Molecular recognition in dissipative systems: A physico-chemical origin of semiosis?

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The study of biological signs, their codification, and their mode of transmission in animal or vegetable communication, all involve biosemiotics.[1] This discipline focuses on the analysis of iconic stimuli (visual, acoustic, tactile, etc.) and the appropriate reactions they trigger. Semiotics itself deals with the biological origins of language. The problem that arises is in defining the precedence of the iconic stimulus in relation to the object that it designates. A mystery which creates the intrusion of a mental process where it has no place. The archaeology of iconic stimuli, in the field of molecular interactions, leads us to consider a type of coupling, which must play a determining role in the dynamics of living organisms. Indeed, the correspondence between the two elements of this coupling are such that each of them seems to act as a signal to the other. But what is the sign? To answer this question, the singular properties of this molecular interaction must be explained, and we must consider in what way they could be at the origin of the semiogenesis.

Recognition molecules

Molecular recognition is one of the fundamental paradigms of molecular biology. Its introduction allowed a unitary interpretation of the different functionalities of the cell and the behaviour of organisms. Enzymologists say that an enzyme "recognises" its molecule (substrate) meaning that it binds specifically to it according to a principle of steric complementarity. In immunology, and in hormonology, the same term is used to describe the coupling of [antigens]-[antibodies]. The site of "ecognition", formed on the surface of proteins is called the "paratope". The "recognised" molecule is fixed on the paratope by a protruding part of its relief; the "epitope". Enzymatic couplings of [epitope]-[paratope] make it possible to channel and regulate the tens of thousands of chemical reactions that take place simultaneously within the cell enclosure.[2] Enzymes sort the molecules, promote their encounters and modulate their interactions. The enzyme, for medical scientist, oncologist and semiotician Giorgiio Prodi, is "*a reader that categorises reality by determining all of the molecules that can react factually with it*".[3] This definition is reminiscent of the microscopic "demons of knowledge" envisioned by Maxwell[4] to explain the irreversibility of the diffusion of a gas. To what extent can enzymes be likened to "readers"? To attempt to answer this question, we must approach not from the field of semiotics, but rather from the field of the dynamics of dissipative systems.[5]

The interaction between [epitope] - [paratope] gives dynamic systems by exceptional reactive and organisational possibilities. This self-organisation comes from an asymmetry in the couple, the paratope playing a reactor role and the epitope a reactant role. Also, the properties of epitopes have certain relationships with those of signs towards their receptor.

1-Non-locality

The effect of the epitope is independent of its site of production. Thus, a circulating hormone causes the same response irrespective of the distance between the emitting cell and the recipient cell. Non-locality allows a systemic response.

2 -Nonlinearity

The effects of the epitope are disproportionate. The intensity of a response does

not increase regularly with that of stimulation, by threshold effect, cooperation, saturation, or amplification.

3-Non-immediacy

The epitope retains all its potential, and its effects may be delayed. The [enzyme]-[substrate] "recognition" has been illustrated by Emile Fischer's lock and key model.[6] The model became dynamic with the American chemist and physicist Linus Pauling[7] who pointed out that the substrate and the enzyme deform during their coupling.[8] Today, biophysicists consider that the shape of a protein is a "statistical ball" that is constantly changing randomly. During the [epitope]-[paratope] coupling process, the force plays just as important a role as form, and their interaction follows precise rules from which we deduce the following two facts:

4- The form outweighs the force

It is futile to force a lock with a key that does not fit. Complementarity of form is a prerequisite for the enzyme-substrate coupling. The forces are ineffective if the steric hindrance resists them.

5- Forms create between themselves the necessary space for the forces to act.

A key must be able to turn the lock in order to activate the mechanism. As a result of this space to act, a "mimetic" key can be introduced into the lock. In other words, a molecule which is close to another can engage in a site of "recognition" without being affected. Morphine, for example, is a "mimetic" of endomorphine through the opioid receptors of the neurons.

Rule 4 reinforces the specificity of the receiver, and Rule 5 in contrast relaxes it, extending the domain of its sensitivity. The paratope achieves a structural compromise, between its specificity and its sensitivity, which explains the spontaneous formation of retroactive loops (feedback). Indeed, the paratope of a receiver acts as a common cycle entry and return point. Competition for the same enzymatic paratope is possible, between a substrate and a synthet-

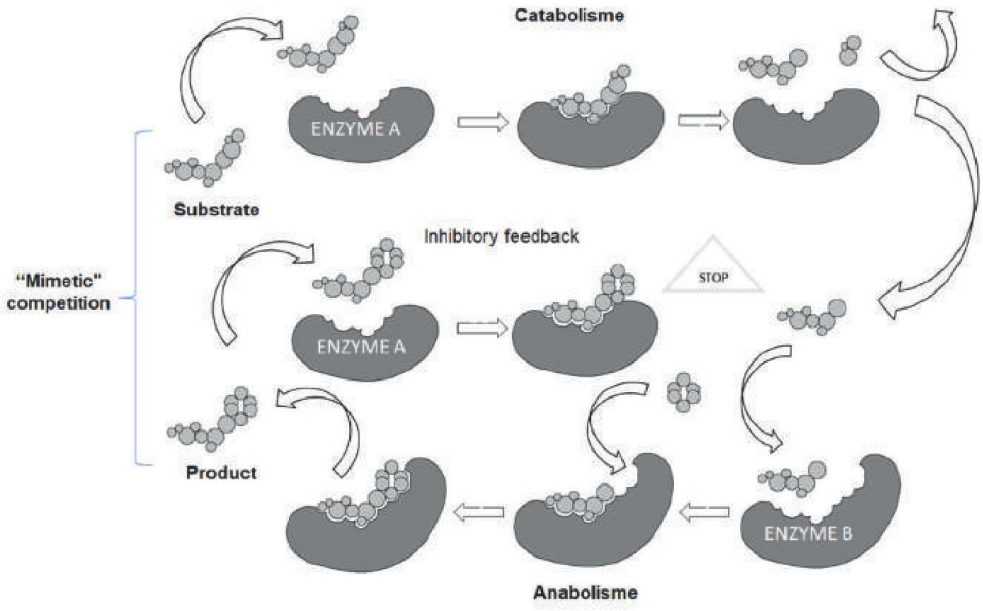

Fig. 1. Regulation of the enzymatic synthesis by mimetic competition. The epitope of the substrate and the epitope of the product presents a steric complementary for the same paratope of enzyme A. This "mimetic" competition for the recognition site of the enzyme limits the overproduction by an inhibitory feedback.

ic product that resembles it. This "mimetic" competition has the effect of curbing production (inhibitory feedback). This feedback is an activator when it unmasks the enzymatic paratope. It is thanks to the combined act of inhibitory and activating feedbacks that the thermodynamics of life are maintained out of balance in the long-term.

The materialisation of time

Life is, according to Prigogine[9], a dissipative system in which time is an ontological actor, just like the molecular constituents. Time, embodied in the DNA, is essentially a chronotopy. That is to say, it comes down to the order of the nucleic acid chain of a gene sequence. This sequence determines the timing of binding of the amino acid of the proteins. This order of binding is key because the protein form results from a complex dynamic winding and progressive contortion, in which the addition of a new amino acid reconfigures the whole. Contrary to C. Afinsen's assertion,[10] the shape of a protein results from a complex dynamic of self-structuring. The materialisation of time has a noticeable effect that prevents the system from constantly rebuilding in the vagaries of a new beginning.

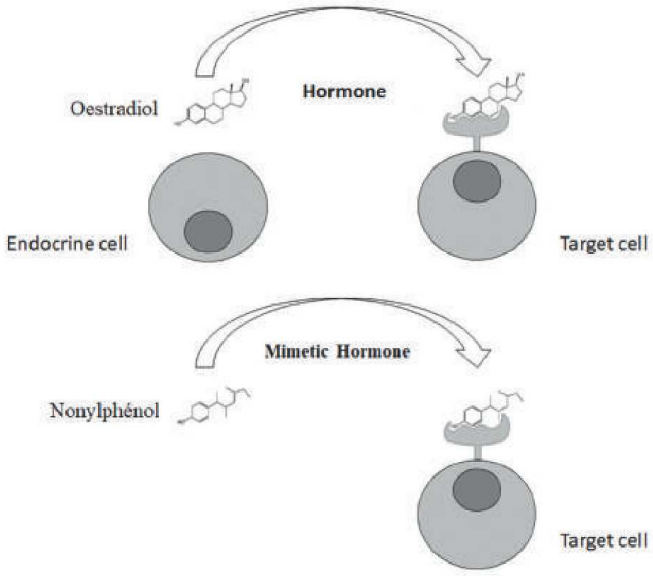

Fig. 2. Mimetic hormone of the oestradiol. The nonylphenol is an organic synthetic molecule belonging to the family of alkylphenols. The epitope of the nonylphenol is similar to the epitope of the oestradiol for the paratope of the receptor of the target cells of the oestradiol. The nonylphenol is an endocrine disrupter.

The dematerialisation of time

Time, frozen in the "chronotropy" of the DNA, becomes an ontological player, in the sense of Prigogine, through [epitope]-[paratope] interaction. Such time is activated during the epitope paratope coincidence which reveals a temporal shift, an anachronism between the footprint of the past and the substrate as it stands. The intrusion of the past profoundly modifies the dynamics of evolution of the dissipative systems, with an alteration to the principle of causality as major consequences. The effect (product) being confused with the cause (substrate), the time-actor is maintained in a reactional circularity. This looping of time is not only stabilising, it can also destabilise the system, pulling it off balance. The functions of the living are then part of a dynamic of rebalancing and updating biological parameters.

At the origin of semiogenesis

The living emerges from a "historisation" of the physico-chemical.[11] The time-actor that presides over the ontogenesis of molecular dynamics also presides over phylogenesis. And it is in the course of this "historisation" that semiosis emerges as a set of signs producing historiated narratives. Time-actor, with the of set, acquires a new possibility of reflexivity. Life becomes the interpreter of a historiated present with a vision of a future.

There is an immeasurable distance between the physico-chemical background of the world and what the world makes through language. From our point of view, however, some operational principles are common to both worlds.

The principle of completion, which implies a structural and functional asymmetry between what is received and what receives it, is already present in the steric complementation of molecules. It finds itself iniconic complementation, which complements fragmentary

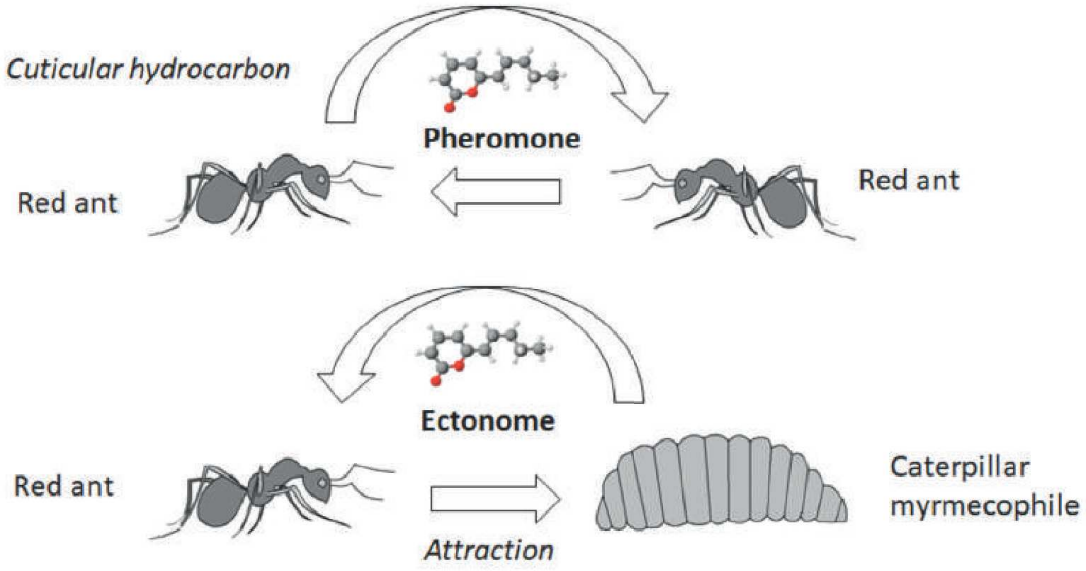

Fig. 3. Molecular mimicry intraspecific and interspecific. The red ant synthesizes a pheromone (hydrocarbon cuticular) which allows a intraspecific recognition. The caterpillar myrmecophile synthetize the same molecule (ectonome) to be admitted in the population of red ants.

sensory impressions from the context. It is still present in the causal complementation, *which* integrates perceptions in the perspective of an experience and a possible future.

The second principle is that of "equivocity". On a molecular scale, it results in assembly errors, inherent to the interlocking game of forms. These errors concern different types of epitopes. According to the organisational level, they are: the substrate for the metabolism, the hormones for functional regulation of organs, pheromone for intraspecific interactions, and ectonomer for relations between different species. At each level, "equivocity" creates new possibilities for interactions. Symbiosis, for example, which plays such an important role in evolution, has its origin in a confusion of form. In the field of semiotics, homonymy, enantiosemy,[12] and the *quid pro quo* are all methods of equivocation.
In each of these areas, time is reactivated in the test of anachronism. Time has momentarily lost its trace and is content with a false semblance to be reborn otherwise. Equivocity prevents the system from repeating itself identically. More importantly, it allows the system to grow through otherness.[13] It allows the system to take care of a unique experience and a shared experience that updates its way of being. It gives the living an autonomy and a remarkable capacity for resistance and resilience to variation.

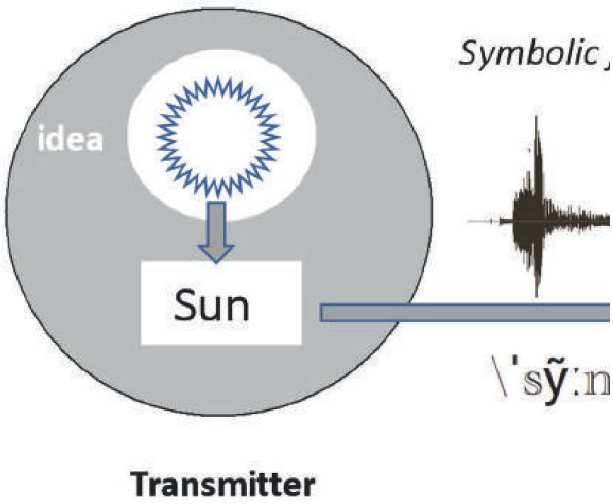

Fig. 4. Homonymy. Words «sun» and «son» have the same pronunciation, they are homonyms. According to the context, the symbolic form associated in concepts can be interpreted by two manners. This equivocity maintains the paradox dynamics of the language.

[1] K. KALEVI (ed.), *Jakob Von Uexküll: A Paradigm for Biology and Semiotics, Semiotica* 134(1-4), Special Issue, 2001.
[2] Cell metabolism involves no less than 75,000 of enzymes, each with an imprint on the surface of the molecule (substrate) that it is likely to transform.
[3] G. PRODI, "Material bases of meaning", *Semiotica* 69(3/4), 1988, 191-241.
[4] M. HEMMO, O. R. SHENKER, *The Road to Maxwell's Demon: Conceptual Foundations of Statistical Mechanics*, Cambridge, Cambridge University Press, 2012, 270-287.
[5] Open system that exchanges energy and matter. It is able to transform dissipated energy and put it at the service of creating an orderly form.
[6] D. E. KOSHLAND Jr., "The Key-Lock Theory and the Induced Fit Theory", A*ngew. Chem-Int. Ed.* 33, 1994, 2375-2378.
[7] L. PAULING, "The valences of transition elements", in *Contribution à l'Étude de la Structure Moléculaire. Victor Henri Memorial Volume. Victor Henri Memorial Volume*, Liège, Desoer, 1948, 1-14.
[8] Transitional configuration of the substrate in the enzymatic site, just before its transformation.
[9] I. PRIGOGINE, I. STENGERS, *Entre le temps et l'éternité*, Paris, Flammarion, "Champs", 1992.
[10] "All the information needed to acquire the native structure of a protein in a given environment is contained in its sequence." (C. Afinsen, Nobel Prize in Chemistry, 1972.)
[11] "The link between physico-chemistry and biology will go through physics-chemical history of matter" (Ilya Prigogine).
[12] An enantiosem is a word that simultaneously designates a thing and its opposite, leaving a free interpretation depending on the context.
[13] D. SCHOËVAËRT-BROSSAULT, "La biodynamique de l'altérité : une complexification par la friction et la fiction", in L-J. LESTOCART (dir.), *Esthétique de la complexité: pour un cognitivisme non-linéaire*, Paris, Hermann, 2017, 317-330.