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An epistemological and bio-physical point of view on complex systems

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Abstract

In this article, after a historical introduction, we give an epistemological point of view of the physics of complex systems. Complex systems are epistemologically interesting because of the fundamental interaction experiment/observer and physicists in their everyday life can experience the paradoxes given by this interaction. Here we describe some of these paradoxes, we make a parallel with quantum mechanics and give a possible philosophical solution, based on notorious physicists/philosopher from the past, transposing and reinterpreting their ideas to modern times. In particular, we analyse the interaction with a complex system such as the living cell, and therefore we also analyse some biophysical implications of complexity.

Keywords: complex systems; epistemology; emergency; experiment/observer interaction.†

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1. Introduction

Here, we are interested in an epistemological view of complex systems, giving insights about some typical problems often faced by researchers in this domain. In particular, the complex system we will focus on is the cell, with its structure, its motility, its cytoskeleton, its ability to reproduce, in one word living. It is impossible to imagine to deal with such a complex system with tools coming from a unique discipline, necessitating, among others, even an epistemological approach.

In this context I think it is important to ask ourselves what we are really doing and what we are looking for, in a general, I would say systemic, way. To tackle these questions, we need to keep some distance from the particular work or the particular experiment, and enter in a deeper, kind of philosophical, thought. I believe that this process is important for every physicist, even every scientist, and probably everyone has his own answers, because a «true» answer is maybe impossible to achieve. Today the high specialisation of science makes it more difficult to take this distance, but to understand complex systems this is necessary. Indeed, in order to find out the exchange of information taking place in a living organism, within itself and with the environment, and the different behaviours at different scales, we need a *global* point of observation. Here I deal with these problems from a complex systems point of view, giving my personal vision.

2. Complex systems: an epistemology point of view

First, let us introduce and discuss the definition of complex systems, which is already not an easy task. Historically, we could say that the first appearance of complexity is with the deterministic chaos from Jules Henri Poincaré at the end of the 19th century [1]. First with the attempt to find a solution of the three-body problem, Poincaré showed that a completely deterministic system can lead to chaotic behaviour, for example via period doubling. The complexity is in the fact that despite the deterministic origin of the system, its behaviour cannot be forecast because of nonlinear terms in the ordinary differential equations of Newtonian mechanics. Epistemologically, this raised fundamental questions, because knowing the mathematical formulation of the problem (Newton equations) does not guarantee its prediction, since the system can yield chaotic behaviour. It was therefore evidence that the scientist dealing with these systems can only do a classification, a phase portrait of the disorder, of the chaotic behaviour [2]. Later on, Edward N. Lorenz [3], in the context of meteorology and weather forecasts elaborated on the dependence of a dynamical system with non-linearities on the initial condition, giving rise to the famous butterfly effect.

In a century we observed the transition from the simple and well calculable universe of Galileo, Newton and Laplace, to a universe of unexpected unpredictable paths.

If Poincaré introduced the first ideas of complexity in Mathematics, giving origin to the field of dynamical systems, in physics, almost contemporary, complexity appeared at the beginning in the context of neural network modelling, with William James [4] and then later, with more mathematical rigour, with the works of Warren S. McCulloch and Walter H. Pitts [5]. But even though these ideas of complexity were already present since many years in an unstructured way, only in the lasts 20-30 years they were accepted in the physics community as a science (the first research institute of complex systems, the Santa Fe Institute, was founded in 1984), giving rise to the physics of complex systems. A complete historical description of complex systems is not our purpose here, let us only cite an example of complex system that will be useful to introduce the main characteristics of complexity: the Ising model [6]. With this example in mind let us move to the definition of complex systems, or, maybe better, to some possible definitions.

In general, we refer to complex systems as systems in which interactions between the objects composing the system, and/or between the system and its environment, are important and give origin to collective behaviour. Complex systems are not necessarily *complicated*: a normal every day pendulum can be considered as a complex system just taking into account the interactions between the pendulum and the environment (friction and an external applied torque), or in interaction with other pendula. Its complexity is given by the fact that varying the control parameter, in this case for example the applied torque, can lead to complex behaviours like period doubling and chaotic oscillations, which are not predictable, in the sense that we cannot have a trajectory of the pendulum indicating the precise position at a given time. This is a complex behaviour that goes out from standard classical mechanics physical tools and therefore needs more adapted statistical and physical instruments to be studied.

At first sight, this can be a good definition, but could lead to the wrong conclusion that since all the objects are connected with all the other objects of the system, and even with the observer, these complex interactions may lead to an impossibility of a complete knowledge (of the type for instance of a phase portrait, being a forecast not possible) of the system behaviour. The essential fact here, as we will see better later, is that the scientist is himself an *active* part of the system, which builds representations, models, interpretations, and not only a passive observer. As expressed by Ignazio Licata [7], the theoretical description, built on our choices, is necessary to give a meaning to vague observations.

This makes the definition of complex systems complicated, therefore it is better to discuss some key properties of them. The most important property, that we did not exploit yet, is *emergence*: complex systems are systems in which interactions between a multitude of objects and/or with the environment lead to emergent collective properties which are not directly explainable by the properties characteristic of each element. The phase transition undergoing in the Ising model, for example, is a collective effect not explainable only with individual spins properties. Life itself is an emergent property, try to mix together 70 kg of hydrogen, oxygen and carbon, shake well, and you will see it start running around and writing PhD theses.

Let us describe better what emergence is. The first appearance of the idea in the physics world was with Philipp Anderson with his famous *More is Different* [8], stating that the formalisms and the concepts needed to understand physical (and in general scientific) phenomena at a given scale are not always linked to the ones at lower scales, and not from them achievable. This was against the dominant reductionist idea (for which everything can be explained starting from a basic, low scale, law) predominating at that time, and even probably nowadays. Besides, he noted a general lower, and in any case different, degree of symmetry while looking at the system at a larger scale. Therefore, the laws of microscopic physics cannot always explain new phenomena emerging at larger scales, for which an adapted theory capturing the essence of the phenomena has to be created. The laws of objects composed by a large number of individuals, in particular living systems, cannot be deduced uniquely from the laws of particle physics, as the reductionist approach would predict. Notably, the lower degree of symmetry observed while increasing the complexity of a system, allows us to say that life can be seen as a breaking of symmetry effect. There are many examples of this, sugar molecules produced by living systems have all a **R** (for right) configuration, while in principle **R** and **S** (*sinister*, latin for left) configurations have the same energy and should be present in the same amount. The same happens for many chiral molecules and cells, like sperm cells, for which chirality is essential for life and which can move in their environment only thank to this symmetry breaking, otherwise the *scallop theorem* would not allow them to move at low Reynolds numbers (*i.e.* at normal life conditions) [9]. In one sentence, emergence is a continuous novelty production in an essentially unpredictable way.

These ideas of emergence were already present at a philosophical level with the idea of *new categories*, ontological entities with a hierarchical organisation needed to describe interactions with different *strata* at least since the late 19th/early 20th century with Nicolai Hartman [10], or also John S. Mill or Charlie D. Broad, but only in the last 20-30 years were accepted in the physics community (more or less at the same time as the definition of physics of complex systems as a science).

Another key feature of complexity is the definition of the border between system and environment. Here the active choice of the scientist comes into play:

to build a model on an aspect of nature we make some assumptions on this border, on the interactions between the system and the environment. These changeable assumptions are the most important active part contribution of the scientist. The definition of them leads to different emergent properties and the modelling of distinct aspects of the system. In the *Middle Way*, citing the Nobel prize Robert Laughlin, standing between the physics of particles and the cosmological theories, there is the realm of incertitude, of randomness, where nature expresses a game of probability resulting from the competition between freedom and constraints. This does not mean at all that we cannot do science, but in contrast to a classical Newtonian universe, where the observer records events resulting from predefined universal laws, allowing in principle for a full prediction of the system, here the active observer has to look for a global comprehension. He has to do a global picture of the possibilities, without being able to predict which one will be realized. For example, the process of protein folding can happen in a myriad of different fashions with exactly the same energy level and the one finally chosen cannot be predicted. In the same way in an Ising system we cannot predict the exact state of the system at a given time, we cannot say which orientation spin i will have at time t, but only say that at some critical temperature a collective behaviour will arise.

In this realm, reductionist approach cannot explain this diversity, nor these emergent properties, but this is not because there is something wrong in it, simply, in these situations, it does not work. The scientist creates a variety of models, not necessarily all convergent in a unique vision, to describe different levels and different behaviours of the systems. Finally, a complex system is a system which is unpredictable, and not reducible to a single formal model, to a single *theory of everything*.

Now it should be clearer what a complex system is and the issues of a scientist studying it. Let us then focus further on the epistemological side of these issues. A direct and common answer to the epistemological problems settled at the beginning, would be a circular vision between experiment and theory, a kind of experimentalism of Galilean memory: *sensate esperienze e necessarie dimostrazioni* (sensible experiences and necessary demonstrations), in which the experimental evidence builds the theory, the theory generalises the results, inducing new experiments to verify its consistency. In some cases, it is sufficient to stop here, and «keep calculating». But after a deeper epistemological analysis, of relevance in particular for complexity given what we said about the observed/observer interactions, this vision would have at least two problems. First, what would be the starting point of the circle? Theory or experiments? We are tempted to say experiments, since physics is an experimental science, but then there would be another question, can an experiment exist without a theory? The answer is: not really. This leads us directly to the second problem of this circular vision. Is the experiment true independently of the framework in which it is operating, therefore independent of the theory or of the tradition (the social structure)? A theory is an (unstable) equilibrium state between the experiment and the observer, but is not unique and never complete. As we said, in complex systems science we select an aspect of our observation and we model this aspect under a certain hypothesis, a theory of all is here not even conceivable, essentially because of emergency. Therefore, maybe a more adapted point of view is the one of Pierre Duhem, who was coincidentally a professor here in Bordeaux. His holistic vision states that experiments and theories are connected to conventional principle which can change during time [11]. The connection to the active observer needed for complex systems is evident, and also the idea that natural phenomena are not pre-existing facts ruled by a unique formula that once discovered will predict everything. A theory and an experiment can be true in a certain set-up, at a certain scale, but could not work at others. So, there is no such thing as a *crucial experiment* allowing us to discern a good from a bad theory. The experiment itself is defined within a set-up, under some hypothesis, ultimately by our cognitive structure.

In this regard you may have thought about the observation of a quantum system, as one of the most evident interaction observed/observer. Therefore, it is very interesting to discuss briefly the idea presented in the nice book edited by Licata and Ammar Sakaji *Physics Of Emergence and Organization* (2008) (in which I cite the articles by Eliano Pessa and by Ignazio Licata [12]) of a systemic science based on quantum or quantum field theories applications to phase transition in biological matter, supported by the indissoluble connection between emergent properties and the observer, the scientist himself. Indeed, this connection observer/observed can be thought to have a link with quantum mechanical properties, in which an observation causes the irreversible collapse of the wave function. However, as pointed out by Pessa himself, the success of this quantum biological theory is still very partial, mostly because while the particles in quantum theories are all considered as identical (if, of course they have same charge, mass, etc ...) the variability of living beings is in striking contrast with that. Moreover, many complex processes studied from a statistical point of view (like the Moran model for evolution genetics [13] or processes on networks [14]) do not have an evident correspondent Hamiltonian from which one could start a quantum approach, and even if we could build one approximated, we would need an out of equilibrium generalisation of the quantum theories. Also, many biological concepts, like, with the example of evolution models, the fitness, and the environmental effects are, if not impossible, very difficult to be tackled with a quantum field formalism.

The richness of complex systems is given by the fact that they are not linked to a particular physical model, which would be confined in a particular domain of science, like for example gravitation or other physical theories, it is rather a result of physical and mathematical research as a whole. This is related to the fact that complex systems deal mostly with the mesoscopic realm, a realm where physics meets many other disciplines and macroscopic and microscopic descriptions melt together. As a matter of fact, the range of applications of the physics of complex systems is very large. Thinking for example of the theory of deterministic chaos and nonlinear theory, which are part of the physics of complex systems, applications go through meteorology, electronics, optics, thermoconvection, chemical reactions, biology and even astrophysics. Its transversal property, creating links, connecting together scientific domains traditionally very far apart from each other, is a unifying factor of science itself and of theory with applications.

To conclude, when we start observing outside well defined ideal conditions, the famous spherical cow, we often must face complexity. That is because interactions with the environment become important and change themselves as the system evolves, therefore the border itself between the system and the environment becomes difficult to be defined, leading to an active choice of modelling a particular phenomenon, made by the observer, and leading then to complexity.

3. What can biologists learn from complex systems?

There are many examples where the physics of complex systems gave important insights on biological systems and helped to better understand them. We have already mentioned protein folding and chiral motion of cells (such as sperm cells, or some bacteria). It is worth to mention, for its historical relevance, also the Lotka-Volterra model, describing the prey-predator competition in simple, but already informative mathematical terms with important implications on ecosystem science [15]. In its simplest version two continuous non-linear differential equations are coupled, to represent the time evolution of both prey and predator populations. Under some assumptions, actually realistic only in ecosystems isolated from other effects and where all the other conditions – weather, temperature, availability of food ... – are constant over the time considered (it is just the simplest version of the model), it can be shown that there are two fixed points of the dynamics. One is the extinction of both populations, and the other is an oscillatory dynamic, with a feedback regulated mechanism: the more prey means the more food for predators, implying a growth of the predator population. Despite its strong assumptions this model was already interesting for the understanding of ecosystems, helping to take decisions on regulatory politics for nature preservation, in particular after human alteration.

More closely related to our system, the living cell, we can cite important

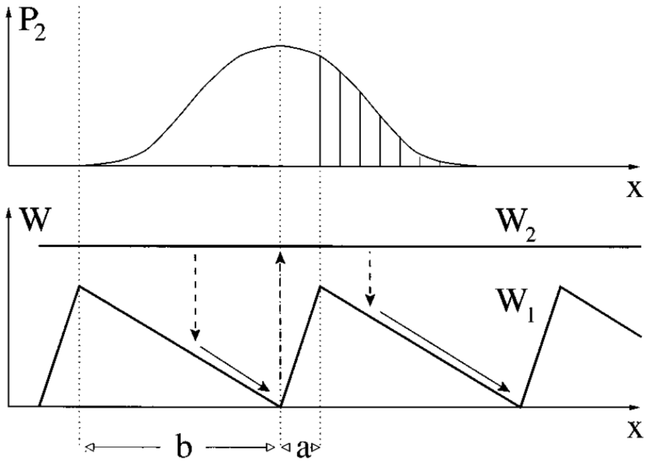

Figure 1. Schematic view of the two states ratchet model, the higher, constant potential (W2) is the Brownian diffusion state, and W1 is the asymmetric ratchet periodic potential. Arrows symbolise stochastic transitions between the 2 states, where up pointing arrows need an active energy injection to jump to the upper state. Adapted with permission from [23].

works proving the existence of long-range correlations in genomic DNA packaging [16, 17], or works on tissue growth showing self-developed homeostatic stresses [18]. The homeostatic stress is the steady stress proper to growing living systems, as biological tissues, arising from the non-equilibrium state of the system, balancing apoptosis and cell division and its regulation is essential in many pathologies, like cancer [19]. This is an important aspect involved in mechano-sensitivity, which appears to be a property shared by all cells of the human body and all phyla, from mammals to plants, fungi and bacteria [20]. Diffusion effects in crowded environments, such as cytoplasm or nuclei, are also fields where physics gave a good contribution. Non-standard diffusion exponents have been put in evidence, different from the standard Brownian motion due to crowding and hydrodynamical back-reflection effects (a molecule moving in a liquid creates a flow which is reflected from other molecules of the same size) [21].

Here, I would like to discuss shortly the modelling of molecular motors, active proteins responsible for transport of vesicles or nutrients along cell cytoskeleton filaments and in general of many other active features of the cell. This is an example of a highly out of equilibrium system with an interesting physical interpretation. First, it should be noticed that at the nano-scale (molecular motors typically move of a few tenths of nanometres per step and apply loads of a few pN) viscosity dominates inertia and the relatively high, with respect to molecular motors power, thermal noise makes standard motor motion impossible. In this context a simple symmetric Brownian ratchet, i.e., a passive motor subject to thermal fluctuations would not lead to a net directed force. The first step to a solution of the problem is to reproduce the symmetry of the filament in an appropriate potential landscape, where we can find the periodical structure of the filament to which the motor is attached and, at the same time, the filament polarisation towards one of its ends, giving an asymmetry in the sawtooth. Again, it can be proved [22] that yet it is not sufficient to have a direct movement, as intuitively we could think: a particle falling randomly on this potential landscape could be expected to have a drift to the right. Actually, what is really important is how the system is driven out of equilibrium, therefore how energy (generally hydrolysis of ATP) is used to switch from the state described by potential W1 to the free diffusion potential described by the constant potential W2, coupling in this way the 2 states [23] (up pointing arrows in Figure 1). Within this picture we can find the transition rates between the two states that optimise directed movement, arriving at the conclusion that there should exist active sites localised along the filament which promote transition from state 1 to state 2. This seems to be supported experimentally, by studying the experimental velocity curves with respect to ATP density [24, 25].

Another field where complex systems and stochastic processes have successfully contributed is population genetics. In this field theoretical models have a huge database of information represented by the famous Lenski's experiment on 12 populations of Escherichia Coli evolving at constant nutrient-poor conditions since 1988 [26]. The popular Moran model [13] gives a stochastic description of evolution, following the path of the pioneering models from Sewall G. Wright and Ronald A. Fisher [27, 28], but introducing individual random births and deaths, allowing for a better mathematical description. In the simplest version of it, the most important parameter governing the dynamics of asexually reproducing individuals is the individual fitness. Without going into the details of the model, we can say that the passage to a mathematical description of evolution was essential to the wide acceptance of Darwin and Wallace theories from the scientific community and took more than a century to be partially achieved (there are still important open problems). An important result is that the mean population fitness increases under selection and the rate of fitness increase is proportional to the amount of genetic variability of the population. Furthermore, this description helped in the explanation of genetic drift (long-term fluctuations of the genetic expression of the population), genetic fixation (the probability that a genetic feature dominates others) and evolution dynamics. These models are related to a branching process, which is another class of stochastic models originally created to explain the extinction of a population, but without a genetic point of view.

Finally, the implications of neural network theory to the understanding of brain mechanisms are still a very active subject, since understanding brain mechanisms can be very difficult, but we can cite a few findings obtained by a statistical mechanics/complex systems analysis. A good picture of what is going on in such a complex network is provided by the statistics of some available data, for example the synaptic weights. Since so far it has not been possible to observe dynamically a single synapse weight change, then a theoretical description can help to understand the underlying mechanism and to infer some properties, as storage capacity, of real neural networks. In different areas of the brain (similar distributions are observed also in cortical networks) [29, 30], the synaptic weight distribution has a skewed form which can be approximated to a log-normal, in fact it has been fitted by a lognormal by Sen Song et al. [31], without considering a large number of silent synapses, up to 60% [32]. Theoretically, this has been associated to memory optimisation in neural network: the condition of maximum storage of memories, together with the constraint of positive synaptic weights (i.e., excitatory synapses), leads to a large proportion of silent neurons and to a truncated Gaussian distribution for the synaptic weights [33]. Behind such ideas there are mechanisms driving the brain to an attractor where memory would be optimised. If optimality has not yet been reached, the decay of the distribution for large weights could be much slower than Gaussian. Other optimality principles, for instance considering the energetic cost of maintaining excitatory synapses [34], lead to similar conclusions. In both cases it was not necessary to specify any details on the plasticity rule, that could bring to a more precise identification of the final distribution. Caution should be adopted with this evolution-driven optimality and with the idea of evolution itself, remembering what we said previously, are not complete unique theories which can explain everything, we should not forget that we are dealing with a complex system. The quantity to be optimised can change with time and even with the observed scale, we do not face an equilibrium system.

In general, we can say that the point of view of complex systems helps to interpret and explain some observations that otherwise would be considered in biology as unexpected events or noise. We think for example of extreme events, or the observation of asymmetric distributions, considered as atypical with respect to the common normal distribution. Moreover, having a global phase diagram of some aspects of a biological system, helps to understand what are the control parameters that can trigger non-trivial collective behaviours essential for life.

To conclude, in all the discussed situations it is now evident that a deterministic description is not even conceivable, because stochastic and out of equilibrium processes are dominant in living systems. Also, we can say that in general we can infer much interesting information on underlying processes just by looking «critically» at statistical distributions or time variations of observable quantities.

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