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## Geocentrism vs Genocentrism:

### Theories without Metaphors, Metaphors without Theories

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#### Abstract

Through the comparison between two major, long-lasting theoretical frameworks – geocentrism and genocentrism – we discuss the different epistemological role played by metaphors in physics and biology. Throughout its history, physics developed theories and mathematical formalisms, which either do not seem to rely on metaphors at all (as geocentrism) or have absorbed initial thrusting metaphors into original theoretical frameworks. When considering genocentrism, in turn, the situation looks different. For some authors, genocentric theories are not metaphorical, but for opposite reasons with respect to geocentrism: pivotal concepts of information theories are straightforwardly imported as theoretical ones into biology. For others, the reference to information in genocentrism is indeed metaphorical, although the similarities and dissimilarities are not spelt out. Some problematic consequences of the application of genocentrism to biology are discussed.

**Keywords:** geocentrism; genocentrism; metaphors; theorizing; biological randomness; organicism; teleology.

## 1 – Introduction: Points of View and Metaphors in Science

Science is a matter of point of view. Without further qualifications, such a claim would appear as provocative at first sight, and unacceptable after reflection. Science aims at elaborating an objective description and understanding of the world, which cannot depend on the choice of a certain “angle”. Of course, it is well known that there is no contradiction between approaching phenomena from a certain perspective and the possibility of generating objective knowledge. All depends on what justifies the choice of the point of view, and to what extent such a choice produces knowledge that satisfies the canons of natural science. In some cases, objectivity may be obtained by relativizing the point of view, in a specific but powerful sense: Galileo’s Relativity first allowed to focus on those “laws of physics” that are invariant with respect to changes (transformations) of inertial *reference systems*; Einstein’s General Relativity then generalized them to transformations in Riemann’s manifolds (diffeomorphisms’ invariance). Physics could thus move from “the subjective-absolute viewpoint to the objective-relative scientific knowledge”, as observed by Weyl (1949), an idea that may be cautiously transferred to biology (Longo, in press).

Our aim here is to examine the epistemological role of metaphors in inducing the adoption of a certain perspective in science. More specifically, we focus on the differences between physics and biology. In spite of being both well-established natural sciences, these two disciplines seem to substantially differ in the way metaphors contribute to the process of theoretical construction. The comparison between geocentrism and genocentrism, which may look strange in many respects, will help us to make that difference explicit. Geocentrism and genocentrism share some general epistemological features. They rely on the decision to look at the solar system or at the organism from a specific point of view, that of the Earth or of DNA, respectively. Once this decision is taken, then some questions become relevant and some research directions are opened, and suitable technical tools are used or created for that

purpose. Geocentrism and genocentrism are also comparable in the fact that they have been challenged by approaches relying on different perspectives: geocentrism was eventually supplanted by heliocentrism, while an increasing number of scholars argue nowadays that genocentrism should be replaced by some form of “organismo-centrism” (Gilbert and Sarkhar 2000; Moreno and Mossio 2015; Walsh 2015; Longo and Soto 2016).

What role did metaphors play in the establishment of geocentrism and genocentrism? For us, there is no obvious reason to claim that Ptolemy’s geometry of epicycles was a metaphor or a consequence of a metaphor. Rather, it appears as a consistent theoretical and mathematical development of the common sense appreciation of the immobility of Earth and the movement of the sky. To establish the framework, Ptolemy and his school used the most advanced tools of Euclid’s geometry, the dominating mathematics of the time.

What about genocentrism? We refer by this label to the view according to which “the special causal and therefore explanatory role of the gene is due to its informational role in storing and transmitting hereditary information, its role in programming the development of the embryo, and its regulatory function in somatic cells” (Rosenberg 2007, 134; see also Mossio, Montévil and Longo 2016, and Godfrey-Smith and Sterelny 2016). Although many other factors do play a role, genocentrism maintains that the distinctive features of biological organisms (in relation to their development, functioning and evolution) are determined by the presence and effects of genes. What makes organism special, when compared with other natural systems, is the fact of being the result of the genetic information or even program.

In contrast with geocentrism, the role of metaphors in the establishment of genocentrism is more intricate. Schrödinger’s original remark concerning the aperiodic structure of chromosomes contained a metaphorical aspect (Schrödinger 1944), although the idea that a *linear* “code-script” could encode a *three-dimensional* structure, such as an organism, was a novel and audacious theoretical proposal. With the simultaneous development of information

theory, a set of specific notions elaborated in that field were imported into biology and adopted as pivotal notions. In Dawkins' words: "... coded characters spell out specific instructions for building willow trees that will shed a new generation of downy seeds. [...] It is raining instructions out there; it's raining programs; it's raining tree-growing, fluff-spreading, algorithms. That's not a metaphor, it is the plain truth." (Dawkins 1986, 111). For a significant part of theoreticians and philosophers of biology, the use of these notions was not supposed to be metaphorical but rather theoretical. Genocentrism then is not metaphorical, but for *opposite* reasons with respect to geocentrism: while geocentrism do not appeal to external notions, genocentrism fully integrate external notions in the theoretical framework: to put it bluntly, biology is conceived as a branch of information theory (Jacob 1974). For many other biologists, presumably the majority, the appeal to these notions is indeed metaphorical in the sense, as underlined by Keller (2015, s1), that they acknowledge that there are both similarities and differences between organisms and computers. In either case, information- or computation-based notions in genocentric biology did not promote any relevant application of existing fundamental results obtained in Information and Computation Theories to biology. They tended instead to remain commonsensical notions while inspiring or supporting *strong consequences* such as the Central Dogma of Molecular Biology or the idea of exact stereospecificity of macromolecular interactions (Monod 1971).

Be it as it may, both attitudes in genocentrism with regard to computational notions had a common outcome, insofar as they did not result in the establishment of an original theoretical framework. And we take this situation as being specific to biology. The difference between physics and biology vis-à-vis the epistemological role of metaphors is also revealed by the fact that geocentrism was supplanted by heliocentrism, whose planetary movements were later shown by Newtonian mechanics to be consistent (actually unified) with Galileo's falling stones. Classical mechanics was developed by relying on the machine metaphor, which promoted the emergence of an original theoretical and mathematical framework. As we will

discuss, even though the machine metaphor is also at play in genocentrism (although the machine is the computer, and not the clock), it seems unable in this case to foster the emergence of a new theoretical framework. The upshot of our analysis is that biology relies too much on metaphors that do not evolve into sufficiently robust theories. For this reason, some central questions cannot be satisfactorily answered: What is the exact notion of information at work (see Longo et al. 2012)? Where are the operating system and the compiler of the genetic program, if any (see Longo 2018b, 2019)? We think that biology should rebuild the link with organicist accounts that, while they became minority in the last few decades, do exist and have much to say. As a matter of fact, organicism and the organization-centred perspective are not metaphorical: they are meant to frame biological phenomena and only them.

If it proved fertile, the comparison between geocentrism and genocentrism would then be quite complex. While the former is not metaphorical and supplanted by an initially metaphorical theory, the mechanical metaphor at the core of genocentrism should be replaced, precisely because it has been unable to generate a theory endowed with sufficient explanatory power.

## **2 - From Epicycles on top of Epicycles to Ellipses and Falling Apples**

Ptolemy (ca. 100-170 AD) described a geocentric planetary system following Hipparchus' (ca. 190-120 BC) approach, based on Euclid's geometry. The theory was based on – and further stimulated – remarkable developments in tridimensional trigonometry. Ptolemy methodically extended the existing tables of data and used complex epicycles to unify them in a coherent geometry for the planetary system. Many more data were later collected by the great astronomers and mathematicians of the Islamic schools (Arabs, Persians and Indians).

The success of the enterprise is mathematically justified by the fact that any finite set of points in an ellipsis around the Sun may be interpolated by enough Earth's centred epicycles, one on

top of the other – in modern terms, this is a matter of the sum of series suitably centred. This allowed the development of a remarkable summa of very rigorous geometric constructions. In this process, we do not see metaphors playing a substantial role. Rather, the enterprise relies on and technically develops the commonsense idea that the Earth is immobile at the centre of the universe and the other celestial bodies turn around it.

In the golden age of Islamic astronomy, both data and geometric interpolations were obtained by centuries of observations that allowed to add precision or to correct the Western computations. For example, out of the numerous Arabic scientists and fine observers of the sky, Ibn Yunus (Egypt, ca 1000 AD) developed spherical trigonometry and computed practically all visible relative positions of planets and celestial bodies in immense astronomical tables, later used to produce the Alfonsine Tables (Catholic Spain, 1483), widely used in navigation. The work of the astronomers was also made possible by the ideas of algebraists, such as Omar Khayyam (Persia, 1048-1131). His classification and solution of cubic equations and intersections of conics was a major contribution for better computations and opened the way to a new marriage of geometry and algebra (Islami and Longo 2017).

The close observations of the sky also allowed to describe geometrically many sound correlations: when Jupiter and Saturn, say, are in conjunction then Mars necessarily appears in this or that constellation. Extremely accurate observations and recordings of the sky allowed to prove that *differences* in the Jupiter-Mars proximity induce *differences* in the relative position of Mars, with great regularity. In today's perspective, we consider as wrong any causal inference drawn from this sort of correlations in a geocentric frame.

As a matter of fact, the Islamic astronomers were only in part motivated by the search for knowledge: astrology was an integral part of their work (Ayduz, Kalin, and Dagli 2014). In the Western world, similar motivations spanned till the early times of the Scientific Revolution. Cardano (1501-1570) and Kepler (1571-1630), extraordinary scientific

personalities of that revolution, were also motivated and financed by their work as astrologers, even though they had adhered to the new geometry of the solar system, while assuming that the Copernican views could also be a tool for predicting human life and behaviour.

As it is well known, Copernicus (1473-1543) introduced a radical change in perspective: look at the Solar system from the point of view of the Sun, not from that of the Earth. Van Fraassen (1970) observes that the invention of the Italian Renaissance perspective in painting helped Copernicus to change perspective: the limit or projective or escape point sets a mobile “point of view” for the spectator - if you change it in the painting, then the spectator’s view point changes symmetrically (Longo and Longo 2020). The new geometry of the Solar System was made possible by – and contributed to corroborate – a new metaphysics. As a consequence, the Earth, thus Rome (and the Pope), would no longer be at the centre of the system of the planets or the Universe. Indeed, a plurality of Christian Churches was born at the time. Tycho Brahe (1546-1601), many years after Copernicus, contributed with more data, yet these were not sufficient for provoking a change of perspective and geometry (and adopting Kepler’s ellipses), which is first a metaphysical decision, and then a theoretical development. As we mentioned above, Ptolemy’s epicycles can always interpolate finitely many data on planetary orbits. Their back-and-forth (or “retrograde”) movements are instead incompatible with the most fundamental principle of the revolution in physics, Galileo's principle of inertia (1564-1642).

The conjunction of Copernicus’ perspective, Galileo’s principle and Kepler’s properties allowed to understand differently also the many correlations between planetary positions and movements (“celestial mechanisms”) observed by the ancient astronomers. Planets were considered “to move and be here and there” for very different reasons and were understood by very different physical (inertia) and geometric properties (Kepler’s laws) with regards to the geocentric approach. The same correlations between planets, such as the ones we mention



among Jupiter, Saturn and Mars, could be given a very different interpretation. Newton (1642 - 1727) then unified the fall of apples and the movements of celestial bodies. Kepler's laws were derived from Newton's laws of universal gravitation, which provided heliocentrism with a wider theoretical foundation in the context of Newtonian Mechanics.

Here we would like to emphasize that, while geocentrism was not metaphorical, the issue is more complex for Mechanics, the new physics that emerged in the modern era. As a matter of fact, it is common knowledge that an analogy between artifactual machines and the entire universe underlay the use of the term "mechanics": one can study and understand the natural world as a machine, i.e. in terms of the movement of, and interplay between, elementary bodies or parts endowed with specific shapes and sizes. More technically, mechanics, as described by Lagrange, Laplace and Fourier (late eighteenth – early nineteenth century), was intended as the analysis of complex dynamics by their decomposition in elementary and simple components. This led to the invention of linear approaches to many relevant systems of equations in terms of Fourier series: by the piecewise (linear) composition of movements of the parts one could describe the totality such as, typically, the Solar System (Marinucci 2011). Upheld by the metaphor of the machine, the new science of Mechanics underwent an extraordinary development that led to its more general formalization after Newton. In this process, the initial metaphor progressively left the place to an autonomous and coherent framework, without playing any further role. Quite the contrary, some aspects of the initial mechanical metaphor are contradicted by the exigencies of the new theory: for instance, Newtonian Mechanics appeals to the 'action at a distance' concept, which is not consistent with a strict mechanical conception. After having achieved its driving role, in a word, the metaphor was absorbed by original theories – from Newton to Einstein.

We know the story. In particular, conservation properties (of energy or of momentum, i.e. inertial movement) allow to write the Lagrangian functional (or the Hamiltonian) by

Hamilton's variational method (Hamilton 1833), and derive Newton's equations, which yield Kepler's laws. The robustness of the proposal allowed also to internally prove its own limits, and guided further changes of perspective. In 1892, Poincaré's "Negative Result", as he called his negative answer to the linear compositionality of the planetary dynamics<sup>1</sup>, sets the limits of classical mechanics and opened the way to the geometry of non-linear dynamical systems. Riemann's geometry hinted to a possible geometric understanding of gravitation as action at a distance and opened to way to Einstein's Relativity. Once some good principles are proposed – that is, conservation properties or (equivalently) symmetries in equations, as proved by Noether (Kosman-Schwarback 2010) – the rest follows. As a result, by Einstein's unification of inertia and gravitation and Noether's theorems, we may understand the fall of apples' and planets' trajectories as due to "symmetry reasons" and thus theoretically frame causality in physics (Longo 2018).

This is the monument of knowledge and scientific method that we inherited from modern physics in which early metaphors – in particular the mechanical one - played a role in the process of establishment of *original* theories and formalisms. Yet, further advances were made also by "saying 'no'", as we noticed, that is by proving the limits even of the late consequence of the mechanistic approach, the potential compositionality or linearity of the dynamics – Poincaré's negative result.

### **3 - From Epicycles to Genes and back**

As we tried to argue, the geocentric theory of epicycles is not metaphorical. It is first grounded on common sense: everybody understands that the sun and the sky turn around us and that the

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<sup>1</sup> This is classically called "the three-body problem": the movements of two planets around the Sun cannot be linearly approximated by Fourier-Lindstedt series, as their gravitational fields interfere with each other.

Earth does not move, otherwise when jumping we would fall back elsewhere. Planets' trajectories were then described by a very complicated but refined geometry. Metaphysics was also crucial: man and its world, if not the Pope, were naturally at the centre of the universe and of Creation.

Let us now turn to genocentrism. The metaphysical choice of giving to the newly isolated molecules a central role in both ontogenesis and phylogenesis was made early in the twentieth century (Keller 2001). The animalcule and the homunculus of the preformationist tradition were made modern and material by seeing them as a chemical structure at the centre of organismal and evolutionary dynamics. A further step, a theoretical one but consistent with this metaphysical decision, was taken when the “War of the code”, World War II, brought to the limelight the alpha-numeric encrypting of information. Schrödinger, by focusing on the non-periodic structure of the chromosomes, proposed that such a structure could be described as a *code-script* for phenotypes. This was an original conjecture at the time, with major consequences. In particular, Schrödinger explicitly stressed the Laplacian nature of his analysis: “In calling the structure of the chromosome fibers a code-script we mean that the all-penetrating mind, once conceived by Laplace, to which every causal connection lay immediately open, could tell from their structure whether the egg would develop, under suitable conditions, into a black cock or into a speckled hen, into a fly or a maize plant, a rhododendron, a beetle, a mouse or a woman” (Schrödinger 1944, 21). Schrödinger was fully aware that “...the term code-script is, of course, too narrow. The chromosome structures are at the same time instrumental in bringing about the development they foreshadow. They are law-code and executive power – or, to use another simile, they are architect's plan and builder's craft – in one” (Schrödinger 1944, 22). The wording “law-codes and executive power” will be later soundly summarized as “program”, including operating systems and compilers, once computer science became a discipline in the early '50s.

Schrödinger's Laplacian conjecture of the genetic program was fully taken on board by the promoters of the Human Genome Project: Once decoded the DNA we will be able to transfer it on a CD-ROM and say: "Here is a human being, this is me" (Gilbert 1992, 96). The search for computers' programs, operating systems and compilers in molecular interactions has continued till now. A peak may be found in the work of Danchin (2003, 2009), a leading molecular biologist and student of Monod, where *lambda-calculus* (Barendregt 1984; Longo 1988; Bezem, Klop and Roelde 2013) is mentioned as a paradigmatic programming language for encoding life, also used to write models "in which "molecules" were programs that act on each other (one program using the other as input data) yielding new programs according to a specific calculus (known as lambda-calculus)" (Fontana, webpage<sup>2</sup>). Danchin's analysis is enriched by a reference to a possible genetic meaning of Gödel's theorem, as a diagonal coding technique in chromosomes that may produce novelty in biological evolution (see Longo 2018a for an analysis of these spurious theoretical correlations).

Like in geocentrism, no metaphors seem to be at play in these accounts, although, somehow paradoxically, for opposite reasons. That is, while geocentrism was elaborated without relying on an analogy with a distinct set of concepts, genocentrism has straightforwardly imported concepts from information theory and computer science as *theoretical* notions. These concepts are the most consequential ones that our culture of digital codes in transmission and elaboration of information in computers' networks can offer as a conceptual frame for the genocentric approach. The idea of coded information, or even genetic program<sup>3</sup>, seems to be the only possible theoretical frame to justify the view of chromosomes as the locus of complete determination of ontogenesis and phylogenesis – how to retrace otherwise a complete

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<sup>2</sup> <https://scholar.harvard.edu/walterfontana/home> (visited on November 24, 2019).

<sup>3</sup> 'Program' is a stronger notion than 'information', as shown by Keller's distinction between two "narratives" of the genetic code: a more restricted one referring to the relation between nucleotide sequences and amino-acid sequences and another, more general one pointing to the relation between genetic information and the organism, the phenotype as a whole (see Keller 2015, s7-s8; also Plomin 2018).

organism in a-periodic molecules? Preformationism finds then a scientific terminology and justification under the form of a set of written code or written instructions. The import of the concept of program into biology goes, however, with an important conceptual shift, which is the one mentioned by Schrödinger. As Nicholson (2014, 165) also notes, computer programs are part of the software of the machine, and they require the hardware to be executed. In turn, the biological program is supposed to generate – so to speak – the hardware required for its own expression. We will come back later to the tension between unidirectional vs. reciprocal determination in machines and organisms. Here, we would emphasize the fact that while computer programs are something that the system does, biological programs are something that makes the system.

Importantly, the conception of DNA as a program was reinforced by Monod and Jacob's paper in 1961, where they refer to: "a co-ordinated program of protein synthesis *and the means of controlling execution*" (Jacob and Monod 1961, 353, our emphasis). The genetic "programme", the French word for computer program, makes genes "both necessary and sufficient to define the structure of a protein", since the mechanism of control of protein expression "operate at the genetic level".<sup>4</sup> Their remarkable discovery of the operon lactose mechanism was thus considered a general paradigm of a control structure of the genetic program, a feedback control on discrete sequences of letters: gene expression is controlled by other genes. Moreover, it seems problematic to understand genetic control as cybernetic control, as done by Monod, on discrete data types without, however, adopting the tools and the frame of Wiener's theory of control – which uses differential equations in continuous structures (Wiener 1948). Rather, control mechanisms as those described in (Monod 1971) may themselves be consistently understood in the computers' language of recursive

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<sup>4</sup> See Peluffo (2015) for a clarification of the question (also mentioned by Keller 2015, s15) concerning the American use of "programme" as in "concert programme, travel programme...". The term used in the first translation in British English of *La Logique du Vivant* (Jacob 1973), was "programme", which also refers, as in French to a "computer program": the control terminology leaves no doubt.

definitions, which apply to discrete data types in a “linguistic/programming” frame (Jacob 1974). As pointed out by Danchin (2003, 2009), lambda-calculus is a suitable, fully alphabetic (re-)writing system for recursion (see references above), far away from continuous-differential cybernetic feedback.

The passage from alphanumeric writing to the genetic program is still alive in university textbooks and encyclopaedias (see for example Gouyon, Henry and Arnoud 2002, and Godfrey-Smith and Sterelny 2016). In passing, it is tempting here to emphasize the analogy between programs that work on other programs in genocentrism, and the epicycles placed on the top of other epicycles in the geocentric framework. Similarly to what happened in Ptolemaic theoretical frames while elaborating epicycles, the genocentric perspective stimulated the birth of new techniques of investigation and the discovery of fundamental mechanisms. Moreover, the view of genes as information carriers had a role for the invention of some new mathematics inspired by networks of gene-expression (Kauffman 1969; Barabasi and Oltvai 2004; just to mention one out of many very popular areas). The reference to information and programs in genetic analysis has had even some influence into computer programming, such as DNA computing (Adleman 1994). More significantly, thanks to the work of top computer scientists as Danos (2009), Cardelli and Shih (2011) and a few others, an entire area of network programming has enriched computer science by new software tools. The future will say whether they are as relevant as the analysis of algebraic equations inspired by the geocentric approach in the Islamic world.

The analogies between geocentrism and genocentrism stop here, where a crucial *disanalogy* must be brought to the foreground. As mentioned, most of the work in Ptolemy’s school and its major Islamic developments soundly used relevant properties of Euclidean geometry and its advancements. With some rare exceptions (such as the work of Danchin – whose mathematical sophistication in the “programming” analysis does not go very far either –, and

of some other authors), biologists do not apply relevant mathematical *results* from computer science or information theory. When they try, they get it wrong as Maynard-Smith (1999) does when he incorrectly compares Turing-Kolmogorov and Shannon-Brillouin's notions of information, entropy and complexity (see Longo et al. 2012; Perret and Longo 2016)<sup>5</sup>.

Such a limited application of the science of programming makes it difficult to maintain that the use of computational notions in biology is indeed theoretical, as advocated by the “founding fathers” of genocentrism. Instead, it seems fair to claim that most biologists make a either commonsensical or *metaphorical* use of these notions in their everyday practice. A large literature shows that generations of biologists have used computational notions by (explicitly or implicitly) acknowledging (or, maybe more precisely, by sensing) that organisms cannot be theoretically assimilated to computational machines. Even authors that are explicitly against the genetic “program” may refer to it in titles and introductions of their work: amongst them, one can mention Farge's (Pouille and Farge 2008; Pouille et al. 2009) and Heard's teams (Heard 2016) – by typically referring to the “re-programming cell fate”.

Then, what epistemological role has this metaphorical use of computational notions played in modern biology? In sharp contrast to the role that mechanical metaphors played in the emergence of modern physics, in the case of genocentrism they did *not* foster the elaboration of an original theoretical framework in biology. The metaphor of the genetic program has remained merely a metaphor for biologists, and genocentric biology has been developing with a metaphorical core. Despite being unable to apply specific mathematical results coming from computer science to build a theory of biological phenomena, biologists have nevertheless

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<sup>5</sup> Some early attempts to use Kolmogorov complexity for alpha-numeric strings, related to the length of programs in Algorithmic Information Theory (Calude 2002), in order to analyze biological complexity, have found an obstacle in the little relation between DNA “complexity” and organismal complexity (plants may have a 50 times larger DNA than a big vertebrate; *C. Elegans*, a microscopic worm of 1,000 cells, has about 16,000 genes; humans seem to have about 20,000 genes). In this perspective, some acknowledge that “DNA sequences possess much more freedom in the combination of the symbols of their alphabet than written language or computer source codes” (Schmitt and Herzel 1997). We will hint to this issue below, in reference to alternative splicing and overlapping genes.

oriented their research *as if* organisms were realizing a genetic program. Guided by the metaphor, they have been mainly focusing on the (supposed) similarities between organisms and computers while neglecting the differences, and the original aspects of the former. The inherent duality of the metaphor was lost and, as Keller writes “Lose this duality, and one loses the vitality of the metaphor” (Keller 2015, s1), even though, as she points out, early metaphors “left a conceptual framework that continued to shape how scientists actually perceived their objects of study” (*ibid.*, s2). The “absorption” of the metaphor by a theoretical framework that makes room to specificities – as it happened for classical mechanics – did not occur.

In spite of their differences, therefore, the two attitudes vis-à-vis genocentrism – theoretical or metaphorical – actually produced the *same* outcome, i.e. the fact of not resulting into the elaboration of a theoretical framework that adequately deals with the distinctive features of biological organisms, and of biological phenomena more generally. A theoretical use of computational notions precludes by definition the possibility of recognizing the epistemological autonomy of biology; the metaphorical use would not, at the condition of either inducing an original theorizing or being abandoned if it were unable to do so. None of the latter outcomes occurred with the metaphorical use, which leads us to claim that the role of metaphors in genocentrism has been peculiar and, in the end, responsible for the limited explanatory power of molecular biology.

Advocates of different research paths have been marginalized in various ways. Waddington and McClintock were not quoted for decades: they had dared to think about or discover epigenetic forms of regulation (Keller 2003). Similarly, the early remarks on heritability of genetic changes induced by nutrition in plants (Durrant 1962) or on stochasticity in gene expression (Kupiec 1983) were considered a heresy for two decades or more. The discovery of prions (Prusiner 1982), that is, proteins that transmit and modify other proteins’ foldings, –



a fact incompatible with the Central Dogma of Molecular Biology – was ignored for more than a decade. In spite of evidence, as observed by Feynman, “it is hard to prove vague theories false”, even when they imply strong consequences. In the following section, we go a bit more into detail, and focus on two fundamental aspects with respect to which genocentrism falls short in explaining biological phenomena: the nature of determination and the status of randomness.

#### **4 – Randomness and Determination**

A key feature of both theories of elaboration (Turing) and transmission (Shannon) of information on discrete data types is their deterministic structure in the sense of Laplace, punctuated though (and unfortunately) by some unavoidable noise. If one elaborates or transmits information, one wants to be able to predict the outcome, and the procedure must be iterable *ad libitum* – a (classical) Discrete State Machine is “Laplacian”, writes Turing (1950). Exact iteration is a key feature of deterministic predictability. What a surprise if the computer program does not do, even if only once, what it is supposed to do exactly, or if the sequence of letters transmitted is shuffled! There must be noise somewhere. Computers are so well designed that, in isolated machines, this practically never happens (otherwise the user gets very upset). So, probabilities may be introduced as a measure of frequencies of sequences (Shannon) or they are artificially posited in computing formal molecular interactions with noise (Cardelli, Kwiatkowska and Laurenti 2016). Instead, when transmitting or elaborating information in actual networks of computers, such as the Internet, the challenge of identical iteration of instructions (the correctness of programs) becomes an intrinsic and major scientific problem. Space and time, that we better understand by the mathematics of continua, may allow fluctuations of all sorts in wires, nodes, waves ... in “access queues” to servers, in time. Yet, computer scientists working on these matters are so good that they call the

unpredictable noise a “do not care” - and they avoid it most of the time, by fantastic techniques (Aceto, Longo and Victor 2003; Longo, Palamidessi and Paul 2010).

From a genocentric perspective, unpredictability or the non-identical iteration of a procedure in biology is therefore due to “noise”, just as it happens in message transmission and in computations: “Evolution [...] stems from the very *imperfections* of the conservative mechanism which indeed constitutes their [of living beings] unique privilege” (Monod 1971, 116). Only noise may disturb the macromolecular interactions that are “necessarily stereospecific”, a necessity at the core of Monod’s book and approach and derived from the need to transmit and elaborate information. Otherwise, genes define completely the tridimensional folding of proteins, a consequence of the Central Dogma, (Crick, 1958) (see the reference to Prusiner's work above). As a matter of fact, the notion of noise is proper to information theories, which deal with the elaboration and transmission of discrete alpha-numeric sequences: in particular, randomness is equated to noise. In contrast, in physics one may distinguish between the notions of randomness and noise. Randomness is “unpredictability with regards to the intended theory” (Calude and Longo 2016) and is *analysed within the theory*. For example, classical randomness (in non-linear systems say) is conceptually distinguished from quantum randomness and mathematics makes the difference by different probability correlations (Bell inequalities, see Aspect, Grangier and Roger 1982). Noise instead is “outside the theory”. Typically, a truck passing by a laboratory where a spin-up/down of an electron is measured may be a source of “noise”, conceptually and mathematically different from the quantum randomness of the electron’s spin. Similarly, the divergence due to a Lyapounov exponent (Devaney 1989) in classical non-linear dynamics allows to evaluate the “limits of (un-)predictability”, that is of randomness; a sudden hearth-quake occurring during measurement, in turn, would add unpredictable noise well beyond the estimated Lyapounov divergence.

A major implication of the Laplacian dimension of genocentrism is the possibility to predict (with some noise) ontogenetic developments, as already hinted by Schrödinger in 1944, even though it can be argued (Keller 2015, s10), that this is precisely what it has been unable to do. “In this alphabet [the nucleotides and the amino acids] can therefore be written all the diversity of structures and performances the biosphere contains” (Monod 1971, 104). As a matter of fact, at the level of individual organisms, predictability has become a major aim in molecular biology and its applications: from monogamous behaviour (Young et al. 1999) to school performance (Selzam et al. 2016). This reminds us of the work in astrology by the Islamic and early western astronomers. Indeed, the relevance of this expectation for the general public and decision makers affected (and affects) scientific projects and financial support (Audétat 2015), in particular due to the amplifying role of newspapers<sup>67</sup>.

Driven by its purported capacity to predict, the computational bias inherent to genocentrism (be it seen from a theoretical or metaphorical viewpoint) forced a narrow understanding of the nature and role of randomness in biology. Yet, 20 years after the early work on “stochastic gene expression” (Kupiec 1983), massive evidence (at least since Elowitz et al. 2002) has confirmed the relevance of both classical and quantum randomness in macro-molecular interactions (Fromion, Leoncini and Robert 2013; Kiviet et al. 2014). As a result, the effectiveness of DNA-based predictions is nowadays the object of a lively debate (Resnik 2018)<sup>8</sup>. Interpreting the variability of gene expression and of macromolecular interactions as

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<sup>6</sup> “Being Rich and Successful Is in Your DNA” (*Daily Mail*, July 12, 2018); “A New Genetic Test Could Help Determine Children’s Success” (*Newsweek*, July 10, 2018); “Our ‘Fortunetelling Genes’ make us” (*Wall Street Journal*, November 16, 2018).

<sup>7</sup> As for the promises of genocentric cancer research, from President Nixon’s 1971 “War on Cancer” to Microsoft’s “computing cancer project” (<http://news.microsoft.com/stories/computingcancer/>, accessed on October, 31, 2018), as well as for alternative approaches, see Sonnenschein and Soto (2016), Baker (2014) and Longo (2018b).

<sup>8</sup> Note that the Laplacian determination proper to dominating molecular analysis, by their alphabetic/information theoretic nature, opposes, in biology, “deterministic” to “random” or “probabilistic”. Once more, this is so because of its nature as intended scientific frame, not as a metaphor. From mathematical physics, instead, we know since long (Poincaré 1892) that classical randomness is *deterministic unpredictability*. As hinted above, quantum indetermination differs from it as well as from stochasticity, a notion proper to statistical physics or more general stochastic dynamics (Chibbaro, Rondoni and Vulpiani 2015).

a supposedly marginal phenomenon appears therefore to be significantly at odds with experimental evidence. Biological organisms host inherent randomness that should be accounted as such, and not reduced to noise. Although they still use the term, recent proposals of “Noise Biology” (Rao, Wolf and Arkin 2002; Simpson et al. 2009), inspired by the methods of Statistical Physics, seem to go in this direction. Yet, making room to randomness, as treated in Statistical Physics, faces major conceptual problems (Bravi and Longo 2015). The latter deals with immense numbers, beyond Avogadro numbers ( $10^{23}$ ), while macro-molecular interactions or stochastic cellular activities (the random production of enzyme in a liver, say) concern a few hundreds or a few hundred millions entities, well below Avogadro numbers. The mathematical treatment cannot therefore be the same. The challenge is then to guess a right “mesoscopic” level where random variations constructively affect the dynamics and are neither corrected nor averaged out (Giuliani 2010).

In addition to stochastic gene expression and the inherent randomness of biological processes, an increasing number of experimental results suggest that the peculiarity of determination in biology, also at the molecular level, radically differs from the one proper to transmission and elaboration of information. Let's just quote here, “alternative splicing” (Brett et al. 2001), that allows a gene to be expressed in different proteins, and “overlapping genes” that infringe any “start and stop” codons supposed to delimit genes (Pavesi et al. 2018). These dynamics also contain random aspects (Skotheim and Nees 2007) that enhance variability and diversity in gene expression and show that biological organisms do not work like the artificial systems to which information theories primarily apply. As a matter of fact, it is not advised to transmit or elaborate information stochastically, unless in some specific use in cryptography, where “hiding” information is independent from the intended effects of transmission and elaboration (it should not affect the “semantics”). Nor do constrained but random oscillations of mediators of information (like in RNA splicing) make any sense in information theories. Even less strings of bits are “read” as varying or overlapping substrings: in programming, parentheses

rigidly force the operational semantics - the much referred lambda-calculus is a paradigm as for the rigorous handling of parentheses (Barendregt 1984) as rigid “start and stop” in the reading of instructions. In summary, determination in biology, even at the molecular level, is a complex blend of predictable dynamics and highly constrained forms of randomness. Chemical affinities, that depend on the context, compartmentalization, torsions and pressures on macromolecular structures and chromatin further and massively constrain and canalize fundamentally random dynamics (Cortini et al. 2016).

The “information carrier” or “programming” role of DNA can be challenged, even at the molecular-physical level, by a different perspective on determination and randomness. Following an idea initially expressed by Darwin, biological randomness may be viewed as implying a *theoretical* unpredictability, due to the “high sensitivity” of organisms to “internal and external conditions” (Darwin 1859). In particular, any reproduction implies a variation - Darwin’s first principle, spelt out in at least four of the first six chapters of the “Origins”. In modern terms, biological unpredictability must be analysed differently from deterministic unpredictability and quantum randomness in physics (while including both of them).

First, biological randomness contributes to functional variability and diversity as well as of organismal and ecosystemic adaptation (Montévil et al. 2016). In particular, it superposes classical and quantum randomness with phenotypic consequences, being at various levels of biological organization (ecosystemic, organismal and molecular), with a dual stabilizing/destabilizing role (Buiatti and Longo, 2013). Given that it concerns low numbers of elements (when compared with statistical physics), biological randomness refers to fluctuations that cannot be statistically dumped out, and generates variability that contributes to adaptation, which is a key component of biological stability, in particular at the evolutionary scale. For example, an intrinsically unpredictable quantum event (a particle’s spin up or down

affecting a mutation, say) may contribute to the formation of a new functional biological observable.

Second, biological randomness implies a stronger sense of unpredictability. In physics, randomness is “what is measured by probabilities” (from Laplace to Kolmogorov: see Mugur-Schachter and Longo 2014; Longo, in press), since each theory fixes a priori its own space of possibilities (or “phase space”, as space of pertinent observables and parameters), within which one can give a measure of probability. Theoretical unpredictability, instead, cannot be evaluated either by probabilities since it includes changes of the very space of possibilities (the space of contingently possible phenotypes) or by the key role of “rare events”, as discussed in (Longo 2017). Probabilities cannot be calculated if the phase space of possibilities is not given, and invariant. Phenotypes are co-constituted with an enabling environment: their possible phylogenetic paths are not given “a priori” and their formation changes the phase space (consider for instance the exaptation of internal hears from double jaws some 250 millions years ago, or that of feathers and wings from front podia ... Gould 2002: all of them were initially non-existing possibilities). Moreover, biological randomness occurs in a context depending on the past: – homology of phenotypes and inherited mutations, which have had a functional role in the past but are not expressed today or are expressed differently (“cryptic mutations”, see Paaby and Rockman 2014), so that their molecular structure and their function can only be understood by a phylogenetic reconstruction of the history of an organism or a phenotype (Longo 2017).

## **5 – Teleology and Organization**

Genocentrism had a major impact on another fundamental aspect of biological explanation: *teleology*. One of the central motivations for advocating the explanatory role of the genetic program in biology was precisely its capacity to frame in a scientifically legitimate way the

study of biological purposiveness (Jacob 1974). As Mayr wrote: “The language of computers” allows us to understand how an individual organism has been “programmed” and makes the question of “purpose” “legitimate” (1961, 1503).

The reason why the genetic program has been considered a satisfactory solution to the scientific problem of biological purposiveness is that it is supposed to provide a *mechanistic* account of the latter. In modern physics, the mechanical metaphor was used to free scientific explanation from teleological implications - somehow paradoxically, considering that machines are purposeful entities. Through a progressive theoretical elaboration achieved with Hamilton, physics could get rid of any purpose (Bailly and Longo 2011), which was still used to understand trajectories: does a light ray or an apple go along the best (optimal) path *towards an end*? From Hamilton on, the answer is unambiguously “No”: a path is a geodetic, the result of the sum (an integral) of gradients of point-wise (conserved) momentum. Hamilton’s variational method allowed the reconstruction of optimal paths with no purpose.

In biology, genocentrism replaces a teleological explanation with a mechanical one through a twofold move. First, organisms are seen as carrying a genetic program that determines ontogenesis and organismal functions in a scientifically legitimate way. Second, the program is considered to be written through an evolutionary process, which is *itself* understood as a mechanical one. As a result, the purposiveness of individual organisms becomes apparent (Mayr’s “teleonomy”) when looking at them as the outcome of evolution by natural selection that acts on sequences of letters and writes the genetic program with them (Gouyon, Henry and Arnoud 2002; Chaitin 2012).

In our view, there are various problems with this picture, beyond the fact that the DNA does not seem to behave as a program in determining the organism, as discussed above. One fundamental issue is the construction of the relationship between the genes and the organism as a *unidirectional* one, such that the genes determine the organism, but not vice-versa. As

discussed above in reference to Lagrange, Laplace and Fourier's celestial mechanics, we understand 'mechanism', in its broadest possible sense, as the conception according to which determination goes from the parts to the whole, and not the other way around. Mechanism does not make room to circular or mutual determination. Now, while this conception has proven fertile in physics (until Poincaré's 1892 result, as hinted above), we think that its relevance for biology is more highly questionable.

As a matter of fact, the entire "organicist" tradition in biology and philosophy of biology has underscored the idea that biological organisms realize a special relation between the parts and the whole, and that no proper understanding of the parts and their activity can be obtained by abstracting from their integrated into a whole organized system. The parts determine the whole just as the whole determines the parts. Many authors throughout the history of biology have emphasized this idea, including Aristotle, Kant, Cuvier, Bernard, Woodger, Bertalanffy, Maturana, Varela, Rosen and, today, Kauffman. As Claude Bernard put it: "The physiologist and the physician must never forget that the living being comprises an organism and an individuality. [...] Indeed, when we wish to ascribe to a physiological quality its value and true significance, we must always refer to this whole and draw our final conclusions only in relation to its effects in the whole" (1865/1984, quoted and translated by Wolfe, 2010).

The very idea of the genetic program or of the DNA as the locus of the complete ontogenetic information denies the circular determination between the parts and the whole. To quote Monod: "Through its properties, by the microscopic clockwork function that establishes between DNA and protein, as between organism and medium, an entirely one-way relationship, this system obviously defies any 'dialectical' description. It is not Hegelian at all, but thoroughly Cartesian: the cell is indeed a machine" (Monod 1971: 110-111). This conception orients biological research by assuming that genes are the *explanans* while the organism is the *explanandum*. The hypothesis is of course legitimate and can be explored. As



a matter of fact, it *has* been massively explored, and a substantial part of experimental biology still considers that it captures a crucial aspect of biological determination. Yet, the recent and thriving “antireductionist” trend in biology – including molecular biology – seems to show that the directional conception inherent to the genetic program has a limited explanatory power, also beyond the unsatisfactory understanding of determination and randomness. More and more research programs suggest that an adequate understanding of biological phenomena requires a shift to a “systemic thinking”, in which epigenetic, cellular, tissular and organismal factors – that cannot be themselves derived from the genetic program, and are therefore presupposed – contribute to determine and regulate gene expression. DNA contributes to determine the organism’s ontogenesis and functioning, and the organism contributes to determine DNA maintenance and expression: determination is circular and cannot be made unidirectional. Also, many phenotypes may originate from organismal and ecosystemic interactions, where genes and/or their expression are increasingly found to be followers in phylogenesis (West-Eberhard 2003) and in ontogenesis (Weinberg 2014; Gatenby 2017).

Within this general antireductionist trend, many scholars have argued that contemporary biology should adopt an *organicist* perspective and reconnect with the tradition mentioned above (Gilbert and Sarkhar 2000). In previous studies, we have put forward a theoretical framework in which the circular organization of biological organisms is put in the foreground (Mossio, Montévil and Longo, 2016). By relying on previous contributions – notably Rosen's (M,R)-systems (Rosen 1991) and Kauffman’s work-constraint cycle (Kauffman 2000) –, we have conceptualized biological organization as a regime in which a set of components acting as constraints in the thermodynamic flow contribute to mutually determine their conditions of existence over time (Montévil and Mossio, 2015). As a result, the whole organization realizes what is usually called a “constraints closure”, which describes how the collective activity of the components achieves self-maintenance. Constraints closure implies a circular relation between causes and effects, insofar as the effects of the collective activity of its components

contribute to determine their own conditions of existence and, thereby, to maintain the entire organism. Closure does not allow a privileged level of causality: DNA is “just” a (very relevant) constraint. The embryogenetic formation and the functioning of the cardio-vascular system in vertebrates (Noble 1979) could be an interesting example of multilevel causality within a closure of constraint. As a matter of fact, it is hard to understand this phenomenon as a pre-programmed phenotype; in particular, the developing embryo regulates gene expression, coordinates initially chaotic neural rhythms, all affecting each other after a critical transition during embryogenetic differentiation (Noble 1979, 2012). When discussing her conception of the “reactive genome”, Keller asks the following question “if the genome is so responsive to its environment, how is it that the developmental process is as reliable as it is?” (2015, s16). We find her answer convergent with the perspective that we are advocating here: “The answer must [*also*] be sought in the dynamic stability of the system as a whole. [...] The range of possible responses [*of genomes*] is severely constrained, both by the organizational dynamics of the system in which they are embedded and by their own structure” (s16).

As one of us has argued in (Mossio and Bich 2017), the acknowledgement of biological organisms' capacity of self-determination (in the precise sense of self-maintenance) goes with the ascription of *intrinsic purposiveness* to them which, in turn, legitimates the relevance of genuine teleological explanations. Indeed, as the effects of organisms' activity participate to determine their existence and features, the relation between causes and effects becomes circular, which allows interpreting the latter as a kind of final causes. The contrast with genocentrism is patent here. Genocentrism takes organisms purposiveness as a phenomenon that can (and should) be explained away in a mechanistic framework that appeals only to unidirectional determination. The genetic program determines the organism, whose behaviour and features play no role in shaping the existence and activity of the program. Therefore, the program explains the organisms, but not vice-versa. Genocentrism cannot accommodate in its theoretical framework intrinsic purposiveness, whereas the organicist tradition takes it as a

fundamental feature of biological organisms. As we mentioned, genocentrism may seem a rationally legitimate hypothesis, which might have proved adequate and fertile in order to discover specific molecular mechanisms, similarly as the geocentric approach stimulated three-dimensional trigonometry and the work on algebraic equations – but it is legitimate to believe that the same could be achieved also within a better theoretical framework. Yet, the current antireductionist and systemic trend in biology, promoted by evidence coming also from molecular biology, such as stochastic gene expression and the role of epigenetics, suggests that the hypothesis is not legitimate, and that biological explanation cannot get rid of circular determination, in particular in the form of constraints within and at all levels of organization, as organicism has been advocating for centuries. While the metaphorical or theoretical use of mechanical concepts did work, at least to some extent, for physics, it did not produce comparable results in biology, nor allowed, so far, a passage comparable to the one from Descartes' mechanism to Newton's gravitational laws and their equations. Genocentrism's inherent incapacity to make sense of intrinsic purposiveness, replaced by the linguistic notion of a written program, constitutes for us a key reason for its explanatory weakness.

## **6 – Conclusions**

What conclusions can be drawn about the role of metaphors in biology? In the previous pages we have tried to argue that metaphors can certainly have an important epistemological role in science, by promoting the elaboration of new and original theoretical frameworks. The example of the mechanical metaphor that elicited the emergence of modern physics seems clear and commonly accepted.

By considering geocentrism and heliocentrism, we have argued that physics can elaborate theoretical frameworks either without the initial support of a metaphor (as it seems to be the

case for geocentrism) or by absorbing initial thrusting metaphors. In both cases, what matters is the fact that, at the end of the process, an original theoretical framework is elaborated to deal with a specific set of natural phenomena.

The comparison between geocentrism and genocentrism suggests that the situation in biology is substantially different. On a first approximation, the two approaches share significant commonalities: they are both characterized by the fact of adopting a specific point of view on a class of phenomena under scrutiny; both of them laboriously try to make uncooperative experimental evidence consistent with their conceptual framework; and in spite of this effort, both of them have been, or might be, replaced by approaches adopting a different point of view. Yet, fundamental epistemological differences exist between geocentrism and genocentrism, precisely vis-à-vis theorizing and the role of metaphors in theorizing. Genocentric biologists and theorists have either imported notions from information theories and straightforwardly used them as theoretical ones, or adopted and continuously used such notions as metaphorical. In both cases, no original theory has emerged, which shows the particular nature of molecular biology in this respect.

One could argue that we are exaggerating the importance of original theorizing in science. Even though genocentrism has imported concepts from Shannon's theory or from computer science, it does not follow that it has been unable to generate significant scientific knowledge. Our reply to this objection is twofold. First, it is not clear how valuable is the knowledge gathered by viewing the organism as determined by a genetic program. We agree that molecular biology, driven by the theoretical or metaphorical use of computational metaphors, has described and explained a vast amount of phenomena, that is of "molecular mechanisms", a term extensively used and in conformity with the mechanical rooting of the metaphor. These are supposedly related to the role of DNA in ontogenesis, physiology and heredity (the Mendelian genes). Without doubt, we know much more about these phenomena now than we

did 100 years ago. However, if the reader agrees with us about the fact that geocentrism induced a strongly biased characterization of biological organisms, then the value of such a knowledge is unclear. What do we really know about molecular phenomena if what we know has been obtained by looking at organisms as if they were computers, while there are various aspects with respect to which organisms do not seem to behave as computers at all? To what extent will this knowledge be conserved when geocentrism is replaced by a new theoretical framework?

The relevance of these questions seems obvious if one keeps comparing geocentrism to geocentrism. The Alfonsine Tables (see above) were based on observations and their soundness or applicability to navigation did not depend on geocentric assumptions. Research in algebra was partly motivated by the interpolation of planetary trajectories by epicycles and scientifically supported astrology. Its validity, though, did not depend on either of them and turned out to be relevant in completely different scientific contexts. So, the (mathematical) “mechanisms” correlating Mars, Jupiter and Venus in the geocentric approach were totally revised in the heliocentric system. Similarly, even though geocentrism has generated scientific knowledge, it is hard to tell what exactly such knowledge consists in, and how one can distinguish between sound and spurious correlations or applications, as well as the influence of the geocentric bias in obtaining it. In addition, doubts concerning the soundness of geocentric knowledge come from the observation that the pivotal notion of 'gene' is not well defined within the framework (Keller 2000).

Second, even if one accepted that robust knowledge was gathered by geocentric research, it does not follow that it could not have been obtained from a different perspective. The claim that geocentrism was a necessary (or at least useful) step in the progress of scientific knowledge is just hypothetical. As a historical counterfactual, it is either untestable or indirectly refuted by the analogy with the Islamic knowledge of the sky and invention of

Algebra in geocentric frames. It might be the case that relevant and robust knowledge about molecular phenomena in biological organisms could have been or could be obtained without relying on computational hypotheses. Once again, the comparison with geocentrism is instructive: did geocentrism and astrology make a necessary or useful contribution to astronomical knowledge? Answers may vary, but ours tends to be ‘no’. Similarly, the financial support for astrology was crucial for the work of the Islamic astronomers, but in which sense does this “justify” astrology?

Assuming that the argument developed so far convinces the reader, the next question is: Why is geocentrism so peculiar with respect to theorizing and the use of metaphors? Though a complete answer is beyond the scope of this paper, we’d like to point to one aspect that we find particularly relevant: the *weight of history*. Understood as a modern natural science, physics is much older than biology, and relies on the monumental theoretical construction briefly discussed in section 2. Modern and contemporary physics is theoretically “dense”, and is able to continuously and endogenously generate new concepts (and even disciplines) as soon as new phenomena require to be addressed and explained. It seems to us that the case of biology is significantly different, especially when considering organismal biology, while evolutionary biology – that does rely on a well-established original theory – would deserve a different analysis in this respect. During its shorter history, organismal (or, as it is sometimes referred to, functional) biology has remained mostly empirical and did not elaborate theoretical frameworks of a kind comparable to those of physics. Even biological “theories” as cell theory are such in a much more informal sense than physical ones. Many good reasons can be invoked to explain this difference, the first one being that biological phenomena are much more recalcitrant than physical or chemical ones to be subsumed to general and yet distinctive laws (Montévil et al. 2016). Be it as it may, the consequence is that biology suffers from a “theoretical void” that geocentrism, and its computational/informational frame, has contributed to fill in, even though it did not succeed in establishing an original theoretical

framework. In the absence of exploitable theoretical alternatives, genocentrism has remained at the heart of functional biology, either in the theoretical “reductive” version or, more frequently, in the metaphorical one. As a matter of fact, because of its theoretical weakness functional biology tends to “import” concepts not only from computing and information sciences, but also from other disciplines as physics itself (think of the whole “biophysics” domain) and even economy. Interestingly, functional biology has also imported concepts and explanatory strategies from the biological field that is the most theoretically robust, i.e. evolutionary biology, notably when natural selection is applied to account for biological phenomena taking place *within* organisms (the so-called “cellular Darwinism”, see for instance Kupiec 1997). To conclude, let us ask again the question at the beginning of this section: what conclusions can be drawn about the role of metaphors in biology? From our point of view, we should be rather skeptical about their positive epistemological role, notably when considering molecular and functional biology. For many reasons metaphors – and in particular the computational one – have been understood as theories or kept as such in the conceptual framework of biology: in both cases, they have been unable to foster a proper biological theorizing as they have tended to neglect distinctive features of biological organisms and phenomena.

## 7 – References

- Aceto, L., G. Longo, and B. Victor, eds. 2003. “The Difference between Concurrent and Sequential Computations.” In *Special Issue, Mathematical Structures in Computer Science*, vol. 13, 4–5. Cambridge University Press.
- Adleman, L. M. 1994. “Molecular Computation of Solutions to Combinatorial Problems.” *Science* 266 (5187): 1021–1024.
- Aspect, A., P. Grangier, and G. Roger. 1982. “New York. Experimental Realization of the

- Einstein-Podolsky-Rosen-Bohm Gedanken experiment: A New Violation of Bell's Inequalities." *Physical Review Letters* 49.
- Audétat, M., ed. 2015. *Sciences et technologies émergentes: Pourquoi tant de promesses?* Paris: Hermann.
- Ayduz, S., I. Kalin, and C. Dagli. 2014. *The Oxford Encyclopedia of Philosophy, Science, and Technology in Islam*. Oxford University Press. p. 64. ISBN 9780199812578.
- Baker, S. 2014. "Recognizing Paradigm Instability in Theories of Carcinogenesis." *British Journal of Medicine and Medical Research* 4 (5): 1149–1163.
- Bailly, F., and G. Longo. 2011. *Mathematics and the Natural Sciences: The Physical Singularity of Life*. London: Imperial College Press.
- Barabasi, A., and Z. N. Oltvai. 2004. "Network Biology: Understanding the Cells' Functional Organization." *Nature Reviews Genetics* 5 (2): 101–113.
- Barendregt, H. 1984. *The Lambda-Calculus: Its Syntax, Its Semantics*. Amsterdam: North-Holland.
- Bernard, C. (1865) 1984. *Introduction à l'étude de la médecine expérimentale*. Paris: Baillière.
- Bezem, M., J. W. Klop, and R. Roelde Vrijer. 2013. *Term Rewriting Systems*. Cambridge MA: Cambridge University Press.
- Bravi, B., and G. Longo. 2015. "The Unconventionality of Nature: Biology, from Noise to Functional Randomness." In *Unconventional Computation and Natural Computation*, edited by Dinneen Calude, 3–34. Springer LNCS 9252.
- Brett, D., H. Pospisil, J. Valcárcel, L. Reich, and P. Bork. 2001. "Alternative Splicing and Genome Complexity." *Nature Genetics* 30.



- Buiatti, M., and G. Longo. 2013. "Randomness and Multi-level Interactions in Biology." *Theory in Biosciences* 132 (3): 139–158.
- Calude, C. 2002. *Information and Randomness*. Berlin: Springer-Verlag.
- Calude, C., and G. Longo. 2016. "Classical, Quantum and Biological Randomness as Relative Unpredictability." *Special Issue of Natural Computing* 15 (2): 263–278.
- Cardelli, L., and W. Shih. 2011. "A Programming Language for Composable DNA Circuits." *Proceedings of the 17th International Conference, DNA 17*, Pasadena, CA, USA.
- Cardelli, L., M. Kwiatkowska, and L. Laurenti. 2016. "Stochastic Analysis of Chemical Reaction Networks Using Linear Noise Approximation." *Biosystems* 149: 26–33.
- Chaitin, G. 2012. *Proving Darwin: Making Biology Mathematical*. New York: Pantheon.
- Chibbaro, S., L. Rondoni, and A. Vulpiani. 2015. *Reductionism, Emergence and Levels of Reality: The Importance of Being Borderline*. Berlin: Springer.
- Cortini, R., M. Barbi, B. Caré, C. Lavelle, A. Lesne, J. Mozziconacci, and J. M. Victor. 2016. "The Physics of Epigenetics." *Reviews of Modern Physics* 88: 025002.
- Crick, F. H. 1958. "On Protein Synthesis." *Symposia of the Society for Experimental Biology* 12: 138–163.
- Danchin, A. 2003. *The Delphic Boat. What Genomes Tell Us*. Cambridge: Harvard University Press.
- Danchin, A. 2009. "Bacteria as Computers Making Computers." *Microbiology Review* 33: 3–26.
- Danos, V. 2009. "Agile Modelling of Cellular Signalling." *Electronic Notes in Theoretical Computer Science* 229: 3–10.
- Darwin, C. 1859. *On the Origin of Species*. London: John Murray.

- Dawkins, R. 1986. *The Blind Watchmaker*. London: Longmans.
- Devaney, Q10 R. L. 1989. *An Introduction to Chaotic Dynamical Systems*. Addison-Wesley.
- Durrant, A. 1962. "The Environmental Induction of Heritable Change in *Linum*." *Heredity* 17 (1): 27–61.
- Elowitz, M. B., A. J. Levine, E. Siggia, and P. S. Swain. 2002. "Stochastic Gene Expression in a Single Cell." *Science* 297.
- Fromion, V., E. Leoncini, and P. Robert. 2013. "Stochastic Gene Expression in Cells: A Point Process Approach." *SIAM Journal on Applied Mathematics* 73 (1): 195–211.
- Gatenby, R. A. 2017. "Is the Genetic Paradigm of Cancer Complete?" *Radiology* 284: 1–3.
- Gilbert, W. 1992. "A Vision of the Grail." In *The Code of Codes: Scientific and Social Issues in the Human Genome Project*, edited by Daniel J. Kevles, and E. Leroy. Harvard U.P.
- Gilbert, S. F., and S. Sarkar. 2000. "Embracing Complexity: Organicism for the 21st Century." *Developmental Dynamics* 219 (1): 1–9.
- Giuliani, A. 2010. "Collective Motions and Specific Effectors: A Statistical Mechanics Perspective on Biological Regulation." *BMC Genomics* 11 (suppl 1): S2.
- Godfrey-Smith, P., and K. Sterelny. 2016. Biological Information. *Stanford Encyclopedia of Philosophy*. <https://plato.stanford.edu/entries/information-biological/>.
- Gould, S. J. 2002. *The Structure of Evolutionary Theory*. Cambridge, MA: Harvard University Press.
- Gouyon, P. H., J. P. Henry, and J. Arnoud. 2002. *Gene Avatars, the Neo-Darwinian Theory of Evolution*. Kluwer.
- Hamilton, W. R. 1833. *On a General Method in Dynamics*. Dublin: Trinity College.

- Heard, E. 2016. “Epigénétique et mémoire cellulaire ». *Léçons inaugurales au Collège de France*. Paris: Fayard.
- Islami, A., and G. Longo. 2017. “Marriages of Mathematics and Physics: A Challenge for Biology”. In *The Necessary Western Conjunction to the Eastern Philosophy of Exploring the Nature of Mind and Life* (K. Matsuno et al., eds), Special Issue. *Progress in Biophysics and Molecular Biology* 131: 179–192.
- Jacob, F. 1973. *The Logic of Life*. Pantheon Books.
- Jacob, F. 1974. “Le modèle linguistique en biologie.” *Critique*, XXX: 322.
- Jacob, F., and J. Monod. 1961. “Genetic Regulatory Mechanisms in the Synthesis of Proteins.” *Journal of Molecular Biology* 3.
- Kauffman, S. 1969. “Metabolic Stability and Epigenesis in Randomly Constructed Genetic Nets.” *Journal of Theoretical Biology* 22 (3): 437–467.
- Kauffman, S. 2000. *Investigations*. Oxford: Oxford University Press.
- Keller, E. F. 2000. “Decoding the Genetic Program: Or, Some Circular Logic in the Logic of Circularity.” In *The Concept of the Gene in Development and Evolution. Historical and Epistemological Perspectives*, edited by Peter Beurton, Raphael Falk, and Hans-Jörg Rheinberger, 159–177. Cambridge: Cambridge University Press.
- Keller, E. F. 2001. *The Century of the Gene*. Cambridge, MA: Harvard University Press.
- Keller, E. F. 2003. *A Feeling for the Organism. Life and Work of Barbara McClintock*. New York: Freeman.
- Keller, E. F. 2015. “Cognitive Functions of Metaphor in the Natural Sciences.” *Philosophical Enquiries* 3 (1): 113–132.

- Kiviet, D. J., P. Nghe, N. Walker, S. Boulineau, V. Sunderlikova, and S. J. Tans. 2014. "Stochasticity of Metabolism and Growth at the Single-cell Level." *Nature* 514: 376.
- Kosman-Schwarback, Y. 2010. *The Noether Theorems: Invariance and Conservation Laws in the Twentieth Century*. Berlin: Springer-Verlag.
- Kupiec, J. J. 1983. "A Probabilistic Theory for Cell Differentiation, Embryonic Mortality and DNA C-Value Paradox." *Speculations in Science and Technology* 6: 471–478.
- Kupiec, J. J. 1997. "A Darwinian Theory for the Origin of Cellular Differentiation." *Molecular and General Genetics* 255: 201–208.
- Longo, G. 1988. "The Lambda-Calculus: Connections to Higher Type Recursion Theory, Proof-Theory, Category Theory. Conference on 'Church's Thesis after 50 Years'." *Annals of Pure and Applied Logic* 40: 93–133.
- Longo, G. 2017. "How Future Depends on Past Histories and Rare Events in Systems of Life." *Foundations of Science*, 1–32.
- Longo, G. 2018a. "Interfaces of Incompleteness." In *Systemics of Incompleteness and Quasisystems*, edited by G. Minati, M. Abram, and E. Pessa. New York, NY: Springer. (preliminary version: "Incompletezza" per *La Matematica*, vol. 4, Einaudi).
- Longo, G. 2018b. "Information and Causality: Mathematical Reflections on Cancer Biology." *Organisms Journal of Biological Sciences* 2 (1).
- Longo, G. 2019. "Information at the Threshold of Interpretation, Science as Human Construction of Sense." In *A Critical Reflection on Automated Science – Will Science Remain Human?*, edited by M. Bertolaso and F. Sterpetti. Dordrecht: Springer.
- Longo, G. in press. "Confusing Biological Twins and Atomic Clocks. Today's Ecological Relevance of Bergson-Einstein Debate on time." *What Is Time? Einstein and Bergson 100 Years Later*, April 4–6, 2019 (proceedings in preparation, Campo, Ronchi eds).

- Longo, G., and S. Longo. 2020. "Infinity of God and Space of Men in Painting, Conditions of Possibility for the Scientific Revolution." In *Mathematics in the Visual Arts*, edited by R. Scheps and M.-C. Maurel. London: ISTE-WILEY Ltd.
- Longo, G., P. A. Miquel, C. Sonnenschein, and A. Soto. 2012. "Is Information a Proper Observable for Biological Organization?" *Progress in Biophysics and Molecular Biology* 109 (3): 108–114.
- Longo, G., C. Palamidessi, and T. Paul. 2010. "Some Bridging Results and Challenges in Classical, Quantum and Computational Randomness." In *Randomness through Computation*, edited by H. Zenil, 73–92. World Scientific.
- Longo, G., and A. M. Soto. 2016. "Why Do We Need Theories?" *Progress in Biophysics and Molecular Biology* 122: 4–10.
- Marinucci, A. 2011. *Tra ordine e caos. Metodi e linguaggi tra fisica, matematica e filosofia*. Roma: Aracne.
- Maynard-Smith, J. 1999. "The Idea of Information in Biology." *The Quarterly Review of Biology* 74: 495–400.
- Mayr, E. 1961. "Cause and Effect in Biology: Kinds of Causes, Predictability, and Teleology Are Viewed by a Practicing Biologist." *Science* 134: 1501–1506.
- Monod, J. 1971. *Chance and Necessity: An Essay on the Natural Philosophy of Modern Biology*. New York: Alfred A. Knopf.
- Montévil, M., and M. Mossio. 2015. "Closure of Constraints in Biological Organisation." *Journal of Theoretical Biology* 372: 179–191.
- Montévil, M., M. Mossio, A. Pocheville, and G. Longo. 2016. "Theoretical Principles for Biology: Variation." *Progress in Biophysics and Molecular Biology* 122 (1): 36–50.

- Moreno, A., and M. Mossio. 2015. *Biological Autonomy. A Philosophical and Theoretical Enquiry*. Dordrecht: Springer.
- Mossio, M., and L. Bich. 2017. "What Makes Biological Organisation Teleological?" *Synthese* 194: 1089–1114.
- Mossio, M., M. Montévil, and G. Longo. 2016. "Theoretical Principles for Biology: Organisation." *Progress in Biophysics and Molecular Biology* 122 (1): 24–35.
- Mugur-Schachter, M., and G. Longo, eds. 2014. *Developments of the Concepts of Randomness, Statistic, and Probability, Special Issue of Mathematical Structures in Computer Science*. Cambridge University Press. vol. 24, n. 3.
- Nicholson, D. J. 2014. "The Machine Conception of the Organism in Development and Evolution: A. Critical Analysis." *Studies in History and Philosophy of Biological and Biomedical Sciences Part C* 48: 162–174.
- Noble, D. 1979. *The Initiation of the Heartbeat*. Oxford: Oxford University Press.
- Noble, D. 2012. "A Theory of Biological Relativity: No Privileged Level of Causation." *Interface Focus* 2 (1): 55–64.
- Paaby, A., and M. Rockman. 2014. "Cryptic Genetic Variation: Evolution's Hidden Substrate." *Nature Reviews Genetics* 15: 247–258.
- Pavesi, Angelo, Alberto Vianelli, Nicola Chirico, Yiming Bao, Olga Blinkova, Robert Belshaw, Andrew Firth, David Karlin, and Eric Jan. 2018. "Overlapping Genes and the Proteins They Encode Differ Significantly in Their Sequence Composition from Non-overlapping Genes." *PLoS ONE* 13 (10): e0202513.
- Peluffo, A. 2015. "The 'Genetic Program': Behind the Genesis of an Influential Metaphor." *Genetics* 200: 685–696.

- Perret, N., and G. Longo. 2016. "Reductionist Perspectives and the Notion of Information." *Progress in Biophysics and Molecular Biology* 122: 11.
- Plomin, R. 2018. *BLUEPRINT. How DNA Makes Us Who We Are*. Penguin.
- Poincaré, H. 1892. *Les Méthodes Nouvelles de la Mécanique Celeste*. Paris: Gauthier-Villars.
- Pouille, P. A., P. Ahmadi, A. C. Brunet, and E. Farge. 2009. "Mechanical Signals Trigger Myosin II Redistribution and Mesoderm Invagination in *Drosophila* Embryos." *Science Signaling* 2: ra16.
- Pouille, P. A., and E. Farge. 2008. "Hydrodynamic Simulation of Multicellular Embryo Invagination." *Physical Biology* 5: 015005.
- Prusiner, S. B. 1982. "Novel Proteinaceous Infectious Particles Cause Scrapie." *Science* 216 (4542): 136–144.
- Rao, C. V., D. M. Wolf, and A. P. Arkin. 2002. "Control, Exploitation and Tolerance of Intracellular Noise." *Nature* 420.
- Resnik, B. 2018. "How Scientists are Learning to Predict Your Future with Your Genes. But What are the Limits?" *Vox*. web journal: <https://www.vox.com/science-and-health/2018/8/23/17527708/genetics-genome-sequencing-gwas-polygenic-risk-score>.
- Rosen, R. 1991. *Life Itself. A Comprehensive Enquiry Into the Nature, Origin and Fabrication of Life*. New York: Columbia University Press.
- Rosenberg, A. 2007. "Reductionism (and Antireductionism) in Biology." In *The Cambridge Companion to the Philosophy of Biology*, edited by D. Hull and M. Ruse, 120–138. Cambridge University Press.
- Schmitt, A. O., and H. Herzel. 1997. "Estimating the Entropy of DNA Sequences." *Journal of Theoretical Biology* 188: 369–377.

- Schrödinger, E. 1944. *What Is Life? The Physical Aspect of the Living Cell*. Cambridge: Cambridge University Press.
- Selzam, S., E. Krapohl, S. von Stumm, P. F. O'Reilly, K. Rimfeld, Y. Kovas, P. S. Dale, J. J. Lee, and R. Plomin. 2016. "Predicting Educational Achievement from DNA." *Molecular Psychiatry* 22: 267.
- Simpson, M. L., C. D. Cox, M. S. Allen, J. M. McCollum, R. D. Dar, D. K. Karig, and J. F. Cooke. 2009. "Noise in Biological Circuits." *WIREs Nanomedicine and Nanotechnology* 1.
- Sonnenschein, C., and A. M. Soto. 2016. "Carcinogenesis Explained within the Context of a Theory of Organisms." *Progress in Biophysics and Molecular Biology* 122 (1): 70–76.
- Skotheim, R. I., and M. Nees. 2007. "Alternative Splicing in Cancer: Noise, Functional, or Systematic?" *The International Journal of Biochemistry and Cell Biology* 39 (7–8): 1432–1449.
- Turing, A. 1950. "Computing Machinery and Intelligence." *Mind; A Quarterly Review of Psychology and Philosophy* LIX: 433–460.
- van Frassen, B. C. 1970. *An Introduction to the Philosophy of Space and Time*. New York: Random House.
- Young, J., Roger Nilsen, Katrina G. Waymire, Grant R. MacGregor, and Thomas R. Insel. 1999. "Increased Affiliative Response to Vasopressin in Mice Expressing the V1a Receptor from a Monogamous Vole." *Nature* 400: 766–768.
- Walsh, D. 2015. *Organisms, Agency, and Evolution*. Cambridge: Cambridge University Press.
- Weinberg, R. 2014. "Coming Full Circle – From Endless Complexity to Simplicity and Back Again." *Cell* 157.



West-Eberhard, M.-J. 2003. *Developmental Plasticity and Evolution*. New York: Oxford University Press.

Weyl, H. 1949. *Philosophy of Mathematics and of Natural Sciences*. Princeton: Princeton University Press.

Wiener, R. 1948. *Cybernetics: Or Control and Communication in the Animal and the Machine*. Cambridge, MA: MIT Press.

Wolfe, C. 2010. "Do Organisms Have an Ontological Status?" *History and Philosophy of the Life Sciences* 32 (2–3): 195–232.

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