Fluctuation-Facilitated Charge Migration along DNA

R. Bruinsma,* G. Grüner, M. R. D'Orsogna, and J. Rudnick

Department of Physics, UCLA, 405 Hilgard Avenue, Los Angeles, California 90095-1547
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We propose a model Hamiltonian for charge transfer along the DNA double helix with temperature-driven fluctuations in the base pair positions acting as the rate limiting factor for charge transfer between neighboring base pairs. We compare the predictions of the model with the recent work of Barton and Zewail on the unusual two-stage charge transfer of DNA.

Charge transport and electrical conduction is known to occur in a wide range of organic linear-chain crystals of stacked planar molecules [1]. Transfer rates from molecule to molecule are determined by the single-particle transfer integral τ, with typical rates of the order of $1/10^{-15}$ sec. Strong interaction between the electronic degrees of freedom and molecular vibrations may reduce this to $1/10^{-12}$ sec, a typical lattice or intramolecular vibration frequency. By comparison, biochemical charge-transfer processes, such as those encountered in the metabolic redox ("oxidation-reduction") chains [2], usually are much slower (down to 1 sec^{-1}). Key steps often involve some form of large-scale motion of the molecule.

DNA can be considered as a one-dimensional, aperiodic, linear chain of stacked base pairs. More than 30 years ago, it was suggested that duplex DNA might support electron transport in a manner similar to that of the linear-chain compounds, namely, by tunneling along overlapping p orbitals located on the base pairs [3,4]. Hall *et al.* [5] first presented evidence that photoinduced, radical cations can travel along DNA molecules in aqueous solution over quite considerable distances (more than 40 Å, or about ten base pairs). If so, DNA might present us with flexible, molecular-size wires able to transport charge in aqueous environments. Possible applications range from microelectronics to long-range detection of DNA damage. Subsequent studies by a number of groups reported a wide range of values for the effective inverse spatial carrier decay length β, ranging from as low [6] as 0.02 Å^{-1} to as high [7] as around 1 Å^{-1}, the different values most probably reflecting differences in charge transfer for different base sequences [8].

Recently, Wan and co-workers (hereafter referred to as BZ) [9] used femtosecond spectroscopy to measure the rates of the DNA charge-transfer process. An unusual two-step decay process was observed with characteristic time scales of 5 and 75 ps, respectively. *Ab initio* molecular-orbital calculations [10–12] find that DNA has a large single-particle band gap, and a transfer integral τ of order 0.1 eV [13]. This would lead to a charge-transfer rate τ/h for coherent tunneling that is comparable to that of the linear-chain compounds, but that is much too high compared to the rates measured by BZ.

Apart from coherent tunneling [3], a number of alternative transport mechanisms have been proposed, in particular, incoherent, phonon-assisted electron hopping between bases, with the electron wave function fully localized on each subsequent base pair [14,15]. This would reduce the transfer rate to a typical intramolecular vibrational frequency (ps^{-1}), but this still is much too large to explain the slow second-stage step of the decay. It was also suggested that a charged radical could induce a polaronic distortion [16] of the DNA internal structure that might control charge transfer. The explanation proposed by BZ for the long relaxation times is that large-amplitude thermal fluctuations of the intercalated photoreceptor sets the rate-limiting step for the charge transfer. The polaronic scenario for charge transport has also been discussed by Ly *et al.* [17] and by Conwell and Rakhmanova [18].

The aim of this Letter is to construct a model Hamiltonian to treat charge transfer along a chain under conditions of *large structural fluctuations,* and suggest that thermally induced structural disorder interferes with the π-orbital overlap mediated charge transfer, leading to long relaxation times. To construct this Hamiltonian, we first must discuss the origin of the structural fluctuations. Figure 1 shows an example of a typical DNA configuration obtained by a molecular dynamics (MD) simulation [19]. The relative orientation of neighboring bases along DNA is characterized by a set of collective variables such as the relative roll and twist angles (R and T) and the relative slide displacement (see lower portion of Fig. 1). Long-time MD simulations of DNA lead to typical rms fluctuation angles for R and T of order 5 and 9 deg [20] in the ps to ns time window, while the mean base pair spacing also shows large-amplitude fluctuations [21]. Structural fluctuations in the ps to ns time window have been observed [22] experimentally as dynamic Stokes shifts in the fluorescence spectrum of DNA. These local fluctuations are extraordinarily strong compared with those due to thermally excited phonon modes in crystalline linear-chain materials. The unusual "softness" of the R, S, and T variables is also reflected by the fact that their *mean values* vary greatly depending on base pair sequence [23].

In our simplified model, we include only two collective modes. The first mode is an angular variable $\theta(t)$, which is
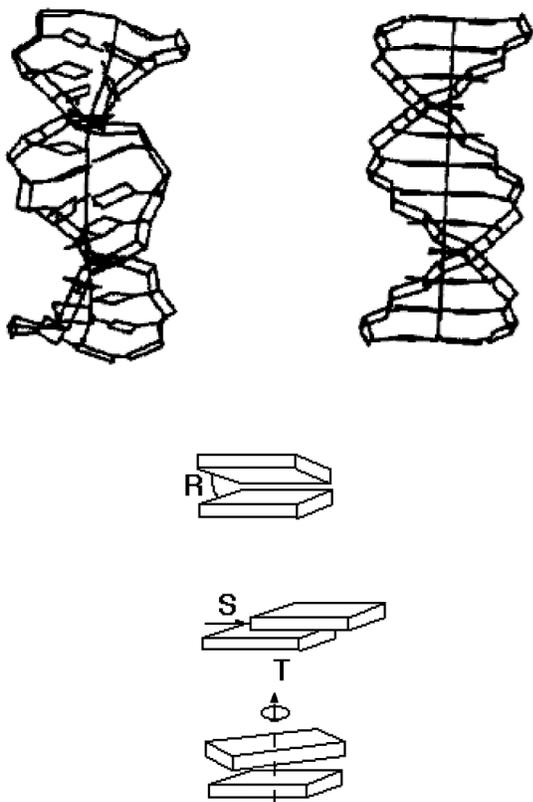
FIG. 1.　Upper left: Snapshot of the result of a 140 ps finite temperature simulation of DNA by Swaminathan *et al.* [19]. Upper right: the ordered $t = 0$ DNA structure. Lower portion: Illustrations of the roll (R), slide (S), and twist (T) motions of adjacent base pairs.

that relative rotation angle of the two bases which couples most efficiently to the π-orbital tunnel matrix element. Next, the displacement variable $y(t)$ represents that collective mode which couples most efficiently to the on-site energy of the radical. This second form of coupling provides the necessary mechanism for energy transfer between the charge and the thermal reservoir required for hopping transport along a random sequence of base pairs with different on-site energies. Both $\theta(t)$ and $y(t)$ are treated as classical harmonic variables that are coupled to a heat bath of oscillators. As a result, $\theta(t)$ and $y(t)$ obey—in the absence of the radical—the following Langevin equations:

$$M \frac{d^2y(t)}{dt^2} + \gamma_y \frac{dy(t)}{dt} + M\Omega_y^2 y(t) = \eta_y(t), \quad (1)$$

$$I \frac{d^2\theta(t)}{dt^2} + \gamma_\theta \frac{d\theta(t)}{dt} + I\Omega_\theta^2 \theta(t) = \eta_\theta(t). \quad (2)$$

In Eqs. (1) and (2), I is the reduced moment of inertia for the relative rotation of the two adjacent bases, Ω_θ is the oscillator frequency of the rotation mode, while M and Ω_y are the reduced mass and natural frequency of the displacement mode. The values of M, I, Ω_θ, Ω_y, and the damping coefficients are obtained by comparing the Fourier power spectra of $y(t)$ and $\theta(t)$ obtained from Eqs. (1) and (2), to power spectra of MD simulations of DNA [24]. From a typical long-time (10 ns) MD time series, we find oscillation periods $2\pi/\Omega$ of order 1–10 ps, a (large) mass M of order 1–10 kdalton, a moment of inertia I of order $10^2 k_B T \Omega_\theta^{-2}$, and relaxation times comparable to the oscillation period (i.e., the slow modes are close to critical damping). The amplitudes of the white-noise variables $\eta(t)$ follow from the fluctuation-dissipation theorem for classical variables. We will neglect mode coupling between different pairs of adjacent base pairs. The two modes are then coupled to a one-dimensional, tight-binding Hamiltonian for single-particle charge transport:

$$H = \sum_i \left\{ \tau(\theta_{i,i+1})(c_{i+1}^\dagger c_i + c_i^\dagger c_{i+1}) + \epsilon_i c_i^\dagger c_i + \frac{1}{2} I_i(\dot{\theta}_{i,i+1}^2 + \Omega_\theta^2 \theta_{i,i+1}^2) + \frac{1}{2} M_i(\dot{y}_i^2 + \Omega_{y,i}^2(y_i + y_{0,i} c_i^\dagger c_i)^2) \right\} + H_{\text{bath}}(\{\theta, y\}). \tag{3}$$

In Eq. (3), ϵ_i is the on-site electronic energy. The distance $y_{0,i}$ is the change in the equilibrium value of the y variable of the ith base when the particle localizes on that site, while $M\Omega^2 y_0^2$ is the typical deformation energy.

Certain limiting cases of this general Hamiltonian are familiar from studies of one-dimensional charge transport. For uniform ϵ_i and for fixed θ, H is the Hamiltonian of a tight-binding polaron [16]. For fixed θ and y and random ϵ_i, H is the Anderson Hamiltonian for localization in one dimension. For the case of DNA, we assume that site-to-site differences in the value of ϵ_i are of order 0.1 eV based on the sequence-dependent differences in the ionization potential [25]. Next, the transfer integral, $\tau(\theta)$ will be assumed to be small compared to the thermal energy, $k_B T$, for θ near a special value, denoted by θ^*, the "rapid decay state" (see below). Finally, the characteristic interaction energy, $M\Omega^2 y_0^2$, between the charged radical and the on-site structural variable, y, is assumed to be large compared to $k_B T$ (e.g., due to electrostatic effects) and of order ϵ.

In this, unusual, high-temperature/strong-coupling regime, the transfer integral $\tau(\theta)$ is the lowest energy scale. Under these conditions, particle motion described by H is, indeed, dominated by incoherent hopping from site to site. We first restrict ourselves to the case of a particle which resides at site A at time $t = 0$ and then hops to the neighboring site B with a different on-site energy. For fixed θ, the transition rate $\Gamma(\theta)$ for incoherent charge transfer between A and B can be computed by applying the method of Garg, Onuchic, and Ambegaokar (GOA) [26]. In Fig. 2 we show the two potential energy surfaces $V^+(y) = \langle A|H|A \rangle$ and $V^-(y) = \langle B|H|B \rangle$ for the particle on the A and B, respectively, sites as a function
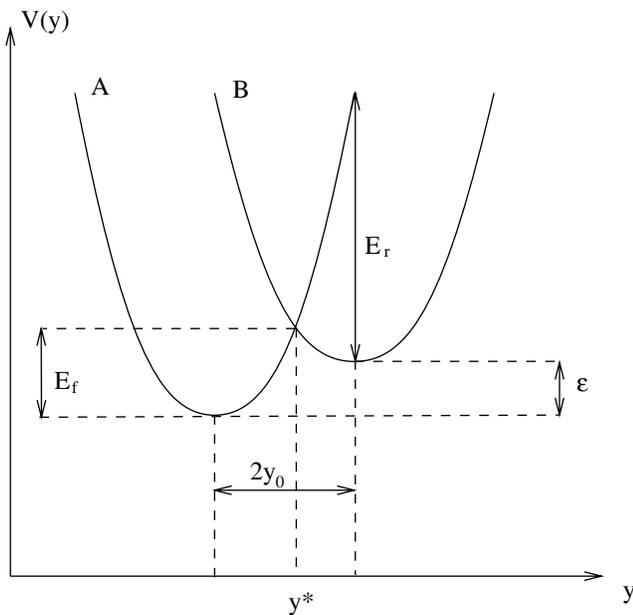
FIG. 2.   Potential energy surfaces for a particle localized on either of two neighboring sites, A and B, as a function of the collective variable, y. The θ variable is assumed fixed. Non-adiabatic transfer between the two surfaces takes place nearly exclusively at the degeneracy point y^*.

of y. If the difference between the on-site energies of the two sites is modest, then the two energy surfaces will cross each other, as shown in Fig. 2. Efficient transfer between the two potential energy surfaces takes place nearly exclusively at the "crossing points" y^*, where $V^+(y^*) = V^-(y^*)$, shown in Fig. 2. Note that an energy barrier E_f must be overcome to reach this crossing point. In the high-temperature, strong-coupling limit, the on-site probability decays exponentially with a rate

$$\Gamma(\theta) \simeq \frac{\tau(\theta)^2}{4\hbar} \left(\frac{\pi}{E_r k_B T}\right)^{1/2} \exp(-E_f/k_B T), \quad (4)$$

where the energy scale E_r defined in Fig. 2, depends on the difference between the on-site energies. The validity condition for Eq. (4) is that $\tau(\theta)$ must be small compared with $(E_r k_B T)^{1/2}$. By itself, Eq. (4) does not account for two-stage decay, as observed by BZ. In a typical ensemble of radical sites (with the same on-site energies) there must be significant heterogeneity, with less likely states characterized by rapid charge transfer and more likely states characterized by low charge transfer rates. This heterogeneity is incorporated by demanding that $\tau(\theta)$ only is appreciable for θ near the special value θ^*, while tunneling plays no role for different θ values [27]. If θ undergoes large-amplitude thermal fluctuations, then there should be considerable heterogeneity for the transfer rates.

Assume then that, at time $t = 0$, an ensemble of particles is prepared on the A site, with the θ(0) variable obeying the Boltzmann distribution. We define the probability density $P(\theta, t)\,d\theta$ to be the fraction of radicals at time t that are still on the A site, and whose θ value is in the

range between θ and $\theta + d\theta$. For the overdamped case of Eq. (2), $P(\theta, t)$ obeys the following equation:

$$\frac{\partial P(\theta, t)}{\partial t} = \left(\frac{k_B T}{\gamma_\theta}\right)\frac{\partial^2 P(\theta, t)}{\partial \theta^2} + \left(\frac{1}{\gamma_\theta}\right)\frac{\partial}{\partial \theta}\left[I\Omega_\theta^2 \theta P(\theta, t)\right]$$
$$- \Gamma(\theta)P(\theta, t). \quad (5)$$

We now use Eq. (5) to discuss the decay rate. For $\Gamma(\theta^*)$ large compared to the thermal equilibrium rate $1/\tau_\theta$ two forms of decay are encountered [28].

(i) Early stage decay.—At time $t = 0$, a certain fraction of the oscillators has an energy exceeding $E = (1/2)I(\Omega_\theta \theta^*)^2$. These oscillators will pass through the $\theta = \theta^*$ point within a time of order max$\{\tau_\theta, \Omega_\theta^{-1}\}$. When this happens, there is a finite probability for charge transfer to take place. On a time scale of order max$\{\tau_\theta, \Omega_\theta^{-1}\}$, these "high energy" oscillators are removed from the probability distribution.

(ii) Late stage decay.—After the high energy oscillators have been removed from the distribution, further decay requires "energy diffusion" along the oscillator energy scale from lower energies towards $E(\theta^*) = (1/2)I(\Omega_\theta \theta^*)^2$. Once the energy of an oscillator reaches this value, efficient charge transfer takes place. After a standard, but lengthy, analysis of Eq. (4), we find that the late-stage decay rate is

$$k_{\text{late}} = \tau_\theta \Omega_\theta^2 \left\{\frac{\theta^* e^{-(1/2)\beta I\Omega_\theta^2 \theta^{*2}}}{\int_{-\infty}^{\infty} e^{-(1/2)\beta I\Omega_\theta^2 \theta^2}\,d\theta}\right\}. \quad (6)$$

The factor in front of Eq. (6) is of order the early-stage decay rate while the term in brackets is of the order of the thermal probability that θ exceeds θ^*. The second-stage decay rate strongly increases with increasing temperature, while early-stage decay is not expected to be strongly temperature dependent although the fraction of sites that exhibits early stage decay should be strongly temperature dependent [of order the term in brackets of Eq. (6)].

The time dependence of $P(\theta, t)$ would be consistent with the observations of BZ if this thermal probability of the θ^* state is of order 0.01. In that case, 1% of the sites would show rapid decay with time scales of order ps, while the remainder would show decay slowed down by a factor of 100. We treated here only the nearest-neighbor hopping process. Charge transport over longer distances described by our Hamiltonian reduces—under the assumed conditions—to classical one-dimensional diffusion in a random medium with site-specific transfer rates. The transport properties of such systems have been extensively discussed elsewhere [29].

In conclusion, we propose that charge transport along DNA proceeds by classical diffusion with high-amplitude thermal fluctuations providing the rate-limiting step for the site-to-site charge transfer. If correct, charge transport along DNA would have unique characteristics as compared to the linear-chain compounds. Since the radical severely deforms the local structure, it might be considered as a polaron in the strong-coupling limit; but, unlike

polaronic transport, hopping is controlled by thermal fluctuations. Indeed, Eq. (6) predicts that the charge-transfer rate should strongly increase with temperature, which is consistent with the observations of BZ. A better description of the mechanism proposed in this paper for charge transfer along DNA would be to consider it as a *repeated sequence of reversible oxidation-reduction reactions*. The site-to-site charge transfer would be viewed as a "chemical reaction," dominated by a "transition state" where the collective variables y and q assume a special value (y^* and θ^*, respectively). We are not aware of any of the linear-chain compounds exhibiting this curious form of charge transfer. On the other hand, a recent single-molecule optical study of a particular reversible oxidation-reduction reaction *did* report [30] two-stage nonexponential behavior but with decay rates much lower than those measured by BZ (in the range of $1 \sec^{-1}$). The higher rates of charge transfer in DNA would be due to the fact that the molecular motion of the bases still is significantly restrained by the backbone. If the present analysis is appropriate, then charge transport in DNA occupies a unique position intermediate between charge transport in solid-state materials and charge transport in biochemical charge-transfer reactions.

Finally, the proposed Hamiltonian obviously incorporates a number of rather serious simplifications. The method described in this paper should apply only to charge transfer between bases with comparable on-site energies, so that the energy difference can be compensated by polaronic deformation energy. This is expected to be the case if the adjacent bases are the same. The two-site energy difference at the border between a GC (guanine-cytosine) string and an AT (adenine-thymine) string may well be so large, however, that the degeneracy point is removed. This would have the effect of dramatically suppressing charge transfer. Detailed quantum-chemical calculations are required to determine whether this is, in fact, the case. We included the collective modes only in a schematic way. We require a large structural on-site distortion of a site by the particle (of order 0.1 eV), but this is likely to require an anharmonic description of the collective modes. We did not include coupling of modes of adjacent pairs, the double-stranded nature of DNA with the possibility of interchain charge transfer or effects related to the "tertiary" structure, i.e., the coiling of the duplex.

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*On leave at Instituut-Lorentz for Theoretical Physics, Universiteit Leiden, Postbus 9506, 2300 RA Leiden, The Netherlands.

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