# Long-Range Coherence and Energy Storage in Biological Systems

## H. FRÖHLICH

Department of Theoretical Physics, University of Liverpool, Liverpool, England

#### Abstracts

Biological systems are expected to have a branch of longitudinal electric modes in a frequency region between  $10^{11}$  and  $10^{12}$  sec<sup>-1</sup>. They are based on the dipolar properties of cell membranes; of certain bonds recurring in giant molecules (such as H bonds) and possibly on pockets of non-localized electrons. In Section 2 it is shown quite generally that if energy is supplied above a certain mean rate to such a branch, then a steady state will be reached in which a single mode of this branch is very strongly excited. The supplied energy is thus not completely thermalized but stored in a highly ordered fashion. This order expresses itself in long-range phase correlations; the phenomenon has considerable similarity with the low-temperature condensation of a Bose gas. General consequences and proposals of experiments are discussed in Section 3.

Dans les systèmes biologiques on peut présumer une branche de modes électriques longitudinaux dans une région de fréquences entre  $10^{11}$  et  $10^{12}$  sec<sup>-1</sup>. Ceux-ci peuvent être associés à des propriétés dipolaires de membranes cellulaires, de certaines liaisons récurrentes dans les molécules géantes (telles que des liaisons d'hydrogène) et peut-être de poches d'électrons non localisés. Dans le Section 2 on montre d'une façon toute générale, que si l'on fournit de l'énergie à une telle branche à une certaine vitesse, un état stationnaire sera atteint, dans lequel un seul mode de cette branche est très fortement excité. L'énergie ainsi fournie n'est donc pas complètement thermalisée, mais reste emmagasinée d'une manière bien ordonnée. Cet ordre apparaît dans les corrélations de phase à longue portée. Le phénomène a une similarité considérable à la condensation d'un gaz de Bose aux basses températures. Dans le Section 3 on discute des conséquences générales et on propose des expériences.

Man kann erwarten dass biologische Systeme einen Zweig von longitudinalen elektrischen Schwingungen in einem Frequenzbereich zwischen  $10^{11}$  und  $10^{12}$  sec<sup>-1</sup> haben. Diese sind auf Dipolareigenschaften von Zellmembranen, von gewissen Bindungen in Riesenmolekülen (z. B. Wasserstoffbindungen) und vielleicht von Taschen von nichtlokalisierten Elektronen gegründet. In Sektion 2 wird im allgemeinen gezeigt, dass wenn Energie mit mehr als einer gewissen Durchschnittsrate einem solchen Zweig zugeführt wird, wird ein stationärer Zustand erreicht, in welchem eine einzige Schwingung dieses Zweigs sehr stark angeregt ist. Die zugeführte Energie ist also nicht vollständig thermalisiert, sondern wird in einer höchst geordnetenr Weise gespeichert. Diese Ordnung zeigt sich in Phasenkorrelationen mit langer Reichweite. Das Phänomen hat beträchtlicle Ähnlichkeiten mit der Kondensation eines Bosegases bei tiefen Temperaturen. Allgemeine Folgerungen und Vorschläge von Experimenten werden in Sektion 3 diskutiert.

#### 1. General

The present paper arises from development and clarification of ideas presented by myself [1] in the opening talk of the recent Versailles conference on Theoretical Physics and Biology. In the past decades biology has been highly successful in the correlation of biological properties with the structure and properties of relevant molecules. This stage of development might be compared with the correlation of the physical and chemical properties of materials with the structure and properties of the atoms and molecules of which the material is composed. These properties modified by interaction with their neighbours account for many features of the substance. Some of the most interesting properties in the physics of materials, however, can be understood in terms of the collective (cooperative) behaviour of a great number of these constituents only, usually associated with some kind of longrange order. Most frequently this order is described in terms of a definite spatial pattern. A much more subtle type of long-range order is found in superfluid helium, and in superconductors. This order is connected with the concept of long-range phase correlation (coherence). Superfluids (and superconductors) undergo at very low temperatures a phase transition. The simplest model available for this transition is the Einstein condensation of a Bose gas in which-with decreasing temperature-more and more particles "condense" into a single quantum state.

At first thought one might consider the order exhibited in these low-temperature phenomena to be quite irrelevant for Biology. Stimulated by a different attitude, however, I have been able to show [2] that under appropriate conditions a phenomenon quite similar to Bose condensation may occur in substances which possess longitudinal electric modes. If energy is fed into these modes and thence transferred to other degrees of freedom of the substance then a stationary state will be reached in which the energy content of the electric modes is larger than in thermal equilibrium. This excess energy is found to be channelled into a single mode—exactly as in Bose condensation—provided the energy supply exceeds a critical value. Under these circumstances a random supply of energy is thus not completely thermalized but partly used in maintaining a coherent electric wave in the substance.

The original reason for considering longitudinal electric modes lay in the extraordinary dielectric properties of biological systems. Furthermore living systems though relatively stable are in some respects far from thermal equilibrium; also they may be expected to exhibit some order of a non-trivial nature. From a very general point of view of physics, three observations may thus be made about living systems.

[1]. They are relatively stable yet in some respects far from thermal equilibrium.

[2]. They probably exhibit some kind of order typical for them yet not of an obvious spatial nature.

[3]. Cells and many of the relevant giant molecules have quite extraordinary dielectric properties.

In connection with (3) it should be remembered that cells have a membrane of about  $10^{-6}$  cm thickness which maintains a very strong dipolar layer. In the (from the point of view of physics) complicated shape of a cell surface, local vibrations of a part of the cell membrane are feasible such that the positive and the negative part of a particular section of the membrane vibrate against each other-leading to an oscillating electric dipole. Its frequency is of the order  $10^{11}$ - $10^{12}$  sec<sup>-1</sup> if a sound velocity in the layer of order  $10^{5}$ - $10^{6}$  cm/sec perpendicular to the surface is assumed.

The giant molecules occurring in biological systems also have extraordinary dipolar properties largely in view of the frequently occurring hydrogen bonds. Careri [3] has pointed out that in the  $\alpha$  helix they may be expected to exhibit collective dipolar oscillations in the same frequency region.

Other sources for dipolar oscillations in the same frequency region might exist. They would arise, for instance, from the presence of "non-localized" electrons in some regions of a cell.

Dielectric systems of the type described here are capable of longitudinal electric oscillations extending over the whole material. The existence of such oscillations follows directly from Maxwell's equations though little use has been made of this possibility in physics. They can have a certain range of macroscopic wavelengths depending only weakly on frequency.

Certain processes in living systems involving the cell membrane, or the hydrogen bonds of molecules, or other dipolar constituents, may be expected to feed energy locally to the particular dipolar oscillations. The long-range Coulomb interaction then causes this energy to be shared with other dipoles. The situation thus is exactly as assumed in the above-mentioned model, so that the dipoles will tend to oscillate coherently provided the energy supply is sufficiently large compared with the energy loss. Non-linear effects are likely to reduce this loss with increasing excitation and effectively transfer the system into a metastable state in which the energy supplied locally to dipolar constituents is channelled into a single longitudinal mode which exhibits long-range phase correlations.

It should be remarked that the present model fits the general conditions for the stability of "dissipative structures" presented by Prigogine [4] at the Versailles conference.

Furthermore the channelling of randomly supplied energy into a single mode described above—should be considered as a special case of long-range quantummechanical phase correlations as pointed out in [1]. Such phase correlations are a common property of superfluids and superconductors as described by Yang [5]. They also may be expected to arise in certain forms of chemical bond as has been emphasized by Löwdin [6].

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#### 2. Coherent Excitations

Consider a suspension of a large number Z of units in a substance which will be treated as a heat bath. Each unit is assumed capable of electric dipole oscillations with a certain frequency  $\omega_0$ . Long-range Coulomb interaction between these individual oscillators then gives rise to a branch of Z longitudinal electric modes in a frequency range say

(1) 
$$\omega_1 \leq \omega \leq \omega_2$$

which may be shifted considerably from  $\omega_0$  but is relatively narrow. The modes of this branch describe longitudinal electric waves in the material as a whole. Oscillations of single units can then be described by appropriate superposition of these waves. Assume that energy is supplied locally to each unit at a mean rate s. This is equivalent with a supply of energy at the same rate s to each mode. Assume furthermore that each unit can exchange energy locally with the surrounding heat bath; this can again be expressed in terms of an exchange of energy in quanta  $\hbar\omega$  with the modes of the branch at a rate which is nearly independent of  $\omega$ . The net rate of loss  $L_{1i}$  of the mode with frequency  $\omega_i$  (containing  $n_i$  quanta) can then be written in the form

(2) 
$$L_{1l} = \phi(T)(n_l e^{\hbar \omega_l / KT} - (1 + n_l))$$

where  $\phi(T)$  may depend on temperature T. In a higher order individual units could exchange two, or more quanta with the heat bath but never a fraction of a quantum. The long-range Coulomb interaction between units gives rise, however, to the whole range (1) of frequencies. In second order, therefore, absorption of a quantum  $\hbar\omega_i$  in conjunction with emission of a quantum  $\hbar\omega_i$ , or vice versa, permits an exchange of energy between the branch of electric modes, and the heat bath in a range

(3) 
$$0 < \hbar |\omega_l - \omega_j| \leq \hbar (\omega_2 - \omega_1)$$

The net range of loss  $L_{2l}$  of the mode  $\omega_l$  due to such processes can be written in the form

(4) 
$$L_{2l} = \chi(T) \sum_{j} (n_l (1 + n_j) e^{\hbar(\omega_e - \omega_j)/KT} - n_j (1 + n_l))$$

The general forms of (2) and (4) are dictated by the requirement that in the absence of energy supply, s = 0, thermal equilibrium  $(L_{1l} = 0, L_{2l} = 0)$  requires a Planck distribution  $n_{lT}$  for  $n_l$ ,

(5) 
$$n_{lT} = \frac{1}{e^{\hbar\omega_l/KT} - 1}$$

Note that  $\chi$  may depend on temperature. A slightly more general form of  $L_{21}$  would permit explicit dependence of  $\chi$  on  $\omega_1$  and  $\omega_j$ .

The condition for stationarity requires for each l,

(6) 
$$s = L_{1l} + L_{2l}$$

With the notations

(7) 
$$N = \sum n_j, \qquad S(T) = s \sum e^{-\hbar \omega_j/KT}$$

one finds

(8) 
$$S(T) = \phi \sum (n_j - (1 + n_j)e^{-\hbar\omega_j/KT})$$

independent of  $\chi$ , and

(9) 
$$n_l = \left(1 + \frac{s}{\phi + \chi N}\right) \frac{1}{Ae^{\hbar\omega_l/KT} - 1}$$

where

(10) 
$$A = \frac{\phi + \chi \sum (1 + n_j)e^{-\hbar\omega_j/KT}}{\phi + N\chi} > 0$$

or making use of (8),

(11) 
$$A = 1 - \frac{\chi}{\phi + N\chi} \frac{S(T)}{\phi} \le 1$$

Clearly s = 0 leads to A = 1 and (9) becomes the thermal equilibrium distribution (5). However,  $\chi = 0$  also leads to A = 1 even if  $s \neq 0$  though in this case  $n_i$  no longer represents a Planck distribution.

Inequality (11) together with the condition  $n_l \ge 0$  leads to

(12) 
$$A = e^{-\mu/KT} \text{ where } \hbar\omega_1 > \mu \ge 0$$

Clearly a Bose type of condensation into the lowest mode  $\omega_1$  will take place when  $\mu$  approaches  $\hbar \omega_1$  very closely. We shall show in the high temperature limit

(13) 
$$kT \gg \hbar\omega_1$$

that this will occur when s exceeds a critical value  $s_0$ . In this approximation one has from (9) and (12),

(14) 
$$n_{l} = \left(1 + \frac{s}{\phi + \chi N}\right) \frac{kT}{\hbar w_{l} - \mu} + \cdots$$

Let  $D(\omega) d\omega$  be the number of modes in  $d\omega$ . Then if no condensation has taken place  $D(\omega_l)n_l$  may be considered a continuous function. Let  $N_n$  be the total number of quanta in this case. From the inequality of (12) one then finds an upper limit for  $N_n$ , for then

(15) 
$$N_n = \left(1 + \frac{s}{\phi + \chi N_n}\right) kT \int_{\omega_1}^{\omega_2} \frac{D \, d\omega}{\hbar \omega - \mu} < \left(1 + \frac{s}{\phi + \chi N_n}\right) N_0$$

or

(16) 
$$\frac{N_n(\phi + \chi N_n)}{\phi + \chi N_n + s} < N_0$$

where

(17) 
$$N_0 = \frac{kT}{\hbar} \int_{\omega_1}^{\omega_2} \frac{D \, d\omega}{\omega - \omega_1}$$

Now the total number N of quanta is quite generally determined by s and  $\phi$ , and may well exceed the maximum of "non-condensed" quanta  $N_n$  imposed by (16). For an introduction of the excess number  $m_l$  of quanta in  $\omega_l$  over the number in thermal equilibrium,

(18) 
$$m_l = n_l - n_{l,T}; \qquad \sum m_l = N - N_T$$

where  $N_T$  is the total number of quanta in thermal equilibrium, one finds from (8), (5), and (13),

(19) 
$$S(T) = \phi \sum m_i (1 - e^{-\hbar\omega/KT}) \simeq \phi \sum m_i \frac{\hbar\omega_i}{kT} = \phi \frac{\hbar\bar{\omega}}{kT} (N - N_T)$$

Here  $\bar{\omega}$  must have the range

(20) 
$$\omega_1 \leqq \tilde{\omega} \leqq \omega_2$$

Also in approximation (13) one has  $S(T) \simeq Zs$ , so that

(21) 
$$N = N_T + \frac{sZ}{\phi} \frac{kT}{\hbar\bar{\omega}}$$

Now  $\bar{\omega}$  is limited by (20) and may therefore vary only slightly with s. Hence according to (21) N is linearly increasing with s. A value  $s_0$  of s therefore exists above which  $N = N_n$  can no longer hold because (16) can no longer be satisfied. In this case

(22) 
$$N = n_1 + N_n = \frac{kT}{\hbar\omega_1 - \mu} + N_n$$

where  $\mu$  approaches  $\hbar\omega_1$  very closely. Its actual value follows from (21) and (22). Condensation into the mode  $\omega_1$  thus takes place.

It is now of great interest to note that apart from the relatively small variations permitted for  $\bar{\omega}$ , the excess  $N - N_T$  is entirely determined by  $Zs/\phi$ . The smaller  $\phi$ , therefore, the smaller is the critical value  $s_0$  required for condensation. Compared with other processes like energy transfer from acoustic (low frequency) vibrations the processes  $L_1$  (cf.(2)) may indeed be expected to be rather slow (i.e.  $\phi$  relatively small) because they must occur in quanta  $\hbar\omega$ . The processes  $L_2$  (4), on the other hand, which can transfer smaller amounts contribute only in a higher order,  $(\hbar\omega/kT)^2$ , which is considered negligible in view of (13).

Assume now that condensation into the mode  $\omega_1$  has been established, so that a coherent longitudinal electric vibration exists in the substance. Non-linear effects associated with this excitation are then expected to lead to its further stabilization as pointed out for a simple model in Appendix I of [1], though the argument used there is very general. Roughly speaking the free energy associated with the vibration can be decreased if the system is permitted to undergo deformations. If these deformations are measured in terms of parameters, say  $\eta$ , then for small  $\eta$  the elastic energy associated with a deformation will be proportional to  $\eta^2$  because in the absence of the vibrations the system was elastically in equilibrium. The energy associated with the electric polarization will, however, be linear in  $\eta$ —for small  $\eta$ . Hence a new equilibrium is established in which  $\eta$  is proportional to  $P^2$ , the mean square of the polarization. The total free energy then consists of a positive term proportional to  $P^2$ , and a negative one proportional to  $P^4$ , thus pointing to an instability at sufficiently large  $P^2$ . This may indicate a rupture or else stabilization under the influence of higher order terms in  $\eta$  and  $P^2$ . In the latter case a metastable state will be reached, and  $\phi$  will then be very small. Further supply of energy s should then lead to instabilities at a later stage.

### 3. Discussion and Proposal of Experiments

Biological systems contain components capable of electric dipole oscillations. These interact through long-range Coulomb forces and thus establish a branch (or several branches) of longitudinal electric modes probably in a frequency range of  $10^{11}-10^{12}$  sec<sup>-1</sup>. The relevant components may be connected with certain regions in the cell membrane, with certain chemical bonds in particular with hydrogen bonds, or with regions containing non-localized electrons. If energy is supplied locally to one component (or removed from there) then in view of the long-range interaction this energy change is shared by all the components which establish the branch of electric modes. If the rate of energy supply is sufficiently large then, as shown in Section 2, the energy gets channelled into a single mode which then presents a strongly excited coherent longitudinal electric vibration. Its wavelength depends on details of the geometrical arrangement of the components. A certain fraction of the supplied energy, therefore, is not thermalized but stored in a single mode which then exhibits long-range phase correlations. With respect to the electric modes the system is thus maintained

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through a flux of energy in a state of high order far from thermal equilibrium. In this excited state the mean value  $P^2$  of the square of the electric polarization may be large and hence lead to deformations (and stresses) in the material. This in turn may lead to a relative stabilization of the excitation so that a relatively small supply of energy is required to maintain it. Continued energy supply of a higher magnitude must then ultimately lead to an instability.

If established the phenomenon proposed here should have a profound influence on biological properties like cell division which may involve relatively extensive regions. Thus it has been suggested in [1] that the deformations connected with the excitation should stimulate cell division. This stimulus would increase with increasing size of the cell. It would be partly due to the vibrations inside the cell under consideration, but partly it would arise from the electric fields based on the dipolar oscillations in other cells. This latter influence would disappear, however, when cells are densely packed for then deformations in the cell membrane no longer influence the dielectric response. Such an influence of packing has actually been observed; it is known as "contact inhibition".

Formation of certain bonds as required in the synthesis of giant molecules will feed energy into the branch if the particular bonds belong to the components which establish the electric modes. The coherent excitation, on the other hand, presents a reservoir of energy in a highly ordered form available for various uses.

Observations by Szent-Györgyi [7] may be of considerable relevance in this connection. He concludes that "cellular activities, like cell division or protein synthesis are dominated, to a great extent, by the electronic charges of the system", and he indicates that some of these electrons may be in non-localized states. Such electrons will take part in the proposed electric vibrations and reinforce them provided their density is not too high. Hence if cell division or protein synthesis are stimulated by our vibrations then additional (electronic) sources for it will increase these effects. A change must be expected, however, when the electron density becomes so high (larger than 1015 cm-3) that their proper frequency exceeds  $\omega_1$ . In this case the reaction on the original vibrations can no longer be neglected. This then may lead to a qualitative change in such cell activities as depend on our vibrations. It is suggestive, of course, to propose that this change characterizes cancer which accordingly would be caused by an excessive density of non-localized electrons in some region of a cell (e.g. in certain giant molecules). Carcinogenic molecules must then have the ability of transferring electrons to the relevant regions of a cell. This hypothesis could possibly be checked if ionizing radiation exists which produces "non-localized" electrons.

Such specific questions must, of course, be studied in detail in connection with the particular structures and processes. Most important in the first place, however, would be experimental establishment of the existence of the coherent vibrations in living systems. The magnitude of the electric polarization should be fairly high, but direct measurement seems difficult in view of the expected high frequency. A very interesting suggestion has been made, however, by Palma [8]. He proposes investigation of the spectral distribution of scattered light of laser beams. One then deals essentially with Raman-like scattering and thus from the frequency shift obtains the frequency of the longitudinal vibrations. One would have to work with low intensities, of course, so as not to kill the organism.

Careri [9] proposes to investigate the infrared properties of biological systems. The oscillations considered here are of course longitudinal, and hence optically not active. Nevertheless they should be expected to produce a certain amount of radiation through surface effects. Also the deformations associated with the establishment of the proposed oscillations would influence the transverse (optical) resonance frequencies.

More indirect methods would work with the proposed biological effects of the electric vibrations. Thus the stimulus on a cell arising from the dipolar oscillations of other cells could be screened with the appropriate use of absorbers or otherwise altered with the use of filters or reflectors.

The proposals discussed in this paper are speculative. The derivation given in Section 2 in conjunction with the striking dielectric properties of biological systems seems to point definitely, however, to the possibility of the storage of supplied energy in a highly ordered form.

#### Note added in proof

I have now found that absorption of light  $(\hbar \omega \gg kT)$  may also lead to energy storage in a single state. This may be relevant to photosynthesis.

#### Bibliography

- H. Fröhlich, Quantum Mechanics and Biology, talk given at the Versailles Conference 1967 on Theoretical Physics and Biology, to be published.
- [2] H. Fröhlich, Phys. Letters 26A, 402 (1968).
- [3] G. Careri, discussion remarks to [1], to be published.
- [4] I. Prigogine, Structure, Dissipation and Life, talk given at the Versailles Conference 1967, to be published.
- [5] C. N. Yang, Rev. Mod. Phys. 34, 694 (1962).
- [6] Per-Olov Löwdin, personal communication.
- [7] A. Szent Györgyi, Charge, Charge Transfer and Cellular Activity, talk given at the Versailles Conference (1967), to be published.
- [8] U. Palma, personal communication.
- [9] G. Careri, personal communication.

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