On the complementarity of Biology and Physics

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Living matter is characterised by three attributes: energy, growth and reproduction. Any abnormality in all or any of these can produce illness, mutation, and abnormal reproduction [1].

To make a thorough and profound study of living matter two main factors must be considered, although they are really inseparable. The fundamental structure needs to be examined and studied at the atomic and subatomic level, while at the same time those energy aberrations that produce changes in, or result in changes of, that fundamental structure should be scrutinised. To proceed from this point biology needs a new beginning, and by this we mean a synthesis of existing knowledge rather than a search for new facts. Only during such a synthesis will it become clear what innovations are likely to be needed and what new knowledge has to be acquired.

We predict that if living matter was studied at the level of its basic structure — that is, the elementary particle energy level — we would find very little difference between it and inanimate matter.

All living matter is made up of elements and particles and therefore should obey the laws of physics, as do all systems of the Universe — from the most complex galaxies to minuscule atomic and subatomic particles.

In their organisation unicellular organism are more complex than the galaxies, in spite of the latter's size. E. coli contains approximately 5,000 different types of compound, of which 3,000 are different proteins and 1,000 nucleic acids.

How much more complex is a mammal, which is composed of billions of cells? Man consists of approximately $10^{20}$ cells, and in a human body there are some 100,000 different kinds of proteins, most of which have molecular weights of more than several thousands.

Starting from the primordial soup life evolved some $2 \times 10^9$ years ago, and through chance and necessity man has adapted, adopted and developed into what he is today.
While it has been calculated that the entire physical Universe is composed of about $10^{80}$ particles (electrons and protons) it is also known that the number of base pairs in one human chromosome is about $4 \times 10^9$.

In theory, as each base pair position could be occupied by any of the 4 bases the real calculation is $4^{4 \times 10^9}$. Taking logs it can be shown quite simply that $\log 4^{4 \times 10^9} = 2.4 \times 10^9$, and therefore the number becomes the colossal figure of 1 followed by $2.4 \times 10^9$ zeros, or 1 followed by 2,400 million noughts. The number of possible genetic combinations is of ungraspable magnitude. The number of particles in the entire physical universe is hardly a drop in the ocean by comparison.

In the beginning of life nucleic acids grouped together randomly and through the evolutionary process and natural selection produced a workable structure. During 2 billion years of history a large number of combinations that proved unworkable have been eliminated. It is quite conceivable that man has not yet arrived at his final genetic composition, and that the future may hold more promising mutations.

It is because of the complexity of living matter that the known laws of physics do not seem to satisfy all its patterns of function and behaviour. For example, the speed by which information is transmitted for the architectural composition of complex proteins could approximate to roughly $10^9$ impulses/second in a mammalian cell. The speed of transmission would then be close to the speed of light. Is this really possible with the energy variations of biological systems as we know them today?

**Complementarity of Biology and Physics**

The reason there is some difficulty in explaining biological behaviour in terms of the laws of physics today could be two-fold. We have already referred to the first, which is that the structure of living matter has not been studied at a sufficiently fundamental level compared with the way physicists and mathematicians have investigated inanimate matter. And in the second place it could be that the laws of physics which are applicable to or will accommodate the behaviour of biological systems remains to be formulated. The gap between biology and physics is very apparent when comparing the difference in depth at which the respective systems have been studied. We need only consider the Hamiltonian which describes the interactions in a certain group of metals — the rare earths. We can formulate it as:

$$H = \sum_i V_{ei} + \sum_{i \neq j} J_{ji} \vec{J}_i \cdot \vec{J}_j + H_{\text{Zeeman}}$$

The first term is the energy due to the electric field created around a particular site of the metal because of the electron cloud around it. The second one, the exchange term, involves interactions between the spins at different sites — that is, between one located at a certain site and all its neighbours. The third term, the Zeeman term, appears when there is a magnetic field that has been imposed on the system.

If we now look at a biological system such as a cell membrane, which is composed of a lipid bilayer and intrinsic proteins, its Hamiltonian can be written as:

\[ H = H_{\text{l lipid-lipid}} + H_{\text{l lipid-protein}} + H_{\text{protein-protein}} \]

The first term corresponds to lipid–lipid reactions (between lipid chains); the third term is the protein–protein interaction, and the second one the mutual reaction between lipids and proteins. They have been written in order of decreasing hierarchy in terms of the strength of each interaction. The Hamiltonian is the same as for a binary alloy (crystalline) in metal physics. But so far each term has been studied at a much grosser level than on metals, for example; it has been looked at in terms of the configurations of lipid chains and the nature of intrinsic proteins embedded in them. Nothing has been attempted in a more detailed fashion because of the inherent complexity of such a study. The same kind of argument holds for most biological products and systems.

In the realm of physics and cosmology we are looking at galaxies on the one hand and into the atom on the other, realising that the behaviour of the former depends on the understanding of the latter. There are great similarities in the comportment of these two vastly different entities. However, the atomic and energy relationships of a galaxy are simplicity itself compared with those demonstrated by a living cell. Galaxies are simple because everything, or almost everything, about them can be calculated — their existence, size, life expectancy, and so on. In a single cell such calculation would hardly be possible as the number of equations involved would be enormous owing to the number of parameters present making the interpretation of the results extremely difficult. For practical purposes that number could be considered to tend to infinity although remaining a very large constant. Introduce this constant into any complex organic system and you maintain life.

In their understanding of this kind of reasoning the biomedical scientists have fallen behind the rest. Conforming to the tradition of considering man to be a divine creature biologists have desisted from the logical pursuit of knowledge derived from investigating the elements, the atomic comportment, and the energy components that constitute life. In the main the
behaviour of biological systems has been studied by physiological biochemistry and at a much too superficial level to be truly revealing. One could make the comparison of studying surface anatomy on a lady fully clothed in Victorian period costume.

Writing in 1943, 10 years before the elucidation of DNA structure, Schrödinger said «chromosome fibres could suitably be called aperiodic crystals» and in his opinion these represented a material carrier of life.

We know now that there are crystalline arrangements — that is to say periodic crystals — in living systems. Perhaps the simplest and therefore the best example is that of the purple membrane (halobacterium halobium) which gives the crystal structure (hexagonal), the size of the unit cell, and the spacing between cells in this membrane [2]. Indeed, the atomic arrangements and their interplay in the most vital parts of an organism do not differ fundamentally from those physicists and chemists have studied in the non-living world. Yet even this knowledge leaves vast lacunae in our understanding: what are the forces that control subatomic relationships in living organisms? and how are these influenced by purely physical changes arising from the internal or external environment? After all, whether living or not, matter is the relationship of elementary particles maintained in time and space by the interplay of available energy.

Biology and statistical quantum mechanics

Living matter is a complex collection of interrelated particles which, unlike inanimate matter, have an infinite capability to alter and change and yet function collectively to remain together. Its individual particles obey the statistical laws of physics.

Physical laws rest on statistical bases, and therefore can give only predictions for the observable quantities during the process of measurement.

If we consider the Fermi–Dirac distribution function for the probability of a single particle state at energy E to be occupied by an electron this can be written as:

\[ f(\varepsilon) = \frac{1}{e^{(\varepsilon - \varepsilon_p)/kT} + 1} \]

With \( f(\varepsilon) \) = probability for a single–particle state at energy E to be occupied by an electron;
\( \varepsilon_p \) = Fermi energy level;
\( k \) = Boltzmann constant;
\( T \) = absolute temperature.
Physical particles can be described by two quantum statistical distributions: the fermions by Fermi–Dirac distribution, and bosons by the Bose–Einstein distribution. Although the formalism of quantum mechanics has been widely accepted its interpretation is still a subject of controversy, particularly with regard to the measurement process — namely the «Copenhagen interpretation» of Bohr; the more statistical approach of Einstein; or more recently the hidden variables theory of Bohm [3] and the many worlds interpretation of Everett [4] and Wheeler [5].

When very large numbers of atoms are interacting statistical laws begin to play a role. These laws are obeyed with increasing fidelity as the number of atoms gets larger. At this stage a semblance of order appears, but it is only a semblance.

There is no reason to assume that the law of statistical mechanics will not apply to particles of living organisms. The body is made up of a very large number of cells — of the order of $10^{20}$ — and each has in its constitu-

![Fig. 1. — Step-functions for accepted normal limits for temperature, sight and sound.](image)

tion a large number of both free and bonded electrons. The DNA molecule exemplifies this well. We need look no further than at the 4 bases — guanine, adenine, cytosine, and thymine. Each one of these contains between 10 and 14 free, and many more bonded, electrons. Even the covalent bonding between the bases themselves are of different strengths. There are also protons in the body which although not readily usable, because they are absorbed internally by surrounding tissue, are still there nevertheless. Therefore we have a very large number of particles, electrons and protons, which should follow the behaviour described by the Fermi–Dirac and Bose–Einstein distributions respectively, provided $\varepsilon_p \ll kT$. Although the arrangement in living systems is more complex than in non-living matter we cannot disregard the basic comportment as predicted by the laws of statistical mechanics.

The arrangement of living matter is much more functionally complex than that of inanimate matter, yet generally speaking because of this complexity it is far less sensitive or responsive to physical disturbance. Surely this is what Claude Bernard called «le milieu intérieur» a hundred years ago — and what Cannon called homeostasis 50 years ago — without either of them using physical or mathematical formulations to explain or expound on their theme, but expressing it simply in terms of physiology.

This can be seen easily if we consider the normal sensory apparatus of man and the normal functioning of the body in relation to temperature changes. In the curves above it is demonstrated that the human body can function normally only within an extremely narrow range of the variables involved.

Although the curves are approximate — for example, the intensity perceived by the human ear is not strictly constant for all frequencies — they serve our purpose in showing how narrow the range is within which we normally function.

**Order and disorder**

The existence of matter — whether living or otherwise — is recognised by the observation that it exhibits a certain orderliness.

This attribute of orderliness is more marked in living than in inanimate matter, and is one of the two differences distinguishing them. The other is of course reproduction.

Max Planck once wrote on the dynamical and statistical types of law. His first type fits the description of a mechanism that allows events to take place producing a new order from existing order, as is the case in cellular function and reproduction. The second type describes events that produce order from disorder, which prevails in almost all inorganic substances [6].

This concept is not acceptable today. The dynamic and statistical laws of physics depend not on two different orders, but rather on the size of the disorder.

The time–dependent Schrödinger equation which gives the time evolution of the system:

\[
i\hbar \frac{d\psi}{dt} = H\psi
\]

already contains the information about the statistical nature of the wave function describing the physical system.
Everything is disorderly to a greater or lesser extent. However, under the influence of certain conditions and driven by chance some order transpires; it is a relative order since no future is ever an exact blue-print of the past or present — for example, no so-called daughter cell is ever exactly like the mother cell; no twin is totally identical and no offspring completely resembles its parent. The energy relationship to different particles commands a certain orderliness; the more complex these objects are the more orderly they become. The more complex an organism is the more built-in safety mechanisms there will be which will tend to correct random mistakes and lend it an appearance of order.

We believe there is a need to develop a study of living systems from the point of view of their statistical mechanics at a subatomic level. We know that the concept of entropy gives the best and most accurate information about the state of order/disorder of a physical system. It has been used extensively to account for both macroscopic properties (as in a Carnot engine) and microscopic ones (entropy of a ferromagnet).

Although the concept of entropy has been used considerably since Boltzmann introduced it at the end of the nineteenth century it has not been suggested before that it can be thought of as the measure of the order of a system which would compete with its disorder measured by its temperature. This can be seen from an extension of a classic example in quantum mechanics — namely, the calculation of the average magnetic moment of an atom in a system of non-interacting atoms (taken for simplicity) at a temperature T in an external magnetic field parallel to the direction of space.

The magnetic energy of an atom is therefore:

$$E = - \mu \cdot H$$

where \(\mu\) is the magnetic moment of the atom.

As \(\mu\) is directly proportional to \(J\), the total angular momentum of the atom, the energy can be expressed as:

$$E \propto - HJ_z$$

where \(J_z\) is the \(z\) component of the total angular momentum \(J\).

\(J_z\) can take any of the \(2J + 1\) possible orientations, and therefore the magnetic moment can have the same number of possible orientations.

The possible magnetic energies in the atom are thus:

$$E_m \propto - Hm$$

if we call \(m\) one of the \(2J + 1\) values of \(J_z\).

The probability for an atom to have a particular value \(m\) is then:

$$P_m \propto e^{-\beta E_m} \propto e^{-\beta H_m}$$
The average value of the magnetic moment of the atom is:

\[
\langle \mu_n \rangle = \frac{\sum_{m=-J}^{+J} e^{\beta \mu_m H_m} (g \mu_n m)}{\sum_{m=-J}^{+J} e^{\beta \mu_m H_m}}
\]

with \( \beta = 1/kT; \) \( k = \) Boltzmann constant; \( g = \) Landé factor; \( \mu_m = \) Bohr magneton.

If we now call \( Z \) the partition function of the atom this is defined as the denominator above, but the entropy associated with the atom can be defined as:

\[
S = k \log Z
\]

Therefore the final expression for the average value of the magnetic moment becomes:

\[
\langle \mu_n \rangle = T \frac{\partial S}{\partial H}
\]

In the next stage of the argument, instead of taking \( H \), the magnetic field, as a measure of the order of the system which is going to compete with the disorder produced by the temperature \( T \), we take \( S \) — the entropy — as a measure of that order.

The range of temperature variation of the human body is extremely narrow. The body has a specific temperature regulating mechanism to ensure this. Even when the normal equilibrium temperature of the body is increased — for example, during an infection — or decreased, as in normal sleep, the new state at a higher or lower temperature is a new equilibrium state of higher or lower disorder, and thus the entropy at the new temperature can be calculated. The body takes care to average out all non-equilibrium situations in order to function in an orderly manner as possible compatible with maintenance of life and in the most efficient way in its new situation of either a higher or a lower temperature.

Let us call \( T_c \) the characteristic time of the system, as given by the Heisenberg uncertainty relationship for energy and time:

\[
T_c \cdot \hbar \sim E
\]

This gives us \( T_c = 10^{-15} \) sec.

A new uncertainty relationship for the order/disorder in the system can now be set up, such as:

\[
T_c \cdot \Delta S \cdot \Delta T \sim \hbar
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If we take $\Delta T = 10^{-6}$ K, $\Delta S$ is of the order of $10^{-13}$ JK$^{-1}$ which shows that an accurate measurement of temperature produces a large error in the measurement of entropy. On the other hand, if there is a large error in the measurement of temperature, such as $1^\circ$K, $\Delta S$ is of the order of $10^{-19}$ JK$^{-1}$, which is a very small error.

In other words, if we reduce $T$ we increase the order of the system. As $S$ decreases at the same time we are increasing the order, and thus can measure $S$ less accurately. Conversely, if $T$ is increased so is the disorder, which increases $S$ and reduces the order of the system, in which event $S$ can be measured more accurately.

We suggest that the same reasoning can be applied to biological systems. Looking no further than the structural configuration of the 4 bases of the DNA molecule: each base contains between 10 and 14 free electrons and a high number of bonded ones. Changes in the environment can alter the interaction within a base and therefore possibly between bases in terms of a change of electronic energy. These changes depend on the stability of the bonding and electron arrangements within one base as well as between base pairs and the relative gaps between the electronic energy levels available.

In writing the Hamiltonian of such a system it is crucial to distinguish between first order, second order, and third order effects. Although they all contribute to the total energy change of the system their relative magnitudes impose such an hierarchy.

The first order effects are changes in the energy levels of and energy transfer between the free electrons in a base. The second order effects involve the bonded electrons of a base. The third order effects include crossover interactions between a base from one pair and another base in a neighbouring pair.

If for simplicity one assumes a short range interaction this would take place between nearest neighbour pairs. It is also possible to assume — although the calculation would be more complex — a more realistic interaction such as a long range one, which would involve neighbours a certain distance apart. This distance would correspond to a calculated correlation length characteristic of the system. It is not unreasonable to imply that these changes will affect nucleic acid function.

From the Heisenberg uncertainty relationship for energy and time, taking $E$ as the mean energy required to unzip the base pairs, we can estimate the value of the characteristic time of our system to be:

$$T_e \sim \frac{\hbar}{E} = 10^{-13} - 10^{-14} \text{ sec}$$
We can then introduce this time into the new uncertainty relationship $T_c \cdot \Delta S \cdot \Delta T \sim \hbar$, and see the effect of raising the temperature of the system by $10^5 K$, for example, on the order of the system as given by the entropy $S$.

We can then calculate the disturbance effect and see whether this would increase further the state of disorder of the system to the extent that it could disturb and even permanently dissociate the relative parts of the strands — thus killing the cell or producing major abnormalities.

Knowing that $T_c$ is of the order of $10^{-13}$ to $10^{-14}$ secs and taking into account the enormous number of demands made for DNA base transcription every second, it is inconceivable that the numerous, rapid, discrete alterations in the dynamic DNA molecule can be under chemical control. Ultimately, initiation and control of transcription must be the result of physical signals — electromagnetic in nature — which respond with the necessary rapidity to the organism’s demands.

These signals trigger off the «chemical train» needed to maintain the production line and process of information transfer.

By studying living matter with the tools of quantum mechanics and the hardware of today’s physics it should be possible to calculate and detect the energy changes — normal and abnormal — and pin-point the location in the DNA where they respectively take place.

It is here that the new uncertainty relationship invoking entropy would be of major relevance, making it possible to reduce the calculation of the probability of the sites where the disorder is most likely to occur.

Energy aberrations are easier to detect than changes in base pair sequence in a mammalian cell. The former will lead us to localisation of the latter, and this premise should form the basis of a new methodology for the deciphering of cancer DNA and other abnormalities [1].

REFERENCES


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