

Direct Measurement of the Dynamics of Hole Hopping in Extended DNA G-Tracts. An Unbiased Random Walk

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Abstract: We report the measurement of distance- and temperature-dependent rate constants for charge separation in capped hairpins in which a stilbene hole acceptor and hole donor are separated by A_3G_n diblock polypurine sequences consisting of 3 adenines and 1–19 guanines. The longer diblock systems obey the simplest model for an unbiased random walk, providing a direct measurement of $k_{\text{hop}} = 4.3 \times 10^9 \text{ s}^{-1}$ for a single reversible G-to-G hole hopping step, somewhat faster than the value of $1.2 \times 10^9 \text{ s}^{-1}$ calculated for A-tract hole hopping. The temperature dependence for hopping in A_3G_{13} provides values of $E_{\text{act}} = 2.8 \text{ kcal/mol}$ and $A = 7 \times 10^9 \text{ s}^{-1}$, consistent with a weakly activated, conformationally gated process.

Random walks have been described for diverse processes including excitation transport in dendrimers,¹ photosynthetic antenna proteins,² and single crystals.³ They have also been invoked in studies of DNA transcription,⁴ structural change,⁵ DNA computing,⁶ and charge transport. Following the initial suggestion by Schuster and co-workers⁷ that long-distance charge transport in DNA might occur via “hopping” of a radical cation or hole localized on one base to a neighboring base, there have been numerous experimental and theoretical studies of DNA hole hopping.⁸ Alternative models involving delocalized holes have also been advanced.⁹ Most experimental studies of the distance dependence of hole transport have employed relative yields as surrogates for rate constants. However, hole transport in DNA is a complex process in which charge recombination and chemical reactions compete with hole hopping. Thus relative yields are not determined solely by hopping kinetics. To our knowledge, no direct measurements of hole hopping dynamics in DNA have been reported to date.

We report here the results of our investigation of the distance and temperature-dependent dynamics of hole transport in stilbene donor–acceptor capped hairpins in which the hole donor (Sa) and hole acceptor (Sd) are separated by A_3G_n diblock polypurine sequences consisting of 3 adenines and 1–19 guanines (Figure 1a). The longer diblock systems obey the simplest model for an unbiased random walk, providing a value of $k_{\text{hop}} = (4.3 \pm 0.2) \times 10^9 \text{ s}^{-1}$ for a single reversible hole hopping step between an oxidized G and its nearest neighbor. The temperature dependence for hopping in A_3G_{13} provides values of $E_{\text{act}} = 2.8 \text{ kcal/mol}$ and $A = 7 \times 10^9 \text{ s}^{-1}$, consistent with a weakly activated, conformationally gated process.

We recently reported measurements of the dynamics and efficiency of photoinduced hole transport in DNA hairpin conjugates

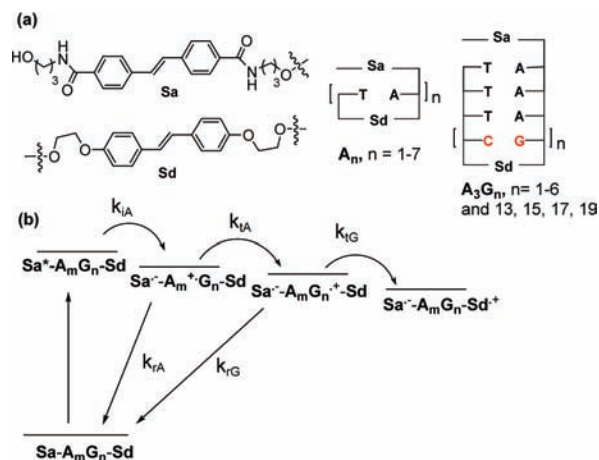


Figure 1. (a) Structures of Sa and Sd chromophores and Sa/Sd capped hairpins having A_n base sequences and A_3G_n diblock sequences. (b) Simplified mechanism for charge separation in A_mG_n diblock systems.

possessing a stilbenedicarboxamide (Sa) hole donor and stilbene-diether (Sd) hole acceptor separated by duplex sequences consisting of either a short A-tract (1–7 adenines) or diblock sequences having a short A-tract (1–4 adenines) followed by a short G-tract (1–7 guanines, Figure 1a).^{10–13} The A_3G_n sequences display distance-dependent rate constants for formation of the $\text{Sa}^{\cdot+}/\text{Sd}^{\cdot+}$ charge separated states (k_{cs}) and efficiencies (quantum yields for charge separation) that are independent of distance. This behavior was explained by the simplified mechanism shown in Figure 1b. Photochemical hole injection (k_{IA}) yields a $\text{Sa}^{\cdot+}/\text{A}^{\cdot+}$ contact radical ion pair that undergoes hole transport and hole trapping by the G-tract (k_{IA}) in competition with charge recombination (k_{rA}). In the case of G-tracts possessing two or more guanines, neither charge recombination to the ground state (k_{rG}) nor hole return to the A-tract competes effectively with G-tract hole transport to Sd. This results in charge separation efficiencies that are independent of the length of the G-tract. Hole transport times for A_3G_7 approach the 6 ns pump–probe time window for our Ti-sapphire-based laser system.¹³ These results suggested that it should be possible to investigate the dynamics of hole transport in much longer G-tracts by means of nanosecond time-resolved transient absorption spectroscopy.

The syntheses and characterization of the diblock systems A_3G_n ($n = 13, 15, 17, \text{ and } 19$) and methods used for transient absorption measurements are described in the Supporting Information. Transient absorption spectra were obtained by exciting samples with 7 ns, 2 mJ, 355 nm laser pulses generated using the frequency-tripled output of a Continuum Precision II 8000 Nd:YAG laser. The transient spectra of A_3G_{17} constructed from single wavelength decays obtained at 10 nm intervals are shown in Figure 2a. These spectra display maxima at ca. 525 and 575 nm, assigned to $\text{Sd}^{\cdot+}$

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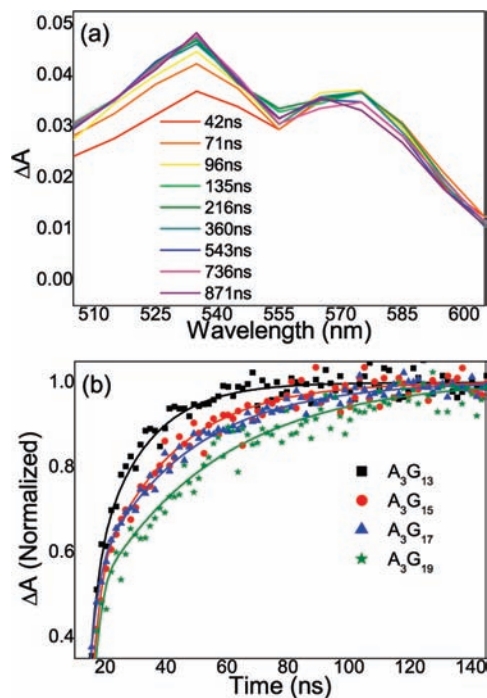


Figure 2. (a) Transient absorption spectra following 355 nm, 7 ns laser pulses for the diblock system A_3G_{17} in an aqueous solution. (b) Normalized kinetic traces for the formation of Sd^{++} in long A_3G_n diblock systems.

and Sa^{--} respectively, with a band intensity ratio of 1.3:1 which is similar to that observed for A-tract Sa – Sd systems in which charge separation is complete on the time scale of the transient absorption measurements (<1 ns).^{10,13} The transient absorption values for the four systems are similar, and none of the signals decay during the 180 ns time window of these measurements. Thus the efficiency of charge separation is similar for these systems, and none of them undergo either charge recombination or chemical reactions on the time scale of these measurements. Rise times for the formation of Sd^{++} at 25 °C are shown in Figure 2b along with single-exponential fits to the kinetic data. A plot of the charge separation rate constants ($k_{cs} = \tau_{rise}^{-1}$) versus number of base pairs for the long G-tracts is shown in Figure 3 along with our published data for A-tracts and for diblock systems having shorter G-blocks.¹³ The absence of data for A_3G_n sequences with $6 < n < 13$ is a consequence of the gap in time scales between our fs and ns transient instruments. The temperature-dependent rise times for formation of Sd^{++} from A_3G_{13} are shown in Figure 4a, and an Arrhenius plot for this data is shown in Figure 4b. Kinetic data with experimental errors are summarized in Tables S1 and S2 (Supporting Information).

The simplest of random walk processes is the unbiased first passage random walk in one dimension, in which the reflection point and trapping site are located at opposite ends of the walk and each forward and return step has the same rate constant.^{14,15} For a long but finite system the first passage time can be described by the simple relationship

$$\tau(N) = (1/2k_{hop})N^2 \quad (1)$$

where $\tau(N)$ is the time required for N hopping steps and k_{hop} is the rate constant for a single hopping step.¹⁴ Since the hole arrival time at the beginning of the A_3G_n G-tracts is <1 ns,¹³ the charge separation times for the longer diblock systems directly provide the first passage times. Thus our experimental lifetime data for the longer $\tau(N)$ can be used with eq 1 to provide a value of $k_{hop} = (4.3$

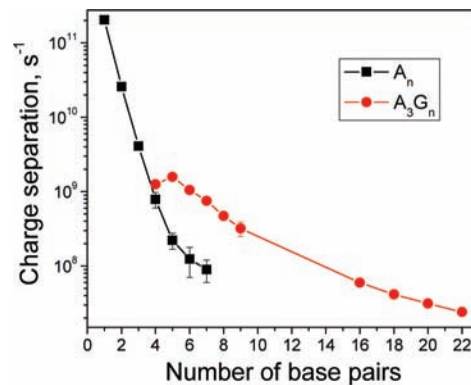


Figure 3. Rate constants for photoinduced charge separation in Sa/Sd systems having A-tract and A_3G_n base sequences. Error bars are smaller than symbols for most A_3G_n sequences.

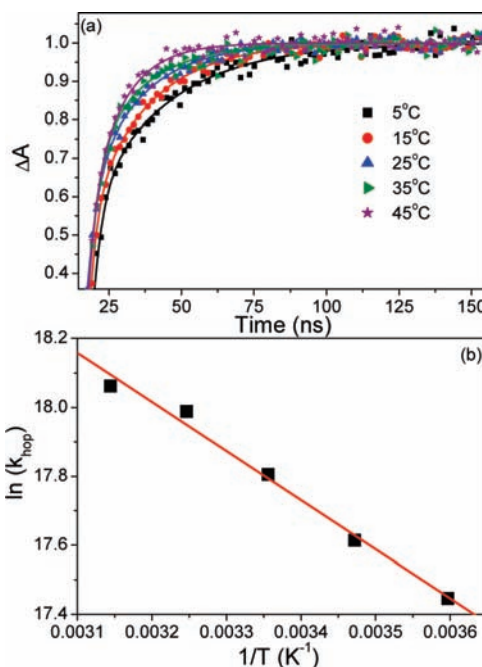


Figure 4. (a) Temperature-dependent kinetic traces for hole arrival times in A_3G_{13} . (b) Arrhenius plot showing the temperature dependence of hole arrival times in A_3G_{13} .

$\pm 0.2) \times 10^9$ s⁻¹ for the longer A_3G_n systems. The same value can be obtained using the kinetic model developed by Blaustein et al. for hole hopping in A-tract systems, which includes hole injection and charge recombination rate constants (see Supporting Information).¹⁶ This value is larger than the value of $k_{hop} = 1.2 \times 10^9$ s⁻¹ for A-tract hole hopping obtained using this model. The experimental values for k_{hop} can be compared to the results recently reported by Steinbrecher et al.¹⁷ for the simulated dynamics of G-to-G and A-to-A hole hopping in single strand $A_4G_2A_4$ and A_{10} sequences obtained using a QM/MM model that explicitly considers solvent interactions. Their model assumes charge localization on a single purine base, in accord with some,¹⁸ but not all, theoretical models.⁹ Their estimated rate constants of 1.3×10^9 s⁻¹ for G-to-G and 4.1×10^9 s⁻¹ for A-to-A hopping are similar in magnitude to our experimental values but inverted in order. Hopping rates are expected to be determined by reorganization energies and, to a lesser extent, electron transfer integrals. The internal reorganization energies calculated using classical Marcus theory are larger for GG vs AA.^{17,19,20} The electron transfer integral for GG is larger than that for AA; however, this does not fully compensate for differences

in reorganization energy.²¹ Consideration of both structural dynamics and quantum mechanical analysis of hole transport may prove necessary to fully understand differences in the dynamics of A- vs G-tract hole transport.

The temperature dependence of the charge separation rates for A₃G₁₃ (Figure 4b) provides values of $E_{\text{act}} = 2.8$ kcal/mol and $A = 7 \times 10^9$ s⁻¹, corresponding to values of $\Delta H^\ddagger = 2.25$ kcal/mol and $\Delta S^\ddagger = -15.5$ eu. An estimated value of $\Delta S^\ddagger = -6.6$ eu per hopping step can be obtained using eq 1 to calculate the temperature-independent component of k_{hop} (see Supporting Information). Whereas the temperature dependence of the dynamics of photoinduced electron transfer²² and quantum yields for product formation in DNA have been reported,²³ our data provide the first experimental determination of the activation parameters for hole hopping. The large negative entropy of activation for a single G-to-G hop is consistent with current theoretical models for conformationally gated hole transport in DNA.^{24,25} Importantly, our experimental value of $E_{\text{act}} = 2.8$ kcal/mol is smaller than the value of 3.9 kcal/mol calculated by Steinbrecher et al. for a single G-to-G hop.¹⁷ Further theoretical analysis will be necessary to understand the temperature dependence of DNA hopping processes.

Most previous studies of A-tract hole transport have employed quantum yields or relative yields for charge separation or chemical reactions as surrogates for rate constants. This has led to results that were difficult or impossible to interpret using a simple random walk model or a combination of superexchange and hopping models.²⁶ For example, in Giese's classic study of oxidative cleavage at G vs GGG in G⁺A_nGGG systems ($n = 1-8, 16$) the ratio of G/GGG cleavage was found to be independent of n when $n > 4$.²⁷ Our results show that the efficiency of an unbiased multistep hole transport process can be independent of distance, whereas the rate constant remains distance dependent even in very long hopping sequences. The shallow distance dependence of A-tract mediated charge separation quantum yields observed by Takada and co-workers²⁸ and the periodic dependence of chemical trapping efficacy observed by Barton and co-workers²⁹ most likely reflect the occurrence of processes that compete with an unbiased random walk. Thus we would caution against the use of chemical yields or quantum yields as surrogates for rate constants in systems as complex as DNA hole transport.

In summary, the distance dependence of the dynamics of hole transport in long diblock A₃G_n systems is consistent with an unbiased first passage random walk model for G-tract hole hopping. A random walk is compatible with hopping between localized holes; however, it does not preclude some degree of charge delocalization. Long G-tracts have not previously been employed in studies of DNA hole transport and are found to have a faster hopping rate than the extensively studied A-tracts. Interruption of either a G-tract or A-tract with a base having a higher or lower oxidation potential or with an abasic site is expected to result in slower hole transport.¹² Thus the potential use of duplex DNA containing natural base pairs in molecular electronic devices is severely limited by slow hole transport rate constants. Finally, we note that theoretical analyses of our results for A-tract hole transport have found that our stilbene-capped hairpins provide "good models" for DNA hole transport.^{20,24}

We fully anticipate that the same will be true of our studies of G-tract hole transport.

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Supporting Information Available: Materials, methods, and kinetic modeling. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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