A Personal Overview

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It is possible to argue that the physicists succeeded in the aim of the conference: to consider and determine whether a theoretical biology might be brought into existence in the same sense that a theoretical physics has. However, despite their self-satisfaction, it is far from certain that the representatives of the other disciplines, particularly the biologists, would accept that conclusion. This personal summary, threading the proceedings in overview, may bind the diversity of physical positions that were expressed.

Bohm sounded a keynote of the troubled metaphysical foundations of modern physics. Partly pure professionalese, his views irritated the non-physicists, and, at the beginning, a substantial number of the physicists. Yet by the end of the conference his insistence that the physicists consider the faulty foundations of quantum mechanics, the foundations of thinking about space-time and of order itself, finally began to stroke sufficient chords among them into resonance. This arose because of the striking parallels between the quantization of elementary physical systems—in nuclear, atomic, molecular physics; and in the biological systems—in the molecular biology of the formation of life; in its evolution—in the internal cellular processes, in the cell, the internal organ systems, the total organism, and in the species in the ecosystem. It really wasn't until positions about the quantization at these other levels had emerged in the conference that any meaningful dialectic began with Bohm's point of view.

Consider, for example, one such exchange. Gradually a (vertical) hierarchy of organizational levels began to appear at the conference; and a (horizontal) heterarchy of diverse elements. One might see at most a finite matrix of this sort; or, by extension, an indefinite denumerable growth which might proliferate emanatively in time. Yet Bohm took exception to this. His point (in this interpretation) was essentially that ordering was non-denumerable. It is the abstraction provided by people that establishes autonomous hierarchical order. However, this ordering, from a 'prime ministering' or 'executing' function (using social system elements as analogue) down to the lowest 'functionaries', represents the orders of the hierarchy, while there is a flux of state identifications upward, which represents information. Such ordering information, however, represents timeless processes. It is the horizontal heterarchial order that gives

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the time order (i.e. time is given by the processes of different variety).

The law of the hierarchy is to govern the hierarchy, and this must flow from the timeless order (e.g. consider the ordering of the king and the duke, etc.).

Now the concept of function cannot be described or defined in terms of function. It must have an aim which is not function. It is for this reason that a functionless (and thus timeless) order must exist. However, function and its opposite, malfunction, lead to harmony and conflict, as objective realities. 'Survival' involves harmonization (e.g. the continued existence of cars is harmonized by the traffic laws). Conflict is dissipative. Every view of function tends to maintain harmony and order.

Ultimately, it is the law of constancy of numbers, of a one-ness other than function, that establishes the relations of order, and it is the time space that determines the hierarchical space.

While no certain idea emerged whether Bohm had any significant positive idea for establishing an abstract structure for quantum mechanics (and no reader could judge this further from these remarks), nevertheless the attack he mounted on the problem of quantization is one of a number of paths that may have some meaning. (The reader may judge for himself from Bohm in July 1966 *Rev. Mod. Phys.*) His attack—it appears in this overview—is that time and space are not to be equated, but, instead, that 'timely' properties emerge from hierarchical ordering itself. Beyond this, Bohm's own remarks on his notion of order will have to speak for themselves.

It is certainly true that Bastin and Lieber were also concerned with such global questions, in seeking a line to view the physical-material universe, and thence, biological processes.

A similar message was received (1967) in a New York Academy of Science meeting ('Interdisciplinary Perspectives of Time', R. Fischer, ed.; *Ann. N.Y. Acad. Sci.*, *138*, 367, 1967), particularly as speaker after speaker made his distinctions between physical time in its many faces (astronomical, radioactive, geological, etc.), and biological time (e.g. physiological, psychological).

This appears to me then to afford the transition to my contribution, which began from a very specialized problem. I had started, as a classical physicist (of a 'systems' persuasion), to try to clarify a few topics in the physics of regulation and control of the macroscopic biological system. Experimentally, instead of finding the small amplitude dynamics of linear regulation and control theory (for example, the variations in regulated metabolic power), I found characteristics much more similar to so-called bang-bang control theory. In a number of related studies I found the system loaded from one end to another with large-amplitude oscillations. 'Limit cycles!' I said. 'The system must be described by spectroscopy.' Thus, purely on empirical grounds, I was led to the same path that emerged in physics, which started from the chemical 'field' spectroscopy of individual atomistic species, and continued to the physical 'temporal' spectroscopy of atoms and molecules. My contribution, thus, is to offer the same path for a theoretical biology that developed as a theoretical physics, namely, that the gross 'material' system is made up of temporally quantized atoms in the case of simple solids, or of atomistic biochemical chains in the case of the biological system, whose everbeating cooperative effort represents the foundation for the characteristics of the overall system.

It is quite pointed of Bohm and others to have asked the question as to what is the foundation for quantization, since this has meaning at many different levels. It is important also to recognize that the ordering relations which may give the meaning at different levels may result in differences in detail and connection at various levels, yet possess great similarities. In the case of the gross biological system, I have chosen to insist that the spectroscopy is due to non-linear limit cycles at the biochemical level, largely.

It was most fortunate (for me) that Warren McCulloch had put me in touch with Goodwin a few years ago (and through whose good offices I have been able to attend this conference). It was clear that Goodwin had taken on for himself the same task at the 'atomistic' biological level, namely at the level of the biological cell, that I had taken for the system as a whole. His advantage was that whereas my chains (I prefer chains to loops or networks to emphasize its chained causal nature without stressing the fixity of the lumped element-to-element connection of networks) were much more complex thermal-mechanical-hydraulic-electrical-chemical systems sweeping cooperatively throughout the system—say as represented in particular by any endocrine system response—his chains were shorter enzyme-linked chains nearly available by a more direct spectroscopic separation. It is to his credit that his quick appreciation of the non-linear exposition of its dynamics became the most direct path to sink it into biological consciousness. This is shown by the acceptance of his book, *Temporal Processes in Cells*, and by the speed with which it has inspired other investigators. In these efforts, Goodwin and my colleagues have therefore been the 'practical' translators of from whence the foundations for a theoretical biology should come.

It was pleasing to Goodwin and me (in the important sense of its fittingness) to find in the remarks of Scriven that the modern chemical engineer was capable of following up the non-linear mechanics of the biological system with his unit processes, transport processes, and reaction systems. It is not surprising, for it was in the works and examples of such people as Onsager, Kirkwood, Eyring, etc., that people like myself learned enough about non-equilibrium mechanics to begin to tackle real systems.

Then Pattee, immersed at the lowest biological level question, the origin of life, better than anyone squared the circle. It turns out that here, too, at the lowest level of biochemical synthesis, the question is the non-linear dynamics of the chain. It is not sufficient to obtain a replication mechanism. A tactical polymerization by which aggraded forms may be created, by condensation reactions, is simply not sufficient. These will limit, reach a static, steady state. There must be a degradation step; and, further, it must be a step which produces a reliable gain from the energetic (free energy) changes. This requires specific catalysis ('No hereditary process can take place without uncatalyzed reactions').

From my point of view, Pattee's remarks are directed at the steps of a non-linear chain that can produce cyclic certainty from a DC potential bath of chemicals. It is not the DNA, RNA geometric specificity that provides the steps. They provide a geometric milieu over which the decisive steps can take place. Specific catalytic reactions are the escapement-like processes that make the non-linear clock run. (See, for example, Pattee *et al.*, *Natural Automata and Useful Simulations*, Sparton, 1966.) The timing phases are possibly the many unit process steps involved in protein synthesis. Thus, Pattee's story is not the completion of the mystery of non-linear limits cycles—the spectroscopy of life formation and maintenance of the molecular biological level—but only its sketchy formal beginning. Room is still left for Nobel prizes at this level. (Arbib's contribution was to emphasize that there is a mathematical apparatus for doing the kind of thing that the complex biological system must do in self-replication. That is, he attempts an elegantly simple proof of the von Neumann result of whether a machine can be built that can reproduce machines as complex as itself.) We can only hope that as investigators like Pattee can elucidate more of the experimental problems of dynamic synthesis, that Arbib's algebraic semi-groups will be able to keep up, and perhaps sometime even surpass the experimental problems in predictive and prognostic value.

There is little doubt that the mathematical-computational complexity will be great. ('Isomorphic' mathematical theories will be quite important.)

While Kornacker directed his attention pointedly at the nervous system elements, he was really casting light on the one intermediate element which is needed to clarify the non-linear mechanisms of both the gross biological system and the microscopic cellular biological system; that is, the membrane. At present, his structure is still formal.

Guided by the statistical mechanics of thermal fluctuations and the formation of thermodynamic averages, he applies these ideas to cellular transport, specifically to electrical excitability of nerve membrane. The basic need, he shows, is to come up with a negative resistance within the membrane model. He finally proposes that a diode rectifier operating in a particular direction against a concentration gradient (sodium is his proposed gradient source) is the necessary and sufficient condition for a negative resistance.

While the details of his own particular problem are exceedingly clever, it is the broader implication that is really more interesting. His modelling contains some fertile seeds for the necessary instability to get the biological membrane to act as an active source for transport—whether at Goodwin's level of the cellular non-linear performance, or my level of the system response of such a system, say, as red cell-capillary interaction in the vascular beds.

Beyond that, Cowan suggests that the next few steps in understanding the electrical activity in the nervous system are coming along quite well. In the path in which Hebb has been so influential, a rough view exists of the relation of cortex and the reticular formation-thalamic link. Cowan has been developing a modelling of the cortico-thalamic nets, proposed as an improvement on the crude McCulloch-Pitts descriptions of processes in neural arcs. Thus, the high-frequency, tens of millisecond, responses in the brain are gradually coming into perspective.

For the gross nature of behaviour, McCulloch and I have recently sketched out a description of what a non-linear patterned model of man has to look like (copies were made available at the symposium, '1967 Behavioral Model of Man—His Chains Revealed', *NASA Contractors Report*, CR-858, July 1967)*. The model, physiological-psychological, is based on a central concept, homeokinesis, which echoes Waddington's homeorhesis. Waddington's thoughts long pre-date ours (apologies are in order for not having stumbled on his concept earlier). However, vanity and religion make me prefer or feel more comfortable with our concept (yet), for the ground we covered with it.

What is clearly missing is the 'theoretical' intermediate structure that covers the behavioural spectrum from 0·1 second to a few days. That it may be dominated

*The paper is now available in *Currents in Modern Biology, 1* (1968), 337.

by endocrine system and neuro-endocrine system responses is quite probable. However, we did not succeed at the conference in covering this ground. Although not represented at the conference, there are 'systems' scientists in endocrinology who have begun the laborious task of outlining the dynamic networks that govern their response. (Illustrative is the modelling of Yates and Urquhart. For example, Yates' most recent model of the adreno-cortical system was presented at an October 1967 conference on 'Hormonal Control Systems in Health and Disease', San Diego.)

However, the biologist claims there are two global questions which these statements of operating mechanisms do not answer:

1. What is the adaptive nature of the individual in his milieu ?
2. What is the operative and adaptive nature of the species in their milieu ?

The first question—which is where Waddington's and Maynard Smith's interests lie, and the 'real' reason for calling this conference—can be examined by default. Let us first pursue the second.

Fortunately, Kerner furnishes the beginnings of an answer. (I was very fortunate to attend a N.Y. Acad. Sci. conference—see *Ann. N.Y. Acad. Sci., 96*, 975, 1962—in which he presented a primary paper on the subject.) Following Volterra dynamics for interacting species, Kerner embeds this in the statistical 'mechanics' of Gibbs' ensemble theory. By this step, he reminds us that—if we can find the interparticulate forces—we can treat all kinds of ensembles, including biological, by this technique. I must confess that his paper inspired me, and in fact I think that I *have* furnished an answer for the 'effective' characterization of the interparticle forces in biological spectroscopy. Just as in theoretical physics—if the energetics presented by the spectroscopy of the underlying atomistic particles can be identified, then in summation, thermodynamic functions can be set up (e.g. the free energy—see for example Landau, Lifshitz, *Statistical Physics*, 1958) and the equations of change can be derived. This technique avoids the description of the detailed 'force' laws (actually it embeds them in a quantized structure which is quite close). Thus, I believe a structure now exists to describe both the individual quantization and the population changes. Kerner has continued with his problem of the application to competition among species.

Thus, we approach the question Waddington wants answered: 'You physical fellows have had your fun, and I've paid for it, now where is the answer to my question ? What is the theoretical basis for evolution ?' (This is a case in which I hope I am only putting my words in his mouth !)

Maynard Smith said that the fitness of an individual species is governed by or related to the number of its children. We will go along with this. The fitness of a species depends upon its ability to achieve a non-decaying number existence in the ecology. It is not a question of brain size or abilities. It is a question whether, for changing ecologies, the genetic content, epigenetically enfolding, has enough survival value to produce a yield slightly greater than one-for-one. This is not a deterministic question, but an emanative evolutionary one. Thus one cannot state the course of future evolution. (Today's species may die; yesterday's certainly have died. This is well illustrated in Gaylord's *Life in the Past*, which shows the growing, peaking, and decline in many phyla.)

However, this again is a quantization problem, i.e. the formation of a stable cycle within a quasi-static changing milieu. The theoretical foundation here is whether the epigenetically produced branchings—of phenotype—are exceedingly rich for changing environmental conditions. This must be at the basis of a science of the theory of evolution. We physicists could start to examine such questions, but the hint is better directed to the geneticist. He knows so many more details than we; we would only fumble. However, he has to absorb from us the static problem, Arbib's theory of automata, and the dynamic problem—Bohm's, Pattee's, Goodwin's, our spatial and temporal quantization by dynamics.

As Pattee indicated on the lowest level, the genotype is the instruction for a working cycle, the phenotype is the enzyme that makes it carry over. In our terms, to illustrate non-linear quantization—using the theory of the (very good) clock as example (very good will mean highly reliable in hereditary terms)—the timing phase (more generally now the spatial phase with a rate governing reaction) is given by a linear isochronous element—pendulum, mass-spring, atomistic element. While this will create a cycling phase, it either will not sustain, or will die down; thus an escapement which injects 'impulsive energy' (the enzyme), carries it over. A variety of phenotypic escapements might do. This governs the direction of evolution.

The contribution of 'practical' Richard Gregory, at this point, is very impressive. We mathematical physical types, prepared to lay out the mathematical and electrical characteristics of the nervous system, and of the emergent patterns of behaviour, may sometimes be casual about one link—the sensory link—and its implied informational data processing. For the species to stay out of trouble—normally to have children and not get eaten—remote 'at-a-distance' processing is desirable. The remote sensory detector (why it arose in the genotype is Waddington's and Maynard Smith's business), the eye, proliferated the whole nervous system, says Gregory. The clue to its origin, likely, is the pervasive darklight variation, that most common signal. Did this start the higher development ? Agreeing with Gregory, we are inclined to say, 'Yes'.

Thus, the fundamental pieces fall into line—obviously not in any well developed sense, but in outline. At this point now it can be (and is being) followed by competent workers clarifying the pieces. At what level description will subsequently break down is not for us to say. However, this era puts the foundation of the living system at every level into quantized limit cycles and their adaptive, emanative evolution.

Some incidental tidbits that concerned us also arose at the conference. In conducting a personal dialectic with Bohm, a thought struck me on a feature common to his presentation and mine, on the nature of creativity. Creativity in humans, to me, meant the establishment of novel emergent cyclic patterns in behaviour. To Bohm, the next instant of time itself was the only 'creative' emanative process. These, I suddenly saw, were the same. The 'creation' of time is the only continuing monotonous thing that is 'created'. In this sense, the 'creation' of man (as a linear chain) is the only act of creation of man to man. Kornacker and I worked this over to the conclusion:

The creation of time order is to the creativity of dynamic process as the hereditary (i.e. reproductive) sequence is to the creativity of evolution.

We presented this as one unifying theme.

Kornacker posed one other problem—of the definition of obscenity—which I attempted to dismiss, until he forced a meaningful dialectic. In my terms, a person whose 'body' image (of both internal and external cyclic events, i.e. his entire 'superego') is well composed and placid, will regard any presentation put before him which is too complex in structure and 'jittery' with regard to his 'ego' image (by definition, one's own ego image is stable, all else is moving—when this is upset, the individual is in trouble), as 'obscene'. To a person whose image is multi-dimensional and darting in time structure, almost no image can be obscene. This is the essence of the concept.

By this means we succeeded further in seeing ourselves, seeing others, and seeing the temporal-spatial problem of ideas, and creativity, and discovery in science, and the central problem of the conference.

Finally, Kornacker proposed, in apt summary, a (hopefully non-obscene) structural picture to unify the conference. I leave that summary to him (see p. 321).