TAUTOMERIC MUTATION IN DNA. A THEORETICAL COMPARATIVE STUDY AND SYNTHESIS BETWEEN VARIOUS PROPOSED QUANTUM MODELS

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The tautomeric mutation and its repair in DNA is discussed from the perspective of a theoretical bio-physicist using quantum tools. Many of the well known concepts and techniques borrowed from condensed matter physics in particular, are found to be quite useful in the analysis of this process and to provide important insight. It is shown that the proposed diverse theoretical models for describing this phenomenon can be unified by making use of these tools. Various experimental results of paramount importance, obtained from living organisms, were highlighted and used as input in the calculations and in the analysis. Possible applications of the theoretical procedure adopted here to investigate many related phenomena, are also briefly discussed.

1 Introduction

The mutation process in DNA and its importance to evolution of living systems is quite well studied by now[1-4]. In fact, mutation plays a very crucial role in the evolution and the appearance of a large variety of species on this earth conforming to Darwinian theory. A mutation introduces a defect in the well ordered arrangement or symmetry pattern of nucleotides' distribution within a double stranded DNA molecule, with non trivial consequences in various bio-physical processes DNA undergoes. To elaborate, even

the partial loss of symmetry involving the complementarity of the nucleotides on the two strands, affects the very important processes like replication and transcription. The process of replication in fact, triggers the cell division processes in a living system and provides the pathway for the development of new multicellular organisms. Moreover, it is also responsible for the growth of population of species through geological time scale. The process of transcription leads to Protein synthesis and hence plays an important role in the development of tissues for a living system.

There are different types of mutation classified on the basis of the origin viz. spontaneous and induced. The spontaneous mutation is the one which occcurs in the absence of any external radiation or chemical agent. They provide the background mutations and are the main contributors to the evolution of species and the variety present on this earth. The induced mutation is brought about by the presence of certain chemical agents known as mutagens or by irradiation of electromagnetic wave.

A special type of point mutation which is of particular interest to condensed matter physicists is "tautomeric mutation". In this mutational process each nucleotide viz. Adenine (A), Thymine (T), Cytosine (C) and Guanine (G) fluctuates between various isomeric forms or tautomers. Furthermore, these nucleotides existing in these various forms viz. keto (most common and stable one) and enol/ imino (rare and unstable ones) can sometimes exhibit pairings which violate the conventional Watson-Crick base pairing rule (BPR) for a double stranded DNA[1-4]. Very often intrinsic quantum fluctuations involving proton tunnelling and causing hydrogen bond alterations are responsible for this anomalous behavior. It may be clarified here that hydrogen atom being the lightest atom, exhibits zero point motion, which is at the root of proton tunneling.

This non trivial role of quantum processes has inspired theoretical biophysicists to construct various types of quantum models for describing the phenomenon of tautomeric mutation in DNA. There is in fact a very deep connection between biology and physics with regard to many diverse phenomena seen in biological systems [5]. This originates from the fundamental relation between various microscopic and macroscopic processes underneath as well as the symmetry of various structures and patterns observed in physical and biological systems.

Coming back to the specific phenomenon of tautomeric mutation, it should be remarked however that, sometimes chemical contamination during synthesis may also be the cause for such tautomers to be created in a DNA molecule.

In this communication, we would like to discuss at length about two such proposed models based on quantum physics and establish a mathematical connection between them. One of them is a "quantum spin-pseudo-spin model" (to be called simply "quantum spin model" for brevity from now onwards) of generalized transverse Ising type, while the other one is a "bosonic model" of tight binding nature [1, 2]. It is worth presenting a brief background review of these two well known models from statistical mechanics and condensed matter physics perspective, before we describe their relevance and connection to the DNA problem.

It is worth recalling that a transverse Ising model has two parts viz.:- (i) a usual Ising model involving coupling between the longitudinal spin components S_z's (taking discrete values) corresponding to the nearest neighbour sites and (ii) a transverse magnetic field (along x or y directions) coupling to the spins [6]. The transverse Ising model can exhibit quantum processes unlike the original conventional Ising model. This is because the transverse magnetic field couples to the spin operators and can flip the spin states from 'up' to 'down' and vice versa.

The 'bosons' are a class of fundamental particles with integral spins and obey Bose-Einstein Statistics [7]. 'Fermions' are the other class of fundamental particles which obey Fermi-Dirac Statistics and hence follow the well known Pauli Exclusion principle [7]. In condensed matter systems various excitations of both collective and composite particle nature, often aquire bosonic character after quantization. They include phonons, magnons, plasmons, excitons etc. [8]. These bosons belong to the class 'quasi-particles' in condensed matter physics and can propagate as well, transporting charge and spin fluctuations in the system. On the other hand, the 'real single particles' which are the original charge carriers and spin carriers in various condensed matter systems, can in general be identified as 'electron' or 'hole' both of which are of fermionic character [8].

Coming back to our original problem of tautomeric mutation, we now describe the two proposed models viz. (i) the quantum spin based model and (ii) the bosonic model at some length. We then show that the second model above can indeed be obtained mathematically from the first one in a perturbative scheme in low orders and furthermore that the two approaches can be unified in a consistent manner even from a bio-physical view point.

2 Mathematical formulation

The quantum spin model proposed and referred to earlier, in fact contains both interacting 'spin' and 'pseudo-spin degrees' of freedom which are operators and also includes a 'generalized transverse field' coupling to them [1]. In this model, the interactions within a DNA molecule is described by an analogous transverse field Ising Hamiltonian (with spin 1/2) corresponding to a 2-legged ladder, with inter-strand coupling of ferromagnetic type between pseudo-spin operators and antiferromagnetic type between the longitudinal components (z-components) of spin operators. The transverse field here couples to both transverse components of spin operators as well as pseudo-spin operators and causes the mutations by flipping the states and breaking the BPR order. In this model, the nucleotides 'A', 'T', 'C' and 'G' are regarded as different quantum states of a DNA molecule at any local site within the molecule and are represented as (X, +1/2), (X, -1/2), (Y, +1/2) and (Y, -1/2) respectively; where the first letter stands for the pseudo-spin label and the second number gives the spin state ("up" or "down"). Thus 'X' and 'Y' themselves are called "pseudo-spin up state" and "pseudo-spin down state" respectively for convenience. Furthermore, the transverse field term is assumed to have contributions of intra-strand type processes only.

It is worthwhile to point out that in a real DNA molecule, the inter-strand coupling is provided by hydrogen bonds which are weaker in strength than the intra-strand coupling between the nearest neighbour nucleotides generated through covalent bonding, by an order of magnitude [3]. Therefore the tautomeric mutation takes place easily by hydrogen bond rearrangements.

Mathematically the full quantum spin model is given by [1]:-

$$\mathcal{H}_{QSM} = \mathcal{H}_{Ising}^{inter-strand} + \mathcal{H}_{Transverse}^{intra-strand} \tag{1}$$

where

$$\mathcal{H}_{Ising}^{inter-strand} = \sum_{i,M,N,s,s'} \lambda_i^{1,2} \sigma^z_{i,M,s;1} \sigma^z_{i,N,s';2} \delta_{M,N} \delta_{s,-s} \tag{2}$$

$$\mathcal{H}_{Transverse}^{intra-strand} = \sum_{i,l} \frac{1}{2} H_i^l \Big[\left(\sigma^+_{i,l} + \sigma^-_{i,l}\right)_{sp} X I_{psp} + I_{sp} X \left(\sigma^+_{i,l} + \sigma^-_{i,l}\right)_{psp} + \frac{1}{2} \left(\sigma^+_{i,l} + \sigma^-_{i,l}\right)_{sp} X \left(\sigma^+_{i,l} + \sigma^-_{i,l}\right)_{psp} \Big] \tag{3}$$

We note that the operators σ 's occurring above in equation 2 are in fact composite operators comprising of both spin operators and pseudo-spin operators and I being the identity operator. The parameter H represents the transverse field. In our calculations later for simplicity, we have assumed it to be spatially uniform i.e. site independent.

Thus the quantum spin model above contains the very elements triggering the process of mutation through the presence of the transverse field term, besides having the usual Watson-Crick base pairing term represented by the Ising-like term.

On the other hand, the proposed bosonic model for DNA is based on the assumption of tunnelling states of protons as two-level systems and involves only an intra-strand Hamiltonian containing a single boson site energy term and a nearest neighbour bosonic hopping term [2]. Mathematically it is expressed as [2]:-

$$\mathcal{H}_{bosonic} = \sum_n E_0 b_n^+ b_n + \kappa \sum_n \left(b_n^+ b_{n+1} + b_{n+1}^+ b_n \right) \tag{4}$$

where the operators b_n and b_n^+ represent the bosonic destruction and bosonic creation operators respectively at the 'n'th site on a strand. In this model the tautomeric mutation is regarded as a bosonic excitation (of excitonic type) with the parameter E_0 ' being the bosonic energy. Thus the first term represents the site energy of this boson. The second term describes the hopping of this boson between the nearest neighbour sites on any one strand, implying the intra-strand propagation of mutation with an amplitude κ. The inter-site hopping amplitude depends upon the dipolar interactions between the nearest neighbour bases, besides many other factors. It may be recalled that this Hamiltonian is analogous to the well known tight binding model corresponding to band theory in condensed matter physics.

It must be pointed out that the full Hamiltonian corresponding to DNA in the bosonic approach, contains additional parts consisting of structural distortion of the DNA molecule from the solid mechanics perspective as well [2, 3]. This arises from the proton tunneling process combined with the hopping of the excitation, leading to a deformation of elastic DNA through the π-electrons' rearrangement [2]. On the other hand, the quantum spin model contains a fictitious transverse field H causing anomalous pairings [1], which can be linked to the physical relocation and reorientation of the Hydrogen bonds, leading again to the phonon-like distortion modes due to the charge redistribution, along the 'rungs' joining the multiple strands generated in the course of replication process. Thus the presence of an intrinsic coupling between the electronic/ ionic degrees of freedom and the phonon-like modes in both the models, provide a very important conceptual bridge between the two approaches.

The bosonic model thus assumes the existence of mutational process already and looks at the consequences only, as is clear from the structure of the Hamiltonian given in equation 4 and the discussions in the above paragraph.

For the quantum spin model the above coupling would imply that the Fourier Transform of the transverse field (H_q) and the phonon creation and destruction operators can be related in the following way:-

$$H_q = C_q \left(v_q + v_{-q}^{+} \right) \tag{5}$$

where v_q and v_q^+ are the phonon destruction and creation operators respectively and the coefficients C_q involve the proton tunneling matrix elements. The above equation exhibits the possible deformation of nucleotides and the lattice (along the rungs) due to proton tunneling. The portion relevant for the pure mutational process however consists only of C_q.

We would now like to explore a possible mathematical connection between the spin model and the bosonic model. For this we make the following assumptions and adopt the following strategy:-

1. We assume that both of the above models become operational physically only after the completion of many many rounds of replication, so that a large number of mutually complementary strands are already formed in the system in accordance with the BPR.

2. There are long range orderings involving both "spins" and "pseudo-spins" along the directions of 'rungs' i.e. perpendicular to the strands with the pseudo-spins exhibiting ferromagnetism and the spins displaying anti-ferromagnetism in the quantum spin model [1]. The arrangements of spins and pseudo-spins along any strand are however random [1].

3. The tautomeric mutation implies excitations in either or both spin channels and pseudo-spin channels brought about by the transverse field H through flipping action in the quantum spin model.

4. We bosonize the entire Hamiltonian corresponding to the quantum spin model for DNA, by making use of Holstein-Primakoff transformations for both spin and pseudo-spin sectors.

   Holstein-Primakoff transformations (HPT) are very well known transformations in condensed matter physics, in particular in the field of magnetism [8-11]. It relates the quantum spin operators to a set of bosonic operators in the ordered phase of a ferromagnet or anti-ferromagnet. It is ensured that these transformations preserve the respective commutation algebras of both spin operators and bosonic operators. These bosonic operators are real space bosonic operators to start with, representing spin flips implying excitations or de-excitations in the ordered phase. The corresponding q-space bosonic operators can easily be constructed by taking Fourier Transforms. At very low temperatures, the spin Hamiltonian for a ferromagnet or anti-ferromagnet can be approximately diagonalized in terms of these q-space bosonic operators, representing collective modes. This scheme is known as 'bosonization'. These above bosonic operators in fact correspond to creation and destruction of new bosonic particles known as "magnons" in the field of magnetism.

   In our case with DNA, we apply the above procedure corresponding to the ordered structures for both 'spin' and 'pseudo-spin' to generate the bosonic excitations. Besides, we take the Fourier Transform along the rungs and proceed accordingly.

5. Treating the inter-strand term as the principal term and the intra-strand term as a perturbation in the bosonized version of the Hamiltonian, we would now like to carry out a Schrieffer-Wolf like transformation and retain terms upto 3rd order in intra-strand part of the spin model.

   Schrieffer-Wolf transformation (SWT) is another well known transformation in quantum mechanics and is widely used in various fields of condensed matter physics involving many-body effects in particular [8-11]. In this transformation, a Hamiltonian consisting of a principal term and a secondary one is transformed by a similarity transformation to generate an effective Hamiltonian where the secondary term does not occur in linear order. Thus this new effective Hamiltonian contains the higher order contributions (from 2nd order onwards) of the secondary term besides the principal term. This gives rise to new interaction processes bringing in a lot of additional physics. This transformation is particularly very useful and popular in the field of superconductivity dealing with electron-phonon interaction based pairing mechanism and other types of boson mediated pairing as well. Besides, SWT is also made use of extensively in the theoretical treatment of Anderson-Kondo-Mixed valency problem [11].

6. We apply SWT to the Hamiltonian corresponding to the quantum spin model for DNA, with the inter-strand Ising part as the principal term and the intra-strand transverse field containing part involving flipping operators, as the secondary term. The rationale for this procedure is that from the operator composition of the original quantum spin Hamiltonian, this scheme is expected to generate an effective Hamiltonian quite similar in structure to the one proposed in the bosonic model, when retaining the low order contributions in the transformed expression. This would then lead to a unification of the two quantum models put forward.

   It should be pointed out here that whereas the bosonic model proposes the intra-strand hopping of only one kind of boson, the calculations with the quantum spin model is very much likely to produce the hopping of two kinds of bosons viz. the HP bosons belonging to both spin sector and pseudo-spin sector. Besides, the effective Hamiltonian generated from this calculation based on SWT, may also contain an additional term of 2nd order in intra-strand part as well, which has no analogue in the bosonic model.

We now present the calculations in somewhat details in the following section.

3 Calculations

We recall that in the quantum spin model, we have the principal part identified with $\mathcal{H}_{Ising}$ and the perturbation part being $\mathcal{H}_{Transverse}$. The standard Schrieffer-Wolf transformation (SWT) then leads to the following expression for the effective Hamiltonian:-

$$\mathcal{H}_{eff} = \mathcal{H}_{Ising} + [\mathcal{H}_{Transverse}, S] + \frac{1}{2}[[\mathcal{H}_{QSM}, S], S] + higherorders(neglected) \qquad (6)$$

by keeping terms up to 3rd order in perturbation, as stated earlier; where the operator $\hat{S}$ satisfies the equation

$$[\mathcal{H}_{Ising}, S] + \mathcal{H}_{Transverse} = 0 \tag{7}$$

ensuring that a term 1st order in $\mathcal{H}_{Transverse}$ does not occur in $\mathcal{H}_{eff}$.

It is assumed here that the operator S has similar structure and is of the same order as $\mathcal{H}_{Transverse}$. Therefore $\hat{S}$ can easily be determined from the above equation (7) as:-

$$S^{mn} = \frac{\mathcal{H}^{mn}_{Transverse}}{(E_n - E_m)} \tag{8}$$

where the corresponding matrix elements of the operators have been related with E's being the eigenvalues of $\mathcal{H}_{Ising}$, which are $\frac{-\lambda i}{4}$ and zero only, as can be seen easily from its form.

Thus making use of the above set of equations, one can extract the corresponding matrix elements of the operator term which is of 3rd order in $\mathcal{H}_{Transverse}$, occurring in $\mathcal{H}_{eff}$. Taking into account the two strands, one needs to evaluate 16 matrix elements. This enables one to write down the full formal expression for $\mathcal{H}_{eff}$, which would be pretty long.

We now show below that the term 3rd order in $_{Transverse}$ indeed contains the 2nd term (hopping term) of the bosonic model. Besides, we also show that $_{Ising}$ of the quantum spin model can easily be identified with the 1st term (site energy term) of the bosonic model as well. To show this explicitly, we need to carry out the bosonization operation as discussed earlier.

The Holstein-Primakoff transformations (HPT) take the following forms here:-

(a): Spins forming anti-ferromagnetic ladder:

$$\begin{aligned} S_i^z &= SI - a_i^+ a_i \\ S_i^+ &= (2S)^{\frac{1}{2}} \left(I - \frac{a_i^+ a_i}{2S} \right)^{\frac{1}{2}} a_i \\ S_i^- &= (2S)^{\frac{1}{2}} a_i^+ \left(I - \frac{a_i^+ a_i}{2S} \right)^{\frac{1}{2}} \end{aligned} \tag{9}$$

for up spin ($\uparrow$) sublattice with $S = \frac{1}{2}$ and

$$\begin{aligned} S_i^z &= -SI + b_i^+ b_i \\ S_i^+ &= (2S)^{\frac{1}{2}} \left(I - \frac{b_i^+ b_i}{2S} \right)^{\frac{1}{2}} b_i^+ \\ \hat{S_i^-} &= (2S)^{\frac{1}{2}} b_i \left(I - \frac{b_i^+ b_i}{2S} \right)^{\frac{1}{2}} \end{aligned} \tag{10}$$

for down spin ($\downarrow$) sublattice with $S = \frac{1}{2}$.

The quantities a_i^+ and b_i^+ are the boson operators representing spin flips at site i corresponding to the up and down sublattices respectively.

(b): Pseudo-spins forming ferromagnetic ladder:

The transformations are very similar to the above equation 9, excepting that there is only one lattice with up pseudo-spin ($\uparrow$) present and that the corresponding boson operator is represented as $\tilde{b_i}$ or $\tilde{b_i^+}$ corresponding to destruction or creation of this bosonic excitation.

Making use of the above transformation equations (HPT) corresponding to both spin and pseudo-spin and incorporating them in the original $\hat{\mathcal{H}}_{QSM}$, we get the following equations keeping the bosonic operators in the lowest order:-

$$\mathcal{H}_{Ising}^{inter-strand} = \left[E_G I + \sum_n \left[E_0 \left(a_n^{1^+} a_n^1 + b_n^{2^+} b_n^2 + \tilde{b_n^{1^+}} \tilde{b_n^1} + \tilde{b_n^{2^+}} \tilde{b_n^2} \right) \right] \right] \tag{11}$$

where

$$E_G = -\frac{\lambda^{1,2}}{16}$$

and

$$E_0 = \frac{\lambda^{1,2}}{8}$$

with 'I' being the identity operator and assuming site independence of the inter-strand coupling; and

$$\begin{aligned} \left[\mathcal{H}_{Transverse}^{intra-strand}\right]^3 = \left(\frac{1}{8}\right) \sum_{i,j,k,l1,l2,l3} [[\ H_i^{sp} H_j^{sp} H_k^{sp} \{\ a_i^{l1^+} a_j^{l2} a_k^{l3^+} \delta_{\sigma_i,\sigma_k} \\ + b_i^{l1^+} b_j^{l2} b_k^{l3^+} \delta_{\sigma_i,\sigma_k} + a_i^{l1^+} a_j^{l2} b_k^{l3^+} \delta_{\sigma_i,-\sigma_k} + \text{terms with} \\ \text{similar combinations involving interchanges between} \\ \text{l1, l2 and l3 } \} \delta_{ij} \delta_{i\pm1,k} \delta_{l1,l2} \delta_{l2,l3} \ ] + [\ H_i^{psp} H_j^{psp} H_k^{psp} \\ \{\ b_i^{\sim l1^+} b_j^{\sim l2} b_k^{\sim l3^+} \delta_{\sigma_{i(psp)},\sigma_{j(psp)}} + \text{terms with similar} \\ \text{combinations involving interchanges between l1, l2} \\ \text{and l3 } \} \delta_{ij} \delta_{i\pm1,k} \delta_{l1,l2} \delta_{l2,l3} \ ] + \text{terms of different types} \\ \text{not contributing to the intra-strand hopping of boson} \\ \text{between nearest neighbors }] \end{aligned} \tag{12}$$

We will assume the transverse field H_i to be site independent (H) later.

The quantities $l1$, $l2$ and $l3$ represent strand indices and take values 1 and 2 considering only the two primary strands.

Comparing these expressions with those from $\mathcal{H}_{bosonic}$ (see equation 4) we get,

$$(E_0)_{bosonic} = \left(\frac{1}{8}\right) \lambda^{1,2} \tag{13}$$

and

$$\kappa \approx \left(\frac{1}{4}\right) H^3 \tag{14}$$

In the above calculations, we have taken into account the contributions to the nearest neighbor hopping of the bosons arising from both spin and pseudo-spin sectors in any one strand. Furthermore, we have also assumed the site independence of the transverse field coupling to both spins and pseudo-spins.

Thus we have been able to identify the parameters occurring in the bosonic model in terms of those of the quantum spin model, as given in the equations 13 and 14. This therefore implies a unification of the two approaches based on quantum modelling.

It must be emphasized however, that the exact or more correct relations between the coefficients of the two models can be obtained only after writing down the full (and very long !) expression for $\mathcal{H}_{eff}$.

4 Results and discussions

The main results and the salient features which follow from the calculation reported here are highlighted below:-

1. The two independent quantum Hamiltonians put forward for modelling the tautomeric mutation of DNA, viz. quantum spin model and the bosonic model can indeed be unified. More precisely, the bosonic model can itself be obtained from the spin model in a perturbation expansion retained upto low order, after carrying out bosonization of the spin model.

2. Through our proposed unification scheme for connecting the two quantum models, the nature of bosons occurring in the bosonic model have become more precisely and clearly physically defined and identified. Moreover these bosons are found to be of two different/ distinct types, arising from the spin and the pesudo-spin sectors, as has been explained earlier.

3. The phonons are implicitly present in our calculations through the presence of the external transverse field H_i appearing in the quantum spin model. The existence of this hidden coupling between the phonons and magnons/pseudo-magnons is however extremely important and crucial for providing the physical basis and rationale in the unification of the two quantum models. Moreover, this coupling also plays the pivotal role in future calculations of some more important properties of DNA, to be discussed in the next section.

4. The lowest order processes present in the calculations described in this article are those involving 1 phonon- 1 magnon/1 pseudo-magnon and 1 phonon- 3 magnon/ 3 pseudo-magnon, as the operator structure of $\hat{\mathcal{H}}_{Transverse}$ would suggest. For our unification calculation relating the quantum spin model with the bosonic model presented in this article, we however have only retained the 1 phonon- 1 magnon/ 1 pseudo-magnon process in the very lowest order for simplicity.

5. The lowest order process referred above, is a virtual process not conserving energy strictly speaking. For the macroscopic size of a DNA molecule with a long time duration of observation, which is the case assumed here in the calculations, the bosons (magnons and the pseudo-magnons) acquire very large life times and become almost "stable particles" for all practical purposes, as expected. Therefore these bosons behave really like genuine quasi-particles and contribute to the various thermodynamic and electromagnetic response functions of DNA, to be touched upon in the next section.

6. In our quantum spin model each strand has been assumed to be of paramagnetic nature in both spin and pseudo-spin [1]. In view of the presence of covalent bonding between the adjacent nucleotides situated in a strand for a real DNA molecule [2-4] however, the spins and pseudo-spins in a strand, introduced in our quantum spin

model, should in fact be correlated. This would reduce the degree of degeneracy of the ground state corresponding to any strand, substantially from the ideal value of 4N assumed in our calculations and would also affect the expression obtained for the repairing efficiency [1]. The relation between the quantum spin model and the bosonic model derived in this article, remains intact though.

5 Applications and future plans

Our calculations presented in somewhat details in this article, bring out the crucial and non-trivial importance of the role played by the quantum fluctuations in the phenomena of tautomeric mutations in DNA. Quite interestingly, this theoretical approach and calculations find ready and promising applications in several other related phenomena. The most notable amongst these are:- Denaturation dynamics of DNA molecule, response of DNA to terahertz radiation and effective mutation rate observed in various organisms. Our calculations involving quantum models can easily be utilized and extended to study these phenomena and properties. These are discussed below in somewhat details.

(i) Denaturation dynamics:

At a sufficiently high temperature a DNA molecule 'melts' i.e. the two complementary strands of DNA get delinked. This is due to the rupture of the hydrogen bonds between the complementary bases. This process is known as denaturation of DNA [4]. Because the G-C bonds are stronger than the A-T bonds, the (G+C) rich DNA configuration has a higher melting temperature than that of (A+T) rich configuration [4]. The melting temperature (T_m) is defined as the temperature at which at least 50 per cent of the hydrogen bonds have been broken.

It may be recalled that in our calculations involving quantum spin model, we had obtained an expression for the Base Pair Transition rate by the 2nd order of perturbation treatment with the transverse field containing term [1]. This contribution would then have an additional effect on the thermally driven melting process and denaturation dynamics in general. Since our calculation has been done at zero temperature, this study would determine the role of pure quantum fluctuations in the melting and denaturation of DNA. Intuitively, it is expected to bring down Tm. It is worthwhile to mention that our treatment has modelled the structure of DNA simply as a pair of linear strands with complementary base pairs facing each other, in accordance with the well known Peyrard-Bishop (PB) model [12]. At the same time it is also to be emphasized that without invoking any inter-ionic potentials i.e. intra-base pair as well as nearest neighbor inter-base pair potentials heuristically, as have been done in several other theoretical approaches using PB model [13], the very quantum origin of tautomeric fluctuations can be made use of readily to directly study the denaturation dynamics in our approach. The parameters in our theoretical procedure would however consist only of 2 quantities viz. the inter-strand coupling λ and the intra-strand transverse field H, as has been explained earlier.

(ii) Response to terahertz radiation:

The mutation rate in DNA under electromagnetic (EM) irradiation shows an enhancement in general [3, 4]. The high energy irradiation with Ultra-violet (UV) rays and X-rays is found to trigger point mutations and the rate/ percentage of mutation grows steeply with increase in radiation dose as well, although exhibiting a linear dependence approximately [4]. This is very much expected as the high frequency EM radiation can easily break the chemical bonds and cause mutations. On the contrary, the effect of low fre-

quency EM radiation on biological systems, more specifically on genetic materials and enzymatic reactions, known as "mw-effect" has been rather debatable [14, 15]. Recently it has been proposed based on improved mathematical modeling (by carrying out calculations on an extension of Peyrard- Bishop model), that a resonance type of interaction between terahertz (THz) radiation and the coupled modes involving torsional modes and the hydrogen bond stretching modes with bond energies in THz range, may cause partial and even complete destruction of hydrogen bonds between the corresponding bases of the two complementary strands of DNA molecule [15]. This idea finds a positive experimental support as well from the study of non-thermal effects of THz radiation on certain biosensor cells [16]. Besides, the experiments with THz radiation can also bring out the nature of phonon modes in DNA molecules [17], which are of great importance in our model calculations.

This phenomenon in turn is very much expected to strongly alter the evolution and dynamics of DNA, influencing various bio-physical processes like replication and transcription. Our formalism and calculational scheme based on quantum spin model can easily be made use of in investigating these aspects by first analysing the nature and properties of the excitations (quasi-particles) in this model of ours and then determining their coupling to an external electromagnetic field. Subsequently, the rates of these processes can be calculated as well through standard quantum mechanical scheme based on Fermi's Golden rule by enumerating the various relevant matrix elements, very similar to the one described in our earlier work [1]. This investigation would be taken up in near future.

(iii) Compensation and the effective mutation rate observed in organisms:

Our quantum spin model based calculations explicitly provide mathematical expressions for the tautomeric mutation rate and its compensation rate in a DNA molecule [1]. These are found to be quite consistent and are in broad agreement quantitatively with the observations for the effective mutation rate corresponding to a living system viz. a bacteria called neurospora, as an example [1-4]. The mutation here is predominantly of 'spontaneous' type and its frequency of occurrence is rather low. The effective mutation rate as observed, however also contains a compensatory contribution, considered arising only from the 'primary repair processes' or 'proof reading', as is called [1-4, 18]. This is believed to be an intrinsic and internal process for a living system carried out by a special class of enzymes. On the other hand, our calculation involving quantum spin modelling very firmly establishes that the observed rate has another hidden non-trivial compensatory contribution in the form of a 'secondary repair' originating entirely from the quantum fluctuations [1]. Therefore the conventional quantitative analyses based upon the observed mutational rate should be relooked into, taking into account this novel compensatory mechanism. It is worthwhile to point out that an estimate of the ratio of secondary repair rate and the primary repair rate shows it to be of the order of 1 per cent [1-4, 18]. Therefore the secondary repair process can't be ignored at all when determining or estimating the effective mutation rate of DNA in various organisms.

6 Concluding Remarks

The understanding of the phenomenon of tautomeric mutation in DNA is very exciting and important for molecular biologists. Nevertheless, it is turning out to be equally challenging for condensed matter physicists to construct appropriate models containing microscopic flavours to describe this phenomenon, which is predominantly of quantum ori-

gin and affects a long-range spatial ordering. In particular, the quantum models proposed and looking quite similar to models or Hamiltonians used to describe various phenomena and processes in condensed matter systems, are found to be very appropriate and extremely powerful in handling the problem of tautomeric mutation. These models have been remarkably successful in explaining the processes of both DNA mutation and compensation/repair in various living organisms, qualitatively as well as semi-quantitatively [1-3]. Besides, a unification between these different types of suggested models has been achieved quite satisfactorily by making use of principles of quantum physics and in a manner analogous to that used in treating various phenomena in condensed matter physics, as has been elaborated in this article.

Furthermore, many other diverse phenomena involving DNA and related to tautomeric mutation, such as denaturation and mutation induced by THz radiation can also be investigated theoretically by applying quantum mechanical formalisms and treatments to these proposed models, in particular the quantum spin model. These extended calculations and the comparison of the corresponding theoretical results with those from experiments performed on DNA extracted from various organisms, would definitely be very crucial to test the strength and the universality of our proposed quantum models further.

This whole endeavour is also greatly expected to throw new light and provide new directions on a meaningful and successful synthesis of molecular bio-physics with condensed matter physics in general and in relation to the problems of DNA in particular.

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