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## *Five Arguments for a New Theory of Biological Individuation*

Biological theories have been propounded since ancient times. In an attempt to grasp the nature of the species and the individual, and in general, the genesis of these two aspects has been considered as distinct phenomena. This is the reason why the evolution of species and the development of organisms is explained by two different theories: natural selection and genetic programming. This separation presents a recurring problem, as these two processes are in fact closely interwoven one with the other. In concrete terms, the species evolves through the reproduction of individuals that succeed each other. There has to be, therefore, a point where the theory of evolution and the theory of embryonic development meet. In the 20th century, this union occurred through what has become known as ‘evolutionary synthesis’. Evolution of the species is considered to arise from transformation due to mutation of the genetic programmes coded in the DNA. This field of research is now called “evo-devo”. While, logically, the two processes can be linked to one another with this theory, the cost is considerable. New problems arise bound very closely with genetic determinism, in which the theory ends. DNA becomes omnipotent. It governs evolution through its mutation, and controls the genesis of organisms through the genetic information it contains. Ever since we developed the ability to sequence genomes, the difficulty of holding such a view has been confirmed.

Firstly, there are considerably fewer differences between the genomes of organisms, including those that are phylogenetically distant, than were foreseen. It is therefore difficult to explain evolution by the addition of DNA point mutations. Secondly, it has not been

possible to decode the genetic programmes that are supposed to control embryonic development by reading these genomes. There are far fewer genes than seem necessary to explain all the functions performed by an organism. As a result of these limits to genetic determinism, we are now seeing a real change of paradigm, with the emergence of systems biology.

Instead of focusing our understanding of organisms on their DNA, we are trying to see and understand them as systems. We are seeking, in this new context, to find the balance between the influences arising from the various levels, which include the DNA, the networks of proteins, the cell tissues, the organism and the environment. This post-genomic biology requires enormous use of bio-computing to integrate the huge quantities of data collected by large-scale transcriptome and proteome analysis. The aim of these programmes is to identify all the RNAs and proteins in a cell in order to establish a map of the interactions they have with each other in the form of networks. It is thus hoped to arrive at a complete description of how a cell functions. However, scientific progress does not result simply from accumulating data. The observations made depend just as much on the theories which guide the research as on the reverse. Systems biology will not succeed in going beyond the contradictions of evolutionary synthesis unless it also resolves the original problem concerning separating evolution from embryogenesis. To do this, a new conceptual framework needs to be developed.

Ontophylogenesis (or cellular Darwinism) resolves this problem and provides a conceptual context in which DNA is not omnipotent. It breaks with traditional theories by considering embryonic development and evolution as a single process. It consists of applying Darwinism to the interior of organisms, no longer just to the DNA but also to how a cell functions as well. It thus leads to a general conception in which the question of biological individuation can be tackled from a new angle. It is this theory which is the subject of this book, in the course of which various extensions of it will gradually be discussed.

The concept of probability will first of all be analysed in order to understand the difference between determinism and probabilism. This prior clarification is necessary in order to grasp what the intrinsically probabilistic character of cellular Darwinism involves, and to differentiate it from the theories of genetics and self-organisation. The latter use the concept of noise or fluctuation but are fundamentally deterministic theories (chapter 2). The principles of genetic determinism will also be studied in detail. We shall see that they are incompatible with recent experimental data because the molecular order that they imply for explaining biological organisation does not exist (chapters 3 and 4). We shall then examine the variants of holism, theories which assert that order, instead of originating from the molecular level as in genetic determinism, originates from higher levels of organisation. The analysis will show that they are not valid alternatives, as they rely on the idea of a creative nature and a return to animism, which are purely and simply a negation of scientific rationality (chapter 5). We will then discuss ontophylogenesis, which differs from reductionism and holism in that it does not presuppose origin in biological organisation, whether concealed at molecular level or at higher levels of organisation. As a result, ontogenesis can really be considered as a process and not as the expression of a static order. The experimental data supporting it have been accumulating for more than forty years. They show that gene expression is a probabilistic phenomenon and that there exist mechanisms exerting selection on cell differentiation. In addition, computer simulations show that cellular Darwinism is in a position to generate reproducible cell structures and that chance can play a positive role in this process (chapter 6). Finally, ontophylogenesis will be placed in a wider historical and philosophical perspective, which will distinguish it as much from Aristotelian (hylemorphic) conceptions, which place the origin of organisation in Form, as from Hippocratic conceptions that place it directly in the material body taken as a whole. This analysis will again show how it differs from genetics and self-organisation which, for their part, remain within these traditional modes of thought (chapter 7).

All these developments will gradually produce support for the five main arguments for cellular Darwinism, which we shall first of all set out rather bluntly in a summarised form.

### **1.1 Ontophylogenesis**

An adult multicellular organism, comprised of numerous differentiated parts, results from the development of an embryo, which itself arises from the multiplication of a germinal cell. During this process, cells which are undifferentiated at the start become specialised and organise themselves into tissues that carry out the functions necessary for life. An organism with the characteristics of a biological species is thus produced. New germinal cells are in turn generated in this organism and the process of embryogenesis is reproduced cyclically. How can this phenomenon be explained? This is a question which is very difficult to answer.

Up until the present time, the functioning of living beings has always been interpreted in line with deterministic theories. For genetics and molecular biology, the organism is inscribed in advance in the genome as a code containing the genetic programme. The cells differentiate according to the instructions in this programme: the genes are activated in sequence during the development and synthesise specific proteins which serve as signals exchanged by the cells. Under the influence of these signals, the cells differentiate for specific purposes, a totally deterministic phenomenon which excludes chance. This theory, which poses serious conceptual problems, is now being refuted by a large number of experimental facts.

Cellular Darwinism renounces the deterministic tradition of embryology and genetics. Cells change state and differentiate because the way they function is intrinsically probabilistic. There is randomness deep inside them, in the way the genes function, where they are supposed to be controlled by the genetic programme. Depending on whether one set or another of these genes is expressed by chance, from all those that make up the genome, the cell acquires certain characteristics that correspond to a particular

differentiated state. Interactions between cells play an important role, but they do not involve signals inducing changes of state, as the theory of genetic programming supposes. Rather, they stabilise genetic expression when a viable combination of differentiated cells has been produced by the genes functioning randomly (Kupiec, 1983). The genetic expression is then frozen and the cells can no longer change their state. If a cell does not adapt to its microenvironment through this random process, it ceases to multiply and dies or becomes pathological. The conceptual structure of this model is therefore a mixture of chance and selection, analogous to the theory of natural selection but transposed to the level of cell behaviour.

However, the analogy with Charles Darwin's theory (1809–1882) goes further. According to cellular Darwinism, embryogenesis is a real extension of natural selection within organisms. Ontogenesis and phylogenesis are the two inseparable sides of a single reality produced by a unique process: ontophylogenesis. Organisms develop and evolve at the same time. Both phenomena are the result of a single mechanism (Kupiec, 1986), so for this reason, the usual definitions of the genome and the environment are not apt. Since it functions randomly, not only is the genome not the bearer of a genetic programme of rigid instructions in which the adult organism is inscribed in advance, but the conception that we have of the environment is equally incorrect. It comprises not only an external environment from which the organism is separated by a hermetic barrier, but it continues inside the organism forming the selective microenvironment of the cell, to which the latter must adapt. This conception of the cell microenvironment corresponds to Claude Bernard's 'internal environment' (1813–1878). For him, organs and cells lead an autonomous life in this internal environment (Bernard, 1878). Cellular Darwinism borrows, therefore, both from Darwin's and Bernard's theories, and consists of applying natural selection to the cells which live in the internal environment. A similarly inspired theory was put forward by Wilhelm Roux (1850–1924) in the 19th century, but it was eclipsed by the expansion of genetic conceptions (Roux, 1881).

## 1.2 Random man

The term ‘Darwinism’ nowadays no longer refers to the original theory set out by Darwin but to evolutionary synthesis. Species evolve in this context due to random mutations of DNA, which produce advantages for certain individuals in using the environment. They are selected therefore owing to their more rapid multiplication. It is a question of simplification, which eliminates the fundamental aspects of Darwin’s thought. His book *On the Origin of Species* (1859) puts forward a theory explaining the transformation of species, but also questions what a species actually is. The word ‘origin’ must be understood as meaning ‘a mechanism generating the species’ and not ‘chronological origin’ in a history of living forms, which is not what Darwin meant. He first of all considered the definition of ‘species’ and its significance. What he said about this is very surprising and runs counter to common sense. He began by defending a nominalist vision. He asserted that species do not actually exist in nature, but are abstract entities created by the classifier by arbitrarily grouping living forms together, depending on his subjective appreciation of them. Darwin’s nominalist position is nowadays totally suppressed or considered as an error of his youth corrected by the adherents of evolutionary synthesis (Mayr, 1993). As we shall see, it is this most revolutionary and most fertile aspect of his thought that contains the germ of a general theory of living beings. In contrast, genetics is not nominalist but is founded on the reality of the species. Evolutionary synthesis is thus forced synthesis between profoundly contradictory elements, which leads to a theoretical and experimental contradiction (Kupiec, 1999).

The special fields of both Bernard and Darwin have found their way into the realms of modern science, but it is unusual for the two to be brought together. Their individual areas of research seem very separate. Bernard’s is concerned with the way the organism functions internally and argues for absolute determinism, while Darwin’s concerns the organism’s relationships with its external environment,

and argues a probabilistic theory.<sup>1</sup> Earlier discussion here has already indicated the similarity between the Darwinian environment and Bernard's internal environment. Their convergence however equally concerns their epistemological conceptions. In the same way that Darwin doubted the objective reality of species, theoretical models of physiology were, for Bernard, creations of the mind, and their reality should be considered as subjective. He goes even as far as doubting the reality of physiological functions. So although nowadays it seems extremely surprising to a biologist who does not know the history of his discipline, the father of the modern theory of evolution did not believe in the reality of the species and the father of modern physiology did not believe in the reality of physiological functions! The profound significance of this shared nominalism must be analysed. It indicates radical anti-essentialism which lets us understand the living being while renouncing any finalism. Cellular Darwinism radicalises this Bernard/Darwinian anti-essentialism.

To break, indeed, with the essentialist biology of Aristotle, Descartes (1596–1650) introduced the idea of the 'Animal Machine' taking the clock as a metaphor for the organism. La Mettrie then extended it to the 'Man Machine'.<sup>2</sup> Reducing the living being to a machine means that the physiological processes follow ordinary physical and chemical laws, like the rest of nature. Living material, like inanimate material, is inert in itself. It is the forces that are each exerted on the parts of a living body<sup>3</sup> that make an organism move and endow it with vital characteristics. However, Mechanism

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<sup>1</sup> Darwin does not actually use the terminology of the theory of probability. As we shall explain in chapter 7, §7.3, his explanation of the origin of hereditary variations was ambiguous. However, it covered what nowadays we call chance variation.

<sup>2</sup> Descartes considered man to be made of two substances, the immaterial mind and the body. The metaphor of the machine only applied to the body. La Mettrie radicalised this position. For him there is only one material substance. What is called the mind only arises from the organs of thought functioning, thus producing the man machine.

<sup>3</sup> Or chemical reactions between molecules.

does not succeed in totally eliminating finalism because a machine is built by its designer according to a plan decided in advance for fulfilling a function. All the parts making it up are adjusted relative to each other to fulfil this overall purpose. Necessity rules supreme. Cellular Darwinism also considers life as an exclusively physical and chemical phenomenon, and from this point of view, it is mechanistic; but, contrary to traditional mechanism, which is fundamentally deterministic, it is based on probabilistic laws. The Man Machine, as far as cellular Darwinism is concerned, is a 'Random Man' and thus escapes totally from finalism and essentialism.

Cellular Darwinism is also different from theories of self-organisation, which postulate that matter is not inert but on the contrary has creative properties producing life. Man, according to these theories, cannot therefore arise from chance.

### **1.3 The same kind of laws govern biology and physics**

In physics, order is subjective because it is related to the level of observation at which the experimenter places himself and to the degree of accuracy that he sets. Macroscopic order at our level of existence arises from microscopic disorder. The behaviour of molecules and atoms when considered individually is intrinsically random but this molecular disorder is insignificant at the macroscopic level. Due to the huge number of particles making up systems, the individual variability of each molecule is negligible compared with the average behaviour of the whole. Erwin Schrödinger (1887–1961) spoke in this respect of the principle of 'order from disorder' which governs physics. In contrast, as regards molecular biology and genetics, biology is supposed to be subject to a principle of 'order from order'. The order is supposed to be real, intrinsic to the living thing and irrespective of the subjectivity of the observer. The macroscopic organisation of living beings is said to be produced from the microscopic order laid down in the chromosomes in the form of genetic information. This theory holds that biological molecules do not collect together according to the probabilistic laws of

physics but fit together according to the instructions relating to this information. There would therefore seem to be a difference in kind between physics and biology. In physics, order would seem to be epistemological<sup>4</sup> whereas it is supposed to be ontological<sup>5</sup> in biology. This analysis by Schrödinger (1944) is the basis for the theory of genetic programming. It has been dominating molecular biology since it started but its historical and philosophical roots are a great deal older. Genetic information is equivalent to the formal cause, or to the soul, in Aristotle's philosophy. It is an order principle which determines an invariable organisation of living beings corresponding to the species. This analogy between genetics and Aristotle's system has already been probed by the founders of molecular biology and evolutionary synthesis (Delbrück, 1971; Mayr, 1982; Mauron, 2002; Vinci and Robert, 2005) without their considering it a problem: the fact that biology uses Aristotelian concepts would only go on to show the relevance of his system. In actual fact, this theoretical structure induces contradictions which undermine the development of the molecular biology research programme.

Indeed, this Aristotelian conception of molecular biology is nowadays invalidated by the most recent observations. Contrary to what it predicts, there is very great molecular disorder in biological systems. Gene expression and interactions between proteins are not rigidly determined, but rather the reverse — they have a fundamentally probabilistic character. Cellular Darwinism goes beyond this contradiction because it takes physical and chemical probabilistic laws fully on board. The behaviour of proteins is subjected to Brownian motion and the laws of diffusion. It does not therefore, as does genetics, introduce a difference in kind between physics and biology. In this respect it is different again from theories of self-organisation which, like molecular biology, consider order to be real.

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<sup>4</sup> i.e. in the knowing subject.

<sup>5</sup> i.e. constituting that which is real, inherent in the world, irrespective of the knowing subject.

#### 1.4 The first principle of biology

The idea that philosophy no longer has very much to contribute to science is very widespread. Just as science is supposed to be capable on its own of providing us with access to real knowledge, sure of its truth owing to experimental method, philosophy is supposed only to be metaphysical speculation, of absolutely no use for scientific research. It could only be used at best to study the methodology and development of science. Seeing it this way is wrong. In all the sciences there are entities or first principles which serve as starting points. These principles are not demonstrated, but are stated *a priori* as constituting the reality. They are not intangible. For example, Newton's physics is based on three-dimensional space and absolute time. Yet this prime structure of the universe was abandoned by Einstein, which led him to work out the physics of relativity. First principles arise from ontology which is an area on the limits between science and philosophy. The choice of first principles is very important because they determine the nature of scientific theories which are constructed from them.

In biology, the question of first principles does not seem to present a problem. It can be formulated thus: What are the primordial entities of the living world? The answer seems to be obvious: when we look at the living world, we can immediately pick out individuals managing on their own, and if we compare them, we observe subsets among them of identical beings. We can thus identify an initial entity, the individual organism, and the species which is coextensive to it.<sup>6</sup> We do not doubt for a moment that these two entities really exist in nature, irrespective of any subjective divisions we make to pick them out, or theoretical suppositions that we apply. A genealogical line is then conceived as a succession of identical ontogeneses but each with its independent individual reality. This seems simple and natural and has always tended to dominate biology. Yet there is another conception, and this is the one that certain classifiers and evolutionists have tended to adopt. It consists of

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<sup>6</sup> Since a species is a set of identical individuals.

extending one's view beyond the individual to see the genealogical line as the prime entity, and no longer the organism. It is possible, indeed, to be interested in the first instance in the relationships between beings that resemble each other. The idea that then appears is that of the relationship which unites them, and is based on the material continuity of living beings occurring through the transmission of a germinal cell and its hereditary material. Earlier we recalled Darwin's nominalism. He did not cling to this negative position. Through this nominalism he rejected the essentialist definition of the species, but in its place he substituted an evolutionary definition. In his eyes, a species is a genealogical line for a group of organisms that have the same common ancestor. In such a concept, the genealogical link becomes the first principle and the organism a secondary entity produced by the process creating that link, i.e. the evolutionary process itself. The organism is an entity which has no existence except as an instant in the continuous process of reproducing organisms. This genealogical idea of the living being is implicit in Darwin and explicitly stated by Bernard (Bernard, 1878).

However, it has nowadays disappeared from contemporary physiology, and biology must confront another contradiction. Since the dawn of genetics, it has been dominated by the point of view which considers the individual organism to be a first principle, whereas living beings are historical productions, the explanation of which requires a genealogical design. Neo-Darwinian synthesis has attempted to resolve this problem but has not managed to do so, as it continues to consider ontogenesis and phylogenesis as arising from two distinct processes. Ontophylogenesis, on the other hand, removes this contradiction because it allows effective synthesis of the two points of view by combining embryogenesis and evolution in a single process.

### **1.5 Man lost in the Amazonian forest**

Another very widely held opinion consists in believing that the difficulties encountered in biology arise from the complexity of the living being. This complexity is supposed to be related to its hierarchical

organisation of one level above another: molecules, cells, tissues, organs, organisms and ecosystems. Corresponding to this structural hierarchy is said to be a hierarchy of controls leading to very complicated networks of multiple interactions between components, that cannot be described by simple laws. This hierarchical organisation seems obvious but raises the same question as that concerning species: Is it a first principle? Is it ontologically real? As concerns genetics and the theories of self-organisation the answer is positive: it would seem to be a structure helping constitute the living being. Each level seems to have properties determining how organisms function. Due to this ontological similarity, genetics and self-organisation are confronted with the same pitfalls. Self-organisation, which sets itself up as an alternative, is no more appropriate than genetics, and leads to the same contradictions.

Hierarchical organisation is not, on the other hand, a first principle for cellular Darwinism. We find it difficult to accept this idea because there is a particular epistemological obstacle to biology. This lies not in any intrinsic complexity of living beings but in the extreme difficulty we have in going beyond essentialism in our relationship with them. We always want to endow them with characteristics which differentiate them from the rest of nature. These characteristics are intrinsic, either those coded in the genetic information, or emerging and creative characteristics postulated by self-organisation.

We can understand this difficulty better using an analogy. Everyone knows the allegory of Plato's cave. Here, the situation is different. The man is not a prisoner in a cave but is lost in the Amazonian forest. He has no idea of the geoclimatic context of where he is and can never see the Amazon, the existence of which is unknown to him. Before his eyes he has this extraordinary accumulation of vegetation comprised of all sorts of plants, large and small, which are intertwined in every direction. This forest, with its innumerable details, appears to him to be extraordinarily complex and he thinks that the explanation for it must be similarly complex: he seeks a meaning and reason for each detail. Why, for example, is this particular plant exactly in this specific place and why are its

branches intertwined with those of that other plant? In this quest for meaning, he succeeds in classifying several types of plant depending on their size, and recognises thus several levels populated with living things that maintain specific relationships which seem to support this complexity: the phenomena connected with small plants that survive close to the ground, with those that occur higher towards the tops of the tall trees, and with those that are at a height in between. This structure seems to him to be inherent to the forest and even to account for it. In fact, each of these levels seems to have its own properties in terms of light, temperature, humidity and sensitivity to wind. Nevertheless, if he were to see the Amazon, he would probably understand that this apparent complexity and apparent hierarchical organisation has a simple explanation related to the abundance of water in this region, which favours the growth of luxuriant vegetation. He would also understand that the multitude of little details that make up the forest are the result of the vagaries produced during this growth, which have neither an explanation nor any particular meaning. As for the levels of organisation, they are not a constitutive structure inherent to the forest but the result of plant growth in the conditions where they are produced. If these conditions change (less water, a different temperature etc.), the structure of the forest would also change, because it is not constitutive but the result of a process conditioned by the structure of the environment.

When we analyse living matter, we are in a situation similar to this man lost in the forest. In the same way that he is unable to see the Amazon, we also have a blind spot. The idea of a natural hierarchy is intimately linked with essentialism which assumes a hierarchy of forms or essences that give structure to the world. This hierarchy ends with Man whose existence has been endowed with a meaning that emanates spontaneously from his nature. It makes him the centre of and ultimate project of Creation. We are incapable therefore of renouncing this because that would mean abandoning our privileged position and recognising in ourselves Random Man, with the loss of meaning that it implies. This prospect is a threat to our integrity and we seek to avoid it at all costs.