Condensed Matter Physics and the Biology of the Future

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In a modern textbook of histology or cell physiology the electron micrographs illustrate the complexity of living matter. As the resolution of electron microscopes improves, more and more details appear. A nerve fiber is usually regarded as a simple structure, yet at high resolution we can recognize a reticulum of fibers named microtubules, microfilaments, and neurofilaments (Nagele and Roisen, 1982). Moreover the fibers are regularly interconnected and in the connections are little rings. What is the function of this network? It looks like a microprocessor.

To take such photographs we have to poison, kill, and embalm the living tissue. We can also mince it up while it is still alive and pick up some of the bits. Biochemistry tells us that there are over 30,000 different proteins in the human body, not to mention all the other molecules. Biophysics uncovers thousands of intricate processes. In intact life these processes occur in an orderly manner. The acinar cell of the pancreas is a factory that manufactures digestive enzymes. It cuts, shapes, inspects, and packages them in a way that prevents the digestion of the cell itself; and as it does so it moves them the length of the cell and then delivers them through the cell wall into the pancreatic duct outside the cell, and so to the gut where the now free enzymes digest the food of the organism.

The task of studying the individual biochemical reactions in minced-up tissue has been so enormous and so interesting that molecular biologists have had little time to devote to how the reactions are organized and how the reactants are moved. Thermal diffusion (Brownian motion) is always present but there are no thermal gradients as in a heat engine. The cell is isothermal, yet efficient in the use of energy. Most biochemical reactions involve at least three molecules, the two or more reactants and an enzyme that is the catalyst. The chance collision of three entities in Brownian motion is an unlikely occurrence. Moreover the collision must be made with the correct orientation for the active parts on the several molecules to mesh. A further oriented collision may have to follow the first. After a three-body collision transfer RNA has its coded-for amino acid attached. It is now a transporter that finds its correct code-word on messenger RNA as this "computer tape" speeds through a ribosome. This is the machine that joins together hundreds of the twenty or so different amino acids, on instructions from messenger RNA, into a specific protein. It is inconceivable that the cell has to wait for the chaotic Brownian movement to bring about all these things by chance. An automated factory would be quite inefficient if it operated by means of a random movement of parts from floor to ceiling. It requires coordination and control, conveyer belts and robots.

As cellular structure is elucidated in more and more detail by electron microscopy, the cell appears less and less like a bag containing molecules dissolved in water, which implicitly was the classical view, and more and more like a solid state structure. A cell 16 μm in diameter has an internal surface area of perhaps 100,000 μm^2 (Clegg, 1983). Such a structure will impose a spacial order of sorts but gives no clue of how motion is ordered in relation to the structure. Back in 1950 Fritz London (1950) speculated that the behavior of superfluids might in some way help in understanding the dynamics of the immensely complicated macromolecular systems of biology. He suggested that a coherent fluid state of zero entropy combines the stability of quantum states with the possibility of motion without the dissipation of energy.

The suggestion of coherent quantum phenomena in biology usually evokes contemptuous dismissal because these phenomena require bizarre, extreme conditions such as extremely low temperature (for superconductivity and superfluidity) or extremely high ones in the laser. There is, however, a bizarre extreme electric field across all the membranes in and around a living cell and the purpose of this field is unknown except in a nerve fiber, where a transient interruption of field is the nerve action potential. If the modest transmembrane potential of the order of 100 mV is divided by the thickness of the membrane (10 nm) the field works out to be enormous ($\approx 10^7$ Vm^{-1}); enormous in comparison even with the lethal field imposed in the electric chair! Herbert Frohlich seems to have been the first to publish this simple but vital calculation (1968) and he went on (1980) to develop a theory of coherent excitations in biological systems based on this elementary observation.

Briefly the theory is this:- All membrane molecules will have the thermal vibrations appropriate to the organism's temperature; but, because the membrane molecules are in an intense

electric field, they will be electrically polarized and will therefore interact giving rise to modes of vibration. These phonon modes will exchange nonlinearly with the random phonons of the surrounding cell water. If energy, above a threshold level, is supplied to these modes, Frohlich's theory predicts that the lowest mode will condense into the coherence of a giant vibration with a frequency in the millimeter wave band. One of the important consequences of this theory is that it predicts the existence of ultra-long-range interactions between macromolecular systems, of much longer range than that of chemical forces. Moreover the forces will be specific in that a cell membrane could recognize a macromolecule by its inherent molecular vibrations and either attract or repel it, depending on the relative phase of the coupled vibrations. The interacting systems may well have other systems in between them. And so we have the beginnings of an explanation of the orderly motion of cellular structures and of macromolecules. There is evidence of such specific action-at-a-distance between living mammalian red blood cells, and the action is mediated by extended macromolecules of molecular weight greater than 40,000. This interaction is experimentally consistent with the requirements of the Frohlich theory (Rowlands et al., 1982; Fritz, 1984).

The energy that an organism gets from food, sunlight, etc. is used in complex metabolic reactions to produce adenosine triphosphate (ATP), which is the "fuel" for many if not all cellular processes. Until ten years ago a most baffling problem in biology was how the 0.5-eV energy from the decomposition of ATP is conserved. It should quickly be degraded into heat by bond vibrations; but actually most of the energy appears as an intact quantum quite a long way, on a microscopic scale, from where it was produced. The work of Davydov (1979) and of Scott (1981, 1985) now makes it look as though the α-helix, so characteristic of proteins, is uniquely designed to carry the quantum of energy of ATP over considerable biological distances with little loss, in the form of solitons (solitary waves). These are well known in theoretical and experimental physics and there is experimental evidence of their existence in crystalline acetanilide which has structural features in common with the much more complicated α-helix of protein molecules. Moreover there is now a theory (del Giudice et al., 1982) that combines those of Frohlich and Davydov into the beginnings of a comprehensive theory of cell dynamics in which the Frohlich vibrations are fed with energy by solitons in molecular chains.

So there is plenty of scope in the years to come for interpreting new experiments and for reinterpreting the old in terms of mechanisms already familiar to condensed-matter physics. But the problem of greatest difficulty (and interest) is the growth and development of organisms. The fertilized ovum of man is about a tenth of a millimeter in diameter and yet it contains all the information for building an adult. If you argue that in 40 weeks gestation much information may come from the mother, then consider a fish, a highly complex animal but one completely lacking in motherly care. Inside the fertilized ovum are all the instructions for building man, given energy, simple chemicals, a few amino acids not synthesized in the body, and vitamins. A human being is much more complex than an airliner. Yet an airliner does not build itself from energy and raw materials; nor can we conceive of packaging the "building instruction book" within a one-tenth-millimeter sphere.

How is it done? There are some clues but it is difficult to see where to make a start experimentally. Fanchon Frohlich (1977) thinks that there is much more to DNA than instructions for building macromolecules. As we understand the genetic code it is like the Morse code in which a group of up to four binary digits corresponds to a letter of the alphabet. In the DNA genetic code a group of three nucleic acids corresponds to the position of a particular amino acid in the primary structure of a protein. In terms of linguistics we are reading DNA in a very primitive fashion. In a language letters form words and the order becomes important. Sentences bring another level of order. Sentence follows sentence and contradictions have to be avoided if there is to be an unequivocal build-up of ideas. When you think of a sonnet, fourteen ten-syllable lines, and all the subtleties that Shakespeare can convey in one, maybe we are reading the genetic code at the level of first-year junior school. In linguistics the distinction is between letter-by-letter coding and the collective complexity of language; so we may be dealing with a collective cooperative phenomenon as in H. Frohlich's theory of coherent excitations in biological systems.

In any living creature there is more DNA than is needed for building proteins. The DNA content per cell for various organisms varies over a wide range, from 0.005 to 200 picograms. *Homo sapiens* weighs in at about 7 pg. The record seems to be held by a marine organism consisting of just a single cell. Less than 2% of its DNA is needed for protein synthesis; the rest is surplus and has been called "junk" DNA. Life is very efficient and I cannot accept that even a single species wastes 98% of its DNA. This marine creature, a dinoflagellate, being a single cell, has no brain. But it has behavior, so perhaps the "junk" DNA is its brain which instructs it how to behave, to react to stimuli, and to reproduce. The code may be different or interpreted in a different way or there may be an entirely different code lodged in the intramolecular vibrations of DNA or elsewhere. Popp, Nagl, and coworkers (1984) suggest that excimer-laser-like excitations in DNA give rise to the so-called ultra-weak photon emission from living cells. They base this suggestion partly on experimental evidence for coherence in this radiation. If this idea is correct, DNA vibrations could constitute an enormous reservoir for information. Most other workers in this field, however, believe that the ultra-weak photon emission arises from the decomposition of lipid peroxides; that is, it has its origin in well-known chemical reactions (Quickenden et al., 1985).

There is certainly plenty of surplus DNA in most organisms, in which the code may be different or interpreted in a different way. In higher organisms there are other possibilities. The support for Herbert Frohlich's theory shows that cells are communicating with organelles, and cells with cells, by mechanisms additional to simple electrical and chemical methods. These excitations have existed since life began, and since life seems to use every available mechanism it may well have developed the use of Frohlich excitations

for very subtle communication. At frequencies of 10^{11} hertz quite a narrow wave-band could transmit a vast quantity of information. For instance a tenfold band could carry 150,000 television programs. There may be a nervous system of higher order than the one we know, a second nervous system (Rowlands, 1983), and the action potential may be just a crude fast transmitter of urgent messages to make us move and to control whole organs. Neurotrophism, which has been defined as "interactions between nerve and other cells which initiate or control molecular modifications in the other cells" and which has not been much studied in comparison with what might be called "action-potential" neurology, may turn out to be much the more interesting.

The vibrations might be transmitted along nerve fiber membranes but they would be interrupted by action potentials. It is more likely that the microtubules, microfilaments, and neurofilaments mentioned in the first paragraph of this essay are used. Nonlinear integrated optics is beginning to replace electronics in communication and an analogous process for Frohlich excitations and/or solitons could transmit masses of information, without loss, in these structures. The cross connections and the associated ring proteins may be switches and parts of a "microprocessor". Already the Naval Research Laboratory in Washington is considering computer elements made of macromolecules and molecular switches in which information is transmitted by solitons. Some patents have been taken out!

In the central nervous system itself there are myriads of neurons (nerve cells) but lots more of neuroglia; they outnumber neurons by about ten to one. They have a complex architecture but we do not really know what they do. Hypotheses range from merely a mechanical support structure to the seat of memory! The membranes of the glial cells invest those of the neurons extensively and the membranes come closer together (10 nm) than any other cells that are not actually in contact. This gap is small enough for the tunnelling of quantum particles between the two moieties of specialized cells in the central nervous system. Glial cells could be processing information from "junk" DNA.

Evidence is very slender for such thoughts, but in science we should keep open minds, though not of course so open that our brains fall out! Wilfred Trotter wrote:- "The mind likes a strange idea as little as the body likes a strange protein and resists it with similar energy. It would not be too fanciful to say that a new idea is the mostquickly-acting antigen known to Science". We must beware of orthodoxy; it is a way of going wrong with confidence.

This essay, written to honor Frohlich's 80th birthday, is a brief account of ideas inspired by reading, in 1980, his theory of coherent excitations in biological systems. Another purpose of the essay is to persuade young scientists, not yet "weighed down with the burden of inert ideas" (Whitehead), that a rigorous training in condensed matter physics would be a major asset for a successful career as a 21st century life scientist.

ACKNOWLEDGMENT

This paper is based on a lecture given at the University of Toronto on 25th February 1984 during the tenure of a Medical Research Council of Canada Visiting Professorship.

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