

Biology with information and meaning

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ABSTRACT

It is shown that information and meaning can be defined by operative procedures, and that we need to recognize them as a new type of natural entities. They are not quantities (neither fundamental nor derived) because they cannot be measured, and they are not qualities because they are not subjective features. Here it is proposed to call them nominable entities, i.e., entities which can be specified only by naming their components in their natural order

Introduction

In 1953, Watson and Crick proposed that the linear sequence of nucleotides represents the *information* carried by a gene. A few years later, the mechanism of protein synthesis was discovered and it was found that the sequence of nucleotides in genes determines the sequence of amino acids in proteins, with a process that amounts to a transfer of linear information from genes to proteins. In both types of molecules, therefore, *biological* (or *organic*) *information* was identified with, and defined by, the specific sequence of their subunits.

The concept of biological information threw a completely new light on the century old mystery of inheritance (*"heredity is the transfer of information"*), and quickly transformed the whole of biology, which turned from an energy-based into an information-based science. Despite this outstanding success, however, it has been repeatedly pointed out that biological information, or *biological specificity* (as some prefer to call it), cannot be measured and cannot therefore be regarded as a physical quantity, neither a fundamental nor a derived one. This is further underlined by the fact that there is another type of information which can be measured and which is a true physical quantity. It is the information of a message that Shannon defined in 1948 with an entropy-like formula, and which can therefore be referred to as *physical information*.

The crucial point is that the information defined by Shannon's formula does not depend on the sequence of subunits, while biological information is defined precisely by that sequence. Physical information, in other words, has nothing to do with specificity, while biological information has everything to do with it. The two concepts are literally worlds apart, and this reinforces the conclusion that biological information is not, and cannot be, a physical quantity. So what is it?

According to a growing number of people, biological information is a *metaphor*. It is a means that we use to describe what we observe in living systems and to communicate our results quickly and easily, but no more than that. It is like those programs that we use to write our computer instructions in English, thus saving us the trouble to write them with the binary-digits of the machine language. Ultimately, however, there are only binary digits at the level of the machine language, and there are only physical quantities at the most fundamental level of Nature.

This conclusion, which can be referred to as *"the physicalist thesis"*, has been proposed in various ways by a number of scientists and philosophers (Chargaff, 1963; Sarkar, 1996; Mahner and Bunge, 1997; Griffiths and Knight, 1998; Griffith, 2001), and is still a hotly debated issue. One of the crucial points is the

very definition of information, but despite the many proposals which have been put forward (Brillouin, 1956; Monod, 1970; Atlan, 1972; Gatlin, 1972; Dretske, 1981; Chaitin, 1987; Devlin, 1990; Küppers, 1990; Yockey, 1992; Sarkar, 2000; Maynard Smith, 2000), a general consensus has not yet been reached.

The definition problem will be addressed in this paper too, but only as a logical consequence of the answer that will be given to a larger problem. The history of science tells us that a new physical entity has been universally accepted only after the discovery of natural phenomena that could not be accounted for by the previous entities. In Newton's times, for example, physicists were recognising only three fundamental quantities (space, time and mass) and a fourth one (electric charge) was added only after the discovery of the electromagnetic realm.

Nothing of the kind has apparently happened in Biology. The century old battle against vitalism was fought, and won, precisely on the issue that life obeys the ordinary laws of physics. This is the strength of the physicalist thesis, and we must accept that biological information can be a real natural entity only if we discover that it is essential for the coming into being of an entirely new realm of molecules. This is the point which lies at the heart of the problem of biological information, and it is precisely this point, as we will see, that the physicalists have overlooked.

The molecules of life

Modern biology is based on three extraordinary experimental facts: (1) the discovery that all specific structures and functions of life are ultimately due to *proteins*, i.e. to strings of amino acids; (2) the discovery that the hereditary instructions for making proteins are carried by strings of nucleotides called *genes*; and (3) the discovery that gene sequences are translated into protein sequences by a universal set of rules which has become known as *the genetic code*.

These discoveries have confirmed that genes and proteins are the key molecules of life, but have also revealed something totally unexpected about them. They have shown that genes and proteins differ from all other molecules not because of their size, shape or composition, but because they are *produced* in a totally different way. In the inorganic world, the structure of molecules is determined by the bonds that exist between their atoms, i.e., by *internal* factors. In living systems, instead, genes are built by molecular machines which physically stick their nucleotides together following the order of a template which is *external* to the growing molecule. In a similar way, proteins are made by molecular machines which bind amino acids in the order prescribed by an external template of nucleotides.

Genes and proteins, in short, are assembled by molecular robots on the basis of outside instructions. They are *manufactured* molecules, as different from ordinary molecules as *artificial* objects are from *natural* ones. Indeed, if we agree that molecules are natural when their structure is determined *from within*, and artificial when it is determined *from without*, then genes and proteins can truly be referred to as *artificial molecules*, as *artifacts made by Nature*.

Names apart, it is a fact that this type of molecule exists only in living systems. There is nothing like them in the inorganic world. This concept has been emphasized by many authors, in particular by Hubert Yockey, one of the patriarchs of Information Theory: "*There is nothing in the physico-chemical world that remotely resembles reactions being determined by sequence and codes between sequences...There is no trace of messages determining the results of chemical reactions in inanimate matter...The origin of a genetic code is a bridge that must be crossed to pass over the abyss that separates chemistry and physics from biology...The existence of a genome and the genetic code divides living organisms from inanimate matter*" (Yockey, 2000).

Molecular biology, in short, has revealed the existence of a totally unexpected gulf between life and non-life. The great divide is not between organic and inorganic structures. It is between structures which are built *from within* and structures which are built *from without*. Between molecules which are made by spontaneous assemblies and molecules which are manufactured by molecular machines. All of which has two outstanding implications. The first is that the very existence of manufactured molecules requires the existence of at least one new natural entity, because the known physical quantities can only account for molecules which are formed spontaneously. The second is that there must have been a point, in the early history of life, when molecular machines appeared on our planet and started producing manufactured molecules.

The first molecular machines

A molecular machine is *a system which is capable of assembling molecules by binding their subunits together in the order provided by a template*. In principle, many molecules could have been used as templates, and many operations could have been performed on any class of templates. In practice, however, all existing molecular machines stick subunits together in the order provided by *linear strings of nucleotides*, and these templates are processed only with the operations of *copying* and *coding*. The result is that we have two great classes of molecular machines: (1) some make copies of a pre-existing string of nucleotides, and for this reason are referred to as *copymakers*; (2) others translate a string of nucleotides into a string of amino acids according to the rules of a code, and for this reason are referred to as *codemakers*.

Today, copymakers and codemakers are highly sophisticated molecular systems, but the main operations of copymaking and codemaking are still performed by a few medium-sized molecules, mainly made of ribonucleic acids. The first molecular machines, therefore, could have been medium-sized RNAs (polymerizing RNAs, pieces of ribosomal RNAs and transfer RNAs), which came into being by chemical evolution and started producing “manufactured” molecules by copying and coding. However they came about, it is important to notice that the appearance of these systems gave rise not only to new molecules but also to new natural entities, and in particular to *biological information*.

Let us imagine a population of nucleic acids which had formed spontaneously on the primitive Earth by the random assembly of nucleotides, and let us consider what happened when a copymaker used one of them as a template and started copying it. During that process, the random sequence of the template became a precise sequence of operations for the copymaker, i.e. it became *information* for it. Nucleic acids alone and copymakers alone have nothing to do with information, just as hydrogen and oxygen in isolation have nothing to do with the properties of water. It is only their combined action in the act of copying that brings information into existence. It was copymakers, therefore, that first brought biological information into the world, and it is they that keep producing it. But this presents us with a problem, because now we have to make up our minds about the scientific “status” of biological (or organic) information.

Organic information

According to a long tradition, the entities of nature are divided into “objective” (or “primary”) and “subjective” (or “secondary”). Objective entities are features which can be evaluated in a reproducible way by any number of observers, and are normally represented by entities which can be measured, i.e. by *quantities*. Subjective entities are features whose evaluation depends upon individual judgements, and which are referred to as *qualities* because they can be described but not measured. By tradition, therefore, we say that science is the study of quantities and qualities, and that any natural entity belongs to one of these two categories.

In the case of organic information, however, this scheme breaks down. Organic information is *a specific sequence of elements*, and the specificity of a sequence cannot be measured, so organic information is not a quantity. But it is not a quality either, because linear specificity is a feature that we find in organic molecules, and is therefore *an objective feature of the world*, not a subjective one. Organic information, in short, is neither a quantity nor a quality, so it must be a new kind of natural entity: *something which cannot be measured but which still is an objective and reproducible entity*. A scheme based on quantities and qualities, in other words, is not enough to describe the world, but we can easily generalize it. All we have to do is to go back to the original distinction between objective and subjective entities, and to accept that there are natural entities which are *objective-but-not-measurable*.

We conclude that organic information is a new type of natural entity, but we also conclude that it belongs to the same class of objective entities that contains all physical quantities. Therefore, *it has the same scientific “status” as physical quantities*. This however gives us a new problem, because there are two main classes of physical quantities: a small group of *fundamental quantities* (space, time, mass, charge and temperature) and a much larger group of *derived quantities*. This distinction remains valid even in the more general framework of the objective entities, so we need to understand whether organic information belongs to the first or to the second group, i.e., whether it is a fundamental or a derived entity.

Luckily, this problem has a straightforward solution because genes and proteins are sequences which have two very special characteristics. One is that *any change to a biological sequence produces a sequence which has an entirely new specificity*. This means that although a biological sequence can be said to have

“components”, it is at the same time a single indivisible whole. The second outstanding feature is that *from the knowledge of n elements of a biological sequence it is impossible to predict the element $(n+1)$* . This is equivalent to saying that *a specific sequence cannot be described by anything simpler than the sequence itself*, so it cannot be a derived entity.

We conclude that organic information has the same scientific status as physical quantities, because it is an objective and reproducible entity. However, we also conclude that it does not have the status of a *derived* physical quantity, because it cannot be expressed by anything simpler than itself. This suggests that it has the same scientific status as *fundamental* physical quantities, i.e., that it is a fundamental entity of Nature. And we can also give it a name. Since organic information can only be described by *naming* its sequence, we can say that it is a *nominable* entity (It will be noticed that this is not equivalent to the concept of *ostensible* entity, because an ostensive procedure does not reveal all the features which are normally associated with the scientific naming of a natural sequence).

Organic meaning

Proteins truly are the stuff of life. They are the key building blocks of all living structures, as well as the engines of the countless reactions that go on within those structures. For all their extraordinary versatility, however, there is one thing they cannot do. Unlike genes, they cannot be their own templates. It is simply not possible to make proteins by copying other proteins. The fact that parents are similar to offspring means that they are made of similar proteins, but the instructions to build proteins are not transmitted by proteins. What is inherited is genes, and it is copies of genes, i.e. strings of nucleotides, that provide the information for making proteins. More precisely, it is a sequence of groups of three nucleotides, called *codons*, that determines the sequence of amino acids in a protein chain.

For an organism to become similar to its parents, however, it is imperative that the same genes always give rise to the same proteins. Without this precondition, there would be no parents and no offspring in the first place. There would be no biological specificity, no heredity, no reproduction. Life itself as we know it on Earth is totally dependent upon this one crucial characteristic of protein synthesis: *the same codon must always be translated into the same amino acid*.

This result would be delivered with absolute certainty if the link between codons and amino acids were determined by some law of physics, but this is not the solution chosen by Nature. The link is provided by molecules called *adaptors* (*transfer RNAs*), which keep the two objects at a distance, so that any codon could, in principle, be associated with any amino acid. There is no law of physics, no chemical necessity for the existence of specific rules of correspondence between codons and amino acids, and we can account for their presence in the world only by saying that they are the result of a code, more precisely of what is referred to as *the genetic code*.

A code is a set of rules which establish a correspondence between the objects of two independent worlds. The Morse code, for example, is a correspondence between combinations of dots and dashes with the letters of the alphabet, and in the same way the genetic code is a correspondence between combinations of nucleotides and amino acids. Let us notice now that establishing a correspondence between, say, object 1 and object 2, is equivalent to saying that object 2 is the *meaning* of object 1. In the Morse code, for example, the rule that “dot-dash” corresponds to letter “A”, is equivalent to saying that letter “A” is the meaning of “dot-dash”. In the code of the English language, the mental object of the word “apple” is associated to the mental object of the *fruit* ‘apple’, and this is equivalent to saying that that fruit is the meaning of that word. By the same token, the rule of the genetic code that a codon corresponds to an amino acid is equivalent to saying that that amino acid is the organic meaning of that codon. Anywhere there is a code, be it in the mental or in the organic world, there is meaning. We can say, therefore, that *meaning is an object which is related to another object by a code*, and that organic meaning exists wherever an organic code exists (Barbieri, 2003).

One could object that meaning must be much more complex than that, but complex entities can be made up of simple elements, especially in the realm of organic molecules. The existence of meaning in the organic world may seem strange, at first, but in reality it is no more strange than the existence of an organic code, because they are the two sides of the same coin. As we have seen, saying that a code establishes a correspondence between two objects is equivalent to saying that one object is the meaning of the other, so we cannot have codes without meaning or meaning without codes. All we need to keep in mind is that meaning is a mental entity when the code is between mental objects, but it is an organic entity when the code is between organic molecules.

The two pillars of life

Modern biology and modern physics have both readily accepted the concept of information and have both carefully avoided the concept of meaning. In the case of physics, this was probably due to the fact that *physical information* could be defined and measured as a true scientific quantity, while for meaning there has never been any serious prospect of a quantitative expression. On top of that, Claude Shannon clearly stated that Information Theory has nothing to do with meaning because the semantic content of messages is irrelevant to the problem of transmitting them.

In the case of biology, the meaning of molecular messages is far from irrelevant, but many went along with Shannon's suggestion that information is the real thing, and that the problem of meaning can be circumvented. After all, one could always say that meaning is inextricably tied up with *context* and can be accounted for only by describing all the fastidious details of context. Some have even suggested that meaning is only a qualification of information, something that allows us to distinguish between the *syntactic* and the *semantic* aspect of information.

There is no doubt, in short, that information is highly popular and that meaning is equally highly unpopular among scientists, both in physics and in biology, and yet we have seen that organic information and organic meaning are both the result of *fundamental* natural processes. Just as it is an act of *copying* that creates organic information, so it is an act of *coding* that creates organic meaning. Copying and coding are the processes; copymakers and codemakers are their agents; organic information and organic meaning are their results, or the kind of natural entity that they belong to. But the parallel goes even further than that.

We have seen that organic information *cannot be measured*, and the same is true for organic meaning. We have seen that organic information is an *objective and reproducible* entity, because it is defined by a specific sequence of molecules, and the same is true for organic meaning, which is defined by a specific set of coding rules between molecules. Finally, we have seen that organic information is a *fundamental* entity, because it cannot be described by anything simpler than its sequence, and the same is true for organic meaning, which cannot be defined by anything simpler than its coding rules.

Organic information and organic meaning, in short, belong to the same class of entities because they have the same general characteristics: they both are *objective-but-non-measurable* entities, they both are *fundamental* entities of Nature, and since we can describe them only by *naming* their components, they both are *nominable* entities. Finally, let us underline that they truly are *the two pillars of life*, because organic information is a result of the copying process that produces *genes*, while organic meaning is a result of the coding process that generates *proteins*. At this point, we can summarize all the above concepts with the following statements:

- (1) *Organic information is the specific sequence produced by a copying process.*
- (2) *Organic meaning is the object which is associated to another object by a coding process.*
- (3) *Organic information and organic meaning are neither quantities nor qualities. They are a new kind of natural entities which are referred to as nominable entities.*
- (4) *Organic information and organic meaning emerge from different biological processes: organic information is a result of copying and organic meaning is a result of coding.*
- (5) *Organic information and organic meaning have the same scientific status as physical quantities because they are objective and reproducible entities.*
- (6) *Organic information and organic meaning have the same scientific status as fundamental physical quantities because they cannot be reduced to, or derived from, simpler entities.*

Operative definitions

The definition of scientific concepts is a notoriously difficult problem in biology, but for a time it was a controversial issue even in physics, despite the fact that there the situation is simpler because most physical entities can be measured. The critical point in physics was the theoretical possibility that the entity which is measured may not be the same entity which had been defined. This led to the idea that there should be no difference between what is measured and what is defined, i.e., to the concept of *operative* (or *operational*) definition: *a physical quantity is defined by the operations that are carried out in order to measure it.*

It was this operational approach that solved the definition problem in physics, and it is interesting to notice that a generalized version can be obtained in a fairly straightforward way. Instead of saying that *a natural entity is defined by the operations that measure it*, we can say that *a natural entity is defined by the operations that evaluate it in an objective and reproducible way*.

The advantage of this generalized approach is that it applies to all *objective entities*, so it can be used not only in physics, but in biology as well. To this purpose, we only need to notice that *a measurement* is an objective and reproducible description of a physical quantity, just as *the naming of a specific sequence* is an objective and reproducible description of organic information, and just as *the naming of a coded object* is an objective and reproducible description of organic meaning. While the physical quantities are evaluated by *measuring*, in other words, our biological entities are evaluated by *naming their components*, but in both cases the entities in question are *defined by the operations that evaluate them*, and this is the essence of the operative approach.

We conclude that organic information and organic meaning can be defined by generalized operative definitions which are as reliable as the operative definitions of physics. This should ensure that they are no longer at the mercy of endless debates on terminology as they have been in the past. The operative definitions are scientific tools, not literary or philosophical statements. They are justified by their own prescriptions, so there is no point in asking if they are right or wrong. All we can ask is whether they contribute to our description and to our understanding of Nature.

Conclusions

One of the most extraordinary results of molecular biology is the discovery that genes and proteins are *molecular artifacts*, i.e., molecules which are assembled by external agents. More precisely, they are manufactured by molecular machines which stick their subunits together in the order prescribed by a template of nucleotides. Genes are manufactured by *copymakers*, machines that make copies of a sequence of nucleotides. Proteins are made by *codemakers*, machines that translate a nucleotide sequence into an amino acid sequence according to the rules of a code.

When a copymaker is copying, the nucleotide sequence of the template becomes *information* for it, so it is an act of copying that brings organic information into existence. In a similar way, when a codemaker is assembling a protein, amino acids are associated to codons and become the *meaning* of those codons, so it is an act of coding that brings organic meaning into existence. In short, organic information and organic meaning are the inevitable results of copying and coding.

Modern biology has readily accepted the concept of information but not the concept of meaning. This cannot be right, because copying and coding are both fundamental processes, so information and meaning are equally important to life. The present exclusion of meaning from biology, however, is not due to the idea that meaning is outside science, like, for example, *phlogiston* or *entelechy*. It is because meaning is regarded as a function of too many variables, an entity too complex to be given a scientific definition. Here it is shown that organic information and organic meaning can be defined by the biological processes of copying and coding that bring them into existence. It is also shown that these biological definitions are *generalized operative definitions*, i.e. definitions where the entities are defined by the operations that evaluate them in an objective and reproducible way.

At the moment, however, we don't know to what extent these biological definitions can be generalized. Can we extend them from the molecular level to the other levels of life? Can we say, for example, that mental information and mental meaning are the results of mental copying and mental coding? The short answer is that we cannot answer yet. We don't know, for example, if we need more general concepts of information and meaning in order to explain a process like embryonic development, so it is far too early to draw conclusions at the higher level of the mind. This, however, should not make us forget the fundamental role of organic information and organic meaning in the history of life.

The organic information which is handed down, generation after generation, by the copying of genes, with occasional mistakes, is the raw material for natural selection to work on. In a similar way, the organic meaning produced by new organic codes would create evolutionary novelties comparable to that of the genetic code, and in fact there seems to be a correspondence between the great events of macroevolution and the appearance of new organic codes (Barbieri, 2003). Organic information, in short, is the raw material for the mechanism of *evolution by natural selection*, while organic meaning is the raw material for the mechanism of *evolution by natural conventions*. This means that the concepts of organic information and

organic meaning – or the equivalent concepts of copying and coding – are the true foundation of biology, even if we may need to extend them with other concepts or with other qualifications at some higher levels of the hierarchy of life.

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