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BIOLOGY AND THE MEASUREMENT PROBLEM

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Abstract—Present-day molecular biology, despite its name, is almost entirely committed to a macroscopic, classical picture of the organism; one in which quantum aspects play no role, except as a source of noise. Particularly is this true when dealing with informational aspects; especially "genetic information". The pervading metaphor here is an identification of "genetic information" with DNA sequence, and thence with program or software. We take a quite different view herein. If we presume, to the contrary, that microphysical processes play a role in primary genetic processes, then the "information" they can convey consists of observables evaluated on states. It is then natural to analogize a complex, consisting of (observed system + observer) with the biological partition between genome (observed system) and phenotype (observer). Such a picture immediately raises the deep issues surrounding "the measurement problem" in quantum mechanics.

In our brief consideration of such matters, we suggest that standard quantum mechanics is too narrow to deal with the biological pictures, because it is inexorably tied to quantifications of classical, conservative systems; there is no such for an organism. Rather, we are led to consider subsystems we call "sites", for which there is in principle no Hamiltonian. We then query the extent to which such "genetic information" is already subsumed in traditional observables a physicist would measure *in vitro* in a laboratory. We suggest there is no reason to believe that "genetic information", manifested in bioactivities, is reducible to these. Finally, we contrast this view of "genetic information" with more traditional ideas of program and computability. We argue that computability (algorithms) are entirely classical concepts, in a physical sense, and quite inadequate for a biology (or even a physics) in which quantum measurement processes are important.

1. INTRODUCTION

The explosive developments of the "New Quantum Theory" in the 1920s were, according to many participants and witnesses, accompanied by a renewed interest in biology on the part of the physics community. Put bluntly, it was widely believed that the new insights into nature, occasioned by these developments, would also serve to illuminate "the nature of life". Bohr himself was always much concerned with such possibilities. So too, to mention only the most eminent, was Erwin Schrödinger, who in his famous essay "What is Life?" repeatedly spoke of a "new physics", required to build the bridges between quantum-theoretic insights and the world of organism. At the very least, no one then doubted that life was heavily intertwined with microphysics.

Since then, however, history seems to have moved in quite the opposite direction. To be sure, biology is now dominated by "molecular biology", one of whose main historical roots was the search for such "new physics" by the physicist Max Delbrück in the realm of the very small (i.e. bacteriophage viruses). But this has grown as an almost exclusively empirical endeavor, and moreover, one in which quantum theory *per se* has played little role. Indeed, at a conceptual level, what passes for theory in molecular biology, is entirely classical; even 18th-century. Molecular biologists in fact tend to be deeply distrustful of "theory"; they regard it, including all of quantum theory, as essentially irrelevant.

And yet, the basic conceptual questions posed by biology remain, as they always have been, unanswered, and even unaddressed; displaced by a naive and optimistic reductionism. In the remarks to follow, we shall briefly re-examine the original proposition that micro-physics is basically intertwined with the nature of organism and of life; not irrelevant to it as currently presumed. In the process, we shall perhaps learn some new things about microphysics itself.

The ideas to be described herein go back a long way. Some of them were originally reported in 1963 (Rosen, 1964), at a time when the Watson–Crick model for DNA was about a decade old, and when the identification of "genetic information" with "sequence" had already become a reflex. The point of departure for the work to be described was an attempt to make this usage of the term "information" consonant with what the term meant in microphysics. That meant talking about measurement.

2. SOME HISTORICAL CONSIDERATIONS

von Neumann, in his classical text on quantum mechanics (von Neumann, 1932), had already tacitly identified the term "physical event" with "evaluation of observables on states", and "information" with the result of such evaluation. Underlying this was the proposition that a material system, the kind of thing with which quantum theory itself dealt, was a collection of such states, and a corresponding family of observables to be evaluated or measured on them. He argued at great length that the former was embodied in a complex Hilbert space, and the latter in self-adjoint operators on that space, whose eigenvalues constituted the values themselves.

This seemed quite general. But it was not, in fact, as general as it looked. Historically, a quantum-mechanical system was always viewed as a quantization of a classical one. And classical physics was then dominated by ideas of conservation, especially in classical mechanics. Accordingly, quantum *mechanics* (as distinguished from quantum *theory*) was entirely dominated by a single basic observable, the Hamiltonian, embodied in a Schrödinger equation. One could not even get started in quantum *mechanics* until that basic observable was specified. As long as a quantum-theoretic system meant a quantification of a classical conservative one, there was no conceptual trouble with this. However, quantum *theory* had inevitably opened far wider possibilities as to what a "microphysical system" could be; namely, an essentially arbitrary family of states, and of observables to be evaluated on them.

Now let us look at the situation in biology. As a material system, whatever a living organism may be, it is certainly not conservative. Quite the contrary; it is wide open in every way. Even its constituent particles are turning over relentlessly. Moreover, there has never been any such thing as a "classical" description of an organism, and hence nothing to even begin to quantize in the standard sense. For these historical reasons, then, standard quantum mechanics has been unable to find a purchase on basic biological questions. It can, to be sure, operate as usual on certain *subsystems*, considered apart from the organism itself, but it is an act of faith to proceed from these subsystems to the organism as a material system in its own right; i.e. to argue that quantum-theoretic characterization of such subsystems is sufficient to establish a quantum theory of the organism.

3. ON "PRIMARY GENETIC INFORMATION"

As we have just seen, a traditional, straightforward application of conventional quantum-mechanical views, which presuppose conservation conditions, and begin from classical views about what systems are, are already too specialized to work well in biology. However, we can retain the essential idea of material events consisting of observables evaluated on states, and the resultant values as embodying "information" about those states. It was in this context that the paper Rosen (*loc. cit.*) attempted to deal with "primary genetic information" in microphysical terms, although we no longer have an immediate interpretation of the term "state" anymore; it is now roughly synonymous with anything on which a given observable, or family of observables, can be evaluated or measured.

We thus presume only that the term "genetic information" is associated with a family **A** of microphysical observables, and that the "information" associated with a particular state ψ, on which the observables in **A** may be evaluated, is embodied in the resultant values. We do presuppose that the familiar rules relating states, observables and values, automatic in the standard Hilbert space picture of ordinary quantum mechanics, hold here; i.e. that the observables in **A** are represented by self-adjoint operators on some appropriate space of states.

If that is so, then the exigencies of the biological situation require that the observables in **A** all commute. Otherwise, we can see that iterations of the evaluation process on a state will quickly corrupt the "information" presumably carried by, or embodied in, that state. That is, the observables in **A** behave "classically" with respect to each other.

Now it is a theorem of von Neumann that, given a family of commuting observables, like **A**, there exists an observable A of which all the observables in the family are all functions. That is, everything in **A** is of the form $f(A)$. Thus, in a precise sense, the "information" obtained by evaluating the observables in **A** on a state is already a function of evaluating A alone on that state. Everything thus reduces to a consideration of the spectrum of A; that is what we studied primarily in Rosen, *loc. cit.*

One of the corollaries of that discussion was, precisely, that *the observable A could not be regarded as a Hamiltonian of anything.* Moreover, if we attempted to attach a Hamiltonian to **A**, to obtain a conventional quantum-mechanical system **S**, the states of **A** disappeared irretrievably into the states of **S**.

I interpreted these curious results as follows. That Hamiltonian-based systems, with which quantum mechanics traditionally deals, contain subsystems like "*active sites*", and that it is these which are involved in biological transactions involving informational exchanges. Such subsystems are not fractionable or separable from, say, whole molecules; there is no physical procedure for breaking a molecule into two parts, by severing chemical bonds, one of which is such a site, and the other of which is "everything else". This is clearly because such subsystems, or sites, are not energetically closed. They are thus not "molecules" in their own right, amenable to the same quantum-mechanical analysis that molecules themselves are; they are more general, as microphysical

systems in themselves, than are inherently conservative molecular structures. And as such, they become invisible in any analysis based on conservation; no analysis of a Schrödinger equation, however detailed, will reveal them.

Thus, for example, it is not possible in principle to determine whether a particular (protein) molecule is an enzyme; even less what its specificity might be, from its description as a conservative structure. As noted, such a description precludes what is needed in drawing such conclusions.

The upshot of these considerations, stated briefly, is that traditional quantum mechanics is, in its reliance upon conservation (in turn, derived from classical descriptions), a very special theory. In particular, it is too special to serve as a basis for biology. As we have indicated, it discards those subsystems in which "informational" transactions are localized; the subsystems we have called "sites".

4. PHENOTYPE AS OBSERVER OF GENOME

Part of the motivation for the above analysis of "genetic information" in microphysical terms was a picture of phenotype, in the broadest sense, as an array of meters for evaluating, or measuring, the values of the observables of **A** on the states ψ present in a biological system or organism. In a sense, the phenotype of an organism is thus regarded as reading out, by virtue of its own changes in state, the "genetic information" which makes it what it is.

This partition of an organism into phenotype and genotype, which we have identified with the analogous partition of a microphysical measurement process into (observer + observed system), actually goes back to Mendel and to Weismann. It was Mendel who initially suggested that an organism phenotype could be partitioned into an overlapping family of "characters", each under the control of distinct "factors" (nowadays called genes). We would now say that these phenotypic characters (e.g. wrinkled cotyledons, five fingers, etc.) *express* the underlying genomic factors, just as a meter expresses a value of something measured. Weismann, in apparent ignorance of Mendel's work, likewise partitioned an organism into *soma* plus *germplasm*; the soma (roughly phenotype) had to be recreated anew in each generation, but the germplasm was propagated essentially unchanged from the beginning.

This kind of genotype/phenotype, or soma/germplasm partition is perhaps the essential characteristic property of organism itself. What we suggest is that this partition is generically related to the partition between observed system and observer. Furthermore, the biologist, as an observer of the entire, unpartitioned system, sees phenotypic behaviors as the set of processes through which meters come to express the values of what they are measuring.

Conceptually, such ideas run directly into the difficulties collectively known in quantum mechanics as "the measurement problem" (cf. e.g. Belinfante, 1975; d'Espagnat, 1976; Wheeler & Zurek, 1983). These arise, roughly, from trying to relate what is measured, and what does the measuring, considered as separate systems, with the complex (measured system + observer) as the measurement is being performed. Of this problem, d'Espagnat says poignantly "the problem of measurement in quantum mechanics is considered as nonexistent or trivial by an impressive body of theoretical physicists, and as presenting almost insurmountable difficulties by a somewhat lesser but steadily growing number of their colleagues" (*loc. cit.*, p. 161).

In the present case, let us recall that the measured system is presumed to consist of states ψ, and what is measured is "genetic information" acquired by evaluating the family of operators **A**, or the single operator A of which these are all functions, on these states. The meters themselves constitute soma or phenotype, through which this "information" is expressed, in the form of dynamical evolutions in the meters. As we have noted, the situation is rendered still more interesting by the fact that the operator A is not itself a Hamiltonian of anything; it pertains rather to a "site".

We cannot, in this limited space, discuss the ramifications of "the measurement problem" in all its generality, nor the impact on it of pursuing the above homology between measurement and organism. Rather, we shall content ourselves with a few corollaries of it, as an indication of the interplay between microphysics and biology which emerges from it.

5. BIOLOGICAL OBSERVABLES

The above remarks bear in a new way on whether quantum mechanics is a "complete theory". We have already seen that, in a number of ways, quantum mechanics limits itself far beyond the scope of classical descriptions, which provide its basic point of departure. Within those assumptions, of course, quantum mechanics provides a far better, more general theory than the corresponding classical one does. Outside those assumptions, based essentially on conservation (Hamiltonians), quantum mechanics provides no theory at all. It is in this latter sense that we talk about "completeness"; not in the traditional senses, embodied, say, in the notion of "hidden variables" (cf. e.g. Belinfante, 1973), and that of the EPR paradox initially proposed by Einstein *et al.* (1935). Our problem has to do rather with limitations of domains of applicability, addressed already by Schrödinger (*loc. cit.*) in his term "new physics", and in particular, with its adequacy in providing a reductionistic basis for biology.

The germ of our problem arises in addressing the kind of microphysical subsystem we called a "site". As we have seen, this kind of subsystem has no

Hamiltonian of its own. Intuitively, it takes energy, coming from a larger structure, to hold it together. As we have argued, such "sites" are the repositories of "information" in biology (we have considered "genetic information" in the preceding discussion). These larger structures can be thought of as traditional molecules, to which standard quantum mechanics does apply. But the sites disappear irreversibly when we look, however carefully, at such a description of a whole molecule.

For the past few years, for instance, there has been considerable effort invested, mainly in biotechnological contexts, into "bioactivity" of molecular structures. A central focus of these activities lies in the concept of a "pharmacophore", which is another kind of name for what we have called a site; with how to recognize one, and above all, with how to design one. A basic tool in these endeavors is called SAR ("structure–activity relationships"), and especially a variant called Q-SAR ("quantitative structure–activity relationships"). Conceptually, I would regard them as an offshoot of what used to be called "absolute reaction rate theory" (cf. e.g. Glasstone *et al.*, 1941).

The idea behind such endeavors is that any measurement of a "bioactivity" associated with a molecule, via a change of biological somatic properties *in vivo*, is already contained in the standard measurements which a physicist would make, or calculate, on that molecule. In other words, that a bioactivity, measured on an organism, is just another name for a class of observable values of that molecule, which a physicist could in principle measure directly. Stated baldly, the presumption behind SAR and Q-SAR is that the "bio-" in "bioactivity" is redundant.

Suffice it to say that this approach has not been very successful, even when supplemented by a host of "semi-empirical" information coming directly from bio-assays.

As suggested above, however, organisms tend to see sites and not molecules which may carry them. Furthermore, we have seen that sites are not independently amenable to standard modes of quantum-mechanical description. Accordingly, there is a strong possibility that observables associated with such sites (i.e. observables like A above), which are actually seen, or evaluated, by an organism, are unrelated to what a physicist would see when looking at a whole molecule carrying such a site as a subsystem.

It was on such a basis that I proposed (cf. Rosen, 1968) the existence of "biological observables" localized in such sites, inherently not expressible in terms of the usual ones of quantum mechanics. In the above language, "bioactivity" of a molecule cannot be reduced to traditional quantum mechanical descriptions of the molecule alone. It is in this sense that such molecular descriptions are incomplete.

Some (admittedly controversial) experimental work, designed to explore this possibility of "biological observables", was undertaken in the context of enzyme–substrate recognition, and measured by standard kinetic means (cf. Comorosan, 1968, 1976). Taken at face value, these experiments support the above analysis. However, other possible explanations of the results could not be completely excluded, and the experiments themselves, though widely repeated by other investigators on a variety of simple enzyme–substrate systems, were apparently not universally so. Interested readers may judge for themselves.

6. ON OBSERVATION AND COMPUTATION

von Neumann himself noted the analogy between measuring the value of an observable and performing a computation; they were both embodiments of effective procedures for generating numbers. Much later, when he became personally involved with the development of digital computers, he came to regard both as embodiments of algorithmic processes. He applied these ideas extensively to biological questions; particularly to "self-reproduction", and to understanding the brain. A useful and encyclopedic guide to his thinking on these matters may be found in Burks (1966).

Although as far as I know he never said so explicitly, von Neumann came to regard computability, the basis for his view of automata, as a law of nature; i.e. as a restriction on physics itself. Specifically, that nature could do nothing which was not computable or algorithmic. Thus, he came to believe that the universal digital *computer* (universal Turing machine) was also a universal *constructor*, able to perform whatever physical acts were required to assemble any material system that could physically exist from material parts.

These ideas found their most noted embodiment in von Neumann's "tesselation models" for self-reproduction. Such ideas tacitly served as a kind of "classical description" of organism itself. They served to partition the physical world into hardware and software; a partition which was quickly identified with the biological partition into phenotype (hardware) and genotype (software). From this, it was an easy step to the prevalent current view of genotype as *program*; a view reinforced by the identification of Mendelian genetic "factors", and hence "genetic information", with sequences in linear DNA strings.

We wish to briefly contrast this view of "genetic information" with the one developed above, based on measurement, and in which microphysical processes play a central role. As we have seen, views like von Neumann's are based on a direct identification of physical measurement with formal computation, and thereby, a complete extrusion of microphysics itself (because the mathematical "machine", like a Turing machine, is in physical terms an entirely classical device). The only role of microphysics in such a picture is as a source of noise; never as a source of message.

The difficulty with identifying "physically effective" with algorithmic or computable here is, in a nutshell, that the entire distinction between microphysics and macrophysics, between quantum and classical, disappears. Or, more precisely, the former disappears into the latter, because "algorithm" itself, the hardware which executes it, and the software on which the hardware operates, are entirely classical. Hence, at this level, it is impossible even to discriminate between a microscopic system and a macroscopic one.

Pursued a bit further, computability is inexorably tied to the finite (indeed, low) dimensionality of both hardware and software; the only thing which can grow indefinitely is time. This may be argued adequate for classical processes, in which state descriptions are presumed finite, but it is the essence of microphysics that "state" is already not finite. In a precise sense, one of the essential difficulties with computability is that the set of messages or inputs which can be processed by a finite-state device is too small to describe the state of a microphysical system.

Hence, microphysical systems are far richer in the "information" carried in their observables than could be conveyed to macroscopic hardware via macroscopic software. We have even argued, in other contexts (cf. Rosen, 1991), that the latter are *non-generic* in the former. These facts have a variety of other conceptual and technological correlates, which we cannot go into here. We merely wish to motivate the proposition that "genetic information", interpreted as the measurement of genotypic observables by phenotypes, is a very different thing from the processing of software by hardware.

7. SUMMARY

We started from the proposition that microphysical events play a basic role in biological processes which involve "information". More specifically, that such "information" involves the quantum-theoretic evaluation of observables on states.

We stressed that the "states" involved, and the observables defined on them, cannot generally be regarded as quantizations of classically describable, conservative systems governed by Hamiltonians. They may be realized as subsystems of them, but inherently of a more general class which we called "sites".

We homologized the evaluation of microphysical observables on sites with the genotype/phenotype duality characteristic of biological organisms, where the sites convey "information", and the phenotypes are the measuring instruments themselves. As we saw, this homology immediately raises the issues comprising "the measurement problem" in microphysics, in a direct biological context.

Finally, we contrasted this picture of "genetic information" with the more customary one of genome as "program", processed by finite-state hardware. As we indicate, such algorithmic pictures are entirely macroscopic, and in fact entirely lose the discrimination between classical and quantum, even in the limited case of Hamiltonian systems.

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ADDENDUM

The following remarks are attached in connection with comments made by the referees, to whom I am grateful for their attention.

First, the present paper is ultimately concerned with the nature of the relations between biology and physics, and most particularly, with the efficacy of reductionisms. Our point of departure is the different ways in which they characterize "information". Actually, our discussion does not so much compare biology and physics, as it compares "molecular biology" and "quantum mechanics". What was argued was that the concept of "site", developed above, evades both, and thus the reductionisms they differently espouse. I had thought this was sufficiently clear from the paper, but if not, I will emphasize it again here.

Second, this subject-matter is large; the paper itself is short. The boundary condition of brevity requires a sacrifice of breadth for depth. That is why I appended a list of references, some of them quite lengthy. But they cannot perform their intended function if they are not consulted.

Finally, I should say that, to me, biology is a subject concerned with organization. Information propagation within organisms is one large facet of this. In their different ways, molecular biology and quantum mechanics provide us with distinct kinds of material surrogates for organisms; surrogates which (in different ways) share their matter, but in which this matter is organized quite differently. Hence the behavior of these surrogates is quite different from those of organisms. The reductionistic claim is always that, if you have enough such surrogates, and know enough about them, then the organization will follow as a corollary. These kinds of claims are almost never true. For instance, you cannot solve a classical N-body problem by solving N one-body problems. There is an inherent non-recursiveness here; something which is not just a technical matter, and makes N bodies in isolation a poor surrogate for those same bodies in interaction.

An immediate example is provided by what was early called the "central problem" of molecular biology; the protein-folding problem. According to the Sequence Hypothesis, which "reduces" all information to sequence information, or "primary structure", the folding of a polypeptide should be entailed from its sequence alone, under any given set of ambient conditions. So there should be an algorithm, a program or software, which converts a given primary structure into a set of spatial coordinates for its residues; i.e. into a shape or tertiary structure. People have looked very hard for such a program, based on the idea that folding is merely a minimization of free energy (i.e. a constrained N-body problem). Suffice it to say that no such program has ever been found, and even more significantly, that the goal appears to recede as it is approached from this direction.

Folding is, to me, the most elementary example of morphogenesis or pattern generation. I would argue that the substitution of "sequence", as a reductionistic surrogate for the Mendelian "factors" (which were characterized initially entirely through their morphogenetic effects) has not illuminated this process much. Conversely, direct approaches to morphogenesis, mainly via attractors in (inanimate) open systems, tacitly involve entirely different surrogate genes, which have nothing to do with sequences.

Biology poses problems. Both quantum mechanics (which says something about matter in general) and in a different way, the experimental techniques of molecular biology, provide methods which can be applied to problems. Both claim that their methods are adequate to the problems; a theoretical assertion. In the present paper, I have argued that: (a) the quantum-mechanical world and the molecular biology world are mutually irreducible; and moreover (b) there are tangible and basic things (e.g. "sites") which evade both.

I would thus suggest keeping an open mind about claims that biology is "reducible", or that it has already been reduced, to one or the other.