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Solitonlike excitations in biological systems

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A model for solitonlike excitation in DNA is presented and assessed in the context of previous models of collective excitations in other biological systems. A qualitative analysis describes the mechanisms of some DNA function, in particular opening of DNA base pairs to initiate protein synthesis. A formalism is presented which analyzes quantitatively the above-mentioned model, predicts the threshold for *B*-DNA→*A*-DNA transition, and specifies the parameters of particular electromagnetic stimulations that can produce or initiate a variety of DNA responses and effects. The example of insulin production is discussed in detail and theoretical predictions are given for the parameters of an electromagnetic signal reproducing the stimulation to a cell which would lead to insulin production as a response.

I. INTRODUCTION

Interest in physical and mathematical modeling of biological systems has been steadily increasing during the last 20 years as it has been understood that a substantial leap is required to bridge the gap between the amount of information gathered about the biochemistry and the structure of living systems and the actual understanding of basic mechanisms underlying their functioning. The main features that any model attempting to explain biological activity must comprise are the following.

(i) Biological systems are complex, highly organized systems[1] that work within a very narrow range of variation of the parameters that characterize them and their function (temperature, sensory mechanisms, energetic balance, etc.). They present features that point to a delicate balance in the state of relative disorder that they endeavor to maintain in order to remain alive.

(ii) They are subjected to a great variety of energy inputs and stimulations from their environment and therefore must have a wide capability of response and adaptability to the above.

(iii) Living systems must have highly efficient means for storage and transfer of energy in order to convert the latter into all the necessary requirements for metabolic activity.

(iv) Living matter contains a very intricate arrangement and superposition of electromagnetic fields arising from its different constituents which effectively constitute the very refined balance needed for the maintenance of life.

(v) As most of the activity of biological systems involves the dynamics of macromolecules (proteins, lipids, carbohydrates, proteins in muscle contraction, DNA, etc.), a formalism must be developed to study the behavior of such complex condensed-matter systems composed of a large number of molecules interacting with each other.

(vi) Due to the major role played by DNA activity in the regulation of normal functioning of living systems, it is essential to understand the mechanisms of DNA function and of information transfer along the DNA chain. Only through such a study can DNA activity be monitored and altered in case of the breakdown of a particular process.

Due to the extreme complexity of biological systems it is of great interest to study energy differences between the actual state of the system and its "ground state" ("resting state") as only these play a role in physical processes. For this purpose we need to analyze the feasibility of formation of collective excitations in biomolecules that may arise as a result of the interactions present in each particular system. Competitive effects of dispersion and coherence are exhibited by most biomolecular chains. In the case of rigid chains, excitations can be created in the form of excitons or phonons. However, these excitations have a short lifetime and energy associated with them is dissipated in the form of heat as oscillations of the molecules. On the other hand, in "soft" chains, other types of excitations can arise due to nonlinear coupling between intramolecular vibrations and chain deformation. This type of collective excitation is such that instead of its energy being rapidly dissipated the chain deformation "traps" the vibrational energy as in a potential well. Under suitable conditions, this results in the formation of a coherent persistent excitation, viz., a solitonlike excitation. This latter can travel along the chain at a velocity lower than that of longitudinal sound and with little attenuation or energy loss. Although topologically different classes of solitons may arise according to the particular system under study, these coherent excitations may be involved in information and/or energy transfer along biomolecular chains. Knowledge of the latter can lead to a better understanding of the dynamics of biological systems and of crucial mechanisms of their functioning.

The purpose of this paper is to review the main current models of the dynamics of certain biomolecules and, in particular, to present a critical evaluation of present models that attempt to describe DNA activity. Section II presents first a review of Davydov's work[2] on soliton formation in α-helix proteins and its application to the phenomenon of muscle contraction. An analysis of the

experimental work of Webb[3] and co-workers on laser Raman spectra of metabolically active cells follows. The existence of "Davydov solitons" in α-helix proteins and the experimental evidence put forward by Webb prompted Scott[4] to further the theoretical analysis of the dynamics of Davydov solitons. His work is also reviewed in Sec. II. After a brief résumé of the work of Fröhlich[5] on coherent electric oscillations that can lead to Bose phonon condensation in biological systems, we present a theory put forward by Del Guidice, Doglia, and Milani[6] to explain the collective dynamics of metabolically active cells through an interplay between Fröhlich's coherent electric oscillations and Davydov's solitons. The work of Englander *et al.*[7] is also described and assessed critically, especially their coupled-oscillator model that proposes soliton formation in DNA.

Finally, in Sec. III, we present our model of the role of solitonlike excitations in DNA function. We discuss soliton propagation in the *B*-DNA state (resting state) and calculate the energy threshold for the transition into the active state or *A*-DNA state. We analyze soliton energy modulation effected by the electromagnetic (e.m.) fields interacting with DNA and discuss theoretical predictions for the particular cases of protein production (synthesis) and cell division. Section IV puts forward our conclusions on the potential importance of soliton formation in biological systems and stresses the urgent need of feedback between theoretical and experimental work.

II. SOLITONS IN α-HELIX PROTEINS

Davydov[2] has shown that collective excitations in the form of solitons exist in α-helix proteins, under suitable conditions. Slowly moving local intramolecular excitations accompanied by chain deformations may give rise to the onset of collective excitations. The solution to the nonlinear Schrödinger equation with which Davydov described the time evolution of the distribution of intramolecular excitations over the molecules of the chain and displacement of molecules about their equilibrium positions is a soliton. The soliton velocity is always lower than the longitudinal sound velocity so that it does not lose energy by phonon emission. This explains the stability of solitons, i.e., they do not spread with time. Davydov applied[8] the concept of soliton formation in α-helix proteins to explain contraction of striated muscles and the efficiency of conversion of soliton kinetic energy into energy of contraction of extension if a load is applied to the muscle. Muscle-fiber molecules can then store a considerable amount of energy in the form of solitons.

Laser Raman spectroscopy has been performed by Webb[9] on metabolically active *eschirichia coli (E. coli)*. The work of Webb covers the range from 10 and 3000 cm^{-1}. Scott[4] became interested in a spectrum from *E. coli* which had nine lines that could be assigned, to a rather close approximation, to sums and differences of two elementary frequencies: (i) the frequency of the interaction of the soliton with unit cells of the α-helix, and (ii) the frequency of an "interspine oscillation" in bond energy between the three spines that run longitudinally along the α-helix. In other words, Scott wanted to compare that particular spectrum to the vibrational structure of an α-helix soliton. Using a formalism modified from Davydov's original one, he was able to show very good agreement between Webb's experimental values and his numerical predictions. The two elementary frequencies mentioned above were calculated to be at 15.35 and 125.7 cm^{-1}. Careri *et al.*[9] have recently discussed formation of Davydov solitons in acetanilide.

Before we proceed to discuss a model[6] that involves the role of Davydov solitons in DNA, we give a brief résumé of the coherent-excitation theory proposed by Fröhlich,[5] as his theory is used in conjunction with Davydov's. Fröhlich considered a set of coupled oscillating electric dipoles kept in a nonequilibrium state by an external energy input, but unable to store the incoming energy. He showed that, for a certain critical value of the energy supply, the lowest vibrational mode is coherently excited and Bose-like condensation takes place in it. The high electric polarizability of biological materials provides the basis for another model proposed by Fröhlich: due to strong coupling between electric and elastic degrees of freedom, biomolecules may be in excited metastable states with large dipole moments. These are the basis of long-range attractive and repulsive forces in systems oscillating coherently with the same frequency. Frölich estimated the frequency of the coherent oscillation to be of the order of 10^{11} Hz for the cell membrane, and of the order of 1 GHz for DNA.[10]

Del Guidice *et al.*[6] have proposed a model for DNA activity based on an interplay of Fröhlich's coherent electrical excitations with Davydov solitons. They proposed that Davydov solitons could dominate the dynamics of *B*-DNA and Fröhlich's mechanism could dominate the behavior of *A*-DNA. This conclusion is arrived at on the basis of Raman spectra of DNA,[11,12] viz., a weak broad band around 830 cm^{-1} in *B*-DNA and a string and sharp line in *A*-DNA at 807 cm^{-1}. They maintain that soliton formation can arise in *B*-DNA under suitable conditions, but not in *A*-DNA. This conclusion is not correct for the following reasons.

(i) Experiments were done at $T<30\,^{\circ}C$ or $T>85\,^{\circ}C$. Clearly, below 30 °C cells are not biologically active, and above 85 °C DNA is denatured. In fact, denaturation seems to start soon after 50 °C.[13]

(ii) How can the cell keep alive if there is no monitoring of *B*-DNA activity? That is, if the conditions are not right and only excitons are formed in *B*-DNA, i.e., no soliton formation, how can energy and/or information be transferred along the DNA chain in order to ensure the maintenance of life? In Sec. III we propose an alternative theory that can resolve this conflict without having to invoke Fröhlich's theory.

(iii) Frequencies of the order of 0.1 cm^{-1} corresponding to oscillation of the full DNA chain correspond to approximately 3 GHz, in good agreement with the parameters described[14] for artificial e.m. stimulation of DNA. They conclude that the Webb lines in the region of 2000 cm^{-1} correspond to processes leading to protein synthesis from DNA. No reason is given as to why this higher-frequency mode should be excited first; then a transition to lower frequencies (790–850 cm^{-1}) is attributed to

binding with water molecules. Nonlinear electric field effects have been observed but, as will be seen in Sec. III, an alternative explanation will be proposed.

In summary, the model of Del Guidice *et al.* rests on an interpretation of experimental results taken under nonphysiological conditions and on the assumption that two different mechanisms, of a very different nature, must be invoked for explaining *B*-DNA and *A*-DNA activity.

Englander *et al.*[7] analyzed the fact that polar hydrogens of the bases in DNA exchange with solvent hydrogens under conditions in which these molecules are ordered. This has lead to the proposal that ordered helices contain small amounts of open states in which bases are unpaired, and these open states mediate the exchange of otherwise inaccessible hydrogen-bonded protons. Englander *et al.* considered the description of the open-state configurations and proposed that these may be described in terms of solitons. They predicted the existence of a unique major open state of DNA at physiological temperatures. They presented a mechanical analog of a mobile defect in DNA which, when traveling, opens base pairs and recloses them behind. This model proposes that the existence of soliton excitations in the double helix arises from nonlinear coupling between the gravitational potential energy and the torsional twist energy of a double linear chain of pendula (the bases) connected by springs (the sugar-phosphate backbones). They themselves recognized the overall simplification of the model, which appears to give them reasonable agreement with some data from hydrogen-deuterium exchange experiments. However, some of the predictions they arrive at may reflect the oversimplification of this model. They predict an optimum frequency ("jitter frequency") associated with this mobile state on the order of 1 MHz, as opposed to experimental observations of frequencies in the range 600 MHz to 1.5 GHz.[15,16] They claim that, although these latter experiments predict higher frequencies than their optimum range, their results would imply very large open structures. This need not be so because (a) coherent oscillation of base pairs involved in the opening of loci associated with a particular demand of a cell may explain long-distance "communication" between base pairs and (b) base pairs belonging to the opening of a particular locus are not contiguous to each other: the configuration is much more "spread out" along the chain, as bases involved might be a considerable distance apart. Also, they have considered a denaturation temperature of 80 °C (which is far too high) and have not really discussed the behavior at physiological temperatures or proposed mechanisms for any process to occur. Krumhansl *et al.*[17] and more recently Alexander[18] have proposed the foundations of a more feasible modes of DNA.

III. PROPOSED MODEL OF DNA ACTIVITY

In this section we describe the model that we have proposed of DNA activity, and present some numerical calculations and predictions that can be tested experimentally or that are being tested at present by the experimental team within our research unit. The purpose of our model is to show a method whereby DNA activity can be selectively controlled and dictated by noninvasive means.

The onset of collective excitations in DNA, viz., solitons, can be due to the nonlinear nature of the coupling between intramolecular excitations and chain deformations. Intramolecular vibrations take place in the O—P—O bonds of the DNA backbone,[12] and these are coupled to chain deformations resulting from the extension and compression of the hydrogen bonding existing between two bases of a base pair. It is to be pointed out that this appears to be an indirect coupling mediated, to some extent, by C=O groups in the base pair. Thus, the class of solitons that we are describing is qualitatively different from the Davydov soliton, being of a different topological nature. Further, we show how the soliton energy has to be modulated in order that the transition from *B*-DNA (resting state) to *A*-DNA (active state) be effective. We first discuss the model qualitatively, describing DNA activity at "rest" (i.e., when routine maintenance processes are being monitored in a cell) and in the "active" state (i.e., when involved in the initiation of a process that has to satisfy a particular demand of the cell). Section III A gives the details of the formalism, including some numerical predictions for certain processes to occur.

A. Description of the model

We have shown that, for and above a certain threshold value of the coupling constant of the nonlinear interaction, soliton formation occurs[19] when DNA is in its *B* state. If solitons are responsible, at least in part, for information and/or energy transfer along DNA, continuous activity has to be ensured at all times. Soliton formation is "switched on" by internal processes occurring in the system and not by an external agent or a change of regime externally effected, as has been suggested by Del Guidice *et al.*[6] This internal switch is of a very complex nature, but it is basically due to the interplay of three phenomena: (i) the strength of the nonlinear interaction (coupling) in DNA, (ii) energy release due to adenosine triphosphate (ATP) hydrolysis, and (iii) the presence of an electromagnetic "background" arising from different components of a cell. The latter contributes to the DNA ground state and, as mentioned before, due to the complexity of the system, we study excitations of that ground state since only processes in which energy differences exist are of interest.

It is to be stressed that electronic interactions have not been considered for two main reasons. (i) The energy released during ATP hydrolysis is 0.5 eV and is considered to be the basic energetic unit utilized in physiological processes or vital of the DNA molecule, this energy release can excite localized intermolecular vibrations in long chain molecules. Such collective excitations, or solitonlike excitations, can arise at sites of local energy release from ATP hydrolysis and propagate along the molecule with great efficiency and very little attenuation. This fact was already noted by Davydov.[8] (ii) The strength of the coupling of the electronic interaction to either vibrations or deformations is therefore a higher-order correction to the Hamiltonian described by Eq. (3.1) (in Sec. III B).

We now describe the way in which the switching from

the B-DNA to A-DNA state can occur as a result of a stimulation requiring the cell to satisfy a need, e.g., a certain product must be synthesized. The metabolic changes associated with the demand of the cell are transduced as an e.m. field signaling the DNA. If the energy change associated with this demand (e.g., related to the amount or concentration of protein to be produced or initiated) is smaller than the threshold value for the B-DNA$\rightarrow A$-DNA transition, the cell need not involve DNA in the synthesis of that product since the energy change may be enough of a stimulation to induce ejection of the product from those constituents of the cell (organelles, vesicles, etc.) that store these products. In other words, it is an "extra-DNA" process. If the energy change associated with the demand is greater than the threshold value, calculated as 0.25 eV,[19] the transition B-DNA$\rightarrow A$-DNA is effected. We now describe the mechanism that may induce this transition. The e.m. field signaling the specific demand of the cell to DNA has linear and nonlinear components. The role of nonlinear electric field effects at selective frequencies in DNA has been shown to be several orders of magnitude greater than the role of the linear one.[20] Such a signal has to couple with a vibrational mode of DNA, and the obvious way would be through an interaction between the e.m. signal and the chain's apparent permanent dipole moment. This coupling may produce a resonant effect in the DNA chain resulting in soliton energy modulation. This is seen experimentally as strong and sharp lines in the A-DNA laser Raman spectrum,[11,12] while weak broader lines are seen in the resting state.[3,21] In turn, this soliton energy modulation can produce strong chain deformation leading to DNA unzipping. Long-range communication effects must come into play at this point as different segments of DNA will be involved: these would oscillate coherently, leaving those segments not involved "dormant." Permanent closures of long segments of DNA (up to 90% of its length) during the life of a cell can be explained, apart from evolutionary and hereditary considerations, by their having a different natural frequency of oscillation and thus not oscillating coherently with the functioning segments. It seems reasonable to think that field strength, power level, and especially frequency of a particular signal are specific for eliciting a particular response in DNA. In that case, as we show in Sec. III B, we can devise a method that would enable us to calculate the parameters of the signal that could artificially reproduce the effect, e.g., of a protein dipole moment on DNA so as to induce or initiate a particular DNA function. In other words, we need not know the exact base sequencing that is associated with the initiation of that DNA function. Instead, we look for the characteristics of an electric signal that could produce the same effect, viz., initiation of that DNA function. The smooth functioning of the mechanism operating during the B-DNA$\rightarrow A$-DNA transition must be ensured by a very sensitive feedback. When the demand is satisfied, the e.m. signal switches itself off and A-DNA returns to its B-DNA configuration. Breakdown in this feedback system could be due to the signal not eliciting the appropriate response from DNA, or, more likely, that the response is inadequate to meet the demand thus resulting in different pathological conditions. In Sec. III B we describe the formalism for DNA activity based on the above model and give certain numerical predictions.

B. Quantitative analysis of the model: a formalism for DNA activity

The Hamiltonian for the B-DNA state[19] can be written as

$$\mathscr{H}_{B-\mathrm{DNA}}=\mathscr{H}_0+\mathscr{H}_1+\mathscr{H}_2\ , \tag{3.1}$$

where

$$\mathscr{H}_0=\tfrac{1}{2}\sum_n\left[\frac{1}{M}\hat{p}_n^2+w(u_n-u_{n-1})^2\right] \tag{3.2}$$

is the energy operator for displacements u_n of molecules of mass M from their equilibrium positions (M represents here the mass of a base pair), $\hat{p}_n$ is the momentum operator canonically conjugate to u_n, and w is the chain-elasticity coefficient. Here

$$\mathscr{H}_1=\sum_n[(\epsilon-D)B_n^\dagger B_n-J(B_{n+1}^\dagger B_n+B_{n+1}B_n^\dagger)] \tag{3.3}$$

is the energy operator for the intramolecular excitations, where ϵ is the excitation energy for a molecule, D is the deformation energy excitation operator, $-J$ is the resonance interaction between neighboring molecules, and $B_n^\dagger$ and B_n are creation and annihilation operators for intramolecular excitation quanta on the nth molecule.

Thus we could call $E_0=\epsilon-D$ the fundamental energy of the intramolecular vibration and $-J$ the nearest-neighbor dipole-dipole interaction energy. The excitations with the lowest energy described by the Hamiltonian (3.3) are solitonlike excitations, which represent a complex combination of intramolecular excitations distributed along a certain portion of the chain and the local chain deformation within this segment. It is therefore correct to attribute the same creation and annihilation operators to both terms in Eq. (3.3). Here

$$\mathscr{H}_2=\chi_{\mathrm{DNA}}\sum_n(u_n-u_{n-1})B_n^\dagger B_n \tag{3.4}$$

describes the interaction between intramolecular excitations displaced from their equilibrium positions.

We have calculated[20] the parameter χ_{DNA}, the coupling constant that gives the strength of the nonlinear interaction in DNA, to be $\chi_{\mathrm{DNA}}=1.26\times10^{-9}$ N. This shows that $\chi_{\mathrm{DNA}}\simeq30\chi_{\alpha-\mathrm{helix}}$,[4] in other words, the threshold for soliton formation in DNA, is approximately 30 times higher than that for the α-helix proteins. There is a conceptual similarity between Davydov's formalism and ours for the α-helix proteins: in the former, soliton formation arises from the direct coupling between the amide bond energy and the compression and extension of the hydrogen bonding associated with it. In DNA, soliton formation may arise from the indirect coupling between the O—P—O bond energy in the DNA backbone and the extension and compression of the hydrogen bonding linking the base pairs.

The energy transfer effected by the soliton when DNA is in its B state is a solution to Eq. (3.1), viz.,

$$E_{\rm sol}^{B} \equiv \epsilon - D - 2J - \frac{\chi_{\rm DNA}^{4}}{3w^{2}J} + \tfrac{1}{2} m_{\rm sol} v_{\rm sol}^{2} , \tag{3.5}$$

where $m_{\rm sol}$ is the soliton mass and $v_{\rm sol}$ the soliton velocity of propagation. We have calculated the soliton mass to be[19]

$$m_{\rm sol} = m_{\rm ex} + \frac{4\chi_{\rm DNA}^{4}(1+\frac{3}{2}s^{2}-\frac{1}{2}s^{4})}{3w^{2}(1-s^{2})^{3} J v_{s}^{2}} ,$$

where

$$s = v_{\rm sol}/v_{s} \quad \text{and} \quad m_{\rm ex} = \frac{\hbar}{2Ja^{2}} ,$$

a being the distance between two neighboring pairs along the DNA chain, $m_{\rm ex}$ the mass of the exciton, and v_s the velocity of longitudinal sound along DNA, which we estimated to be 3892 $\rm m\,s^{-1}$ in B-DNA. The $v_{\rm sol}$ was estimated to be 428 $\rm m\,s^{-1}$.[20] These agree with other values reported.[22] Thus

$$m_{\rm sol} = \frac{\hbar}{2Ja^{2}} + \frac{4\chi_{\rm DNA}^{4}(1+\frac{3}{2}s^{2}-\frac{1}{2}s^{4})}{3w^{2}(1-s^{2})^{3} J v_{s}^{2}} . \tag{3.6}$$

In order to describe the B-DNA$\rightarrow$$A$-DNA transition, an extra term has to be added to Eq. (3.1) to account for the interaction between the external e.m. field inducing the transition and the chain dipole moment. This term will be responsible for possible initiation of DNA function. This is then

$$\mathscr{H}_{A\text{-DNA}} = \mathscr{H}_{B\text{-DNA}} + \mathscr{H}_{\rm int} , \tag{3.7}$$

where $\mathscr{H}_{\rm int}$ is the operator that will allow for soliton energy modulation induced by the external e.m. field. Physically, it describes the energetic changes occurring to B-DNA in the presence of this external e.m. signal which, if above the threshold value, can induce transition to the A state. $\mathscr{H}_{\rm int}$ is composed of two terms, of which the first one described below is the dominant one: (i) the interaction between the e.m. field and the longitudinal dipole-dipole coupling of the chain, and (ii) the interaction between the e.m. field and the coupling between intramolecular vibrations and chain displacements about equilibrium positions. The energy transfer along the DNA chain in the A state is the solution to Eq. (3.7), viz.,

$$E_{\rm sol}^{A} = \epsilon - D - 2J - \frac{\chi_{\rm DNA}^{4}}{3w^{2}J} + \tfrac{1}{2} m_{\rm sol}^{*} v^{2} , \tag{3.8}$$

where $E_{\rm ex} = \epsilon - D - 2J$. the term $\chi_{\rm DNA}^{4}/3w^{2}J$ is the energy correction introduced by the soliton formation in B-DNA, which is more favorable than exciton formation in a soft chain. The term $\frac{1}{2} m_{\rm sol}^{*} v_{2}$ describes the A-DNA chain energy, where v is the new soliton velocity in the A-DNA configuration and m^{*} the new effective soliton mass that introduces the coupling between the external e.m. field and both J and $\chi_{\rm DNA}$.

We now proceed to discuss the second term in Eq. (3.7), viz., $\mathscr{H}_{\rm int}$. We have already recognized the importance of nonlinear-electric-field effects on DNA.[20] If P is the polarization vector, the energy density due to an electric field E is

$$\mathscr{E} = \mathbf{P}\cdot\mathbf{E} , \tag{3.9}$$

where $\mathbf{P}$ can be written in terms of a series expansion in only the odd powers of E. This is

$$P = N\epsilon_{0}(\alpha E + \gamma E^{3}) , \tag{3.10}$$

N being the number of molecules per unit volume, ϵ_0 the permittivity of free space, α and γ the linear and nonlinear polarizabilities, respectively. Thus Eq. (3.9) becomes

$$\mathscr{E} = N\epsilon_{0}(\alpha E^{2} + \gamma E^{4}) , \tag{3.11}$$

where the first term describes the linear contribution to the energy and the second term the nonlinear contribution. This latter one is thus

$$\mathscr{E}_{\rm non} = N\epsilon_{0}\gamma E^{4} . \tag{3.12}$$

The nonlinear polarizability can be written explicitly as[23]

$$\gamma = \frac{1}{6\pi N\epsilon_{0} S E^{3}} \frac{I}{f} , \tag{3.13}$$

where I is the displacement current, f the frequency of the signal, and S the cross-sectional area of the measuring cell which can be taken as 1 $\rm cm^2$. Combining (3.12) and (3.13) we get

$$\mathscr{E}_{\rm non} = \frac{1}{6\pi s} \frac{IE}{f} .$$

Taking $1/6\pi s \simeq 500$ we arrive at the general result

$$\mathscr{E}_{non} = 500 \frac{IE}{f} . \tag{3.14}$$

If $\mathscr{E}_{non}$ is to produce a disturbance in the chain dipole, we can calculate the values of the other three parameters that would produce this effect.

Another effect that we can calculate is that of the interaction of a protein dipole moment with the transmembrane electric field which is of the order of 7×10^{6} $\rm V\,m^{-1}$.[14] The idea is that $\mathscr{E}_{\rm non}$ will produce the soliton energy modulation that can be required to produce chain deformation and lead to the B-DNA$\rightarrow$$A$-DNA transition. We have recently calculated[24] such an effect in the case of a signal that simulated the conditions for DNA-mediated insulin synthesis that is triggered by a very specific stimulation to the cell: an increase in the level of glucose. We can think of this chain of events in the following way.

(i) Arrival of glucose molecules to the cell membrane.

(ii) Interaction between glucose dipole moment and transmembrane electric field creates an e.m. signal that encodes instructions for DNA response and propagates towards the cell nucleus.

(iii) Interaction occurs between signal and the DNA apparent permanent dipole moment. Under physiological conditions, the energy due to this interaction is above the threshold for the B-DNA$\rightarrow$$A$-DNA transition,[19] thus creating soliton modulation which can result in the above-mentioned conformational change.

(iv) Once the B-DNA$\rightarrow$$A$-DNA transition has been effected, opening of loci occurs to send instructions encoding the message to synthesize insulin. This will continue until negative feedback stops the instruction.

We have calculated the $\mathscr{E}_{non}$ at the cell membrane due to interaction (ii) and this is of the order of 5.75×10^{-18} J.[24] After traveling a distance equal to 500 times the cell-membrane thickness, the energy reaching the cell nucleus decreases as the inverse square of distance, viz., the value of $\mathscr{E}_{non}$ at the nucleus is equal to 2.3×10^{-23} J, or 1.44×10^{-4} eV. This is the energetic disturbance effected on the nucleus by one molecule of glucose. It can be seen that approximately 1800 molecules of glucose are sufficient to produce an effect just greater than the threshold for the B-DNA$\rightarrow A$-DNA transition, viz., 0.25 eV. We have predicted[24] the values of the main parameters describing the signal arising at the cell membrane which would create this particular effect on DNA loci: an electric field $E=0.02$ V m^{-1} and a frequency of the order of 1.7 GHz. These theoretical predictions are being tested experimentally at present.

We can therefore see through this quantitative analysis the importance of the role of $\mathscr{H}_{int}$ in Eq. (3.7) in the total Hamiltonian describing A-DNA. The example of insulin shows that it is possible, by knowing the parameters of the e.m. signal that reproduces a particular stimulus to the cell, to achieve a wide variety of DNA-mediated responses which can in turn lead to a wide range of effects.

IV. CONCLUSIONS

We have discussed formation of solitonlike excitations in biological systems and have concentrated our work in particular on the DNA biomolecule. Our model predicts transition of the B-DNA to A-DNA state and allows for the calculation of the parameters describing an e.m. signal which could artificially reproduce the stimulation needed to produce or initiate a variety of DNA responses and effects. If found to be experimentally verified, the potential importance of this model would be such that it could supersede the present trend of base sequencing for DNA decoding. Indeed, only knowledge of the particular e.m. signal that would trigger the desired DNA response would be required, thus leading to a completely new field of medical and clinical applications. We very much hope that this paper will encourage researchers in the field that possess suitable experimental facilities to perform tests that could help elucidate the usefulness of this new methodology.

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