

## OLD AND NEW BIOLOGY

*Homo sapiens* and his “cousins” (*H. Denisovianus*, *H. Neanderthalensis*, *H. Floresensis*) are very peculiar “animals” due to the innovative organization of their brain when confronted with that of other species, Primates included. Our brain contains hundred billions of neurons liable to be organized in a million billions different configurations and is therefore a container of an incredible levels of information, much higher than the human genome only endowed with 23000 genes. Moreover, in the last part of our evolution, a small number of genes accelerated their change and allowed us to exchange ideas and concepts with an incredible speed and efficiency. Hans Jonas, a philosopher of last century, wrote that humans were different from other animals for three emblematic features, the “image”, the “tool”, the “grave”. By image he meant the capacity of developing and “imaging” in human brains original thoughts and projects not present in nature and then to modify the external matter according to them, thus adapting to changes in the environment through the planned modification of it using the constructed “tools”. The third feature proposed by H. Jonas was the “grave”, as a symbol of the capacity of transcendent thought. Humans have always been conscious of their original features and probably since the early days of civilization used them into two different ways mainly derived from two opposite conceptions of their relationship with the outer world. Particularly, one current of thought aimed at the planned “humanization” of the contexts considered as made of independent “objects”, using human-made tools. The second one on the other hand was taking into account the existence of a different category, namely living systems, that is “subjects”, liable to actively react to external human and not human inputs. We may call the two ways of thinking “mechanistic” the first and “vitalist” the second, the best description of the differences between living and not living systems ever written being in my opinion a chapter in the famous book by Jean Baptiste Lamarck “*Philosophie Zoologique*” where he says:

“The molecules of an inorganic body are all independent one from another.... On the contrary the molecules of a living body, according to their conditions depend one from another because all of them are influenced by a cause which animate them and induces them to act; because that cause induces all of them to help reaching a common goal both in single organs and in the whole individual.... Moreover, every living body is permanently animated by a specific force which, without ever stopping, induces the excitation of the movements of its interior parts continuously producing changes in the states of these parts resulting in the repair, renewals, developments and a large amount of processes present only in living beings; this induces excited movements in the interior parts which modify and destroys them but also repairs and renews them leading to the extension of the duration of the existence of the individual.”..... “Finally, no inorganic body will die because inorganic bodies never are alive. On the contrary all living bodies will inevitably are subjected to death...”... “Life, in the parts of the bodies endowed with it, is an organic phenomenon which leads to many others; and this phenomenon only derives from the relations between the parts components of this body, the fluids contained by it and moving, and the cause of the excitement and the movements and the resulting changes”. The main concepts derived from the Lamarckian vision of life, absent in non-living bodies may therefore be defined in the following way: a) The components of living systems are connected with dynamic and co-operative interactions the result of which is by no ways simply additive, meaning by that that “A” connected with “B” never forms “AB” but on the contrary leads to the formation of an unpredictable “whole” whose features may not be known through the simple study of the parts; b) The “excitability” of all living bodies, meaning by that the active response to the environment needed to preserve the specific dynamic rules of life; c) The continuous changes of life from birth to death allowing the “active” adaptation to the modifications of the environment.

One conclusion of this definition of the differences between life and “no-life”, very relevant to the discussion contained in the present paper is that living systems are “excitable subjects” while non-living ones are “objects”. It is worth stressing moreover that, if we agree with the Lamarckian definition, non-living systems are totally predictable if we know their independent components,

liable to be easily assembled without any “unintended effects” derived from interactions among them. This is not true in the case of living systems where the interaction between parts is not simply the sum of them ( $A+B=AB$ ) but rather ( $A+B=?$ ). Rather unfortunately in my opinion, human beings, very proud of their capacity of modifying the world according to projects, have very often chosen an anti-Lamarckian position and did not consider the differences between the two kinds of systems. This attitude favored what I call the “Prometeian Utopia”, that is the common feeling that humans may and should construct a totally humanized world by the assemblage of living and not living components all considered objects, therefore devoid of any capacity of unintended reactions to human actions. A side effect of this position became the concept of “possession”, by single humans, groups of them, and the whole humanity as such, of the products deriving from the development of the project. This way of thinking has been supported by the efforts of philosophers and scientists to demonstrate the “substantial equivalence” of living and non-living systems. Just to quote a few of them, René Descartes (1596–1650) attributed the contraction of muscles to a hydraulic flow of “nervous fluid” down the nerves into the muscle tissue, William Harvey (1578–1657) compared the animal heart to a pump with valves to insure one-way flow, Giovanni Borelli (1608–1679) described flight in birds as the compression of a “wedge”, etc. In the nineteenth and twentieth centuries that mechanistic view gained further considerable support by the school of Berlin scientists headed by the physicist Hermann von Helmholtz (1821–1894) who wrote the famous “Manifesto of medical materialists” of 1847, together with Ernst Brücke and Emil Du Bois-Reymond. The “Manifesto” stated that living organisms have no special “vital force,” and thus research on organisms should be based only on the known laws of physics and chemistry meaning by that that the study of single molecules (components of a system) may lead to the total knowledge of the whole. This statement, in other words completely equated living to the non-living systems discussed by Lamarck and was coherent with the human project of constructing ex-novo the world by assembling its pieces following a human project as it really happens in the case of automobiles whose components are totally independent one from the other. A well-known successor of the authors of the Manifesto has been, in the next generation, the German-born physiologist Jacques Loeb, who published a widely read book whose title *The Mechanistic Conception of Life* (1912) wholly defined the content. It is worth mentioning here that a good friend and follower of the “Medical materialists” was also Mendel, who applied their concepts to plants, studying for the first time the dynamics of inheritance of the characters of the plant “*Pisum sativum*”, choosing for his experiments only single, discrete and independent characters but avoiding quantitative ones. The choice of these characters and not others was derived from the concept of discreteness and lack of interactions between components in living systems according to the mechanistic vision of life and disregarding its multiversity, that is the presence of both discrete and interacting genes in the same organisms. Obviously Mendel found what he wanted to find, namely independent and discrete genes randomly sorted at each generation not showing any influence of the environment. In other words Mendel’s experiments have been biased by the “Spirit of his times” coherent with the general thought that humans can modify the world at will without negative unpredictable effects, thus obtaining the total possession of it. These concepts, deriving from the vision of a wholly man-made world, have been apparently confirmed in Biology when a new discipline was born in the twentieth century, namely Molecular Biology, and Francis Crick and James Watson described DNA as one string of four small molecules which they equated to the “letters” of a program (A,T,G,C), wholly defining the lives of organisms from birth to death, again independently from the environment. This statement was called the “Central Dogma of Molecular Biology”, disregarding the fact that the word “Dogma” should never be applied to scientific theories, science being the acquirement of ever-changing knowledge. It is needless to say that if this Dogma had been true we could make projects of plants and animals and then assemble their parts according to them, thus obtaining plants and animals “optimal” for our well-being. Unfortunately this has been the basic informative conception of plant and animal breeding during the so-called “Green revolution”. In those times, students of plant breeding were taught to be coherent with the “Dogma” of the so-called “Donald’s

ideo-type". According to the ideo-type, plants and animals were considered to be made of independent parts and, as a consequence, the aim of the breeder should be to improve independently all single characters after having assembled them on a piece of paper. In other words students were supposed to describe the supposedly optimal structure of each part, thus assembling a project ( the "ideotype") leading to single, totally uniform varieties for each plant and animal species and disregarding the possible interactions between parts, between the plant and animal selected and the different environments both natural, human made and social. Those omissions were based on the concepts deriving from the "Central Dogma" according to which the whole life of every living being is simply the unbiased "transcription and translation" of a single program "written" in DNA. Within this frame single genes and the whole program itself were moreover supposed to be transferred to the future generations without internal or external-driven modifications. It is worth noting that it was in this period that breeders, more and more united into larger commercial firms, started the first World-wide organisation ( UPOV) entitled to release patents on living systems ( the "cultivated varieties"= cul-tivars) thus protecting their ownership by breeders who had "selected" them. This, in my opinion, has been the final demonstration of the acceptance by humanity of the full equivalence between living and non-living systems conceptually transforming living subjects into man-made objects, thus inevitably leading to the failure of the Green revolution and later on of Genetic engineering applied to plants and animals. We know now that the reason for this failure was the total, almost religious "faith" in the "Central Dogma", challenged by science itself in the last decade of the twentieth century and in the first decade of the second millennium, when the "New Biology" allowed a better knowledge of the complex living systems, thus "falsifying" the former concepts of life. . It is worth recalling however that throughout the whole history of Biology here however that there has always been a current of thought rejecting the transformation into objects of living subject and dynamic systems, although the science of the "Modern Era" had reduced it to a minority. Let us then shortly discuss what we know now:

#### a) Living systems are "complex"

As I said before, living systems are "complex". That means that their components are not independent one from the others but rather do "communicate" and the results of the interactions among the parts are intrinsically unpredictable and always "new". This concept is easily understandable using a couple of examples. For instance if we take away the door of a car both the door and the rest of the car remain the same as they were when united. If, on the other hand we cut a finger of a living hand the finger will eventually die and the animal or human who has lost it also will change as it will bleed, the cells of his hand will try to divide thus putatively reconstructing the finger, and so-on. Another example may be the birth of a human being. In this case the child derives from the union of two different cells but his features certainly will not be predictable as they would be if the son or daughter were the result of the simple addition of the two programs "written in DNA". On the contrary, we now very well that the new-born will be a "new" complex system totally original, being derived from the union of two genomes and therefore a brand new pattern of non-additive interactions between the genes inherited by the parents. Moreover we know very-well that the result of a union among two living system will be modified during its life according to the environment and its interactions with it. To make it even more clear with an example, it is obvious that a human being, although born from a tall mother and father, may, this notwithstanding, not reach their height if he happens to belong to a poor family and therefore does not have a sufficient amount of food available. These examples therefore tell us that all living systems are composed by dynamically interacting parts, the results of their interactions being at least partially unpredictable and changing according to the environmental inputs. Now, all this shows that the so-called program written in DNA, in the real life changes in time both throughout generations but also within them. If this is true as we know that this obviously means that not necessarily the genes themselves, but rather the products of single genomes, may change with time due to the interactions between the

components within the organisms and according to the unpredictable signals coming from the interior and/or the environment.

#### b) What then about DNA?

DNA molecules, contrary to what is commonly said, are probably the most inert component of living systems not being able to be transcribed into a different molecule ( RNA) to be later translated into protein(s), but needing for that the interaction with a complex of proteins and other molecules at the end of a long chain due to start from a signal coming from inside or outside the cell. The signaling chain starts from a “receptor”, that is on or more proteins located across the membrane, an external part of which is liable to recognize specific signals from outside, the remaining part being “swimming” in the internal solution (the “cytoplasm”). When the molecular signal comes and is recognized by the receptor, the whole configuration of it changes, thus becoming liable to lead to the organization of a chain of proteins present in the cytoplasm. Eventually, the last protein of this dynamic chain will become able to form a complex with a part of the DNA to be activated, and only with that. However, this is only the start of the process of production of the protein(s) needed in this case because we know now that “genes” are highly “ambiguous”, in the sense that one gene has enough information to induce the synthesis of many different proteins each of them being constructed only in the presence of a specific signal coming from the external context. A clear proof of this apparent redundancy of gene products and its key role for life is for instance the fact that, humans are endowed with 23000 genes but may produce about one million different proteins. This is due to a series of processes developed throughout evolution capable of multiplying the number of putative proteins synthesized using the information of only one gene. This is made possible by the “ambiguity” of the different passages from DNA to RNA ( transcription), from initial RNAs to a series of RNAs, from their “translation” into chains of amino-acids, the “letters” of the proteins. The production of many different RNAs from a single gene can happen through a series of processes. We know now that RNA transcription can be initiated and stopped beginning and ending at different sites of the DNA molecule. Moreover, in animals and plants, the transcribed RNA can be cut into pieces, a part of which will be eliminated the remaining ones being connected in final molecules in different sequences, thus leading each to the production through a process called “translation”, of different amino-acid chains. Furthermore, single protein chains may be assembled into a range of functional proteins, liable to be complexed with many small molecules. All these steps determine an increase of variability of the final products each of which will be used only in the presence of specific signals coming from the environment or deriving from a modification of the internal network of a cell.

Therefore we can state that DNA is very far from containing a single program, but on the contrary is endowed with the information sufficient for building a very high number of “tools” ( the proteins) needed for the ever-changing cells and organisms, the choice of which of those should be produced in different moments and contexts is not “written” but dictated by external and internal signals. In other words evolution does not lead by any means to the construction of “optimal” organisms but, on the contrary, has been and still is increasing the number of “tools” for change or, in other words, the diversity to be used for the continuous adaptation to the ever-changing environment and internal networks. We know now, as thoroughly discussed by the book “The four dimensions evolution” published by MIT Press by E.Jablonka and F.Lamb in 2004, that living beings are using four classes of tools for the increase of diversity differentially chosen by the different groups of organisms developed throughout evolution. The four classes, according these authors, are : genetic variability, epi-genetic variability, behavioral variation, symbolic variability. Genetic variability is that coming from changes in order and nature of the “letters” of the DNA sequences ( A,T,G,C), The epigenetic differences on the other hand are changes not of the sequence but of the levels of expression of genes, leading to quantitative and qualitative changes of the final products of them but not to modifications of the DNA chains. The most relevant groups of epigenetic changes determines the blockage of single genes by the attachment to DNA of small molecules (the “methyl groups”) or the

opposite, that is their release of them and the subsequent activation of the genes involved. It is worth stressing here that both epigenetic blockages or releases can be transmitted from generation to generation without any change in DNA sequence composition and that in animals this occurs also through changes in signals coming from other members of the same or different species through modifications in their behavior. Finally, to further clarify the real nature and function of DNA, we know now that only a small part of it contains the information needed for the synthesis of proteins, the main tools of change of living beings, the remaining sequence being “non-coding” but involved in epigenetic processes from the activation and inhibition of genes to chromosome organization etc. Just to give an example of this we know that coding DNA of human beings only covers 1.5% of the total, the remaining one being non coding but very relevant for a number of epigenetic processes.

As we said, a third class of processes leading to variability is behavior, namely the “active” part of adaptation to environmental changes leading to the modification of the context by the organisms. This class of processes is particularly relevant in the organisms endowed with central nervous organization but does exist also in other ones and also in bacteria.

The fourth kind of variability, finally, is peculiar to humans as they are the species endowed with the highest level of information exchange among individuals, leading to the transmission of knowledge throughout generations.

All the four classes of variability described are present in all the organisms living on our Planet but the different groups of living beings assign to them different relevance. Bacteria, as we said before, mainly exploit genetic variability for adaptation, also due to the fact that bacterial lives are very short and therefore do not need to frequently change during them. Moreover in bacteria, mutations are immediately expressed and used, at variance with what happens in plants and animals both needing, a few generations to exploit them.

Plants may have very long lives and therefore need to change during them according to environmental modifications. This is the reason for the prevalence of epigenetic tools in this group of organisms, as also shown by the fact that it has been in plants that the first cases of epigenetic modification were described. Animals use both genetic and epigenetic tools but, particularly in those endowed with central nervous systems, fully exploit their capacity of changing behaviors, thus choosing according to the need the contexts where they are. Finally, as anticipated earlier, humans, are endowed with a brain containing hundred billion neurons liable to be connected in one million billions different configurations and therefore the amount of information of a human brain is incredibly higher of that present in our DNA . Moreover in humans a small number of genes accelerated their evolution and a specific group of them (the so-called Fox P genes) improved our capacity to exchange information through the exchange of symbols or, in other terms, words and sentences. Therefore many languages were born and with them many cultures, all leading to a previously unknown capacity of using the variability of the brain in the modification of the environment. Our main class of variation therefore is the symbolic one, an extremely powerful tool allowing the construction of projects of the transformation of our Planet although liable to unfortunately lead to the ideology of its construction and possession of living and non-living systems present on Earth.