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Quantum Mechanical Coherence in Human Red Blood Cells

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Fritz London predicted that the behavior of the quantum fluids "...might prove useful for an understanding of the macromolecular systems of biology which behave... much more simply than would be expected in view of the apparent great complexity of their structure." The Fröhlich theory is of an energy-driven laserlike process in living cells which should drive cellular phonons into coherence. Fröhlich's theory predicts specific ultra-long-range forces which can explain the presently mysterious, ordered tensor interactions within and without the living cell. Several different types of experiments demonstrate a specific ultra-long-range interaction between mammalian red blood cells which accords with the postulates of the Fröhlich theory. One phenomenon seems to be compatible with processes analogous to self-focusing and trapping in nonlinear optics. As work progresses more and more biological mechanisms appear to be similar to those known in condensed matter physics.

KEY WORDS: Erythrocytes, quantum coherence in; condensed state physics and biology; quantum biology; nonlinear biology.

1. INTRODUCTION

In 1950 Fritz London[1] predicted that the behavior of the quantum fluids "...might prove useful for an understanding of the macromolecular systems of biology which behave in many respects much more simply than would be expected in view of the apparent great complexity of their structure... certain actions between macromolecules in biochemistry could not be understood unless they could be conceived as conditioned by some quantum mechanism involving the system as a whole. In some biological

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processes the concept of a fluid state of entropy zero could play a decisive role, for it combines the characteristic stability of quantum states with the possibility of motion without necessarily implying transitions between quantum states."

In 1968 Herbert Fröhlich[2,3] suggested that an energy-requiring laserlike process in living cell membranes, organelles, and macromolecules should drive cellular phonons, via a Bose–Einstein condensation, into coherence. The theory predicts *specific* forces, of range much longer than chemical forces, that could explain the presently mysterious, ordered, inter- and intracellular tensor interactions which occur in living cells. There is now a substantial number of experiments that are compatible with Fröhlich's theory.[4] One such series of experiments on the red cells of human blood is reviewed in this paper.

2. OUTLINE OF FRÖHLICH'S THEORY

The body consists of cells and connective tissue. Across every membrane around or within a cell there is a modest electrical potential difference of 10–100 mV. But the potential difference acts across membranes of thickness only 10 nm, so the field ($\sim 10^7$ V m^{-1}) is enormous, sufficient to polarize membrane molecules nonlinearly into metastable or electret states.[3] Even if the metastable states have a short life their occupancy may remain high by the exchange of thermal phonons with the surrounding water, which is a constant temperature heat bath in the thermodynamic sense. If energy from cell metabolism is supplied to the modes of the collective polar excitations a process may arise whereby there is an exchange of the *difference* in energy between two quanta with the heat bath. If this process dominates single phonon exchange, the supply of energy will be channeled into the mode of highest wave number which will become a giant vibration by a mechanism analogous to a Bose–Einstein condensation. According to Fröhlich[3] the vibrations will have a frequency of the order of 10^{11} Hz, in which range lie many of the natural frequencies of biological macromolecules. The most important conclusion of the Fröhlich theory, with regard to the experiments to be described, is the existence of ultra-long-range forces between cells and within cells; forces of much longer range than the London–van der Waals' forces, perhaps ranging over distances of several micrometers.[3]

3. EXPERIMENTS ON THE RED CELLS OF HUMAN BLOOD

Blood is a suspension of cells in a complex liquid which is called "plasma." Plasma is a watery solution of many species of molecules and

macromolecules. The predominant macromolecule is albumin (MW 60,000 daltons) with a concentration of about $60\,g\,l^{-1}$. At concentrations an order of magnitude less, there is fibrinogen (which clots to fibrin in shed blood) and the many immunoglobulins which fight (and sometimes cause!) disease.

The predominant cell of blood is the red cell or erythrocyte which carries oxygen. The platelets are 20 times less numerous and the white cells are 50 times less numerous again. When blood ceases to flow and there are no shearing forces, the red cells aggregate. Red cells are flexible biconcave discs of diameter 8 μm and, when they aggregate naturally, they form themselves into regular columns, face to face.[5,6] These columns of cells are called rouleaux and the process is peculiar to those mammals which have flattened red cells. Rouleau formation can be observed, under a microscope, in blood which is prevented from clotting by an added chemical. Most of the red cells must be removed to give a clear field of view. In these circumstances the cells execute a very slow Brownian movement on which there is superimposed a tendency to move toward each other.[7]

To measure this interaction we observed the movement in a hemacytometer, a precision glass chamber normally used in counting the cell content of blood. The motion was recorded with a time-lapse ciné camera and the rate of aggregation was calculated. This measured rate was compared with the rate expected by Brownian motion alone, in accordance with a well-authenticated analysis of the coagulation of colloids by Smoluchowski.[8] Artifical microspheres aggregate at the rate expected for Brownian motion but red cells aggregated three times faster than expected.[9,10] According to Smoluchowski[8–10] this implies that the red cells are attracting each other at a membrane-to-membrane distance of 4 μm, i.e., at a range well beyond chemical interactions.

A Fröhlich-type interaction requires (a) an organized array of molecules as in a cell membrane, (b) an electrical potential difference across the membrane, and (c) a supply of energy.

When we (a) disorganized the membrane with glutaraldehyde the interaction disappeared[7,9,10]; (b) lowered the membrane potential to zero the interaction disappeared reversibly, i.e., when the membrane potential was restored in the *same* cells, the interaction returned[7,9,10]; (c) depleted the cells of their energy stores the interaction disappeared and was restored in the *same* cells by feeding them with adenosine.[7,9,10]

These observations have been confirmed by an independent method, quasielastic laser light scattering,[11] which measures the diffusion coefficient of the red cells directly.[12,13]

The above-described experiments were done with the red cells suspen-

ded in their own natural plasma, which is a very complex fluid. Red cells will continue to live for a time in salt solutions of an appropriate composition and osmotic pressure. But there is no Fröhlich interaction (nor rouleau formation) unless there are also *extended* macromolecules of sufficient concentration in the salt solutions.[14] The molecular weight of such extended macromolecules needs to be greater than 40,000 daltons (unpublished observation). Albumin, which is the major macromolecule of blood and which has a molecular weight of 60,000 daltons, does *not*, however, transmit.[14] Albumin is a *globular* molecule but it can be unraveled into an extended form by gentle heat; after which it becomes a transmitter of the Fröhlich interaction.[15] Fibrinogen, the macromolecule which polymerizes into the structured fibrin gel of a blood clot, is a good transmitter when partially purified[14] and in this state it is used for treating disorders of fibrinogen production in patients. But when it is highly purified[16] it does not transmit at all unless most of the clotting factors of the "extrinsic pathway" of blood coagulation are added.[17] Fibrinogen consists of globules attached to each other by extended chains. There is evidence[18] that pure fibrinogen is a flexed multinodular molecule and we interpret our results[17] as an unraveling of the flexion when the clotting factors are added.

There is some evidence of specificity of the Fröhlich interaction which comes from experiments on mixtures of red cells from different mammalian species. These will aggregate into rouleaux but the ordering of the cells in the rouleaux is not random. The cells from the same species show a preference for each other.[19] A flaw in the argument that this indicates specificity in the attraction is that colliding cells may come apart again, for instance when two cells from different species touch. We have eliminated this possibility and have also shown that the rate of aggregation in mixtures of cells is significantly lower than for pure suspensions of the cells of the species used.[20]

Quite different experiments on rouleaux offer further evidence for a Fröhlich interaction. A rouleau can be pulled apart by micromanipulation. As tension is applied along the axis of the rouleau the cells come apart but remain attached to each other by contractile fibrils ("contractils") which will pull the chain of cells back into a rouleau when the tension is released. As in the Brownian experiments described above, this phenomenon is profoundly affected by disorganizing the cell membrane, by abolishing the membrane potential, and by depleting the cells of their source of energy.[21] The "contractils" cannot be photographed under light microscopy but with the scanning electron microscope they show a regular discontinuity between the fibril and the cell membrane.[21] It is possible that the contractils owe their existence to a phenomenon analogous to self-focusing and

self-trapping in nonlinear optics[4] and that the critical self-focusing for trapping is only established over a distance equal to length of the discontinuity. A triple contractil can be formed by manipulating a branched rouleau with a side arm.[22] In this way three contractils meet at a point. The inevitable positive and negative curvatures of the surface of the three contractils at their junction eliminate any possibility that the forces holding the contractil together are of the nature of surface tension.

4. DISCUSSION

The triumphs of molecular biology in the second half of the twentieth century have uncovered ever more unanswered questions. An organism wastes very little energy and the innumerable chemical reactions occur in an ordered fashion. It is now inconceivable that the reacting molecules simply wander around inside a cell by Brownian motion until, by chance, they come together and react. Most cellular reactions need an enzyme (a protein macromolecule which acts as a catalyst) in addition to the reactants. In other words three-particle collisions are widespread, yet their chance occurrence is vanishingly small. The tangled "rope" of DNA has to be unraveled in an orderly fashion for its "message" to be decoded or reproduced (which requires enzymes) and it is unraveled at extraordinary speed. The "information" needed to build a human being is packed into the fertilized ovum, a cell no bigger than 0.1 mm in diameter. A Boeing 747 is less complex than a human being but can you imagine the "instruction book" for building one being packed into a tenth millimetre sphere? Moreover the ovum is self-building. The mother supplies the raw materials and energy, and the body (aircraft) builds itself! If you argue that the mother contributes information during the 40 weeks of gestation, think of a salmon. That is pretty complex too and yet it builds itself from an eggcell in the complete absence of mother love.

The problems facing biology at the end of the twentieth century are as complex as those facing physics a hundred years ago—the constancy of the velocity of light, the structure of the atom, the line spectra, and the origin of the universe. The answers will come from quantum mechanics and nonlinear phenomena, as predicted 30 years ago by London,[1] because they are the only conceivable explanations. Biologists must embrace these concepts or condemn themselves to the nihilism of "vitalism," discredited since the experiments of Pasteur in the last century.

Clegg[4] has shown that, as cellular structure is elucidated in more and more detail by electron microscopy, the cell appears to be more and more a solid state structure, with an internal surface area to a 16-μm cell of 100,000 μm^2 or more. A lattice of macromolecular structures extends from

the cell surface throughout the cytoplasm and to within the nucleus. This extensive network could be carrying quantum mechanical signals in the manner postulated by Fröhlich.[3,4] The energy efficiency of the cell is beginning to be explained by the transmission of quanta in the form of solitons, without loss, over vast biological distances.[23,24]

There are other possibilities. By using the analogy of the complexity and subtlety of linguistics, Fanchon Fröhlich[25] has suggested that, presently, we may merely be reading the code of DNA at a level similar to first year Junior School English. Rowlands[4] has argued that there is a "second nervous system," much more complicated than what we know, to control all the multitude of intracellular mechanisms by zero entropy signaling. Perhaps the most fascinating possibility arises from the existence of "junk" DNA. All organisms have more than enough DNA to code for all their proteins and the surplus DNA has been denoted "selfish," "parasitic," or "junk." This surplus may amount to 98% in some protozoa!! These protozoa consist of one cell only and so they have no "nervous system." Maybe the "junk" DNA is the brain, coded with the organism's behavior and programmed with its responses to outside stimuli. Right or wrong, at all events, condensed matter physics seems to offer the key to the understanding of biological function.[26]

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