the coding factor, the IdEP-IdLA model has proved to be an agile tool for simulating a wide range of aggregative processes, albeit with limitations discussed in paragraph 3. The model has in fact provided an exhaustive description of complete as well as incomplete aggregation processes, in both autopoietic and heteropoietic modes. In particular, it demonstrated that the heteropoietic mode of assembly implies that the ordering agents, custodians of the aggregation code, must necessarily also be the seat of specific dissipative processes. Moreover, the good aptitude of the model to represent the thermodynamics of aggregative reactions in open systems has led to an effective description of what conditions must occur for order to arise from disorder in dissipative structures.

The transfer in the biochemical and, in particular, biogenetic field of the general conclusions to which the use of the model leads, seems to suggest the existence of a telecausal dynamics of events, alongside the usual causal dynamics. Such a conclusion, although based on objective physical and mathematical evidence, do not claim to prove anything. But, if the IdEP-IdLA model is correctly set up and free from errors, if the simplifications that characterize it are acceptable in the scientific context in which it was intended to be used, then the fact that telepoiesis exists and that it can at least contribute to bio-aggregative dynamics presents itself as an epistemological possibility to be taken into account. We actually believe that the use of the IdEP-IdLA model allows us to conjecture in an argued way the existence, in natural phenomena and superimposed on the powerful causal forces that we are accustomed to know and study, a sort of fine vibrations whose exploration could perhaps shed new light on the deep why of things.

Admitting Arianna's conjecture as a working hypothesis does not mean opening the door to metaphysical solutions. It does not mean giving up the secularity of science. It simply means approaching an unconventional speculative proposal without preconceptions, with rigor and without ideological reservations.

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