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MOLECULAR CODES AND SIGNALS[1]

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The general conceptual background of my talk is this: The discovery of the genetic information enciphered on the DNA molecule of the cell remains underestimated because of a deliberate conceptual and interpretative poverty of modern natural sciences. Several fundamental and primarily descriptive concepts were consciously eliminated from the modern scientific frame of mind. An unfair scepticism was injected into the minds of scientists by hypercritical philosophers – Hume and Immanuel Kant are typical representatives of that band. In modern sciences the doctrine of Kant is not accepted in a coherent way. The concepts of space and time were reinstalled by physicists – who – curiously enough – do not really care what Kant said a propos of space and time. But the concepts of a whole, of an efficient and material cause are virtually forgotten or reduced to a ridicule. The discovery of the molecular cryptography illustrates the need for the restoration of those concepts within the scientific conceptual framework.

To illustrate the crisis in the concept of causality, I shall tell a story. The other day I was walking along a street in Barcelona, and a small dog approached me saying: „Excuse me sir, I am going to visit my fiancée in New York, could you tell me, how to get to the airport?" I said: „Unfortunately, I can't tell you this, sir. I am a foreigner. You must ask somebody else." So the dog bowed, walked away and I heard that it was asking the same question an elderly lady on the other side of the street. Now, the whole event was properly registered on the video tape. The dog was found to be a legitimate descendant of a quite respectable dog's family.

Here the modern (conceptually mutilated) paradigm of sciences enters:

How to explain this unusual activity of the dog? The most plausible explanatory hypothesis is that the dog was intoxicated, or drugged. It possibly swallowed a wrong pill or drunk from a wrong glass – a proper laboratory procedure will certainly discover the reasons for its strange behaviour. If not, the reasons should be looked for more deeply. Perhaps one of its chromosomes was unnaturally spliced or duplicated. Anyway, the answer would not be satisfactory unless it is done in terms of the thermodynamics, or quantum mechanics. The dog's brain is to be analyzed upon the biochemical level. The sounds produced by it have to be analyzed down to the level of attoseconds.

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[1] This is the full text of the talk given during the n Meeting of the European Jesuit Scientists, Sant Cugat, Barcelona, 11-15 September, 1991.

What about the old paradigm? The old fashioned, Aristotelian paradigm would accept for granted that the dog's eyes, muscles and its brain were working properly, and that its neurotransmitters were secreted in the right place. The old paradigm would concentrate upon the necessary conditions for comprehending the concepts of aims and proportional means, the idea of searching for information, the idea of a distance in space, the concept of aerial transport, finally on the necessary conditions for communicating those concepts with the aid of the acoustic signals of the English language code.

This may be enough as far as the problem of causality is concerned. I shall return to it by the end of my talk. The idea of the whole is also quite crucial. But how does all this enter into the problem of the molecular signals?

To answer this question we have first to prepare a proper conceptual background.

The current but quite erroneous idea of a living being, equals it with the adult structure of the organism. The error is threefold:

(1) Many people, mostly physicists, but even some biologists, seem to forget that all the organisms we know, pass through a stage in which they are building their functional structures from inorganic matter, or from the organic nonfunctional scraps[2].

(2) Few people remember, or realize that any organic food taken by a living body, be it a cell or an elephant, is chemically degraded, down to the level of simple organic molecules. From those simple chemical units every cell is building *de novo* its hierarchical, functional structures. The alien, relatively big molecules of the fatty acids taken in the food are stored sometimes without being disassembled, but I never heard they would be incorporated into functional structures of the cell.

(3) Few people are aware that all the structural elements of the living body, whatever is the stage of its life cycle, undergo a continuous and relatively fast replacement – the process of this replacement is called metabolic turn-over.

So, one may say that the development is the most essential property of biological life. But the development means the ceaseless tendency to build not just the *complex,* but the *functional* structures. A dead, decaying body is much more complex than the living one. So not just **complexity** but **functionality** is the right descriptive concept in biology.

Summing up:

I. biological life does not mean just **structure – but a dynamism** of structures

[2] It is rather hard to find the reasons of a statement like this: „Darwin could not have suspected the existence of self-organization, a recently discovered (sic! – PL), innate property of some complex systems". Cfr. Kauffman S. A. [prof. of biochem. and biophys. Univ. of Pennsylvania School of Medicine] (1991). *Antichaos and Adaptation.* Sci. Am. Aug. 64-70. Ancient Greeks, Hippocrates and Aristotle among them, did know this quite well. Aristotle considered the *epigenesis* as the most fundamental and essential manifestation of biological life.

II. biological life does not mean just **complexity – but integrated** complexity (functionality)

III. biological life does not mean just a **set of organs –** but primarily a process of building an **integrated set** of organs.

DNA codons						aminoacid 1 & 3 letter symbol
		GCT	GCC	GCA	GCG	= A = Ala
CGG	CGT	CGC	CGA	AGA	AGG	= R = Arg
				AAT	AAC	= N = Asn
				GAT	GAC	= D = Asp
				TGT	TGC	= C = Cys
(Stop)			TAA	TAG	TGA	= = End
				CAA	CAG	= Q = Gln
				GAA	GAG	= E = Glu
		GGT	GGC	GCA	GGG	= G = Gly
				CAT	CAC	= H = His
			ATT	ATC	ATA	= I = Ile
TTA	TTG	CTT	CTC	CTA	CTG	= L = Leu
				AAA	AAG	= K = Lys
(Start)					ATG	= M = Met
				TTT	TTC	= F = Phe
		CCT	CCC	CCA	CCG	= P = Pro
TCT	TCC	TCA	TCG	AGT	AGC	= S = Ser
		ACT	ACC	ACA	ACG	= T = Thr
					TGG	= W = Trp
				TAT	TAC	= Y = Tyr
		ATT	GTC	GTA	GTG	= V = Val

Now what about signals? The molecular signals and codes have no sense whatsoever apart from the function and the development. To reach this part of biological dynamism upon which the idea of a DNA signal makes sense, we have first to descend several levels of mental **abstraction.** I repeat – mental abstraction. Without this abstraction we could not grasp the actual meaning of a molecular signal. However, if we make an abstrac-

tion, and especially if we make this abstraction again and again, we shouldn't forget that it is just a mental process. Otherwise we would create pseudo-beings which exist in our phantasy but not in the reality.

The first level of the abstraction, I am talking about, separates the biochemical level from cytological level, or the anatomical level.

The second level of abstraction separates a molecule from its functional context within a concrete organellum of a cell.

The third separates the biosynthetic pathway which produced that molecule, from other biosynthetic pathways.

The fourth step separates a single molecule of an enzyme from the whole set of the enzymes constituting this biosynthetic pathway.

The fifth step of abstraction forgets about the dynamism of this particular enzyme and concentrates on the aminoacid sequence (primary structure) of a polypeptide – and so we have come to the tiny details of the DNA molecule of the φX174 virus[3].

The variety and number of signals already discovered in the DNA molecule is astonishing. Almost every year new signals and new kinds of them are discovered. I intended to say something on the most recent discoveries, but after a reflection I decided to turn back to the elementary facts – I prefer to reconsider the most basic elements rather than to glide superficially on things which are still poorly understood.

To illustrate my point I selected a stretch of a single file of the DNA-molecule hidden in the capsid (envelope) of the φX174 virus. The whole DNA molecule of this particular virus is composed of 5386 complex chemical subunits (average mol. weight = 300) of four different kinds (A,C,G,T). The selected stretch is only 37 subunits long. The distance between the subunits is 0,34 nm. The actual length of the whole stretch is some twelve nanometers.

DNA ..... GCGGAAGGAGTGATGTAATGTCTAAAGGTAAAAAACG .....
0 ...⟸.. .831. ..... 841 ..... 851 ..... 861 ..... 867 .....⟹.. 5386

The chemical structure of the DNA subunits is such, that they are interchangeable. In other words those subunits could be rearranged in the form of 4^{37} different sequences – each sequence being perfect DNA – as far as the purely physico-chemical aspect of this molecule is concerned.

Now I am going to discuss the *technical* signals of the DNA. I am using the term „technical signal" to denote those signals which refer to the properties of the translating dynamism of the cell. In the „technical" sense some physically possible DNA sequences are useless.

For instance, the sequence TAA, or TAG or TGA (called the „stop" codons) provoke the arrest of the translating dynamism of the cell. They mean „stop here", „do not translate any longer". In our stretch we have four such signals.

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[3] Cfr Stryer L. (1981) *Biochemistry.* Freeman & Co., San Francisco, p. 632, or Freifelder D. (1987) *Molecular Biology.* Jones & Bartlett Publ., Inc., Boston, 407-410.

If within a stretch of the DNA those signals are too numerous, no functional message could be encoded there. It would be too often interrupted by the „stop codons". How long must be the space free of the stop signals? The so called open reading frame (ORF) for a relatively crude catabolic enzyme must be at least 4 hundred subunits long, but the ORF for an anabolic (biosynthetic) enzyme is usually three times longer.

The presence of the stop signals tells us nothing about the functional meaning of the stretch. However, it does tell us something about the dynamism of the translating machinery.

I didn't finish yet with the technical meaning of this stretch of the viral DNA. We have another technical signal here (the so called Shine-Delgarno sequence).

The six subunits underlined inform the translating machinery of the cell that the sequence ATG which is 4–7 subunits to the right signifies the beginning of the new functional message. In other words the sequence ATG (which usually codes for methionine aminoacid) *because* of the presence of the Shine-Delgarno sequence is to be interpreted as the beginning of a bigger whole. That methionine aminoacid subunit may be discarded (cut oft) in the further (posttranslational) processing of the protein molecule.

We may now translate the sequence starting with the codon ATG (start)[4]

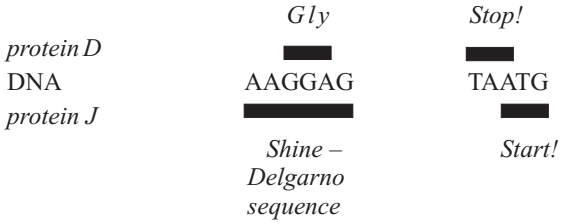
The first stop codon of this ORF appears after 114 nucleotide subunits. That means it contains 38 aminoacid codons. This relatively short message dictates the primary structure of the viral protein J. The protein regulates the packing of the newly synthesized viral DNA into the newly synthesized viral capsid.

[4] The symbolism in molecular biology needs a comment, I think. It does not reflect the actual complexity of the interacting structures. For instance, the three-letter, arbitrary symbols denote a single aminoacid, a relatively simple organic molecule (average mol. w. = 100). On the other hand the three capital letters used to denote a codon, refer to three relatively complex organic molecules (av. mol. w. = 300). So in the DNA each aminoacid is enciphered by an almost 10 times bigger chemical structure.

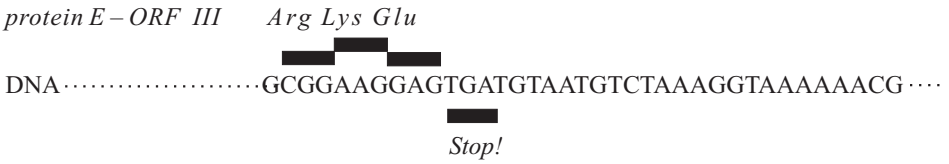
But it is not the end of the story. There are other messages written on the same stretch of the DNA molecule:

The TAA signal marks the end of the 456 subunits long ORF for the protein D. This protein is necessary in the process of the proper assembly of the new viral capsid.

We can see that the same elements of the DNA molecule can have different meanings.



Still it is not the end of the story. On the same stretch a fragment of another protein is encoded. It is the protein E, which, if released in the proper moment, induces the destruction of the bacterium and thus liberates the newly synthesized viral units[5].



We can see that on the same sequence of 9 nucleotide subunits the following signals are encoded:

(1) aminoacid glycine and valine codons (protein D)

(2) aminoacid lysine and glutamic acid codons (protein E)

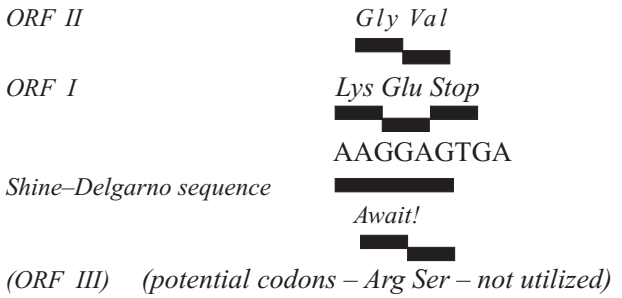
(3) warning signal „beware the start signal" (protein J)

A purely formal possibility is left unused, namely the potential codons in the third open reading frame.

(4) (potential codons for the aminoacids arginine and serine).

We discussed just two kinds of signals found in the DNA molecule. One kind of signals (I called them *technical* signals) cannot be treated without the reference to the mechanism of translating machinery of the cell. The other kind of signals (aminoacid

[5] The ORF for the protein E is 273 subunits long.



codons) has reference to the functional structure of protein molecules, and their sense or lack of sense cannot be evaluated without the reference to a higher level of dynamisms – but which level? That depends upon the nature of a particular organism and the nature of the particular protein enciphered in the concrete ORF of the concrete DNA molecule. Some proteins are functional within the framework of a single cell, some other are functional upon the level of anatomical structures. But that is another story[6].

The facts discussed above demonstrate a variety of signals and codes utilized by a relatively simple bacterial cell[7]. In the enciphered DNA molecule of such a cell several other kinds of signals were discovered. Every kind of a signal hidden in the physical structure of the DNA has its own reference framework. Apart from that framework – in isolation from the proportionately complex and proportionately dynamic system of interpretation, those signals make no sense, and I doubt if they could be discovered at all[8].

What I would like to stress is this. The molecular signals reintroduce the concept of an objective whole – not just a single whole, but a variety of wholes. Their indivisibility is not physical, but dynamic. From the purely physical point of view those wholes

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[6] The details of the messages enciphered on the DNA of 0X174 virus are described after Sanger F., Air G. M., Barrell B. G., Brown N. L., Coulson A. R., Fiddes J. C., Hutchison III C. A., Slocombe P. M. Smith M. (1977) *Nucleotide sequence of the bacteriophage (fX174 DNA.* Nature 265, 687-705; Fiddes J. C. (1977) *The nucleotide sequence of a viral DNA.* Sci. Am. 237/6 (December), 55-67; Freifelder D. (1987). *Molecular Biology.* Jones & Bartlett Publ., Inc., Boston, p. 408-410. According Sanger et all (1977) and Fiddes (1977) the length of the DNA of the phage is 5375 nucleotide subunits, while according Freifelder (1987) their number is 5386.

[7] The virus complex structure is only used by the bacterial cell, but it is completely passive source of the molecular information. It might be compared with the videocassette, which is unable to produce a picture or a sound without being processed by a proper dynamism of the videotape player.

[8] It seems that this rather obvious truth is universally ignored. Cfr. for instance the following text: „A genome [the informational DNA molecule - PL] acts like a complex parallel-processing computer, or network, in which genes regulate one another's activity either directly or through their products. The coordinated behaviour of this system underlies cellular differentiation". Kauffman S. A. [prof. of biochem. and biophys. Univ. of Pennsylvania School of Medicine] (1991) *Antichaos and Adaptation.* Sci. Am., Aug. 64-70.

are rather fragile, and yet the basic, fundamental dynamism of life depends upon their perfect integration. The awareness of this fact should reintroduce into scientific methodology the forgotten concepts of nonarbitrary wholes and provoke the reconsideration upon the concept of the proportional integrating cause.

Now what is the reason behind the story about the little dog in Barcelona? The current paradigm of the natural sciences, with its reluctance to see anything which goes beyond a limited set of concepts invented and selected to cope with the astrophysical, or subatomic realities, and their mathematical processing – this paradigm seems to me equally shortsighted in the case of the molecular signals as it was in the case of the Barcelona dog. The ideas of the whole, and the idea of the *proportional integrating efficient cause* must be reconsidered, while the validity of Kant's critical statements should be – in my opinion – reanalyzed.