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A MODEL ANALYSIS OF MICROWAVE INDUCED MUTATIONS

by

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ABSTRACT

We show that the resonant excitation of localized vibrational modes by microwaves recently reported in DNA, cannot account for the enhancement of the mutation rate observed in viruses irradiated with microwaves of 130 MHz. This conclusion was obtained within the tautomeric shift model of mutations.

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INTRODUCTION

Experiments performed in the sixties [1] on bacteriophages showed that the number of mutants as a function of the frequency of the microwave with which they were irradiated during the reproduction had a resonance around 130 MHz with a line width of about 30 MHz. This is shown in Fig. 1. The peak value is about 4 times larger than the background mutation rate.

At that time, attempts to interpret these results with a model of mutations based on the induction of tautomeric forms [2] of the nucleotides were unsuccessful, mainly because the energy of the microwave photon is too low by several orders of magnitude to induce the required transition. Furthermore, calculations showed that during the separation of the strands of DNA the protons of the hydrogen bonds in the base pairs become more localized making difficult a tautomeric transformation [3].

Recently, a series of papers [4,5] appeared in which the resonant absorption of microwave energy by DNA is reported. This energy excites vibrational modes of the molecule and suggests a possible connexion between the resonant absorption of microwaves and the resonance in the mutation rate.

This connexion becomes particularly plausible considering that a detailed calculation of the vibrational modes of DNA chains shows that when excited with microwaves, localized vibrational modes are also excited at the extremes. As a result, the amplitude of the oscillations of the base pairs linked by hydrogen bonds at the extremes of DNA may be very large (a tenth of an Angstrom) [6]. But it is precisely at the end

of the DNA chain where the replication takes place and the mutations are more likely to happen. Thus, the mutation rate would probe the localized vibrational modes at the replication sites.

Encouraged by these ideas we revisited the old tautomeric model in a very simplified version and incorporated the vibrational modes. Here we show that the localized vibrational modes, at least in this model with a reasonable set of parameters, can not induce either the required rate of tautomeric transformations.

MODEL

Let us consider a double hydrogen bond as occurs in the A-T pair of DNA [2]. Each proton is in an asymmetric double well potential. The protons are in a ground state (normal position) and from time to time tunnel to the opposite well (tautomeric form), Fig. 2. Due to their coulomb charge and proximity, the motion of the two protons is highly correlated (if one jumps, the other has to jump also). Thus, we consider the dynamics of only one proton. The asymmetric double well potential will be described by two delta functions; admittedly this is not a realistic potential but it contains the essential physical features and it can be solved analytically. The separation of the potential wells will be considered as an external dynamical variable driven by the localized modes and treated by perturbation theory in the adiabatic approximation. The unperturbed Hamiltonian is

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$$H = \frac{p^2}{2M} - J\{(1+\alpha)\delta(x-a) + (1-\alpha)\delta(x+a)\}, \quad (1)$$

where M is the proton mass, J is a coupling constant describing the strength of the delta potentials, α is a measure of the asymmetry of the potential and $2a$ is the separation between the wells.

Schroedinger's equation $H\psi = E\psi$ has bounded state solutions of the form

$$\psi(x) = \begin{cases} A e^{-kx} & \text{for } x > a \\ B e^{-kx} + C e^{kx} & \text{for } |x| < a \\ D e^{kx} & \text{for } x < -a \end{cases}, \quad (2)$$

with $E = -\hbar^2 k^2 / (2M)$. The continuity of ψ requires that

$$B = \frac{D - A e^{-\rho}}{2 \sinh \rho}, \quad C = \frac{A - D e^{-\rho}}{2 \sinh \rho}, \quad (3)$$

where $\rho = 2ka$. The solution at the singular points $x = a, -a$, together with Eqs. (3), require that [7]

$$A [e^{\rho} - (2\mu/\rho)(1+\alpha)\sinh\rho] - D = 0 \quad (4)$$

$$A - [e^{\rho} - (2\mu/\rho)(1-\alpha)\sinh\rho]D = 0$$

where we defined the dimensionless parameter $\mu = 2MJ a / \hbar^2$. Eqs.

(4) yield the secular equations for ρ :

$$\rho = \mu \{1 + q [\alpha^2 + (1 - \alpha^2) e^{-2\rho}]^{1/2}\} \quad (5)$$

where $q = 1$ corresponds to the ground state and $q = -1$ to the excited state. This system has only two bounded states and Eqs. (3-5) provide the exact solution. We are, however, interested in the case of large separation between wells, namely $e^{-2\rho} \ll 1$. In that limit the normalized solutions are

$$(D/A)_g \approx [(1 + \alpha)/(2\alpha)] e^{-\rho_g} \quad (6)$$

$$(B/A)_g \approx [(1 - \alpha)/(2\alpha)] e^{-2\rho_g} \quad (7)$$

$$(C/A)_g \approx e^{-\rho_g} \quad (8)$$

$$A_g = \sqrt{k_g} e^{\rho_g/2} \quad (9)$$

with

$$E_g \approx -J\mu (1 + \alpha)^2 / (4a) \quad , \quad \rho_g \approx \mu(1 + \alpha) \quad , \quad (10)$$

where the subindex g stands for ground state. For the excited state (e) one has

$$(A/D)_e \approx - [(1 - \alpha)/(2\alpha)] e^{-\rho_e} \quad (11)$$

$$(B/D)_e \approx e^{-\rho_e} \quad (12)$$

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$$(C/D)_e = -[(1 + \alpha)/(2\alpha)] e^{-2\rho_e} \quad (13)$$

$$\rho_e \approx -\sqrt{k_e} e^{\rho} e^{1/2} \quad (14)$$

with

$$E_e \approx -J\mu(1 - \alpha)^2/(4a) \quad ; \quad \rho_e \approx \mu(1 - \alpha) \quad . \quad (15)$$

The activation energy is

$$\Delta E = E_e - E_g = J\mu\alpha/a \quad . \quad (16)$$

In this approximation both E_g and E_e are independent of a .

PERTURBATION THEORY

The perturbation Hamiltonian is

$$\begin{aligned} H_{int} &= (\partial H/\partial a)_a \xi \\ &= J\{(1 + \alpha)\delta'(x - a) - (1 - \alpha)\delta'(x + a)\}\xi \end{aligned} \quad (17)$$

where $\xi = \xi_0 \sin \Omega t$ is the varying distance between the potential wells. Since the energy of the localized mode $\hbar\Omega$ is much smaller than the activation energy ΔE , the adiabatic approximation is adequate [8]. To lowest order the unperturbed ground state is given by

$$\phi = \psi_g(t) e^{-iE_g t/\hbar} + \kappa(t) \psi_e(t) e^{-iE_e t/\hbar} \quad (18)$$

where $\psi_{g,e}(t) = \psi_{g,e}(x, a(t))$ and the time dependence of E_g and E_e has been neglected (this is quite accurate in the limit of large separation). Then, $\kappa(t)$ is given by Eq. (31.11) of Ref. 8:

$$\kappa(t) = \frac{\Omega \langle \psi_e | H_{int} | \psi_g \rangle_0}{i(\Delta E)^2} (e^{i\Delta E t/\hbar} \cos \Omega t - 1) \quad (19)$$

Although ψ has discontinuous derivatives at $x=a$ and $-a$, the matrix element can be easily calculated using the formal relation

$$\int_{-\infty}^{\infty} f(x) \delta'(x) dx = -\frac{1}{2} [f'_+ + f'_-] \equiv -\overline{f'(0)} \quad (20)$$

where f'_+ and f'_- are the derivatives of the function $f(x)$ to the right and to the left of the point $x = 0$. If $f(x)$ has continuous derivatives Eq. (20) yields the usual relation. In the limit of large separation, using Eqs. (6-15), it results

$$\langle \psi_e | H_{int} | \psi_g \rangle_0 = 2 J \xi_0 (1 - \alpha^2)^{3/2} (\mu/2a)^2 e^{-\mu} \sinh(\mu a) \quad (21)$$

THE TAUTOMERIC STATE

The ratio of the probabilities of finding the tautomeric state and the normal state is identified with the ratio, P_t , of the densities of probability at $x = -a$ and $x = a$. At finite temperatures, in particular at room temperature, the main con

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tribution P_T , to P , comes from the thermal population of the excited state, that is

$$P_T = \frac{|\psi_e(-a)|^2}{|\psi_g(a)|^2} e^{-\Delta E/T} \approx \frac{1+\alpha}{1-\alpha} e^{-\Delta E/T}, \quad (22)$$

The mixture of wavefunctions due to vibrations produces the additional contribution

$$P_L = \frac{|\psi_e(-a)|^2}{|\psi_g(a)|^2} \overline{|\kappa|^2} \approx \frac{1+\alpha}{1-\alpha} \frac{3}{16} \frac{(1-\alpha^2)^3}{\alpha^4} \left(\frac{\hbar\Omega}{J/\xi_0}\right)^2 e^{-2\mu(1-\alpha)}, \quad (23)$$

where a time average has been taken over $|\kappa(t)|^2$.

NUMERICAL EXAMPLE

Fig. 3 shows $\text{Log } P_T$ and $\text{Log } P_L$ as a function of the ground state energy of the proton between 0.5 and 1.2 eV and for two values of the asymmetry $\alpha = 0.3$ and $\alpha = 0.5$. For this plot we used the values $a = 0.5 \text{ \AA}$, $\xi_0 = 0.05 \text{ \AA}$, $\Omega/2\pi = 100 \text{ MHz}$, $T = 0.025 \text{ eV}$. In this model P_T is related to the natural mutation rate and it has been estimated to be in range $10^{-9} - 10^{-7}$. [2]

CONCLUSIONS

It can be seen in Fig.3 that the value of P_L is in every case several orders of magnitude smaller than P_T . Thus, at least

within this model, the vibrational modes cannot account for the amplification factor of 4 in the mutation rate induced by the microwave energy.

FIGURE CAPTIONS

- Fig. 1 - Mutation rate as a function of the microwave frequency.
- Fig. 2 - Pair of nucleotides adenine (A) - thymine (T) showing the hydrogen bonds and the corresponding asymmetric well potential. (a) Schematic diagram of the adenine (A)-thymine (T) base pair. (b) Potential energy corresponding to the upper hydrogen bond in a).
- Fig. 3 - Mutations rates, P , due to thermally induced (T) and vibrationally induced (L) tautomeric shifts as a function of ground state energy for two values of the asymmetry parameter.

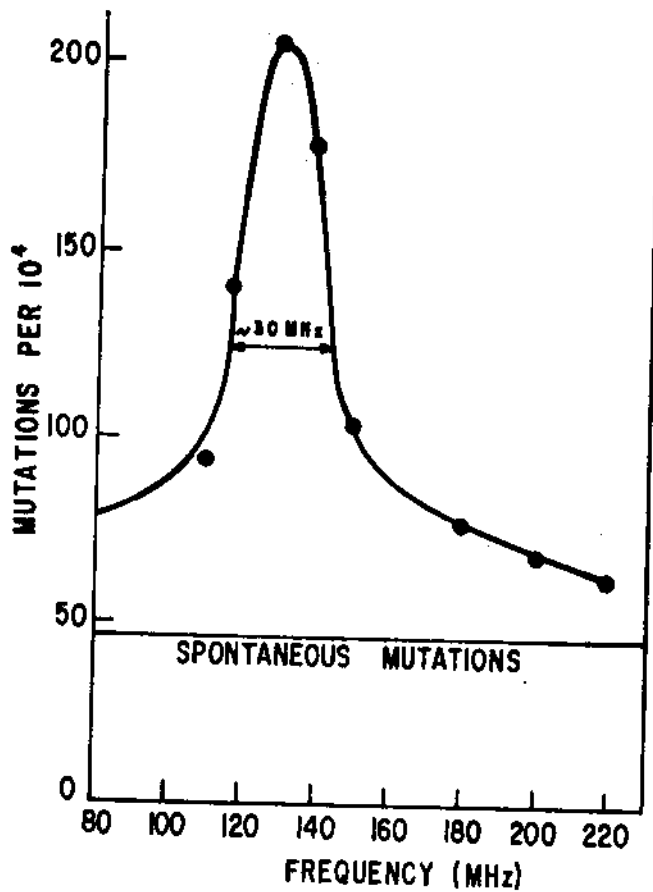


Fig. 1

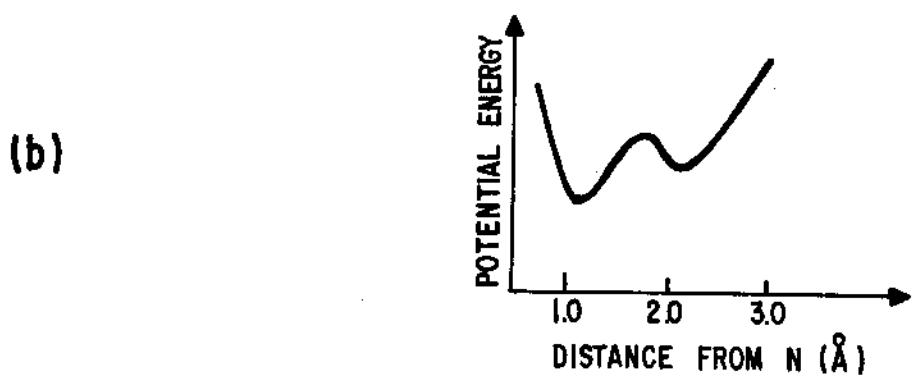
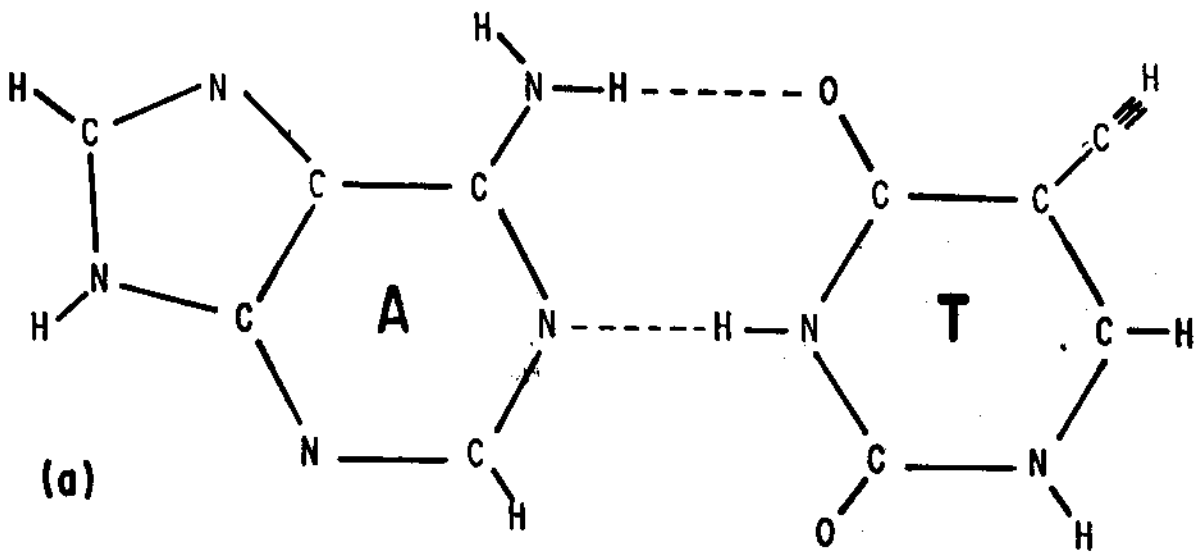


Fig. 2

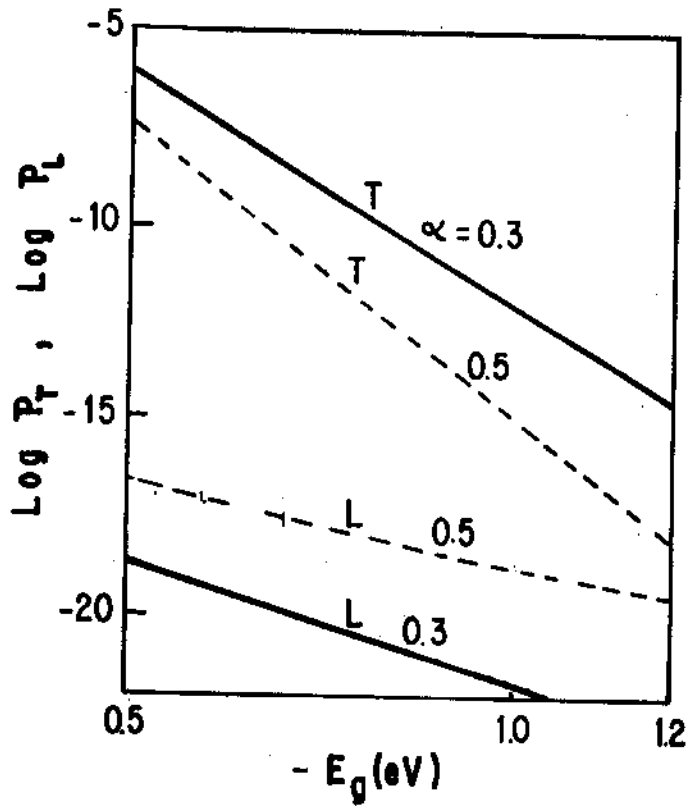


FIG. 3

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