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# From Axiomatic Systems to the Dogmatic Gene and Beyond

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## ABSTRACT

The positivistic views that dominated the early debate on the foundations of mathematics, at the beginning of the 20th century, survived the “negative results” that have shown the limits of the axiomatic approach since the 1930s. Rigour, abstraction and symbolism have been confused with formalism, based on finite strings of signs, pre-given axioms, and potentially mechanisable rewriting rules. This contributed to major clarifications in the mathematical praxes but obscured the limits of formalisms due to the exclusion of the historical creation of sense proper to any science. We expand on this sometimes fruitful confusion with some case studies. We then hint to the historical creation of sense as a component of an epistemology of mathematics. We continue with an analogy with genocentric approaches in biology, as similar positivistic views resurfaced there fifty years later. Finite sequences of letters in the DNA would completely determine ontogenesis and phylogenesis, according to the Central Dogma of molecular biology. Limits and “negative evidence” have been disregarded while searching for the “gene for” everything. Alternative perspectives require a reconstruction of the sense of history as locus for the constitution of any object of biological knowledge. In particular, the historicity of biological evolution will be understood in terms of changing phase spaces and of the role of rare events in all phylogenetic trajectories. The analysis of the evolutionary production of variability, adaptivity and ecosystemic diversity is a key component of the project we hint to, as part of a renewed relation to the biological environment.

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## 1. Proofs, meanings and invariants

With integers and their ratios mapping perfectly to musical forms and aesthetic criteria, ancient Greek thought easily associates intimate knowledge of reality and production of beauty. As early Greek thinkers lay the groundwork for Western philosophy, Pythagoras thought that not only rigour but the very essence of reality was to be found in numbers, within the rules governing arithmetic (Huffman, 2019; Chiurazzi, 2017). Ancient Greeks had a reason to give such importance to integers: their role was central in their societies. This went from the political rule — with strict quorums for assemblies and some tediously recorded voting tallies (Canevaro, 2018) — to the currency systems used in one of the first highly commercial societies with complex import-export networks (Ober, 2011).

But suddenly, after decades of detailed examination of integers and their ratios, the crash. The perfect *logos* of integers creates in its midst the irrational, the “*a-logos*”, inside the unitary square itself: in its diagonal one finds a number,  $\sqrt{2}$ , lying outside of the bounds of arithmetic reasoning and integer ratios.

How to make sense of this nonsensical evidence, this first negative result? As it often does when confronted with powerful negative results, reason itself expands. At the time, it did so by including drawing motions, producing lines, evoking meaning through the use of diagrams at the core of geometry, in Euclid’s account (Longo, 2009). The breadthless border of plane figures that is the line is not an approximation, but a new foundation to reground geometric reasoning away from arithmetic principles.

This new geometrical foundation lies in diagrams (Panza, 2012), but not simply in the final diagrams themselves. Instead, it is the common element between the diagram, the motions that create the diagram, and the oral description of both diagram and motions to one’s peers. The motion and the description seek

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The authors’ order is alphabetical.

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to capture that which is not in the particular physical instantiation. Following Proclus, the discoveries in geometry are *measured*, in a physical sense, through perception (αἰσθητικός). To truly grasp mathematical concepts which reside in the intellect, one has to extract their essence, using one's imagination while inspired by the diagrams (Helmig and Steel, 2020).

Geometry then arises in the interplay that allows the tracing motion in the sand to show a continuous line — a trajectory, we could say — and the language that then allows one to say “the line I'm drawing is breadthless”. By this, Greek geometry invented at once a notion of trajectory independent of the object moving along it and the difficult notion of border, which served as foundation for later developments, up to Thom's general theory (Thom, 1954).

Symmetries also play a central role in this new non-numerical foundation for geometry. Looking at the five Euclidean postulates, they all implicitly try to maximise symmetries in the constructions they allow, with the central elements being straight lines between points (forming the most symmetric and simplest trajectories) and circles (Longo, 2009). And although this was not formalised and might have gone unnoticed until Desargues or even Joseph Diaz Gergonne, the postulates — and the first theorem — themselves explicit some conceptual symmetry in how they allow a duality between points and lines: if any line is defined by a pair of points, a point is also defined by a pair of lines<sup>1</sup> (Pedoe, 1975). Symmetries will continue to play a key role in the foundations of mathematics from Klein's Erlangen program (1872) to Weyl's approach to mathematical knowledge (Weyl, 1952).

There is a common pattern behind the use of such elements as basis for mathematical thoughts: a search for abstraction. As the very concept of abstraction is hard to define and manipulate, let us focus instead on the construction of explicit invariants. What is numerosity but the abstraction that seeks to find the common invariant between seven coins and seven sheep? Between three lions and three roars? What is symmetry but the search for patterns that remain the same after simple transformations? What is continuity but the common property shared by all motions and trajectories?

The fact that we human mathematicians decided to collectively focus on invariants such as those — maybe unconsciously, through the process of finding them easy to work with — is grounded in these pre-human practices. Each of the early ones apparently corresponds to a pattern that our brain is able to notice and then stabilise as invariants of action: being able to iterate an action, anticipate the trajectory of a prey or of a predator, independently of changing environments, forces the selective memory of the invariant properties of trajectories. Our early invariants are practiced in actions before becoming generalised and abstract forms of small set of intuitions — that result from praxes — for which we now even have neuronal evidence, as traces of the interfacing of the brain with the world, through action. The brain allows ecosystemic activities while shaping itself in them. Like the practice of trajectories, counting small amounts of distinct objects is a practice shared with many animals — again a practical invariant, in this case in comparing quantities. What is the sense of numerosity for larger numbers except the extension of our inner capacity for subitising — instantly knowing the number of objects in a small set, of size generally less than five. This primary sense can also be isolated and traced back to — and perhaps produced by — some dedicated neuronal structures in our brains, where initial simple connections are reinforced by their use (Dehaene, 2011; Anobile, Arrighi and Burr, 2019; Longo and Viarouge, 2010). There is also evidence that the integer number line itself, with the numbers sorted from left to right in our writing cultures<sup>2</sup>, could be a common invariant on how humans can write and “see” numbers internally, linking arithmetic and geometric intuitions.

What is the common element in all lines and curves we draw? The pattern that is independent of the thickness, colour, or medium in which we draw — be it sand or paper — but the continuity of the gesture? Is it a coincidence that the essence of the line might be in the continuity of the artist's hand's trajectory, and that we chose this as one of the central invariants of early geometry, when we as a species share such an uncanny innate ability to visualise and predict such trajectories effortlessly? Following Poincaré's intuition, our inner representations of the distance of an object in space might be related to the set of muscular tensions necessary to reach it. This is facilitated by our saccadic movements — or eye jerks — which trace in advance the paths needed to reach an object, to capture a prey. More precisely, tracing in advance a trajectory by our eyes allows to anticipate the next position where they look to follow a prey, escape a predator, capture

<sup>1</sup>To be more accurate, this requires the two lines not to be parallel — as seen in the reference to the first theorem of Euclid's Elements below — or for one to be in a projective space.

<sup>2</sup>From right to left in Arabic, as any Arabic mathematised person can witness.

a ball, and to move there following “the pursuit line” also traced by eye jerks — fractions of a second in advance (Berthoz, 1997). The Poincaré-Berthoz isomorphism relates our visual perception of continuity and our vestibular perception of trajectories that are continuous in not only space but also time (Teissier, 2012). Attuned with our perspective, Teissier observed, in a lecture which became famous at the Philosophy and Mathematics seminar at ENS Paris: “I understand a theorem when, for sure, I can follow the logical argument, yet the actual understanding and mastering of the argument comes only when it becomes evident to my monkey’s brain”.

Finally, symmetries contain an aesthetic component. They please our brains and we often recognise them from a distance, even if they are imperfect — and can now teach artificial neural networks to do the same, starting with the simplest patterns of continuity in the early stages of AI and going to complex symmetries more recently (Scharcanski and Venetsanopoulos, 1997; Cao, Pang and Li, 2016). If their design shows anything, it is that it is relatively easy to create neural networks that detect exactly those simple properties: continuity, borders, symmetry, and sometimes even numerosity. The symmetries of the world, those of our animal bodies may have forced our brain structures and perpetuate this influence on any new brain in a similar environment. An extreme case is seen in the empirical evidence from studies where cats where raised in environments consisting entirely of stripes (horizontal or oblique). Once adults, the cats had visual deficiencies in their capacity to recognise shapes that differed from the pattern they were used to, visible in both behaviour and neural cell networks (Blasdel, Mitchell, Muir and Pettigrew, 1977; Maffei, 1998).

When explaining axiomatic systems to young students, we often find ourselves describing axioms as self-evident properties and neglecting their evolutionary and historical formation, the way they result from a friction between our brains and the world by our living bodies, later enriched and specified by language and writing. It is then reasonable to wonder whether many early axioms are exactly this: attempts to abstract a felt intuition, a pattern perceived by most human minds, the proposal of a relevant invariance property. We hinted at the role of active tracing and symmetries in the proposal of Euclid’s axioms. Their universality — as understandable by any human — is due to the pre-linguistic nature of this construction of sense that precedes human languages. The proof is then inextricably linked to the discourse that allows generalisation of this early intuition, as a result of an active relation to the world, into rigorous knowledge. It then becomes a social object that relies, by language, on rhetoric and sometimes esoteric knowledge (often in a master/disciple setting<sup>3</sup>). Despite the relative fascination of Greek philosophers for the written word, proofs were still mostly oral objects, with people learning from each other instead of using textbooks. Every mathematician experiences the huge efficiency gains one obtains when discussing complex results face to face as opposed to in a textbook, and how many proofs are elaborated during discussions in front of black-or white- boards. Proofs are still now mostly oral objects, supported by sketched computations or very informal drawings just hinting to structures of imagination by gestures.

We then reach a kind of informal rigour. A proof is whatever convinces its audience — sometimes one well-versed in rhetorical tricks — of the veracity of a proposition. Explicit references to previously proved results contribute to such rigour. But certain central statements can remain unexamined. For example, the consideration of a line as breadthless border can be formally interpreted as taking the asymptotic limit of a sequence of geometric objects, but this limit is never formally defined — and would have been impossible with the tools present at the Greeks’ time. Teissier’s very argument about the Poincaré-Berthoz isomorphism makes use of this peculiarity: his isomorphism is not a true, formal isomorphism, but only a linguistic trick to give his readers an intuition of the relationship he infers between the visual and vestibular lines — and he says as much in his article (Teissier, 2012).

Getting back to Greek mathematicians, let’s consider Euclid’s *Elements* again. On one side, it is correct to say that they figure a systematic approach with an axiomatisation that was not present in earlier texts. The results in the *Elements* indeed have proofs, albeit lacking some examination of what proofs are exactly<sup>4</sup>. On the other side, a mathematical proof is also — or even mainly — a historical construction of meaning, through a dialogue in the informal rigour proper to the praxis of mathematics. If it is too complex, it

<sup>3</sup>Legends abound on Hippasus of Metapondum and his potential murder as punishment for revealing the irrationality of  $\sqrt{2}$  to the public outside of the Pythagorean school (Huffman, 2019).

<sup>4</sup>For example, the analysis of modus ponens and the examination of the rules of deduction that are used within the text are far from the consideration present in the text itself, at least from the evidence subsisting today.

must be — and is in practice — re-written over time, by distilling lemmas, and by proposing more general underlying invariants, thus making the corresponding intuition easier to grasp. It might then be ahistorical to interpret Euclid’s project as a predecessor to Hilbert’s that was only lacking the proper tools to found mathematics in a formal way (see the remarks on Euclid’s first theorem in chapter one and on other critiques in Heath (1908)).

## 2. The role of formalism

Looking at the last two millennia, we can observe that formalism and codification of thought both appear over time, and are steeped in the evolution of language. As in other fields, there is a desire to simplify patterns that everyone observes. If most mathematicians talk about powers of an unknown number, it is more efficient to use  $x^7$  than a complex sentence. Common examples can be found in older works such as Muḥammad ibn Mūsā al-Khwārizmī’s treatise on algebra (as translated by Rosen (1831)):

“I have divided ten into two parts, and having multiplied each part by itself, I have subtracted the smaller from the greater, and the remainder was forty. Then the computation is — you multiply ten minus thing by itself, it is a hundred plus one square minus twenty things and you also multiply thing by thing, it is one square. Subtract this from a hundred and a square minus twenty things, and you have a hundred, minus twenty things, equal to forty dirhems.”

Or, equivalently:

$$\left| (10 - x)^2 - x^2 \right| = 40 \rightarrow 100 - 20x = 40$$

Here, formalism has the advantage of making proofs more intelligible by making them more concise, through the adoption of a common language. And this process of formalisation is in itself social: with dozens of potential formalisms proposed, the selection of one of them depends on their relative popularity among other authors until one reaches hegemony. The choice of the symbol’s calligraphy itself is not neutral: quite a few of them evoke meaning through both the motion necessary to draw them and the mental associations this creates. For example, the choice of using  $\widehat{ABC}$  — and sometimes  $\angle ABC$  — to denote an angle is the result of a non-trivial evolution. As related by Florian Cajori, the symbol  $<$  was used from for angles in 1634 and continued being used until the eighteenth century, in parallel with the “smaller than” signification (Cajori, 1928). The period in between saw a multiplication of options appear:  $\angle$  for an angle, and  $\angle\angle$  for plural angles,  $\widehat{a\ b}$  for an angle between lines  $a$  and  $b$ , or even  $\sphericalangle$ , among dozens of other possibilities, each carrying a possibly different reference to meaning<sup>5</sup>).

Going back to early Greek mathematicians, the representation of numbers was dual, with on one hand numbers written as letters, and on the other manipulation through pebbles ( $\psi\eta\phi\omicron\varsigma$ ) on a table — or maybe an early abacus. Thus, the representation was not only through an abstract symbol that was drawn, but mentally incorporated the manipulation of a number of dots, linking the concept and the numerosity (Lang, 1957). Hence, the process of sharing the initial meaning that one ascribes to a symbol is an essential part: without it, the symbol cannot be used and remains unknown. Hence, before the symbol acquires any autonomy and becomes stable through the same rules as general linguistic terms<sup>6</sup>, it must be used by a small community for which it represents a shared meaning born through common interactions — oral or written<sup>7</sup>.

The symbol — from the Greek  $\sigma\upsilon\mu\beta\acute{\alpha}\lambda\lambda\omega$ , “I throw together” — can then be said to unite multiple sources of meaning. It represents the invariant at the heart of the abstraction process, and its multiple

<sup>5</sup>One curious effect is that old notations had a symbol for an indeterminate angle ( $\angle$ ), but few possibilities for one that goes through given points or lines. Reciprocally, contemporary notations allow for a specific angle given three points:  $\widehat{ABC}$ , but do not directly allow the representation of a generic angle. Of course, it is still possible to denote a generic angle by using  $\widehat{ABC}$  with generic A, B, and C. Some use  $\angle ABC$  for specific angles, but the symbol  $\angle$  by itself has become rare. Questions on the nature of angles are still debated today, especially as they relate to physical measurements, as in Krystek (2021).

<sup>6</sup>For example, the most commonly used terms are those that are most stable and evolve more slowly (Pagel, Atkinson and Meade, 2007).

<sup>7</sup>For what is probably the first time in history, mathematicians interact mainly through papers and most of the exchanges on what could be shared meanings happen via impersonal publications, instead of oral exchanges — or even regular epistolary correspondence. It remains to be seen how this will impact the evolution of symbol-concepts.

meanings interact. As such, it is not just a formal sign that can be manipulated by automated syntactic rules without losing something — some form of meaning — in the process. In this context, the initial invariant is not just a symbol, but the motion that allows one to draw said symbol. The meaning evoked arises from both motion and association with other symbol-concepts.

In the historical mathematical practice, after one removes or simplifies redundant passages of proofs to make them clearer to check (and sometimes to understand), it seems natural to hope that we can reach some point where the whole process becomes quasi-mechanical. In this context, Hilbert's project initially appears reasonable, as is the general objective of finding a common axiomatisation of mathematics that can lead to a fully formal, fully verified, and ideally all-encompassing tower of mathematical knowledge. In this way, the stabilisation of symbols is a prerequisite for the axiomatisation project, providing both the tools and the motivation for the latter. The issue is when one goes from this initial formalisation of simple concepts and towards the formalisation of our actions on concept-symbols themselves, in a self-referential way.

Mathematics is rigorous, but true mathematical rigour can only be meaning-making, and in this way can only be “in-formal”. A formalism without this meaning-making can only manipulate symbols as signs — and not signifiers — and easily falls into the absurd. Shortly after Frege explicitly formalised Cantor's set theory, Russell shows an easy contradiction.

The solution, which uses both sets and classes, illustrates how important types are in mathematics — although this is not always fully apparent. Types contribute greatly to the creation of meaning in proofs, by allowing us to state on which set a function is defined and in which set it has its values.

Thirty years after this first paradox, Alonzo Church proposes a theory of functions that could be applied to themselves. As this allows a brand of pure formalism with no intrinsic meaning, it leads to Curry's paradox, a more technical rewriting of the initial circular contradiction. Two paths avoid this contradiction: bringing meaning into the formalism by reintroducing types (Church, 1941) or limiting the simultaneous interplay of self-application and negation (Barendregt, 1984). This happens once again with Martin-Löf and his formal universe of Types, which is a Type in itself. Once Girard points out this paradox in the theory, illustrating both its expressive power and a profound flaw (Coquand, 1986), Martin-Löf repairs it by restoring the link to meaning-making in a novel theory of types (Martin-Löf and Sambin, 1984).

Those paradoxes do not negate the importance or usefulness of formalism, but underline its limits when it comes to the creation of meaningful statements. Studying the paradoxes themselves is a fruitful activity even outside of theoretical contexts, as is shown by the developments of early computer science but also contemporary development paradigms inspired by intuitionistic logic. The system that rose out of this thanks to Curry's fixed-point operator is expressive and led to new meaningful insights in topology (Amadio and Curien, 1998; Longo, 2001).

That said, almost each time mathematicians tried to avoid the requirements of only considering meaningful statements — by trying to replace it with the rigour of a pure formalism — they ended up with flaws in the system leading to a syntactic contradiction.

A common feature of many such paradoxes is that they rely on some form of encoding. This is extremely present in Gödel's initial incompleteness theorems: the goal was after all to encode provability of arithmetic statements in arithmetic itself. This is powerful, but the process tends to remove all links to intuition and meaning to achieve certain results, and was already decried by Girard (2001): “the practice of artificial codings corresponds to a logical ideology for which the language is a mere bureaucratic device, with no intrinsic properties”. The intuition-removing effect of encoding can also be found in another object commonly studied by set theory: bijections. There are many — discontinuous — bijections between  $\mathbb{R}$  and  $\mathbb{R}^2$ , and creating one is trivial by “mixing” the numerical representations of two numbers, a very simple encoding indeed. Here, the encodings typically destroys continuity, one of our main sources of intuition, or what “gives meaning” to the real line and spaces. This makes such objects harder to handle than ones related by stronger relations (ideally an isomorphism). The only operations doable on such structures are syntactic operations: rigorous, but rarely meaningful.

Thus, despite a century of debate over the role of formalism and numerous attempts to push mathematicians to follow stricter rules, proofs remain social objects — the most stable of our conceptual constructions, yet the result of a historical inter-subjective activity.

Let us give three examples of diverging reactions to objects that look like proofs, where the interplay between intuition, sense and formal (even computational) rigour has had a major role. First, we can take the



first “proof” of the four-colour theorem in 1976, which relied on the automatised checking of a disjunction of 1834 cases, as well as extensive manual checking<sup>8</sup> (Wilson, 2003). Its status as proof was disputed for at least two decades, as it left most unsatisfied with the methodology and the reliance on automated checking. This lasted at least until further proofs appeared and the automated checking of the proof was formalised in Coq, requiring mathematicians to have to accept a much smaller codebase<sup>9</sup>. In a way, the proof did not fully respect the norms of being both manually checkable and of bringing meaning and new intuitions to mathematicians who would check the proof<sup>10</sup>.

One key issue in this direction is that program correctness is not decidable, as a consequence of Rice’s theorem Rogers (1987) — moreover “few” properties of programs are even semidecidable (Giannini and Longo, 1984). That is, no program can be guaranteed to find a proof of the correctness of other programs, and no general method can perfectly rigorously prove the correctness of very long programs, without special insights. So, the solution comes from the robustness and transparency of the programming style: Coq is such an example, thanks to its robust foundation in Type Theory. This is thus a matter of the historical formation of a programming style after avoiding logical paradoxes (Curry’s, Girard’s ...). By this, we can trust a proof written and deduced in Coq, even though a proof of correctness is impossible in the general case.

On the opposite side, we have the article on Quantum Bit Commitment published in 1993 by Brassard, Crépeau, Jozsa and Langlois (Brassard, Crépeau, Jozsa and Langlois, 1993). This article featured a short proof (the whole article being 9 pages long) of a surprising result, and was quite well received initially — and published in what might have been the most prestigious venue in the field at the time. It had all the required elements to be accepted as a proof: it was formal, made sense, and gave new intuitions about the field. And yet it was shown to be invalid three years later, with the central counterargument fitting in a single line (Lo and Chau, 1997). One common explanation for this gap is that the field has very little reliance on intuition (or rather, offers very little in the way of intuition for people to work with), and that most proofs depend on formal sign manipulation. Non-visual formalisation as a tool of creation (and not only of verification) might then be easily misled.

Our last example is contemporary, and illustrates the fuzzy boundary between proof and non-proof. In 2012, Shinichi Mochizuki put online a string of four preprints proposing a proof of the abc conjecture<sup>11</sup>, totalling 646 pages in the versions last updated in December 2020 — and requiring the assimilation of nearly 2000 pages of his previous research on anabelian geometry. After eight years, the community is still undecided about the solidity of the proof, due to both its length and its complexity. After the first few years of general evaluation, the debate has now focused on Corollary 3.12 of the fourth article. This corollary states that the theory developed over all the preceding works applies to the problem at hand. The problem is then one of semantics, and not one of syntax: does the new theory apply to the object considered, and how would that make sense? Interestingly, quite a few arguments against the proof are linked to heuristics developed over time and not to formal considerations of what proofs are. Central to this is the fact that the new theory has so far found no other application or usable intermediate result, which would be a first for a theory of this scale. So far, the mathematical community is still debating the issue<sup>12</sup> (Castelvecchi, 2015; Roberts, 2019).

Considering proofs — or at least verified knowledge — as social objects is not a new idea, as Henri Poincaré wrote in 1905: “Anything objective must be common to multiple minds, and consequentially be

<sup>8</sup>Ironically, there was a small — and fixable — gap in the original proof, located in the “human” side of the proof and not in the massive disjunction (Wilson, 2003).

<sup>9</sup>One could then interpret proof checks as force multipliers, allowing mathematicians to only have to check a small kernel that then bootstraps by building upon itself up to the point where it can check the whole proof.

<sup>10</sup>One could wonder about the status of matrix multiplication algorithms, whose complexity grows further and further away from most mathematicians’ capacity to review as they get steadily closer to the  $\tilde{O}(n^2)$  bound, with proofs now regularly sporting more than 30 pages of formalism (Gall, 2014; Alman and Williams, 2021). One wonders if the proofs of future  $\tilde{O}(n^{2+\epsilon})$  algorithms will have lengths in  $\Omega(\frac{1}{\epsilon})$ .

<sup>11</sup>The abc conjecture was proposed in 1985, and constrains the relative sizes of  $c$  and  $abc$ , where  $a$ ,  $b$ , and  $c$  are three positive integers who are relative primes and satisfy  $a + b = c$ .

<sup>12</sup>There are social factors making this issue more complex. First, the author refused to leave his home country of Japan to talk about his solution abroad, limiting the opportunities for others to exchange with him. Second, he recently published the four articles in a journal for which he is chief editor, which is unorthodox and has been badly received — although he recused himself from the process.

transmitted from one to the other”<sup>13</sup>. We could then follow René Thom and his provocation — “anything rigorous is insignificant” — and wonder about the relationships between abstractness, rigour, symbolism, and their links to formalism, being careful not to assume one is the other (Thom, 1973).

The “linguistic turn” at the beginning of the 20th century made us think we could identify these notions, with formalised axioms and well chosen strings of symbols handled by appropriate rewriting rules trying to replace the abstract symbolic and rigorous practice of mathematics, beyond the question of meaning and context. This attempt to limit the legitimate expressions of meaning in non formal but rigorous settings has consequences on other fields, which we will now investigate.

### 3. Tempered expectations

After the failure of the end-goal of the Hilbertian project, mostly through Gödel’s incompleteness theorems, mathematicians had to revise the objective of mathematics themselves. More concretely, and well beyond the fantastic diagonal trick of Gödel’s, interesting unprovable statements of Formal Number Theory (Arithmetic) of the 1970s and 1980s more blatantly show the “concrete or mathematical” incompleteness of formalisms. One can even point out where a “geometric judgements” or the use of “genericity” of a considered number, not expressible by induction, steps in the proof of these number theoretic examples. A close analysis of the formal unprovability of Kruskal-Friedman “tree-theorem” (Harrington, Morley, Šcedrov and Simpson, 1985) and Girard’s Normalization theorems (Girard, Taylor and Lafont, 1989) is developed in Longo (2011).

Then, gone was the ideal of finding a complete set of formal axioms and theorems and their associated proofs in a search for “complete knowledge”. Hence Hilbert’s speech of “We must know — We will know”<sup>14</sup>, in response to du Bois-Reymond’s *ignorabimus* speech on the limits of scientific knowledge in 1872 (McCarty, 2004) and in search for the “definitive solution” to the problem of foundation, as said by Hilbert of mathematics in the 1920s. Fortunately, in science, there are rarely definitive solutions. So, the focus went to the interplay of axioms and theories, to find their relationships with one another, to find which results depend on which ones, continuing, in a sense, Hilbert’s 1898 seminal work in the foundations of Geometry and the diversity of axiomatic systems (Hilbert, 1902). Thus, the field went from a search for a unique set of rigorous “truths” to a relativising framework and many think about mathematical proofs in a broader sense - in reference to the historicity and contextuality of mathematical activity “generated in our space of humanity from a human activity”, as written by Husserl in 1933 while stressing the “crisis” of the formalist approach to knowledge (Husserl, 1970).

One of the few common formal invariants is the use of the axiom of choice. This axiom plays an interesting role as it tends to help our intuitions and be a boon when it comes to proving new results. That said, in many cases, this is only a shortcut, and alternative proofs that do not rely on it are often found in the following years — or the result is shown to imply or be equivalent to the axiom of choice.

Mathematics show us that almost any important proof, even if it is of an *a posteriori* fully formalisable statement, requires new concepts and structures, and often an investigation of their properties, in a dynamic construction of meaning. This is true from Euclid’s first theorem to Wiles’ proof of Fermat’s conjecture. The first requires a reference to the meaning of breadthless continuous lines: two continuous trajectories intersecting in good conditions produce one and only one point, assumes the first theorem in the first book of Euclid’s — and this also defines continuity for a breadthless line. Its foundation is anchored in lines as (continuous) motion, as “produced” as Euclid says, and on the Greek metaphysics of pure ideas. The second refers to the historical meaning construction of the Galois representations of the semi-stable modular curves and the corresponding original notions and properties that emerge in Wiles’ proof.

There still exists a dynamic struggle on the question of formalism, which still plays a role, but mostly to rigorously check proofs. On one side, we have the hard border made by impossibility results that limit any attempt at a full formalisation of non-trivial theories. On the other side, we have a frustration with the limits of mathematics as they are performed, with the many errors that are eventually found in published

<sup>13</sup>“Ce qui est objectif doit être commun à plusieurs esprits, et par conséquent pouvoir être transmis de l’un à l’autre.” as quoted in Thomas (2015).

<sup>14</sup>Wir müssen wissen — wir werden wissen.



work despite the peer-review<sup>15</sup>. A human example of this struggle can be found in the career of Fields medalist Vladimir Voevodsky. His efforts on formal verification — through the development of univalent foundations — might have been motivated by the doubts related to potential errors in his own published work, one of which was confirmed only after 15 years (for more information, see Andrei Rodin’s article on “Voevodsky’s unfinished project: filling the gap between pure and applied mathematics” in this very issue or Rodin (2020)).

In recent years automatic proof assistance has been making miracles, particularly in very abstract areas of mathematics, Voevodsky’s work being just one example. Robust systems help mathematicians develop incredibly complex computations, by formally implementing some fragments of proofs that can be fully carried on by a machine. Note though, that the formal provability of a statement is undecidable, thus it is up to the mathematician experience and good taste to understand which fragments of its reasoning may be soundly passed over to a machine. When it works, the mathematician is then free to “think”, while passing to a machine some boring computations, that is, to invent new concepts and structures, what really matters in mathematics since the invention of the breadthless line. The other advantage is also that errors tend to appear in the computational parts of a proof, hidden in “minor” lemmas, as it was in Poincaré’s early version of the Three Body problem — avoiding them by machines is just fantastic.

The search for certainty, as pursued by Voevodsky — but this was also Martin-Löf’s quest after Girard’s paradox demolished his early Type Theoretic construction — is a sound concern, in particular for the certainty in the robustness of a proof. Proving theorems, and doing so correctly, is surely essential to mathematics, and it is the mathematician’s job. However, it is even more important to “understand” which are the theorems worth proving.

The philosophical teachings of the Gödelian limits and of more recent formal impossibility results in number theory have, alas, been often ignored beyond the horizons of their initial field. Interestingly, despite the limited communication between the fields when it comes to the philosophical underpinnings of formalism, physics has also greatly evolved over the 20th century, with a similar direction. The initial end goal of physics<sup>16</sup> was to obtain a predictive power over dynamic systems that was hindered only by instrumental capacity — and hence unboundedly growing.

This idea played well with technological advances, from logarithm tables for artillery ballistic computations that are performed manually to the more intricate computational physical models designed in the second half of the 20th century. Representing objects as single points with finite-precision arithmetic means that one can be exact and rigorous, and running the same predictive program over the same inputs gives the exact same results. Some elements were considered to be random in appearance, as the product of continuous non-linear dynamics, but this randomness was a classical one, linked to physical fluctuations/perturbations and mathematical non-linearity, not to a mathematical limit of what is knowable.

However, this project also ran into an immovable object with the elaboration of Heisenberg’s uncertainty principle, nearly simultaneously with mathematics — being published in 1927, barely four years before Gödel’s incompleteness theorems. The discrete character of the black-body radiation discovered in 1900 by Max Planck could have bolstered this interpretation, limiting the impact of continuity (and the corresponding unavoidable noise). As it turned out, what physicists found instead was a completely new framework where non-deterministic fluctuations made impossible any prediction on a small scale. The “rigour” of exact computation and repeated iterations fails, as Schrödinger’s equation does not give us any single answer, but at best a superposition of results or a distribution of probabilities.

In a way, this is much worse than the initial measuring problems of classical physics, but it forces the redefinition of physics end-goals themselves. Instead of trying to obtain unbounded predictive power, rigour becomes knowing which elements behave deterministically, to which precision they can be known, and to understand the probability distributions when they cannot.

The nature of noise is then questioned, and split into a randomness due to classical physical phenomena — the random fluctuations of a double pendulum, say, and its non-linear dynamics, against quantum un-

<sup>15</sup>Although many errors can be found in work before the 20th century, there is a perceived recent increase among some mathematicians — such as those of the Xena project — sometimes blamed on the working conditions which increase the workload of reviewers because of extreme publishing pressure.

<sup>16</sup>And, it could be argued, of mathematics too in some of their earliest incarnation as a computational tool for Babylonian and Indian astronomy (Rochberg, 2002).

certainty. Knowing a system then acquires a different meaning, even randomness depends on the intended theory, on the frame of physical meaning.

## 4. Foundational back and forth, biology versus mathematics

### 4.1. The Dogmatic Gene

Hilbert's program was rediscovered by molecular biology, after World War II. The genocentric approach, though, grounded on the isolation of "chromosomes" by colouring them, is due to several authors and goes back to the end of the 19th century (Keller, 2009). Soon, research focused on them as an immensely important chemical structure at the core of all biological activity — which luckily was also easy to see. A high moment of their role in the assumption of their "completeness" with respect to ontogenesis is surely due to the discovery in Beadle and Tatum (1941) that a mutation in an "eye colour gene" was responsible for a change in an enzyme acting in the metabolic pathway of pigment synthesis (Horowitz, 1995). The "one-gene / one enzyme" hypothesis became then a founding principle of molecular biology, that spanned at least 60 years. Still in 1999, F. Collins claimed (Collins, 1999), on these grounds and in view of the correlations to phenotypes attributed to genes, that he, as head of the Human Genome Project, expected to find about 80,000 genes in the Human DNA, a lot more than the 16,000 genes found in *C. Elegans*, a microscopic worm of 1,000 cells — a significant difference, on the behalf of our human dignity. Two years later human genes were claimed to be 25,000, soon downplayed to 20,000. The number of *C. Elegans*' genes remained stable. In between these 60 years, the grandiose march of the completeness assumption had its strong point in the "Central Dogma" (CD) of molecular biology:

The transfer of information from nucleic acid to nucleic acid, or from nucleic acid to protein may be possible, but transfer from protein to protein, or from protein to nucleic acid is impossible. Information means here the precise determination of sequence, either of bases in the nucleic acid or of amino acid residues in the — Francis Harry Crick (1958)

In spite of some subtle interpretations still trying to justify the CD, enriched by some recursive cycle from RNA to DNA, it remains an instructive perspective on life with a predominantly unidirectional flow of coded information from DNA to RNA and then to proteins (Istrail, De-Leon and Davidson, 2007).

Of course, even in the perspective of the CD, more is needed to understand the DNA as the "complete book of life" containing the instructions for ontogenesis — "written by God", as stated by F. Collins in 2001 upon announcing the decoding of the DNA. One needs proteins to completely describe phenotypes. They do so, since the bio-chemical cascades taking place in a cell, are "a Cartesian mechanism", a "boolean algebra" as "found in computers", gears based on "the exact, stereospecific" interactions (geometric and chemical affinities) of macromolecules in the cell (Monod, 1970). The old "key-lock paradigm", proposed for small molecules at the end of 19th century, was thus transferred to huge ones, an essential feature of the computational model of the organism (Istrail, De-Leon and Davidson, 2007; Karr, Sanghvi, Macklin, Gutschow, Jacobs, Bolival Jr, Assad-Garcia, Glass and Covert, 2012).

We recognize in the CD, enriched with the assumption of exact, mechanical macro-molecular cascades in the cell, the hypothesis of completeness of formal axioms: these are finite strings of signs, from which "potentially mechanisable" deduction rules, as association of strings to strings (gears of a boolean algebra), would allow to deduce all true assertions of mathematics. Thus, life dynamics originate in finite strings of G, C, A and T, four chemicals, an alphabet: "The surprise is that the genetic specificity is written down, not with ideograms as in Chinese, but with an alphabet as in French, or rather in Morse" (Jacob, 1965). We also write mathematical axioms in an finite alphabet (some logograms or special symbols are also required, such as " $\rightarrow$ "). This is rarely done with ideograms as these need to be interpreted, are highly context dependent, rich of ambiguities, far from the "unshakable certainties" that the axiomatic/alphabetic approach (and the focus on DNA) may give to knowledge. Both the analysis of axioms and the decoded DNA would give the Hilbertian "definitive solution" to the main problems of biology, as claimed by the decoders of the human genome (Gilbert, 1992), promising in 2001 to defeat genetic diseases in a few years, to "Eliminate Suffering And Death Due To Cancer By 2015" (von Eschenbach, 2003) and a lot more (see Longo (2018b) for references and a discussion). The complete driving role of genes, as programming feature of DNA (Danchin, 2002, 2008), lead to invent "genes for" such things as language (Cohen, 1998) and aggressive behavior (Perbal, 2013).

## 4.2. Beyond axioms and dogmas

Let's go back to mathematics. In Type Theoretic programming languages, a program is a (formal) proof — this is the rigorous frame that makes Coq a very reliable proof assistant: Coq brings in programming the rigour of (constructive) Proof Theory. Conversely, a formal proof, in Coq, is a program. Yet, we learned from the story we told above that the notion of mathematical proof must be complemented by “human sense”, more precisely by the invention of concepts and structures, beginning with the first and most fundamental one of western mathematics: Euclid's breadthless line. Moreover, the “concrete or mathematical incompleteness” of proofs as programs even applies to pure combinatorial statements of Number Theory, as mentioned above: geometric judgements step in even along these proofs, as part of a shared creation of meaning, shared in history (Longo, 2011). This meaning is transferable to other human contexts as it is based — in mathematics more than in any other form of knowledge — in action in space, in pre-linguistic constructions that single out invariant trajectories, in subitising. The construction of the concept, in language, is a further stabilisation in humans of those pre-linguistic experiences, made definitely robust by the invention of writing. But this (finite, alphabetic) writing does not allow even a posteriori to reconstruct the constitutive path that gives meaning to it, since reference to meaning, action, symmetries and gestures provably enter into the proof. A historical context thus gives meaning to the practice of mathematics: its human universality and historical stability is due to its basis in prelinguistic activities in the ecosystem, as hinted above. The aim of mathematics though is to turn these historical constructions into maximally invariant concepts and proofs. In a sense, historicity, as origin of meaning making, enables and constrains the mathematical invention, later stabilised by forgetting history as much as possible — though without ever reaching a meaning-independent complete reconstruction.

The formal approach to foundation did contribute to a rich debate during the 20th century: it gave us a robust notion of rigor, highly required after a century rich of mathematics as well as of mistakes due to fuzzy definitions and proofs — such as the famous mistakes concerning the continuity of sum of series of continuous functions, of left and right derivability — mostly due to wrong alternation of quantifiers and imprecise writing. The result has been a monument of rigour and results, the detection of errors and paradoxes and their fixing, lively and productive controversies. More importantly, it set the guidelines to the invention of formal computing machines, since the “negative results” of the 1930s. As hinted in Section 1, since the irrationality of  $\sqrt{2}$ , negative results opened new ways for knowledge construction, from Poincaré's Three Body Theorem, to Gödel's theorem to Einstein's EPR “paradox”<sup>17</sup>. The myth of the “positive” construction of knowledge, typical of Hilbertian views or of unbounded genocentrism is unfounded: mathematics is not done by formally deriving theorems from pre-given axioms, nor biology by discovering new “genes of ...” — i.e. by deducing phenotypes from finite sequences of letters of DNA. Even within Computer Science, the limits of formalisms stimulated the debate between “syntax oriented” and “semantic oriented” approaches in Theory of Programming (Scott, 1980; Longo, 2001).

As for biology, mainstream molecular biology highlighted many fundamental molecular “mechanisms” and proposed enormous amounts of data. Longo and Mossio (2020), compares the geo-centric (Ptolemaic) approach in astronomy and the geno-centric one in biology. The fantastic astronomy in the Arabic world (7th to 14th centuries) provided us with fantastic data and correlations: all visible celestial bodies were named, classified and their movements correlated. The Alphonsine Tables of the late 15th century allowed geographic explorations that changed the world. Yet, the theoretical frame was totally wrong. This means that any assertion correlating data, by causality typically, such as “the position of Jupiter in this constellation causes Mars to be there ...”, was *wrong*.

Similarly, the “genes for everything”, from intelligence (Stewart, 2004) to marital fidelity (Young, Nilsen, Waymire, MacGregor and Insel, 1999) or the ad hoc “oncogenes”, one for each cancer type, diverted research from understanding and fighting this life threatening disease (Sonnenschein and Soto, 1999; Weinberg, 2014). Typically, it distorted analyses from the investigation of carcinogenes, such as endocrine disruptors, since these mostly small molecules would not fit the exact, boolean, key-lock paradigm of macromolecular interactions — thus, they could not interfere, by principle, with molecular cascades and cellular receptors. Instead they do, with lower probabilities, but sufficient to disrupt cellular processes (Diamanti-Kandarakis,

<sup>17</sup>See Longo (2019) for a comparative analysis and their creative fall-out. Note also that the EPR paradox of entanglement is at the core of Quantum Computing (Zorzi, 2016).

Bourguignon, Giudice, Hauser, Prins, Soto, Zoeller and Gore, 2009). This is a catastrophic consequence of a bad philosophy of biology. A change of perspective is emerging from within molecular biology itself, in particular since the results on stochasticity of gene expression in Elowitz, Levine, Siggia and Swain (2002). Similarly, proteins in the cell's cytoplasm have large enthalpic random movements and at least 30 percent of them are considered to be intrinsically unstructured. Moreover, their shape and biological functionality depends on the context, from pH levels, to pressures and torsions on their physical structure, including on the DNA chromatin, to the presence of other proteins in their subcellular locales (Uversky, 2011). The new views belong still a minority and Prusiner's ideas, who discovered prions in early 1980's, were ousted for a decade as these badly folded proteins modify the conformation of close ones, against the CD (Prusiner, 1982).

A philosophical bias made many ignore the evidence accumulated by some as above and by many others — the marginalisation of the epigenetic approach by C. Waddington and B. McClintock is yet another example (Keller, 1984). Today, an increasing trend in research closely considers the crucial role of the enthalpic quasi chaotic movements of macro-molecules, with changing chemical affinities according to the context. This justifies the richness of the interactions in the quasi turbulence of the proteome, while stressing that they are canalised, constrained and selected by the context and the cell structure (Kupiec, 2010). It is the context that “gives sense” by canalising and allowing to function many highly improbable macro-molecular networks that, in turn, contribute to the construction of the cellular, tissular, organismal and ecosystemic constraints (for a general role of constraints formation and dynamics in organismal biology, see Montévil and Mossio (2015)).

In spite of the paradigm shift which is taking place, immense interests forbid a faster pace for it. For example, Genetically Modified Organisms (GMOs) in agriculture are yet another consequence of the mechanistic philosophy of biology. They are a direct application of the Central Dogma: we can drive the plant in the ecosystem by manipulating the genetic information and program, somehow like formal axioms and rules completely drive a mathematical theory. The biological consequences though are severe: typically, a major decrease of biodiversity (Bizzarri, 2012) and a destruction of the microbioma of roots (Kowalchuk, Bruinsma and van Veen, 2003).

## 5. Historicity

What is, in biology, the analogue of the way out from formalist frames (the complete coding of an organism in the DNA) by “contexts of historical creation of meaning”, as hinted above in reference to the role of meaning and of mathematical invention in proofs?

The key is again in the role of the historical dynamics of life. Nothing in biology can be understood unless in a temporal perspective, both phylogenetic and ontogenetic. We stressed above the historical creation of meaning in mathematics, while acknowledging that at each epoch, mathematics' aim is to give a “universal” definition of new concepts and structures, to pass beyond history by searching the maximal conceptual — and historical — invariance. In biology, historicity is even more radical. There is no way to define a “mouse” without referring to a history, no way to propose a historically stable concept of mouse. The notion of mouse is not a historical invariant. That is, no detailed description of its phenotypes is ever complete nor stable: other species may fit it or some phenotype may differ or change over time and still you may have a mouse. Mice do change, as they evolve, typically they differentiate in strains, a major concern as for the diversity of their reactions in experimental work, where measurement strictly depend on the animal's history, in the broadest sense (Montévil, 2019). In short, the only way to define a mouse is by its phylogenetic history (Lecointre and Le Guyader, 2001).

Similarly, homologies — common evolutionary origins of an organ, as in Gould (2002) — allow us to understand organ structures and functions: the strange structure of the wings of bats is only understood as homologous to our hands, while the wings of birds are homologous to our arms. Insects wings are not homologous to birds, yet they have the same function (they are analogous). Some birds have wings that do not allow to fly (penguins), in some cases this function has been lost in relatively recent evolutionary times (the New Zealand kiwi). Most of evolutionary novelty comes from historical readjustment and adaptation of previous functions and structures that “make sense” in new contexts — they acquire new functions and change structure and may thus be understood (West-Eberhard, 2003). Ex-aptation, as adaptation ex-post, is

a key notion in evolutionary biology Gould (2002). No formal definition of a structure nor of a function allows to characterize a phenotype: only its history may help to understand both structure and function. Consider also the physical nonsense of the blood vessels and nerves passing in front of the eye, between cellular sensors and the incoming light (as Helmholtz allegedly observed, we should fire God for making such an engineering mistake), can only be understood by the vertebrates eye's phylo- and onto-genesis. Cephalopods have more suitably back-vascularised and innervated eyes, because of the very different phylogenetic and ontogenetic paths of their very modular brains, of which the eyes are an extension (Serb and Eernisse, 2008).

In synthesis, a mathematical proof is *also* a historical creation of meaning, a biological organism is *only* a historical formation of an individual.

A sense of history, both phylogenetic and ontogenetic, motivates alternative knowledge paths in biology. The formation of constraints to processes that evolve over time is at the core of the novel theory of organisms in Montévil and Mossio (2015); Montévil (2020). Constraints act upon processes, are conserved at the relevant time scales and are based on mutual dependence such that they both depend on and contribute to maintaining each other. In particular, cellular constraints canalise and enable, within cells, biochemical networks that are chemically highly improbable (with almost zero probabilities as physical phenomena). These chemical processes then co-construct the constraints that make them possible. Variability is probably the main invariant in biology, canalised by organismal and ecosystemic historical constraints. A unified perspective is proposed in Soto, Longo and Noble (2016).

Let us note finally that the notion of gene is not “well-defined”, to put it in mathematical terms — in contrast to axioms and to the very notion of “axiom”. More precisely, the latter has had some historical plasticity, yet in each conceptual frame, mostly in continuity with previous ones, it found a rigorous frame. The notion of “gene”, instead, not only changed at least five times in the 20th century (Keller, 2009), but each time turned out to be fuzzy. First, early in the century, they were meant to be some parts of the chromosomes acting as “Mendelian genes” (directly related to phenotypes, like in the colors of peas). Later, they were associated to proteins and enzymes but this gradually turned out more of the many-to-many type, in contrast to the one-to-one claim in Beadle and Tatum (1941) — so that no linear nor functional deduction is in general possible from genes to proteins. More recently, alternative splicing and overlapping genes (Pavesi, Vianelli, Chirico, Bao, Blinkova, Belshaw, Firth and Karlin, 2018) destroy any myth of the complete encoding of the “information” for phenotypes in genes, viewed as well delimited segments of DNA, as well as of the leading role of genes in development and evolution: these dynamics largely depend on the epigenetic contexts, in the broadest sense. For example, pressure and torsions on the chromatin, as already mentioned, modify gene expression (Lesne, Becavin and Victor, 2012) and this has a major role in embryogenesis in view of the physically changing constraints acting on cells. Genes have more the role of followers than of programmers in either process (West-Eberhard, 2003). So, hybrids of cave-fish — more than a hundred species of fish that have lost their eyes by evolving in caverns — do have eyes (Gatenby, Gillies and Brown, 2011). The corresponding “genes”, whatever this notion may mean, or the parts of the DNA used in the formation of eyes, are still there, but no longer used by the organism in ontogenesis, in that context.

Organisms are not self-organised processes, like flames or hurricanes, but a historically changing formation of constraints to flows of energy and matter, that enable the use of these flows to reconstruct the constraints (for example, the vascular systems constrains flows, thus enables metabolism, which contributes to the reconstruction of the constraint). Note that flames and hurricanes have an irreversible processual time, not a historical time: their physico-mathematical structure did not change in the last four billions years, in contrast to life. The time of history is a time of changing phase spaces (the space of pertinent observables and parameters) and marked by rare events (Longo, 2018a). The Darwinian principles of reproduction with variation and selection, can be seen as the a priori of life (reproduction with variation), in co-constituted contexts that may enable (as “positive selection”) the (new) possible or may exclude it as incompatible (do not enable it, or “negative selection”). These principles guide the intelligibility of life, both in phylo- and onto-genesis, as proposed in Soto, Longo and Noble (2016).

DNA is a major constraint and a physico-chemical trace of evolution inside each cell; it constrains Brownian flows of molecules and, thus, the type of possible proteins in a given moment and context. So, as the foundation of mathematics is the clarification of principles in a historical praxis — possibly by trying to write axioms — where invariance plays a major role, similarly the foundation of biology must refer to



(Darwinian) principles of reproduction with modifications and reconstruction with correlated variations, enablement and negative selection, while taking the point of view of the organism and its dynamics in the historical time of an ecosystem. The role of axioms in mathematics and of DNA in biology, while preserving their relevance, are then re-understood in their historical process of formation, use and activity.

## 6. Concluding remarks

Besides the reference to Montévil and Mossio (2015), Soto, Longo and Noble (2016) and correlated work in an organismal/evolutionary (historical) perspective, we did not venture in details in the ongoing re-inventions of foundational analysis in mathematics for biology as there are many growing projects, such as the work by Ehresmann (2017). A sort of Manifesto of the new trends, recovering the role of meaning and structures in meta-mathematical analyses may be found in the Editorial Policy of the “Annals of Mathematics and Philosophy” ([https://spartacus-idh.com/amp/MxPhi\\_en.pdf](https://spartacus-idh.com/amp/MxPhi_en.pdf)). A reference book along similar perspectives, with particular emphasis on contemporary mathematics, is Zalamea (2012). In biology, we point to the papers and new openings in “Organisms, a journal in biological sciences” and its Editorial. Time is required to appreciate the philosophical (and mathematical) relevance of the new ideas in mathematics proposed by “heterogenesis” in Sarti, Citti and Piotrowski (2019), among new bridging perspectives. They propose an analysis of the “genesis *of* and *from* diversity” in the changing space of observables and parameters: the historical frame of semiotics (their original field of interest) and of the Darwinian ecosystem along evolution. By this, they aim to describe by mathematics the dynamics of changing phase spaces, typical to historical sciences such as biology, which has no counterpart in physical morphogeneses. Our common perspective (see Longo (2018a); Montévil (2020)) sets a new foundational bridge between mathematics and biology as it changes the most fundamental mathematical invariants of physical theories, the underlying symmetries in the “background spaces” (or in the “conditions of possibilities”) of all existing systems of equations for physics. As Weyl observes in 1952: “All a priori statements in physics have their origin in symmetry”, a remark justified by Noethers theorems. These a priori symmetries characterize the pregiven structure of observables and parameters — an invariance unsuitable for theorising biological evolution as well as any historical science.

In the approach hinted here, we first observe that Darwin’s first principle, the a priori of heredity, that is *descent with modification*, is a “non-conservation principle” for phenotypes. Thus we propose a fundamental breaking of symmetry, the non conservation of the space of all possible dynamics or phase space, at the core of biological evolution, as production of variability and diversity. This may also help to modify our bugged, mechanistic relation to the ecosystem, its diversity and its historicity.

## References

- Alman, J., Williams, V.V., 2021. A refined laser method and faster matrix multiplication, in: Proceedings of the 2021 ACM-SIAM Symposium on Discrete Algorithms (SODA), SIAM. pp. 522–539.
- Amadio, R.M., Curien, P.L., 1998. Domains and lambda-calculi. 46, Cambridge University Press.
- Anobile, G., Arrighi, R., Burr, D.C., 2019. Simultaneous and sequential subitizing are separate systems, and neither predicts math abilities. Journal of Experimental Child Psychology 178, 86 – 103. URL: <http://www.sciencedirect.com/science/article/pii/S0022096518300870>, doi:<https://doi.org/10.1016/j.jecp.2018.09.017>.
- Barendregt, H., 1984. The lambda calculus, its syntax and semantics. Studies in logic and the foundations of mathematics; 103.
- Beadle, G.W., Tatum, E.L., 1941. Genetic control of developmental reactions. The American Naturalist 75, 107–116.
- Berthoz, A., 1997. Le sens du mouvement. Odile Jacob.
- Bizzarri, M., 2012. The new alchemists: The risks of genetic modification. Wit Press.
- Blasdel, G.G., Mitchell, D.E., Muir, D.W., Pettigrew, J.D., 1977. A physiological and behavioural study in cats of the effect of early visual experience with contours of a single orientation. The Journal of Physiology 265, 615–636. doi:<https://doi.org/10.1113/jphysiol.1977.sp011734>.
- Brassard, G., Crepeau, C., Jozsa, R., Langlois, D., 1993. A quantum bit commitment scheme provably unbreakable by both parties, in: Proceedings of 1993 IEEE 34th Annual Foundations of Computer Science, pp. 362–371. doi:10.1109/SFCS.1993.366851.
- Cajori, F., 1928. A history of mathematical notations (volume 1). Open Court Publishing Company.
- Canevaro, M., 2018. Majority Rule vs. Consensus: The Practice of Democratic Deliberation in the Greek Poleis. Edinburgh University Press. pp. 101–156. doi:10.3366/edinburgh/9781474421775.003.0005.
- Cao, J., Pang, Y., Li, X., 2016. Pedestrian detection inspired by appearance constancy and shape symmetry, in: Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, pp. 1316–1324.
- Castelvecchi, D., 2015. The biggest mystery in mathematics: Shinichi Mochizuki and the impenetrable proof. Nature News 526, 178. URL: <http://www.nature.com/news/the-biggest-mystery-in-mathematics-shinichi-mochizuki-and-the-impenetrable-proof-1.18509>, doi:10.1038/526178a.
- Chiurazzi, G., 2017. Dynamis. Ontologia dell'incommensurabile. volume 9. Guerini & Associati.
- Church, A., 1941. The Calculi of Lambda Conversion. Princeton University Press, USA.
- Cohen, P., 1998. Excited researchers think they have found a gene for language. New Scientist 2119, 77.
- Collins, F.S., 1999. Medical and societal consequences of the human genome project. New England Journal of Medicine 341, 28–37. PMID: 10387940.
- Coquand, T., 1986. An analysis of Girard's paradox, in: In Symposium on Logic in Computer Science, IEEE Computer Society Press. pp. 227–236.
- Crick, F.H., 1958. On protein synthesis, in: Symposia of the Society for Experimental Biology, Number XII: The Biological Replication of Macromolecules, Cambridge University Press. pp. 138–163.
- Danchin, A., 2002. The Delphic Boat: what genomes tell us. Harvard University Press.
- Danchin, A., 2008. Bacteria as computers making computers. FEMS microbiology reviews 33, 3–26.
- Dehaene, S., 2011. The number sense: How the mind creates mathematics. Oxford University Press USA.
- Diamanti-Kandarakis, E., Bourguignon, J.P., Giudice, L.C., Hauser, R., Prins, G.S., Soto, A.M., Zoeller, R.T., Gore, A.C., 2009. Endocrine-disrupting chemicals: an endocrine society scientific statement. Endocrine reviews 30, 293–342.
- Ehresmann, A., 2017. Applications of categories in biology and cognition. Categories for the Working Philosopher.
- Elowitz, M.B., Levine, A.J., Siggia, E.D., Swain, P.S., 2002. Stochastic gene expression in a single cell. Science 297, 1183–1186.
- von Eschenbach, A.C., 2003. NCI sets goal of eliminating suffering and death due to cancer by 2015. Journal of the National Medical Association 95, 637.
- Gall, F.L., 2014. Powers of tensors and fast matrix multiplication, in: Nabeshima, K., Nagasaka, K., Winkler, F., Szántó, Á. (Eds.), International Symposium on Symbolic and Algebraic Computation, ISSAC '14, Kobe, Japan, July 23–25, 2014, ACM. pp. 296–303. URL: <https://doi.org/10.1145/2608628.2608664>, doi:10.1145/2608628.2608664.
- Gatenby, R.A., Gillies, R.J., Brown, J.S., 2011. Of cancer and cave fish. Nature Reviews Cancer 11, 237–238.
- Giannini, P., Longo, G., 1984. Effectively given domains and lambda-calculus models. Information and Control 62, 36 – 63. URL: <http://www.sciencedirect.com/science/article/pii/S0019995884800091>, doi:[https://doi.org/10.1016/S0019-9958\(84\)80009-1](https://doi.org/10.1016/S0019-9958(84)80009-1).
- Gilbert, W., 1992. A vision of the Grail. Harvard University Press.
- Girard, J.Y., 2001. Locus solum: From the rules of logic to the logic of rules. Mathematical Structures in Computer Science 11, 301506. doi:10.1017/S096012950100336X.
- Girard, J.Y., Taylor, P., Lafont, Y., 1989. Proofs and types. volume 7. Cambridge University Press.
- Gould, S.J., 2002. The structure of evolutionary theory. Harvard University Press.
- Harrington, L.A., Morley, M.D., Šcedrov, A., Simpson, S.G., 1985. Harvey Friedman's research on the foundations of mathematics. Elsevier.
- Heath, T.L., 1908. The thirteen books of Euclid's Elements. Cambridge University Press.
- Helmig, C., Steel, C., 2020. Proclus, in: Zalta, E.N. (Ed.), The Stanford Encyclopedia of Philosophy. fall 2020 ed.. Metaphysics Research Lab, Stanford University.
- Hilbert, D., 1902. The foundations of geometry. Open court publishing Company.

- Horowitz, N.H., 1995. One-gene-one-enzyme: Remembering biochemical genetics. *Protein Science* 4, 1017–1019.
- Huffman, C., 2019. Pythagoreanism, in: Zalta, E.N. (Ed.), *The Stanford Encyclopedia of Philosophy*. fall 2019 ed.. Metaphysics Research Lab, Stanford University.
- Husserl, E., 1970. *The crisis of European sciences and transcendental phenomenology: An introduction to phenomenological philosophy*. Northwestern University Press.
- Istrail, S., De-Leon, S.B.T., Davidson, E.H., 2007. The regulatory genome and the computer. *Developmental Biology* 310, 187–195.
- Jacob, F., 1965. Génétique cellulaire: Leçon inaugurale prononcée le vendredi 7 mai 1965, in: Paris: Collège de France.
- Karr, J.R., Sanghvi, J.C., Macklin, D.N., Gutschow, M.V., Jacobs, J.M., Bolival Jr, B., Assad-Garcia, N., Glass, J.I., Covert, M.W., 2012. A whole-cell computational model predicts phenotype from genotype. *Cell* 150, 389–401.
- Keller, E.F., 1984. *A feeling for the organism*, 10th anniversary edition: the life and work of Barbara McClintock. Macmillan.
- Keller, E.F., 2009. *The century of the gene*. Harvard University Press.
- Kowalchuk, G.A., Bruinsma, M., van Veen, J.A., 2003. Assessing responses of soil microorganisms to gm plants. *Trends in Ecology & Evolution* 18, 403–410.
- Krystek, M.P., 2021. The term ‘angle’ in the international system of units. *arXiv:2101.01023*.
- Kupiec, J.J., 2010. On the lack of specificity of proteins and its consequences for a theory of biological organization. *Progress in Biophysics and Molecular Biology* 102, 45–52.
- Lang, M., 1957. Herodotos and the abacus. *Hesperia: The Journal of the American School of Classical Studies at Athens* 26, 271–288. URL: <http://www.jstor.org/stable/147100>.
- Lecointre, G., Le Guyader, H., 2001. Classification phylogénétique du vivant. Belin.
- Lesne, A., Becavin, C., Victor, J.M., 2012. The condensed chromatin fiber: an allosteric chemo-mechanical machine for signal transduction and genome processing. *Physical biology* 9, 013001.
- Lo, H.K., Chau, H.F., 1997. Is quantum bit commitment really possible? *Physical Review Letters* 78, 3410.
- Longo, G., 2001. Some topologies for computations, in: *Invited paper, proceedings of the Conference Géométrie au XXè siècle*.
- Longo, G., 2009. Theorems as constructive visions, in: *Proceedings of ICMI 19 conference on Proof and Proving*, Springer.
- Longo, G., 2011. Reflections on concrete incompleteness. *Philosophia Mathematica* 19, 255–280.
- Longo, G., 2018a. How future depends on past and rare events in systems of life. *Foundations of Science* 23, 443–474.
- Longo, G., 2018b. Information and causality: Mathematical reflections on cancer biology. *Organisms. Journal of Biological Sciences* 2, 83–104.
- Longo, G., 2019. Interfaces of incompleteness, in: *Systemics of Incompleteness and Quasi-systems*. Springer, pp. 3–55.
- Longo, G., Mossio, M., 2020. Geocentrism vs genocentrism: theories without metaphors, metaphors without theories. *Interdisciplinary Science Reviews* 45, 380–405.
- Longo, G., Viarouge, A., 2010. Mathematical intuition and the cognitive roots of mathematical concepts. *Topoi* 29, 15–27.
- Maffei, L., 1998. *Il mondo del cervello*. Laterza.
- Martin-Löf, P., Sambin, G., 1984. *Intuitionistic type theory*. volume 9. Bibliopolis Naples.
- McCarty, D.C., 2004. *David Hilbert and Paul du Bois-Reymond: Limits and Ideals*. Gruyter.
- Monod, J., 1970. *Le hasard et la nécessité*. Le Seuil.
- Montévil, M., 2019. Measurement in biology is methodized by theory. *Biology & philosophy* 34, 35.
- Montévil, M., Mossio, M., 2015. Closure of constraints in biological organisation. *Journal of theoretical biology* 372, 179–191.
- Montévil, M., 2020. Historicity at the hearth of biology. *Theory in Biosciences* doi:10.1007/s12064-020-00320-8.
- Ober, J., 2011. Wealthy hellas. *The Journal of Economic Asymmetries* 8, 1–38.
- Pagel, M., Atkinson, Q.D., Meade, A., 2007. Frequency of word-use predicts rates of lexical evolution throughout indo-european history. *Nature* 449, 717–720. URL: <https://doi.org/10.1038/nature06176>, doi:10.1038/nature06176.
- Panza, M., 2012. The twofold role of diagrams in euclids plane geometry. *Synthese* 186, 55–102.
- Pavesi, A., Vianelli, A., Chirico, N., Bao, Y., Blinkova, O., Belshaw, R., Firth, A., Karlin, D., 2018. Overlapping genes and the proteins they encode differ significantly in their sequence composition from non-overlapping genes. *PloS one* 13, e0202513.
- Pedoe, D., 1975. Notes on the history of geometrical ideas ii. the principle of duality. *Mathematics Magazine* 48, 274–277. URL: <https://doi.org/10.1080/0025570X.1975.11976511>, doi:10.1080/0025570X.1975.11976511, arXiv:<https://doi.org/10.1080/0025570X.1975.11976511>.
- Perbal, L., 2013. The warrior gene and the maōri people: the responsibility of the geneticists. *Bioethics* 27, 382–387.
- Prusiner, S.B., 1982. Novel proteinaceous infectious particles cause scrapie. *Science* 216, 136–144.
- Roberts, D.M., 2019. A crisis of identification. *Inference, International Review of Science* 4.
- Rochberg, F., 2002. A consideration of babylonian astronomy within the historiography of science. *Studies in History and Philosophy of Science Part A* 33, 661 – 684. URL: <http://www.sciencedirect.com/science/article/pii/S0039368102000225>, doi:[https://doi.org/10.1016/S0039-3681\(02\)00022-5](https://doi.org/10.1016/S0039-3681(02)00022-5).
- Rodin, A., 2020. *Axiomatic architecture of scientific theories*, Habilitation thesis. St. Petersburg State University.
- Rogers, H., 1987. *Theory of Recursive Functions and Effective Computability*. MIT Press, Cambridge, MA, USA.
- Rosen, F.A., 1831. *The Algebra of Mohammed Ben Musa* Edited and Translated by Frederic Rosen. Oriental translation fund.
- Sarti, A., Citti, G., Piotrowski, D., 2019. Differential heterogenesis and the emergence of semiotic function. *Semiotica* 2019, 1–34.
- Scharcanski, J., Venetsanopoulos, A.N., 1997. Edge detection of color images using directional operators. *IEEE Transactions on Circuits and Systems for Video Technology* 7, 397–401. doi:10.1109/76.564116.
- Scott, D., 1980. Lambda calculus: some models, some philosophy, in: *Studies in Logic and the Foundations of Mathematics*.

- Elsevier. volume 101, pp. 223–265.
- Serb, J.M., Eernisse, D.J., 2008. Charting evolutions trajectory: using molluscan eye diversity to understand parallel and convergent evolution. *Evolution: Education and Outreach* 1, 439.
- Sonnenschein, C., Soto, A.M., 1999. The society of cells: cancer and control of cell proliferation. Bios Scientific Pub Limited.
- Soto, A., Longo, G., Noble, D., 2016. From the century of the genome to the century of the organism: New theoretical approaches. Special issue of *Progress in Biophysics and Molecular Biology* 122.
- Stewart, J., 2004. La vie existe-t-elle. Vuibert, Paris .
- Teissier, B., 2012. Why are stories and proofs interesting ? *Circles Disturbed: The Interplay of Mathematics and Narrative* .
- Thom, R., 1954. Quelques propriétés globales des variétés différentiables. *Commentarii Mathematici Helvetici* , 17–86.
- Thom, R., 1973. La science malgré tout.
- Thomas, E., 2015. L'objectivité scientifique, hier et aujourd'hui. Catalogue de l'exposition "Boîtes noires - Empreintes du monde et paysages intérieurs".
- Uversky, V.N., 2011. Intrinsically disordered proteins from a to z. *The international journal of biochemistry & cell biology* 43, 1090–1103.
- Weinberg, R.A., 2014. Coming full circle from endless complexity to simplicity and back again. *Cell* 157, 267–271.
- West-Eberhard, M.J., 2003. Developmental plasticity and evolution. Oxford University Press.
- Weyl, H., 1952. Symmetry. Princeton, New Jersey .
- Wilson, R., 2003. Four colours suffice: how the Map Problem was solved. Allen Lane, London, UK. URL: <http://oro.open.ac.uk/7716/>.
- Young, L.J., Nilsen, R., Waymire, K.G., MacGregor, G.R., Insel, T.R., 1999. Increased affiliative response to vasopressin in mice expressing the v1a receptor from a monogamous vole. *Nature* 400, 766–768.
- Zalamea, F., 2012. Synthetic philosophy of contemporary mathematics. MIT Press.
- Zorzi, M., 2016. On quantum lambda calculi: a foundational perspective. *Mathematical Structures in Computer Science* 26, 1107.

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