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Effects of intrinsic base-pair fluctuations on charge transport in DNA

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We investigate propagation of a charge carrier along intrinsically dynamically disordered double-stranded DNA. This is realized by the semiclassical coupling of the charge with a nonlinear lattice model that can accurately describe the statistical mechanics of the large amplitude fluctuations of the base pairs leading to the thermal denaturation transition of DNA. We find that the fluctuating intrinsic disorder can trap the charge and inhibit polaronic charge transport. The dependence of the mean distance covered by the charge carrier until its trapping, as a function of the energy of the fluctuations of the base pairs is also presented.

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Charge transfer in DNA is of great biological importance because of the role that it can play in damage occurring under conditions of oxidative stress [1]. In particular, efficient long-range hole migration can oxidize sensitive parts of the DNA sequence (clusters of two or three guanine bases), resulting in increasing probability for mutations and carcinogenesis. Many experiments have addressed the distance and sequence dependence of charge transfer through DNA between selectively located donor and acceptor sites [1–5]. It appears that the microscopic mechanism that is responsible for long-range transport of a charge carrier is incoherent hopping among the stacking bases [1,4–8].

Several studies have recently been devoted to direct measurements of current-voltage relations and conductivity calculations of this biomolecule [9–13]—exploring its potential application in mesoscopic electronic devices, in addition to its obvious value as an important building block in nanostructures due to its unique assembly and recognition properties [14].

It is plausible that when an electron or a hole is injected into a soft (deformable) macromolecule such as DNA, it will induce local distortions of the structure as the latter adjusts to the excess charge and lowers the system energy; in other words a "polaronic" distortion will be formed. Both polaron hopping [4,7] and drifting [15,16] have been discussed in this context. The time required for polaron formation when an excess charge is introduced into DNA has been calculated to be of the order of a few picoseconds [16]. It has been conjectured that the current observed in homogeneous DNA in Ref. [11] is due to polaron drifting [16].

An open question that has not yet been adequately addressed concerns the influence of the local fluctuations of the bases on the long range charge transport in DNA [14]. In the present work we report an investigation in this direction by simulating polaron transport in an *intrinsically* fluctuating underlying lattice. For simplicity, and in order to isolate the intrinsic dynamical disorder effects from static or extrinsic disorder, we consider a homopolymer DNA chain consisting of a sequence of identical base pairs. Such homogeneous double helices have been synthesized and used in experiments (i.e., poly(G)-poly(C) oligomers [11,13]).

Theoretical models have recently been proposed [17,18] to explain femtosecond spectroscopic results [3] revealing a double characteristic time nature in short-range charge transfer, controlled by base-pair motions. These models use fluctuating tunneling amplitudes to effectively represent structural dynamics characteristics in reaction coordinate schemes. Our approach here is quite different since we directly couple the charge with the lattice degrees of freedom. Many different kinds of motion of base pairs may interact with an excess charge [4]. Here we focus on the structural dynamics relating to the stretching of the hydrogen bonds connecting the bases of each pair. Hydrogen bonds fluctuations can form dynamic denaturation bubbles, and large local openings of the double strand can be expected to strongly affect the charge transport.

A nonlinear dynamical model has been introduced previously which accurately describes central observed features of the thermal denaturation of DNA [19–21] (in the absence of charge carriers). In this one-dimensional model each base pair is described by a single variable y_n, representing the stretching of the two complementary bases at this site. There are two kinds of nonlinearities, each of them having a specific role. In the initial version of the model the anharmonicity of the relative motion of the two bases comprising each pair was shown to initiate the denaturation process through collective nonlinear local excitations [19]. Later, cooperativity was included through nonlinear stacking interactions between adjacent base pairs [20] (corresponding to elastic deformation effects). This had a striking effect on the thermal denaturation, leading to a sharp first order transition [20] in quantitative agreement with experimental observations. The fundamental role of the nonlinearity close to the melting transition was also demonstrated [20,21]. This model has been successfully tested against recent experimental melting studies in short DNA chains [22].

The Hamiltonian of the model reads

$$H_{\mathrm{lat}}=\sum_n \left[\frac{1}{2}m\dot{y}_n^2+V(y_n)+W(y_n,y_{n-1})\right], \tag{1}$$

where the sum is over the base pairs of the stack, m is the mass of a nucleotide, and the Morse potential

$$V(y_n)=D(e^{-ay_n}-1)^2 \tag{2}$$

describes the anharmonic relative motion within a particular base pair. The nearest-neighbor potential

$$W(y_n,y_{n-1})=\frac{k}{2}(1+\rho e^{-\beta(y_n+y_{n-1})})(y_n-y_{n-1})^2 \quad (3)$$

describes the stacking interaction which is not characterized by individual base-base coupling, but rather by a base-pair–base-pair overall coupling.

To include the effect of an added charge, we augment this model with a tight-binding Hamiltonian to describe the charge (electron or hole) hopping between adjacent base pairs

$$H_{ch}=-V\sum_n (c_n^\dagger c_{n+1}+c_n^\dagger c_{n-1}). \quad (4)$$

Here c_n and $c_n^\dagger$ are annihilation and creation operators, respectively, for the charge carrier at the nth base pair of the double strand, and V represents the transfer integral between neighboring sites. Since we use homopolymer DNA, we choose to measure the energy from the identical on-site energies ϵ of each site and we have omitted the term $\Sigma_n \epsilon c_n^\dagger c_n$ in the last expression.

Regarding the charge-lattice interaction, we use an on-site Holstein type [23,24] coupling. This means that we assume that the local stretching of a base pair affects the on-site energy of the charge carrier through the interaction term

$$H_{\rm int}=\chi\sum_n y_n c_n^\dagger c_n, \quad (5)$$

where χ is the coupling constant. An intersite type of interaction [25] could also be important. This kind of coupling implies that the relative transverse distortion of adjacent base pairs alters the overlap of the corresponding π orbitals and consequently modifies the transfer integral V. Since, *a priori*, we do not know which of these two different couplings is dominant, we use the Hamiltonian (5) to describe the interaction in this initial study.

We use semiclassical equations of motion in order to study the dynamics of the system; i.e., we treat the charge quantum-mechanically and the bases' motion classically [24]. This is justified because of the much larger mass of the bases. From Schrödinger's equation we obtain

$$i\hbar\frac{d\Psi_n}{dt}=-V(\Psi_{n+1}+\Psi_{n-1})+\chi y_n\Psi_n, \quad (6)$$

where Ψ_n is the probability amplitude for the charge carrier located at the nth base pair. Newton equations of motion for the stretchings y_n yield

$$m\frac{d^2y_n}{dt^2}=-V'(y_n)-W'(y_n,y_{n-1})-W'(y_{n+1},y_n) -\chi|\Psi_n|^2, \quad (7)$$

where the prime denotes differentiation with respect to y_n.

The parameter values we have used in our simulations are as follows. (i) In the lattice Hamiltonian (1)–(3) we use the values given in Ref. [20] that yield agreement with the experimental melting curves; viz., $m=300$ amu, $D=0.04$ eV, $a=4.45$ Å^{-1}, $k=0.04$ eV/Å^2, $\rho=0.5$, and $\beta=0.35$ Å^{-1}. (ii) The estimate of the hopping overlap V in Eq. (4) is of the order of 0.1–0.3 eV [16,27]. We use $V=0.1$ eV as a representative value. (iii) There is no information regarding the coupling constant χ of Eq. (5). In Refs. [15,16] the value 0.6 eV/Å has been used for intersite coupling of the charge with longitudinal displacements of individual bases. Here, we use this value also for on-site coupling χ.

The static polaron [26] that we find with these values of parameters is a large polaron extending over about ten base pairs. Its energy is -0.207 eV, i.e., slightly below the lower edge of the band of extended states at -0.2 eV. The static polaron in our case is slightly more extended than the corresponding one presented in Refs. [15,16]. The motion of such a polaron is a continuous translation (drifting)—due to the existence of a translational mode with almost zero frequency [28]—rather than discrete hopping events that characterize small polaron transport.

In order to examine how dynamical disorder affects the charge transport, we could initialize a polaron moving in a segment with random fluctuations of the base pairs and follow its evolution for different total initial energies. Alternatively, instead of starting with a moving polaron, we have observed that if we initially place, in a randomly fluctuating chain, a charge carrier which has the distribution of the static polaron but without the accompanying lattice distortion, then it induces the appropriate base pairs' distortion in its local neighborhood and starts moving in random directions. This resembles the phonon assisted polaron transport discussed in Refs. [4,7]. We determine the initial random lattice fluctuations by attributing a stretching at each base pair obtained through a uniform random distribution with a maximum amplitude Y, symmetrically centered around zero. The initial velocities of the lattice sites are zero.

Due to the nonlinearities in model (1)–(3), the initial disorder evolves to form opening bubbles of various sizes. Small fluctuations do not disturb the polaron motion. However, when a sufficiently large bubble is encountered, it interacts with the polaron leading typically to its trapping. We emphasize the dynamical character of this interaction. The bubble could disappear after a while, or a part of its energy could be repelled. Also the polaron may directly trap, or sometimes it is reflected backwards and then trapped through the interaction with another bubble. In Fig. 1 we demonstrate such a dynamical interaction. It is clearly seen that a temporary local accumulation of the lattice energy (bubble) around the 80th site of the chain traps the polaron. After the trapping the bubble disappears.

In Fig. 2 we show the trapping for a few representative polaron trajectories with different strengths of the lattice fluctuations. As can be seen, all the depicted trajectories start with similar velocities, about 1 base pair per 50 psec, independently of the width of the fluctuations. After some time, depending on the energy in the lattice, each trajectory devi-

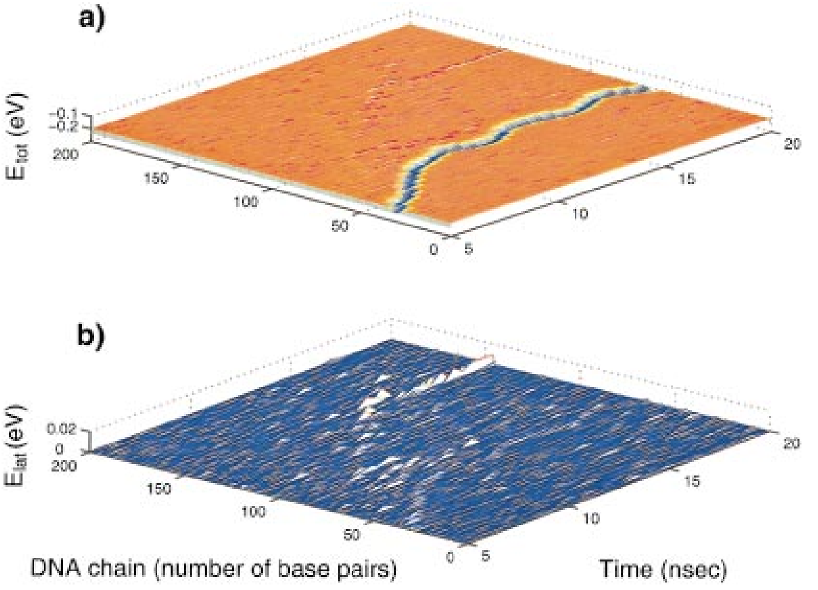

FIG. 1. (Color) Example of a polaron trapping through dynamical interaction with a large bubble. Lattice distribution of (a) the total energy $E_{\mathrm{lat}}+E_{\mathrm{ch}}+E_{\mathrm{int}}$ and (b) the lattice energy E_{lat}, as a function of time. In (a) the polaronic trajectory can be easily distinguished due to the substantial negative energy of the polaron. In (b) the bubbles are displayed. The total energy of the system is $E=-0.101$ eV. The values of the parameters are given in the text.

ates from the initial straight line of the propagation, when it starts to interact with large bubbles that finally lead to its trapping.

The larger the initial energy of the lattice the sooner the polaron is trapped by encountering large bubbles, and the smaller the average distance that it travels. In Fig. 3 we present the mean distance traveled by the polaron until its trapping, as a function of the total energy of the system. The mean values have been averaged over twenty simulations with different initial random fluctuations of the base pairs. The error bars represent statistical errors. We should note here a detail of the procedure that we use to obtain different realizations of the dynamical disorder in different initial conditions. For the same maximum amplitude Y, different realizations will have slightly different energies. This is merely a consequence of the nonlinearity of the model. However, our goal is to average over several runs with different initial conditions but with the same energy. We impose the fixed total energy on the system as follows: to produce the initial condition for the simulation we vary the maximum disorder amplitude Y in a systematic way, which is a variation of the bisection method, and begin the simulation only when the disordered system has the desired energy.

A log-log plot of the data of Fig. 3 (see the inset of the figure) exhibits an almost straight line. This implies the dependence

$$\langle L\rangle=\frac{c}{E^{p}}, \tag{8}$$

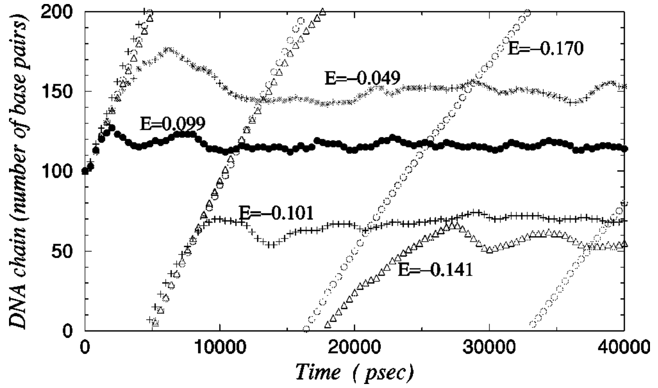

FIG. 2. Polaron trajectories for different energies of the lattice. E denotes the total energy of the system in each case. The energy values are given in eV. We have used periodic boundary conditions in chains consisting of 200 base pairs. For this reason a polaron that exits from the one side of the chain (top of the figure) enters from the other side (bottom of the figure).

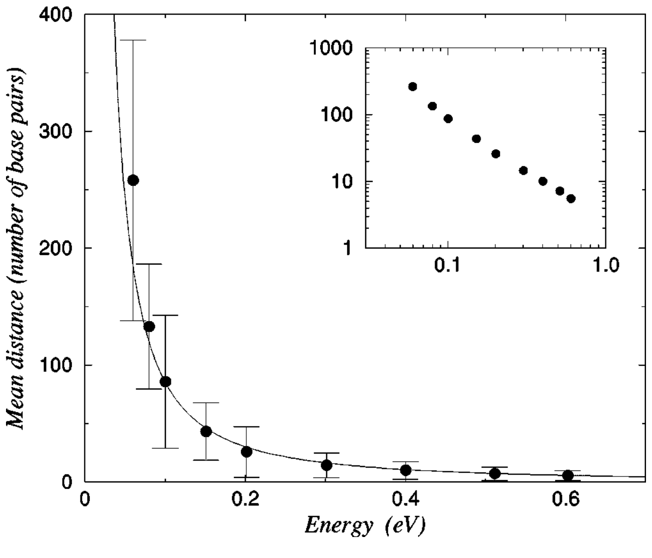

FIG. 3. The mean distance that a polaron travels before trapping, as a function of the total energy of the system. The energy values have been shifted by $+0.2$ eV (the lower band edge). The average is over an ensemble of 20 different initial randomizations of the lattice, having the same energy. The continuous line results from fitting the calculated points with the formula $y\sim 1/x^{p}$. The obtained value of the inverse power dependence is $p\approx\frac{3}{2}$. The inset shows the same data on logarithmic scales.

where $\langle L \rangle$ is the mean transport distance. By fitting the data with the above expression we find that $p \approx 1.5$ and $c \approx 2.69$. If we assume, as a rough measure, that the total energy of the system is proportional to its temperature T, this yields a $T^{-3/2}$ dependence of the mean transport range of the carrier.

In this preliminary report we have used a naive way to represent thermal fluctuations by giving random initial displacements in the base pairs of the chain. Our results for the trapping of the polaron and the particular decay of the transport distance remain to be verified by more accurate descriptions. For this purpose Langevin molecular dynamics simulations are currently under consideration [29].

Another interesting direction is the incorporation of a sequence of different bases in the double strand, instead of the homopolymer case we have considered in this study. Then one has to add the term $\Sigma_n \epsilon_n c_n^\dagger c_n$ to the tight-binding Hamiltonian (4), where ϵ_n represents the on-site energy of the nth base pair. For this, the relative on-site energies of the carrier at the different DNA bases are needed. If the width of the differences of these on-site energies is large compared to the hopping integral V, a small polaron extending over only a few lattice sites is expected. Then the continuous transport that we have obtained in our simulations would change to discrete hopping. Such a mechanism should result in quite different dependence on the kinetic energy of the base pairs. In particular, the hopping probability may increase with the strength of the dynamical disorder ($\sim$ thermal fluctuations), resulting in enhanced diffusivity and more efficient transport with increasing total energy [30].

In conclusion we have presented results on the influence of intrinsic dynamical disorder in the transport of a charge carrier through the stacking path of a DNA chain. We have focused on the large amplitude openings of the strands, that lead to a thermal denaturation at sufficiently large temperature. We find that the fluctuations of these large denaturation bubbles, characterized by multiple length and time scales, result in polaron trapping. Under the influence of this intrinsic colored noise, the charge transport distance has been found to decay with an inverse power law dependence on the total energy of the system, as $(\text{energy})^{-3/2}$. Further studies using different types of couplings and interactions with other kinds of motions of bases would probably reveal different dependences. Appropriately designed experiments are clearly needed to determine which is the dominant interaction of the local fluctuations affecting the long range charge transport in DNA.

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