# Code biology: A bird's-eye view

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Biosemiotics is the synthesis of biology and semiotics and its founder, Thomas Sebeok, was a student and a strong supporter of Charles Peirce, which explains why biosemiotics has been, since the beginning, a field firmly based on Peircean semiotics and Peircean philosophy.

In the history of biosemiotics, however, there has been a brief period – between 2004 and 2012 – when a serious attempt was made to build an '*extended biosemiotics*', one that was not confined into the straitjacket of the Peircean approach. Eventually, however, that attempt was officially rejected by the majority of the biosemioticians, and the result was that in 2012 a small group of people broke away from biosemiotics and founded the new research field of code biology.

The motivations of that break have been described in an article entitled "From biosemiotics to code biology" (Barbieri 2014) and will not be repeated here. The validity of that break, on the other hand, has been contested by Federico Vega in an article entitled "A critique of Barbieri's code biology through Rosen's relational biology: Reconciling Barbieri's biosemiotics with Peircean biosemiotics" (Vega 2018). This critique has already been discussed (Barbieri 2018) and will not be repeated here.

After this brief account of the beginning of code biology, this article will try to give an overall view of that field and will do so by summarizing the results obtained in the study of three problems: the first is the origin of the genetic code; the second is the origin of the other organic codes that exist in living systems; the third is the idea that there has been a universal neural code at the origin of mind as there has been a universal genetic code at the origin of life.

Code biology has proposed novel solutions in all three cases and the present article is dedicated to illustrating them, so it is ideally divided into three parts.

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## 1. The genetic code

### 1.1. Two explanations for the genetic code

In *Chance and Necessity* (1971) Jacques Monod wrote that there are two alternative explanations for the genetic code. The first is chemical, or more precisely stereochemical: "… if a certain codon was 'chosen' to represent a certain amino acid it is because there existed a certain stereochemical affinity between them". The second is that "…The code's structure is chemically arbitrary: the code as we know it today is the result of random choices which gradually enriched it" (Monod 1971: 135).

Monod declared that the first hypothesis is far more appealing but added that "the numerous attempts to verify this hypothesis have up to now proved negative. […] Pending the unlikely confirmation of this first hypothesis we are reduced to the second one, displeasing from the methodological viewpoint because it does not explain the code universality, and because it does not provide any model of primitive translation" (Monod 1971: 136).

Ten years later, in *Life Itself* (1981) Francis Crick wrote that "[…] the genetic code is as important for biology as Mendeleev's Periodic Table of the Elements is for chemistry, but there is an important difference. The Periodic Table would be the same everywhere in the universe. The genetic code appears rather arbitrary, or at least partly so. [...] If this appearance of arbitrariness in the genetic code is sustained, we can only conclude that all life on earth arose from one very primitive population" (Crick 1981: 46–47).

The '*appearance of arbitrariness*' envisaged by Francis Crick became a certainty only a few years later, because it was shown that any codon can be associated with any amino acid (Schimmel 1987; Hou, Schimmel 1988; Schimmel *et al.* 1993) thus proving that there are no deterministic links between them. It is an experimental fact, in other words, that the genetic code is made of *arbitrary rules*, and the idea of descent from a common ancestor does explain its presence in all living organisms.

One may expect that this put an end to the *stereochemical theory*, but in reality it did nothing of the kind. As the history of science has taught us, when some data are in contrast with an established theory, what happens is that a *protective belt* is built around it and it is claimed that the contrast is only apparent.

In our case the protective argument has been the idea that the genetic code is arbitrary *today*, but not at the beginning, when the code first appeared on the primitive Earth. For that event we have no direct evidence and only two theoretical options: it was either chemical determinism or

arbitrariness. The first, as Monod underlined, is "far more appealing" whereas the second is "displeasing from the methodological viewpoint" because it implies that "the code as we know it today is the result of random choices".

The arbitrariness of the code, in other words, appears to imply that its evolution is, to all practical purposes, unknowable. This is why the stereochemical theory is still holding the field, despite the fact that "[…] the numerous attempts to verify this hypothesis have up to now proved negative", a conclusion that is as valid today as it was in Monod's times.

A way out of this impasse, however, does exist, because it has been shown that the arbitrariness of the genetic code does not prevent us from reconstructing its evolution (Barbieri 2019), and the sections that follow provide a brief summary of this point.

### 1.2. The ancestral adaptors

The origin of the genetic code was due, in principle, either to chemical determinism or to arbitrariness. In the case of chemical determinism, any codon would have been associated with one and only one amino acid and there would have been no ambiguity in the code; in the case of arbitrariness, any codon could have been associated with any number of amino acids and the first genetic code that appeared on Earth would have been *ambiguous*. This means that a sequence of codons was translated some time into a protein and some other time into a different protein, and the ancestral apparatus was inevitably producing *statistical* proteins. Which in turns means that the evolution of the code was necessarily a process that reduced its original ambiguity. But how did it take place?

The rules of the genetic code are realized by *adaptors*, structures that are formed by transfer-RNAs and synthetases (more precisely *aminoacyl-tRNA synthetases*), the molecules that first activate amino acids with ATP and then attach them to the transfer-RNAs.

The transfer-RNAs are small molecules (75–90 nucleotides long) with a basic cloverleaf structure that has been highly conserved in evolution, which strongly suggests that they descended from a common ancestor. The synthetases belong instead to two distinct superfamilies and descended therefore from two ancestors. In both cases, the ancestral transfer-RNAs and the ancestral synthetases were far fewer and less diversified than their modern descendants, and this means that in the course of evolution they became increasingly *diversified* and increasingly *interdependent*, until the point was reached in which any codon was associated with one and only one amino acid and a *non-ambiguous* genetic code came into existence.

This evolution has been illustrated by Jacques Ninio (1982) with a beautiful metaphor. He pointed out that in any hotel, in addition to the familiar keys that open individual doors, there is a pass-key that opens all doors. At first, one may think that the pass-key is the most complex of all, but the truth is exactly the opposite. The pass-key is the simplest because what is complex in a key is not the ability to open a door but the ability to open one particular door *and not all the others*.

Ninio remarked that the transfer-RNAs can be compared to keys that open individual doors, whereas their common ancestor was like a pass-key that could open all doors. The evolution of the genetic code, in other words, was a process of diversification of the transfer-RNAs that steadily increased their complexity by *decreasing* the number of amino acids that they could associate to each codon.

The amino acids are attached to the transfer-RNAs by synthetases that perform two distinct operations: on one side they recognize a specific amino acid, and on another side they recognize a specific structure of a transfer-RNA. The result is that each transfer-RNA gets attached to a specific amino acid because it contains a region that is recognized only by the synthetase that is carrying that amino acid. This means that the evolution of the genetic code consisted in two parallel evolutions: one that differentiated the transfer-RNAs by evolving individual features in each of them, and one that differentiated the synthetases in such a way that they could recognize those individual features.

The transfer-RNAs, in other words, evolved in parallel with the synthetases, very much like a set of locks that evolved in parallel with a set of keys until the point was reached in which any key could fit into one and only one lock. But why did the adaptors evolve in that way? What were the *causes* that induced them to diversify and to acquire unique individual features?

### 1.3. The ancestral ribosomes

The molecular machines that make proteins, the *ribosomes*, are made of ribosomal-RNAs and ribosomal proteins. The ribosomal RNAs are among the most conserved molecules in evolution (Woese 1987; 2000) and contain regions that have the ability to form peptide bonds (Nitta *et al.* 1998). This suggests that the ribosomal-RNAs appeared very early on the primitive Earth and some of them could stick amino acids together in no specific order and produce statistical proteins (Woese 1965). The first ribosomal proteins were therefore statistical proteins, but what were their functions?

A particularly illuminating information has come from the discovery that ribosomes are formed by the self-assembly of their components and it has been possible to find out the contribution of individual ribosomal proteins by studying what happens when the ribosomes are reassembled without anyone of them in turn. These experiments have shown that the ribosomal proteins fall into three major categories: some are necessary for function, others are required for self-assembly, and those of the third group have a stimulating effect but are fundamentally disposable (Kurland 1970; Fox 2010).

At first sight there does not seem to be a reason for the presence of disposable proteins, but in reality an explanation does exist. It comes from a general principle in engineering that Burks (1970) expressed in this way: "there exists a direct correlation between the size of an automaton – as measured roughly by number of components – and the accuracy of its function". In our case, this principle means that there was an evolutionary advantage in increasing the number of ribosomal proteins because that was making the ribosomes more heavy, more resistant to thermal noise and therefore less prone to errors.

A similar principle accounts for the evolution of an increasing number of functional ribosomal proteins. Any complex system can improve its efficiency by increasing the number of controlling operations (Ashby 1962), and it is probably for this reason that the number of ribosomal proteins with functional roles did increase in evolution. The same is true for the ribosomal proteins involved in self-assembly: by increasing their number it was possible to produce ribosomes that could reassemble more easily and more efficiently from their components.

By increasing the number of the ribosomal proteins, in short, it became possible to reduce the translation errors and to improve the performance of the ribosomes in protein synthesis, and this does explain why the number of those proteins did increase in evolution. In effect, the number of ribosomal proteins is 57 in *Bacteria*, 68 in *Archaea* and 78 in *Eukaryota*, which clearly show there has been a tendency to increase their number (Lecompte *et al.* 2002). On the other hand, there are 34 ribosomal proteins which are universally conserved in all organisms and they are probably the ribosomal proteins that evolved in the primitive systems before the common ancestor split into *Bacteria*, *Archaea* and *Eukaryota*.

The increase in number of the ribosomal proteins, on the other hand, was accompanied by a parallel increase in size of the ribosomal RNAs, and the ancestral ribosomes steadily expanded their dimensions and eventually

gave origin to enormous machines with molecular weights of over 2 million in prokaryotes and over 4 million in eukaryotes. But what were the *causes* of this evolution?

### 1.4. The mechanism of ambiguity-reduction

The ancestral systems could only produce statistical proteins and yet life went on and evolved even in those times. There were two main reasons for this. The first is that the primary functions were performed by the RNAs and these molecules were fairly faithfully transmitted from one generation to the next by molecular copying. The second is that the same protein functions could be implemented by different molecules, and life could continue even if the proteins of the descendants were slightly different from those of the progenitors. More precisely, life could continue even if the progenitors transmitted to the descendants the same RNAs and the same *families* of statistical proteins. There was however a condition that had to be met: the statistical proteins of a progenitor could reappear in a descendant only if the statistical differences between them were not cancelled out by the ambiguity of the genetic code.

The ancestral systems, in other words, could produce viable descendants only if the ambiguity of the genetic code was low enough to allow the same families of statistical proteins to reappear in each generation. This amounts to saying that the ambiguity of the genetic code could not exceed a prefixed limit, but within that limit the ancestral systems could go on indefinitely producing descendants that were statistically similar to the progenitors.

Evolution was bound to favour any improvement in the translation apparatus of the ancestral systems, and we have seen that the translation errors could be reduced by increasing the number of the ribosomal proteins. This increase, on the other hand, could be *perpetuated* only if a higher number of protein families could reappear in the descendants, and this was possible only if the ambiguity of the genetic code was reduced. The ambiguity of the code, in turn, could be reduced only by increasing the number and the diversity of the synthetases that were attaching amino acids to the transfer-RNAs.

An increase of the ribosomal proteins, in short, was favoured by evolution because it was reducing the translation errors, but could be achieved only by reducing the ambiguity of the genetic code, and this in turn could be achieved only by increasing the number of the synthetase proteins.

The evolution of the ribosomal proteins and the evolution of the synthetases, in other words, were two interdependent processes and both were favoured because the first was reducing the translation errors and the second was reducing the ambiguity of the genetic code (Barbieri 2019).

The synthetases and the ribosomal proteins, in conclusion, evolved in parallel and the mechanism at the heart of their evolution was a systematic reduction in the ambiguity of the genetic code, a reduction that went on until any ambiguity was completely erased. At that point any sequence of codons was translated into one and only one protein and *biological specificity* came into existence.

The above scenario may look entirely speculative, at first, but in reality it does have consequences that can be tested. It implies, for example, that the universal ribosomal proteins and the synthetases were the first *specific* proteins that appeared in the history of life, and this is in agreement with the molecular phylogenies (Woese 2000; Fox 2010; Petrov *et al*. 2015).

What is particularly important, in our case, is that chemical determinism is no longer a theoretical necessity. The arbitrariness of the genetic code is an experimental reality but its existence does not prevent us from reconstructing the evolution of the genetic code.

## 2. The organic codes

### 2.1. From the common ancestor to the first cells

The fact that all living organisms contain a virtually universal genetic code implies that that code evolved in a population of primitive systems that is known as the *common ancestor*. The phylogenetic trees, on the other hand, have shown that all cells belong to three primary kingdoms, *Archaea*, *Bacteria* and *Eukaryota*, and the first cells that appeared on Earth were the first representatives of these kingdoms (Woese, Fox 1977; Woese *et al*. 1990; Woese 2000). The cells share a few universal features in all kingdoms, but most of their characteristics are unique to each kingdom, which means that they evolved independently in the descendants of the common ancestor. They have, in particular, different types of cell membrane, and this gives us a major evolutionary problem.

The cell membrane is the site of two fundamental processes – the exchange of matter and energy with the environment– but it is also the site of *signal transduction*, the process that transforms the signals from the environment (*first messengers*) into internal signals (*second messengers*). First

and second messengers belong to two independent worlds and laboratory experiments have shown that the same first messenger can activate different second messengers and that different first messengers can activate the same second messenger (Alberts *et al.* 2007) which means that there are no necessary connections between them.

The membrane receptors that implement signal transduction, furthermore, are molecular adaptors that create links between first and second messengers just as the transfer-RNAs create links between codons and amino acids. In signal transduction, in short, we find all the essential components of a code: (a) two independents worlds of molecules (first messengers and second messengers), (b) a set of adaptors that create a mapping between them, and (c) the proof that the mapping is arbitrary because its rules can be changed in many different ways. All of which amounts to saying that signal transduction is based on *signal transduction codes* (Barbieri 2003), and we have the problem of understanding why did they evolve.

The origin of the genetic code was a major turning point in the history of life, and yet it was not enough to create a modern cell. The reason is that the descendants of the common ancestor could produce specific proteins but not *specific responses to the environment* because they had not yet evolved an efficient system of interactions with the outside world. They had biological specificity in protein synthesis, but not in their relationships with the environment. This suggests that the descendants of the common ancestor evolved along independent lines and gave origin to distinct types of cells by combining the universal genetic code with different types of signal-transduction codes (Barbieri 2016).

The genetic code and the signal transduction codes appeared very early in the history of life and have been highly conserved ever since. In addition to these foundational codes, however, many other organic codes have been discovered in living systems. Among them, the *sequence codes* (Trifonov 1989, 1996, 1999), the *sugar code* (Gabius 2000, 2009), the *splicing codes* (Barbieri 2003; Fu 2004; Wang, Cooper 2007), the *histone code* (Strahl and Allis 2000; Turner 2000, 2007; Kühn, Hofmeyr 2014), the *compartment codes* (Barbieri 2003), the *tubulin code* (Verhey, Gaertig 2007; Janke 2014), the *ubiquitin code* (Komander, Rape 2012), the *molecular codes* (Görlich *et al.* 2011; Görlich, Dittrich 2013; Dittrich 2018) and the *lamin code* (Maraldi 2018). Our next problem, therefore, is to find out the roles that these codes had in life.

### 2.2. Two types of evolution

The reconstruction of the molecular trees of life was first obtained by comparing individual molecules in different species (Zuckerkandl, Pauling 1965; Woese, Fox 1977), but a much more powerful approach became possible by comparing entire genomes (Snel *et al*. 2005; Jun at al 2010). One of the most important results of this extended technology was the discovery that all modern eukaryotes belong to 5 or 6 major groups that radiated from a common ancestor (Baldauf 2003; Adl *et al*. 2005; Keeling *et al*. 2005).

This tells us that there have been two major events in the evolution of the cells. The first was the appearance of a population of primitive systems that evolved the genetic code and has become known as the *Last Universal Common Ancestor* (LUCA); the other was the appearance of the *Last Eukaryotic Common Ancestor* (LECA) the population from which all modern eukaryotes have descended.

The universal ancestor appeared around 3.5 billion years ago, whereas the eukaryotic ancestor arrived two billion years later, around 1.5 billion years ago (Harold 2014). The crucial point is that throughout that immensely long period the evolution of the cells took place in two completely different ways.

The fossil record has revealed the presence of fossilized bacteria in Precambrian rocks, and has shown that the stromatolites built by cyanobacteria two and three billion years ago are virtually identical to those built by their modern descendants (Barghoorn, Tyler 1965; Knoll 2003). The bacteria, in other words, appeared very early in the history of life and have conserved their complexity (in terms of size, shape and number of components) ever since. This point has been beautifully illustrated by Nick Lane: "... the bacteria and archaea have barely changed in 4 billion years of evolution. There have been massive environmental upheavals in that time. The rise of oxygen in the air and oceans transformed environmental opportunities, but the bacteria remained unchanged. Glaciations on a global scale (snowball earths) must have pushed ecosystems to the brink of collapse, yet bacteria remained unchanged. [...] Nothing is more conservative than a bacterium" (Lane 2015: 158).

The eukaryotes, instead, did the opposite. They repeatedly increased the complexity of their cells and eventually broke the cellular barrier and gave origin to countless multicellular creatures. This gives us a major problem: why have the prokaryotes *not* increased their complexity throughout the history of life while the eukaryotes have become increasingly more complex?

An unexpected solution to this problem has come from the discovery that the eukaryotes evolved many more organic codes than prokaryotes. This suggests that the prokaryotes did not become more complex because they did not evolve new organic codes whereas the eukaryotes increased their complexity because they continued to bring new organic codes into being (Barbieri 2017).

### 2.3. Codes and complexity

In prokaryotes there are far less organic codes than in eukaryotes, but can we explain that experimental fact? A natural explanation does exist, and is suggested by the fact that the prokaryotes became committed to fast replication and adopted a drastic *streamlining strategy* in order to achieve that goal. Let us illustrate this point with two examples.

In bacteria, the transcription of the genes is immediately followed by their translation into proteins, but such a fast link could hardly have been present in the ancestral systems. A direct coupling between transcription and translation required the abolition of all intermediate steps and could be achieved only by the descendants of the common ancestor that adopted a streamlining strategy. The other descendants maintained a physical separation between transcription and translation and this allowed them to introduce the operations of splicing in between. The prokaryotes, in other words, could not evolve a splicing code simply because they had abolished the separation between transcription and translation that is the very precondition of splicing.

A second example comes from the histone code. The ancestral DNAs were negatively charged molecules that inevitably attracted positively charged ones, but in order to maximize the replication rate it was necessary to remove any interposition of material between genes and signalling molecules, and this is why the streamlining strategy produced genes with no protein wrapping around them. Some ancestral systems, however, did not follow that strategy and continued to carry genes surrounded by positively charged molecules that eventually evolved into histones. The potential to evolve the histone code, in other words, survived only in the descendants of the common ancestor that did not adopt the streamlining strategy of the bacteria.

We have in this way a solution to the problem of complexity: the cells that adopted a streamlining strategy lost the potential to evolve new organic codes and have conserved the same complexity throughout evolution; the

cells that did not adopt a streamlining strategy maintained the potential to evolve new organic codes and gave origin to increasingly complex systems (Barbieri 2017).

Another increase in complexity took place with the origin of multicellular creatures, and here too we find that new levels of complexity were associated with new organic codes. Among them: the *Hox* code (Hunt *et al.* 1991; Kessel, Gruss 1991), the *adhesive code* (Redies, Takeichi 1996; Shapiro, Colman 1999; Faria 2018), the *transcriptional codes* (Jessell 2000; Marquard, Pfaff 2001; Ruiz i Altaba *et al.* 2003), the *apoptosis code* (Basañez, Hardwick 2008; Füllgrabe *et al.* 2010), the *bioelectric code* (Tseng, Levin 2013; Levin 2014) and the *acoustic codes* (Farina, Pieretti 2014; Farina 2018).

The experimental evidence, in conclusion, does suggest that there is a link between the complexity of the living systems and the number of their organic codes.

## 3. The neural codes

### 3.1. Hints of a universal neural code

There is a large consensus today that mind is a natural phenomenon and that mental events are caused by brain events. More precisely, it is widely accepted that mind is made of higher-level brain processes, such as feelings and instincts, that are caused by lower-level brain processes such as neuron firings and synaptic connections (Searle 2002). We need therefore to understand *how* does the brain produce the mind and to this purpose it is useful to start from what all animals have in common.

There is ample evidence that virtually all animals have the same basic instincts and feelings. They all have the imperative to *survive* and to *reproduce*. They all experience hunger and thirst, fear and aggression, and all are capable of reacting to stimuli such as light, sound, pressure and temperature. The basic feelings and instincts, in short, are virtually universal in animals, and this means that they appeared in an ancestral animal population and have been highly conserved ever since.

The conservation of the basic instincts and feelings, on the other hand, has been accompanied by an explosive diversification of the brain, a pattern that has also been observed in the evolution of the cell, where the genetic code has been highly conserved whereas the apparatus of protein synthesis has continued to change. In both cases we have a system where virtually everything is on the move, except a fundamental set of rules, and this strongly

suggests that a neural code has been highly conserved after its appearance in a common ancestor. This conclusion is also suggested by comparative anatomy.

The processes of the brain are set in motion by signals from the sense organs, but these organs arise from the histological tissues of the body, and these tissues (epithelial, connective, muscular and nervous tissues) are the same in all triploblastic animals. All signals that are delivered to the brain, in other words, are produced by sense organs that arise from a limited number of universal tissues, and represent therefore a limited number of universal *inputs*. The basic feelings and instincts, on the other hand, are found in all triploblastic animals and represent a limited number of universal *outputs*.

What we observe, in short, is a universal set of sense organs on one side, a universal set of animal instincts and feelings on the other side, and a set of neural processes in between. The most parsimonious explanation is that the neural processes in between are also a universal set of operations. And since there is no necessary link between sense organs and instincts or sense organs and feelings, we conclude that the bridge between them is provided by the rules of a *universal neural code*.

The existence of a universal neural code, in other words, is the most parsimonious explanation of the fact that the basic animal instincts and feelings have been conserved in evolution. But of course we would like more evidence in support of this conclusion, and there is in fact a variety of research results that point in that direction.

### 3.2. A variety of neural codes

The Nobel Prize for Medicine in 2014 was awarded to John O'Keefe, May-Britt Moser and Edvard Moser for the discovery that the cells of the hippocampus use the rules of a unique space code to build an internal map of the environment (O'Keefe, Burgess 2005; Hafting *et al*. 2005; Brandon, Hasselmo 2009).

The existence of a space code in the hippocampus is based on solid experimental evidence and this is important because the neural codes are much more difficult to grasp than the organic codes. The difference between them comes from the fact that organic molecules are *space-objects*, in the sense that their properties come from their three-dimensional organization in space, whereas neural states are *time-objects* in the sense that they arise from sequences of neuron firings in time.

Despite this objective difficulty in the study of the neural codes, a significant number of results has already been obtained. It has been discovered, for example, a *neural code for mechanical stimuli* (Nicolelis, Ribeiro 2006; Nicolelis 2011), a *neural code for taste* (Di Lorenzo 2000; Hallock, Di Lorenzo 2006), a *synaptic code* for cell-to-cell communication (Hart *et al*. 1995; Szabo, Soltesz 2015) and an *olfactory code* (Grabe, Sachse 2018). The processing of many neural signals, in other words, takes place according to codified rules, and our purpose is to figure how they came into being.

The nervous system is made of three types of neurons: (1) the *sensory neurons* transmit to the brain the signals produced by the sense organs, (2) the *motor neurons* deliver signals from the brain to the motor organs (muscles and glands), and (3) the *intermediate neurons* provide a bridge between them. In some cases the sensory neurons are directly connected to the motor neurons, thus forming a *reflex arch*, a system that produces a quick stimulus-response effect known as *reflex action*.

The first nervous systems were probably a collection of reflex arches, as it is still the case in a few primitive animals, and it is likely that the first intermediate neurons evolved as an extension of those arches. Once in existence, however, in addition to *transmitting* electrical signals they started *processing* them and this new function fuelled their evolution into increasingly complex systems. This is because the behaviour of an animal must take into account a variety of cues from the environment, and to that purpose it is necessary that a motor organ receives signals from many sense organs and that a sense organ delivers signals to many motor organs.

The intermediate neurons solved that problem by developing multiple connections between sensory inputs and motor outputs, but they evolved in two very different directions. One was the formation of neural networks that are totally non-conscious and provide a sort of *automatic pilot* for the body. The other was the generation of *sensitive neural states*, the precursors of instincts and feelings, and it was this second process that started evolving the neural codes of the conscious brain.

### 3.3. The revolution of the universal neural code

Instincts and feelings are referred to as *first-person* experiences because they are experienced directly, without intermediaries. They make us feel that we *control* our body, that we are in charge of its movements, that we live a personal life. Above all, they are quintessentially *private* internal states, and this makes it impossible to share them with other people.

The goal of science is to produce models of what exists in nature, and first-person experiences are undoubtedly part of nature, so we need models that help us to understand them.

Let us take, for example, the case in which a toe is injured. We know that signals are immediately sent to the brain that processes them and delivers orders to the motor organs that spring the body into action. Here we have two distinct players where one (the brain) is the observer and the other (the injured toe) is the observed. It is the observer that receives signals from the toe and transforms them into a feeling of pain, but then something extraordinary happens. We do not feel the pain in the brain, where the feeling is created, but in the toe. Observer and observed have collapsed into one, and the feeling is displaced to the place that gave origin to the whole neurological process.

Something similar takes place when we receive signals from the environment, for example when we look at a tree. In this case, an image is formed on the retina and the retina sends signals to the brain. Again, there is a physical separation between the sender and the receiver of signals, and yet we do not see an image on the retina, where the visual signals are generated, nor in the brain, where they are processed. What we see is a tree in the outside world. This again is generated by a short-circuit between observer and observed followed by a displacement of the end result to the place where the process originated.

This tells us that first-person experiences are nothing elementary and indivisible. On the contrary, they are the result of complex operations where highly differentiated cells act in concert to create a physiological short-circuit between body and brain, between observer and observed, between senders and receivers of neural signals. That kind of complexity was necessarily the result of an evolutionary process that was set in motion when feelings and instincts started playing specific roles in animal behaviour, i.e., when the universal neural code came into being.

The origin of this code, in other words, set in motion a true biological revolution, a major transition that transformed the non-conscious brain of the ancestral animals into the feeling brain of the modern animals. The result was an absolute novelty: it was the origin of *consciousness*, the origin of *subjectivity*, the origin of *first-person* experiences, in short, the origin of *mind*.

This is the *code theory of mind*, the idea that there has been a *universal neural code* at the origin of mind as there has been a universal genetic code at the origin of life; it is also the idea that there are neurological processes

that create short-circuits between brain and body and give origin to first-person experiences, to the feeling that we are conscious beings and not automatons (Barbieri 2011, 2015).

## Conclusion

Today there are two major paradigms in biology. One is the idea that '*life is chemistry*' or, more precisely, '*an extremely complex form of chemistry*'. The other is the idea that '*life is chemistry plus information*', a paradigm based on the view that hereditary information does not exist in inanimate matter and is *ontologically* different from chemistry. The nature of this ontological difference has been the object of countless debates but a shared conclusion has never been reached, and this explains why the *chemical paradigm* and the *information paradigm* continue to exist side by side. The discovery of the genetic code, on the other hand, has brought to light another fundamental component of the living systems, and this has raised a challenge to both paradigms.

A code is a set of rules that establish a correspondence between the objects of two independent worlds, and can be described as *a mapping between signs and meanings*. Saying that there is a correspondence between object 1 and object 2, is equivalent to saying that object 1 is the *sign* of object 2, or that object 2 is the *meaning* of object 1. In the Morse code, for example, the rule that 'dot-dash' corresponds to letter 'A', is equivalent to saying that letter 'A' is the meaning of 'dot-dash'. In the same way, the rule that a codon corresponds to a certain amino acid is equivalent to saying that that amino acid is the *organic meaning* of that codon.

Meaning, in short, is the inevitable product of a code because there cannot be codes without meaning (Barbieri 2003). All we need to keep in mind, is that meaning is a mental entity when the code is between mental objects, but it is an organic entity when the code is between organic molecules. Meaning, on the other hand, is ontologically different not only from matter and energy but also from information, and this tells us that it cannot be accommodated into the two existing paradigms.

The discovery of the genetic code, in other words, suggests that biology requires a third paradigm, a theoretical framework that can be referred to as the *code paradigm* because it states that "*life is chemistry, information and codes*".

The idea that meaning is a natural entity, ontologically distinct from matter, energy and information has been proposed more than 30 years ago, in *The Semantic Theory of Evolution* (Barbieri 1985) but of course it can be accepted by the scientific community only if it is proved that the genetic code is a real code and not a metaphorical entity. Now this proof has finally arrived and we can look forward to a future where biology fully acknowledges that meaning is a fundamental component of life.

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