ORIGINAL PAPER

Origin and Evolution of the Brain

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Abstract Modern biology has not yet come to terms with the presence of many organic codes in Nature, despite the fact that we can *prove* their existence. As a result, it has not yet accepted the idea that the great events of macroevolution were associated with the origin of new organic codes, despite the fact that this is the most parsimonious and logical explanation of those events. This is probably due to the fact that the existence of organic codes in all fundamental processes of life, and in all major transitions in the history of life, has enormous theoretical implications. It requires nothing less than a new theoretical framework, and that kind of change is inevitably slow. There are too many facts to reconsider, too many bits of history to weave together in a new mosaic. But this is what science is about, and the purpose of the present paper is to show that it can be done. More precisely, it is shown that the whole natural history of the brain can be revisited in the light of the organic codes. What is described here is only a bird's-eye view of brain macroevolution, but it is hoped that the extraordinary potential of the organic codes can nevertheless come through. The paper contains also another message. The organic codes prove that life is based on semiosis, and are in fact the components of *organic semiosis*, the first and the most diffused form of semiosis on Earth, but not the only one. It will be shown that the evolution of the brain was accompanied by the development of two new types of sign processes. More precisely, it gave origin first to *interpretive semiosis*, mostly in vertebrates, and then to *cultural semiosis*, in our species.

Keywords Organic codes · Macroevolution · Origin of brain · Origin of mind · First-person experiences · Organic semiosis · Modelling systems

Introduction

The genetic code appeared on Earth at the origin of life, whereas the codes of culture arrived almost four billion years later. This may give the impression that evolution

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went on for almost the entire history of life without producing any other code, but that is not what happened. Many other organic codes came into being, and we can actually *prove* their existence with the very same procedure with which we have proved the existence of the genetic code (Barbieri 2003, 2008).

Any code is a set of rules of correspondence between two independent worlds, and is necessarily implemented by structures, called *adaptors*, that perform two independent recognition processes. The genetic code, for example, is a set of rules that link the world of nucleotides to the word of amino acids, and its adaptors are the transfer-RNAs. The adaptors are required because there is no necessary link between the two worlds, and a set of rules is required in order to guarantee the specificity of the correspondence. The adaptors, in short, are essential components in all organic codes and their presence in a biological process is a sure sign that that process is based on a code.

Signal transduction, for example, creates a link between first and second messengers, but these molecules belong to two independent worlds because any first messenger can be coupled with any second messenger (Alberts et al. 1994). Without adaptors there would be no bridge between the two worlds, and without the rules of a code there would be no biological specificity. The signal receptors of the cell membrane have in fact the defining characteristics of true adaptors and this reveals the existence of a *signal transduction code* (Barbieri 1998, 2003). Molecular adaptors have also been found in many other biological processes, thus bringing to light the existence of *splicing codes*, *cell compartment codes* and *cytoskeleton codes* (Barbieri 2003, 2008). Other organic codes have been discovered with different criteria. Among them, the *metabolic code* (Tomkins 1975), the *sequence codes* (Trifonov 1987, 1989, 1996, 1999), the *adhesive code* (Redies and Takeichi 1996; Shapiro and Colman 1999), the *sugar code* (Gabius 2000; Gabius et al. 2002), the *histone code* (Strahl and Allis 2000; Turner 2000, 2002; Gamble and Freedman 2002), the *transcriptional codes* (Jessell 2000; Marquardt and Pfaff 2001; Perissi and Rosenfeld 2005; Flames et al. 2007), a *chromosome folding code* (Boutanaev et al. 2005; Segal et al. 2006), an *acetylation code* (Knights et al. 2006), the *tubulin code* (Verhey and Gaertig 2007), and the *splicing code* (Pertea et al. 2007; Barash et al. 2010; Dhir et al. 2010).

The living world, in short, is literally teeming with organic codes, and this means that at some point in history they came into being. They had origins and evolutions and we simply cannot write the history of life without them. This paper is an attempt to reconstruct the history of the brain by taking the organic codes into account, and to this purpose it is divided into two parts. The first is about the events that culminated in the origin of the brain. The second is dedicated to the evolution of the brain.

PART 1 — The Origin of the Brain

Organic Codes and Macroevolution

The existence of many organic codes in Nature is an experimental fact—let us never forget this—but also more than that. It is one of those facts that have extraordinary theoretical implications. It suggests that the great events of macroevolution were

associated with new organic codes, and this idea—the *code view of life*—gives us a totally new understanding of history. It is a view that paleontologists have never considered before and yet we have at least one outstanding example before our eyes. We know that the very first event of macroevolution—the origin of life itself—was associated with the genetic code, because it was that code that brought biological specificity into existence. But let us examine a few other examples of the deep link that exists between organic codes and macroevolution.

(1) The three domains of life

     The data from molecular biology have revealed that all known cells belong to three distinct primary kingdoms, or domains, that have been referred to as Archaea, Bacteria and Eucarya (Woese 1987, 2000). The fact that virtually all cells have the same genetic code suggests that this code appeared in precellular systems that had not yet developed a modern cell design. According to Woese, those systems were not proper cells because they had not yet crossed what he called the "Darwinian threshold", an unspecified critical point after which a full cell organization could come into being (Woese 2002). According to the code view, the ancestral systems that developed the genetic code were not modern cells simply because they did not have a signal transduction code. It is this code that gives a context-dependent behaviour to a cell because it allows it to regulate protein synthesis according to the signals from the environment. A signal transduction code was therefore of paramount importance to the ancestral systems, which explains why there have been various independent attempts to develop it. It is an experimental fact, at any rate, that Archaea, Bacteria and Eucarya have three distinct signalling systems, and this does suggest that each domain arose by the combination of the universal genetic code with three distinct signal-transduction codes.

(2) The difference between prokaryotes and eukaryotes

     According to the code view, the ancestral cells of the three primary kingdoms adopted strategies that channelled them into two very different evolutionary directions. Archaea and Bacteria chose a *streamlining* strategy that prevented the acquisition of new organic codes and for that reason they have remained substantially the same ever since. The Eucarya, on the contrary, continued to explore the 'coding space' and evolved new organic codes (splicing codes, compartment codes, histone code, etc.) throughout the whole three thousand million years of cellular evolution. In this theoretical framework, the key event that gave origin to the eukaryotes was the appearance of the splicing codes, because splicing requires a separation *in time* between transcription and translation, and this was the precondition for their separation *in space*, a separation that eventually became physically implemented by the nuclear membrane.

(3) The origin of multicellular life

     Any new organic code brings into existence an absolute novelty, something that has never existed before, because the adaptors of a code create associations that are not determined by physical necessity. Any new organic code was therefore a true macroevolution, a genuine increase in complexity, to the point that the best measure of the complexity of a living system is probably the

number of its organic codes. This means that the evolution of the eukaryotes was due to a large extent to the addition of new organic codes, a process that turned the eukaryotic cells into increasingly more complex systems. Eventually, however, the complexity of the cell reached a limit and new organic codes broke the cellular barrier and gave origin to three completely new forms of life, the great kingdoms of plants, fungi and animals (Barbieri 1985, 2003).

The Codes of the Body-Plan

The origin of animals was a true macroevolution, and gives us the same problem that we face in all major transitions: how did real novelties come into existence? In the case of the first animals the starting point was a population of cells that could organize themselves in space in countless different ways, so how did they manage to generate those particular three-dimensional structures that we call animals?

The solution was obtained by three types of experiments. More precisely, by the attempts to form multicellular structures with one, two or three different types of cells (the *germ layers*). The experiment with one cell type produced bodies which have no symmetry (the sponges); two cell types built bodies with one axis of symmetry (the *radiata* or diploblasts, i.e., hydra, corals and medusae), and three cell types gave origin to bodies with three axes of symmetry (the *bilateria* or triploblats, i.e., vertebrates and invertebrates) (Tudge 2000). In principle, the number of three-dimensional patterns that the first animal cells could form in space was unlimited, so it was imperative to make choices. These choices, or constraints, turned out to be sets of instructions that specify a body-plan. More precisely the cells are instructed that their position is anterior or posterior, dorsal or ventral and proximal or distal *in respect to the surrounding cells*. These instructions are carried by genes, and consist of molecules which are referred to as the *molecular determinants* of the body axes (Gilbert 2006).

The crucial point is that there are countless types of molecular determinants and yet all triploblastic animals have the same axes (top-to-bottom, back-to-front and left-to-right). This shows that there is no necessary link between molecular determinants and body axes, and that in turns means that the actual links that we find in Nature are based on conventional rules, i.e., on the rules of organic codes that can be referred to as the *codes of the body-axes*.

It must be underlined that the relationships of the body axes are between *cells*, and this means that they do not determine only the axes of the body, but also those of all its constituent parts. In the hand, for example, the proximo-distal axis is the direction from wrist to fingers, the antero-posterior axis is from thumb to little finger, and the dorsal-ventral axis is from the outer surface to the palm of the hand. Right and left hands have different symmetries because their axes are one the mirror image of the other. There is therefore a multitude of axes in the animal body, and it turns out that many of them have the same molecular determinants. The products of the gene *Sonic hedgehog* (*Shh*), for example, determine the dorso-ventral axis of the forebrain as well

as the antero-posterior axis of the hand, which again shows that molecular determinants are mere labels and represent the conventional rules of a code.

The antero-posterior axis of the body (the head-to-tail direction), is determined by two small depressions that are formed very early on the outer surface of the embryo and that mark the signposts of mouth and anus. Between those two points, a third depression is produced by the movements of a colony of migrating cells that invade the space between the first two germ layers (ectoderm and endoderm) to form the middle germ layer (the mesoderm). The invagination point (the blastopore) can be set either near the mouth-signpost (the *stomodeum*) or near the anus-signpost (the *proctodeum*) and that choice determines the future organization of all organs in the body. The animals where the blastopore is formed near the signpost of the mouth (*stoma*) are invertebrates (technically *protostomes*): they have an outside skeleton, a dorsal heart and a ventral nervous system. The animals where the blastopore is formed away from the mouth signpost are vertebrates (more precisely *deuterostomes*): they have an inside skeleton, a ventral heart and a dorsal nervous system.

The whole organization of the body, in other words, is a consequence of a few parameters that determine the migrations of the mesoderm in respect to the body axes. The crucial point is that these migrations (the *gastrulation* movements) take place in countless different ways in both vertebrates and invertebrates, and this shows that they are not due to physical necessity but to the conventional rules of a *gastrulation code*. We realize in this way that the three-dimensional organization the animal body is determined by a variety of organic codes that together can be referred to as the *codes of the body-plan*.

Cell Fate and Cell Memory

All free-living cells, from bacteria to protozoa, react swiftly to environmental changes, but the cells of multicellular animals have a more sophisticated behaviour. Their reactions do not take into account only their present conditions but also their history. This is because in embryonic development the cells learn not only to become different, but also to *remain* different. They acquire, in short, a *cell memory*. In technical terms, they go through embryonic processes that fix their *histological* fate for the rest of their life.

This great discovery was made by Hans Spemann, in 1901, by studying what happens when small pieces of tissue are transplanted from one part of an embryo to another. Spemann found that the embryonic cells can change their histological fate (skin cells, for example, can become nerve cells) if they are transplanted *before* a critical period, but are totally unable to do so if the transplant takes place *after* that period. This means that for every cell type there is a crucial period of development in which *something* happens that decides what the cell's destiny is going to be, and that something was called *cell determination*.

Other experiments proved that determination does not normally take place in a single step but in stages, and that the number and duration of these stages vary from one tissue to another. The most impressive property of determination is the

extraordinary stability of its consequences. The process takes only a few hours to complete but leaves permanent effects in every generation of daughter cells for years to come. The state of determination, furthermore, is conserved even when cells are grown in vitro and perform many division cycles outside the body. When brought back in vivo, they express again the properties of the determination state as if they had never 'forgotten' that experience (Alberts et al. 1994).

The determination of cell fate, in short, amounts to the acquisition of a *cell memory* that is maintained for life and is transmitted to all descendant cells. The various steps of determination are controlled by molecules, known as *molecular determinants*, which can be passed on by the mother on fertilization or produced by the embryo at various stages of development. The crucial point is that the basic histological tissues are the same in all animals, but their molecular determinants are of countless different types, which shows that the link between determinants and histological fate is not dictated by physical necessity but by the rules of codes that have been referred to as *histological codes*, or *transcriptional codes* (Jessell 2000; Marquardt and Pfaff 2001; Perissi and Rosenfeld 2005; Flames et al. 2007).

This is dramatically illustrated by the most fundamental of all cell distinctions, that between somatic and sexual cells. In *Drosophila*, for example, that distinction is determined by the *pole plasm*, a substance that is deposited by the mother at the posterior end of the egg. All cells that receive molecules from the pole plasm become sexual cells and are potentially immortal, whereas all the others become somatic cells and are destined to die with the body. The distinction between somatic and sexual cells takes place in all animals but is produced by widely different molecules, in some cases produced by the mother and in other cases by the embryo, all of which shows that it is an outstanding example of histological code.

During embryonic development, in conclusion, the cells undergo two distinct processes of determination: one for their three-dimensional pattern and the other for their histological fate. Both processes are totally absent in free-living cells, which again shows that the origin of animals was a true macroevolution. Both processes, furthermore, are based on conventional rules of correspondence between molecular determinants and cell states because the determinants can be of countless different physical types. In all animals, in other words, the body plan and the histological fate of tissues and organs are based on the rules of organic codes.

Evolving the Neuron

The organs of an animal are not larger versions of the cell organelles, but there is nonetheless a parallel between them because there is a similar division of labour at the two different levels of organization. The same basic proteins, for example, are expressed in the muscles of an animal and in the contracting region of a cell, so it is likely that the evolution of the animal organs took advantage of the molecular mechanisms that had been developed in the organelles and compartments of the ancestral protozoa.

This makes sense from an evolutionary point of view, and suggests that the first animals already had the potential of expressing an internal division of labour. Some of their cells, for example, could preferentially express the genes of locomotion, thus becoming the precursors of the future motor organs. Other cells could preferentially express the genes of signal transduction and become the precursors of the future sense organs. A third type of cells could establish a link between them and prefigure in this way the future *nervous system* because this system is, by definition, a bridge between sense organs and motor organs. Whatever happened, at any rate, we know that the cells of the nervous system have two key characteristics, both of which could be obtained by modifying pre-existing protozoan structures.

The first major feature of the neuron is the ability to communicate with other cells by chemicals that are released from vesicles at points of close contact between their cell membranes (the synapses). It is those vesicles that provide the components of the brain signalling system, but they did not have to be invented from scratch. They are very similar to the standard vesicles that exist in all eukaryotic cells and are routinely used for transporting molecules across membranes.

The second great feature of the neuron is the ability to transmit electrical signals, and this too can be explained with a modification of pre-existing structures. The cell is constantly exchanging molecules with the environment and most of them are electrically charged, so there is a constant flux of positive and negative ions across the cell membrane. These ions can travel only through channels provided by specialized proteins, and their movements take place either by active transport or by passive diffusion. In the first case they are called 'ion pumps' and in the second case 'ion channels'. Most channels, furthermore, are opened only by specific stimuli (electrical, mechanical, chemical etc.). The *voltage-gated sodium channels*, for example, are protein systems that let sodium in only when they are stimulated by electrical signals.

The transport of all ions across the cell membrane is influenced by the fact that the interior of the cell is always electrically negative in respect to the outside because most of the great molecules that are trapped inside carry negative charges. The combination of this structural electrical asymmetry with the currents produced by ion pumps and ion channels leads to a stationary state characterized by an electrical difference across the cell membrane that is referred to as the *membrane potential*.

This potential is the result of a dynamic equilibrium of forces and any perturbation of it produces an electric pulse known as *action potential*. An electrical stimulus, for example, can open a sodium channel and let in a flux of positive ions that rapidly change the local value of the membrane potential. Such a change, however, is confined to a very small region under the cell membrane and can be propagated to other regions only if the membrane contains many other sodium channels at a close distance from each other. All cells, in short, have ions pumps and ion channels, but only an uninterrupted distribution of sodium channels can propagate an action potential. That was the novelty that allowed a cell to transmit electrical signals.

Chemical-releasing vesicles, ion pumps and ion channels, in conclusion, had all been invented by free-living cells during the first three thousand million years of

evolution, and did not have to be redesigned. All that was required for the origin of the neuron was a new way of arranging them in space.

The Intermediate Brain

The nervous system is made of three types of neurons: (1) the *sensory neurons* transmit the electrical signals produced by the sense organs, (2) the *motor neurons* deliver electrical signals 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 provides a quick stimulus-response reaction known as a *reflex*. Intermediate neurons, therefore, can be dispensed with, and a few animals do manage without them. It is a fact, however, that most animals do have intermediate neurons, and what we observe in evolution is that brains increased their size primarily by increasing the number of their intermediate neurons. The evolution of the brain, in other words, has largely been the evolution of the 'intermediate brain'.

It is well known, today, that most brain processing is totally unconscious, and we can say therefore that the intermediate brain is divided into a conscious part and an unconscious one. But when did this split occur? When did consciousness appear in the history of life? Here, unfortunately, we come up against the difficulty that consciousness is too large a category. It is associated with feelings, sensations, emotions, instincts, thinking, free will, ethics, aesthetics and so on. Some of these entities appeared late in evolution and only in a restricted number of species, so we can regard them as special evolutionary developments. The origin of consciousness, in other words, can be restricted to its most essential features. To the origin of something primitive and universal, something that even simple animals could have. Feelings and instincts are probably the most universal of all conscious processes, and here it is assumed that consciousness came into existence when the primitive brain managed to produce them. Let us see how that could have happened.

The first nervous systems were probably little more that a collection of reflex arches, and it is likely that the first intermediate neurons came into being as a physical extension of those arches. Their proliferation was favoured simply because they provided a useful *trait-de-union* between sensory neurons and motor neurons. Once in existence, however, they could start exploring other possibilities.

Their first contribution was probably the development of a multi-gated reflex-arch system. The behaviour of an animal must take into account a variety of clues from the environment, and to this purpose it is useful that a motor organ receives signals from many sense organs and that a sense organ delivers signals to many motor organs. This inevitably requires multi-gated connections between sensory inputs and motor outputs, and that probably explains why intermediate neurons had such a great evolutionary success.

In addition to transmitting electrical signals, however, the intermediate neurons could do something else. They could start *processing* the signals, and that opened up a whole new world of possibilities. In practice, the processing evolved in two great directions and produced two very different outcomes. One was the formation of

neural networks that give origin to feedback systems and provide a sort of 'automatic pilot' for any given physiological function. The other was the generation of feelings and instincts.

The first processing was totally unconscious and was carried out by a component of the intermediate brain that here is referred to as the *cybernetic brain*. The second processing was adopted by another major component of the intermediate brain that here is referred to as the *instinctive brain*. The intermediate brain, in short, evolved from a primitive reflex-arch system and developed two distinct types of neural processing, one completely unconscious and the second controlled by instincts. But why *two* types of processing? Why develop feelings and instincts if a cybernetic brain can work perfectly well without them?

The Instinctive Brain

A cybernetic brain can control all physiological functions and can cope with the vagaries of the environment, so there doesn't seem to be any need to evolve also feelings and instincts. We should not forget, however, that a cybernetic brain is an intermediary between sense organs and motor organs, and can work only if there is a *continuous* chains of reactions between inputs and outputs. This means that all the operations of a cybernetic brain are linked together in a physically continuous sequence, and the initial input is inevitably a signal from the outside world. An animal with a fully cybernetic brain, in other words, is virtually a puppet in the hands of the environment. An instinctive brain, instead, is a system where the orders to act come from within the system, not from without. An animal with an instinctive brain takes decisions on the basis of its own instincts, of its own internal rules, and has therefore a certain autonomy from the environment. But does such autonomy have an evolutionary advantage?

In circumstances when there is no food and no sexual partner in the immediate surroundings, a cybernetic animal would simply stop eating and mating, whereas an instinctive animal would embark in a long journey of exploration well beyond its visible surroundings and even in the absence of positive external signals. An internal drive to act, irrespective of the circumstances, in short, can have a survival role, and that is probably why most animals evolved both a cybernetic brain and an instinctive brain.

It must be underlined, however, that an instinctive brain is not a system that can simply be 'added' to a cybernetic brain. An instinctive brain is a system that acts on the basis of internal drives, and that means that it has the ability to send its own orders to the motor organs, i.e., to generate its own electrical signals. That in turn means that the signals delivered to the motor organs do not come all from the sense organs.

The evolution of the instinctive brain, in brief, required a major change in brain circuitry. The bridge between sense organs and motor organs provided by the cybernetic brain was *interrupted*, and the gap was filled by a new bridge made of feelings and instincts. The instinctive brain did not simply *add* feelings to a pre-existing system. It physically broke the continuity of the cybernetic bridge and introduced a new bridge in between. As a result, the intermediate brain, acquired

three distinct control systems, that are based respectively (1) on chemical signalling, (2) on neural networks, and (3) on feelings and instincts. The first two make up the cybernetic brain, whereas the third system is the instinctive brain of an animal.

The origin of feelings and instinct, furthermore, can be associated with the origin of consciousness, but in order to appreciate this point we need to discuss the concept of 'first-person' experience because it is this concept that is largely regarded, today, as the key component of consciousness.

The 'First-Person' Experiences

Feelings, sensations, emotions and instincts are often referred to as 'first-person' experiences because they are experienced directly, without intermediaries. They make us feel that we know our body, that we are in charge of its movements, that we are conscious beings and 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 testable models of what exists in nature, and first-person experiences are undoubtedly part of nature, so we should be able to make models of them. Models, of course, are not reality ("the map is not the territory"), but they are ideas of reality and what really matters is that these ideas can be tested and improved indefinitely. In our case, the problem is to build a model that makes us understand, at least in principle, how first-person experiences can be produced.

Let's take, for example, the case in which a toe is injured. We know that electrical pulses are immediately sent to the central nervous system and that the intermediate brain processes them and delivers orders to the motor organs that spring the body into action. Here we have two distinct players: an observer system (the intermediate brain) and an observed part (the injured toe). It is the observer that gets the information and transforms it into the feeling of pain, but then something extraordinary happens. We do not feel the pain in the intermediate brain, where the feeling is created, but in the toe, where the injury took place. Observer and observed have become one, and it is precisely this collapse into a single feeling unity that generates a 'first-person' experience.

Something similar takes place when we receive signals from the environment, for example when we look at an outside object. In this case, an image is formed on the retina and electrical signals are sent to the intermediate brain. Again, there is a separation between observer (the brain) and observed (the retina). What we see, however, is not an image on the retina, where the visual information is actually produced. The intermediate brain and the retina collapse into a single processing unity and what we see is an image in the outside world. This is again a first-person experience, and again it is generated by a physiological process that short-circuits the physical separation between sense organs and intermediate brain.

What we call 'first-person' experiences, in brief, is nothing elementary, undifferentiated and indivisible. The exact opposite is true. They are the result of complex neural processes where many highly differentiated cells act in concert and create a physiological short-circuit between observer and observed. First-person experiences, in other words, cannot exist in single cells. They could evolve only in

multicellular systems and their origin was a true macroevolution, an absolute novelty. Our problem, therefore, is to understand *how* it could have happened. What was the mechanism that brought them into existence?

The Difference Between Brain and Mind

Feelings, sensations, emotions and instincts are traditionally known as *mental* processes, or products of the *mind*. There is a large consensus today that mind is a natural phenomenon, and that mental events are produced by brain events. At the same time, it is also widely acknowledged that there is a gulf between the physiological processes of the brain and the subjective experiences of the mind. Our problem, therefore, is to understand not only how does the brain produce the mind but also what is the *difference* between them. Probably the best way to deal with this problem is by comparing it with the parallel problem that exists between matter and life. It is largely accepted, today, that life evolved from matter, but also that life is fundamentally different from matter, because entities like natural selection and the genetic code, to name but a few, simply do not exist in the inanimate world.

But how can we explain that? How can something give origin to something fundamentally different from itself? How could matter produce life if there is a fundamental difference between them? Many have decided that no such difference can exist, and therefore that "*life is chemistry*", a conclusion that goes in parallel with the idea that "*mind is brain*".

The chemical view of life is still popular today, and it would be perfectly plausible if primitive genes and primitive proteins could have evolved all the way up to the first cells by spontaneous chemical reactions. But that is precisely what Molecular Biology has ruled out, because genes and proteins are never formed spontaneously in living systems. They are manufactured by molecular machines that physically stick their components together in the order provided by a template. Primitive genes and primitive proteins did appear spontaneously on the primitive Earth but they could not give origin to the first cells because they did not have biological specificity. They gave origin instead to molecular machines, and it was these machines and their products that evolved into the first cells.

Genes and proteins, in short, are assembled by molecular robots on the basis of linear *information*, and this makes them as different from spontaneous molecules as *artificial* objects are from natural ones. Genes and proteins are *molecular artifacts*, i.e., *artifacts made by molecular machines* (Barbieri 2003, 2008). They came from inanimate matter because their components were formed spontaneously, but they are different from inanimate matter because they need entities, like information and coding rules, that do not exist in spontaneous reactions. Only molecular machines can bring these entities into existence, and when they do they produce artifacts, but above all they produce *absolute novelties*, objects that are completely different from whatever is formed spontaneously in the Universe.

This is the logic that explains, in principle, how genuine novelties appeared in evolution. Any biological system that makes objects according to the rules of a code is generating biological artifacts, and a world of artifacts is fundamentally different from the world where it came from. This makes us understand why life arose from matter and yet it is fundamentally different from it, as well as why mind is produced

by the brain and yet it is fundamentally different from it. There is the same logic, the same underlying principle behind the origin of life and the origin of mind. This is the *code model of mind*, the idea that there was a *neural code* at the origin of mind as there was a genetic code at the origin of life (Barbieri 2006, 2010).

The Code Model of Mind

The parallel between the origin of life and the origin of mind can become a scientific model only if it takes the form of a coherent set of hypotheses, so let us see how this can be done.

In the origin of life, the key event was the appearance of *proteins*, and the genetic code played a crucial part in it precisely because it was instrumental to protein synthesis. In the origin of mind, the key event was the appearance of *feelings*, and our hypothesis is that a neural code was as instrumental to the production of feelings as the genetic code was to the production of proteins. The parallel, therefore, is between feelings and proteins, and this immediately tells us that there are both similarities and differences between the two cases.

Proteins are *space-objects*, in the sense that they act in virtue of their three-dimensional organization in space, whereas feelings are *time-objects* because they are 'processes', entities that consist of flowing sequences of states. The same is true for their components. Proteins are assembled from smaller space-objects like amino acids, and feeling are assembled from lower level brain processes such as neuron firings and chemical signalling.

The idea of a deep parallel between life and mind leads in this way to a parallel between proteins and feelings, and in particular to a parallel between the processes that produce them. We already know that the assembly of proteins does not take place *spontaneously* because no spontaneous process can produce an unlimited number of identical sequences of amino acids. The *code model of mind* is the idea that the same is true in the case of feelings, i.e., that feelings are not the spontaneous result of lower level brain processes. They can be generated only by a neural apparatus that assembles them from components according to the rules of a code. According to the code model, in short, *feelings are brain-artifacts* and are manufactured by a codemaker according to the rules of the *neural code*.

In the case of proteins, the codemaker is the ribonucleoprotein system of the cell, the system that provides a bridge between genotype and phenotype. It receives information from the genotype in the form of messenger RNAs and assembles the building blocks of the phenotype according to the rules of the genetic code. It must be underlined, however, that the codemaking system has a logical and a historical priority over genotype and phenotype, and for this reason it is a third category that has been referred to as the *ribotype* of the cell (Barbieri 1981, 1985).

In the case of feelings, the codemaker is the intermediate brain of an animal, the system that receives information from the sense organs and delivers orders to the motor organs. The sense organs provide all the information that an animal is ever going to have about the world, and represent therefore in an animal what the genotype is in a cell. In a similar way, the motor organs allow a body to act in the

world, and have in an animal the role that the phenotype has in a cell. Finally, the intermediate brain is a processing and a manufacturing system, an apparatus that is in an animal what the ribotype is in a cell.

The parallel between life and mind, in conclusion, involves three distinct parallels: one between proteins and feelings, one between genetic code and neural code, and one between cell and animal codemaking systems. The categories that we find in the cell, in other words, are also found in animals, because at both levels we have information, code and codemaker. The details are different, and yet there is the same *logic* at work, the same strategy of bringing absolute novelties into existence by organic coding.

The Neural Code

The term 'neural code' is used fairly often in the scientific literature and stands for the unknown mechanism by which the signals produced by the sense organs are transformed into subjective experiences such as feelings and sensations. It must be underlined that the term is potentially ambiguous, because it may indicate either a universal code or the code that an animal is using to create its own species-specific representations of the world. A similar ambiguity arises, for example, with the term 'language', which can mean either a universal human faculty or the specific language that is spoken in a particular place.

The parallel with the genetic code removes this ambiguity from the start and makes it clear that the Code model of mind assumes the existence of a *universal* neural code. Our problem is therefore the scientific basis of that idea: on what grounds can we say that a (nearly) universal neural code exists in all animals as a (nearly) universal genetic code exist in all cells?

Let's consider, for example the transformation of mechanical stimuli into tactile sensations. Rats have mechano-receptors on the tip of their whiskers while we have them on the tip of our fingers, and there is no doubt that our tactile exploration of the world is different from theirs, but does that mean that we use a different neural code? The evidence is that the physiological processes that transform the mechanical stimuli into tactile sensations are the same in all animals, and this does suggest that there is a universal mechanism at work (Nicolelis and Ribeiro 2006). As a matter of fact, the evidence in question comes from animals with three germ layers (the triploblasts), but they represent the vast majority of all animal taxa, so let us concentrate our attention on them. How can we generalize the experimental data and conclude that virtually all triploblastic animals have the same neural code?

We do know that the starting point of all neural processing is the electrical signals produced by sense organs, but we also know that the sense organs arise from the basic histological tissues of the body, and that these tissues (epithelial, connective, muscular and nervous tissues) are the same in all triploblastic animals. All signals that are sent to the brain, in other words, come from organs produced by a limited number of universal tissues, and that does make it plausible that they represent a limited number of universal inputs. But do we also have a limited number of universal outputs?

The neural correlates of the sense organs (feelings and perceptions) can be recognized by the *actions* that they produce, and there is ample evidence that all triploblastic animals have the same basic *instincts*. They all have the imperative to *survive* and to *reproduce*. They all seem to experience hunger and thirst, fear and aggression, and they are all capable of reacting to stimuli such as light, sound and smells. The neural correlates of the basic histological tissues, in short, are associated with the basic animal instincts and these appear to be virtually the same in all triploblastic animals.

What we observe, in conclusion, is a universal set of basic histological tissues on one side, a universal set of basic animal instincts on the other side, and a set of neural transformation 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 physical link between sense organs and feelings, we can conclude that the bridge between them can only be the result of a virtually universal *neural code*.

Theories on Mind

It is widely accepted, today, that the mind is produced by the brain, and our problem is to understand *how* that happens. At the moment, the scientific models that have been proposed on this issue can be divided into three major groups.

(1) The *computational theory* is the idea that lower-level brain processes, such as neuron firings and synaptic connections, are transformed into feelings by neural processes that are equivalent to *computations*. Brain and mind are compared to the hardware and software of a computer, and mental activity is regarded as a sort of data processing which is implemented by the brain but is in principle distinct from it, rather like a software is distinct from its hardware (Fodor 1975, 1983; Johnson-Laird 1983).

(2) The *connectionist theory* states that lower-level brain processes are transformed into higher-level brain events by neural networks, i.e., by webs of synaptic connections that are not the result of computations but of explorative processes. The reference model, here, is the computer-generated neural networks that simulate the growth of the synaptic web in a developing brain (Hopfield 1982; Rumelhart and McClelland 1986; Edelman 1989; Holland 1992; Churchland and Sejnowski 1993; Crick 1994).

(3) The *emergence theory* states that higher-level brain properties emerge from lower-level neurological phenomena, and mind is distinct from brain because any emergence is accompanied by the appearance of new properties (Morgan Lloyd 1923; Searle 1980, 1992, 2002).

The theory described in this paper is that the brain produces the mind by assembling neural components together with the rules of a neural code, very much like the cell produces proteins with the rules of the genetic code (Barbieri 2006). This implies that feelings are no longer *brain objects* but *brain artifacts*. It implies that feelings are not side-effects of neural networks (as in connectionism),

that they do not come into existence spontaneously by emergence, and that they are not the result of computations, but of real manufacturing processes. According to the code model, in short, feelings and instincts are *manufactured artifacts*, whereas according to the other theories they are *spontaneous products* of brain processes.

This does make a difference, because if the mind were made of spontaneous products it could not have *rules of its own*. Artifacts, instead, do have some autonomy because the rules of a code are not dictated by physical necessity. Artifacts, furthermore, can have *epigenetic* properties that add unexpected features to the coding rules. The autonomy of the mind, in short, is something that spontaneous brain products cannot achieve whereas brain artifacts can.

PART 2 — The Evolution of the Brain

Two Universal Strategies

There is both unity and diversity in life. The unity comes from the presence of a universal genetic code in all living cells. The diversity from the existence of different organic codes in different groups of cells. The first cells, for example, were divided into three primary kingdoms (Archea, Bacteria and Eukarya) by three distinct signal-transduction codes. After that original split, some cells (Archea and Bacteria) adopted a streamlining strategy that prevented them from developing new organic codes, with the result that they have remained substantially the same ever since. The other cells (Eukarya) continued to explore the coding space and became increasingly more complex.

If we now look at the evolution of animals, we find again a split between a streamlining strategy and an exploring strategy. In this case, it was the split that divided invertebrates from vertebrates. The invertebrates adopted a streamlining strategy that reduced their brain development to the bare essentials, whereas the vertebrates appear to have explored almost without limits the potentialities of the brain space. In evolution, in other words, there seem to be two universal strategies at work, one that promotes streamlining and one that favours exploration. At the cellular level these strategies divided prokaryotes from eukaryotes, and at the animal level they divided invertebrates from vertebrates.

At the cellular level, furthermore, the exploring strategy of the eukaryotes was primarily based on the development of new organic codes, and this suggests that, at the animal level, the exploring strategy of the vertebrates could also have been based on organic codes. But can we prove it? Can we actually show that many organic codes appeared in vertebrate evolution?

Brains do not normally fossilize, but we can still obtain information on their ancestral organic codes. We can get it from embryology, because the main driving forces of animal evolution were changes in embryonic development that have been passed on to their modern descendants. The embryonic brain, in short, is probably the best place where we can find information about the evolution of the brain and its organic codes.

Mechanisms of Brain Development

The embryonic development of the vertebrate nervous system takes place in four stages. The first begins when a strip of ectoderm is induced to become neural tissue by the underlying mesoderm, and comes to an end when the newly formed neuroblasts complete their last cell division, an event which marks the 'birth' of the neurons. This is a truly epochal event because everything that a neuron will ever do in its life is largely determined by the time and the place of its birth. Somehow, these two parameters leave an indelible mark in the young neuron and become a permanent memory for it.

The second phase of neural development is the period in which neurons migrate from their birthplace to their final destination, a target that they 'know' because it is somehow 'written' in the memory of their birth.

The third phase begins when neurons reach their definitive residence. From this time onwards, the body of a neuron does not move any more but sends out 'tentacles' that begin a long journey of exploration in the surrounding body. Any tentacle (a *neurite*) ends with a roughly triangular lamina (called *growth cone*) which moves like the hand of a blind man, touching and feeling any object on its path before deciding what to do next. The axons of motor neurons are the longest of such tentacles, and their task is to leave the neural tube for the rest of the body in search of organs that require nerve connections. This is achieved with an exploration strategy that takes place in two stages. In the first part of the journey, the growth cones move along tracks provided by specific molecules, with a preference for those of other axons (which explains why growth cones migrate together and form the thick bundles that we call *nerves*). They do not have a geographic knowledge of their targets but this is compensated by an overproduction of cells, which ensures that some of them will actually reach the targets. At this point the second part of the strategy comes into play. The organs that need to be innervated send off particular molecules, known as *nerve growth factors*, that literally save the neurons from certain death. More precisely, neurons are programmed to commit suicide—i.e., to activate the genes of cell death, or *apoptosis*—at the end of a predetermined period, and nerve growth factors are the only molecules that can switch off this self-destruction mechanism. The result is that the neurons that reach the right places survive, and all the others disappear (Levi-Montalcini 1975, 1987; Changeaux 1983).

The fourth phase of brain development begins when the growth cones reach the target areas. At this point, some unknown signal instructs the axon to stop moving and to begin a new transformation. The growth cone looses its flat shape and generates a variety of thin long fingers that are sent off in various directions towards the surrounding cells. When a contact is established, the tips of the finger-like extensions expand themselves and become the round buttons of the *synapses*, the structures that specialize in the transmission of neurochemicals. This turns the neuron into a secretory cell and from that moment on the neuron is committed to a life of uninterrupted chemical communication with other cells.

The making and breaking of synaptic connections is the actual wiring of the nervous system and takes place with a mechanism that is based first on molecular recognitions and then on functional reinforcements. Each neuron

generates an excess number of synapses, so the system is initially over-connected. The synaptic connections, on the other hand, are continuously broken and reformed, and only those that are repeatedly reconnected become stable structures. Those that are less engaged are progressively eliminated and in the end only the active synapses remain. This mechanism continues to operate long after birth and in some part of the brain it goes on indefinitely, thus providing the means to form new neural connections throughout the life of an individual. According to Donald Hebb (1949) it is this mechanism that lies at the heart of memory, and the results obtained from natural and artificial neural networks have so far confirmed his prophetic idea.

Codes of Brain Development

Cell adhesion, cell death and cell signalling are major tools of brain development, and in all of them we can recognize the presence of organic codes. Let us briefly examine a few examples.

(1) Cell adhesion

In the 1940s, Roger Sperry severed the optic nerve of a fish and showed that its fibres grow back precisely to their former targets in the brain. More than that. When the eye was rotated 180° in its socket, the fish was snapping downward at a bait placed above it, thus proving that the connections are extremely specific. This led Sperry (1943, 1963) to formulate the 'chemo-affinity hypothesis', the idea that neurons recognize their synaptic partners by millions of 'recognizing molecules' displayed on their cell membranes. The wiring of the brain is essentially accomplished by molecules that bridge the synaptic cleft and decide which neurons are connected and which are not. They function both as synaptic recognizers and synaptic glue, and recently it has been shown that cadherins and protocadherins are good candidates for these roles. Protocadherins, in particular, have an enormous potential for diversification because their genes contain variable and constant regions like the genes of the immunoglobulins. They could, therefore, provide the building blocks of a neural system that is capable of learning and memorizing, and, like the immune system, can cope with virtually everything, even the unexpected (Hilschmann et al. 2001). This suggests that the chemoaffinity hypothesis of Roger Sperry should be re-formulated in terms of a code. Rather than listing millions of individual molecular interactions, an organic code can generate an enormous diversity with a limited number of rules, and this is why various authors has proposed that the wiring of the nervous system is based on an *Adhesive code* (Redies and Takeichi 1996; Shapiro and Colman 1999).

(2) Cell death

Active cell suicide (apoptosis) is a universal mechanism of embryonic development, one that is used to shape virtually *all* organs of the body. The key point is that suicide genes are present in all cells and the signalling molecules that switch them on and off are of many different types. This means that the recognition of a signalling molecule and the activation of the suicide genes are

two independent processes, so we need to understand what brings them together. Since there are no necessary connections between them, the only realistic solution is that the link is established by the rules of an *Apoptosis code*, i.e., a code that determines which signalling molecules switch on the apoptosis genes in which tissue.

(3) Cell signalling

Neurons communicate with other cells by releasing chemicals called *neurotransmitters* in the small space (the *synaptic cleft*) that separates their cell membranes. There are four distinct groups of neurotransmitters and dozens of molecules in each of them, but the most surprising feature is that the same molecules are employed in many other parts of the body with completely different functions. Adrenaline, for example, is a neurotransmitter, but it is also a hormone produced by the adrenal glands to spring the body into action by increasing the blood pressure, speeding up the heart and releasing glucose from the liver. Acetylcholine is another common neurotransmitter in the brain, but it also act on the heart (where it induces relaxation), on skeletal muscles (where the result is contraction), and in the pancreas (which is made to secrete enzymes). Neurotransmitters, in other words, are *multifunctional molecules*, and this suggests that they are used as molecular *labels* that can be given different meanings in different contexts. The most parsimonious explanation is that their function is determined by the rules of an organic code that can be referred to as the *Neurochemical code*. The idea that neurotransmitters act like the words of a chemical language is reinforced by the fact that small structural variations can have vastly different meanings. This is very common in language (compare, for example, the meanings of *dark*, *park* and *bark*), but it is also common in brain signalling. Serotonin, for example, is a normal neurotransmitter, but a slightly modified version of it, such as mescaline, produces violent hallucinations. The same is true for lysergic acid (LSD), which is related to dopamine, and in general for many other chemicals that are structurally similar to neurotransmitters.

In brain development, in conclusion, we see at work mechanisms that have all the defining characteristics of organic codes, and we might as well come to terms with this fact of life.

The Evolution of Vision

The human retina is made of three layers, one of which contains about 100 million *photoreceptor cells* (rods and cones) that react to light by producing electrical signals. These are sent to the *bipolar cells* of the second layer which in turn deliver signals to the one million *ganglion cells* of the third layer whose axons form the optic nerve. The 100 million signals of the photoreceptor cells undergo therefore a first processing on the retina, the result of which is one million pulses delivered via the optic nerve to the brain. Here the signals are sent to the midbrain, and after the *optic chiasm* (where 50% swap direction) are transmitted to the *visual cortex*, at the back of the head, where they are further processed by groups of *cortical cells*

arranged in distinct *areas*. It turns out that the operations performed in areas 17, 18 and 19 maintain a certain topological coherence with the visual field of the retina, in the sense that adjacent points in the retina are processed by adjacent points in those areas of the visual cortex In area 17, furthermore, Hubel and Wiesel have found that some cells react only to horizontal movements on the retina, other cells react only to vertical movements and still others to sharp edges (Hubel and Wiesel 1962, 1979). After areas 18 and 19, the visual inputs go on to other cortical areas, but the topological coherence with the retina is rapidly lost, probably because the information on spatial relationships has already been extracted.

The key point, at the higher processing level, is that the brain does not merely *register* the information from the retina but can literally *manipulate* it. When an object is approaching, for example, its image on the retina becomes larger, but the brain still perceives an object of constant size. When the head is moving, the image of an object on the retina is also moving, but the brain decides that the object is standing still. When the light intensity is lowered, the retinal image of a green apple, for example, becomes darker, but the brain compensates for that and concludes that the apple has not changed its colour.

These (and many other) results prove that what we 'perceive' is not necessarily what the sense organs tell us. 'Perceptions', in other words, are distinct from 'sensations'. A sensations is what comes from the senses and has a specific physiological effect (colour, sound, smell, tickle and so on). A perception is what the brain decides to do of the information from the senses, according to its own set of processing rules.

We realize in this way that there are many types of processing going on in the brain, and such a complex hierarchy can only have been the result of a long history, so let us take a brief look at the evolution of vision.

Some of the most primitive eyes are found in flatworms and are little more than clusters of photoreceptor cells that can distinguish day from night. They are also able to detect the direction of the light source, a feat that allows flatworms to swim towards the dark. But flatworm eyes do not have a lens and thus cannot form visual images of the surrounding objects.

The first camera-eye, with a lens that projects an image on the retina, probably appeared in fish. The fish retina already has a three-layered structure (rods and cones, bipolar cells and ganglion cells) and an optic nerve that transmits the visual inputs to the midbrain. In fish, however, all nerve fibers change direction at the optic chiasm, and the midbrain is the final destination of the visual inputs, the place where the signals from all sense organs are converted into orders to the motor organs.

This primitive structure was substantially conserved in amphibians and reptiles, and it was only birds and mammals that started evolving a more advanced design. In their visual system, not all the fibers of the optic nerves crossed direction at the optic chiasm and the final destination of the visual inputs was moved from the midbrain to the visual cortex and then to other regions of the neocortex. These changes went hand in hand with a gradual transition from an olfactory and tactile mode of life to a life where vision was acquiring an increasingly important role.

The evolution of vision is an outstanding example of the changes that took place in the *cybernetic* brain, more precisely in that part of the cybernetic brain that is in charge of the automatic processing of visual information. The cybernetic brain,

however, was only a part of the evolving brain, and we need to consider also the evolution of the bran in its entirety.

Three Modelling Systems

The results of brain processing are what we normally call feelings, sensations, emotions, perceptions, mental images and so on, but it is useful to have also a more general term that applies to all of them. Here we follow the convention that all products of brain processing can be referred to as brain *models*. The intermediate brain, in other words, uses the signals from the sense organs to generate distinct *models* of the world. A visual image, for example is a model of the information delivered by the retina, and a feeling of hunger is a model obtained by processing the signals sent by the sense detectors of the digestive apparatus.

The brain can be described in this way as a *modelling system*, a concept that has been popularized by Thomas Sebeok and that has acquired an increasing importance in semiotics (Sebeok and Danesi 2000). The term was actually coined by Juri Lotman, who described language as the 'primary modelling system' of our species (Lotman 1991), but Sebeok underlined that language evolved from animal systems, and should be regarded as a secondary modelling system. The distinction between primary, secondary and tertiary modelling system has become a matter of some controversy, so it is important to be clear about it. Here we use those terms to indicate the modelling systems that appeared at three different stages of evolution and gave origin to three different types of brain processing.

(1) The First modelling system

This is the system that appeared when the primitive brain managed to produce feelings and sensations. These entities can be divided into two great classes because the sense organs deliver information either about the outside world or about the interior of the body. The first modelling system consists therefore of two types of models, one that represents the environment and one that carries information about the body. Jakob von Uexküll (1909) called these two worlds *Umwelt* and *Innenwelt*, names that express very well the idea that every animal lives in two distinct subjective universes. We can say therefore that *Innenwelt* is the model of the internal body built by the instinctive brain, and that *Umwelt* is the model of the external world built by the cybernetic brain of an animal. The brain as we know it—the brain with feelings—came into being when the primitive brain split into instinctive brain and cybernetic brain, and these started producing the feelings and sensations that make up the first modelling system of all triploblastic animals (vertebrates and invertebrates).

(2) The Second modelling system

Some animals (like snakes) stop chasing a prey when this disappears from sight, whereas others (like mammals) deduce that the prey has temporarily been hidden by an obstacle and continue chasing it. Some can even learn to follow the footsteps of a prey, which reveals a still higher degree of abstraction. This ability to 'interpret' the signals from the environment, is based, as we will see, on a new type of neural processing that represents the *second modelling system*

of the brain, a system that appeared when a part of the cybernetic brain became an 'interpretive brain'.

(3) The Third modelling system

The last major novelty in brain evolution was the origin of language, and that too required, as we will see, a new type of neural processing, so it is legitimate to say that language represents a third modelling system.

There have been, in conclusion, three major transitions in the evolution of the brain and each of them gave origin to a new type of neural processing that was, to all effects, a new modelling system.

The Interpretive Brain

The instinctive brain delivers orders to the motor organs, and is the directive centre of an animal, the main responsible for its ability to survive and reproduce. The cybernetic brain is essentially a servomechanism, and it is precisely this function that explains its enormous increase in evolution. The instinctive brain has changed very little in the history of life, and the greatest changes have taken place precisely in the cybernetic tools that animals evolved in order to provide the instinctive brain with increasingly sophisticated servomechanisms.

The neural networks are probably the most powerful of such tools. Their ability to create feedback loops allows them to produce a goal-directed behaviour in a system, but they also have other outstanding properties. In artificial systems, for example, it has been shown that neural networks can provide the basis of *learning* and *memory* (Kohonen 1984), and it is likely that they have similar properties in living systems. It is possible, therefore, that neural networks were the physical tools that evolved learning and memory, but that still leaves us with the problem of understanding the role that learning and memory had in evolution.

Memories allow a system to compare a phenomenon with previous records of similar phenomena, and it is from such a comparison that a system can 'learn' from past experiences. Memories are clearly a prerequisite for learning, but what does learning achieve? What is the point of storing mental representations and comparing them?

So far, the best answer to this problem is probably the idea, proposed by Charles Sanders Peirce, that memories and learning allows animals to *interpret* the world.

An act of interpretation, on the other hand, consists in giving a meaning to something, and this is, by definition, an act of semiosis. Interpretation, therefore, is a form of semiosis and its elementary components are signs and meanings. According to Peirce (1906), there are three major types of signs in the world, and he called them *icons*, *indexes* and *symbols*.

(1) A sign is an *icon* when it is associated with an object because a *similarity* is established between them. All trees, for example, have individual features, and yet they also have something in common and it is this common pattern that allows us to recognize as a tree any new specimen that we happen to encounter for the first time. Icons, in other words, lead to pattern recognition and are the basic tools of *perception*.

(2)   A sign is an *index* when it is associated with an object because a *physical link* is established between them. We learn to recognize any new cloud from previous clouds, and any new outbreak of rain from previous outbreaks, but we also learn that there is often a correlation between clouds and rain, and we end up with the conclusion that a black cloud is an index of rain. In the same way, a pheromone is an index of a mating partner, the smell of smoke is an index of fire, footprints are indexes of preceding animals, and so on. Indexes, in short, are the basic tools of *learning*, because they allow animals to infer the existence of something from a few physical traces of something else.

(3)   A sign is a *symbol* when it is associated with an object because a *conventional link* is established between them. There is no similarity and no physical link between a flag and a country, for example, or between a name and an object, and a relationship between them can exist only if it is the result of a convention. Symbols allow us to make arbitrary associations and build mental images of future events (projects), of abstract things (numbers), and even of non-existing things (unicorns).

The part of the intermediate brain that allows an animal to interpret the world can be referred to as the *interpretive brain*, or the *second modelling system* of the brain. It was the result of a specific phase in brain evolution and we need therefore to understand, at least in principle, how interpretation came into being.

The Origin of Interpretation

The ability to interpret the world is a form of semiosis, because it is based on signs and meaning, but is it a *new* form of semiosis? More precisely, did interpretation appear only in animals or did it exist also in free living single cells? We have seen that many organic codes appeared on Earth in the first three thousand million years of evolution, and this is equivalent to saying that single cells were capable of coding and decoding the signals from the environment. But coding and decoding is *not* the same as interpreting. Interpretation takes place when the meaning of a sign can change according to circumstances, whereas coding takes place when meaning is the fixed result of a coding rule.

The idea that single cells are capable of interpreting the world is still very popular, today, because single cells have a context-dependent behaviour, and it is taken virtually for granted that context-dependency can only be the result of interpretation. In reality, it takes only two organic codes to produce a context-dependent response in a cell. A context-dependent behaviour means a context-dependent expression of genes, and this is achieved by linking the expression of genes to signal transduction, i.e., by putting together the genetic code with a signal transduction code (Jacob and Monod 1961). And if it takes only two context-free codes to produce a context-dependent behaviour, one can only wonder at how much more complex became the cell behaviour when other organic codes appeared in the system.

The origins of animals, of embryonic development and of the brain, furthermore, were also associated with new organic codes, and were based on coding not on

interpretation. The ability to interpret the world came into being at a later stage, when animals started exploring the potentialities of learning. Neural networks have the ability to form memories, and a set of memories is the basis of learning because it allows a system to decide how to behave in any given situation by comparing the memories of what happened in previous similar situations. A large set of memories, in other words, amounts to a model of the world that is continuously updated and that allows a system to *interpret* what goes on around it.

Such a model, on the other hand, is formed by a limited number of memories whereas the real world offers an infinite number of possibilities. Clearly, a model based on memories can never be perfect, but it has been shown that neural networks can in part overcome this limit by interpolating between discreet memories (Kohonen 1984). In a way, they are able to 'jump-to-conclusions', so to speak, from a limited number of experiences, and in most cases their 'guesses' turn out to be good enough for survival purposes.

This 'extrapolation from limited data' is an operation that is not reducible to the classical Aristotelian categories of 'induction' and 'deduction', and for this reason Charles Peirce called it 'abduction'. It is a new logical category, and the ability to interpret the world appears to be based precisely on that logic.

We realize in this way that interpretation is truly a new form of semiosis because it is not based on coding but on abduction. What is interpreted, furthermore, is not the world but *representations* of the world, and this means that interpretation can exist only in multicellular systems.

Single cells decode the signals from the environment but do not build internal representatioms of it and therefore cannot interpret them. They are sensitive to light, but do not 'see'; they react to sounds but do not 'hear'; they detect hormones but do not 'smell' and do not 'taste' them. It takes many cells which have undertaken specific processes of differentiation to allow a system to see, hear, smell and taste, so it is only multicellular creatures that have these experiences.

The evolution from single cells to animals was a true macroevolution because it created absolute novelties such as feelings and instincts (the first modelling system). Later on, another major transition allowed some animals to evolve a second modelling system that gave them the ability to *interpret* the world. That macroevolution gave origin to a new type of semiosis that can be referred to as *interpretive* semiosis, or, with equivalent names, as *abductive* or *Peircean* semiosis.

The Uniqueness of Language

We and all other animals do not interpret the world but only mental images of the world. The discovery that our perceptions are produced by our brain implies that we live in a world of our own making, and this has led to the idea that there is an unbridgeable gap between mind and reality. Common sense, on the other hand, tells us that we better believe our senses, because it is they that allow us to cope with the world. Our perceptions 'must' reflect reality, otherwise we would not be able to survive. François Jacob has expressed this concept with admirable clarity: "*If the image that a bird gets of the insects it needs to feed its progeny does not reflect at least some aspects of reality, there are no more progeny. If the representation that a*

monkey builds of the branch it wants to leap to has nothing to do with reality, then there is no more monkey. And if this did not apply to ourselves, we would not be here to discuss this point" (Jacob 1982).

Any animal has a modelling system that builds mental images of the world, and we have learned from Darwin that natural selection allows organisms to become increasingly adapted to the environment, i.e., increasingly capable of reducing the distance that separates them from reality. Natural selection, in other words, is a process that allows animals to catch increasing amounts of reality. This is because mental images are not about things, but about *relationships* between things, and have been specifically selected so that the relationships between mental images represent at least some of the relationships that exist between objects of the physical world. To that purpose, natural selection can definitely use relationships based on icons and indexes, because these processes reflect properties of the physical world, but it cannot use symbols, because symbols are arbitrary relationships and would increase rather than decrease the distance from reality. Natural selection, in short, is actively working *against* the use of symbols as a means to represent the *physical* world.

Language, on the other hand, is largely based on symbols, and this does give us a problem. The idea that language is based on arbitrary signs, or symbols, is the legacy of Saussure, in our times, whereas the idea that animal communication is also based on signs has been introduced by Sebeok and is the main thesis of zoosemiotics. This extension of semiosis to the animal world, however, has not denied the uniqueness of language. On the contrary, it has allowed us to reformulate it in more precise terms. Such a reformulation was explicitly proposed by Terrence Deacon in *The Symbolic Species* with the idea that animal communication is based on icons and indexes whereas language is based on symbols (Deacon 1997).

Today, this is still the best way to express the uniqueness of language. It is true that some examples of symbolic activity have been reported in animals, but in no way they can be regarded as primitive languages or intermediate stages toward language. Deacon's criterion may have exceptions, but it does seem to contain a fundamental truth. A massive and systematic use of symbols is indeed what divides human language from animal communication, and we need therefore to account for its origin. How did language come into being?

The Ape with a Double Brain

In the 1940s, Adolf Portmann calculated that our species should have a gestation period of 21 months in order to complete all processes of foetal development that occur in mammals (Portmann 1941, 1945; Gould 1977). A newborn human baby, in other words, is in fact a premature foetus, and the whole first year of his life is but a continuation of the foetal stage. This peculiarity is due to the fact that the human tendency to extend the foetal period (fetalization) leads to a greater foetus at birth, but the birth canal can cope only with a limited increase of foetal size. During the evolution of our species, therefore, any extension of the foetal period had to be accompanied by an anticipation of the time of birth. The result is that our foetal development became split into two distinct phases—intrauterine and extrauterine— and eventually the extrauterine phase (12 months) became the longest of the two.

It is not clear why this evolutionary result is uniquely human, but it is a historical fact that it took place only in our species. In all other mammals, foetal development is completed *in utero*, and what is born is no longer a foetus but a fully developed infant that can already cope with the environment.

The crucial point is that the last part of foetal development is the phase when most synaptic connections are formed. It is a phase of intense 'brain wiring'. The fetalization of the human body has produced therefore a truly unique situation. In all other mammals the wiring of the brain takes place almost completely in the dark and protected environment of the uterus, whereas in our species it takes place predominantly outside the uterus, where the body is exposed to the lights, the sounds and the smells of a constantly changing environment. In our species, in short, the split between intrauterine and extrauterine foetal development created the conditions for two very different types of brain wiring.

A second outstanding consequence of the fetalization split was an enormous increase in brain-size, a phenomenon that was probably caused by embryonic 'regulation', the ability that embryos have to regulate the development of their organs in the critical period of organogenesis. This point is vividly illustrated by a classic experiment. In vertebrate embryonic development, the heart arises from two primordia that appear on the right and left side of the gut, and then migrate to the centre and fuse together in a single organ. If fusion is prevented by inserting an obstacle between them, each half undergoes a spectacular reorganization and forms a complete and fully functional beating heart. The formation of the two hearts, furthermore, is followed by the development of two circulatory systems, and the animal goes through all stages of life in a double-heart condition that is known as *cardia bifida* (DeHaan 1959).

This classic experiment shows that two profoundly different bodies, one with a single heart and the other with two hearts, can be generated *without any genetic change at all*. A modification of the epigenetic conditions of embryonic development is clearly an extremely powerful tool of change, and may well be the key to human evolution. The foetal development of our brain has been split into two distinct processes, one within and one without the uterus, and this is a condition that can be referred to as *cerebra bifida* (Barbieri 2010). It is similar to *cardia bifida*, except that in the case of the heart the two organs arise from a separation in space whereas in *cerebra bifida* they are produced by a separation in time.

The *cardia bifida* experiment is illuminating because it shows that the enormous increase in brain size that took place in human evolution could well have been a *cerebra bifida* effect, a duplication of brain tissue caused by the regulation properties of embryonic development.

Extrauterine foetal development and increased brain size, in conclusion, set the stage for a radically new experiment in brain wiring, thus creating the precondition for a uniquely human faculty. Let us not forget, however, that a precondition for language was not yet language. It was only a potential, a starting point.

The Third Modelling System

The primary modelling system allows an animal to build a representation of the environment, an *Umwelt*, and the second modelling system allows an animal to

extract more information from the incoming signals by *interpreting* them. A process of interpretation is an abstraction (more precisely an abduction) that is based on signs, but not all signs are reliable modelling tools. Icons and indexes can indeed favour adaptation to the environment because they reflect properties that do exist in the world, whereas symbols are completely detached from reality. This explains why animals have modelling systems that are massively based on icons and indexes but are virtually incapable of symbolic activity. It does not explain, however, why our species was such an outstanding exception to that rule. How did we manage to communicate by symbols? The solution proposed here is that we did *not* substantially change the first and the second modelling systems that we inherited from our animal ancestors. What we did, instead, was to develop a *third* modelling system.

The human brain is about three times larger than the brain of any other primate, even when body weight is taken into account. This means that the first ad second modelling systems that we have inherited from our animal ancestors required, at most, a third of our present brain size. The other two thirds could be explained, in principle, by a further extension of our animal faculties, but this is not what happened. We have not developed a sharper eyesight, a more sensitive olfactory system, a more powerful muscular apparatus, and so on. As a matter of fact, our physical faculties are in general less advanced than those of our animal relatives, so it was not an improvement of their modelling systems that explains our increased brain volume. It is likely, therefore, that the brain increase that took place in our species was largely due to the development of those new faculties that collectively make up our *third* modelling system, the system that eventually gave origin to language. The brain matter of this system was provided by the extrauterine phase of foetal development, the *cerebra bifida* effect, but that accounts only for the hardware of the third modelling system, not for its software.

The solution proposed here is that our brain used the traditional neural tools that build an 'Umwelt' but used them to build an Umwelt made exclusively of human relationships, a *cultural Umwelt* that exists side by side the environmental Umwelt. We learned to live simultaneously in two distinct external worlds, one provided by the physical environment and one by the cultural environment. Natural selection, as we have seen, is working against symbols as a means to represent the physical world, but can no longer work against them when they are part of a cultural world that becomes as important as the physical world.

Our third modelling system, in short, evolved in parallel with the first two systems that we have inherited from our animal ancestors, and created a condition whereby we live simultaneously in two environments that not only coexist but somehow manage to merge together into a single reality.

The Code of Language

Noam Chomsky and Thomas Sebeok are the founding fathers of two research fields that today are known respectively as Biolinguistics and Biosemiotics, and the architects of two major theoretical frameworks for the study of language.

Chomsky's most seminal idea is the concept that our ability to learn a language is *innate*, that children are born with a mechanism that allows them to learn whatever language they happens to grow up with (Chomsky 1957, 1965, 1975, 1995, 2005). That inner mechanism has been given various names—first *Universal Grammar*, then *Language Acquisition Device (LAD)*, and finally *Faculty of Language*—but its basic features remain its *innateness* and its *robustness*. The mechanism must be innate because it allows children to master an extremely complex set of rules in a limited period of time, and it must be robust because language, is acquired in a precise sequence of developmental stages. For this reason, Chomsky concluded that the rules of universal grammar, or the principles and parameters of syntax, must be based on very general principles of economy and simplicity that are similar to the *Principle of Least Action* in physics and to the rules of the *Periodic Table* in chemistry (Baker 2001; Boeckx 2006).

Thomas Sebeok maintained that language is first and foremost a modelling system, the quintessential example of semiosis, and that 'interpretation' is its most distinctive feature (Sebeok 1963, 1972, 1988, 1991, 2001). He forcefully promoted the Peirce model of semiosis, which is explicitly based on interpretation, and insisted that semiosis is always an interpretive activity. Sebeok underlined that concept in countless occasions and in no uncertain terms: "There can be no semiosis without interpretability, surely life's cardinal propensity" (Sebeok 2001).

This is the bone of contention between the two frameworks. Is the faculty of language a product of universal principles or the result of interpretive processes? Chomsky insisted that the development of language must be precise, robust and reproducible like the development of any other faculty of the body, and therefore it cannot be left to the vagaries of interpretation. Sebeok insisted that language is semiosis and that semiosis is always an interpretive process, so it cannot be the result of universal principles or physical constraints.

Here, a third solution is proposed. Organic semiosis is a semiosis based on coding not on interpretation, and an embryonic development that follows coding rules is not subject to the vagaries of interpretation. The ontogeny of language, on the other hand, is precise, robust and reproducible even when based on organic codes rather than universal laws. The genetic code, for example, has guaranteed precise, robust and reproducible features in all living system ever since the origin life. Language does require rules, but these rules are much more likely to be the result of organic codes rather than the expression of universal principles.

The third solution, in short, is that there was an organic code at the origin of language just as there was a genetic code at the origin of life and a neural code at the origin of mind. It could have been, for example, a code that provided new rules for the brain-wiring processes that take place in the extrauterine phase of foetal development. It is also possible that the codemaker was not the individual brain bus a *community* of brains, because language is critically dependent upon *human* interactions in the first few years of life. This is the lesson that we have learned from feral children (Maslon 1972; Shattuck 1981), and the study of the 'creole' languages has clearly shown that the major role in the making of new linguistic rules is played by children (Bickerton 1981).

It must be underlined that today we have no evidence in favor of a foundational code of language. This is pure speculation, at the moment, but it does have a logic.

All great events of macroevolution were associated with the appearance of new organic codes, and language *was* a macroevolution, so it makes sense to assume that in that case too Nature resorted to the same old trick, to creation by coding.

Conclusion

Life is based on the copying of genes and on the coding of proteins. The copying of genes is the elementary act that leads to *heredity*, but when it is repeated indefinitely it brings another phenomenon into being. Copying mistakes become inevitable and in a world of limited resources not all changes can be implemented, which means that a process of selection is bound to take place. Molecular copying, in short, leads to heredity, and the indefinite repetition of molecular copying in a world of limited resources leads to *natural selection*. That is how natural selection came into existence. Molecular copying started it and molecular copying has perpetuated it ever since.

The present theoretical framework of biology is the Modern Synthesis, the paradigm where natural selection is regarded as the sole mechanism of evolution, but the Modern Synthesis was built in the 1930s and 40s, when the genetic code was completely unknown. The discovery of this code uncovered a second fundamental mechanism, and proved that life requires both copying and coding, two mechanisms that are distinct because coding cannot be reduced to copying (proteins cannot be copied). The discovery of other organic codes, furthermore, allows us to generalize this conclusion because it proves that coding is not limited to protein synthesis. This gives us a new understanding of life, a new framework where evolution is based on copying and coding, on natural selection and natural conventions.

Modern biology has not yet come to terms with the presence of many organic codes in Nature, but here we have seen that we can prove their existence and that they have outstanding implications for the history of life. We have seen, in particular, that organic codes had a key role in the origin and evolution of the brain. Neurochemical signalling, neural adhesion, synaptic connections, apoptosis and brain wiring are all based on molecular adaptors and are therefore codified processes. In other cases, the presence of organic codes cannot yet be proved but remains the most parsimonious explanation of the facts. This is particularly true for the codes of the three major events in brain macroevolution, the transitions that produced the three modelling systems of the brain and gave origin, respectively, to feelings, to interpretation and to language.

The organic codes are the components of *organic semiosis*, the first and the most diffused form of semiosis on Earth, but not the only one. The evolution of the brain was accompanied by the development of two new types of sign processes, one that gave origin to *interpretive semiosis*, mostly in vertebrates, and one that produced *cultural semiosis*, in our species.

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