Chapter 2
Is There an Explanation for . . . the Diversity of Explanations in Biological Studies?

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Abstract The multiplicity of explanations in the biological sciences has already been amply discussed by philosophers of science. The field of Evo-Devo has been a focus of much attention, with the obvious coexistence and competition of evolutionary and developmental explanations. In this contribution I borrow examples from hugely different areas of biological research to show that this multiplicity of explanations is common to all branches of biology. I will emphasize three explanations for this diversity. The first is the ambiguity of the questions raised, which can be understood in different ways and require different answers. One recurring ambiguity concerns the local or general nature of the questions (and answers). The second explanation is in the historicity of life, which makes every situation unique, and may require different models for the explanation of apparently similar situations. Another cause of this plurality is the existence of long-lasting competing traditions of explanations. These traditions result from the existence of distinct approaches to reality in scientific thinking, such as the opposition between reductionism and holism, and from a complex history of scientific ideas, models, and theories proper to each biological field. The multiplicity of explanations in the biological sciences therefore has a heterogeneous origin, both epistemic and ontological.

Keywords Historicity • Holism • Plurality of explanations • Research traditions • Reductionism • Themata

1 Introduction

This contribution has a dual objective. It aims to understand the origin of the multiplicity of explanations of a singular phenomenon in science, but also to explain why this diversity is particularly high in the biological sciences. This question is not new. In 1961 Ernst Mayr clearly distinguished two types of explanations in

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biology, those answering to "how" questions by describing mechanisms, and those responding to "why" questions by proposing evolutionary scenarios (Mayr 1961). The distinction was not new, but it was clearly outlined by Ernst Mayr. Later, Nikolaas Tinbergen distinguished two kinds of questions within each category, one concerning the appearance of the trait, and the other its present state (Tinbergen 1963). These first contributions underlined the relation between the diversity of explanations and the multiplicity of the questions that can be raised concerning a unique phenomenon. In 1983, John Dupré launched a wide philosophical debate about the ontological origin of the "disunity of science" (Dupré 1983) that persisted for many years (Dupré 1993). This debate had a wider scope than the one I want to address in this contribution, and a different one since it raised ontological issues that will not be discussed here. Nevertheless, interesting clues emerged during this debate about the origin and nature of the plurality of explanations in the biological studies that were nicely summarized and extended by Sandra Mitchell in 2003 (Mitchell 2003). One of the most demonstrative examples of the plurality of explanations in biology presented in her book concerned the origin of the division of labour in insect colonies.

A very important perspective on the issue underlined by Sandra Mitchell and the one that I will describe first is that the diversity of explanations originates in part in the diversity, explicit or more often implicit, of questions that are raised. The second point that I will discuss is the relation between the diversity of explanations in biology and the historical nature of the biological objects.[1] This question was present in Mitchell's book through the notion of biological complexity, but I prefer to focus the discussion on the origin of this complexity, that is, the historical process that generated it, in order to show that interesting lessons can be borrowed from the work of historians. But the diversity of explanations in the biological sciences also emerges from the existence of different types of explanations. They are not Kantian categories, but instead belong to long-lasting scientific traditions. The time when these traditions reveal themselves in the most obvious way is when the question to be answered remains vague and strategies to address it are progressively elaborated. Conceiving them in different ways illuminates more about the plurality of explanatory schemes than the simple observation of competing explanations.

To discuss these three points, I will use examples from different branches of biology, not from Evo-Devo, where this plurality of explanations has been the most extensively scrutinized,[2] but from other fields, from research on ageing and cancer, and even from well-established and apparently non-problematic disciplines as biochemistry. I will also use many historical examples.

In contrast, three alleged reasons for the plurality of explanations in biological sciences will receive only limited attention in this contribution. I consider not only that they have already been amply studied, but also that they are peripheral to the

[1]The historical and contingent nature of biological objects and processes is also discussed by Turner (2015, this volume).

[2]See Brigandt (2015, this volume) for a discussion of the explanatory diversity in Evo-Devo.

main issue: the involvement of different disciplinary approaches within biology; the existence of "levels" in biological objects; and the importance of mechanistic explanations in biology. While different disciplines within biology may favour different types of explanations, one discipline, and even one unique type of research within this discipline, such as the study of social insects discussed by Sandra Mitchell, may harbour many different coexisting and/or competing explanations. So appealing to multi-disciplinarity to explain the plurality of explanations is not sufficient. Certain explanations are limited to one level of organization of biological objects, and different explanations correspond to the numerous levels at which the phenomenon can be studied, but different explanations can also compete at the same level. In addition, the distinction between levels is nothing less than problematic. Finally, the importance of mechanistic explanations in biological sciences is obvious, but mechanistic explanations are a heterogeneous category: a reference to machines can be a metaphor or a precise comparison, and very different types of machines can be used.[3]

2 In Many Cases, the Diversity of Explanations Originates from the Diversity of Questions That Are Raised

This point was raised by Ernst Mayr (1961) and discussed at length by Sandra Mitchell (2003). I will illustrate it by the case of the explanation of cancer. Different explanations are currently in competition. In the somatic mutation theory, cancer results from an accumulation of mutations in tumour cells, whereas in the stem cell theory cancer results from the proliferation of a small fraction of the cells present in the tumour called stem cells, and these stem cells are responsible for the tumours' resistance to the treatments tested so far. To explain the origin of cancer by the occurrence of somatic mutations or by the existence of a small subpopulation of stem cells does not exactly answer the same set of questions, although these two sets are overlapping. To be simple, let us say that the somatic mutation theory explains the progression of tumours, whereas the stem cell model mainly explains why treatments have so far been unsuccessful. In fact, the two explanations are fully compatible, and can be combined: these mutations occurred in a population of stem cells.

The existence of two different explanations can be the result of the nature – general or particular – of the answer that is expected. There is a heated debate about the function of what some have called "junk" DNA: the large fraction of the genome that does not give rise to functional RNAs or proteins and has no known regulatory functions. Two explanations coexist. The first is that this DNA has no functions and

[3]For critical discussions of mechanistic explanations see (Mekios 2015, this volume; Théry 2015, this volume; Zednik 2015, this volume; Baetu 2015, this volume; Issad and Malaterre 2015, this volume).

persists for generations because its presence is neutral, and is therefore not sieved by natural selection. The second type of explanation is that this DNA has a role in organizing the genome or controlling its expression in one way or another that has not yet been discovered. Since it has been recently shown that a large part of this DNA is copied into RNAs, a new debate has emerged concerning the role of this transcriptional process.

The answer may be different for different fragments of this "junk" DNA. One fragment may have an essential role in the regulation of the expression of a gene localized elsewhere in the genome; and another fragment may have no obvious role, its presence being the result of contingent DNA rearrangements, and its persistence the consequence of its invisibility to the control exerted by natural selection.

If the answers can be different, depending upon the fragment that is examined, an overall quantitative answer nevertheless has its place. It would, at least theoretically, be possible to estimate quantitatively the percentage of "junk" DNA that has a function. For instance, 10 % of the "junk" DNA could be shown to have a function, and 90 % to have no function. In this case, it would be possible to state that, in general, "junk" DNA has no function. It is interesting to notice that, in the case of "junk" DNA, the two explanations are incompatible, whereas they were compatible in the case of cancer.

An additional layer of complexity comes from the fact that this "junk" DNA was introduced in the genome at a specific time in the evolutionary history of organisms. To the question of the present function of such a fragment of "junk" DNA can be added another: What explains the progressive invasion of the genomes of eukaryotic organisms by "junk" DNA? According to Michael Lynch, the increase in the size of the genomes of eukaryotes, concomitant with the increasing percentage of "junk" DNA, was the result of contingent events, and of the neutrality of this increase towards natural selection (Lynch 2007). This event is independent of the later acquisition by some of these sequences of regulatory functions, by a process of exaptation whose importance was emphasized by Stephen Jay Gould (Gould and Vrba 1982). Therefore, as I emphasize in the next section, the diversity of explanations is also the result of the historical trajectories of organisms: the extant presence of a sequence of "junk" DNA can be explained both by a neutral process that allowed its acquisition, and the selection of its present function.

Another example – in which the historical dimension has not yet been introduced – is the origin of the catalytic power of enzymes. Traditionally, the catalytic efficiency of enzymes has been explained by their capacity to stabilize, through the formation of specific weak bonds, the transition state of the reaction, and by their direct participation in the catalytic mechanism, for instance, by providing protons at some specific steps in the catalytic process. More recently, it has been proposed that it was necessary to appeal to quantum physics, to strange phenomena such as the tunnel effect, to explain the catalytic efficiency of enzymes. Other quantum effects would explain the high efficiency of photon capture by photosynthetic systems (Scholes et al. 2011), or the measurement by migrating animals of the weak magnetic field of Earth in order to position themselves (Arndt et al. 2009). Do these recent results require a "revisionist's view" of enzymology? Is enzymology

at a turning point? And is it correct to say that the "origin of enzyme catalysis has remained unresolved"? (Nagel and Klinman 2009, 543). In this case, as in the previous one, it seems possible to reconcile the two opposite visions of enzymatic catalysis: the catalytic power of most enzymes can be accounted for by "traditional" chemistry, but in some cases, quantum effects have a dominant role that gives the previous explanatory schemes a limited contribution to the catalytic power. Some of the parties to these controversies present the debate as the necessary choice between two opposed and incompatible explanations; this can only be understood by the fact that the two types of explanations belong to long-lasting, different, and opposing scientific traditions (see below).

The coexistence of different explanations is also the consequence of the often long causal chains responsible for the production of the phenomena under study. In the case of cancer, the explanation of the formation of a particular lung tumour is the accumulation of mutations in the cells of the lung tissues. But the explanation of cancer is also the numerous cigarettes that the patient has smoked. The two explanations are in fact a single one, but the attention is focused on different steps in the long causal chain that led from the cigarettes to the development of the tumour. The explanation by the smoking habit will be probably favoured, not only because smoking precedes the occurrence of mutations in the causal chain, but also because this explanation offers concrete ways to reduce the incidence of lung cancer.

In the previous example, different explanations concern different steps in a linear causal chain. The situation can be more complex. One explanation may target one step in the causal chain, whereas the other describes the context that permitted the deployment of the causal chain. In a search for an explanation of the emergence of life on Earth, some researchers will put forward the role played by self-replicating macromolecules (RNAs or other types of nucleic acids). Others will argue that the explanation of the emergence of life on Earth is to be found in the abundance of liquid water on its surface. The two explanations are of a different nature. The first explanation concerns what is considered as the most important step in the formation of the first organisms; the second is simply a description of the conditions without which life would not have been possible – and that explain what specialists call the "habitability" of Earth. Both explanations are partial and necessary, and they are not in competition. The first may appear more central, but the second is also essential. If the causal chain leading to the formation of the first organisms is a deterministic one, the second type of explanation will receive more attention because, once the conditions for life were present, life would automatically arise. It is the present *credo* that guides the work of astrobiologists. But if the causal chain leading to the formation of organisms is a complex one, a mixture of deterministic and historical, contingent, events, the formation (or not) of life will be explained only through a precise description of the succession of events that led to the first organism, and not by a description of the conditions that obviously were not sufficient to explain its later formation.

Thermodynamic explanations belong to the second type of explanation. The laws of thermodynamics explain the whole of metabolism. The role of ATP, as well as the mechanisms of its production, is explained by thermodynamics. But

the characteristics of the metabolic map cannot be deduced from knowledge of thermodynamics: a molecule different from ATP might have been selected by evolution, and ATP can be produced by different pathways (and may well have been produced by an even greater number). Without water or the existence of thermodynamic laws, life or the central role of ATP would not have been possible. This type of explanation corresponds to the *sine qua non* rule that lawyers use to ascribe responsibilities in trials. Often, in human affairs, the *sine qua non* explanations are more important than the direct causal explanations: when an airplane crashes, the errors of the pilot will be considered as less important, at least less likely to be sanctioned, than the indirect unfavourable conditions that made the occurrence of the catastrophe possible.

In this case, as in the previous one, it is obvious that the way the question is formulated will lead to one or another type of explanation. If the question is: "What explains the formation of life on Earth?" the answer will be automatically directed towards a description of the physicochemical conditions at the surface of Earth that favoured the emergence of organisms. If the question is: "How can we explain the formation of the first organism?" the answer will seek to describe the causal chain leading to this organism.

The situation is exactly the same in the field of cancer research, with the supposed opposition between the somatic mutation theory and the tissue organization field theory of cancer (Soto and Sonnenschein 2011). In the latter, disorganization of the tissues is considered as *the* cause of cancer. Its authors refuse to accommodate the observations in favour of their theory within the somatic mutation theory, convinced that the two theories are incompatible. In contrast, I have the feeling that the two explanations are fully compatible but of a different nature. Somatic mutations are the cause of cancer, but the disorganization of the tissue creates the conditions favourable for the occurrence of the mutations, their selection and their expression.

I will discuss a final example of an ambiguous question that can elicit different answers, and different explanations, because of the importance it had in the history of biological thought. The (simple) question is: "What is the explanation for the presence in organisms of a particular mutation?" It is a question that is often raised in Evo-Devo. This question has two different meanings: what is the explanation for the occurrence of such a mutation? And what is the explanation for its continued presence? The first question could (theoretically) receive a deterministic physicochemical answer, such as the specific impact of radiation on a precise part of the genome, the wrong incorporation of a nucleotide at a specific place in the genome, the absence of a repair process during replication, etc. The answer to the second question will be of a very different nature: this mutation gave the organisms in which it was present a specific advantage in the conditions in which they were living at that time, or, possibly, this mutation had no obvious effect, but by contingent sorting during reproduction has invaded the population. In both cases, the second explanation leaves much room for contingency: the occurrence of mutations and the effects they have on organisms belong to different causal chains, the meeting of which is unpredictable. The ambiguous nature of the question generated a lot of confusion in the answers. The wish of many biologists to give a non-deterministic

explanation for the presence of mutations in organisms led them, as did Jacques Monod in *Chance and Necessity*, to propose that the contingency of evolution had its origin in the quantum indeterminacy of nucleotide electronic structure and the errors it generates during DNA replication (Monod 1971). While quantum indeterminacy can explain some mutations, it is clearly not the one and only cause of mutation, and obviously does not explain the contingency of the evolutionary process.

3 The Diversity of Explanations as the Natural Consequence of the Historicity of Life

Sandra Mitchell nicely described the competition between evolutionary and developmental explanations in Evo-Devo. Whereas evolutionary explanations were dominant until the 1970s, Stephen Jay Gould, Pere Alberch and many others argued in the following years in favour of the importance of developmental explanations: many traits cannot be explained by the action of natural selection, but are a consequence of the programme of development.

Sandra Mitchell suggests a piecemeal approach: a choice between the two explanations may be possible – at least in some cases – but has to be made independently in each case. Ideally, every situation might be located somewhere on a line running from "fully explainable by evolutionary explanations" to "fully explainable by developmental ones". This impossibility of establishing general rules originates in the complexity of the developmental process as well as in the diversity of situations faced by different organisms. The diversity of explanations is the consequence of the diversification process generated by the complex history of life.

The situation is even more complex since each of the characteristics of organisms that have to be explained is the result of a causal chain formed of different steps, each of which may receive a different explanation. For instance, the origin of a trait can be due to developmental constraints, the side effect of another modification in the developmental programme; but the precise characteristics of the trait observed today can be the result of a selective process that has altered later steps in development, a situation similar to that we described in part one.

This situation is familiar to historians. When they try to explain a historical event, such as the Battle of Waterloo, they know that what happened that day was the result of long heterogeneous causal chains, containing events of a very different nature and apparent importance. The error against which historians had to fight was the introduction of an a priori hierarchy between the different steps and their explanations (Veyne 1984). For instance, for Marxists, economic and social transformations were used to explain events such as the French Revolution. But the errors made by the Governor of the Bastille had a major role: no one knows what would have happened if the Bastille had not been taken!

The absence of a predetermined hierarchy in the explanation of historical events is a lesson that not all biologists have yet learned. The development of an epidemic

or of a pandemic is the result of long causal chains, including events that differ greatly in nature and importance. However, these tiny events can have dramatic consequences. Many epidemiologists overlook this when they are questioned about whether or not an epidemic or pandemic will develop, and their answers are awkward and incautious.

Historians have also learned to be very cautious in the way they ask (or do not ask) questions. Most would be reluctant to ask general questions such as: "What is the explanation of the French Revolution?" They would either provide multiple explanations in parallel, or limit their scope to one episode, and give a precise explanation of it. This back-and-forth movement between general and local explanations is also valid, as we have seen, in the biological sciences.

Another reason for the multiplicity of explanations in the biological sciences is the place occupied by etiological explanations. Initially, this type of explanation was put forward in medicine to explain the development of a disease. More generally, they consist in the construction of likely scenarios to account for the transformations that occurred in the past, and are no longer observable. The constraints on the elaboration of these scenarios are weak; this, in conjunction with the highly developed spirit of contradiction of scientists, leads to the proliferation of conflicting hypotheses.

The resulting multiplicity of explanatory hypotheses will not endure indefinitely. New observations, or new possibilities to test some of these scenarios by synthetic experimental evolution (Erwin and Davidson 2009), will limit the number of competing scenarios to one or a small set.

4 The Diversity of Explanations as a Consequence of the Existence of Competing Types of Explanations

The diversity of explanations in the biological sciences also stems from the coexistence of different types of explanations. What appears at a given time as transiently competing explanations may on a longer timescale be seen as different ways of looking at reality and of searching for explanations. One example will illustrate what I mean by "types of explanations". Accounting for the functions of organisms by the existence within them of mechanisms has a long tradition initiated in antiquity by Aristotle and Galen, pursued in the Renaissance by William Harvey, Galileo Galilei, and René Descartes, and continued today in the life sciences through the mechanistic explanations of molecular biology.

But another tradition has coexisted with the previous one, which might retrospectively be called a "chemical" tradition. As early as antiquity, a comparison was made between the progressive formation of organisms and the action of ferments responsible for the production of wine and bread. Present during the Renaissance within the alchemical tradition, it gained a dominant position in the first part of the twentieth century with the so-called "enzyme theory of life" (Olby 1974).

Epigenetics is probably an extant avatar of this tradition. Such an opposition is reminiscent of the themata studied by Gerald Holton (1978). However, I will diverge from the approach of Gerald Holton on two points. The first is that I will emphasize their continuity rather than their alternance. The second is that I will show that they may coexist at the same time, and even in the same person. For instance, the mechanical and chemical explanations of the properties of organisms coexist in Aristotle's writings.

In most cases, it is difficult to precisely designate these types of explanations. They do not fit perfectly with the opposition of categories favoured by philosophers such as the one between holism and reductionism. The reason is that they are a combination of historical traditions and categories of thinking. They certainly correspond to different "styles" and "epistemic cultures", but they transcend these categories. They are the result of this complex history of disciplines, and for this reason their characteristics are partially contingent. The best way to characterize them and to show their importance is through examples, and by looking at an early step in the formation of scientific knowledge, at the time when scientists, faced with a phenomenon they wanted to explain, looked for the best strategies to discover these explanations.

A good example is the search for the nature of the gene in the 1930s. After the "rediscovery" of Mendel's laws at the beginning of the twentieth century, genes played an increasingly important role in the explanations of biological phenomena over the following three decades. They were considered the "atoms of biology" localized on the chromosomes. The nature (and structure) of genes had become a central issue in biology.

The first approach to this question, developed by Max Delbrück, one of the founders of the American Phage Group and later a leader in the young science of molecular biology, was indirect. It consisted in targeting the genes with X-rays and deducing the gross characteristics of the gene from the effects of this irradiation. Results of this experimental approach were published in what was called the "Three-Man Paper" (Sloane and Fogel 2011). The second strategy, developed the same years by the Russian biologist Nikolai Koltzoff (Kol'tsov), was simply to use the chemical knowledge accumulated on the constituents of the cells and, in particular, of the nucleus, to elaborate a reasonable model of the gene (Koltzoff 1928, 1939; Morange 2011a). Both attempts were unsuccessful, but for different reasons. However, the discovery of the double helix structure of DNA by Jim Watson and Francis Crick in 1953, based on a precise chemical knowledge of the constituents of this macromolecule, obviously belonged to the same chemical tradition as the one favoured by Koltzoff.

This dual approach was not limited to the gene. In the same period, two different methodologies were also developed to gain information about the structure of proteins. One, initiated by Emil Fischer at the beginning of the twentieth century, consisted in progressively improving the description of the building blocks of the proteins, the amino acids, and the way they are linked within proteins. The second physicochemical approach was more global and external, and focused on the study of the shape of proteins and of their electric properties.

This second tradition did not become immediately obsolete with the development of X-ray diffraction studies, and the elucidation of the first precise three-dimensional structures of proteins. In the 1960s, a new category of proteins, the allosteric proteins, was identified. The activity of these proteins is regulated by interaction with molecules distinct from their substrates. This interaction triggers a conformational change that alters the activity of these proteins. What was the best experimental approach to explain the remarkable properties of allosteric proteins? One strategy was to describe their three-dimensional structure, i.e., the precise position of the different atoms forming them. The second strategy, favoured by Jacques Monod, the father of the allosteric theory, was indirect. It consisted in altering the equilibrium between the different conformations of these proteins to extract from the results of these perturbation experiments information on the global organization of the proteins.

These two related examples illustrate the persistence of similar approaches despite transformations in the nature of the objects under study, and dramatic changes in the state of knowledge. Interestingly, as seen previously, the same scientist could successively choose the two different approaches. In 1941, Max Delbrück proposed a model of gene duplication in which he identified the gene with a long protein chain (Delbrück 1941).

Despite the fact that these experimental approaches differ greatly, they cannot easily be put into simple categories. The first, that of Delbrück and Monod, was more "physical", and the second, Koltzoff's, more "chemical". The first was global, whereas the second paid more attention to the details of the chemical structure. The proponents of the first were more interested by the search for principles of organization, the existence of symmetries and rules that would have simplified the description of the structure, while the proponents of the second were not intimidated by the terrible chemical complexity of the objects under study. But to contrast the two attitudes as holist versus reductionist is clearly not the appropriate way to investigate their differences.

This does not mean that these general categories cannot be useful in some cases to contrast different types of explanations. Let us consider again the question of the origin of the catalytic power of enzymes. Those who support the hypothesis that quantum effects play a major role clearly belong to a long-lasting reductionist tradition that seeks to discover the secrets of life at the most fundamental level. In the 1960s, some researchers unsuccessfully advocated the conversion of biochemistry to quantum biochemistry (Pullman and Pullman 1963). Recent observations on the "tunnel effect" in catalysis can be viewed as the accomplishment of this reductionist programme, simply postponed by the absence of appropriate technologies.

Symmetrically, the emphasis placed by Emmanuel Farge and other researchers on the role of mechanical deformations in development (Brouzés and Farge 2004; Farge 2011) aims to show that the molecular descriptions are not sufficient, and that a more global view of development is required to understand it fully.

As we have already seen, these contrasts are hardened by the participants. Both sides demand that a choice be made between the different explanations. In most cases, the need for a choice vanishes when knowledge of the system under study

increases. Since their first description, mechanical deformations and tensions now have a recognized place in cell biology, and the discontinuity between mechanical and molecular explanations is progressively disappearing: mechanical effects can alter the production or the activity of molecular signals, or change protein conformations, two categories of phenomena familiar to molecular biologists. Another interesting contrast that provides some clues to understanding many debates in biology is between a static and a dynamic vision of biological phenomena. At the beginning of the twentieth century, the gene was considered by many geneticists not as an object, but as a dynamic process. Another illustration of the contrast between these two different views is to be found in the explanation of the phenomenon of memory. The first mechanisms of memory that were favoured in the 1950s were dynamic: memories corresponded to the stabilized circulation of the nerve impulse in neuron circuits. This dynamic view was challenged in the 1960s by the identification of memories and behaviours with certain types of macromolecules, RNAs, or proteins (Morange 2006). After some years of intense debate, these static models of memory disappeared, and a dynamic model of memory re-emerged – although the dynamics of the circulation of the nerve impulse may be dependent on the structural modifications occurring at the synaptic junctions between neurons.

The way I have presented the debate about the existence of memory macromolecules is not the usual one. However, it casts some new light on the controversy, and in particular explains the major role played by George Ungar at the beginning of the 1970s. Many observers conclude that Ungar's results prolonged a debate that, without him, would have ceased earlier, with the abandonment of the idea that macromolecules can be bearers of memories. Is this prolongation explained by the quality of Ungar's results? The harsh criticisms of his experiments obviously show that the answer is no. The reason is different: Ungar proposed a model in which the peptides (small proteins) that he characterized as the bearers of memories were "signposts" present in the membranes of neurons. With this model he apparently reconciled the static and dynamic views, and made the hypothesis of "bearers of memories" acceptable to all.

This contrast between the static and dynamic visions of biological phenomena is still present in current biological debates. One of the reasons for the present success of epigenetics – the study of the modifications of DNA and surrounding proteins that do not alter the sequence of the DNA but have an effect on its expression – is that epigenetic marks are unstable, dynamically added and erased in response to signals from the organism and from the environment, whereas genetic information appears, in part erroneously, as static. To harden this opposition, the supporters of epigenetics include in it dynamical genetic regulatory models such as the operon model, although this model was considered to fully belong to genetics when it was initially proposed!

Similarly, the static vision of protein structure is progressively being replaced by a dynamic one in which proteins oscillate between different conformations (Morange 2012a). The present interest in this dynamic view of protein (and macromolecular, in general) structure is the consequence of the development of new technologies, such as NMR, which permit direct access to molecular dynamics.

But these technologies were developed because some researchers were convinced that the static, rigid view of proteins was unable to account for their properties. Philosophers have recently wondered whether dynamic models are alternatives or complements to mechanistic explanations (Kaplan and Bechtel 2011). Both types of models are related: what distinguishes them is simply the emphasis put on structures, or on their variations.

To conclude this survey of the long-lasting competing types of explanations, I want to discuss the recurrent opposition between models and explanations in which the final state reached by a system is the result of a "positive" process, and those in which the system evolves "by default", simply through the loss of its previous characteristics.

One historical example of this "evolution by loss" was the model proposed by Theodor Boveri at the beginning of the twentieth century to explain the role of chromosomes in development and differentiation. For Boveri, development was linked with the progressive loss of chromosomes during cell division. The specialization of the cells was the direct consequence of this loss of genetic material.

A similar model "by loss" explains ageing (Morange 2011b). In the simplest evolutionary models, ageing results from the progressive loss of functions with age, or increase in dysfunctions, defects that have not been eliminated by natural selection because they occur too late in the life of organisms to alter reproduction.

Interestingly, various positive models of ageing have been proposed regularly since the Renaissance, such as ageing being the result of poisoning of the body by toxins that accumulate during life. At the beginning of the twentieth century, Elie Mechnikov thought that he had discovered the source of those toxins in the microbes present in the gut, and he designed a special diet to eliminate them. Today, many researchers believe that the formation of protein aggregates during ageing, which is well demonstrated in Alzheimer's and Parkinson's diseases in the brain but that in fact occurs in all the tissues of ageing organisms, has toxic effects. Negative and positive explanations of ageing are not incompatible: the toxic effects of these protein aggregates might explain the dysfunctions observed in ageing. As previously seen, what is significant is negative (the effects) or positive (the existence of a toxic substance) emphasis of the explanations.

In the case of evolution, the situation is the same, but the dominant place of the positive explanations – evolution by the emergence of novelty – is obvious. This has not prevented recurrent support among biologists for an alternative model, evolution by loss. In the 1940s, the French biologist André Lwoff proposed a model of evolution by loss of biochemical functions (Lwoff 1944). More recently, human evolution was explained by the loss, in our ancestors, of genes involved in specialized functions (Olson 1999) or of their regulatory sequences (McLean et al. 2011). Gene loss is seen as the way for the organism to free itself from the constraints accumulated during evolution.

Explanations by loss have also recurrently been used to explain the origin of tumours. Cancer has been considered as a loss of the differentiated characteristics of the cells, their return to a "primitive" stage and/or a loss of regulation – cancer cells

escaping the body's control (Morange 2012b). The vision of cancer as a deregulation was dominant in the 1970s, before the adoption of the somatic mutation theory (Morange 1997).

An explanation by loss does not require further explanations. It can be limited to a description of the obstacles that had to be overcome to reach the basal level. This is obvious in the case of cancer. When John Cairns looked for explanations of cancer in his book *Cancer*: *Science and Society* published in 1978 (Cairns 1978), he found them in the failure of the mechanisms that prevent cells from returning to an uncontrolled state of proliferation.

The fact that explanations by loss are self-sufficient has been contested by Daniel McShea and Robert Brandon who propose that the loss of homogeneity between different cells – a process characteristic of multicellular organisms called cell differentiation – is in fact the result of what they called "a zero force" or "biology's first law" (McShea and Brandon 2010). A similar debate concerns innovation in evolution. Must innovation be specifically explained, as Marc Kirschner and John Gerhart among others propose (Kirschner and Gerhart 2005), or is it the unavoidable consequence of any process of evolution by variation (and selection)?

I have, in previous publications, tried to list the different types of explanations (Morange 2009, 2012c). Today, I am more sceptical about the success of such a project. Some types of explanation are relatively well defined, such as the mechanistic and Darwinian types, but others, such as what I have called "chemical" explanations, are much more difficult to delineate. The reason is simple: types of explanations are also the result of a complex historical process. Some have acquired a well-defined shape, whereas others have successively existed under different, more or less well defined, avatars.

5 Conclusion

The plurality of explanations in the biological sciences has different causes. One is ontological, linked with the historical dimension of biological objects. Two others are epistemic. The first is mundane, the consequence of the formulation of ambiguous questions. In particular, it is not always obvious whether a question concerns a particular phenomenon, or an ensemble of similar phenomena. The second epistemic origin of the plurality of explanations is to be found in the existence of long-lasting traditions of explanations that persist and recurrently conflict with one another, despite the transformations of scientific knowledge. These two epistemic causes of plurality are not totally independent. The description of the conditions that allowed the occurrence of the phenomena under study, what I have called the *sine qua non* explanations, answers a particular type of question. But it can also be considered as a specific type of explanation, competing in some cases with other explanations such as mechanistic explanations. This complex conjunction gives to the landscape of explanations in biology its richness and diversity. My

description is clearly at odds with the too simple vision that many scientists have that knowledge is acquired through the simple fitting of scientific facts to alternative theories and models (Soto and Sonnenschein 2012). Data have a major role in the evolution of scientific knowledge, not simply as a means of choosing between competing explanations, but through the far more indirect process of reshaping the complex landscape of biological explanations.

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