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*Journée du 26 juin 1967*

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## CONCEPTS THEORIQUES

*2ème séance*

PRÉSIDENT S. L. SOBOLEV

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J. D. COWAN

Some Remarks on Neurocybernetics

W. M. ELSASSER

What is Theoretical Biology?

General discussions

## SOME REMARKS ON NEUROCYBERNETICS

JACK D. COWAN

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The last quarter of a century has seen the emergence and development of cybernetics, the science of information and control. As a result, a new language has evolved out of the continued efforts of scientists and engineers to make precise such concepts as "communication channel", "automaton", and "control system". This language has been widely used in those sciences which have to deal with the interaction of animals and machines with their environments. One science that has drawn heavily on this language is neurology. Cybernetic concepts have been used in many different ways to investigate how the brains of men and animals might work.

Perhaps the earliest example of the use of this language in neurology is to be found in the 1943 publication by W. S. McCulloch and W. H. Pitts of "A logical calculus of the ideas immanent in nervous activity" [1]. In this paper, the concept "formal neuron" was introduced, essentially an abstraction from then current details of neuronal operation. These formal neurons operated upon and emitted, at specified times, binary "all-or-none" signals. Their junctions, called "synapses", were either excitatory or else totally inhibitory. They functioned by computing the algebraic sum of the values of their inputs, 1 and 0, subsequently emitting an output signal if, and only if, this sum exceeded a certain specified threshold. Formal neurons could be made to represent the elementary operations of two-valued logic, and *a fortiori*, formal neuronal networks to represent complicated logical formulas [2]. To the extent to which the concept "formal neuronal network" symbolizes the process whereby brains respond to and represent stimuli, the McCulloch-Pitts theory is similar to that of K. J. Craik's [3] regarding the nature and function of neuronal networks. A corollary of the McCulloch-Pitts theorem is also of interest: formal neuronal networks plus "receptors" and "effectors" are equivalent to Turing machines. A Turing [4] machine is itself a formalization of, and an abstraction from, the processes underlying computing. The equivalence of the two concepts, therefore, led immediately to the idea that in at least some aspects of signal processing, brains and computers are similar. N. Wiener, in his now classic book "Cybernetics" [5] developed this analogy, incorporating chapters on computing machines and the nervous system, on *gestalts* and *universals* and on cybernetics and psychopathology.

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Any direct analogy between formal neuronal networks and brains requires the existence in brains of specific circuits, so that there has to be a process of selection of nerve-cells and of the pattern of interconnection, the anatomy or the "wiring-diagram", and a rejection of all other possibilities. However, ablation studies on the brains of many animals [6] apparently indicated that such complex signal processing tasks as visual integration were independent of the specific details of the wiring diagrams of the visual cortex. Even extensive destruction of this tissue did not produce marked disintegration of function, although those activities that persisted were somewhat retrenched. This suggested that perhaps the circuits were redundant throughout areas of nervous tissue and that only gross parameters of the tissue such as the mean number of cells and their interconnections were reliable measures of the tissues' functioning. Wiener [5] suggested that nervous tissue might be similar to large telephone exchanges in containing redundant cells and interconnections, and that messages might be simultaneously transmitted from area to area along many distinct pathways, and might be repeated several times along each pathway, the final decision concerning the validity of signals reaching any area of nervous tissue being determined by some kind of voting procedure. J. von Neumann [7] in the paper, "Probabilistic logics and the synthesis of reliable organisms from unreliable components" gave the first proof of the existence of designs for the construction of neuronal networks which might survive extensive malfunctions of components, or failures of individual formal neurons and of errors in and damage to their connections. Von Neumann's designs utilized the replication of many individual circuits, the simultaneous transmission of messages by many circuits, and "majority-voting" circuits to ensure the overall reliability of signal processing and transmission. Von Neumann was not satisfied with the results. He considered his treatment of error to be rather *ad hoc*, and he suggested that error should be the subject of a thermodynamical theory, as C. E. Shannon had treated the concept of information [8]. He was also aware that formal neuronal networks were digital in their mode of operation, whereas those comprising brains were not, despite their use of pulses in some operating modes [9].

S. Winograd and the author applied Shannon's theorem concerning the reliable transmission of messages through a noisy communication channel to include computation, and so provided part of von Neumann's suggested thermodynamical theory of error for formal neuronal networks [10]. The resulting design for the construction of formal neuronal networks that function correctly in spite of malfunctions of individual neurons, or of errors in and of damage to wiring diagrams, differs in interesting ways from von Neumann's. The ability of formal neuronal networks to function correctly in spite of vicissitudes depends on their composition by anatomically redundant circuits. In von Neumann's prospectus, this kind of redundancy was sought by incorporating many copies of the one and only one circuit necessary for the representation of the specified functions which

are intended to determine the behaviour of the network. In the Winograd-Cowan theory, however, the redundancy is obtained, not by multiplication of identical circuits, but by replacing the specified functions by a greater variety of more complicated functions which require circuits containing many more and richer formal neurons and interconnections than the circuits required for the original specified functions. The key to theory is that the rules governing this replacement constitute error-correcting codes (*see* [11]). The network that results from such an encoding is immune to many kinds of error, i.e., it is largely "error-insensitive". The degree of error-insensitivity obtained depends upon the complexity of the requisite behaviour, on the frequency of errors, and on the level of redundancy introduced by whatever code is used. Because the code operates on functions and not on circuits, the redundancy obtained is functional, i.e., more functions are represented in the encoded network than in its precursor. Because of the nature of error-correcting codes, any one specified function appears in many of these encoded functions, and any one encoded function is essentially a different mixture of many of the specified functions. It is the multiple representation of a multiplicity of specified functions which leads to error-insensitive operation, rather than the mere replication of circuits. In short, it is the diversity of the encoded function that is computed by each individual formal neuron comprising the encoded network which leads to the efficiency of design. So the number of formal neurons required to realize any given mode of behaviour at some level of error-insensitivity, despite probability of malfunction of individual formal neurons and of error in the wiring, is ultimately as small as Shannon's theorem indicates is possible. Naturally, the formal neurons required to represent encoded functions are much more complicated than those which would be required to represent only the original specified functions. The application of Shannon's theorem thus requires that the more complicated formal neurons be no less reliable than the simpler ones, a requirement which is equivalent to assuming that the extra "hardware" required for coding is completely error-insensitive, as in Shannon's theorem. The Winograd-Cowan theorem is, in fact, like von Neumann's theorem, an existence theorem; but it differs from it in requiring a minimal number of very complicated circuits and formal neurons rather than a large number of simple circuits of threshold formal neurons. Our theory is the other extreme to von Neumann's theory wherein complication is minimized at the cost of increased replication, in that redundancy is minimized at the cost of increased complication, to attain some requisite level of error-insensitivity. Suitable combinations of the two techniques, functional coding followed by the replication of the resulting circuits, plus a randomization of the interconnections between them, lead to efficient and practical error-insensitive networks.

However, these networks can persist only for lifetimes that are limited by the error and failure rates of their components. There is an ageing effect, so that the reliability of function of these networks degrades under the cumulating effects

of uncorrected failures. W. H. Pierce [12] has shown how "adaptive" networks may be designed whose lifetimes are substantially longer than those of the above networks. A basic defect of the techniques outlined, in which majority voting effectively controls errors, is that, since those inputs to a given formal neuron which issue from a failed one will be permanently in error, a consistently reliable minority may be outvoted by a consistently unreliable majority. Such a limitation may be overcome by using more complicated formal neurons whose inputs are weighted according to their reliabilities. This requires computation by the recipient formal neuron of these reliabilities. Pierce has proved that such computations can be carried out. If input errors are statistically independent, the input weights  $\alpha_i$  can be selected so that the output of the formal neuron is the digit most likely to be correct, on the assumption that what is required of the formal neuron is the representation of the majority function [13]. One variant of this is particularly interesting. In this, if  $p_i$  is the number of coincidences and  $q_i$  the number of disagreements between the  $i$ th input to, and the output from a given formal neuron in a cycle of  $m$  operations, then the selections  $\alpha_i = \log(p_i/q_i)$  lead to the computation of the most likely estimate of the reliabilities of the inputs for the representation of the majority function.

There are evidently good grounds for asserting that reliable networks of competent formal neurons can be constructed, using the techniques of functional coding followed by replication of the resulting circuits, together with feedback controlled selection of vote-weights, which would be efficient and long-lasting compared with their components. However, the question remains of how such networks are to be constructed. The existence of specific circuits in a network requires the selection of components and wirings. For these redundant networks the problem is crucial; i.e., the amount of selective information required to specify them is very large. Not only do the wirings and thresholds have to be specified, but also particular patterns of synaptic interactions. Vote weights do not have to be selected because the process is automatic, but the necessary wirings of formal neurons need to be more complicated than those of non-adaptive networks. Thus, a very complicated programme is required for the construction of these networks, that contains all the requisite information. An important and interesting question concerns the possibility of leaving the bulk of the selection process to be performed during the lifetime of the network, i.e., by adaptation. A. M. Uttley [14] has outlined how certain replicated circuits might arise by chance in a randomly interconnected network, thus diminishing the amount of selective information what has to be supplied either "genetically" or "epigenetically". What remains is the problem of specifying the complicated functions required for functional coding. For high levels of functional coding, each formal neuron need only represent a random selection of the specified functions of the network, provided it correctly decodes its inputs. It is interesting that recent work on the design of adaptive machines capable of learning to classify, represent,

and recognize patterns of stimuli, has given rise to machines whose functional organization is apparently very similar to the redundant networks we have designed. [See 15, 16].

The combination of such theories of automata and information-processing with what might be called machine theories of adaptation, provides a not unreasonable model of what might be the organization of those parts of brains concerned with perception, learning, and perhaps with memory. We have cited Lashley's work on ablation effects. Lashley concluded that it was not possible to demonstrate the isolated localization of the memory trace or "engram" anywhere within the nervous system. He supposed that there was no special reservoir of cells which would serve as the seat of special memories, every instance of recall requiring the activity of millions of neurons. Moreover, the same neurons which retained the engram must also participate in countless other activities. [See also 17 and 18]. Sperry has suggested a number of principles that might give rise to this property: multiple interconnections between nerve-cells, the fidelity of the wiring being controlled by specific biochemical factors, much overlapping of interconnections; multiple reinforcement of any given function from numerous different sources any one of which may itself be capable of sustaining the activity; reciprocal and surround inhibition between and among neurons; the arrangement of cortical circuits in vertical, rather than horizontal, dimensions and the bilateral duplication of the cerebral hemispheres. J. C. Eccles [19] and A. E. Fessard [20] have inferred from their own experimental studies that presynaptic and lateral inhibition between and among neurons are important features contributing to error-insensitivity. In considering changes in the "evoked potentials" in various areas of the brain, associated with the engramming of conditioned responses, E. R. John [21] demonstrated an effect related to the replication of circuits and the delocalization of function which we have discussed, namely that evoked potentials following the engramming have similar shapes, even over many anatomically distinct regions of the brain.

In the light of these experiments we note certain logical requirements on the structure of the error-insensitive networks obtained by functional coding techniques. These are the existence of large numbers of both excitatory and inhibitory synapses at all units, the existence of many presynaptic "axo-axonal" interconnections, a great deal of multiple interconnection and overlap, and the existence of lateral inhibition between groups of neurons. Furthermore, as a consequence of functional coding, there is an extensive representational system in these networks, any unit of which can be activated by many different patterns. Finally, the reliable activation of any complete pattern of activity would require the synergic activity of many units. All these features of functionally coded networks appear to have experimental correlates, most of which are the result of experiments performed on the central nervous system proper. We should not expect to find high levels of functional coding in peripheral areas, but rather many replicated



circuits more in line with the "telephone-exchange" analogy. At some intermediate stage where the degree of synaptic interaction among neurons is sufficiently high to sustain functional coding as well as circuit replication there will emerge assemblies of synergic neurons, which may be taken to be the "functional units" of the network. Perhaps the vertically organized groups of neurons found in sensory projection areas [22, 23] may be taken to be the experimental correlates of these functional units.

We consider it to be of some importance that deductive models of the organization of neuronal networks be forthcoming which lead to the specification of such entities as functional unit, engram, and so on. R. L. Gregory [24] has made the point that a knowledge of function is required to classify observed biological features into "essential" or "accidental" properties, and that it is only when the functional units of the system being studied can be identified, that deductive inference and not mere description becomes possible. Gregory made the further point that the neurologist is never able to identify functional units directly by observing neurons and their interconnections; in all cases, knowledge is needed of what neurons do, and of how they do it. This raises a peculiar and difficult problem common to almost all attempts to apply cybernetics to biology. For, in order to do this, one must know precisely what is the ensemble of possibilities upon which operates the selection process that alone gives meaning and utility to the ideas of message and information. For the neurological problem, this is equivalent to saying that one needs to know the code, or codes, of the nervous system. Thus, any real application of theories of formal neuronal networks can follow only from a knowledge of what neurons do and of how they do it. This takes us far from the ablation experiments of the physiological psychologist, to the electrophysiologists who measure not behaviour deficits and the like, but the firing patterns of neurons and the changing electrical potentials of nervous tissue, the ECoG and EEG.

Once we enter the domain of experimental neurophysiology, however, it becomes difficult to see how the automata models apply to data.

It is clear that the automata approach is seriously deficient in many respects. In the automata, we have considered changes in the firing patterns occur only at instants specified by an external clock, i.e., they are already "synchronized" in the time domain. There is no clear evidence that the CNS operates in such a fashion. In any case, the formal neuron is a rather crude abstraction of neuronal behaviour, and the theory covers special aspects such as functional stability and does not serve to help us understand the responses of nets comprising many thousands or many millions of cells. The theory, in fact, was designed for the analysis of small-scale local interactions between abstract functional units. Digital computer simulations of neuronal nets [26, 27] together with some combinatorial analysis [27, 28] have given us some indication of the type of activity to be found in homogeneous networks of randomly interconnected formal neurons. If there

are only excitatory synapses in the net, the only stable states of activity are either a large proportion of all the units in the net are active, or else the net is quiescent. This is the "switching effect", discovered by many workers. It has been suggested that a neuronal network which acts itself as a switch might serve as a functional unit, and so correspond to one of McCulloch and Pitts' formal neurons. In case there are also inhibitory synapses, the behaviour is more complex and several intermediate stable levels of activity can persist. Farley has shown that even small networks comprising about one hundred cells can exhibit quite complicated behaviour, recruiting responses, augmenting responses, rhythms and so on, that are reminiscent of experimental phenomena. What is lacking in this approach, however, are the concepts and mathematical tools that would further the analysis of the responses of very large networks, nor is there any real attempt to face the problems of coding in these networks.

There has been one interesting attempt at a mathematical treatment of the responses of large nets [29]. In this, neurons are assumed to be randomly distributed in a mass with a given volume density. The neurons have thresholds, synaptic delays, EPSPs and IPSPs, and a summation time constant. Attention is directed to the proportion of cells becoming "sensitive" per unit time. Sensitive cells are those which are not refractory and can, therefore, be fired by a sufficiently potent stimulus. Although the mathematical treatment is not rigorous, the conclusions are essentially correct. The switching effect is discovered, and the conditions for the distortion-free propagation of plane waves of neuronal excitation are given. It is shown that the connection function which gives such propagation is equivalent to that one found empirically by D. A. Sholl [30]. Since only excitatory synapses are present, this wave propagation is unstable and depends critically on the stimulus, on the cell properties, and on the local density of interconnections. Beurle introduced two mechanisms of interest. Waves were stabilized by "servo" control from external nets which acted by firing off cells ahead of the wavefronts. And cell thresholds were assumed to be dependent upon past activity. These extensions of the random network assumptions are important. The servo idea is an attempt to treat network interactions, the control of one network by another. Threshold modification by past activity changes the responses of a network, according to past responses. So the network can be trained, given the proper feedbacks, to act as a permanent store of messages. Indeed, all the possibilities of behaviour, functional stability, adaptation, and so on, which we considered to be present in functionally stable automata, are to be found in these networks. However, the scale has been changed, so to speak, in that complete networks play the role of functional units, and dynamical variables play an important role in the encoding of stimuli.

There is, therefore, the intriguing possibility that some kind of answers to the problems of modelling some aspects of the activity of neuronal networks in the CNS might be forthcoming from a mathematical formulation closely related to

Beurle's. But there are a number of problems that must be solved before this approach can be made useful. The analysis has some defects. For example, the effects of refractoriness, of the finite size of the network, and of delays, are not properly formulated. To some extent, these defects are not too serious. Correct formulations of similar problems have been given by J. S. Griffith [31] and by M. ten Hoopen [32]. Their conclusions are similar to Beurle's concerning switching and stability, if somewhat less far-reaching in scope. However, what is really lacking from the whole approach is that it does not make contact with the experimental variables of the neurophysiologist, the histograms, correlograms, ECoGs and so forth, and so, in this sense, it is not a testable model for the responses of neuronal network in the central nervous system. Moreover, while the image of interacting waves of neuronal excitation suggests many possibilities for the coding of messages, it has not been used so far to produce precise, quantitative predictions of how and where permanent changes take place in the networks of the central nervous system, and what they represent.

What is required, then, is a novel mathematical formulation of the responses of neuronal networks that takes account of many of the organizational features of the central nervous system that we have listed, in which the variables relate to measurable quantities by current experimental and data processing techniques, and in which there is a precise hypothesis concerning the nature of neuronal coding. It is not too much to hope that this theory will be forthcoming during the next decade.

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## WHAT IS THEORETICAL BIOLOGY?

WALTER M. ELSASSER

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One may trace the beginning of modern efforts in theoretical biology to a celebrated paper of Niels Bohr that appeared in 1933. I should say here at once that my personal interest in theoretical biology was largely aroused by this work. My basic ideas began to develop during my stay in Paris in 1934/35. I am therefore particularly grateful to the Organizing Committee of this Meeting for the opportunity to return to the places of my early stimulation and development.

Bohr's paper indicates how one can apply the ideas of quantum theory to biological problems. What quantum physics has taught us on a more philosophical level is that each progress in our understanding of the behavior of matter is achieved at the price of a corresponding loss: We are no longer able to trace in detail the geometrical arrangements and clearcut causal relationships that govern motions in classical physics. It is a familiar fact that the concept of well-defined orbits of particles ceases to exist in quantum theory. Instead, one has a statistical theory in which prediction is profoundly limited. In theoretical biology, analogous arguments hold but they apply now to a higher level of organization.

This raises at once the question whether changes are required in the mathematical apparatus of quantum mechanics. Our answer is that such changes are unnecessary. Organisms differ from other bodies by their extraordinary complexity. Their dynamics, however, takes place at the energetic levels of ordinary chemical reactions. There are no plausible grounds for changing the laws of physics solely because of an increase in complexity. What then is the new element which appears in the analysis of living systems? We claim that this novelty lies precisely in complexity itself.

On combining the uncertainty relations with this complexity, Bohr concluded that the perturbations which result from quantum measurements are of fundamental importance in biology. Such measuring processes interfere with the delicate operation of a system of as complex a design as an organism. In order to gain a thorough knowledge of the system, which is indispensable for precise prediction, the measurements must be so thorough as to disturb the organism seriously; eventually the animal will become sick and die. But on the other hand, in the absence of prediction science ceases to be analytical and remains on a purely descriptive level.

In my own writings I have emphasized that predictions may be derived from two different procedures. One of these is the determination of initial values,

as already mentioned. The other may be called the method of the sampling of classes. One can for instance predict the behavior of some variety of molecules by measuring other molecules of the same kind, notwithstanding the fact that the measured molecules may be destroyed in the process. This is of course a common method in physics and chemistry. I have been able to show that the application of this method to the classes of biology, e.g., species, leads also to fundamental limitations of prediction. These limitations arise from the fact that organisms of the same class differ from each other in very numerous particulars by virtue of the pervasive inhomogeneity of all living matter.

The totality of these limitations imposed on prediction corresponds to what may properly be called the semi-autonomous character of living matter. If we had chosen to apply a similar terminology in quantum theory, we could have said that the stability of atoms and molecules is a semi-autonomous phenomenon, in the sense that an explanation of this stability in terms of classical physics is not possible. In a similar fashion the stability of organisms and even more the tremendous precision of developmental processes are properties which cannot be fully explained by means of ordinary physics. Undoubtedly, a great part of this stability can be explained in mechanistic terms, for instance by feedback devices. But owing to the intrinsic complexity of living matter one cannot make the purely physical mode of explanation an exhaustive one.

An important reservation is needed at once. This is that physics and chemistry are never false in the organism. They are incomplete. What is meant here is that the initial conditions can never be determined with the required accuracy; nor can one select a biological class whose members would be sufficiently similar to each other to allow adequate prediction based on the method of sampling. The primary distinguishing characteristic of living matter is, therefore, the essential complexity, inhomogeneity, and variability of this matter. We are thus able to define theoretical biology in the following manner: Theoretical biology is the science of radically inhomogeneous classes. Physics, on the other hand, is the science of homogeneous classes, *if not a priori*, then at least in fact and by usage.

In the course of my investigations I have become convinced that complexity, inhomogeneity, and variability are not only necessary conditions for the existence of life; they are also sufficient in a simple sense: Any proposition about life inasmuch as it deals with it as a semi-autonomous phenomenon must be based upon this inhomogeneity, beyond the purely physico-chemical properties of the system considered. Again, we may be confident that this is the only new principle required when we want to characterize life in a general and essentially abstract manner.

We can exhibit the same ideas in a different form, mostly to show their relationship with what is usually called molecular biology. We know that the organism possesses many well-defined constituent parts which one can synthesize in the laboratory; or else one will certainly be able to do so in the future. We shall

designate these as homogeneous components. They are primarily macromolecules. In the living organism, these homogeneous components are immersed into a radically inhomogeneous environment. This inhomogeneity of the internal environment arises out of the almost endless variation of geometrical relationships among parts, and out of the almost limitless variability of the low-energy chemical reactions which this entails. One may express this by saying that in the organism the dynamics of the homogeneous components needs must be coupled into the inhomogeneity of the internal environment.

In order to gain a better understanding of the implications one ought to compare inhomogeneity with what the physicist calls noise. Although noise is a statistical phenomenon, one presumes always that one can form averages over any variable whatsoever. I propose then to define an inhomogeneous class in the following manner: It is a set composed of a finite number of objects such that one can never obtain enough samples to give an operational significance to all averages that it may be possible to define from a purely mathematical standpoint. From this there results an essential limitation of prediction as compared to the case where homogeneous classes would be available.

Bohr had long ago proposed that every fundamental progress in our knowledge of the properties of matter is tied to a loss of so called explanation. This idea found its original application in quantum mechanics. Uncertainties of a quite analogous kind turn out to be basic in theoretical biology. The abstract apparatus which expresses these new uncertainties is the theory of inhomogeneous classes. One fact stands out: When we go from abstract models in the more conventional sense to a theory of abstract *classes* which are not necessarily homogeneous, we introduce a freedom and a generality which are not to be found in traditional theoretical science. I have convinced myself in the course of many years that we have in hand here the chief tool that is required in theoretical biology.

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See also a forthcoming paper by the author in vol. 3 of the series *Towards a Theoretical Biology*, ed. by C. H. Waddington (Edinburgh Un. Press, 1969).

## GENERAL DISCUSSIONS

A. LICHNEROWICZ: M. Grassé nous disait qu'il fallait trouver un langage commun: un premier thème est revenu, entre M. Prigogine et M. Fröhlich: l'expression "non linéaire". Je voudrais dire à la fois mon accord et les limitations qui me semblent s'imposer.

Il faut d'abord faire très attention, en parlant linéaire et non linéaire. Il s'agit de choses dans lesquelles le linéaire peut sécréter des êtres non linéaires et des effets non linéaires. Et par conséquent il faut dire exactement ce qui est, dans chaque cas, effectivement non linéaire. Mais enfin nous serons d'accord, je crois... Et je pense que le mot "non linéaire", qui embrasse le linéaire, est une des clés de notre dialogue.

Secundo: je voudrais rendre hommage, en particulier, à l'effort d'arrachement à la thermo-quasi-statique, en faveur d'une vraie thermodynamique, fait par M. Prigogine; là est probablement l'un des modes d'approche de nos problèmes. C'est l'étude de régimes permanents stables. Et je voudrais peut-être poser, en même temps, à M. Prigogine, une question. Un certain nombre des choses qu'il a dites sont en exact parallèle avec certaines des méthodes contemporaines et anciennes de l'économie mathématique. Nous savons d'ailleurs qu'il y a des parallèles entre thermodynamique et économie. Et en économie les fonctions convexes jouent un rôle important pour les problèmes de stabilité (de stabilités un peu plus globales que les siennes). En fait, Monsieur Prigogine, votre condition du second ordre est une condition de convexité locale.

Je crois que l'introduction de symboles mathématiques du type fonctions convexes, pour certains problèmes, avec contraintes, doit jouer dans l'avenir un rôle important.

Tertio: je voudrais affirmer ma foi dans la biologie théorique, mais je ne crois pas qu'elle doive avoir, à ce stade, un instrument privilégié. Je pense que nous devons également avoir confiance en ce qui a été dit tout à l'heure, par exemple par M. Elsasser, qui est une approche très intéressante des classes hétérogènes aussi dans la *vraie* thermodynamique. Sous les réserves qu'il faut tout de même bien prévenir nos amis biologistes que le mot "entropie", qu'on met à toutes les sauces, n'est pas toujours parfaitement aussi clair et aussi mesurable que nous souhaiterions. Je pense que ces approches convergentes doivent être poursuivies distinctement, et que nous ne pouvons pas, en ce moment, espérer *une* seule approche.

Bien entendu, la mécanique quantique jouera son rôle. Pour le moment, elle est linéaire. Essentiellement en ce sens que ses équations fondamentales sont linéaires. Mais on sait que des essais sont faits pour sortir du linéaire. En gros,



j'ai l'impression que c'est la description qui s'applique aussi à M. Prigogine. Nous avons des équations, disons en gros, rigoureuses, non linéaires, comme équations fondamentales, dans beaucoup de situations; et nous étudions la stabilité à partir des équations aux variations qui forment le système linéaire canoniquement associé. C'est cela que nous faisons constamment, sous des formes et avec des discours, physiques ou chimiques, de type varié.

W. M. ELSASSER: Je suis tout à fait d'accord avec M. Lichnerowicz: j'ajoute l'idée que la théorie des classes hétérogènes joue un rôle similaire à l'usage qu'on fait de la géométrie riemannienne dans la cosmologie. Sans quoi, on aura la contradiction que Kant, le philosophe, constatait il y a deux cents ans: la contradiction entre le problème d'un univers infini et la possibilité de construire un univers sensible. Alors, avec l'introduction de la théorie des classes hétérogènes, des contradictions semblables, entre la nécessité et l'indéterminisme (c'est-à-dire la liberté et le potentiel créateur), . . . ces choses-là disparaissent. Mais naturellement, il faut aussi avoir des méthodes beaucoup plus concrètes, qu'on trouvera en appliquant la mécanique statistique à la biologie moléculaire.

A. LICHNEROWICZ: Je veux dire mon accord. Votre théorie fournit un "background" fondamental pour la suite. L'image est excellente! . . . "Back-ground" dans lequel on mettra des choses assez variées.

I. PRIGOGINE: Au sujet de l'intervention de M. Lichnerowicz, je voudrais dire qu'il existe effectivement une certaine analogie formelle entre les problèmes que j'ai traités et des problèmes sociaux et économiques. Je pense même qu'il doit être possible d'aboutir à de tels éléments d'une théorie des structures sociales. Toutefois à un point de vue précis les problèmes dont j'ai parlé sont plus simples car je puis utiliser les conditions classiques de stabilité thermodynamique. Il faudrait voir si de telles conditions existent dans les problèmes sociaux. Il faut aussi, je crois, souligner combien les notions d'hétérogénéité et de complexité sont ambiguës. Quant à moi je ne sais pas ce qui est plus complexe, une particule élémentaire ou un être vivant.

TH. VOGEL: Je voudrais toucher à deux questions. On a beaucoup parlé du caractère quantique des modèles qui ont été présentés. Je sais bien que "per fas et nefas perseverare diabolicum . . ." Cependant je n'ai pas été convaincu.

Il est bien évident que la théorie quantique doit couvrir, dans un certain domaine, tout ce que couvre la théorie classique, et doit en plus donner des renseignements complémentaires. Cela est vrai également de la théorie de la relativité, dont personne n'a parlé. Mais dans un domaine où la mécanique classique permet de rendre compte de tous les phénomènes qui ont été mentionnés, il est inutile de faire intervenir les quanta.

On nous a présenté, le cas d'illustration d'une lumière cohérente. Illustration qui pourrait être reprise, mot pour mot, des travaux de Bernouilli, sur la vibration d'une file de points matériels. Par conséquent, cela n'a rien de très nouveau. Il ne faut donc pas faire intervenir les quanta, tant qu'on n'a pas montré ce qu'ils peuvent donner, que la théorie classique ne peut pas donner.

Ma deuxième observation a trait à ce que disait M. Elsasser, et qui m'a vivement intéressé.

Il y a longtemps que je pense que l'outil le plus communément utilisé en physique — c'est-à-dire les équations différentielles — n'est pas un outil extrêmement approprié. Je pense, en tout cas, qu'en biologie mathématique, en biologie théorique, comme dans la plupart des théories que l'on peut être amené à bâtir, les équations différentielles, généralement utilisées en physique mathématique, ne sont pas l'outil le mieux adapté pour cette discipline. En tout cas, je suis convaincu — et M. Elsasser a achevé de me convaincre — qu'il n'est pas le plus adapté à la biologie théorique.

Alors, je voudrais signaler la possibilité et l'intérêt d'études sur les systèmes évolutifs sans unicité. Voici quelques années que je m'occupe des équations au paratingent qui peuvent couvrir une assez large part de ces problèmes, mais ces équations ne sont elles-mêmes qu'un cas particulier: il faut considérer des inégalités fonctionnelles qui permettraient d'avoir toutes les solutions possibles, l'ensemble des solutions possibles d'un système incomplètement déterminé.

La solution qui consiste à faire intervenir la probabilité est une fausse solution, à mon sens, parce que l'introduction de la probabilité suppose une axiomatique qu'on laisse généralement implicite et qui est beaucoup plus difficile à défendre que tout le reste de la théorie. Autrement dit, on fait une théorie qui est claire, facile, mais elle n'est valable que moyennant des hypothèses que généralement on ne spécifie pas et qu'il serait extrêmement difficile de vérifier par expérience.

L. TISZA: The discussions concerning the relation of physics and biology seem to be dominated by the intricacies of biology as if the nature of physics were clear to everyone. In reality, I believe, that a satisfactory characterization of physics is a difficult task, and one not to be ignored if the interdisciplinary discussion is performed with a reasonable measure of precision. The task is difficult because of the wide ramification of the branches of physics, and it is aggravated by the fact that all this is in a state of rapid evolution. I will have to confine myself to the discussion of a few characteristic points.

Let me consider the case of quantum mechanics that in the course of a few decades has undergone already essential changes. I am tempted to compare the course on quantum mechanics I took almost forty years ago in Göttingen with the course now being offered to second year undergraduates at M.I.T. The old course, among the first to be offered anywhere on the new discipline, was nominal that of Max Born, but actually it was given by his assistants, among them

Dr. Rosenfeld who is here with us today, and who may check up on my recollections. Well, the old course seemed paradoxical and outright mysterious, whereas the new one is being accepted with striking ease; in discussing the resolution of some of the "paradoxes" of quantum mechanics sometimes the hardest point is to convince the students that there is anything paradoxical involved at all. Needless to say, this comparison is not intended to cast any reflection on Professor Rosenfeld's teaching ability. It is, of course, to be expected that the novelty of a discipline wears off, the rough edges polished, and there are plenty of reasons why its teaching should become a great deal simpler. The point I wish to make is that the metamorphosis of quantum mechanics is more profound than might be expected on such grounds.

An elementary introduction to quantum mechanics necessarily starts with classical physics and a great deal depends on the kind of bridge that we construct between the two disciplines. The most striking difference between the above mentioned two stages of quantum mechanics is that they are tied in with very different parts of classical physics. In fact, I am convinced that the key to the clarification of most of the paradoxes of quantum mechanics is that we have to come to grips with some of the paradoxes and illusions of classical physics. The first illusion to be given up is that there *is* such a thing as a coherent body of classical physics. It is, indeed, well known that Newtonian physics had from the outset two main departments: first, an inductive phenomenological one in which the objects of everyday life and of the laboratory are taken for granted; and, second the analytical mechanics of rigid bodies and mass points. To the extent that this mechanics is applied only to macroscopic motion, these two departments are compatible with each other. This is no longer the case for the wider interpretation of Newtonian mechanics in which the validity of this discipline is postulated even for the smallest, atomic constituents of matter, and where it is assumed, or rather taken for granted that the entire phenomenological physics is reducible to mechanics. For the sake of brevity I shall refer to the two departments of classical physics as PCP (phenomenological classical physics) and MCP (mechanistic classical physics) respectively. The wide range of achievements of classical physics belong primarily to PCP, but its philosophy is altogether dominated by MCP. We know at present that PCP is not reducible to MCP. However, the origin of this failure is not as well understood as it might be. I wish to introduce a few concepts in the hope of shedding some light on the situation.

There are two types of regularities discernible in natural phenomena that are in a way complementary to each other. The first is the well known determinism of classical mechanics. I like to call it *temporal determinism* in order to emphasize that we are dealing with temporal sequences in which the arbitrarily chosen initial state determines the state at a later time. The initial state itself is arbitrary in the sense that it is not restricted by a law of nature within this discipline. This kind of ordering of natural phenomena was distilled from celestial mechanics.

The second type of order manifests itself most obviously in chemistry, say the periodical table of the elements, in which we find the systematization of certain configurations of nuclei and electrons forming the chemical elements. Such configurations are very much favored by stability among infinitely many other configurations that are not observable except in a most transient fashion. Some years ago I have suggested that this type of regularity be called *morphic*. I believe that the success of quantum mechanics is in a large measure due to the fact that this discipline provides a mathematical expression to morphic ideas. Thus, the quantum mechanical "pure state" can be conceived as the ultimate of chemical purification and the samples of a class of systems in the same pure quantum state are absolutely identical to each other. This property may be designated as "morphic invariance". It is also noteworthy that in quantum mechanics temporal and morphic considerations appear jointly in a consistent scheme. In strong contrast with this situation MCP has a purely temporal character, whereas PCP deals with the world as it is and implicitly contains morphic elements. Experimental spectroscopy is a good example for morphic aspects appearing in experiments set up entirely by classical means.

The granting to morphic invariance an independent conceptual status that cannot be reduced to temporal determinism enables us to envisage some of the problems raised from a fresh perspective.

The replacement of MCP by quantum mechanics no longer appears as the replacement of one mechanics with a somewhat different variant, but a fundamentally new conceptual element, namely the morphic point of view, is added to the theory. This explains why the traditional introduction of quantum mechanics as an analog of classical mechanics has a purely formal character giving no allowance to intuitive conceptual understanding. In contrast, the new quantum mechanics referred to above builds a bridge between quantum mechanics and PCP and the transition is a great deal smoother since both disciplines contain morphic elements.

I wish to comment now from the point of view just outlined on Dr. Elsasser's discussion of homogeneous classes. This concept has a clearly morphic character and I agree with Dr. Elsasser that it is of crucial importance for the discussion of the relation of biology and physics. However, I must take exception to the claim that physics deals *only* with homogeneous classes. First of all, we must not speak summarily of all of physics. Thus, MCP knows nothing of homogeneous classes. This concept emerged only within quantum mechanics as the set of systems in the same pure state. Second, quantum mechanics deals not exclusively with homogeneous classes, but contains actually rules for constructing more complicated situations. Let me mention only that we take the homogeneous classes of electrons, protons and neutrons and we build up the classes of nuclei, atoms and molecules. All of these systems can exist in homogeneous classes of pure quantum states, but in actual practice we are more likely to encounter them as various kinds of

