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MOLECULAR CODES AND SIGNALS¹

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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.

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 scraps².

(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	= 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 ϕ X174 virus³.

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 ϕ X174 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..... GCGGAAGGAGTGATGTAATGTCTAAAGGTAAAAACG
 0 ... \leftarrow ... 831. 841 851 861 867 \Rightarrow .. 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.

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.

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

protein D – ORF II *Ala Glu Gly Val Met*



DNA..... GCGGAAGGAGTGATGTAATGTCTAAAGGTA AAAAACG
Stop!


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.

	<i>Gly</i>	<i>Stop!</i>
<i>protein D</i>	█	█
DNA	AAGGAG	TAATG
<i>protein J</i>	████████	█
	<i>Shine – Delgarno sequence</i>	<i>Start!</i>

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 units⁵.

protein E – ORF III *Arg Lys Glu*



DNA..... GCGGAAGGAGTGATGTAATGTCTAAAGGTA AAAAACG ...
Stop!

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.

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.