OFF-PRINT FROM

ADVANCED TECHNOBIOLOGY

edited by

BORIS RYBAK

Professeur à la Sorbonne nouvelle

SIJTHOFF & NOORDHOFF 1979
Alphen aan den Rijn — The Netherlands
Germantown, Maryland, USA

WELCOME ADDRESS

B.Rybak

I.E.L.P.,Université de Paris III,
F 75005 Paris

It is a great honour and a great pleasure for me to chair this NATO-ASI on Advanced Technobiology.

A great honour because the Science we are dealing with is the fundamental logistic in any experimental science - experimenter included (the History of Science and of Technology tell us a lot about these intermingled processes).

A great pleasure,also,because we are "Hommes de métier" and the bright international panel of speakers we have and the young scientists who attend this Session of teaching Bio-sciences research are all "Men of Truth" according to the challenging expression of the late Jean Rostand. So that it is always a deep enjoyment to put together, in the "melting pot" - some kind of "Biotron" - of the interdisciplinarity of Truth , people of great insight and creativity, because Truth is Reality plus wisdom.

This Meeting is a School where one will speak Science using the English and French language. According to the NATO-ASI rule this kind of session has "primarly a high level teaching activity..." The subject being treated in considerable depth by lecturers prominent in their field is presented to other scientists of international standing already specialized in the field and to top students with advanced background. This is the case and I salute the leading senior

Scientists of notable achievements and our young Colleagues of high qualification.

Compliments and ave , yes ! Because the distinguished group who will actively participate here for a while in the life of Biotechnology is characterized notably by the fact that one can be aware , in our period of inflation, that one can publish and perish - but by their precise and concise works anyone here is perfectly alive .

We are dealing with Bio-sciences and consequently concerned with experimentation with vegetals and animals and, in Medicine, with assistance of patients. Now our deontology is founded on the constat that the human hope of life in the Prehistoric period was about 25 years while actually it turns around 70. So, as technobiologists we are Nature lovers and we can afford the responsability to be tutorial humanistic sapiens and faber altogether. In such a way that , according to our aim - and success - to develop a systematic non-invasive,non-traumatic methodology for approaching bio-systems, we suspect that those who cry for "world (or international) coalition for the abolishment of vivisection",etc. have no idea about the know-how and the spirit-how we work for health and welfare including self-recognition. At the limit we suspect that they are obscurantists.

This puts the problem of another radicalism on the mat : abstract formalisms are one thing but technocratic (= oversimplified ,schematized) modelizations another, versus scientific discoveries and inventions as severe ludic permanent(even subconsciously) promotions. But technology should more degenerate into phantasmatic "appareillomanie", thanks to the reificative "principle of economy" through mental and experimental interactive controls.

In our field, apparatus or instruments are tools permitting, by one way or another,to capture signals and extract informations from them by an integrative function of the central neuronic system of the scientist .A non-integrated signal is not an information. Hertzian wave examplifies this concept since we are traversed by radio-frequencies but, because we are not devised to transduce directly such signals , we have no idea about the existence of these signals except if we use a set-up called a radio-receptor. The same aperceptual affair affected the situation of our ancestors

when they did not know the laws of the gravity field. And today we move merely in the interrogative epistemology if not metaphysics as far as our transcendant limits are concerned . Therefore,Bioinformatics is the Science which allows us to penetrate more and more into the deepest,cryptic endogeneous and exogeneous coded signals ⟷ informations transforms: we move from complete ignorance to a never-reached total knowledge.Discovery or invention is then the critical phase where a set of signals becomes a sub-set of informations, i.e. correlated informations. Conversely an information can fade and its extinction increases the entropy.

Practice of communications in terms of informations (1) is the federative principle of the present School as it is for any bio-system according to the genetic code $\mathcal{R}$ and the three phenotypic codes : 1) P_m metabolic(basic), 2)P_e endocrine (including,eventually,exhormones like pheromones) and 3) P_n nervous (except in primitive living forms : virus,bacteria, yeasts, certain protozoa,etc.). The phenotype is dependant on the conjugated action of $\mathcal{R}$ and on the multiple biotopes $\mathcal{C}$... via molecules and physical forces constituting fields of affinities, of pattern recognitions.

Let us consider an Universe $\mathcal{U}$. According to Schrödinger (2), any living system is an order and to maintain its order, a living system must suck order from the external environment. But there is a need to put the problem in terms of informations circulations (the precluding signals circulation is thus implicated in a series of active sites reactions decoding some signal in a definite information,immediately

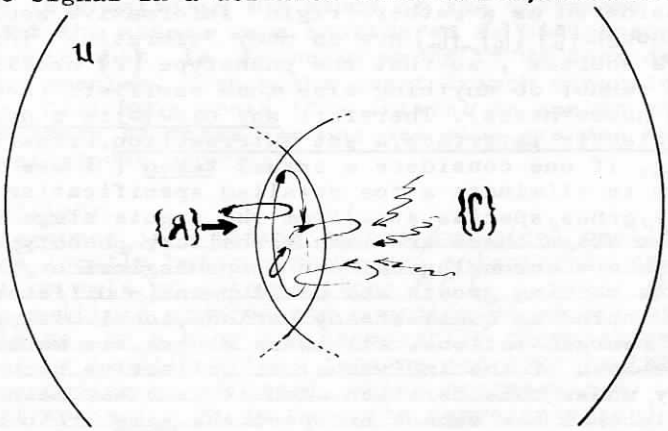


Fig.1

increasing the negentropy of the bio-system bio-{S}). To imagine such bio-{S} as a cybernetic network, for maintaining its order it should have not <u>one</u> source of informations (potential or effective at a certain time) but <u>two</u> sources ,like any energetic (specially thermic) machine. It is what represents figure 1 :<u>any bio-{S} is an informational motor</u> ,the concept of which I developped some years ago (3) (4).The "cold"source of informations is the <u>conservative</u> {A} since it maintains the specificity of living species(admitting mutations)over centuries or more;the "hot"source of informations is the Schrödingerian external biotope,which is strongly variable so that the bio-{S} works as a <u>semi-dissipative</u> system.The different biotopes are themselves semi-dissipative because they provide energy and structured molecules which act as conservative components for the bio-{S};but,for a definite bio-{S} with a finite number of active sites, depending on the biotope this one could be highly dissipative - carrying at the limit only signals - and one understands that such an uninformative biotope is potentially lethal and then it could be only a transitory biotope. It seems to me that this could explain the transfer of the different forms of parasite from one host to another and,maybe, it could intervene in the explanation of migrations. The coaptation of a living system to a certain biotope then depends on the minimum complementarity between active sites of the bio-{S} operating as transformers of signals into informations and depends also on this variable instantaneous and spatially circumscribed flux of adequate signals, <u>i.e</u>. potentially "understandable" as informations by the bio-{S} through as many transformations as needed . {A} could consequently be considered as a rather "rigid" informative source, although $\{I_1\}, \{I_2\}, \ldots \{I_n\}$ are as many "vibrating" informative sources , so that the phenotype {P} oscillates and cannot do anything else than oscillate (homeostasis and homeorhesis). Therefore <u>any bio-{S} is a dynamic symplectic interface,a set intersection</u>.Properly speaking, if one considers a sexual <u>taxon</u> (I use this term to eliminate a too detailed specification of family,genus,species,etc.)from the zygote stage to the adult stage there are many transitory phenotypes as there are chronological and morphological organizations meaning growth and development(= differenciation) and including quasi-steady periods,local disappearances and reorganizations. All these stages are marks of the life-span of the individual or collective natural history under consideration. And it is clear methodologically that one cannot prospect the <u>same</u> organ of the

same organism without paying attention not only to the clone $\{\mathcal{A}\}$ but also to the age, the time-course with anteriorities (like conditioned reflexes and all kinds of memories) as well as to the spatial restraints . $\{\mathcal{A}\}$ itself is submitted to ageing - even inside a particular individual - , so that , insofar as we consider the whole individual of a taxon, the oscillatory bio-$\{S\}$ is intrinsically - and not only extrinsically (= ecologically) - submitted to chrono-alternations . But as a system showing resultant incremential functions during growth ,and differenciation, quasi-stationary turnover during the adult period, and resultant decremential function during senescence. Consequently the bio-informational motor is a non-linear adaptative motor where the instantaneous and remanent combinations of $\{\mathcal{A}\}$ and the different $\{\mathcal{C}\}$ render it $\{\mathcal{P}\}$ or fuzzy . That means that the distribution densities of the events are different and not so sharply built that the bio-$\{S\}$ could not adapt . Briefly speaking : a bio-$\{S\}$ is not a finite recurrent automaton.Furthermore the hodographs or trajectories of the circulating forces and molecules move along intero-internal, intero-external, externo-internal channels ;inside the bio- $\{S\}$ they cross other intersections defining as many compartments (nuclear, mitochrondrial membranes...,intestinal coat,etc.).These points direct our representation of the biospace and put the fundamental problem of mathematical realism against the schematized mathematical models I just mentioned.

Before the celebrated "Erlangen's Program" of Felix Klein (5) Geometry was dedicated to the study of figures; after this inaugural lecture,Geometry became much more interested in the study of the different spaces. But the spaces were considered as homogeneous and isotropic,what is obviously wrong if we consider the living species. Anyhow,the great French mineralogist Alfred des Cloizeaux wrote :"Un cristal de quartz homogène dans toute sa masse est une des plus grandes raretés minéralogiques connues".

Definition:

A bio-space is a finite global dynamical oscillatory space locally heterogeneous and anisotropic resulting from sets of intersections $\mathcal{A} \cap \mathcal{C}$, never $\varnothing$, including multiple ordered and coordinated vicariant vector fields, on a body non necessarily commutative and admitting locally affine tensors and torsors (and the corresponding co-affixes), which represents a functional space (= $\aleph_4$ in Cantor's representation) ,

n-dimensioned, of singularities involving conditional stochastic ergodicity with inaccessible, fully aleatory terms.

This complexity is immediately understood as soon as we cast a glance at a metabolic map or at a microscopic cyto- or histo-logical slide. This complexity expresses a programme, precisely the programme which is our challenge as Biologicians.

We shall move now to the singularities. Let us turn then to the topological interpretation of the mechanical catalysis I discovered (6) and which corresponds to the biophysical princeps factors to induce and to maintain durable, periodically regular revolutions of an adult vertebrate heart: the heart, or a piece of it (7), should be very generally under liminar mechanical restraints to contract and relax for hours. This is an all-or-none law, while Starling's law is a proportional one. Zeeman (8) (9) treated the problem according to the surface of Riemann-Hugoniot which is one of the "catastrophes" of Thom's theory (10) : the orthogonal projection on a flat plane gives the cusp (figure 2). The frontal Z-shape of the Riemann-Hugoniot pucker generated by the singularity called

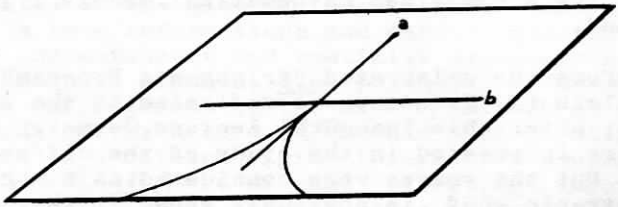


Fig.2.

Hopf bifurcation, is shown in figure 3. Now, what Zeeman's analysis described is, in fact, concerned with an explanation of driven auricular or ventricular parts of the heart when using intracellular microelectrodes and showing the well-known plateau, and not the pacemaker event. Figure 4 recapitulates the types of intracellular electrical patterns for the two different characteristic regions of a vertebrate heart.

The electrical instability of the pacemaker membrane is characterized by a depolarization effect as

soon as repolarization reaches the isoelectric point;

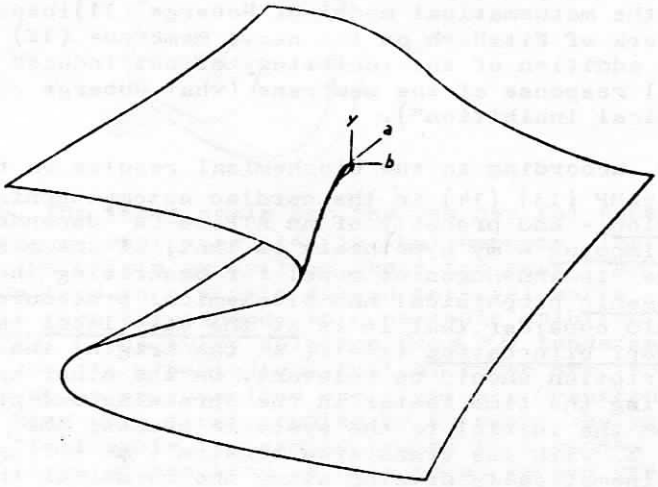
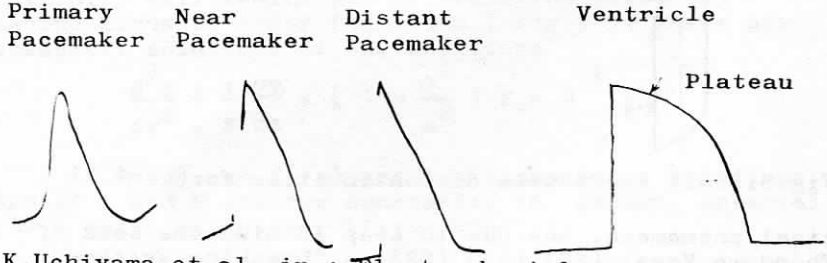


Fig.3.

while a driven tissue (here the ventricle) displays a plateau and, in addition, an isoeletric time lapse



K.Uchiyama et al. in : Electrophysiology and Ultrastructure of the Heart, ed.by T.Sano et al., Grune & Stratton, New York 1967.

Fig.4. Time course of transmembrane potentials.

until a new induced depolarization operates. Thus, as far as automatogenic processes are involved , one should turn to the mathematical model of Roberge (11)inspired by the work of FitzHugh on the nerve membrane (12) with the addition of the inhibitory effect induced by the local response of the membrane (what Roberge called "paradoxical inhibition").

Now, according to the biochemical results on the role of cAMP (13) (14) in the cardiac automatogenic contraction - and probably of an ATPase-Ca^{++}dependent for the impetus - my hypothesis is that, if one preserves the Riemann-Hugoniot model for describing the automatogenic biophysical and biochemical procedures, one should consider that it is at the very local level of the Hopf bifurcation itself(at the origin) that the description should be relevant. On the other hand, considering the time factor in the spreading out process from the initial to the systolic phases, the frontal Z with its transverse tension (≠ spring) should cinematically develop along the border of the pucker into a breaking wave. Now a way of approaching the full set of the representation is to consider the limit cycle of Poincaré for the Van der Pol equation and the overall self-excited oscillations [cf.graphical construction of Liénard (15) (16) (17) (18) (19)]. Figures 5 & 6 . In addition.for the approach of cri-

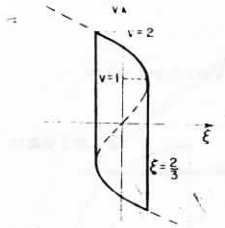


Fig.5.Limit cycle with discontinuities for $\epsilon = \infty$

tical phenomena, one has to keep in mind the work of Théodore Vogel (20) (21) (22) on "breaking systems", another candidate - heuristic - being the physics of transitions (23) (24) .

But a more important problem has to be presented. The general theory of representation considers the projection of a geometrical or a topological being according to the trirectangular trihedral,curvilinear, polar... coordinates. In any case the reference sur-

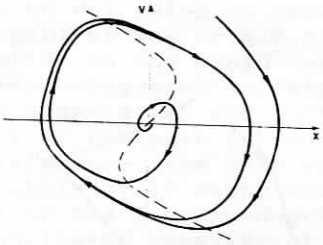


Fig.6. The limit cycle for the van der Pol equation.- The figure indicates clearly what happens. The spirals near the origin as well as those far away from the origin tend to a single closed integral curve ,which in its turn corresponds to a periodic solution of $\ddot{x}+\epsilon f(\dot{x})+x=0$ In other words,every solution for $\epsilon > 0$ tends,as $t \longrightarrow +\infty$, to a periodic solution. These are the salient facts about self-excited oscillations. Occurrences of this kind were first studied by Poincaré who gave the name limit cycle (or simply cycle) to a closed solution curve of the kind we have found in the present case(classical formulation,but cf.J.J.Stoker for example).

faces are flat,homeogeneous and isotropic,without singularity (planes of the 0x,0y,0z coordinates). I will now consider projections of a three dimensional (as well as n-dimensional) geometric or topologic being on any uneven surfaces and to do so I will choose, to do it here, the surfaces of Bessel. To introduce these dramatic landscapes in the theory of representation, I will remind you of Besselian first and second kinds of order functions (Fig.7). There are classical solutions of the equations

$$\frac{d^2y}{dz^2} + \frac{1}{z}\frac{dy}{dz} + \left(1 - \frac{\nu^2}{z^2}\right) y = 0$$

If $J_\nu(z)$ and $Y_\nu(z)$ are two independant solutions and if A and B are two constants, the general integral for ν positive integer (first kind) is

$$y = Z_\nu(z) = A\, J_\nu(z) + B\, Y_\nu(z)$$

(If ν is not a positive integer : second kind).

Figure 7 represents the surfaces $z = f(x,\nu) = J_\nu(x)$ and how it can deform when x and ν continuously vary. We note that :
when $\nu = 0$, $J_0(x) = 1$ for $x = 0$
when $\nu > 0$,all $J_\nu(x) = 0$ for $x = 0$.

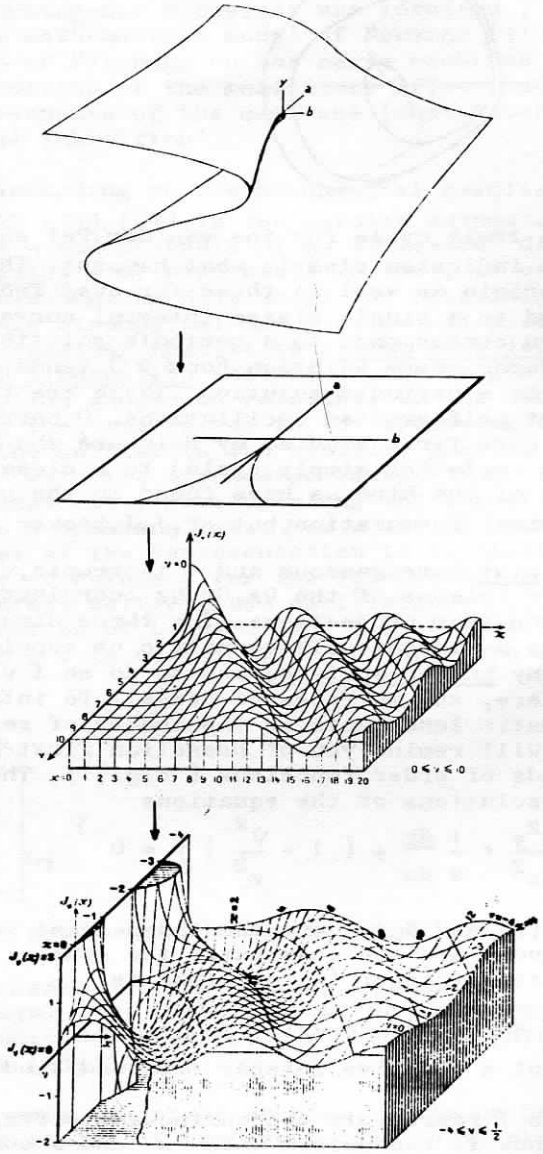


Fig. 7

Now I am not going to consider here what is related to the tangent at the origin,etc. I prefer to drive your attention to the evolution of the cusp generated by the Riemann-Hugoniot surface. When this surface as such is translating and continuously projected at the surface or surfaces of Besselian panorama as surfaces of reference, the cusp will continuously change its shape while still being the same expression on a flat plane of the Riemann-Hugoniot surface;this indicates a non-linear behavior of a definite type of the pucker - a "catastrophe" when the receptor surface (or the three receptor surfaces of the tridimensional geometry) is itself some kind of "catastrophe".Thinking along this line is as useful as considering embeddings.

I will not of course develop here this field which will be implemented elsewhere. I would just like to emphasize that,what ever might be the mode (orthogonal, etc.) of projection,it is also possible to consider three co-ordinates represented by three similar or non-similar reference surfaces so that, conversely, one can project according to two modalities every point of these three co-ordinates: 1) in such a way that we rebuild the chosen morphological being (for example the Riemann-Hugoniot surface); 2) in such a way that by conjunctions of the three systems of projection in the space they define and depending on the scale of each projection, one constructs as many morphological beings as there are projective potentialities from the singular surface(s). In the one way or the other : the classical projections on surfaces without singularity (spherical,plane co-ordinates) are only particular cases of surfaces of co-ordination, this lemma introducing then the more general concept of spatial coordinates as singular surfaces. One can already think how this "anamorphic" reference enlarges the concepts of homotopy, homeo- and diffeo-morphisms,etc. and how the conditions of superimposition are a part of this mode of representation which allows us to give a calculable approach of the heterogeneity and anisotropy of any living space (and other surfaces in microphysics and megaphysics or astrophysics).

With this conception in mind, let us now consider any bio-$\{S\}$ as a beat frequency oscillator ; it follows the heterodyne principle.I have transposed this very classical concept to our problematics in Biology. A heterodyne works with two frequency oscillators, one of which operates on a fixed frequency (it is $\mathcal{R}$ considered as the potentially perpetual driver of a

bio-{S},while -generally speaking- the frequency of the other ($\mathcal{C}$) is modified ,supposing an equivalent capacitor.Because there are many biotopes $\mathcal{C}_1, \mathcal{C}_2 \ldots \mathcal{C}_n$, then there are many eco-frequencies. The resulting frequency of {P} in a certain spatio-temporal state is obtained as a difference between the two series of frequencies. For heuristic purposes I shall recall the wellknown frequency translation (= frequency conversion = mixing = beating) when two alternating waves of different frequencies are superimposed.Figure 8 (25) "illustrates how superimposing 2 waves of different

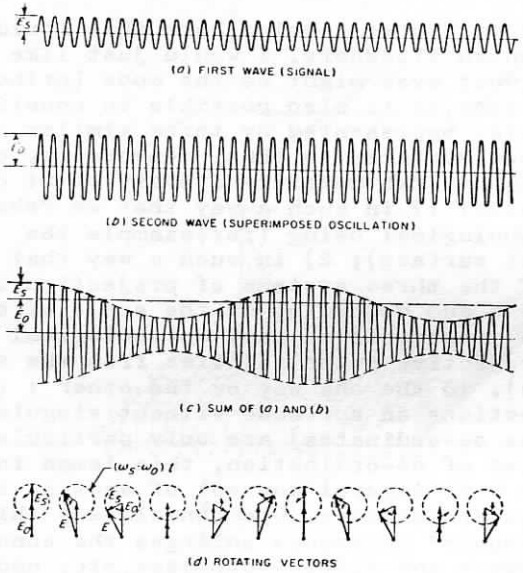


Fig.8.

frequencies results in a wave that pulsates in amplitude at the different frequency of the component waves. The associated relating vectors are also shown".In this case,as has just been reminded, " the higher frequency wave continuously gains in phase position relative to the lower frequency wave because of its greater angular velocity", the result of the combined waves system showing an envelope fluctuating in amplitude (the 2 waves add and substract successively through the variations in the relative phase).Considering an isotaxon or an heterotaxon group, there are external

modulations for each bio-{S} tuned or not. A superheterodyne bio-{S} management permits an increased selectivity of the cybernetic channels, elimination of noise, in short:improvements (cf.the nervous system).

This heuristic conceptualisation offers a general basis for participating in the understanding of the internal and external milieux intérieurs of Generalized Semiotics (including forces,molecules,organisms,etc.). The hodographic reticulum of the bio-cybernetics implies the existence of reflexes with memory - viscero-vegetative stored reflexes partcipating in the bio-rhythms + percepto-motor stored reflexes "intellecting" the conscious reactions as well as the viscero-vegetative vis a tergo. As Biotechnologists we reach there our central preoccupation of increasing by instruments the field of our perceptions and actions,developing metric tools and useful quality .A book :"The Design of Design" by Gordon L.Glegg (26) is instructive in this frame work. Its "Table of Contents" speaks eloquently. Let us read it : I. The design of the problem.II.The design of the designer.III.The design of design the inventive.IV.The design of design the artistic.V. The design of design the rational and - and! - VI. Safety margins...

We are moving in Science and Technology with tremendous serendipity.Bio-informatics is a good guide therein to give the conceptual tools we need as soon as, instead of taking promenades,we have expeditions to prepare.

Now at the opening of this School,I would welcome our elders, respectfully questionning our Past . "Who was the first biomedical engineer?" asked ten years ago L.A.Geddes and H.E.Hoff (27). While Geddes and Hoff first nominated William Gilbert (1450-1603),they supinated d'Arsonval and Helmholtz,judging that the latter should be awarded the title. Personally I have another candidate: unfortunately I do not know his name, except that he is our prehistorical ancestor : the faber-sapiens of Acheulean (wood against stone)or of Chellean(stone against stone), i.e. from a locality which in the present Department is not farther than some kilometers from us , hic et nunc .

REFERENCES

1. Bio-Informatics and Bio-Process Studies in the Physiology of Communication, Biosc.Comm.,1978,4, n°3-4,157-240,Special European Issue ed.by B.Rybak.
2. E. Schrödinger,What is Life ?,Cambridge Univ.Press, 1955, 92 pp.
3. B.Rybak, Encyclopaedia universalis,Paris,1973,XV, 687.
4. B.Rybak,in:"L'idée de régulation dans les sciences", Recherches interdisciplinaires,Maloine,Paris,1977,147.
5. F.Klein, Le programme d'Erlangen ,Coll."Discours de la méthode",dir.B.Rybak,Gauthier-Villars,Paris,1974, 72 pp.
6. B.Rybak,Nouvelles perspectives en physiologie cardiaque,Conf.Palais Découverte,Paris,1957,fasc.226.
7. B.Rybak,a) Life Sc.,1962,5,201 ;b)Arch.mal.coeur & vaisseaux,1965,n°5,711.
8. E.C.Zeeman, in "Towards a Theoretical Biology",C.H. Waddington ed.,Edinburgh Univ.Press,1972,8.
9. E.C.Zeeman, Catastrophe Theory,Addison-Wesley,London 1977, 675 pp.
10. R.Thom,Stabilité structurelle et morphogénèse, Benjamin,Reading,Mass.1972,362 pp.
11. F.A.Roberge, Automatica,1969,5,407.
12. R.FitzHugh, Biophys.J.,1961,1,445.
13. B.Rybak, Proc.Can.Fed.Biol.Soc.,1973,16, 58.
14. B.Rybak & J.C.David, Biochem.Biophys.Res.Comm. 1977,79,n°4,1065.
15. E.& H.Cartan, Ann.Postes,Télégraphes et Téléphones, 1925,XIV, 1196.
16. P.Janet, Ann.Postes,Télégraphes et Téléphones,1925, XIV, 1193.
17. B.van der Pol , The philosophical Magazine,1926,II, 7e ser.,978.
18. A.Liénard, Rev.gén.électricité,1928,XXIII,901.
19. A.Liénard, Rev.gén.électricité,1928,XXIII,946.
20. T.Vogel, Actes du Coll.int.vibrations non linéaires, Ile de Porquerolles,1951, Publ.Scient.Techn.Ministère de l'air, n°281.
21. T.Vogel, Bull.Soc.mathém.France,1953,81,63.
22. T.Vogel, Théorie des systèmes évolutifs ,Gauthier-Villars,Paris,1965,172 pp.
23. N.Boccara, La Physique des transitions,Coll.Que sais-je ? n° 1389,P.U.F.,Paris,1970,126 pp.
24. D.R.Nelson, Nature,1977, 269, 379.
25. F.E.Terman,R.A.Helliwell,J.M.Pettit,D.A.Watkins & W.R.Rambo, Electronic and Radio Engineering, McGraw-Hill,New York,1955, 1078 pp.

26. G.L.Glegg, The Design of Design,Cambridge Univ.Press, 1969,93 pp.
27. L.A.Geddes & H.E.Hoff, Bio-medical Engineering, dec.1968,551.

This Opening Perusal was delivered
June 30,1978 at 9 a.m.