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A model describing charge (hole) transport in DNA has been developed. The individual charge transfer steps in the transport process are described by Marcus theory modified to account for electron delocalization over adjacent identical nucleobases. Such a modification, as well as introducing a distance dependence in the reorganization energy, is necessary in order to reach an agreement with the observed transfer rates in well defined model systems to DNA. Using previously published results as a reference for the reorganization energy and with the delocalization described within the Hückel model we obtain an excellent agreement with experimental data. © *2008 American Institute of Physics.* [DOI: 10.1063/1.2981803]

I. INTRODUCTION

DNA, the carrier of genetic information, also has very interesting and hot debated charge transport properties.[1,2] The mechanism of charge transport has many similarities with the mechanisms found in other organic systems such as molecular crystals and conjugated polymers, materials that are well known to transport electrons over large distances.[3] The majority charge carrier in DNA are holes, which are transported over long distances via a multistep hopping process.[4–8] The possible hopping sites are the four different nucleobases, i.e., guanine, cytosine, adenine, and thymine, irregularly positioned along the DNA strand. These bases have different ionization potentials, which give rise to a strong variation in the on-site energies. As a result of these variations, the electronic wave functions become localized over essentially a single base molecule or a sequence of identical neighboring base molecules.[9,10] This is the underlying physics which results in nonadiabatic hopping transport in DNA. Since guanine has the lowest ionization potential, hole transport occurs predominantly via hopping between guanine sites. The limiting factors are the distance between nearest neighbor guanine bases and the energy barrier for hopping to a different nucleobase molecule.

At temperature T, the nonadiabatic rate constant k_{DA} for charge transfer between donor (D) and acceptor (A) can be expressed as[11]

$$k_{DA} = \frac{2\pi}{\hbar} |H_{DA}|^2 \frac{1}{\sqrt{4\pi\lambda k_B T}} \exp\left[-\frac{(\Delta G^0 + \lambda)^2}{4\lambda k_B T}\right], \quad (1)$$

where H_{DA} is the electronic transfer integral, ΔG^0 the difference in Gibbs free energy between donor and acceptor, and λ the reorganization energy. The square dependence on the electronic transfer integral, H_{DA}, is obtained from perturbation theory. This factor represents the electron tunneling (or superexchange), a process for which the rate decreases exponentially with the donor-acceptor distance.[12]

It was shown experimentally that the rate of charge transfer between two guanine bases along a DNA strand follows an exponential behavior but only when the guanines are separated by no more than three base pairs.[13] For larger guanine separations the distance dependence becomes much weaker, a result which is attributed to the second term in Eq. (1). This term accounts for (classically) the thermal excitations that are needed for charge transfer to occur between sites with different Gibbs free energies (different ionization potential). In addition to this energy barrier for transport, there is also a reorganization energy λ, associated with the charge transfer between bases. The reorganization energy has contributions both from internal nuclear relaxations and from the solvent. There is an extensive literature discussing the reorganization energy in the case of DNA.[14–20] In particular, it has been shown that the extent of solvent relaxation varies with the distance the charge carrier moves, an effect which results in a fairly strong dependence of λ on the donor-acceptor distance. Thus, a distance dependence appears in both the exponential terms in Eq. (1) [H_{DA} is exponential, see Eq. (2) below].

The aim of this work is to create a model for charge transport in DNA which properly describes the above mentioned distance dependences. The model is based on Marcus theory[11] and we use the Monte Carlo method along with the experimental data of Giese *et al.*[13] to establish the details of the process of charge transfer between nucleobases. Their experiment is performed on a well defined system for which the transfer rate is studied as a function of the length of an adenine bridge between guanine donor and acceptor sites (Fig. 1). In particular, we reach the same conclusion as Renger and Marcus[9] that charge transport cannot be based on individual nucleobases as donor or acceptor sites. Instead, the model has to account for electron delocalization over neighboring identical bases. Furthermore, we also stress the importance of including the distance dependence of the reorganization energy λ in order to correctly describe the transition from superexchange to hopping type of transport.

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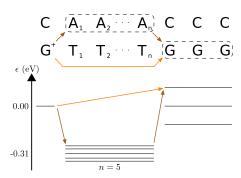
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FIG. 1. (Color online) The DNA sequence used in this study and the energy levels of the different delocalized states, as given by Eq. (3), relative to the energy level of the initial guanine donor.

II. METHOD

The Monte Carlo method applied to the problem of nonadiabatic charge transfer in DNA can be viewed as a random walk of a charge carrier between the nucleobases of the sequence shown in Fig. 1. This system corresponds to the DNA model system used by Giese et al.[13] in their measurement of the transfer rates. The sequence represents a donor-bridge-acceptor system in which the donor is the leftmost guanine, the acceptor is the guanine trimer to the right, and the bridge system is given by the adenine-thymine sequence of length n.

The rate constant k_{DA} [Eq. (1)] is calculated for each possible acceptor. This rate is proportional to the probability for that step to occur next in the random walk. The only nucleobase not considered as an acceptor candidate is the conjugate base in the donor base pair due to the small overlap of the π orbitals between these two bases[21] along with the significant difference in ionization potential.[10] The drawn acceptor is made the new donor and the process is repeated until the charge carrier reaches the guanine trimer at the opposite end of the duplex.

Time is introduced as a sum of dwell times τ_D at the donors that are occupied during the simulation. These are randomly drawn from an exponential distribution with a mean value of[22]

$$\langle \tau_D \rangle = \left(\sum_A k_{DA} \right)^{-1},$$

i.e., the inverse of the total transfer rate from the current donor (D) to any potential acceptor (A) of the charge. The transfer rate (transfer time) thus calculated is made statistically reliable by repeating the above procedure a large number of times.

The DNA duplex is modeled as standard B-DNA with a rise of 3.38 Å and a twist of 36° per base pair. Two nucleobases forming a Watson–Crick pair are equidistant to the helical axis and positioned so that the intrastrand and interstrand nearest neighbor distances become 3.54 and 4.66 Å, respectively. The ionization potentials are specified relative to guanine: 0.31 eV for adenine, 0.42 eV for cytosine, and 0.77 eV for thymine.[10]

The electronic transfer integral H_{DA} in Eq. (1) depends on the donor-acceptor distances R_{DA} according to

$$H_{DA} = H_{DA}^0 \exp\left[-\frac{\beta}{2}(R_{DA} - R_0) \right], \qquad (2)$$

where H_{DA}^0 are constants taken from Hartree–Fock calculations by Voityuk et al.[21] R_0 is either the distance to the nearest intrastrand or interstrand acceptor. β determines the distance dependence of H_{DA} and is approximately equal to $2/l$,[12] where l is the localization length of the donor and acceptor states. As already discussed, the donor-acceptor distance enters Eq. (1) in the reorganization energy as well and hence these two contributions determines the effective distance dependence of the transfer rate. In order to match the reorganization energy as closely as possible to previously reported results,[19] we set β to 0.39 Å^{-1} which corresponds to $l \approx 5$ Å. This localization length is completely consistent with the fact that the wave function extends over a sequence of neighboring identical nucleobases but localizes to a, single nucleobase when this sequence is altered.

If the difference in the Gibbs free energy ΔG^0 is small compared to H_{DA}, the electronic state as well as the charge occupying this particular state has the possibility to delocalize over several nucleobases. In particular, this occurs for identical and adjacent bases in the DNA double helix (illustrated by bases grouped together inside dashed rectangles in Fig. 1), since these have the same ionization potential and are close enough for the electronic transfer integral in Eq. (2) to overcome possible differences in the Gibbs free energy caused by disorder.[9,10,23]

A wave function describing such a delocalized state can be approximated as a linear combination of the molecular orbitals (MOs) of the contained nucleobases. Each MO (each nucleobase) added will yield one additional solution of the Schrödinger equation with an energy ϵ_k. If, in accordance with the Hückel model, the spatial overlap of the MOs are neglected and assuming that the electronic transfer integral for two non-neighboring bases vanish, these energy levels for n bases are given by

$$\epsilon_k = \epsilon_0 + 2H^0 \cos\frac{k\pi}{n+1}, \quad k = 1, \ldots, n, \qquad (3)$$

where ϵ_0 is the ionization potential of the contained nucleobases and H^0 the electronic transfer integral between two identical adjacent bases.

The same assumption implies that the electronic transfer integral between two such delocalized states can be approximated as the transfer integral between the MOs of the two nearest nucleobases, one from each state, multiplied by their expansion coefficients in the linear combination forming the delocalized states. With the assumption that the MOs of the nucleobases participating in a delocalized state contribute about the same to the wave function, the normalization condition implies that the coefficients are all equal to $1/\sqrt{n}$. If we denote the MOs of the two nearest nucleobases by d and a, a crude estimate of the electronic transfer integral is
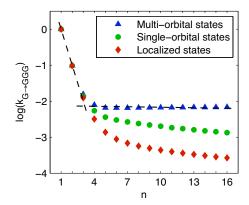
FIG. 2. (Color online) The charge transfer rate dependence on the adenine bridge size n for localized and delocalized holes. The dashed lines are fitted to the results of Giese et al.[13]

$$H_{DA} = \frac{H_{da}^0}{\sqrt{n_D \cdot n_A}} \exp\left[-\frac{\beta}{2}(R_{da} - R_0)\right]. \qquad (4)$$

Note that this equation is valid when D and A correspond to states delocalized over several nucleobases and it is equivalent to Eq. (2) for states localized to single nucleobases.

III. RESULTS AND DISCUSSION

In the following figures, the charge transfer rate for an adenine bridge size of one base pair is set to unity and the rest of the points in the plot are measured relative to this reference value. The first simulation, where the donor and acceptor sites correspond to individual nucleobase molecules, is shown by the diamonds in Fig. 2. The agreement with the experimental results of Giese et al. (the dashed lines) is satisfactory for an adenine bridge size up to three base pairs. However, for a bridge consisting of more base pairs, the charge transfer rate deviates considerably from the experimental results. A closer study of the charge transfer process in the DNA duplex shows that the charge carrier, which makes a thermally induced hop to the initial adenine of the bridge, will have a high probability to immediately jump back to the guanine donor. The further away the acceptor guanine triplet (with a lower ionization potential) is, the more likely the jump back to the single guanine will be. This explains why the charge transfer rate presented in Fig. 2 depends on the bridge size even when the distance between the guanines is large enough to exclude superexchange as the transport mechanism. Tweaking of the parameters involved (β, λ, and the relative ionization potentials) cannot compensate for this behavior while keeping them within acceptable physical limits. The only reasonable correction of the model is to account for electron delocalization in the DNA duplex over identical adjacent nucleobases, which is the same conclusion Renger and Marcus made in their related work.[9]

The circles and triangles in Fig. 2 show the transfer rate when the molecular orbitals of the nucleobases in the adenine bridge have been replaced by delocalized states extending over the whole bridge. The difference between the two sets is that the circles only take into account the state with the lowest ionization potential, i.e., the most probable acceptor state, while the triangles correspond to a simulation
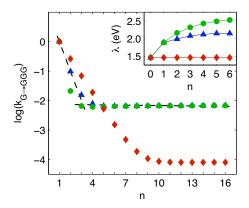

FIG. 3. (Color online) The charge transfer rate dependence on the adenine bridge size n for different distance dependencies of the reorganization energy λ. The markers in the inset correspond to the same marker in the main figure. The circles are the estimates of the reorganization energy made by Siriwong et al.[19]

in which all states with energies according to Eq. (3) have been included (see Fig. 1). Figure 2 makes it apparent that, for larger bridge sizes, the delocalized states with higher ionization potential start to influence the charge transport process, as their energy levels spread out and form a band which decreases the ΔG^0 term in Eq. (1) for hopping from the guanine donor over to the adenine bridge. Clearly, the best agreement with the experimental data is obtained if all states in the band are included as possible acceptor states. In combination with a correct description of the reorganization energy (see below) we can conclude that electron delocalization plays a very important role for long distance charge transport in DNA.

As already pointed out, the reorganization energy depends on the distance between the donor and acceptor involved in the nonadiabatic charge transfer. This is confirmed in our simulations since this dependence is necessary in order to reach agreement with the experimental results. The experimental data show a very abrupt transition from superexchange to hopping. In our case, hopping always occurs between nearest neighbor sites whereas superexchange is associated with charge transfer over a distance of n sites (see Fig. 1). In order to turn off the latter transport channel as abruptly as the experimental result indicates the reorganization energy has to be significantly larger for the long distance superexchange process as compared to the nearest neighbor hopping process. This observation is in agreement with the previously reported distance dependence of λ.[14–19]

In Fig. 3 we illustrate how the transition rate varies with the three different shapes of the distance dependence shown in the inset of the figure (with $\beta = 0.39$ Å^{-1}, see Sec. II above). The diamonds correspond to a constant reorganization energy over the donor-acceptor distance while the triangles represent results in which the reorganization energy has been adjusted in order to match the simulations to the experimental results. In particular, the simulation data show how the crossover from a superexchange process to thermally assisted hopping moves towards shorter distances with increasing distance dependence of the reorganization energy. The circles correspond to the reorganization energy calculated by Siriwong et al.,[19] which has a stronger distance de-
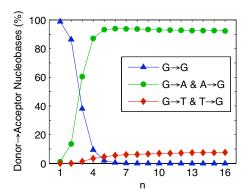
FIG. 4. (Color online) The type of donor and acceptor nucleobases plotted against the bridge size n. The transition from superexchange to thermally assisted hopping over the bridge is apparent.

pendence for transitions further than two base pairs compared to the energy that fits the experimental results. It should be noted that these two results are obtained using completely different approaches. The result presented in Ref. 19 is obtained from classical molecular dynamic simulations using standard force fields whereas our approach is based entirely on fitting of our simulated transfer rate results to the experimental data. Nevertheless these two approaches give qualitatively very similar results for short range electron transfer. For longer transfer distances the deviation could be due to the fact that our model describes the bridge as one delocalized state which is not the case in the classical approach used by Siriwong *et al.*

The characteristic knee in the donor-acceptor distance dependence of the transfer rate is attributed to a change in transport process from superexchange between the guanine donor and the guanine trimer acceptor to a hopping process over the adenine bridge.[13] However, by recording the details of the random walk in our Monte Carlo simulations we can conclude that the actual transition between these two processes is more continuous than expected. In Fig. 4 the charge transfer processes for the DNA donor-bridge-acceptor system are shown, including the superexchange process and two different hopping processes, via the adenine and thymine bridge molecules, respectively. Starting with a bridge size of one adenine-thymine (A-T) base pair, the transport is almost exclusively a superexchange process from the guanine donor (G) to the guanine trimer (GGG) acceptor. However, already at a bridge size of two A-T base pairs ($n=2$), hopping contributes with about 14% to the total charge transfer process. For three A-T base pairs the hopping process is actually slightly more abundant than the G-to-GGG superexchange process, even though this bridge length is assigned to the superexchange part of the transport process. At a bridge size of $n=4$ and above the superexchange process has negligible impact on the charge transport. Instead, guanine-to-adenine hops dominate and to some extent also guanine-to-thymine hops, as the ionization potential of the bridge states decreases with increasing length of the bridge. Most probably, however, due to the presence of extrinsic disorder,[9] electron delocalization will not extend over the full bridge for these very long A-T sequences. In this regime, our results therefore

overestimate the transfer rates as also shown by the deviation between our simulated transfer rates and those given by experiment for $n>9$.

IV. SUMMARY

In order for the results of our Monte Carlo simulation to be in full agreement with the experimental results of Giese *et al.*,[13] we found that the model used has to fulfill the following criteria: (i) The distance dependence of the charge transfer rate has to be stronger than that stemming from the exponential decay of the electronic tunneling. This rules out the Miller–Abrahams model[12] and promotes Marcus theory since several recent studies[14–19] have shown that the reorganization energy introduced in the Marcus theory does in fact have a distance dependence of its own. Furthermore, (ii) the holes cannot be completely localized to individual nucleobase molecules in the DNA duplex since this introduces a bridge size dependence in the trapping potential of the initial guanine donor which is not seen experimentally. Extending the hole states over identical adjacent nucleobases of the same strand abolishes this dependence. If these extended states are treated according to the Hückel model, (iii) all hybridized states have to be accounted for in order to reach agreement with experiment data. We also stress that (iv) the transfer integral has to be scaled with the proper normalization constant of the nucleobase MOs that contribute to the overlap between the donor and acceptor units in the system. The final agreement with the experimental results is excellent. We have also shown that if any of the features described above is neglected the results of the simulations completely fail to represent the experimental data.

Any arbitrary DNA sequence can be construed as a number of guanine-cytosine base pairs separated by varying number of adenine-thymine (bridge) pairs. Hence the model created in this work can be used to study the conductivity of DNA further and in particular the temperature and electric field dependence since these properties enters naturally in the expression for the Marcus transfer rate [Eq. (1)]. These studies are currently in progress.

ACKNOWLEDGMENTS

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