Classical, Quantum and Biological Randomness as Relative Unpredictability

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Abstract
We propose the thesis that randomness is unpredictability with respect to an intended theory and measurement. From this point view we briefly discuss various forms of randomness that physics, mathematics and computing science have proposed. Computing science allows to discuss unpredictability in an abstract, yet very expressive way, which yields useful hierarchies of randomness and may help to relate its various forms in natural sciences. Finally we discuss biological randomness — its peculiar nature and role in ontogenesis and in evolutionary dynamics (phylogenesis). Randomness in biology has a positive character as it contributes to the organisms' and populations' structural stability by adaptation and diversity.

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Abstract We propose the thesis that randomness is unpredictability with respect to an intended theory and measurement. From this point view we briefly discuss various forms of randomness that physics, mathematics and computing science have proposed. Computing science allows to discuss unpredictability in an abstract, yet very expressive way, which yields useful hierarchies of randomness and may help to relate its various forms in natural sciences. Finally we discuss biological randomness—its peculiar nature and role in ontogenesis and in evolutionary dynamics (phylogenesis). Randomness in biology has a positive character as it contributes to the organisms' and populations' structural stability by adaptation and diversity.

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1 Introduction

Randomness is everywhere, for the better or for the worse: vagaries of weather, day-to-day fluctuations in the stock market, random motions of molecules or random genetic mutations are just a few examples. Random numbers have been used for more than 4,000 years, but never have they been in such scrutiny and demand as in our time. What is the origin of randomness in nature and how does it relate to the only access we have to phenomena, that is, through measurement? How does randomness in nature relates to randomness for sequences of numbers? The theoretical and mathematical analysis of randomness is far from obvious. Moreover, as we will show, it depends on (and is relative to) the particular theory one is working on, the *intended* theoretical framework for the phenomena under investigation.

1.1 Brief history

Probably the first philosopher thinking about randomness was Epicurus (341–270 BC). He argued that "randomness is objective, it is the proper nature of events". Democritus (460–370 BC) pinned down the causes of things to necessity and chance alike, justifying, for example, the fact that the atoms disorderly motion can produce an orderly cosmos.

For centuries, though, randomness has been mathematically analysed only in games and gambling. Luca Pacioli, in his *Summa de aritmetica, geometria, proporzioni et proporzionalita* of 1494, studied how the stakes had to be divided among the gamblers, in particular, in the difficult case when the game stops before the end. It is worth noticing that Pacioli, a top Renaissance mathematician, invented also the modern bookkeeping techniques (Double Entry): human activities, from gambling to financial investments, where considered as the

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locus for chance. As a matter of fact, early Renaissance Florence was the place of the invention of banks, paper currency and (risky) financial investments and loans.[1]

Cardano, in *De Ludo Aleae* (The Game of Dice) of 1525 further developed Pacioli's analysis. His book was published only in 1663, so Fermat and Pascal independently and more rigorously rediscovered the "laws of chance" for interrupted games in a famous exchange of letters in 1654. Pascal clarified the independence of history in the games of chance, against common sense: dice do not remember the previous drawings. Probabilities were generally considered as a tool for facing the lack of knowledge in human activities: in contrast to God, we cannot predict the future nor master the consequences of our (risky) actions. For the thinkers of the scientific revolution, randomness is not in nature, which is a perfect "Cartesian Mechanism": science is meant to discover the gears of its wonderful and exact mechanics. At most, as suggested by Spinoza, two independent, well determined trajectories may meet (a walking man and a falling tile) and produce a random event. This may be considered a weak form of "epistemic" randomness, as the union of the two systems may yield a well determined and predictable system and encounter.

Galileo, while still studying randomness only for dice (*Sopra le scoperte de i dadi*, 1612), was the first to relate measurement and probabilities (1632). For him, in physical measurement, errors are unavoidable, yet small errors are the most probable. Moreover, errors distribute symmetrically around the mean value, whose reliability increases with the number of measurements.

Almost two centuries later, Laplace brought Pascal's early insights to the modern rigour of probability theory in [50]. He stressed the role of limited knowledge of phenomena in making predictions by equations: only a daemon with complete knowledge of all the forces in the Universe could "embrace in a single formula the movements of the greatest bodies of the universe and those of the tiniest atom; for such an intellect nothing would be uncertain and the future just like the past would be present before its eyes". The connection between incomplete knowledge of natural phenomena and randomness is made, yet no analysis of the possible "reasons" for randomness is proposed: probability theory gives a formal calculus of randomness, with no commitment on the nature of randomness. Defining randomness proved to be a hugely difficult problem which has received acceptable answers only in the last 100 years or so.

1.2 Preliminary remarks

Randomness is a delicate concept which can come in many flavours [30]. Informally, randomness means *unpredictability*, *lack of patterns or correlations*. Why randomness is so difficult to understand and model? An intuitive understanding comes from the myriad of misconceptions and logical fallacies related to randomness, like the the gambler's fallacy. In spite of the work of mathematicians since the Renaissance, this is the belief that after a coin has landed on tails ten consecutive times there are more chances that the coin will land on heads at the next flip. Similarly, common sense argues that there are "due" numbers in lottery (since all numbers eventually appear, those that have not come up yet are 'due', and thus more likely to come up soon). Each proposed definition of randomness seems to be doomed to be falsified by some more or less clever counter-example.

Even intuitively, the quality of randomness varies: tossing a coin may seem to produce a sequence of zeroes and ones which is less random than the randomness produced by Brownian motion. This is one of the reasons why users of randomness—like casinos, lotteries, polling firms, elections, clinical evaluations—are hard pressed to "prove" that their choices are "really" random. A new challenge is emerging, namely to "prove randomness".

For physical systems, the randomness of a process needs to be differentiated from that of its outcome. Random (stochastic) processes have been extensively studied in probability theory, ergodic theory and information theory [77]. Process or genesis randomness refers to such processes. On one hand, a "random" sequence need not necessarily be the output of a random process (e.g. a mathematically defined "random" sequence) and, conversely, a random process (e.g. a quantum random generator) is expected, but not guaranteed, to produce a "random output". Outcome (or product) randomness provides a *prima facie* reason for the randomness of the process generating that outcome [31, p. 762], but, as argued in [37, p. 431], process and outcome randomness are not extensionally equivalent. Process randomness has no mathematical formalisation and can be accessed/validated only with theory or output randomness.

Measurement is a constantly underlying issue: only by measurement we may associate a number to a "natural" process. Most of the time we actually associate an interval (an approximation), an integer or rational number, as forms of counting or drawing.

[1] Such as the loan, in 1332, to the King of Britain Edward III who never returned it to the Bank of Bardi and Peruzzi—as all high school kids in Italy and our colleague Alberto Peruzzi in Florence know very well . . . .

Let us finally emphasise that, in spite of the existing theoretical differences in the understanding of randomness, our approach allows to unify the various forms of randomness in a relativised perspective:

randomness is unpredictability with respect to the intended theory and measurement.

We will move along this epistemological stand that will allow us to discuss and compare randomness in different theoretical contexts.

2 Randomness in classical dynamics

A major contribution to the contemporary understanding of randomness was given by Poincaré. By his "negative result" (his words) on the Three Body Problem (1892, a relatively simple deterministic dynamics, see below), he proved that minor fluctuations or perturbations below the best possible measurement may manifest in a measurable, yet unpredictable consequence: "we then have a random phenomenon" [68]. This started the analysis of deterministic chaos, as his description of the phase-space trajectory derived from a non-linear system is the first description of a chaotic dynamics, [16].

Poincaré analysis is grounded on a mathematical "tour de force". He proved the non analyticity of the (apparently) simple system of non-linear equations describing two planets and a Sun in their gravitational fields (three bodies). The planets disturb each other's trajectories and this gives the formal divergence of the Lindstedt-Fourier series meant to give a linear approximation of the solution of the equations. More precisely, by using his notions of bifurcations and homoclinic orbit (the intersection of a stable and an unstable manifold), he showed that the "small divisors", which make the series diverge, physically mean that an undetectable fluctuation or perturbation may be amplified to a measurable quantity by the choice of a branch or another in a bifurcation or a manifold along a homoclinic orbit. It is often difficult to give a physical meaning to the solution of a system of equations; it is particularly hard and inventive to make sense of the absence of a solution. Yet, this made us understand randomness as deterministic unpredictability and non-analyticity as a strong form of classical unpredictability.[2]

In this classical framework, a random event has a cause, yet this cause is below measurement. Thus, Curie's principle[3] is preserved as "the asymmetries of the consequences are already present in the causes" or "symmetries are preserved"—the asymmetries in the causes are just hidden.

For decades, Poincaré's approach was quoted and developed only by a few, that is, till Kolmogorov's work in the late 1950s and Lorentz in the 1960s. Turing is one of these few: he based his seminal paper on morphogenesis [74] on a non-linear dynamics of forms generated by chemical reactants. His "action/reaction/diffusion system" produces different forms by spontaneous symmetry breaking. An early hint of these ideas is already given by him in [73, p. 440]: "The displacement of a single electron by a billionth of a centimetre at one moment might make the difference between a man being killed by an avalanche a year later, or escaping". This Poincarian remark by Turing preceded by 20 years the famous "Lorentz butterfly effect", proposed in 1972 on the grounds of Lorentz's work from 1961.

Once more, many like to call this form of classical randomness "epistemic" unpredictability, that is, as related to our knowledge of the world. We do not deal with ontologies here, although this name may be fair, with the due distinction from the understanding of randomness as the very weak form of unpredictability proposed by Spinoza. Poincaré brought to the limelight a fact known since Galileo: classical measurement is an interval, by principle.[4] Measurement is the only form of access we have to the physical world, while no principle forbids, a priori, to join two independent Spinozian dynamics. That is, even epistemic, classical physics posits this limit to access and knowledge as "a priori" measurement. Then this lack of complete knowledge yields classical randomness, typically in relation to a *non-linear mathematical modelling*, which produces either positive Lyapunov exponents or, more strongly, non-analyticity. In other words, classical systems (as well as relativistic ones) are deterministic, yet they may be unpredictable, in the sense that

[2] Non-analyticity is stronger than the presence of positive Lyapunov exponents in a non-linear function. These exponents may appear in the solution of a non-linear system or directly in a function describing a dynamics; they quantify how a minor difference in the initial conditions may be amplified along the trajectory. In this case, one has a form of "controlled" randomness, as the divergence of the trajectories starting within the same best interval of measurement will not exceed an exponentially increasing, yet pre-given value. In the absence of (analytic) solutions, bifurcations and homoclinic orbits may lead to sudden, "uncontrolled", divergence.

[3] A macroscopic cause cannot have more elements of symmetry than the effect it produces. Its informational equivalent—called data processing inequality—states that no manipulation of the data can improve the inferences that can be made from the data [27].

[4] Also Laplace was aware of this, but Lagrange, Laplace, Fourier firmly believed that any (interesting or "Cauchy") system of equations possesses a linear approximation [61].

> randomness is not in the world nor it is just in the eyes of the beholder, but it pops out at the interface between us and the world by theory *and* measurement.

By "theory" we mean the equational or functional determination, possibly by a non-linear system of equations or evolution functions.

3 Quantum randomness

Quantum randomness is hailed to be more than "epistemic", that is, "intrinsic" (to the theory). However, quantum randomness is not part of the standard mathematical model of the quantum which talks about probabilities, but about measurement of individual observables. So, to give more sense to the first statement we need to answer (at least) the following questions: a) what is the source of quantum randomness?, b) what is the quality of quantum randomness? c) is quantum randomness different from classical randomness?

A naive answer to a) is to say that quantum mechanics has shown "without doubt" that microscopic phenomena are intrinsically random. For example, one cannot predict with certainty how long it will take for a single unstable atom in a controlled environment to decay, even if one could have complete knowledge of the "laws of physics" and the atom's initial conditions. One can only calculate the probability of decay in a given time, nothing more! This is *intrinsic randomness guaranteed*.

But is it? What is the cause of the above quantum mechanical effect? One way to answer is to consider a more fundamental quantum phenomenon: *quantum indeterminism*. What is quantum indeterminism and where does it come from? Quantum indeterminism appears in the measurement of individual observables: it has been at the heart of quantum mechanics since Born postulated that the modulus-squared of the wave function should be interpreted as a probability density that, unlike in classical statistical physics [64], expresses fundamental, irreducible indeterminism [14]. For example, the measurement of the spin, "up or down", of an electron, in the standard interpretation of the theory, is considered to be pure contingency, a symmetry breaking with no antecedent, in contrast to the causal understanding of Curie's principle.[5] The nature of individual measurement outcomes in quantum mechanics was, for a period, a subject of much debate. Einstein famously dissented, stating his belief that "*He does not throw dice*" [15, p. 204]. Over time the assumption that measurement outcomes are fundamentally indeterministic became a postulate of the quantum orthodoxy [78]. Of course, this view is not unanimously accepted, see [49].

Following Einstein's approach [32], quantum indeterminism corresponds to the *absence of physical reality*, if reality is *what is made accessible by measurement*: if no unique element of physical reality corresponding to a particular physical observable (thus, measurable) quantity exists, this is reflected by the physical quantity being indeterminate. This approach needs to be more precisely formalised. The notion of *value indefiniteness*, as it appears in the theorems of Bell [11] and, particularly, Kochen and Specker [45], has been used as a formal model of quantum indeterminism [2]. The model has also empirical support as these theorems have been experimentally tested via the violation of various inequalities [75]. We have to be aware that, going along this path, the "belief" in quantum indeterminism rests on the assumptions used by these theorems.

An observable is *value definite* for a given quantum system in a particular state if the measurement of that observable is pre-determined to take a (potentially hidden) value. If no such pre-determined value exists, the observable is *value indefinite*. Formally, this notion can be represented by a *(partial) value assignment function* (see [2] for the complete formalism).

When should we conclude that a physical quantity is value definite? Einstein, Podolsky and Rosen (EPR) define *physical reality* in terms of certainty of predictability in [32, p. 777]:

> If, without in any way disturbing a system, we can predict with certainty (i.e., with probability equal to unity) the value of a physical quantity, then there exists an element of physical reality corresponding to this physical quantity.

Note that both allusions to "disturbance" and to the (numerical) value of a physical quantity refer to measurement, as the only form of access to reality we have. Thus, based on this accepted notion of an element of physical reality, following [2] we answer the above question by identifying EPR notion of an "element of physical reality" with "value definiteness":

[5] A correlation between random events and symmetry breakings is discussed in [57]. In this case, measurement produces a value (up or down), which breaks the in-determined or in-differentiated (thus, symmetric) situation before measurement.

EPR principle: If, without in any way disturbing a system, we can predict with certainty the value of a physical quantity, then there exists a *definite value* prior to observation corresponding to this physical quantity.

The EPR principle justifies the following

Eigenstate principle: A projection observable corresponding to the preparation basis of a quantum state is *value definite*.

The requirement called *admissibility* is used to avoid outcomes impossible to obtain according to quantum predictions which have overwhelming experimental confirmation.

Admissibility principle: Definite values must not contradict the statistical quantum predictions for compatible observables on a single quantum.

Finally, the last assumption is

Non-contextuality principle: Measurement outcomes (when value definite) do not depend on other compatible (i.e. simultaneously co-measurable) observables which may be measured alongside the value definite observable.

The Kochen-Specker Theorem [45] states that no value assignment function can consistently make *all* observables value definite while maintaining the requirement that the values are assigned non-contextually. This is a global property: non-contextuality is incompatible with *all* observables being value definite. However, it is possible to localise value indefiniteness by proving that even the existence of two non-compatible value definite observables is in contradiction with admissibility and non-contextually, without requiring that all observables be value definite. As a consequence we obtain the following "formal identification" of a value indefinite observable:

Any mismatch between preparation and measurement context leads to the measurement of a value indefinite observable.

This fact is stated formally in the following two theorems. As usual we denote the set of complex numbers by $\mathbb{C}$ and vectors in the Hilbert space $\mathbb{C}^n$ by $|\cdot\rangle$; the projection onto the linear subspace spanned by a non-zero vector $|\phi\rangle$ is denoted by P_ϕ. For more details see [49].

Theorem 1 ([2]) *Consider a quantum system prepared in the state $|\psi\rangle$ in dimension $n \geq 3$ Hilbert space $\mathbb{C}^n$, and let $|\phi\rangle$ be any state neither orthogonal nor parallel to $|\psi\rangle$. Then the projection observable P_ϕ is value indefinite under any non-contextual, admissible value assignment.*

Hence, accepting that definite values *exist* for certain observables (the eigenstate principle) and behave non-contextually (non-contextuality principle) is enough to locate and *derive rather than postulate* quantum value indefiniteness. In fact, *value indefinite observables* are far from being scarce [4]:

Theorem 2 ([3]) *Assume the eigenstate, non-contextuality and admissibility principles. Then, the (Lebesgue) probability that an arbitrary observable is value indefinite is one.*

Theorem 2 says that all value definite observables can be located into a small set, a set of probability zero. Consequently, value definite observables are not the norm, they are the exception, a long time held intuition in quantum mechanics.

The above analysis not only offers an answer to the question a) from the beginning of this section, but also indicates a procedure to generate a form of quantum random bits [22,2,3]: *Locate and measure a value indefinite observable*. Quantum random number generators based on Theorem 1 were proposed in [2,3]. Of course, other possible sources of quantum randomness may be identified, so we are naturally lead to question b), what is the quality of quantum randomness certified by Theorem 1, and, if there exist other forms of quantum randomness, what qualities do they have?

To this aim we are going to look in more details at the unpredictability of quantum randomness certified by Theorem 1. We will start by describing a non-probabilistic model of prediction—proposed in [5]—for a hypothetical experiment E specified effectively by an experimenter.[6]

The model uses the following key elements.

[6] The model does not assess the ability to make statistical predictions—as probabilistic models might—but rather the ability to predict precise measurement outcomes.

1. The specification of an experiment E for which the outcome must be predicted.
2. A predicting agent or "predictor", which must predict the outcome of the experiment.
3. An extractor ξ is a physical device the predictor uses to (uniformly) extract information pertinent to prediction that may be outside the scope of the experimental specification E. This could be, for example, the time, measurement of some parameter, iteration of the experiment, etc.
4. The uniform, algorithmic repetition of the experiment E.

In this model a predictor is an effective (i.e. computational) method of uniformly predicting the outcome of an experiment using finite information extracted (again, uniformly) from the experimental conditions along with the specification of the experiment, but *independent* of the results of the experiments. A predictors depends on an axiomatic, formalised theory, which allows to make the prediction, i.e. to compute the "future". An experiment is predictable if any potential sequence of repetitions (of unbounded, but finite, length) of it can always be predicted correctly by such a predictor. To avoid that prediction is successful just by chance, we require that a correct predictor—which can return a prediction or abstain (prediction withheld)—never makes a wrong prediction no matter how many times is required to make a new prediction (by repeating the experiment) and cannot abstain from making predictions indefinitely, i.e. the number of correct predictions can be made arbitrarily large by repeating the experiment enough times.

We consider a finitely specified physical experiment E producing a single bit $x \in \{0, 1\}$. Such an experiment could, for example, be the measurement of a photon's polarisation after it has passed through a 50-50 polarising beam splitter, or simply the toss of a physical coin with initial conditions and experimental parameters specified finitely.

A particular trial of E is associated with the parameter λ which fully describes the "state of the universe" in which the trial is run. This parameter is "an infinite quantity"—for example, an infinite sequence or a real number—structured in a way depending on the intended theory. The result below, though, is independent on the theory. While λ is not in its entirety an obtainable quantity, it contains any information that may be pertinent to prediction and any predictor can have practical access to a finite amount of this information. We can view λ as a resource that one can extract finite information from in order to predict the outcome of the experiment E.

An *extractor* is a physical device selecting a finite amount of information included in λ without altering the experiment E. It can be used by a predicting agent to examine the experiment and make predictions when the experiment is performed with parameter λ. So, the extractor produces a finite string of bits $\xi(\lambda)$. For example, $\xi(\lambda)$ may be an encoding of the result of the previous instantiation of E, or the time of day the experiment is performed.

A *predictor* for E is an algorithm (computable function) P_E which *halts* on every input and *outputs* either 0, 1 (cases in which P_E has made a prediction), or "prediction withheld". We interpret the last form of output as a refrain from making a prediction. The predictor P_E can utilise as input the information $\xi(\lambda)$ selected by an extractor encoding relevant information for a particular instantiation of E, but must not disturb or interact with E in any way; that is, it must be *passive*.

A predictor P_E provides a *correct prediction* using the extractor ξ for an instantiation of E with parameter λ if, when taking as input $\xi(\lambda)$, it outputs 0 or 1 (i.e. it does not refrain from making a prediction) and this output is equal to x, the result of the experiment.

Let us fix an extractor ξ. The predictor P_E is *k-correct for ξ* if there exists an $n \geq k$ such that when E is repeated n times with associated parameters $\lambda_1, \ldots, \lambda_n$ producing the outputs $x_1, x_2, \ldots, x_n$, P_E outputs the sequence $P_E(\xi(\lambda_1)), P_E(\xi(\lambda_2)), \ldots, P_E(\xi(\lambda_n))$ with the following two properties:

1. no prediction in the sequence is incorrect, and
2. in the sequence there are k correct predictions.

The repetition of E must follow an algorithmic procedure for resetting and repeating the experiment; generally this will consist of a succession of events of the form "E is prepared, performed, the result (if any) recorded, E is reset".

The definition above captures the need to avoid correct predictions by chance by forcing more and more trials and predictions. If P_E is k-correct for ξ, then the probability that such a correct sequence would be produced by chance $\binom{n}{k} \cdot 3^{-n}$ is bounded by $\left(\frac{2}{3}\right)^k$, hence it tends to zero when k goes to infinity.

The confidence we have in a k-correct predictor increases as $k \to \infty$. If P_E is k-correct for ξ for all k, then P_E never makes an incorrect prediction and the number of correct predictions can be made arbitrarily large by repeating E enough times. In this case, we simply say that P_E *is correct for* ξ. The infinity used in the above definition is *potential* not actual: its role is to guarantee arbitrarily many correct predictions.

This definition of correctness allows P_E to refrain from predicting when it is unable to. A predictor P_E which is correct for ξ is, when using the extracted information $\xi(\lambda)$, guaranteed to always be capable of providing more correct predictions for E, so it will not output "prediction withheld" indefinitely. Furthermore, although P_E is technically used only a finite, but arbitrarily large, number of times, the definition guarantees that, in the hypothetical scenario where it is executed infinitely many times, P_E will provide infinitely many correct predictions and not a single incorrect one.

Finally we define the prediction of single a bit produced by an individual trial of the experiment E. The outcome x of a single trial of the experiment E performed with parameter λ is predictable (with certainty) if there exist an extractor ξ and a predictor P_E which is correct for ξ, and $P_E(\xi(\lambda)) = x$.

Applying the model of unpredictability described above to quantum measurement outcomes obtained by measuring a value indefinite observable, as for example, obtained using Theorem 1, we obtain a formal certification of the unpredictability of those outcomes:

Theorem 3 ([5]) *Assume the EPR and Eigenstate principles. If E is an experiment measuring a quantum value indefinite observable, then for every predictor P_E using any extractor ξ, P_E is not correct for ξ.*

Theorem 4 ([5]) *Assume the EPR and Eigenstate principles. In an infinite independent repetition of an experiment E measuring a quantum value indefinite observable which generates an infinite sequence of outcomes $\mathbf{x} = x_1 x_2 \ldots$, no single bit x_i can be predicted with certainty.*

According to Theorems 3 and 4 the outcome of measuring a value indefinite observable is "maximally unpredictable". We can measure the degree of unpredictability using the computational power of the predictor. In particular we can consider weaker or stronger predictors than those used in Theorems 3 and 4 which have the power of a Turing machine [1]. This "relativistic" understanding of unpredictability (fix the reference system and the invariant preserving transformations, is the approach proposed by Einstein's relativity theory) allows us to obtain "maximal unpredictability", but *not absolutely, only relative to a theory*, no more no less. In particular and from this perspective, Theorem 3 should not be interpreted as a statement that quantum measurement outcomes are "true random"[7] in any absolute sense: true randomness—in the sense that no correlations exist between successive measurement results—is mathematically impossible as we will show in Section 5 in a "theory invariant way", that is, for sequences of pure digits, independently of which measurements (classical, quantum, ...) they may have been derived from, if any. Finally, question c) will be discussed in Section 6.2.

4 Biological randomness

Biological randomness is an even more complex issue. Both in phylogenesis and ontogenesis, randomness enhances variability and diversity, hence it is core to biological dynamics. Each cell reproduction yields a (slightly) random distribution of proteomes[8], DNA and membrane changes, both largely due to random effects. In [55], this is described as a fundamental "critical transition", whose sensitivity to minor fluctuations, at transition, contributes to the formation of new coherence structures, within the cell and in its ecosystem. Typically, in a multicellular organism, the reconstruction of the cellular micro-environment, at cell doubling, from collagen to cell-to-cell connection and to the general tensegrity structure of the tissular matrix, all yield a changing coherence which contributes to variability and adaptation, from embryogenesis to ageing. A similar phenomenon may be observed in an animal or plant ecosystem, a system yet to be described by a lesser coherence of the structure of correlations in comparison to the global coherence of an organism.[9]

Similarly, the irregularity in the morphogenesis of organs may be ascribed to randomness at the various levels concerned (cell reproduction and frictions/interactions in a tissue). Still, this is functional, as the irregularities of lung alveolus or of branching in vascular systems enhance ontogenetic adaptation [35]. Thus, we do not call "noise" these intrinsically random aspects of onto-phylogenesis, but consider them as essential components of biological stability, a permanent production of diversity [10]. A population, say, is stable also because it is diverse "by low numbers": 1,000 individuals of an animal species in a valley are more stable if diverse. From

[7] Eagle has argued that a physical process is random if it is "maximally unpredictable" [31].

[8] Some molecular types are present in a few tenth or hundreds molecules. Brownian motion may suffice to split them in slightly but non-irrelevantly different numbers.

[9] An organism is an ecosystem, inhabited, for example, by about 10^{14} bacteria and by an immune system which is, per se, an ecosystem [34]. Yet, an ecosystem is not an organism: it does not have the relative metric stability (distance of the components) nor global regulating organs, such as the neural system in animals.

low numbers in proteome splitting to populations, this contribution of randomness to stability is very different from stability derived from stochasticity in physics, typically in statistical physics, where it depends on huge numbers.

We next discuss a few different manifestations of randomness in biology and stress their positive role. Note that, as for the "nature" of randomness in biology, one must refer at least to both quantum and classical phenomena.

First, there exists massive evidence of the role of quantum random phenomena at the molecular level, with phenotypic effects (see [18] for an introduction). A brand new discipline, quantum biology, studies applications of "non-trivial" quantum features such as superposition, non-locality, entanglement and tunnelling to biological objects and problems [9]. "Tentative" examples include: a) the absorbance of frequency-specific radiation, i.e. photosynthesis and vision, b) the conversion of chemical energy into motion, c) DNA mutation and activation of DNA transposons.

In principle, quantum coherence—a mathematical invariant for the wave function of each part of a system—would *be destroyed almost instantly* in the realm of a cell. Still, evidence of quantum coherence was found in the initial stage of photosynthesis [66]. Then the problem remains on how can quantum coherence last long enough in a poorly controlled environment at ambient temperatures *to be useful in photosynthesis?* The issue is *open*, but it is possible that the organismal context (the cell) amplifies quantum phenomena by intracellular forms of "bio-resonance", a notion defined below.

Moreover, it has been shown that double proton transfer affects spontaneous mutation in RNA duplexes [48]. This suggests that the "indeterminism" in a mutation may also be given by *quantum randomness amplified by classical dynamics* (classical randomness, see Section 6).

Thus, quantum events co-exist with classical dynamics, including classical randomness, a hardly treated combination in physics—they should be understood in conjunction—, for lack of a unified understanding of the respective fields. Finally, both forms of randomness contribute to the interference between levels of organisation, due to regulation and integration, called bio-resonance in [18]. Bio-resonance is part of the stabilisation of organismal and ecosystemic structures, but may also be viewed as a form of proper biological randomness, when enhancing unpredictability. It corresponds to the interaction of different levels of organisation, each possessing its own form of determination. Cell networks in tissues, organs as the result of morphogenetic processes, including intracellular organelles . . . , are each given different forms of statistical or equational descriptions, mostly totally unrelated. However, an organ is made of tissues, and both levels interact during their genesis as well as along their continual regeneration.

Second, as for classical randomness, besides the cell-to-cell interactions within an organism (or among multicellular organisms in an ecosystem) or the various forms of bio-resonance in [17], let us focus on macromolecules' Brownian motion. As a key aspect of this approach we observe here that Brownian motion and related forms of random molecular paths and interactions must be given a fundamental and positive role in biology. This random activity corresponds to the thermic level in a cell, thus to a relevant component of the available energy: it turns out to be crucial for gene expression.

The functional role of stochastic effects was known since long in enzyme induction [65], and even theorised for gene expression [46]. In the last decade [33], stochastic gene expression finally came to the limelight. The existing analyses are largely based on classical Brownian motion [7], while local quantum effects cannot be excluded.

> Increasingly, researchers have found that even genetically identical individuals can be very different and that some of the most striking sources of this variability are random fluctuations in the expression of individual genes. Fundamentally, this is because the expression of a gene involves the discrete and inherently random bio-chemical reactions involved in the production of mRNAs and proteins. The fact that DNA (and hence the genes encoded therein) is present in very low numbers means that these fluctuations do not just average away but can instead lead to easily detectable differences between otherwise identical cells; in other words, gene expression must be thought of as a stochastic process. [7]

Different degrees of stochasticity in gene expression have been observed—with major differences in ranges of expression—in the same population (in the same organ or even tissue) [24].

A major consequence that we can derive from this views is the key role we can attribute to this relevant component of the available energy, *heath.* The cell uses it also for gene expression instead of opposing to it. As a matter of fact, the view of DNA as a set of "instructions" (a program) proposes an understanding of the cascades from DNA to RNA to proteins in terms of a deterministic and predictable, thus programmable, sequence of stereospecific interactions (physico-chemical and geometric exact correspondences). That is, gene expression or genetic "information" is physically transmitted by these exact correspondences: stereospecificity is actually "necessary" for this [62]. The random movement of macromolecules is an obstacle that the "program" constantly fights. Indeed, both Shannon's transmission and Turing's elaboration of information, in spite of their theoretical differences, are both designed to oppose noise, see [54]. Instead, in stochastic gene expression, Brownian motion, thus heath, is viewed as a positive contribution to the role of DNA.

Clearly, randomness, in a cell, an organism, an ecosystem, is highly constrained. The compartmentalisation in a cell, the membrane, the tissue tensegrity structure, the integration and regulation by and within an organism, all contribute to restrict and canalise randomness. Consider that an organism like ours has about 10^{13} cells, divided in many smaller parts, including nuclei: few physical structures are so compartmentalised. So the very "sticky" oscillating and randomly moving macromolecules are forced within viable channels. Sometimes, though, it may not work or it may work differently and this belongs to the exploration proper to biological dynamics: a "hopeful monster" [29], if viable in a changing ecosystem, may yield a new possibility in ontogenesis or even a new branch in evolution.

Activation of gene transcription, in these quasi-chaotic environments, with quasi-turbulent enthalpic oscillations of macro-molecules, is thus canalised by the cell structure, in particular in eukaryotic cells, and by the more or less restricted assembly of the protein complexes that initiates it [47]. In short, proteins can interact with multiple partners (they are "sticky") causing a great number of combinatorial possibilities. Yet, protein networks have a central hub where the connection density is the strongest and this peculiar "canalisation" further forces statistical regularities [13]. The various forms of canalisation mentioned in the literature include some resulting from environmental constraints, which are increasingly acknowledged to produce "downwards" or Lamarckian inheritance or adaptation, mostly by a regulation of gene expression [69]. Even mutations may be both random and not random, that is highly constrained or even induced by the environment. For example, organismal activities, from tissular stresses to proteomic changes, can alter genomic sequences in response to environmental perturbations [71].

By this role of constrained stochasticity in gene expression, molecular randomness in cells becomes a key source of cell's activity. As we hinted above, Brownian motion, in particular, must be viewed as a positive component of cell's dynamics [63], instead of being considered as "noise" that opposes the elaboration of the genetic "program" or the transmission of genetic "information" by exact stereospecific macro-molecular interactions. Thus, this view radically departs from the understanding of the cell as a "Cartesian Mechanism" occasionally disturbed by noise [62], as we give heath a constitutive, not a "disturbing" role (also for gene expression and not only for some molecular/enzymatic reactions).

The role of stochasticity in gene expression is increasingly accepted in genetics [76] and may be more generally summarised, by saying that "macromolecular interactions, in a cell, are largely stochastic, they must be given in probabilities and the values of these probabilities depend on the context" [57]. The DNA then becomes an (immensely important) physicochemical trace of a history, continually used by the cell and the organism. Its organisation is stochastically used, but in a very canalised way, depending on the epigenetic context, to produce proteins and, at the organismal level, biological organisation from a given cell. Random phenomena, Brownian random paths first, crucially contribute to this.

A third issue is worth being briefly mentioned. Following [42], we recall how the increasing phenotypic complexity along evolution (organisms become more "complex", if this notion is soundly defined) may be justified as a random complexification of the early bacteria along an asymmetric diffusion. The key point is to invent the right phase space for this analysis, as we hint next: the tridimensional space of "biomass $\times$ complexity $\times$ time" [56].

Note first that the available energy consumption and transformation, thus entropy production, are the unavoidable physical processes underlying all biological activities, including reproduction with variation and motility, organisms "default state" [59]. Now, entropy production goes with energy dispersal, which is realised by random paths, as any diffusion in physics.

At the origin of life, bacterial exponential proliferation was (relatively) unconstrained, as other forms of life did not contrast it. Increasing diversity, even in bacteria, by random differentiation, started the early divergence of life, a process never to stop—and a principle for Darwin. However, it also produced competition within a limited ecosystem and a slow down of the exponential growth.

Gould [41, 42] uses the idea of random diversification to understand a blatant but too often denied fact: life becomes increasingly "complex", if one accords a reasonable meaning to this notion. The increasing complexity of biological structures, whatever this may mean, has been often denied in order to oppose finalist and anthropocentric perspectives, where life is described as *aiming* at *Homo sapiens*, in particular at the reader of this paper, the highest result of the (possibly intelligent) evolutionary path (or design).

It is a fact that, under many reasonable measures, an eukaryotic cell is more complex than a bacterium; a metazoan, with its differentiated cells, tissues and organs, is more complex than a cell ... and that, by counting neurones and their connections, cell networks in mammals are more complex that in early triploblast (which have three tissues layers) and these have more complex networks of all sorts than diplobasts (like jellyfish, a very ancient life form). This non-linear increase can be quantified by counting tissue differentiations, networks and more, as very informally suggested by Gould and more precisely quantified in [8] (see also [56] for a survey). The point is: how are we to understand this change towards complexity without invoking global aims?

Gould provides a remarkable, but very informal answer to this question. He bases it on the analysis of the *asymmetric* random diffusion of life, as constrained proliferation and diversification. Asymmetric because, by a common assumption, life cannot be less complex than bacterial life.[10] We may understand Gould's analysis by a general principle: *Any asymmetric random diffusion propagates, by local interactions, the original symmetry breaking along the diffusion.*

The point is to propose a pertinent (phase) space for this diffusive phenomenon. For example, in a liquid, a drop of dye against a (left) wall, diffuses in space (towards the right) by local bumps of the particles against each other. That is, particles transitively inherit the original (left) wall asymmetry and propagate it *globally* by *local* random interactions. By considering the diffusion of *biomass*, after the early formation (and explosion) of life, over *complexity*, one can then apply the principle above to this fundamental evolutionary dynamics: biomass asymmetrically diffuses over complexity in time. Then, there is no need for a global design or aim: the random paths that compose *any* diffusion, also in this case help to understand a random growth of complexity, *on average*. On average, as there may be local inversion in complexity; still, the asymmetry randomly forces to "higher complexity", a notion to be defined formally, of course,

In [8] and more informally in [56], a close definition of phenotypic complexity was given, by counting fractal dimensions, networks, tissue differentiations ..., and a mathematical analysis of this phenomenon is developed. In short, in the suitable phase space, that is "biomass × complexity × time", one can give a diffusion equation with real coefficients, inspired by Schrödinger's equation (which is a diffusion equation, but in a Hilbert space). In a sense, while Schrödinger's equation is a diffusion of a law (an amplitude) of probability, the potential of variability of biomass over complexity in time was analysed when the biological or phenotypic complexity is quantified, in a tentative but precise way, as hinted above (and better specified in the references).

Note that the idea that complexity (however defined) of living organisms increases with time has been more recently adopted in [70] as a principle. It is thus *assumed* that there is a trend towards complexification and that this is intrinsic to evolution, while Darwin only assumed divergence of characters. The very strong "principle" in [70], instead, may be *derived*, if one gives to randomness, along an asymmetric diffusion, a due role also in evolution.

A further, but indirect fall-out of this approach to phenotypic complexity results from some recent collaboration with biologists of cancer, see [59]. One must first distinguish the notion of complexity above, based on "counting" some key anatomical features, from biological organisation. The first is given by an "anatomy" of the dead animal, the second usually refers to the functional activities of a living organism. It seems that cancer is the only disease that diminishes functional organisation by increasing complexity. When a tissue is affected by cancer, then ducts in glands, villi in epithelia ... increase in topological numbers (e.g. ducts have more lumina) and fractal dimensions (as for villi). This very growth of mathematical complexity reduces the functionality, by reduced flow rates, thus the biological organisation. This is probably a minor remark, but in the still very obscure aetiology of cancer, it may provide a hallmark for this devastating disease.

5 Random sequences: a theory invariant approach

Sequences are the simplest mathematical infinite objects. We use them to discuss some subtle differences in the quality of randomness. In evaluating the quality of randomness of the following four examples we employ various tests of randomness for sequences, i.e. formal tests modelling properties or symptoms intuitively associated with randomness.

The *Champernowne sequence* $012345678910111213,\cdots$ is random with respect to the statistical test which checks equal frequency—a clearly necessary condition of randomness.[11] Indeed, the digits $0, 1, 2, \cdots 9$ appear with the right frequency 10^{-1}, every string of two digits, like 23 or 00, appears with the frequency 10^{-2},

[10] Some may prefer to consider viruses as the least form of life. The issue is controversial, but it would not change at all Gould's and our perspective: we only need a minimum biological complexity which differs from inert matter.

[11] This was Borel's definition of randomness [12].

and, by a classical result of Champernowne [23], every string—say 36664788859999100200030405060234234 or 00000000000000000000000000000000000—appears with the frequency $10^{-(\text{length of the string})}$ (10^{-35} in our examples). Is the condition sufficient to declare the Champernowne sequence random? Of course, not. The Champernowne sequence is generated by a very simple algorithm—just concatenate all strings on the alphabet $\{0, 1, 2, 3, \cdots, 9\}$ in increasing length order and use the lexicographical order for all strings of the same length. This algorithm allows for a prefect prediction of every element of this sequence, ruling out its randomness. A similar situation appears if we concatenate the prime numbers in base 10 obtaining the *Copeland-Erdös sequence* $235711131719232931374143\cdots$ [26].

Consider now your favourite programming language L and note that each syntactically correct program has an end-marker (end or stop, for example) which makes correct programs self-delimited. We now define the binary *halting sequence* $H(L) = h_1 h_2 \cdots h_n \cdots$ in the following way: enumerate all strings over the alphabet used by L in the same way as we did for the Champernowne sequence and define $h_i = 1$ if the ith string considered as a program stops and $h_i = 0$ otherwise. Most strings are not syntactical correct programs, so they will not halt: only some syntactically correct program halt. Church-Turing theorem—on the undecidability of the halting problem [25]—states that there is no algorithm which can calculate (predict) correctly all the bits of the sequence $H(L)$; so from the point of view of this randomness test, the sequence is random. Does $H(L)$ pass the frequency test? The answer is negative.

The Champernowne sequence and the halting sequence are both non-random, because each fails to pass a randomness test. However, each sequence passes a non-trivial random test. The test passed by the Champernowne sequence is "statistical", more quantitative; the test passed by the halting sequence is more qualitative. Which sequence is "more random"?

Using the same programming language L we can define the *Omega sequence* as the binary expansion $\Omega(L) = \omega_1 \omega_2 \cdots \omega_n \cdots$ of the Omega number, the halting probability of L:

$$\sum_{p \text{ halts}} 2^{-(\text{length of } p)}.$$

It has been proved that the Omega sequence passes both the frequency and the incomputability tests, hence it is "more random" than the Champernowne, Copeland-Erdös and halting sequences [19,30]. In fact, the Omega sequence passes an infinity of distinct tests of randomness called Martin-Löf tests—technically making it Martin-Löf random [19,30], one of the most robust and interesting forms of randomness.

Did we finally find the "true" definition of randomness? The answer is negative. A simple way to see it is via the following infinite set of computable correlations present in almost all sequences, including the Omega sequence [21], but not in all sequences: that is, for almost all infinite sequences, there exists an integer $k > 1$ (depending on the sequence) such that for every $m \geq 1$:

$$\omega_{m+1}\omega_{m+2}\cdots\omega_{mk} \neq \underbrace{000\cdots0}_{m(k-1)\text{times}} .$$

In other words, every substring $\omega_{m+1}\omega_{m+2}\cdots\omega_{mk}$ has to contain at least one 1, for all $m \geq 1$, a "non-randomness" phenomenon no Martin-Löf test can detect. A more general result appears in [21], Theorem 2.2.

So, *the quest for a better definition continues!* What about considering not just an incremental improvement over the previous definition, but a definition of "true randomness" or "perfect randomness"? If we confine to just one intuitive meaning of randomness—*the lack of correlations*—the question becomes: *Are there binary infinite sequences with* no *correlations? The answer is negative*, so our quest is doomed to fail: *there is no true randomness*. One can prove this statement using Ramsey theory.[12] see [43,72] or algorithmic information theory [19]

Here is an illustration of the Ramsey-type argument. Let $s_1 \cdots s_n$ be a binary string. A monochromatic arithmetic progression of length k is a substring $s_i s_{i+t} s_{i+2t} \cdots s_{i+(k-1)t}, 1 \leq i$ and $i + (k-1)t \leq n$ with all characters equal (0 or 1) for some $t > 0$. The string 01100110 contains no arithmetic progression of length 3 because the positions 1, 4, 5, 8 (for 0) and 2, 3, 6, 7 (for 1) do not contain an arithmetic progression of length 3; however, both strings 011001100, and 011001101 do: 1, 5, 9 for 0 and 3, 6, 9 for 1.

Theorem 5 (Van der Waerden) *Every infinite binary sequence contains arbitrarily long monochromatic arithmetic progressions.*

[12] The British mathematician and logician Frank P. Ramsey studied *conditions under which order must appear*.

This is one of the many results in Ramsey theory [72]: it shows that in *any sequence* there are arbitrary long simple correlations. We note the power of this type of result: the property stated is true for *any sequence* (in contrast with typical results in probability theory where the property is true for *almost all sequences*). Graham and Spencer, well-known experts in this field, subtitled their *Scientific American* presentation of Ramsey Theory [43] with the following sentence:

> Complete disorder is an impossibility. Every large[13] set of numbers, points or objects necessarily contains a highly regular pattern.

Even if "true randomness" doesn't exist, can our intuition on randomness be cast in more rigorous terms? Randomness plays an essential role in probability theory, the mathematical calculus of random events. Kolmogorov axiomatic probability theory assigns probabilities to sets of outcomes and shows how to calculate with such probabilities; it assumes randomness, but does not distinguish between individually random and non-random elements. So, we are led to ask whether it is possible to study classes of random sequences having precise "randomness/symptoms" of randomness? So far we have discussed two symptoms of randomness: statistical frequency and incomputability. More general symptoms are unpredictability (of which incomputability is a necessary but not sufficient form), incompressibility and typicality.

Algorithmic information theory (AIT) [19,30], developed in the 1960s, provides a close analysis of randomness for sequences of numbers, either given by an abstract or a concrete (machine) computation, or produced by a series of physical measurements. By this, it provides a unique tool for a comparative analysis between different forms of randomness. AIT shows also that there is no infinite sequence passing all tests of randomness, so another proof that "true randomness" does not exist.

As we can guess from the discussion of the four sequences above, randomness can be refuted, but cannot be mathematically proved: one can never be sure that a sequence is "random", there are only forms and degrees of randomness [19,30].

Note finally that, similarly to randomness in classical dynamics, which was made intelligible by Poincaré's negative result, AIT is also rooted in a negative result: Gödel's incompleteness theorem. As recalled above, a random sequence is a highly incomputable sequence. That is, algorithmic randomness is in a certain sense a refinement of Gödel's undecidability, as it gives a fine hierarchy of incomputable sets that may be related, as we will hint below, to relevant forms of randomness in natural sciences.

6 Classical and quantum randomness revisited

6.1 Classical vs. algorithmic randomness

As we recalled in Section 2, classical dynamical systems propose a form of randomness as unpredictability relatively to a specific mathematical model *and* to the properties of measurement. Along these lines, [51] recently gave an evaluation of the unpredictability of the position (and momentum) of planets in the Solar system, a system that motivated all the classical work since Newton and Laplace (their dynamics are unpredictable at relatively short astronomical time). How can one relate this form of deterministic unpredictability to algorithmic randomness, which is a form of pure mathematical incomputability? The first requires an interface between mathematical determination, by equations or evolution functions, and "physical reality" as accessed by measurement. The latter is a formal, asymptotic notion.

A mathematical relation may be established by considering Birkhoff ergodicity. This is a pure mathematical notion as it does not (explicitly) involve physical measurement, yet it applies to the non-linear systems where one may refer to Poincaré's analysis or its variants, that is to weaker forms of chaos based on positive Lyapunov exponents (see footnote [2]) or sensitivity to initial conditions and "mixing" (see paragraph below). Birkhoff's notion is derived from his famous theorem and it roughly says that a trajectory, starting from a given point and with respect to a given observable quantity, is random when the value of a given observable over time coincides asymptotically with its value over space.[14]

A survey of recent results that relate deterministic randomness—under the form of Birkhoff randomness for dynamical systems—to algorithmic randomness is presented in [52]. This was mostly based on the relation between dynamical randomness and a weak form of Martin-Löf algorithmic randomness (due to Schnorr) [38,

[13] The adjective "large" has precise definitions for both finite and infinite sets.

[14] Consider a gas particle and its momentum: the average value of the momentum over time (the time integral) is asymptotically assumed to coincide with the average momenta of all particles in the given, sufficiently large, volume (the space integral).

39]. A subtle difference may be proved, by observing that some "typically" Birkhoff random points are not Martin-Löf random, some are even "pseudo-random", in the sense that they are actually computable. By restricting, in a physically sound way, the class of dynamical systems examined, a correspondence between points that satisfy Birkhoff ergodic theorem and Martin-Löf randomness has been obtained in [36]. These results require an "effectivisation" of the spaces and dynamical theory, a non-obvious work, proper to all meaningful dynamical systems, as the language in which we talk about them is "effective": we formally write equations, solve them, when possible, and compute values, all by suitable algorithms. All these results are asymptotic as they transfer the issue of the relation between theory and physical measurement to the limit behaviour of a trajectory as determined by the theory: a deterministic system with sensitive to initial (or border) conditions, a mathematical notion, produces random infinite paths. To obtain these results it is enough to assume weak forms of deterministic chaos, such as the presence of dense trajectories, i.e. topological transitivity or mixing. The level of their sensitivity is reflected in the level of randomness of the trajectories, in the words of [36]:

> Algorithmic randomness gives a precise way of characterising how sensitive the ergodic theorem is to small changes in the underlying function.

6.2 Quantum vs. algorithmic randomness

We already summarised some of the connections between quantum and algorithmic unpredictability. The issue is increasingly at the limelight since there is a high demand of "random generators" in computing. Computers generate "random numbers" produced by algorithms and computer manufacturers needed a long time to realise that randomness produced by software is only pseudo-random, that is, the generated sequences are perfectly computable though with no apparent regularity.

This form of randomness mimics well the human perception of randomness, but its quality is rather low because computability destroys many symptoms of randomness, e.g. unpredictability.[15] One of the reasons is that pseudo-random generators "silently fail over time, introducing biasses that corrupt randomness" [6, p. 15].

Although no computer or software manufacturer claims today that their products can generate truly random numbers, these mathematically unfounded claims have re-appeared for randomness produced with physical experiments. They appear in papers published in prestigious journals, like Deutsch's famous paper [28] (which describes two quantum random generators (3.1) and (3.2) which produce "true randomness") or *Nature* 2010 editorial (titled *True randomness demonstrated* [67]). Companies commercialise "true random bits" which are produced by a "True Random Number Generator Exploiting Quantum Physics" (ID Quantique) or a "True Random Number Generator" (MAGIQ). "True randomness" does not come necessarily from the quantum. For example, "RANDOM.ORG offers true random numbers to anyone on the Internet" (Random.Org) using the atmospheric noise.

Evaluating the quality of quantum randomness can now be done in a more precise framework. In particular we can answer the question: is a sequence produced by repeated outcomes of measurements of a value indefinite observable computable? The answer is negative, in a strong sense [22],[2]:

Theorem 6 *The sequence obtained by repeating indefinitely the measurement of a value indefinite observable under the conditions of Theorem 1 produces a bi-immune sequence (a strong form of incomputable sequence for which any algorithm can compute only finitely many exact bits).*

Incomputability appears *maximally* in two forms: *individualised*—no single bit can be predicted with certainty (Theorem 4), i.e. an algorithmic computation of a single bit, even if correct, cannot be formally certified; and *asymptotic* via Theorem 6—only finitely many bits can be correctly predicted via an algorithmic computation. *It is an open question whether a sequence as in Theorem 6 is Martin-Löf random or Schnorr random* [19,30].

7 Conclusion and opening: towards a proper biological randomness

The relevance of randomness in mathematics and in natural sciences further vindicates Poincaré's views against Hilbert's. The first stressed since 1890 the interest of negative results, such as his Three Body Theorem, and further claimed in *Science et Méthode* (1908) that

[15] It is not unreasonable to hypothesise that pseudo-randomness rather reflects its creators' subjective "understanding" and "projection" of randomness. Psychologists have known for a long time that people tend to distrust streaks in a series of random bits, hence they imagine a coin flipping sequence alternates between heads and tails much too often for its own sake of "randomness." As we said, the gambler's fallacy is an example.

> ... unsolvable problems have become the most interesting and raised further problems to which we could not think before.

This is in sharp contrast with Hilbert's credo—motivated by his 1900 conjecture on the formal provability (decidability) of consistency of arithmetic—presented in his address to the 1930 Königsberg Conference:[16] [44]

> For the mathematician, there is no unsolvable problem. In contrast to the foolish Ignorabimus, our credo is: We must know, We shall know.

As a matter of fact, the investigation of theoretical ignorabimus, e.g. the analysis of randomness, opened the way to a new type of knowledge, which does not need to give yes or no answers, but raises new questions and proposes new perspectives and, possibly, answers—based on the role of randomness, for example. Hilbert was certainly aware of Poincaré's unpredictability, but (or thus?) he limited his conjectures of completeness and decidability to formal systems, i.e. to *pure mathematical statements*. Poincaré's result instead, as recalled above, makes sense at the interface of mathematics and the physical world. The results mentioned in Section 6.1 turn, by using Birkhoff randomness in dynamical systems, physico-mathematical unpredictability into a pure mathematical form: they give relevant relations between the two frames, by embedding the *formal theory* of some physical dynamics into a computational frame, in order to analyse unpredictability with respect to that theory.

As for biology, the analysis of randomness at all levels of biological organisation, from molecular activities to organismal interactions, clearly plays an increasing role in contemporary work. Still, we are far from a sound unified frame. First, because of the lack of unity even in the fragments of advanced physical analysis in molecular biology (typically, the superposition of classical and quantum randomness in a cell), to which one should add the hydrodynamical effect and the so called "coherence" of water in cells pioneered by del Giudice [40].

Second, biology has to face another fundamental problem. If one assumes a Darwinian perspective and considers phenotypes and organisms as proper biological observables, then *the evolutionary dynamics implies a change of the very space of (parameters and) observables*. That is, a phylogenetic analysis cannot be based on the a priori physical knowledge, the so called condition of possibility for physico-mathematical theories: space-time and the pertinent observable, i.e. the phase space. In other words, a phylogenetic path cannot be analysed in a pre-given phase space, like in all physical theories, including quantum mechanics, where self-adjoint operators in a Hilbert space describe observables. Evolution, by the complex blend of organisms and their ecosystem, co-constitutes its own phase space and this in a (highly) unpredictable way. Thus, random events, in biology, do not just "modify" the numerical values of an observable in a pre-given phase space, like in physics: they modify the very biological observables, the phenotypes, as is more closely argued in [56]. If we are right, this poses a major challenge. In the analysis of evolutionary dynamics, randomness may be not measurable by probabilities [58, 55]. This departs from the many centuries of discussion on chance only expressed by probabilities.

If the reader were observing Burgess fauna, some 520 million years ago [41], she would not be able to attribute probabilities to the changes of survival of Anomalocaris or Hallucigenia or to one of the little chordates nor their probabilities to become a squid, a bivalve or a kangaroo. To the challenges of synchronic measurement, proper to physical state determined systems, such as the ones we examined above, one has to add the even harder approximation of diachronic measurement, in view of the relevance of history in the determination of biological state of affairs [53].

Note that in Section 4 we could have made a synthetic prediction: phenotypic complexity increases along evolution by a random, but asymmetric, diffusion. This conclusion would have been based on a global evaluation, a sum of all the numbers we associated to biological forms (fractal dimensions, networks' numbers, tissue folding ... all summed up). In no way, though, one could "project" this global value into specific phenotypes. There is no way to know if the increasing complexity could be due to the transformation of the lungs of early tetrapods into a swim bladder and gills (branchia) or of their "twin-jointed jaw" into the mammalian auditory ossicles [60].

Can AIT be of any help to meet this challenge? From a highly epistemic perspective, one may say that the phenotypes cannot be described before they appear. Thus, they form an incompressible list of described/describable phenotypes, at each moment of the evolutionary process .... It seems hard to turn such a contingent/linguistic statement into an objective scientific analysis.

In contrast to AIT, in which randomness is developed for infinite sequences of numbers, in a measurement-independent way, any study of randomness in a specific context, physical or biological, for example, depends on the *intended theory* which includes its *main assumptions* (see, for example, Section 3 for the "principles" used in the analysis of quantum randomness and for the theory-and-measurement-dependent notion of predictor).

[16] Incidentally, the conference where Gödel presented his famous incompleteness theorem.

As a consequence, our focus on unpredictability and randomness in natural sciences, where access to knowledge crucially requires physical or biological measurement, cannot and should not be interpreted as an argument that "the world is random" and even less that it is "computable"—we, historical and linguistic humans, effectively write our *theories* and compute in order to predict from them (see [20] for a discussion of the hypothesis of lawless of the (physical) Universe).

We used (strong forms of) relative unpredictability as a tool to compare different forms of determination and stability in natural sciences, sometimes by a conceptual or mathematical duality (showing the "relevance of negative results"), other times by stressing the role of randomness in the robustness or resilience of phenomena. The ways we acquire knowledge may be enlightened by this approach, also in view of the role of symmetries and invariance in mathematical modelling and of the strong connections between spontaneous symmetry breaking and random events discussed in [57].

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