Chapter 16

Fröhlich's Theory of Coherent Excitation – A Retrospective

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16.1 Introduction

Many biological systems have been extensively studied with regard to their structure, function and detailed biochemical and chemical content. However, very little work has been done on the effects of microwave electromagnetic radiation on biological systems. Such work has recently taken on new importance due to the development of novel methods of measurements, which generated widespread reports on suspected effects of microwaves on biological systems including membranes, proteins, nucleic acids and cells. At the same time, theoretical interpretations have been presented in terms of collective excitations in biological systems.

Most large non-biological, physical systems (such as crystals, atomic nuclei, large molecules, spin arrays) which are built up from smaller, more fundamental constituents, possess vibrational modes characterized by a coherent motion of many constituent parts of the large system. It is likely that biological systems such as cell membranes, large biological macromolecules, or intact cells, also possess vibrational modes which will couple weakly or strongly to electromagnetic radiation. To illustrate this, let us consider a cell membrane which, in the simplest model, consists of a bilayer of phospholipid molecules interspersed with protein. These macromolecular assemblies contain dipolar molecules arranged in such a way as to give rise to an ordered array of dipoles. Each dipole is embedded in a complex structure, and it is possible that the interaction between the dipole and the underlying superstructure manifests itself in a vibrational excitation. The charge groups of the dipoles are displaced relative to each other with some frequency f. The detailed nature of this excitation is very complex, involving deformations of the underlying structure. In addition, each dipole also interacts with all other dipoles via electromagnetic forces. Other types of interactions mediated by the structure are also possible. The net result of these mutual interactions is to spread the frequency f into a narrow band and to provide for energy sharing between the individual dipoles. If a particular dipole is perturbed, the perturbation propagates to other dipoles until the whole array of dipoles is excited to some collective quantum state, which we will call a 'dipole wave' or 'electromagnetic oscillation'. The excitation energy of this electromagnetic oscillation is expected to lie in a narrow band close to hf where h is Planck's constant.

Fröhlich¹⁻³ has estimated the frequency of the oscillation to be in the order of $10^{11}Hz$. His estimation is based on the relation $f = v/\lambda$, where v is the velocity of sound in organic material and λ is the wavelength. If we take $v \sim 10^5 cm/sec$, which is the approximate velocity of sound in water and many organic liquids, and $\lambda \sim 10^{-6}cm$, which is a typical dimension of a large biological molecule, then the frequency is equal to $10^{11}Hz$. In general, the expected frequencies are $10^{10} - 10^{11}Hz$ for membranes, $10^{12} - 10^{14}Hz$ for proteins or more general for certain bond-stretching groups, and 10^9Hz for DNA or RNA molecules. There is a lot of experimental evidence in support of the existence of these millimeter waves in biological systems. We will only mention a few cases.

Kiselev and Zalyubovskaya⁴ have examined the influence of millimeter band electromagnetic waves on isolated human and animal cells. Their experiments, as all of the others described in this section, were performed using low intensity microwaves so that thermal effects of irradiation could be excluded. Individual cells were arranged in a monolayer readily accessible to microwave exposure. This also facilitated the subsequent examination of the effects of microwave exposure. Their results showed a decrease in the viability of cells after irradiation at certain electromagnetic wavelengths (see Fig. 16.1). Within the range 5.9 to 7.5 mm, the wavelength 6.50 mm gave a conspicuously higher effect in all three cell lines. The dependence of the biological effect on the frequency of the radiation is thus of a resonant nature as predicted by Fröhlich.

The studies also indicated that millimeter wave irradiation of isolated cells resulted in damage to the cell membrane, the degeneration of protoplasm, an increase in the size of the cells and cell nuclei, and an increase in the total nucleic acid and albumin contents. All of these effects are specific to the resonant wavelength of 6.5 mm. Similarly, microwave irradiation of several viruses (such as adenoviruses, measles virus, and vesicular stomatitis virus) caused a reduction in the number of virus particles by a factor of 2 to 3. The lowered infectious activity of irradiated adenoviruses and the measles virus manifested itself in a delay of the cytopathogenic effect in a tissue culture.

Smolyanskaya and Vilenskaya⁵ studied the effect of millimeter waves on the colfactor of E. coli. Col-factor is an extra-chromosomal genetic element whose activity is normally repressed in E. coli. The suppression of the col-factor results in the



Figure 16.1: Influence of millimeter wave irradiation on survival of tissue cultures.

synthesis of a proteic substance called *colicin*, which causes the cells to die. The activity of colicin synthesis was determined by using the induction coefficient of colicin synthesis, $K_i = \frac{L_e/K_e}{L_c/K_c}$, where L_e and L_c are the number of cells forming colicin in the experiment and in the control respectively; K_e and K_c are the total number of colicinogenic cells in the experiment and in the control respectively.

As illustrated in Figure 16.2, the induction coefficient, K_i , of colicin synthesis has a strong correlation with certain electromagnetic wavelengths, representing a further example of resonance phenomena in biological systems. In Figure 16.3, the induction coefficient is plotted against the power flux density of the radiation. There is no noticeable variation in colicin synthesis compared to the control as the power fluxdensity increases from zero to 0.01 mW/cm² (not shown in Fig. 16.3). However, when density was raised to above 0.01 mW/cm², the induction coefficient increases abruptly from 1.0 to more than 3.0, and remains at the same value as the power density is further increased. The power flux density at which the induction coefficient of colicin synthesis rapidly increases, ie, 0.01 mw/cm², can be regarded as the energy density threshold for the biological effect.

Sevast'yanova and Vilenskaya⁶ also examined the effects of millimeter waves on the bone marrow of mice. They counted mouse bone marrow cells that remained undamaged by x-rays (700 rad) after prior irradiation with the millimeter waves at 10 mW/cm². The microwave field was turned on 60 minutes before the x-rays.



Figure 16.2: Induction coefficient K_i of colicin synthesis as a function of wavelength.



Figure 16.3: Induction coefficient of colicin systhesis as a function of power density.



Figure 16.4: Variation of the relative number of bone-marrow cells, N/N_o , as a function of the wavelength of irradiation. N, number of undamaged cells; N_o , number of cells without radiation. 1, control; 2, X-ray irradiated; 3. X-ray and microwave irradiated.

Despite the fact that microwaves are absorbed in the surface skin layer of the animals up to a depth of about 3×10^{-2} cm, they observed a decrease in the number of bone marrow cells that were damaged by the x-rays when the animals were pre-exposed to microwaves (see Fig. 16.4).

The protective effect of the pre-exposure of the animals to millimeter waves is strongly dependent on the wavelength. The normalized undamaged cell count rises from 0.5 to 0.85 at λ values of 6.7 - 6.82 mm, 7.09- 7.16 mm, and 7.26 - 7.7 mm, whereas no protective effect appeared at the same power density at other wavelengths. This dependence of protective effects on millimeter wavelength again suggests a resonant mechanism for the action of millimeter fields on biological systems. In Figure 16.5, changes in the number of bone marrow cells of irradiated animals is plotted as a function of microwave power density. The plot shows that pre-irradiation of the animals has no influence on undamaged cell count up to a power density of 9 mw/cm². Thus, there is a threshold power density below which the millimeter field has no effect. As the power density is increased beyond 9 mW/cm², the normalized undamaged cell increases rapidly to about 0.85 and stays almost constant thereafter.

Grundler et al^{7,8} have observed resonant behavior in the growth of yeast cells exposed



Figure 16.5: Variation of the relative number of bone-marrow cells N/N_o as function of power density of microwave irradiation. N, number of undamaged cells; N_o , number of cells without radiation. 1, control; 2, X-ray irradiated; 3, X-ray and microwave irradiated; 4, change in skin temperature as a function of microwave power density.

to millimeter electromagnetic radiation. They monitored the intensity of a light beam which passed through a sample of yeast cells placed in a glass cuvette; as the yeast cells multiplied, the transmittance decreased. The growth rate of the sample irradiated with microwaves was divided by the rate of a sample not irradiated. The ratio obtained showed resonance in the region 41.63 to 41.96 GHz.

16.2 Bose-Einstein Condensation in Biological Systems

In order to demonstrate the possibility of coherent behaviour in biological systems, Fröhlich⁹⁻¹³ wrote down rate equations and showed that if energy is supplied above a critical rate to the branch or branches of electromagnetic vibration modes, Bose-Einstein condensation into the lowest energy state occurs. The general forms of the rate equations were dictated by requiring a Bose-Einstein distribution for thermal equilibrium when there is no energy supplied. Using microscopic theory and perturbation calculations, Wu and Austin¹⁴⁻¹⁸ were able to obtain the rate equations of Fröhlich from the Hamiltonian of the biological system under study.

In this section, we consider a simple model suggested by Fröhlich. It is presumed that the biological system consists of three parts: (i) the main oscillating units of giant dipoles occurring approximately along the length of the macromolecule, (ii) the rest of the biosystem constituting a heat bath, and (iii) an external energy source which couples to the oscillating units. The interaction between the dipoles will produce a narrow band of energy, $\omega_i(\omega_o \leq \omega_i \leq \omega_{max})$, which corresponds to the normal modes of the electromagnetic vibrations. The heat bath is, of course, a very complex system. Interaction with the heat bath will lead to emission and absorption of quanta by these oscillating electromagnetic modes, and we consider processes involving one and two quanta only. The interaction involves several factors: dipoles of water and other molecules, mobile ions, certain electronic degrees of freedom, and, to some extent, elastic displacements.

Instead of rate equations, we will approach this theoretical problem with microscopic techniques¹⁹ which are used extensively in quantum field theory. To each mode, ω_i , we assign a creation operator, a_i^+ , and a destruction operator, a_i . The normal modes of oscillation will interact with the remainder of the biological system (the heat bath) which is represented by a set of independent excitation, Ω_k , associated with creation and destruction operators, b_k^+ and b_k respectively. Furthermore, the external energy supply, associated with creation operator, p_f^+ and destruction operator p_f , and excitation energy, θ_f , feeds into the electromagnetic oscillatory units and acts as impetus for the initiation of the biological effects. The Hamiltonian of the biosystem can then be written as:

$$H = \sum_{i} \omega_{i} a_{i}^{+} a_{i} + \sum_{k} \Omega_{k} b_{k}^{+} b_{k} + \sum_{f} \theta_{f} p_{f}^{+} p_{f}$$

+ $\frac{1}{2} \sum_{ijk} (\varphi b_{j} b_{k}^{+} a_{i} + \varphi^{*} b_{j}^{+} b_{k} a_{i}^{+}) + \frac{1}{2} \sum_{ijk} (\chi a_{j}^{+} a_{i} b_{k}^{+} + \chi^{*} a_{j} a_{i}^{+} b_{k})$
+ $\sum_{if} (\varsigma p_{f} a_{i}^{+} + \varsigma^{*} p_{f}^{+} a_{i})$ (16.1)

where φ , χ and ς are the coupling constants for the one quantum process, the two quantum process, and the energy source with the vibration modes respectively. Strictly speaking, we should consider higher order and possibly anharmonic terms; however, it can be shown^{15,16} that accounting for those terms have only minor effects and, within certain limits, they may be ignored altogether. The electromagnetic oscillations are Bosons. The excitations within the heat bath and the energy source can be either Bosons, or fermions, e.g. phonons or electrons. The operators a_i^+ , a_i , b_k^+ , b_k , p_f^+ and p_f satisfy the commutation relations:

$$a_{i} a_{j}^{+} - a_{j}^{+} a_{i} = \delta_{ij}$$

$$a_{i}^{+} a_{j}^{+} - a_{j}^{+} a_{i}^{+} = a_{i} a_{j} - a_{j} a_{i} = 0$$

$$b_{k} b_{e}^{+} \pm b_{e}^{+} b_{k} = \delta_{ke}$$

$$b_{k} b_{e} \pm b_{e} b_{k} = b_{k}^{+} b_{e}^{+} \pm b_{e}^{+} b_{k}^{+} = 0$$

$$p_{f} p_{g}^{+} \pm p_{g}^{+} p_{f} = \delta_{fg}$$
(16.2)

(+ sign for fermions and - sign for bosons).

The rate of change of the number of quanta in the i^{th} mode is given by

$$\dot{n}_i = \frac{1}{\hbar}[n_i, H] = \frac{1}{\hbar}(n_i H - H n_i)$$
 (16.3)

with $n_i = a_i^+ a_i$; the number of quanta in the i^{th} mode and \hbar is the Planck's constant divided by 2π . Using the commutation relations in Equation (16.2) and the finite Green functions¹⁸, the expectation value of the rate of change of the number of quanta to infinite order of interactions is

$$\langle \dot{n}_{i} \rangle = s_{i} - \Phi(T, \omega_{i}) \left[\langle n_{i} \rangle e^{\beta \omega_{i}} - (1 + \langle n_{i} \rangle) \right]$$

$$- \sum_{j} \Lambda(T, \omega_{i}, \omega_{j}) \left[\langle n_{i} \rangle (1 + \langle n_{j} \rangle) e^{\beta \omega_{i}} - \langle n_{j} \rangle (1 + \langle n_{i} \rangle) e^{\beta \omega_{j}} \right]$$

$$(16.4)$$

where the angular brackets refer to the thermal averaging in the grand ensemble appropriate to the entire system; $s_i = 4\pi |\varsigma|^2 \langle p_i^+ p_i \rangle$ is the energy density supplied to the i^{th} mode from the external source, and $\Phi(T,\omega_i)$ and $\Lambda(T,\omega_i,\omega_j)$ are given by

$$\Phi(T,\omega_i) = 4\pi |\varphi|^2 e^{-\beta\omega_i} [1 \pm N(\omega_i)]$$
(16.5)

$$\Lambda(T,\omega_i,\omega_j) = 2\pi |\chi|^2 e^{\beta(\omega_j - \omega_i)} \begin{cases} N(\omega_j - \omega_i) & \text{for } \omega_j > \omega_i \\ [1 \pm N(\omega_i - \omega_j)] & \omega_i > \omega_j \end{cases}$$
(16.6)

where $N(\omega)$ is the number of exitations with energy ω in the heat bath, and the plus or minus sign corresponds to bosons or fermions respectively. Note that the second and third terms in Eq. (16.4) possess exactly the same forms as Fröhlich's Ansätze for loss rate of the i^{th} quanta in one and two quanta processes respectively.

For the stationary state, one requires that $\langle \dot{n}_1 \rangle = 0$. As a result, the average of the i^{th} quanta is

$$\langle n_i \rangle = \left[1 + \frac{s_i}{\Phi(T,\omega_i) + \sum_j \Lambda(T,\omega_i,\omega_j) < n_j > e^{\beta\omega_j}} \right] (e^{\beta(\omega_i - \mu_i)} - 1)^{-1} \quad (16.7)$$

where

$$e^{\beta\mu_i} = 1 + \frac{\sum\limits_j \Lambda(T, \omega_i, \omega_j)(e^{\beta\omega_j} - 1)}{\Phi(T, \omega_i) + \sum\limits_j \Lambda(T, \omega_i, \omega_j)(1 + \langle n_j \rangle)} \ge 1$$
(16.8)

and μ_i is the chemical potential of the i^{th} mode.

The inequality of Eq. (16.8) together with the requirement that $\langle n_i \rangle \geq 0$ dictates that $\omega_i \geq \mu_i \geq 0$. Equations (16.7) and (16.8) are exactly the same form as those derived by Fröhlich. (For details see Appendix I.) If there is no energy supplied, that is s = 0, then $\mu = 0$, and Eq. (16.7) becomes the thermal equilibrium distribution as required. From Eqs. (16.7) and (16.8), one notices that as s increases, μ will increase. When s exceeds a critical value s_o, μ approaches ω_o , where ω_0 is the lowest energy in the excitation band. Therefore, a large number of quanta are condensed into the lowest energy state. This is exactly the Bose-Einstein condensation in a Bose gas system when the temperature is lower than a certain critical value. In our case, the corresponding phase transition is not induced by lowering the temperature. Rather, it occurs by keeping the temperature constant and increasing the energy supply beyond the critical value s_o . From Eq. (16.8), it should be noted that when $\Lambda(T, \omega_i \omega_j) = 0$, $\mu = 0$. Thus, it is the two-quanta processes that are responsible for Bose-Einstein condensation; the larger the $\Lambda(T, \omega_i \omega_j)$, the greater the effect.

16.3 One- and Two-Dimensional Cases

In this section we will use two simple cases to demonstrate the enhancement of excitations in biological systems by external stimulation.

16.3.1 One-Dimensional Case

Let us consider a linear electric dipolar chain; this could correspond to the long chain of a protein, or a DNA chain, etc. Using the Debye model for the phonon in the heat bath, we are able to solve the coupling equations, Eqs. (16.7) and (16.8) numerically and obtain the values of the chemical potential μ and $\langle n_i \rangle$ as a function of the rate of energy supply s_i . For simplicity as before, we assume $s_i = s$, for all modes, and the coupling constants $\Phi(T, \omega_i)$ and $\Lambda(T, \omega_i, \omega_j)$ are assumed to be mode independent. Thus, for a biological system at a stable temperature, these coefficients Φ and Λ can be treated as constants. In Figure 16.6, we plot μ/ω_o as function of the energy supply rate s using $\omega_o/kT = 0.1$ for a constant χ and several values of ϕ for temperature $T = 300^{\circ} K$.

One sees that μ/ω_o approaches 1 when s increases to infinity. This clearly shows that for the one-dimensional case there is no Bose-Einstein condensation as expected. Figure 16.7 shows how the number of excited phonons in the biosystem increase with s.

Though there is no Bose-Einstein condensation, as s increases, the total numbers of the excited phonons in the biosystem is greatly increased. The largest enhancement of the phonon excitation in the biosystem occurs in the very low energy modes which is just above the lowest energy ω_o . Therefore, even if there is no phase transition, the biological system will be greatly affected due to the enhancement of induced phonons when the energy supply rate is sufficiently large.

16.3.2 Two-Dimensional Case

The two-dimensional case could correspond to cell membranes. Using the same assumptions as in the one-dimensional case, we plot μ/ω_o as a function of s in Figure 16.8.

One notices that when s exceeds a certain value s_o , μ/ω_o becomes 1. Thus, the phase transition surely occurs and the phonon will begin to condense to the lowest energy



Figure 16.6: The normalized chemical potential vs. energy supply rate S for $\chi = 0.1, \phi_1 = 0.05, \phi_2 = 0.1$ and $\phi_3 = 0.2$ respectively. The energy is in ω_o units.



Figure 16.7: The ratio of the number of enhanced phonons in the biosystem to that of the thermal equilibrium phonons vs. energy supply rate S for $\chi = 0.1$, $\phi_1 = 0.05$, $\phi_2 = 0.07 \phi_3 = 0.1$ and $\phi_4 = 0.2$.



Figure 16.8: The normalized chemical potential vs. energy supply rate S for $\chi = 0.1, \phi_1 = 0.05, \phi_2 = 0.1$ and $\phi_3 = 0.2$.

mode as s increases beyond the value of s_o . The critical rate of energy supply, s_o , is strongly dependent on the coupling strengths ϕ and χ . Note that as the relative magnitude between ϕ and χ increases, the critical energy supply rate s_o increases. This shift to higher critical energy supply can easily be explained as follows. Recall that χ describes the degree to which the interaction processes channel absorbed energy between the different phonon modes in the biosystem and ϕ describes the tendency of the mode's energy to be channelled to the heat bath. As long as the modes have an external energy source, if ϕ gets larger for a fixed χ , then more energy will be transmitted to the heat bath and less energy will be retained in the system. Therefore, the Bose-Einstein condensation will occur at high energy supply rate s_o . If s is smaller than s_o , there is no Bose-Einstein condensation, but the number of excited phonons will increase as s increases, just as in the one dimensional case. When s is larger than s_o , one expects not only the number of excited phonon to increase, but also the system to undergo a phase transition, i.e. a large number of the excited phonons in the system will be accumulated in the lowest energy state, ω_o .

In the examples above, we kept the coupling constant χ fixed, and ϕ variable. Actually we can change the values of χ ; the results are similar. The only difference is that when χ increases, the number of phonons of lower energy will increase faster and the phase transition in the two-dimensional case will occur at lower s_o .

The experiments for Stokes and anti-Stokes Ramman spectra has been done by Webb et al^{20-22} on synchronized active cells of E coli B.The incident microwave of frequency f_o will force the dipoles in the system to undergo oscillations and re-emit radiation. The spectrum of the oscillation - the Raman spectrum - will be composed of three lines. The central line has the frequency of the incident microwave, f_o , and is due to Rayleigh scattering. The two shifted lines are the result of Stokes and anti-Stokes scattering; they will have frequencies of $f_o - f$ and $f_o + f$ respectively. The frequency shift is equal to the vibrational frequency f, of the system. Figures 16.9-16.11 show the spectra taken at 40, 50, and 60 min. respectively after incubation.

Note that the line near 120 cm^{-1} range between 118 and 125 cm^{-1} . The experimental value of the ratio of the intensities anti-Stokes and Stokes is between 0.9 to 1. The theoretical value of this ratio is given by $n/(1+n)^{22}$, where n is the excitation number. At these frequencies and at room temperature, the thermal equilibrium distribution n^T is smaller than one; this gives values between 0.55 and 0.57 for the ratio of anti-Stoke and Stoke intensities. However, these values are much too small compared to the values obtained experimentally. In order for the ratio of these intensities to approach 1 as shown in the experiments, it is required that the number of excitation, n, should be much larger than 1. Thus, the Stokes and anti-Stokes lines in the active cell spectra may arise from a condensation or enhancement of the excited phonons in the biosystem induced by the energy supply from metabolic processes.



Figure 16.9: Stokes and anti-Stokes Raman spectra of synchronized active cells of E. coli B bacteria, taken at 40 min. after incubation.



Figure 16.10: Stokes and anti-Stokes Raman spectra of active cells of E. coli bacteria, taken at 50 min. after incubation.



Figure 16.11: Stokes and anti-Stokes Raman spectra of active cells of E. coli B bacteria, taken at 60 min. after incubation.

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16.4 Time Threshold for Biological Effects

Frölich's model has been particularly useful in understanding recent experiments revealing the effects of low level microwaves on various biological systems. One important general characteristic reported in these experiments is the existence of a time threshold for the initiation of the differing biological effects. Recall Sevastyanova and Vilenskaya's experiment⁶ involving the simultaneous irradiation of mice bone marrow cells. The time threshold for a protective effect was 30 minutes of microwave exposure. On the induction coefficient of colicin synthesis⁵, they also found that a minimum irradiation time is needed to produce measurable biological effects, again of the order of 30 minutes. The threshold will depend on the particular biological activity being monitored as well as the temperature. An example of the latter is clearly demonstrated in Smolyanskaya and Vilenskaya's experiment on E coli. Irradiation for 30 minutes at 20° produced no change in the rate of colicin synthesis, whereas at 37°, colicin synthesis increased. Therefore, it is expected that the analysis of the time threshold will not be a trivial matter. Both the detailed microscopic structure of the biological system and its thermodynamic behaviour must be considered in order to provide a full understanding of the specific time thresholds encountered for different biological systems.

Using Fröhlich's model, we intend to obtain an approximation for a segment of this time threshold.²³ In applying the Fröhlich hypothesis, one sees that the biological effects cannot begin until condensed phase occurs. It has not been determined how long this condensation has to be maintained in order to produce biological effects. Generally, the time needed to initiate biological effects will consist of two parts, τ_1 and τ_2 . τ_1 represents the time from the beginning of irradiation to the onset of condensation; τ_2 represents the time elapsed from the onset of the condensed phase to the production of the actual biological effects. Thus, the total time, τ , elapsed before biological effects occur from the initiation of irradiation, is given by $\tau = \tau_1 + \tau_2$ In the following analysis, we will evaluate τ_1 using the Hamiltonian given in Equation (16.1). τ_1 represents the minimum time required for the biological system to exhibit effects after irradiation and is the lifetime of the collective excitations in the biological system under scrutiny and is beyond the scope of the present study. However, τ_2 represents an important part and should be studied in future.

As mentioned in the previous section, the heat bath is a very complex system. The excitation modes in the heat bath can be either Bosons or Fermions. For simplicity, we will only consider the case that the excitations in the heat bath are also Bosons and only to the first order in interaction. This method can also easily be extended to other kinds of excitations. The lifetime of τ_1 is given by the relation

 $\tau_1 = h/ | Im\Sigma | where Im\Sigma$ is the imaginary part of the self-energy of vibration mode in the energy band.

It should be noted that the lifetime (and thus the self-energy) of interest is due

to terms with coupling constants χ and χ^* because these terms are responsible for creating the condensed phase. The rest of the terms in the Hamiltonian do not contribute to the condensation in the lowest order of coupling constant and therefore are not relevant to the present calculation.

Using the finite temperature Green's function, the self-energy, $\Sigma(p_i\omega_i)$ for the biological system phonon associated with operator a_i and a_i^+ yields

$$\sum(p_i,\omega_i) = |\chi|^2 \sum_j \left[\frac{1+n(\Omega_{p_j})+n(\omega_{p_i-p_j})}{\omega_{p_i}-\Omega_{p_j}-\omega_{p_i-p_j}+i\delta} + \frac{n(\Omega_{p_j})-n(\omega_{p_i-p_j})}{\omega_{p_i}+\Omega_{p_j}-\omega_{p_i-p_j}+i\delta} \right]$$
(16.9)

where $n(\omega) = (e^{\beta\omega} - 1)^{-1}$, Ω_p is the energy of a phonon with momentum p in the heat bath and ω_p is the energy of a phonon with momentum p in the biological system. At room temperature, these energy bands are much smaller than kT, therefore $n(\omega_{p_i})$ and $n(\Omega_{p_j})$ are much larger than 1. Also, $\Omega_{p'} = \pm(\omega_{p_i} - \omega_{p_i - p_j})$ is smaller than the width of the narrow energy band of biological system under consideration, which in turn is smaller than a typical energy in the set of vibration modes (i.e., $\Omega_{p_j} < \omega_p$). Thus, $n(\Omega_{p_j}) > n(\omega_{p_i - p_j})$. Therefore, the self-energy can be approximately written as

$$\sum(p,\omega_p) = \frac{|\chi|^2}{4\pi^2\hbar\beta} \qquad \int_{-1}^{1} dx \int_{0}^{\infty} \frac{p'^2 dp'}{\Omega_{p'}} \left(\frac{1}{\omega_p - \Omega_{p'} - \omega_{p-p'} + i\delta} + \frac{1}{\omega_p + \Omega_p - \omega_{p-p'} + i\delta}\right)$$
(16.10)

where the summation over heat bath momenta has been converted to an integration. Using the Debye model for the excitations in the heat bath, $\Omega_{p'} = v'p'$, where v' the velocity of sound in the heat bath.

The form of the dispersion relation for the biological system is unknown at present and depends in an intricate manner upon the biological structure. However, to obtain an approximate result, it is assumed that $\omega_p - \omega_{p-p'} = \pm \gamma \Delta$ where Δ is the width of the energy band which is very narrow and γ is a positive quantity less than 1. The value of γ depends on the form of the dispersion relation for the biological system. The real part of self-energy in Eq. (16.10) is impossible to evaluate without knowing the form ω_p . Fortunately we are only interested in the imaginary part which can be obtained easily from Eq. (16.10) as

$$Im\Sigma = -|\chi|^2 \frac{\gamma \Delta}{\beta \pi \hbar^3 v'^3} \tag{16.11}$$

Therefore, the lifetime τ_1 becomes

$$\tau_1 = \pi \hbar^2 v^{\prime 3} / |\chi|^2 \gamma kT \Delta \tag{16.12}$$

which is inversely proportional to the temperature T and to the square of the coupling constant. Thus, as the temperature is raised, the condensed phase should occur sooner, in turn causing the biological effects to begin sooner. This agrees, at least qualitatively, with Smolyanskaya and Vilenskaya's experiment where changing the temperature from 20°C to 37°C brought the biological effects into play, while holding the irradiation time fixed at 30 minutes.

The τ_1 given in Eq. (16.12) represents the irradiation time needed to produce the condensation and is the minimum time needed to produce biological effects. In order to apply this equation to specific circumstances, model studies and more experiments need to be performed to obtain expressions for the coupling constants and the dispersion relations in the energy bands. Given this information, a more complete understanding of the Fröhlich model and all its implication can be obtained.

16.5 Long Range Interaction

Further understanding of cooperative behavior of biological systems requires the development of models which represent the specific biological substance being analyzed. This is a difficult but very important problem which should be investigated carefully in order to understand the implications of the theory and make meaning-ful experimental comparisons. As an example, consider two biological systems at a distance R, larger than their linear dimensions, capable of giant dipole vibrations with frequencies f_1 and f_2 respectively (assuming $f_1 > f_2$). Through the coulombic interaction of these giant dipoles, the combined system then has two normal modes f_+ and f_- which can be expressed as³,

$$f_{\pm}^{2} = \frac{1}{2} (f_{1}^{2} + f_{2}^{2}) \left[1 \pm \left(A^{2} + \frac{B^{2}}{\epsilon_{\pm}} \right)^{1/2} \right]$$
(16.13)

and

$$A = \frac{f_1^2 - f_2^2}{f_1^2 + f_2^2} \ge 0 \tag{16.14}$$

$$B = \left(\frac{be^4 z_1 z_2}{M_1 M_2 R^6}\right)^{1/2}$$
(16.15)

where ϵ_{\pm} is the dielectric constants; z_1, z_2 are the numbers of the bound ions of charge $e; M_1, M_2$ are the molecular masses; and b is a numerical constant of order unity but depends on various angles. The interaction energy, U, is defined as the

difference in the free energy F at a distance R from its value at R going to infinite. The interaction energy is then given as

$$U_{\pm} = F_{\pm}(R) - F_{\pm}(\infty)$$

= $n_{\pm}h[f_{\pm}(R) - f_{\pm}(\infty)]$ (16.16)
= $\frac{n_{\pm}h}{\sqrt{2}} (f_1^2 + f_2^2)^{1/2} \left[\left(1 \pm \sqrt{A^2 + B^2/\epsilon_{\pm}^2} \right)^{1/2} - (1 \pm A)^{1/2} \right]$

where n_{\pm} is the number of quanta of the coherently excitated state. If $f_1 \neq f_2$, and at sufficient large distance, then $B^2 < A^2$. Using Equations (16.14) and (16.15), we find that

$$U_{\pm} \doteq \frac{n_{\pm}h}{\sqrt{2}} (f_1^2 + f_2^2)^{1/2} \frac{B^2}{\epsilon_{\pm}^2 A^2 (1 \pm A)^{1/2}} \alpha \frac{1}{R^6}$$
(16.17)

Thus U_{\pm} is proportional to R^{-6} , i.e., the interaction is short range regardless of which coherent state.

However, if $f_1 \doteq f_2$, then

$$U_{\pm} \doteq \pm \frac{nh}{\sqrt{2}} (f_1^2 + f_2^2) \frac{B}{\epsilon_{\pm}} \alpha \pm \frac{1}{R^3}$$
(16.18)

In this case of near resonance, the interaction has very long range. The interaction is attractive for the lower frequency f_{-} and repulsive for the higher frequence f_{+} respectively.

The long-range interaction from the above discussion may have considerable biological significance. Many biological processes depend on a certain molecule 'recognizing' another molecule. An enzyme and its substrate(s) must interact in a very specific manner both spatially and temporally. A similar situation exists for the antibodies of immune systems; antibodies must distinguish whether a molecule is foreign or belongs to the host. The fundamental biological question is "How does an enzyme or antibody recognize its own very specific target against the enormously high background found in living systems?" Each of these biological molecules can be considered as a unique entity, each with its own characteristic frequency or frequencies. How these molecules interact with each other may be governed by the state of the biological system. One notices that if the system condenses into f_- state, then the interaction is attractive; conversely, if the system condenses into f_+ state, then the interaction is repulsive. This provides a possible mechanism by which an enzyme or antibody can distinguish its target from other molecules. It is possible that the biological system can control which way it will condense into by supplying sufficient chemical energy to one normal mode of the vibration or the other. It can also be perturbed by external microwave radiation which acts by pumping energy into one or the other normal mode of the oscillation.

16.6 Appendix

The Bose-Einstein condensation in biosystems can be demonstrated explicitly as follows: summing over j in Equation (16.4) and set $\langle \dot{n}_i \rangle = 0$ for stationary state, one gets

$$S = \sum_{i} s_{i} = \sum_{i} \Phi(T, \omega_{i}) \left[< n_{i} > e^{\beta \omega_{i}} - (1 + < n_{i} >) \right]$$
(16.19)

On introducing the excess m_i over the thermal equilibrium distribution $\langle n_i \rangle^T$

$$< n_i > = < n_i >^T + m_i, \qquad < n_i >^T = (e^{\beta \omega_i} - 1)^{-1}$$
 (16.20)

we obtain

$$S = \sum_{i} \Lambda(T, \omega_i) m_i (e^{\beta \omega_i} - 1) < N \Phi_{max}(e^{\beta \omega_i} - 1)$$
(16.21)

where

$$N = \sum_{i} m_{i} \tag{16.22}$$

and Φ_{max} is the largest of the $\Phi(T, \omega_i)$. Thus we have a lower limit of the total number N of excess quanta, which increases proportionally to the total rate of supply of energy. Using Eq. (16.8) and Eq. (16.20), Eq. (16.7) can be written as

$$< n_i > = \left[1 + s_i \frac{1 - e^{-\beta \mu_i}}{\sum_j \Lambda(T, \omega_i, \omega_j) m_j(e^{\beta \omega_j} - 1)} \right] (e^{\beta(\omega_i - \mu_i)} - 1)^{-1}$$
 (16.23)

We now consider the simple case such that all $\Phi(T, \omega_i)$ are equal to Φ , and all $\Lambda(T, \omega_i, \omega_i)$ are equal to Λ . Equation (16.19) with Equation (16.20) then becomes

$$S = \Phi \sum_{i} m_i (e^{\beta \omega_i} - 1) \tag{16.24}$$

From Eq. (16.8), it follows that all μ_i are equal to μ such that,

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$$\omega_o \ge \mu \ge 0 \tag{16.25}$$

Eq. (16.23) for $\langle n_i \rangle$ then becomes

$$< n_i > = \left[1 + s_i \frac{1 - e^{-\beta\mu}}{\Lambda \sum_j m_j (e^{\beta\omega_j} - 1)} \right] (e^{\beta(\omega_i - \mu)} - 1)^{-1}$$
 (16.26)

or making use of Eq. (16.24), $< n_i >$ becomes

$$\langle n_i \rangle = \left[1 + \frac{s_i \Phi}{S\Lambda} (1 - e^{-\beta\mu})\right] (e^{\beta(\omega_i - \mu} - 1)^{-1}$$
(16.27)

Using Eqs. (16.20), (16.21), and $N^T = \sum_i < n_i > T$, we find

$$N + N^{T} = \sum_{i} \left[1 + \frac{s_{i} \Phi}{S\Lambda} (1 - e^{-\beta \mu}) \right] (e^{\beta(\omega_{i} - \mu)} - 1)^{-1}$$
(16.28)

Substituting s_i by S and μ by ω_o , and because $s_i \leq S$, $\mu < \omega_o$, we obtain

$$N + N^T \le \left[1 + \frac{\Phi}{\Lambda} (1 - e^{-\beta\omega_o})\right] \sum_i (e^{\beta(\omega_i - \omega_o)} - 1)^{-1}$$
(16.29)

In the particular case where the energy supply s_i to all modes is the same, $S = zs_i$, where z is the number of states in the energy band, then Eq. (16.28) becomes

$$N + N^{T} = \left[1 + \frac{\Phi}{z\Lambda}(1 - e^{-\beta\mu})\right] \sum_{i} \frac{1}{exp[\beta(\omega_{i} - \mu)] - 1}$$
(16.30)

The dependence of both Eqs. (16.29) and (16.30) on S is implicit through μ only. Furthermore, N increases with increasing energy supply S, as seen from Eq. (16.21). One also notices that, by Eqs. (16.7) and (16.8), when S has surpassed a critical value S_o , μ approaches ω_o . Therefore, in both Eqs. (16.29) and (16.30), N becomes very large, as a large number of quanta are condensed into the lowest energy state. This is exactly the Bose-Einstein condensation in a Bose gas when the temperature is lower than a certain critical temperature. In our case the corresponding phase transition is not by lowering temperature but is enforced by increasing the energy supply beyond the critical value S_0 and keeping the temperature constant.

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