Demolishing prejudices to get to the foundations

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Abstract

Commonly accepted views on foundations of science, either based on bottom-up construction or top-down reduction of fundamental entities are here rejected. We show how the current scientific methodology entails a certain kind of research for foundations of science, which are here regarded as insurmountable limitations. At the same time, this methodology allows to surpass the bounds classically accepted as fundamental, yet often based on mere “philosophical prejudices”. Practical examples are provided from quantum mechanics and biophysics.

1 Reductionism and foundations

Tackling the question of “what is fundamental?” seems to boil down, in one way or another, to the long-lasting problem of reductionism. This is customarily intended to mean “that if an entity \(x\) reduces to an entity \(y\) then \(y\) is in a sense prior to \(x\), is more basic than \(x\), is such that \(x\) fully depends upon it or is constituted by it” [1]. Accordingly, reduction is sometimes thought to be equivalent to the action of digging into the foundations of science [1]. Despite this generally accepted view, we show that the reductionist approach to “foundations”, which seems prima facie legitimate and very productive, is absolutely unnecessary to answer the posed question on what is fundamental.

Reductionism commonly “entails realism about the reduced phenomena” [1]. It is the case of a stronger form of reductionism known as physicalism [2]. Physicalism advocates “the thesis that everything is physical” [2], namely that everything can be reduced to fundamental interactions between physical elementary entities. In this view, the entities are the “building blocks” of Nature, and their interactions fully account for all the possible natural phenomena. This is however a typical primitive approach to subtle questions because it is a philosophical prejudice, and it requires the higher order philosophical pre-assumption of realism [3].

Reductionism is justified merely on historical arguments, that is, looking at “specific alleged cases of successful reductions” [1]. However, there are much more cases where reductionism has exhausted its heuristic power, and it is only the arrogant approach of some physicists to regard physics as the foremost among sciences, maintaining that every biological or mental process can be eventually reduced to mere physical interactions. Feynman, for instance, would maintain that “everything is made of atoms. [...] There is nothing that living characterized the leading mindset of the (positivist) scientific community. D. Stoljar indicated an entire group of views as the “Physicalist World Picture” [2]; this includes “the idea that every particular event or process [or entity] which falls under a law of the special sciences (i.e. sciences other than physics) also fall under a law of physics”. [3]

Though the problem of realism is indeed one of the most important in the philosophy of science and surely deserves a great deal of attention, it is auspiscious that this problem finds its solution within the domain of science (this will be discussed in the Subsection [3]).
things do that cannot be understood from the point of view that they are made of atoms acting according to the laws of physics". On the contrary, we believe, with David Bohm, that “the notion that everything is, in principle, reducible to physics [is] an unproved assumption, which is capable of limiting our thinking in such a way that we are blinded to the possibility of whole new classes of fact and law”. Moreover, the reductionist program has failed even within physics alone, not having so far been capable to unify the fundamental forces nor its most successful theories (quantum and relativistic physics). It has been proposed that even a satisfactory theory of gravity requires a more holistic (i.e. non-reductionist) approach and it could have an emergent origin. Furthermore, it is the belief of many contemporary scientists (especially from the promising field of complex systems studies) that emergent behaviors are inherent features of Nature, not to mention the problem of consciousness. So, essentially, “the hope that the actual progress of science can be successfully described in terms of reduction has vanished”.

Another tempting path to approach the question of “what is fundamental”, is the use of conventionalist arguments. “The source of conventionalist philosophy would seem to be wonder at the aesterely beautiful simplicity of the world as revealed in the laws of physics”, p. 80. The idea, however, that our descriptions being simple, elegant, or economical or the like, constitute a guarantee of “fundamentality” is a mere utopia. Conventionalism, despite being totally self-consistent, fails when it comes to acquire empirical knowledge. In a sense, for the conventionalist, the theory comes first, and observed anomalies are “re-absorbed” into ad hoc ancillary hypotheses. It thus appears quite unsatisfactory to address foundations of natural science from the perspective of something that has hardly any empirical content.

In conclusion, a research for foundations of science that involves the intuitive decomposition of systems in basic building-blocks of Nature seems to lead to a dead end; to be meaningful, this would require the assumption of a strong form of realism that, although in principle totally defensible, it seems a way too strict and rather dogmatic assumption to take it as a starting point. Nor it seems promising to rely on purely conventional (e.g. aesthetic) factors, though they can be fruitful in non-empirical sciences. Indeed, while reduction-based foundations clash with the ontological problem (the assumption of realism), conventional-based foundations clash with the epistemological problem (the empirical content of theories). What we are left with is to go back to the very definition of science, to its method, and try to understand what science can and cannot do.

2 Methodology

As it is generally known, Karl R. Popper showed the untenability of well established criterion of demarcation between science and non-science based on inductive verification. Popper proposed instead that theories are conjectures that can only be (deductively) falsified. Popper’s method requires that scientific statements (laws, consistent collections of laws, theories) “can be singled out, by means of empirical tests, in a negative sense: it must be possible for an empirical scientific system to be refuted by experience. [...] Not for nothing do we call laws of nature ‘laws’: the more they prohibit the more they say”, p. 40-41.

One of the leading historians of science of our times, Helge Kragh, recently pointed out that “Karl Popper’s philosophy of science [...] is easily the view of science with the biggest impact on practicing scientists”. For instance, the Nobel laureate for medicine, Peter Medawar, acknowledged to Popper’s falsificationism a genuine descriptive value, stating that “it gives a pretty fair picture of what actually goes on in real-life laboratories”. Or the preeminent cosmologist Hermann Bondi declared that “there is no more to science than its method, and there is no more to its method than Popper has said”. Besides these appraisals, it is a matter of fact that “many scientists subscribe to some version of simplified

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4 In particular, Popper’s criticisms were leveled against the logical positivism of the Vienna Circle. He indeed came back to Hume’s problem of induction; Hume maintained that there is, in fact, no logically consistent way to generalize a finite (though arbitrarily large) number of single empirical confirmations to a universal statement (as a scientific law is intended to be). Popper embraced this position, but he proposed a new solution of the problem of induction and demarcation (see further).
Popperianism” [10], and this happens especially to physicists, and specifically to those who are concerned with fundamental issues. In this section, we will support this claim with several quotations from different prominent physicists who do not share a common philosophical standpoint; and we show that they do actually think of their scientific praxis as based on a form of deductive hypothesis-testing-falsification process. We then show that this methodological choice, has indeed profound consequences on the development of theories, and that it has been extremely efficient in the modern results of foundations of different branches of physics. We are here not concerned with the justification of falsificationism as the right methodology to aspire to; we avoid any normative judgement. We just assume as a working hypothesis - build upon a number of instances - that this is what scientists do, or at least what they are convinced to do: this is enough to lead them to pursue certain (theoretical) directions. Methodological rules are a matter of convention. They are indeed intuitively assumed by scientists in their everyday practical endeavor, but they are indispensable meta-scientific (i.e. logically preceding scientific knowledge) assumptions: “they might be described as the rules of the game of empirical science. They differ from rules of pure logic rather as do the rules of chess”. However, a different choice of the set of rules, would necessarily lead to a different development of scientific knowledge (meant as the collection of the provisionally acknowledged theories). The methodology that one (tacitly) assumes entails the type of development of scientific theories, insofar as it “imposes severe limitations to the kind of questions that can be answered” [16]. Our fundamental theories look as they look also backwards, at a given time after the beginning of a game, this would probably look very different from any game played with standard rules of chess.

Coming back to the physicists who, more or less aware of it, loosely adhere to falsificationism, we deem it interesting to explicitly quote some of them, belonging to different fields. It is worth mentioning a work by the Austrian physicist Herbert Pietschmann with the significant title: “The Rules of Scientific Discovery Demonstrated from Examples of the Physics of Elementary Particles”. Elementary particle physics was particularly developed in the Post-war period to revive scientific (especially European) research. It is well known that this field developed in a very pragmatic and productivist way (see e.g. [13]). Nevertheless, the author shows that falsificationist methodological rules are applied by the working physicist. Thus these rules are shown to be actual tools rather than abstract norms in the development of physics. [...] Predictions by theories and their tests by experiments form the basis of the work of scientists. It is common knowledge among scientists that new predictions are not proven by experiments, but are ruled out if they are wrong. [14]

While Pietschmann has a vast knowledge of the philosophy of science, one of the most brilliant physicist of all times, the Nobel laureate Richard P. Feynman was rather an ignoramus in philosophy. Feynman belonged to a generation of hyper-pragmatic American scientists, whose conduct went down in history with the expression “shut up and calculate!” (see e.g. [15]). However, in the course of some public lectures he gave in the 1960s, Feynman’s audience was granted the rare opportunity to hear the great physicist addressing the problem of scientific method. It turns out that he also adheres to falsificationism:

[scientific] method is based on the principle that observation is the judge of whether something is so or not. [...] Observation is the ultimate and final judge of the truth of an idea. But “prove” used in this way really means “test,” [...]

It is well known that Popper’s methodology has today hardly any supporter among philosophers of science, who have severely criticized it as a too strict and naive description of scientific development. Moreover, falsificationism has for Popper a normative value, i.e. it is seen as the most rational, and therefore the best, possible methodology. Among Popper’s foremost critics and commentators, we ought to mention Imre Lakatos, who developed a weaker and more complex form of falsificationism, which encompasses part of Thomas Kuhn’s critiques.
idea really should be translated as, “The exception tests the rule.” Or, put another way, “The exception proves that the rule is wrong.” That is the principle of science. [16]

Coming to some contemporary leading figures in the field of foundations of quantum mechanics (FQM), David Deutsch has been a staunched Popperian since his student years. Deutsch maintains that

we do not read [scientific theories] in nature, nor does nature write them into us. They are guesses bold conjectures. [...] However, that was not properly understood until [...] the work of the philosopher Karl Popper [17].

We ought to stress that one of the major critiques to Popper’s falsificationism is that it demarcates scientific statements from not-scientific ones on a purely logical basis, i.e. in principle independently of the practical feasibility. In fact, for Popper, a statement is scientific if and only if it can be formulated in a way that the set of its possible falsifiers (in the form of single existential statements) is not empty. On this regard, Č. Brukner and M. Zukowski, who significantly contributed to FQM in recent years, slightly revised Popper’s idea. Whilst maintaining a falsificationist criterion of demarcation, they attribute to falsifiability a momentary value:

Philosophical propositions could be defined as those which are not observationally or experimentally falsifiable at the given moment of the development of human knowledge.[6][18]

Hereinafter, we will accept this updated version of falsificationism as our working definition of the current scientific method, focusing on foundations of physics.[7]

To conclude, we agree with Bohm when he states that “scientists generally apply the scientific method, more or less intuitively” [5]. But we also maintain that since scientists are both the proposers and the referees of new theories, the form into which this theories are shaped is largely entailed by the method they (more or less consciously) apply. Methodology turns therefore into an active factor for the development of science. As we will show in the next section, the falsificationist methodology, vastly adopted in modern physics, has opened new horizons for the foundations of physics.

3 What is fundamental

Provided with a working methodology, we can now propose a criterion to define what is fundamental. Reaching the foundations consists of a pars descripto; that aims at eliminating the constraints that a naive empiricist approach has constructed as a fix framework for our theories. In fact, “we do not begin with white paper at birth, but with inborn expectations and intentions and an innate ability to improve upon them using thought and experience”.[17] At a naive stage of observation, our intuitive experience leads to the conviction that concepts the likes of determinism, absolute simultaneity, local realism, conservation laws (e.g. of parity) were a priori assumptions of scientific investigation. What it turns out, however, is that there is in principle no reason to pre-assume anything like that: they are mere “philosophical prejudices”. Modern physics, with the revolutionary theories of quantum mechanics and relativity, has washed away some of them, and recent developments are ruling out more and more of these “prejudices”. Feyerabend’s words sound thus remarkable, when he states that it

becomes clear that the discoveries of quantum theory look so surprising only because we were caught in the philosophical thesis of determinism [...].

What we often refer to as a crisis in creative activity, and while every synthesis implicitly and trivially tries to falsify some deep-seated fundamental law, the science and art of synthesis as a whole does not explicitly and non-trivially try to falsify any particular theory. That does not mean that falsification is absent or untrue, it just means that it is rather irrelevant in this field:
Figure 1: A sketch of fundamental research here proposed as a series of successive experimental violations of the "philosophical prejudices" assumed by our "established theories", towards the actual fundamental constraints (see main text). "Physical theories" here means "physically significant", i.e. they carry an empirical content. "Formulable" theories are in general all the theories one can think of, and they are characterized solely by the formalism.

Using a methodology as expounded in previous section, we are able to put to the test concepts that were classically not only considered part of the domain of philosophy (metaphysics), but even necessary a priori assumptions for science. Reaching the foundations of physics, then means to test each of this concepts and remove the constraints built upon a prejudicial basis, pushing the frontier of scientific domain up to the "actual" insurmountable constraints which demarcate the possible from the impossible (see Fig. 1), yet within the realm of science on an empirical basis. These actually fundamental constraints (FC) are so transdisciplinary, and should be considered in the research in every natural science. Yet, contrarily to the physicalist program, the search for FC does not elevate one particular science to a leading, more fundamental position. Moreover, this view does not entail any pre-assumption of realism, but rather it allows to test, and possibly empirically falsify, certain forms of realism (see further). For instance, physicists from any field know very well how careful they should be in carrying out their calculations to avoid a violation of the bound imposed by the (finite) speed of light. But why is it so? Why should be the impossibility of instantaneous signaling considered a more fundamental (i.e. insurmountable) limitation of physics, than the bound imposed by determinism? Because the knowledge of the most fundamental bounds are also limited by our methodology. Since falsificationism requires some "cause-effect" relations to meaningfully test theories, then instantaneous signaling would break this possibility, and any meaning of the current methodology along with it. There could however be cases where this relation to methodology are not so unambiguous. Then, they should be considered more fundamental those concepts which independently arise from different theories; they are thus more corroborated (the impossibility of instantaneous signaling implied by both quantum formalism and special relativity, is again an example). In this case, "fundamental" is thought also as a degree of "generality".

To sum up, we maintain that one of the aims of science is to approach the actual foundations (red edge in Fig. 1) through a discrete process of successive falsifications of the allaged a priori assumptions, which obviously have to be formulated in terms of scientific statements. If these are falsified, then they can be dismissed as "philosophical prejudices".

3.1 Foundations of quantum mechanics

A large part of the research on modern foundations of physics has developed along the directions that we have thus far described. It is the case of what are usually referred to as “no-go theorems”\footnote{Recent lines of research show that quantum mechanics may not present a definite causal order\cite{21}. However, these new possibilities do not undermine testable cause-effect relations, and thus do not clash with falsifiability.} They require a falsifiable statement (e.g. in the form

\footnote{Historically, no-go theorems are associated to the conditions of compatibility with quantum formalism. Here, however, we consider them in a more general context. They are regarded as decidable statements that discriminate between any two classes of theories, possibly beyond QM (see further).}
of an inequality) that is deductively inferred (i.e. formally derived) from a minimal set of assumptions, which are chosen to include the “philosophical prejudices” (in the sense expounded above) that one wants to test. A no-go theorem therefore allows to formulate one or more of this “philosophical prejudices” in terms of a statement that can undergo experimental test: what till then was believed to be a philosophical assumption, suddenly enters the domain of science. If this statement is experimentally falsified, its falsity is logically transferred to the conjunction of the assumptions (modus tollens) that thus becomes untenable\(^{10}\). The no-go theorem is the statement of this untenability.

But there is more to the epistemological power of “no-go theorems”: they can sometimes be formulated in a way that they do not include any particular scientific theory in their assumptions (device-independent formulation). In this case the no-go theorem assumes the form of a collection of measurements and relations between measurements (operational formulation), yet it holds directly independently of any specific experimental apparatus, its settings, or the chosen degrees of freedom to be measured. In practice, if a particular theory assumes one of the “philosophical prejudices” that have been falsified by a certain no-go theorem, then this theory needs to be revised (if not completely rejected) in the light of this evidence. Furthermore, the falsification of a no-go theorem rules out the related “philosophical prejudice” for every future scientifically significant theory.

We shall review some of the by now classical no-go theorems in quantum theory, in the spirit of the present paper. It is generally known that quantum mechanics (QM) provides only probabilistic predictions, that is, given a certain experiment with measurement choice \(x\) and a possible outcome \(a\), quantum theory allows to compute the probability \(p(a|x)\) of finding that outcome. Many eminent physicists (Einstein, Schrödinger, de Broglie, Bohm, Vigier, etc.) made great efforts to restore determinism and realism\(^{11}\). A way to achieve this is to assume the existence of underlying hidden variables (HV), \(\lambda\), not experimentally accessible (either in principle or provisionally), that if considered would restore determinism, i.e. \(p(a|x, \lambda) = 0\) or 1\(^{12}\). In a celebrated work \(^{24}\), Bohm proposed a full developed model of QM in terms of HV. However, the HV program started encountering some limitations. To start with, S. Kochen and E. Specker\(^{22}\) assumed (1) a deterministic HV description of quantum mechanics and (2) that these HV are independent of the choice of the disposition of the measurement apparatus (context)\(^{13}\) and showed that this leads to an inconsistency\(^{14}\). Thus if HV exist, they must depend on the context. John Bell, however, noticed that this is not so surprising, since

there is no a priori reason to believe that the results [...] should be the same. The result of observation may reasonably depend not only on the state of the system (including hidden variables) but also on the complete disposition of apparatus. \((25), \text{p. 9}\)

We must stress that this theorem rules out the conjunction of the assumptions only logically. It is only with an experimental violation, recently achieved \(^{26}\), of its falsifiable formulation that contextuality is ruled out.

But it was with a seminal paper by Bell \(^{23}\), that one of the most momentous no-go theorems was put forward\(^{15}\). Consider two distant (even space-like separated) measurement stations \(A\) and \(B\). Each of them receives a physical object (information)
In the realm of QM (see further), some authors try to do (e.g. [27]) to justify the "non-local" correlations that have interacted in the past. At station A (B) a measurement is performed with settings labeled by x (y), and the outcome by a (b). Since the stations are very far away and the local measurement settings are freely chosen, common sense (or a "philosophical prejudice") would suggest that the joint probability of finding a and b given x and y is independent (i.e. factorizable). Nevertheless, in principle (i.e. without "prejudices"), the local measurement settings could somehow statistically influence outcomes of distant experiments, such that \( p(a,b|x,y) \neq p(a|x)p(b|y) \). It is important to notice that "the existence of such correlations is nothing mysterious. [...] These correlations may simply reveal some dependence relation between the two systems which was established when they interacted in the past" [27]. This 'common memory' might be taken along by some hidden variables \( \lambda \) that, if considered, would restore the independence of probabilities. The joint probability then becomes

\[
p(a,b|x,y) = \int_{\Lambda} d\lambda \, q(\lambda) \, p(a|x,\lambda) \, p(b|y,\lambda).
\] (1)

This condition is referred to as local realism (LR)\(^{[16]}\)

Let us consider dichotomic measurement settings and outputs (i.e. \( x, y \in \{0, 1\} \) and \( a, b \in \{-1, +1\} \)) and define the correlations as the averages of the products of outcomes given the choices of settings, i.e. \( \langle a \, b \rangle = \sum_{a,b} \, p(a,b|x,y) \), it is easy to prove that the condition (1) of LR leads to the following expression in terms of correlations:

\[
S_{(LR)} = \langle a_0b_0 \rangle + \langle a_0b_1 \rangle + \langle a_1b_0 \rangle - \langle a_1b_1 \rangle \leq 2.
\] (2)

This is an extraordinary result, known as Bell’s inequality\(^{[23]}\)\(^{[18]}\). Indeed, a condition such as (1) gives a mathematical description of the profound philosophical concepts related to locality and realism, whereas its derived form transforms LR into an experimentally falsifiable statement in terms of actually measurable quantities (correlations). Indeed, the conjunction of all assumptions of Bell inequalities is not a philosophical statement, as it is testable both experimentally and logically [...]. Thus, Bells theorem removed the question of possibility of local realistic description from the realm of philosophy. [18]

Since the 1980s, experiments of increasing ambition have tested local realism through Bell’s inequalities [28], and have empirically violated them. Namely, LR has been falsified and this removed the possibility of scientific theories based on local realistic description\(^{[19]}\)

Quantum mechanics is a compatible theory, because its formalism gives a results that is out of the bounds of local realism. Indeed, quantum mechanics allows the preparation of pairs of information carriers called entangled\(^{[20]}\). From elementary calculations (see e.g. [27]), it follows that using quantum entanglement, the relation between correlations as defined in (2) reaches a maximum value (Tsinel’son’s bound) of

\[
S_{(Q)} = 2\sqrt{2} > 2 = S_{(LR)}.
\] (3)

This is the second crucial result of Bell’s inequalities: the quantum formalism imposes a new bound.

\(^{[16]}\)\( \lambda \) can in general be governed by a probability distribution and be a continuous variable over a domain \( \Lambda \), as considered below. The final probability \( p(a,b|x,y) \) should eventually not explicitly depend on \( \lambda \), which should be averaged out.

\(^{[17]}\)The name comes from the fact that decomposition (1) was derived under the mere assumption of having some real quantities \( \lambda \) that factorize the joint probability distribution into local operations only. Notice, however, that LR is here a compound condition, given by the mathematical expression (1), and cannot be formally separated into two distinct conditions as some authors try to do (e.g. [27]) to justify the “non-local” nature of QM (see further).
that is out of the bounds of local realism. At the moment this new bound imposed by \((3)\) has never been experimentally violated, and QM survived experimental falsification. There is yet another condition that one might want to enforce, namely that the choice of measurement settings cannot direct influence the outcomes at the other stations (not in terms of correlations but actual information transfer). This is called no-signaling (NS) condition and reads

\[
\sum_b p(a,b|x,y) = p(a|x); \quad \sum_a p(a,b|x,y) = p(b|y),
\]

(4)

The NS constraint is where we set the FC. Indeed, a theory that would violate this condition allows for instantaneous signaling and it thus would mean a failure of the scientific method as we conceive it. It would be in principle not falsifiable (besides being incompatible with relativity theory) \(^{22}\).

It is possible to show that LR correlations are a proper subset of quantum correlations and that both are strictly included in the NS set of theories.

(see Fig. 2) To summarize, local realistic theories have been falsified, and we have a theory, QM, which comes outside its borders. However, it is not the most fundamental theory we think of, since there is potentially room for theories that violates the bounds imposed by QM, and still lies in the domain of “physically significant” theories (i.e within the NS bound).

In the literature of modern FQM there is plenty of other no-go theorems that quantify the discrepancy between “classical” and quantum physics, ruling out different “philosophical prejudices” than the mentioned contextuality and local realism. For instance, one of the present authors (F.D.S.) has recently proposed, with B. Dakić \(^{30}\), a new no-go theorem. Consider a scenario in which information should be transmitted between two parties, A and B, in a time window \(\tau\) that allows a single information carrier to travel only once from one party to the other (“one-way” communication). At time \(t = 0\), A and B are given inputs \(x\) and \(y\) and at \(t = \tau\) they reveal outputs \(a\) and \(b\). The joint probability results in a classical mixture of one-way communications:

\[
p(a,b|x,y) = \gamma p_A(a|x)p_{A\rightarrow B}(b|x,y,a) + (1-\gamma)p_B(b|y)p_{B\rightarrow A}(a|x,y,b),
\]

(5)

where symbol \(\prec\) denotes the direction of communication, e.g. \(A \prec B\) means that A sends the information carrier to B. This distribution leads to a Bell’s-like inequality that, in the case of \(x, y, a, b = 0, 1\), reads:

\[
p(a = y, b = x) \leq \frac{1}{2}.
\]

(6)

In Ref.\(^{30}\) is shown that an information carrier in quantum superposition between A and B surpasses this bound, and leads to \(p(a = y, b = x) = 1\). This bound, logically violated by quantum formalism, has been also experimentally falsified, and results in a violation of “classical” one-way communication.

\(^{22}\)In general, for every number of values that \(x, y, a, b\) can take, it is possible to prove that in the space of all the possible probabilities \(p(ab|xy)\), the LR condition \((1)\) forms a polytope whose vertices are the deterministic correlations \((D)\), and whose facets (the edges in the 2-d representation of Fig. \(2\)) are the Bell’s inequalities (Minkowski’s theorem assures that a polytope can be always represented as the intersection of finitely many hyperplanes). Also NS correlations form a polytope, whereas the quantum correlations form a convex, closed and bound set, but that has no facets.
tion.

### 3.2 “Foundations” of biophysics

The process of reaching foundations here proposed can be pursued also in branches of physics considered more “complex” (i.e. the opposite of fundamental in the reductionist view), like the physics of biological systems.

Proteins are a class of polymers involved in most of natural processes at the basis of life. The 3D structure of each protein, of which the precision is essential for its functioning, is uniquely encoded in a 1D sequence of building blocks (the 20 amino acids) along a polymer chain. This process of encoding is usually referred to as design. The huge variability of all existing natural proteins is originated solely by different sequences of the same set of 20 building blocks. Proteins are very complex systems and the understanding and prediction of the mechanism behind their folding, that is the process with which they reach their target 3D structure, is still one of the biggest challenges in science. Until now, no other natural nor artificial polymer is known to be designable and to fold with the same precision and variability of proteins.

A more fundamental approach to understand proteins, that can possibly go beyond the observed natural processes, is to ask a different question: are proteins such unique polymers? In other words: is the specific spatial arrangement of the atoms in amino acids the only possible realization to obtain design and folding? According to the mean field theory of protein design [31], given an alphabet of building blocks of size $q$, a system is designable when

$$q > M,$$

where $M$ is the number of structures that the chain can access, divided the number of monomers along the chain.\[23\] For instance, a simple bead and springs polymer will have a certain number of possible structures $\tilde{M}$, defined only by the excluded volume of the beads. If one adds features to the monomers (e.g. directional interactions), this can result in a smaller number of energetically/geometrically accessible structures for the polymer $M < \tilde{M}$. With fewer accessible structures, it will be easier for the sequence to select a specific target structure - and not an ensemble of degenerate structures. Hence, to make a general polymer designable (from Eq. (7)) one can follow two strategies: i) increasing the alphabet size $q$ and, ii) reducing the number of accessible structures per monomer $M$. In the works [32, 33] one of the present authors (C.C.) and collaborators show with computational polymer models that one can indeed reduce the number of accessible structures by simply introducing a few directional interactions to a simple bead-spring polymer. This approach is already enough to reduce the number of accessible structures $M$ to obtain designability.\[24\] The resulting polymers (bionic proteins) can have different numbers and geometries of those directional interactions and, despite not having at all the geometrical arrangement of amino acids, are designable and able to fold precisely into a specific unique target structure, with the same precision of proteins. These bionic proteins are also in principle experimentally realizable on different length scales. Introducing directional interactions is not the only approach to reduce the number of accessible configurations, therefore there can be other examples of polymers that are able to be designable and fold into a target structure. This view teaches us to look beyond the prejudice that the particularism of the amino acids is the only way to achieve design and folding, and search the functioning of proteins into more fundamental principles, that can be applied to a wider range of possible folding polymers.

### 4 Conclusions

We have shown that the search for foundations is a dynamical process that aims at removing “philosophical prejudices” by means of empirical falsification. This search tends however to an end, given by the FC (which are the most general, physically significant constraints under a certain methodology). A theory $T_1$ is thus more fundamental than a theory $T_2$ when $T_1$ includes $T_2$, but it comes out of the boundaries of $T_2$ (e.g. $T_1$ = quantum theory

\[23\] $M$ is $\exp(\omega)$, where $\omega$ is the so called configurational entropy per monomer

\[24\] The designability was obtained for size of the alphabet $q = 20$ such as in proteins or even less down to $q = 3$.  

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Figure 3: Relations between polymers at a fixed $q = 20$: natural proteins, “bionic” proteins (i.e., all polymers that are designable to fold into a specific target structure) and all “formulable” polymers. The boundary between “bionic” proteins and not folding polymers is the inequality (7) (see main text).

and $T_2 = $ deterministic contextual theories; or local realistic theories).

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