Diffusion Approach to Long Distance Charge Migration in DNA: Time-Dependent and Steady-State Analytical Solutions for the Product Yields

Marina Roginskaya and William A. Bernhard*

Department of Biochemistry and Biophysics, University of Rochester, Rochester, New York 14642

Yuriy Razskazovskiy

Department of Physics, East Tennessee State University, Johnson City, Tennessee 37614

Received: May 14, 2003; In Final Form: November 13, 2003

In this study we report analytical solutions for both time-dependent and steady-state problems of unbiased charge transfer through a regular DNA sequence via a hopping mechanism. The phenomenon is treated as a diffusion of charge in a one-dimensional array of equally spaced and energetically equivalent temporary trapping sites. The solutions take into account the rates of charge hopping (k), side reactions (k_r), and charge transfer to a terminal charge acceptor (k_t). A detailed analysis of the time-dependent problem is performed for the diffusion-controlled regime, i.e., under the assumption that $k_t \gg k$, which is also equivalent to the fast relaxation limit of charge trapping. The analysis shows that the kinetics of charge hopping through DNA is always multiexponential, but under certain circumstances it can be asymptotically approximated by a single-exponential term. In that case, the efficiency of charge transfer can be characterized by a single rate constant $k_{CT} = 1.23kN^{-2} + k_r$, where N is the DNA length expressed in terms of the number of equidistant trapping sites and k_r is the rate of competing chemical processes. The absolute yield of charge transfer under steady-state conditions in general is obtained as $Y_\infty = \omega[\alpha \sinh(\alpha N) + \omega \cosh(\alpha N)]^{-1}$, where $\alpha = (2k_r/k)^{1/2}$ and $\omega = 2k_t/k$. For the diffusion-controlled regime and small N, in particular, it turns into the known "algebraic" dependence $Y_\infty = [1 + (k_r/k)N^2]^{-1}$. At large N the solution is asymptotically exponential with the parameter α mimicking the tunneling parameter β in agreement with earlier predictions. Similar equations and distance dependencies have also been obtained for the damage ratios at the intermediate and terminal trapping sites in DNA. The nonlinear least-squares fit of one of these equations to experimental yields of guanine oxidation available from the literature returns kinetic parameters that are in reasonable agreement with those obtained by Bixon et al. [*Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11713−11716] by numerical simulations, suggesting that these two approaches are physically equivalent.

Introduction

There is growing experimental evidence that long-distance charge migration through DNA is controlled by a multistep site-to-site hopping and not by a single-step long-distance tunneling.[1−5] In parallel, several attempts have been made to describe this process quantitatively by treating charge hopping in DNA as a random walk. Most of the progress to date has been made in describing the yields of charge transfer under steady-state conditions. In 1997 we published an analytical solution for the yield of excess electron scavenging in DNA as a function of DNA length N in the case of random charge injection.[6] The solution explicitly included the rate constants of hopping k, competing chemical reactions k_r, and irreversible charge trapping k_t by the terminal acceptor. A year later another approximation[7] was suggested for the yield of hole trapping in the case of point charge injection:

$$Y_\infty \cong [1 + (k_r/k)N^2]^{-1} \qquad (1)$$

Equation 1 does not include k_t and, therefore, implicitly presumes that this process is not a rate-determining step. In other words, eq 1 describes a diffusion-controlled process in terms

of classic condensed-phase kinetics. Later it was shown that the asymptotic distance dependence of Y_∞ is better described by an exponential function $Y_\infty \propto \exp[-(k_r/k)^{1/2}N]$ rather than the "algebraic" dependence (eq 1).[8] A matrix expression for the product yields was obtained in the same case.[8,9] An alternative solution of the same problem was also obtained in a compact and convenient form by Berlin et al.[10,11] and Li et al.[12] Neither of these solutions, however, depends on the rate of hole trapping k_t. Therefore, all these approaches apply to the processes controlled by hopping or, in other terms, describe the fast-relaxation limit of charge transfer.[11]

No analytical solution has been suggested so far for the time-dependent problem of charge transfer through a DNA bridge via hopping mechanism, which would include the following three critically important parameters: k, k_r, and k_t. Numerical simulation showed that the process is not exponential in general,[13] but asymptotically may turn into a single-exponential dependence characterized by a "rate constant" k_{CT}. It is stated[7] that the characteristic time of hole transfer $\tau_{CT} = k_{CT}^{-1}$ is proportional to the characteristic time of hopping $\tau_o = k^{-1}$ and the square of the DNA length:

$$\tau_{CT} \propto \tau_o N^2 \qquad (2)$$

Equation 2 is not an exact relationship and does not include

---

* To whom correspondence should be addressed.

either k_r or k_t. Diffusion control and the absence of competing processes are, therefore, implicitly presumed in this equation. These presumptions limit the use of eq 2. All time-dependent solutions suggested afterward[14−16] have the same drawback since they ignore the presence of competing processes and, therefore, cannot be used for prediction of the damage distribution along the DNA strand.

On the experimental side, there are several studies in which the accumulation of a modified acceptor was indeed described by a single-exponential function for both hole[17−19] and excess electron migration.[20,21] There are, however, several studies in which a more complex behavior was observed, typically described as a sum of several exponential terms.[18,22] Interpretation of such complex behavior requires caution because, as noted above, the kinetics of charge hopping are not described by a single-exponential dependence in general.

In this study, we apply the diffusion approximation to charge migration in DNA to obtain analytical solutions for product accumulation under both time-dependent and steady-state conditions. The diffusion approximation is a special case of the "unbiased" random walk problem addressed in the publications cited above, which presumes that temporary trapping sites in DNA are separated by energy barriers of equal height and width. A physical example of such a system is a double-stranded DNA containing CG base pairs separated by AT bridges of the same sequence and length, and terminated with GG doublets or GGG triplets. In this study we show that most of the basic predictions discussed above can be obtained as special cases of the diffusion-based solutions.

Results

We consider a system consisting of a hole donor and a hole acceptor, A, bridged by double stranded DNA. While we consider hole migration for the sake of specificity, the same treatment is applicable to excess electron migration. In a typical experiment, the hole is injected by the donor at a known distance from the acceptor. The progress of charge migration is monitored by the concentration of the oxidized acceptor A_{ox} and, optionally, by oxidation of intermediate trapping sites (typically single guanines).

The DNA duplex is considered as a one-dimensional array of N equally spaced and energetically equivalent trapping sites. The distance between the traps is δ, so the total length of the bridge is $L = \delta N$. We also presume the following: (a) Both hole injection into DNA and hole trapping by A are irreversible processes, in a sense that once the hole is trapped, it is never injected back to the strand. The trapping process is characterized by its rate k_t, while no specific condition is imposed on this rate. It can be slower or faster than the hopping rate in general. (b) The hole is injected into DNA at $x = 0$ instantly and migrates to the acceptor located at the distance $L = \delta N$. (c) Hole migration in the bridge can be treated as an unbiased one-dimensional diffusion. The diffusion coefficient D is expressed through the hopping distance δ and the characteristic time of hopping τ_o through the classic relationship

$$D = \delta^2/2\tau_o = k\delta^2/2 \qquad (3)$$

where k is the rate constant of hopping. (d) After reaching the boundary with the acceptor, the hole can either be reflected from this boundary or irreversibly trapped by the acceptor with the rate constant k_t. Effectively, k_t is equivalent to the relaxation rate of the trapping site with use of the terminology of Berlin et al.[11] The definition of the boundary depends on the nature of

the acceptor site. (e) The diffusion process competes with an irreversible chemical transformation of the hole characterized by a cumulative rate constant k_r.

Time-Dependent Solution. The probability density function $W(x,t)$ describing the distribution of holes across the DNA bridge is found by solving the diffusion eq 4 with the appropriate set of initial and boundary conditions.

$$\frac{\partial W(x,t)}{\partial t} = D\frac{\partial^2 W(x,t)}{\partial x^2} - k_r W(x,t) \qquad (4)$$

$$W(x,0) = \delta(x - 0) \qquad (4a)$$

$$D\frac{\partial W(x,t)}{\partial x}\bigg|_{x=0} = 0 \qquad (4b)$$

$$D\frac{\partial W(x,t)}{\partial x}\bigg|_{x=L} = -k_t\delta W(L,t) \qquad (4c)$$

The boundary condition 4c is a one-dimensional analogue of the "gray sphere" approximation used in traditional homogeneous condensed-phase kinetics. It takes into account the possibility that the migrating charge reaching the acceptor can be reflected back or pass through, and, therefore, is an equivalent of the "slow relaxation limit" of charge trapping.[11]

Equation 4 can be solved by using a standard Fourier technique described elsewhere[23] that produces $W(x,t)$ in the form of a converging series

$$W(x,t) = \frac{2}{L}e^{-k_r t}\sum_n e^{-\lambda_n^2 Dt}\cos\lambda_n x \qquad (5)$$

where eigenvalues λ_n are the roots of a transcendent equation

$$\tan\lambda_n L = \frac{k_t\delta}{\lambda_n D} \qquad (6)$$

The probability density function $W(x,t)$ is further used to calculate the amount of oxidized acceptor accumulated by time t, $A_{ox}(t)$, by integrating the flux of the holes, $J(0,\tau)$, to the acceptor from 0 to t:

$$A_{ox}(t) = h_o\int_0^t J(0,\tau)\,d\tau = -h_o D\int_0^t \partial W(x,\tau)/\partial\tau|_{x=L}\,d\tau \qquad (7)$$

where h_o is the total number of injected holes. The final expression for $A_{ox}(t)$ is obtained as a converging series

$$A_{ox}(t) = h_o\frac{2D}{L}\sum_{n=0}^{\infty}\frac{\lambda_n\sin\lambda_n L}{\lambda_n^2 D + k_r}(1 - e^{-(\lambda_n^2 D + k_r)t}) \qquad (8)$$

Equation 8 is an analytical solution that can be used in modeling time-resolved kinetics of charge transfer. In particular, it immediately shows that accumulation of the oxidized acceptor is an infinite sum of exponential terms, wherein the effective "rate constants" have no simple interpretation. To gain a better understanding of the physical meaning of these parameters, we analyze a diffusion-controlled case ($k_t = \infty$). Physically this situation is equivalent to the "black sphere" approximation traditional for homogeneous chemical kinetics in condensed phase, and could be solved by using eq 4 with a boundary condition (4c) in the form $W(L,t) = 0$. We, however, prefer to analyze it as a special case of the more general approach formulated above. So, if $k_t = \infty$, then eq 6 turns into a simple

trigonometric equation $\cos\lambda_n L = 0$, leading to further simplifications:

$$A_{ox}(t) = h_o \frac{\pi k}{2N^2} \sum_{n=0}^{\infty} a_n(1 - e^{-\gamma_n t}) \qquad (9)$$

$$Y(t) = A_{ox}(t)/h_o = \frac{\pi k}{2N^2} \sum_{n=0}^{\infty} a_n(1 - e^{-\gamma_n t}) \qquad (9a)$$

where

$$\gamma_n = (2n + 1)^2 \pi^2 \frac{k}{8N^2} + k_r \text{ and } a_n = \frac{(-1)^n(2n + 1)}{\gamma_n}$$

Equation 9a defines the time dependence of the yield of hole transfer $Y(t)$. At $t = \infty$, $Y(t)$ reaches its maximum value Y_∞, which is equivalent to the yield of hole trapping measured under steady-state conditions:

$$Y_\infty = \frac{\pi k}{2N^2} \sum_{n=0}^{\infty} a_n \qquad (10)$$

Steady-State Solution. An alternative expression for Y_∞, in a more convenient closed form, can be obtained through solving a steady-state diffusion problem:

$$D\frac{d^2 W(x)}{dx^2} - k_r W(x) = 0 \qquad (11)$$

$$D\frac{dW(x)}{dx}\bigg|_{x=0} = -I \qquad (11a)$$

$$D\frac{dW(x)}{dx}\bigg|_{x=L} = -k_t \delta W(L) \qquad (11b)$$

where I is the constant rate of hole injection. Both the problem and the approach to its solution are similar to the one solved earlier for random charge injection.[6] The probability of finding the hole at the nth trapping site $W(n)$ is obtained in the form

$$W(n) = Ae^{\alpha n} + Be^{-\alpha n} \qquad (12)$$

$$A = \frac{Ie^{-\alpha N}(\alpha - \omega)}{\alpha k \delta[\alpha \sinh(\alpha N) + \omega \cosh(\alpha N)]}$$

and

$$B = \frac{Ie^{-\alpha N}(\alpha + \omega)}{\alpha k \delta[\alpha \sinh(\alpha N) + \omega \cosh(\alpha N)]}$$

where

$$\alpha = (2k_r/k)^{1/2} \text{ and } \omega = 2k_t/k$$

and results in eq 13 for Y_∞

$$Y_\infty = \frac{\omega}{\alpha \sinh(\alpha N) + \omega \cosh(\alpha N)} \qquad (13)$$

that further turns into eq 13a in the diffusion-controlled case of $k_t \gg k$ ($\omega \rightarrow \infty$).

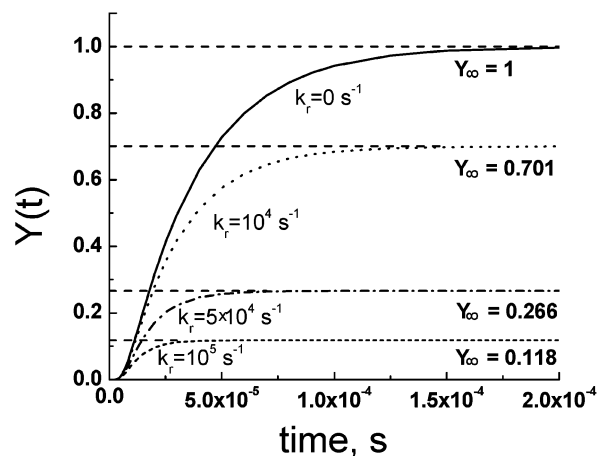$$Y_\infty = \frac{1}{\cosh(\alpha N)} = \text{sech}(\alpha N) \qquad (13a)$$

Figure 1. Time dependence of charge-transfer yields $Y(t)$ calculated for $N = 20$, $k = 10^7$ s^{-1}, and the values of k_r shown in the plot. The asymptotic values Y_∞ shown in the plot are predictions of eq 13a.

Another characteristic of practical interest is the damage ratio, defined as the ratio of product yields at two selected locations within the strand. The rate of product formation at the nth site within the bridge is described as

$$\frac{dP_n}{dt} = k_r \delta W(n) \qquad (14)$$

that results in the following expression for the ratio of the oxidation yields of the terminal acceptor and the first single guanine in the bridge (the distal-to-proximal damage ratio):

$$\frac{Y_\infty}{Y(P_1)} = \frac{\omega}{\alpha[\alpha \cosh(\alpha N) + \omega \sinh(\alpha N)]} \qquad (15)$$

or

$$\frac{Y_\infty}{Y(P_1)} = \frac{1}{\alpha \sinh(\alpha N)} \qquad (15a)$$

for the diffusion-controlled case of $\omega \rightarrow \infty$. The ratio of the yield of oxidized acceptor Y_∞ to the total yield of oxidation at all nonterminal sites Y_{tot} (the distal-to-total damage ratio) is simply obtained as

$$\frac{Y_\infty}{Y_{tot}} = \frac{Y_\infty}{1 - Y_\infty} = \frac{\omega}{\alpha \sinh(\alpha N) + \omega \cosh(\alpha N) - \omega} \qquad (16)$$

In the diffusion-controlled case of $\omega \rightarrow \infty$, eq 16 turns into eq 16a:

$$\frac{Y_\infty}{Y_{tot}} = \frac{1}{\cosh(\alpha N) - 1} \qquad (16a)$$

Discussion

Time Course of A_{ox} Formation. Time dependence of the trapping yield $Y(t) = A_{ox}(t)/h_o$ in the diffusion-controlled case is given by eq 9a, which depends on three parameters: the DNA length N (expressed in terms of the number of equidistant trapping sites), the diffusion rate constant k, and the reaction rate constant k_r. The plots of $Y(t)$ vs t are shown in Figure 1 for $k = 10^7$ s^{-1}, $N = 20$, and four values of k_r. The value of k used in Figure 1 is the average of the rate constants of hole transfer from a single guanine to a guanine doublet and back across a single adenine in a double-stranded DNA, reported by Lewis

Long Distance Charge Migration in DNA

J. Phys. Chem. B, Vol. 108, No. 7, 2004 **2435**

TABLE 1: Values of the First Five Parameters γ_n and Their Relative Statistical Weights a_o/a_n in the Expression for $R(t)$ (eq 18, $k = 10^7$ s^{-1})

| | | k_r, s^{-1} | | | | | | | |
| | | 0 | | 10^4 | | 10^5 | | 10^6 | |
N	n	a_n/a_o	γ_n, s^{-1}	a_n/a_o	γ_n, s^{-1}	a_n/a_o	γ_n, s^{-1}	a_n/a_o	γ_n, s^{-1}
	0	1.00	4.93×10^5	1.00	5.03×10^5	1.00	5.93×10^5	1.00	1.49×10^6
	1	−0.33	4.44×10^6	−0.34	4.45×10^6	−0.39	4.54×10^6	−0.82	5.44×10^6
5	2	0.20	1.23×10^7	0.21	1.23×10^7	0.25	1.24×10^7	0.56	1.33×10^7
	3	−0.14	2.42×10^7	−0.15	2.42×10^7	−0.17	2.43×10^7	−0.41	2.52×10^7
	4	0.11	4.00×10^7	0.12	4.00×10^7	0.13	4.01×10^7	0.33	4.10×10^7
	0	1.00	1.23×10^5	1.00	1.33×10^5	1.00	2.23×10^5	1.00	1.12×10^6
	1	−0.33	1.11×10^6	−0.36	1.12×10^6	−0.55	1.21×10^6	−1.60	2.11×10^6
10	2	0.20	3.08×10^6	0.22	3.09×10^6	0.35	3.18×10^6	1.37	4.08×10^6
	3	−0.14	6.05×10^6	−0.15	6.06×10^6	−0.25	6.15×10^6	−1.11	7.05×10^6
	4	0.11	1.00×10^7	0.12	1.00×10^7	0.20	1.01×10^7	0.92	1.10×10^7
	0	1.00	3.08×10^4	1.00	4.08×10^4	1.00	1.31×10^5	1.00	1.03×10^6
	1	−0.33	2.78×10^5	−0.42	2.88×10^5	−1.04	3.78×10^5	−2.37	1.28×10^6
20	2	0.20	7.71×10^5	0.26	7.81×10^5	0.75	8.71×10^5	2.89	1.77×10^6
	3	−0.14	1.51×10^6	−0.19	1.52×10^6	−0.57	1.61×10^6	−2.89	2.51×10^6
	4	0.11	2.50×10^6	0.15	2.51×10^6	0.46	2.60×10^6	2.68	3.49×10^6

et al.[24] Therefore, the model corresponds to hole migration in an alternating GAGAGA···•CTCTCT··· duplex about 40 base pairs long.

As can be seen from Figure 1, $Y(t)$ gives an S-shaped function, which asymptotically approaches the Y_∞ values predicted by the steady-state solution (eq 13a). Equations 9a and 10 can be combined to obtain the time-dependent solution in a multiexponential form that is convenient for analysis:

$$R(t) = 1 - \frac{Y(t)}{Y_\infty} = \frac{\sum_{n=0}^{\infty} a_n e^{-\gamma_n t}}{\sum_{n=0}^{\infty} a_n} \qquad (17)$$

The truly exponential asymptotic behavior of $R(t)$ requires that all but one exponential terms in eq 17 turn into zero at late times. This is possible if among all γ_n there is only one γ_m, which along with its statistical weight a_m satisfies the following two conditions: (i) $\gamma_m \ll \gamma_{n \neq m}$, and (ii) a_m is greater or at least comparable with all other statistical weights. If these conditions are met, then the accumulation of oxidized acceptor $R(t)$ is asymptotically described by a single-exponential dependence with γ_m playing the role of the formal "rate constant" of charge transfer k_{CT}.

$$R(t) = 1 - \frac{Y(t)}{Y_\infty} = \frac{a_m e^{-\gamma_m t}}{\sum_{n=0}^{\infty} a_n} \qquad (18)$$

The next step to be taken is to determine whether the conditions i and ii can be met in realistic situations and what is the value of m that satisfies these conditions. The answer to this question will fully define the expressions for γ_m and, therefore, for the rate constant of charge transfer k_{CT}. Table 1 reports the first five ($n = 0-4$) relative weights a_n/a_o and the "rate constants" γ_n calculated for the fixed value of $k = 10^7$ s^{-1} and variable k_r and DNA lengths. The data show that if k_r is less than 10^5 s^{-1} (for $N = 5$ or 10) or less than 10^4 s^{-1} ($N = 20$), then the first "rate constant" γ_o is at least 7 times smaller than any other γ_n, and the corresponding exponential term has the greatest statistical weight in the sum. Therefore, the conditions i and ii are satisfied with $m = 0$, resulting in an
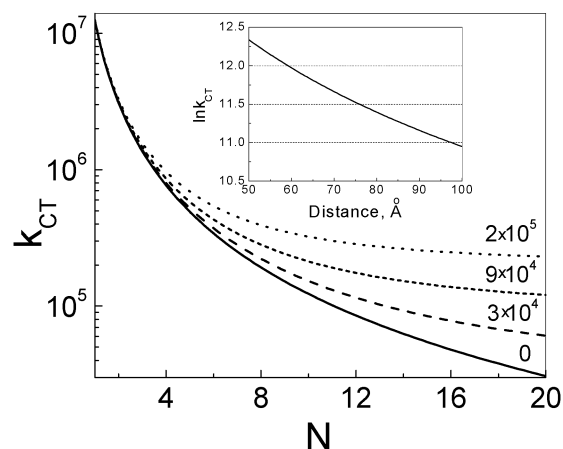

Figure 2. The logarithmic plot of k_{CT} vs N for $k = 10^7$ s^{-1} and the values of k_r (s^{-1}) specified above each curve. The inset shows a fragment of the same plot ($k_r = 0$ s^{-1}) in coordinates ln k_{CT} vs distance, where the distances are expressed in Å. The distances are calculated for $\delta = 6.8$ Å. This situation approximately corresponds to a double-stranded B-form DNA fragment from 15 to 30 base pairs long.

exponential asymptotic behavior with $k_{CT} = \gamma_o$:

$$k_{CT} = \gamma_o = \frac{\pi^2 k}{8N^2} + k_r = 1.23\frac{k}{N^2} + k_r \qquad (19)$$

Equation 19 predicts the same distance dependence for k_{CT} as eq 2 (if the latter is expressed in terms of rate constants instead of lifetimes), but it also depends on k_r. It turns exactly into eq 2 for $k_r = 0$, i.e., the processes competing with charge migration are absent. The effect of k_r on k_{CT} obviously increases with DNA length as illustrated in Figure 2, and should not be neglected in long strands even if k_r is much smaller than k. Equation 19 also justifies the way of extracting both k and k_r from time-resolved kinetics by using linear regression of k_{CT} vs N^{-2}. An attempt to analyze the distance dependence of k_{CT} as it is typically done for direct tunneling would result in abnormally low values for the tunneling parameter β. This situation is also illustrated in Figure 2 where the "β" value calculated for the fragment shown in the inset is about 0.03 Å^{-1}.

The situation with greater k_r (10^6 s^{-1} for $N = 5$ or 10 and $\geq 10^5$ s^{-1} for $N = 20$) is not that straightforward. In these cases, there are several values of γ_n with comparable magnitudes and
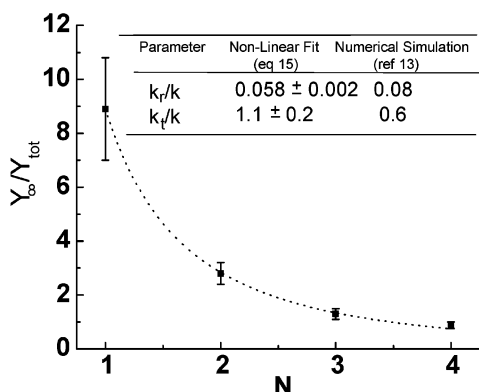
Figure 3. Nonlinear least-squares fit with eq 16 (shown by the dotted line) to the experimental damage ratio for guanine oxidation in a G(TTG)$_N$GG strand with $N = 1-4$ (shown as solid squares with error bars). The yields for $N = 1, 2$, and 4 are taken from ref 28, the yield for $N = 3$ is taken from the graph in ref 13. The parameters obtained from the fit and the literature data are compared in the graph.

statistical weights of opposite signs. In this situation the slopes obtained from the ln$R$ vs t plots cannot be associated with any meaningful "rate constant". This situation is unlikely for hole migration in relatively short bridges since G$^{+•}$ seems to be a fairly unreactive species. However, this possibility should be kept in mind since in other cases such as excess electron migration the situation may be different.

Distance Dependencies of Chemical Yields under Steady-State Conditions. This problem was analyzed extensively in the past both by numerical and analytical techniques.[7,8,10–13,25–27] The advantage of our approach is that it allows one to obtain the solutions in a form that is more compact and convenient for analysis of both diffusion and kinetically controlled situations. In general, the yield of oxidized acceptor Y_∞ and the relative oxidation yields depend on two parameters $\alpha = (2k_r/k)^{1/2}$ and $\omega = 2k_t/k$. From this it follows immediately that the only characteristics that can be extracted from steady-state experiments are the ratios of these rate constants. The use of eq 16 in fitting the damage ratio for guanine oxidation reported by Giese et al.[28] in a regular DNA sequence returns the values of $k_r/k = 0.058 \pm 0.002$ and $k_t/k = 1.1 \pm 0.2$ (Figure 3). Bixon et al.[13] used numerical simulations to reproduce the same experimental data and obtained the values of $k_r/k = 0.08$ and $k_t/k = 0.6$. The agreement between the two sets of results shows that the diffusion treatment is a powerful alternative to numerical analysis of complex kinetic schemes.

As a further illustration of this equivalence, eq 13a turns into eq 1 if αN is fairly small. The latter condition is easily satisfied if either k_r is much smaller than k or the DNA strand is short enough, or both. One obtains

$$Y_\infty = \mathrm{sech}(\alpha N) = [\cosh(\alpha N)]^{-1} \approx [1 + (\alpha^2/2)N^2]^{-1} =$$
$$[1 + (k_r/k)N^2]^{-1} \quad (20)$$

which is eq 1 for the yield of hole transfer through a DNA bridge presented by Jortner et al.[7]

For large N and no constraints imposed on k_t, the more general eq 13 should be applied. The asymptotic behavior of hyperbolic functions at large values of N immediately results in the approximations $\sinh(\alpha N) \approx \cosh(\alpha N) \approx e^{\alpha N}/2$ and, hence, gives the asymptotically exponential distance dependence for the yield of oxidized acceptor:

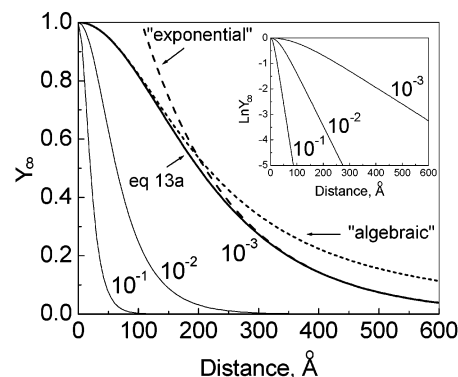$$Y_\infty = \frac{2\omega}{\alpha + \omega}e^{-\alpha N} \quad (21)$$

Figure 4. Distance dependencies of the steady-state yields of charge transfer calculated with eq 13a with $\delta = 6.8$ Å and the k_r/k ratios shown in the plot. The inset shows the same data plotted in coordinates ln Y_∞ vs distance. Dotted and dashed lines show the approximations to eq 13a for small and large charge-transfer distances ($k_r/k = 10^{-3}$) given by eqs 1 and 21a, respectively. The approximations are labeled using the terminology borrowed from ref 8.

In the diffusion-controlled situation eq 21 turns into eq 21a:

$$Y_\infty = 2e^{-\alpha N} \quad (21a)$$

This result is in full agreement with the predictions made in earlier studies.[8,10] Equations 1 and 21a are compared with eq 13a in Figure 4 for $k_r/k = 0.001$, illustrating the "crossover from an algebraic to an exponential asymptotic N dependence".[8] In eqs 21 and 21a the parameter $\alpha = (2k_r/k)^{1/2}$ mimics the falloff parameter β in the tunneling kinetics. Since α is typically small (<0.1 in the cases considered above), any attempt to plot the yields of hole transfer vs distance for a multistep process would result in abnormally small values of "β" as illustrated in the inset in Figure 4. It can be shown that the same exponential drop-off holds for the damage ratio for guanine oxidation expressed in eqs 15 and 16. Therefore, the diffusion approach is consistent with the previously suggested treatments.

Finally we would like to show the equivalence of the set of equations derived by Berlin et al.[10] for the damage ratio and the corresponding set derived from the diffusion approximation. For example, the expression obtained for one of the damage ratio discussed above (eq 15a) was obtained by Berlin et al.[10] in the original form

$$k_{\mathrm{rel,CT}} = \frac{Y_\infty}{Y(P_1)} = \frac{\sinh(\lambda)}{\lambda^2 \sinh(\lambda N)} \quad (22)$$

where $\lambda = (k_r/k)^{1/2} = 2^{-1/2}\alpha$ if expressed in the parameters used in our study. If λ is small, then $\sinh(\lambda) \approx \lambda$ and eq 22 turns directly into eq 15a, which describes the same physical situation.

Conclusions

The major advantage of the approach used in the present work is the capability of describing analytically both time-resolved and steady-state kinetics of charge migration in DNA. The major conclusions of this study are the following:

(i) The distance dependence of the effective rate constant of charge migration k_{CT} measured from the rate of product accumulation at late times is obtained in the form

$$k_{\mathrm{CT}} = \frac{\pi^2 k}{8N^2} + k_r = 1.23\frac{k}{N^2} + k_r$$

which includes both the rate constants of hopping and those of

Long Distance Charge Migration in DNA

J. Phys. Chem. B, Vol. 108, No. 7, 2004 **2437**

side reactions. The equation applies if the rate constant of charge transfer from the bridge to the acceptor k_t is greater than the diffusion rate k (the diffusion-controlled regime). This expression suggests the "inverse-square" distance dependence of k_{CT} as a function of DNA length in agreement with earlier predictions.

(ii) The yield of oxidized acceptor under steady-state conditions Y_∞ depends on DNA length in the form

$$Y_\infty = \frac{\omega}{\alpha \sinh(\alpha N) + \omega \cosh(\alpha N)}$$

where $\alpha = (2k_r/k)^{1/2}$ and $\omega = 2k_t/k$. The diffusion-controlled case given by (13a) corresponds to $\omega \rightarrow \infty$.

(iii) For the damage ratio the diffusion approach results in expressions that take into account the finite rate of hole transfer to the terminal acceptor:

$$\frac{Y_\infty}{Y(P_1)} = \frac{\omega}{\alpha[\alpha \cosh(\alpha N) + \omega \sinh(\alpha N)]}$$

$$\frac{Y_\infty}{Y_{tot}} = \frac{\omega}{\alpha \sinh(\alpha N) + \omega \cosh(\alpha N) - \omega}$$

At large N the steady-state yield of oxidized acceptor is approximated by an exponential function similar to the one used in the description of one-step tunneling:

$$Y_\infty = \frac{2\omega}{\alpha + \omega} e^{-\alpha N}$$

but now with the parameter $\alpha = (2k_r/k)^{1/2}$ playing the role the falloff parameter β in the kinetics of tunneling.

References and Notes

(1) Meggers, E.; Michel-Beyerle, M. E.; Giese, B. *J. Am. Chem. Soc.* **1998**, *120*, 12950−12955.

(2) Giese, B.; Amaudrut, J.; Kohler, A. K.; Spormann, M.; Wessely, S. *Nature* **2001**, *412*, 318−320.

(3) Giese, B. *Curr. Opin. Chem. Biol.* **2002**, *5*, 612−618.

(4) Henderson, P. T.; Jones, D.; Hampikian, G.; Kan, Y.; Schuster, G. B. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 8353−8358.

(5) Schuster, G. B. *Acc. Chem. Res.* **2000**, *33*, 253−260.

(6) Razskazovskii, Y.; Swarts, S. G.; Falcone, J.; Taylor, C.; Sevilla, M. D. *J. Phys. Chem.* **1997**, *101*, 1460−1467.

(7) Jortner, J.; Bixon, M.; Langenbacher, T.; Michel-Beyerle, M. E. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 12759−12765.

(8) Bixon, M.; Jortner, J. *J. Phys. Chem. B* **2000**, *104*, 3906−3913.

(9) Bixon, M.; Jortner, J. *J. Phys. Chem. A* **2001**, *105*, 10322−10328.

(10) Berlin, Y. A.; Burin, A. L.; Ratner, M. A. *J. Phys. Chem. A* **2000**, *104*, 443−445.

(11) Berlin, Y. A.; Burin, A. L.; Ratner, M. A. *J. Am. Chem. Soc.* **2001**, *123*, 260−268.

(12) Li, X.-Q.; Zhang, H.; Yan, Y. *J. Phys. Chem. A* **2001**, *105*, 9563−9567.

(13) Bixon, M.; Giese, B.; Wessely, S.; Langenbacher, T.; Michel-Beyerle, M. E.; Jortner, J. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 11713−11716.

(14) Wang, X.; Nau, W. M. *ChemPhysChem* **2001**, 761−766.

(15) Biscout, D. J.; Kats, E. *Phys. Lett. A* **2002**, *300*, 479−484.

(16) Petrov, E. G.; Shevchenko, Y. V.; May, V. *Chem. Phys.* **2003**, *288*, 269−279.

(17) Wagenknecht, H.-A.; Stemp, E. D. A.; Barton, J. K. *J. Am. Chem. Soc.* **2000**, *122*, 1−7.

(18) Wagenknecht, H.-A.; Rajski, S. R.; Pascaly, M.; Stemp, E. D. A.; Barton, J. K. *J. Am. Chem. Soc.* **2001**, *123*, 4400−4407.

(19) Pascaly, M.; Yoo, J.; Barton, J. K. *J. Am. Chem. Soc.* **2002**, *124*, 9083−9092.

(20) Anderson, R. F.; Patel, K. B.; Wilson, W. R. *J. Chem. Soc., Faraday Trans.* **1991**, *87*, 3739−3745.

(21) Anderson, R. F.; Wright, G. A. *Phys. Chem. Chem. Phys.* **1999**, *1*, 4827−4831.

(22) Delaney, S.; Pascaly, M.; Bhattacharya, P. K.; Han, K.; Barton, J. K. *Inorg. Chem.* **2002**, *41*, 1966−1974.

(23) Defares, J. G.; Sneddon, I. N. *An introduction to the mathematics of medicine and biology*; Year Book Medical Publishers INC.: Chicago, IL, 1961.

(24) Lewis, F. D.; Liu, X.; Liu, J.; Miller, S. *Nature* **2000**, *406*, 51−53.

(25) Bixon, M.; Jortner, J. *J. Am. Chem. Soc.* **2001**, *123*, 12556−12567.

(26) Jortner, J.; Bixon, M.; Voityuk, A. A.; Rosch, N. *J. Phys. Chem. A* **2002**, *106*, 7599−7606.

(27) Bixon, M.; Jortner, J. *Chem. Phys.* **2002**, *281*, 393−408.

(28) Giese, B.; Wesseley, S.; Spormann, M.; Lindemann, U.; Meggers, E.; Michel-Beyerle, M. E. *Angew. Chem., Int. Ed.* **1999**, *38*, 996−998.