

## Increasing the Speed Limit for Hole Transport in DNA

Arun K. Thazhathveetil, Anton Trifonov, Michael R. Wasielewski,\* and Frederick D. Lewis\*

Department of Chemistry and Argonne–Northwestern Solar Energy Research (ANSER) Center, Northwestern University, Evanston, Illinois 60206-3113, United States

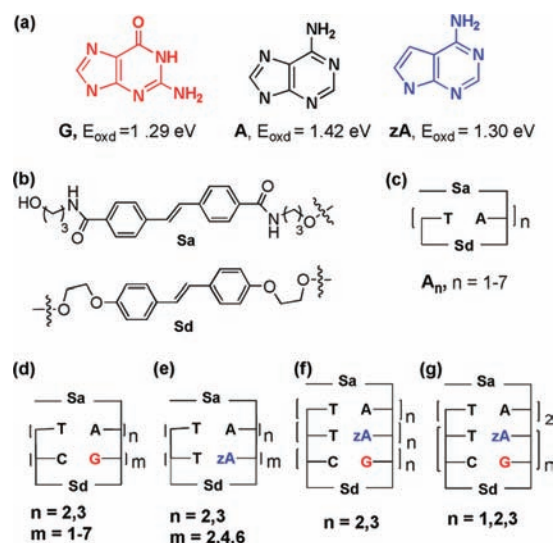
Supporting Information

**ABSTRACT:** Transport of positive charge or holes in DNA occurs via a thermally activated multi-step hopping mechanism. The fastest hopping rates reported to date are those for repeating poly(purine) sequences in which hopping occurs via a random walk mechanism with rate constants of  $k_{\text{hop}} = 4.3 \times 10^9 \text{ s}^{-1}$  for poly(dG) and  $1.2 \times 10^9 \text{ s}^{-1}$  for poly(dA). We report here the dynamics of charge separation in DNA conjugates possessing repeating 7-deazaadenine (zA) sequences. These data provide an estimated value of  $k_{\text{hop}} = 4.2 \times 10^{10} \text{ s}^{-1}$  for poly(zA), an order of magnitude faster than for poly(dG).

Significant progress toward understanding the mechanism and dynamics of photoinduced charge transport through DNA has been made during the past decade.<sup>1</sup> It is now generally accepted that transport of positive charge (holes) over multiple base pairs in DNA occurs via a hole hopping process.<sup>2</sup> Both delocalized<sup>3</sup> and localized<sup>4</sup> hole transport models have been proposed. The hopping process is inherently slow, thus limiting potential applications of duplex DNA as a conducting molecule in molecular-scale devices. We have recently reported the experimental measurements of rate constants for reversible hole hopping in poly(dA) and poly(dG) sequences ( $k_{\text{hop}} = 1.2 \times 10^9$  and  $4.3 \times 10^9 \text{ s}^{-1}$ , respectively).<sup>5</sup> Our value of  $k_{\text{hop}}$  for poly(dG) is consistent with the hole mobility ( $\mu = 10^{-4} \text{ cm}^2 \text{ V}^{-1} \text{ s}^{-1}$ ) calculated by Senthilkumar et al.<sup>6</sup> but is 2 orders of magnitude lower than the value derived by time-resolved microwave conductivity from measurements on a poly(purine)-containing duplex in organic solvents.<sup>7</sup> To place these values in a broader context, our value of  $\mu$  is similar to that for poly(*N*-vinylcarbazole)<sup>8</sup> but much smaller than those for some columnar discotic materials.<sup>9</sup> Hopping rates for alternating or mixed-base DNA sequences are slower still.<sup>10–12</sup>

Slow hole hopping rates constitute a major impediment to achieving wire-like behavior (fast rates and high efficiency) in DNA, in effect determining the speed limit for multi-step hole transport in DNA. A promising solution to this problem was recently reported by Kawai et al.,<sup>13</sup> who observed a significant increase in the apparent hole transport rate between guanines in a GA<sub>5</sub>G sequence when the A<sub>5</sub> bridge was modified by replacing some or all of the adenines with 7-deazaadenine (zA, Chart 1a). This change was attributed to the higher HOMO energy level for zA vs A, which provides a better match for the HOMO level of G. Stimulated by this report, we have investigated the effects of zA incorporation on the dynamics and efficiency of charge separation in DNA diblock, triblock, and alternating systems possessing A, G, and zA bases. Our measured value of  $k_{\text{hop}} = 4.2 \times 10^{10} \text{ s}^{-1}$

**Chart 1.** (a) Structures and Oxidation Potentials for the Purine Bases A, G, and zA (ref 20), (b) Structures of the Stilbenes Sa and Sd, and (c–g) Structures of Capped Hairpins Having the Sequences A<sub>n</sub>, A<sub>n</sub>G<sub>m</sub>, A<sub>n</sub>zA<sub>m</sub>, A<sub>n</sub>zA<sub>n</sub>G<sub>m</sub>, and A<sub>2</sub>(GzA)<sub>n</sub>

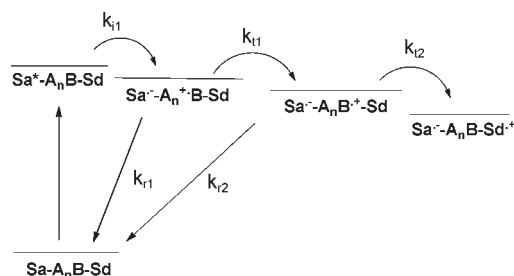


for a poly(zA) sequence is an order of magnitude faster than that for G-hopping, resulting in faster and more efficient hole transport in the base sequences containing zA.

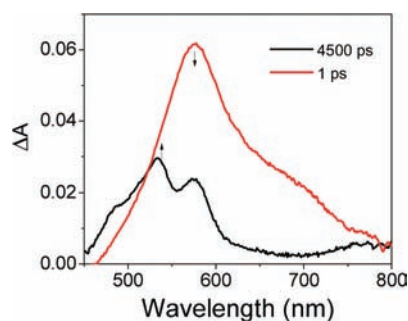
We have employed capped hairpins possessing a stilbenedi-carboxamide (Sa) capping group and a stilbenediether (Sd) hairpin linker separated by various base-pair domains in our investigations of photoinduced charge separation in DNA (Chart 1b).<sup>10,11,14,15</sup> Singlet Sa serves as an electron acceptor and Sd serves as a hole trap in these systems. Differences in the transient absorption spectra of <sup>1</sup>Sa, Sa<sup>-\*</sup>, and Sd<sup>+\*</sup> facilitate investigation of the dynamics and efficiency of charge separation by means of optical pump–probe spectroscopy on the femto-second and nanosecond time scales. When the capped hairpins have a poly(purine) sequence consisting of an A-tract or G-tract (Chart 1c) adjacent to the photoexcited hole injector (e.g., <sup>1</sup>Sa), charge recombination is faster than hole transport over multiple bases, resulting in highly inefficient charge separation.<sup>10,11,15</sup> However, shorter hole transport times and higher efficiencies can be achieved by the use of A<sub>n</sub>G<sub>m</sub> diblock purine sequences containing a short A-block (2 or 3 base pairs) followed by a

Received: May 25, 2011

Published: July 05, 2011



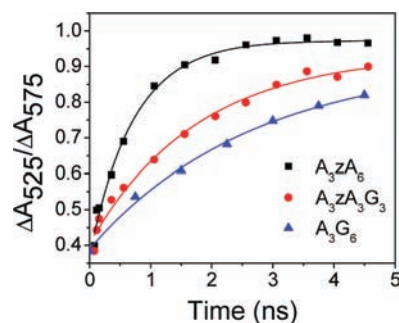
**Figure 1.** Mechanism for charge separation in  $A_nB$  polypurine systems.  $B = \text{poly(G)}, \text{poly(zA)}, \text{zA}_n\text{G}_m$  or  $(\text{GzA})_n$ . See Chart 1c–g for structures.



**Figure 2.** Transient spectra of  $A_2zA_2G_2$ . The red trace represents the locally excited singlet state ( $^1\text{Sa}$ ) immediately after photoexcitation, and the black trace represents the transient spectra after 4500 ps. The  $\text{Sa}^{\bullet-}$  radical anion absorbs primarily at 575 nm and the  $\text{Sd}^{\bullet+}$  radical cation at 535 nm.

longer G-block (Chart 1d).<sup>5,11</sup> Once the hole reaches the G-block in these diblock systems, return electron transfer requires thermal repopulation of the A-block, a process which is slower than hole hopping (Figure 1). Our studies have provided rate constants for reversible G-to-G and A-to-A hole hopping,  $k_{\text{hop}} = 4.3 \times 10^9$  and  $1.2 \times 10^9 \text{ s}^{-1}$ , respectively, and activation parameters of  $E_{\text{act}} = 2.3 \text{ kcal/mol}$  and  $A = 7 \times 10^9 \text{ s}^{-1}$  for hole transport across a  $G_{13}$ -block, consistent with a weakly activated, conformationally gated hole transport process.<sup>11</sup>

Capped hairpins possessing zA bases in diblock, triblock, and alternating purine sequences (Chart 1e–g) were prepared and characterized by the methods previously described for the  $A_n$  and  $A_n\text{G}_m$  hairpins (see Supporting Information).<sup>11</sup> Values of  $T_m$  are lower for the  $A_n\text{zA}_m$  and  $A_n\text{zA}_n\text{G}_n$  systems than for the corresponding  $A_n\text{G}_m$  systems, in accord with the reported effect of isolated  $\text{A} \rightarrow \text{zA}$  replacement on duplex stability.<sup>16,17</sup> However, all of the zA-modified hairpins have well-defined melting curves with values of  $T_m > 60^\circ \text{C}$ . Femtosecond time-resolved transient absorption spectra in aqueous solution were obtained as previously described using 350 nm excitation (which provides selective excitation of Sa) from a Ti-sapphire-based system having a time resolution of ca. 180 fs, a spectral range of 425–800 nm, and a time window of 0–6 ns.<sup>11</sup> The transient absorption spectra shown in Figure 2 for  $A_2zA_2G_2$  are typical of our data for zA-containing systems. Charge separation times ( $\tau_{\text{cs}}$ ) are determined from first-order fits to plots of the ratio of the transient absorbance at 525 nm ( $\text{Sd}^{\bullet+}$  band maximum) and 575 nm ( $\text{Sa}^{\bullet-}$  band maximum) vs time (Figure 3). This ratio increases from ca. 0.4 for the  $\text{Sa}^{\bullet-}-\text{A}_3^+\text{B}_2-\text{Sd}$  ( $\text{B}_2 = \text{G}_6, \text{zA}_6, \text{ or } \text{zA}_3\text{G}_3$ ) charge-separated state formed at short delay times to ca. 1.0 for the



**Figure 3.** Plot of  $\Delta A_{525}/\Delta A_{575}$  vs time for  $A_3G_6$ ,  $A_3zA_3G_3$ , and  $A_3zA_6$  sequences.

**Table 1. Quantum Yields for Charge Separation ( $\Phi_{\text{cs}}$ ) and Charge Separation Times ( $\tau_{\text{cs}}$ ) for Capped Hairpins<sup>a</sup>**

sequence	$\Phi_{\text{cs}}$	$\tau_{\text{cs}}$ , ns	sequence	$\Phi_{\text{cs}}$	$\tau_{\text{cs}}$ , ns
$A_4$	0.23	1.3	$A_9^b$	0.05	20
$A_2G_2^c$	0.38	0.22	$A_3G_6^c$	0.27	3.1
$A_2zA_2$	0.56	0.052	$A_3zA_6$	0.33	0.72
$A_6$	0.09	9.0	$A_3zA_3G_3$	0.34	2.2
$A_2G_4^c$	0.32	1.0	$A_2\text{GzA}$	0.54	0.11
$A_2zA_4$	0.41	0.15	$A_2(\text{GzA})_2$	0.38	0.33
$A_2zA_2G_2$	0.42	0.42	$A_2(\text{GzA})_3$	0.37	0.93

<sup>a</sup> Structures of capped hairpins are shown in Chart 1. Data shown are the averages of at least two measurements. Errors are ca. 10%. <sup>b</sup> Values for  $A_9$  are estimated. <sup>c</sup> Values taken from ref 7.

$\text{Sa}^{\bullet-}-\text{A}_3\text{B}_2-\text{Sd}^{\bullet+}$  charge-separated state at longer delay times. The transient spectra do not decay on the time scale of our measurements, indicative of the formation of long-lived charge-separated states. Quantum yields for charge separation ( $\Phi_{\text{cs}}$ ) are estimated by comparing the integrated band intensities of the transient absorption spectra at long delay times with those for  $A_1$  ( $\Phi_{\text{cs}} = 1$ ).<sup>15</sup>

Values of  $\tau_{\text{cs}}$  and  $\Phi_{\text{cs}}$  for zA-containing systems are reported in Table 1, along with our published data for selected  $A_n$  and  $A_n\text{G}_m$  diblock conjugates. Estimated values for  $A_9$  are obtained by extrapolation of the data for shorter A-tracts. Comparison of the results for the diblock  $A_2zA_2$ ,  $A_2zA_4$ , and  $A_3zA_6$  systems with the corresponding  $A_n\text{G}_m$  systems shows a pronounced decrease in  $\tau_{\text{cs}}$  and increase in  $\Phi_{\text{cs}}$  upon replacement of G with zA. Values of  $\tau_{\text{cs}}$  for two triblock systems ( $A_n\text{zA}_n\text{G}_m$ ,  $n = 2$  or  $3$ ) and three alternating GzA systems ( $A_2(\text{GzA})_n$ ,  $n = 1-3$ ) are shorter than those for the  $A_n\text{G}_m$  systems but longer than those for the  $A_n\text{zA}_m$  systems having the same total number of base pairs. Values of  $\Phi_{\text{cs}}$  for the triblock and alternating GzA systems are larger than those for  $A_n\text{G}_m$  but slightly smaller than those for  $A_n\text{zA}_m$ . Thus, the replacement of A or G with zA in diblock, triblock, and alternating systems results in a decrease in the time required for charge separation and an increase in the charge separation efficiency.

More efficient charge separation in our diblock  $A_n\text{G}_m$  vs poly(A) systems (Chart 1c,d) was attributed to faster hole hopping in a  $G_n$  vs  $A_n$  track as well as the lower oxidation potential of G vs A, which effectively prevents charge return from the G-block to the A-block on the nanosecond time scale of our experiments (Figure 1).<sup>11</sup> The decrease in  $\tau_{\text{cs}}$  for the  $A_n\text{zA}_m$  vs  $A_n\text{G}_m$  diblock systems requires that the rate constant for traversal of a  $zA_m$ -block be faster than that for a  $G_m$ -block ( $k_{12}$ ). Assuming

that the time required for traversal of the A-block in the  $A_3zA_6$  system is the same as that for  $A_3$  (0.29 ns),<sup>18</sup> the traversal time for the  $zA_6$ -block is 0.43 ns (0.72 – 0.29 ns). This traversal time provides an estimated value of  $k_{\text{hop}} = 4.2 \times 10^{10} \text{ s}^{-1}$  for an unbiased  $zA$ -to- $zA$  random walk in the  $zA_6$ -block ( $k_{\text{hop}} = N^2/2\tau$ , where  $N$  is the number of hops and  $\tau$  is the traversal time).<sup>19</sup> This hopping rate is an order of magnitude faster than for a G-to-G random walk and 30 times faster than for an A-to-A random walk. Faster hole hopping for  $zA$  vs G permits hole transport to compete more effectively with either charge recombination from the  $zA$ -block ( $k_{r2}$ , Figure 1) or thermal repopulation of the A-block, resulting in an increase in  $\Phi_{\text{cs}}$ . The increase in  $\Phi_{\text{cs}}$  is limited by charge recombination within the A-block ( $k_{r1}$ ) prior to arrival at the  $zA$ -block ( $k_{t1}$ ).

Values of  $\tau_{\text{cs}}$  for two triblock systems  $A_nzA_nG_n$  ( $n = 2$  or  $3$ ) are longer than those for the corresponding diblock  $A_nzA_m$  systems. This is consistent with slower G-to-G vs  $zA$ -to- $zA$  hopping. Values of  $\Phi_{\text{cs}}$  for the triblock systems are, however, essentially the same as those for the  $A_nzA_m$  diblock systems. This indicates that the efficiency of charge separation is determined largely within the  $A_nzA_n$  segment of our triblock systems and that little or no charge recombination occurs once the hole reaches the G-block. The three alternating  $A_2(\text{GzA})_n$  systems have values of  $\tau_{\text{cs}}$  slightly longer and values of  $\Phi_{\text{cs}}$  slightly smaller than those for the  $A_nzA_m$  diblock systems. Thus, the alternating (GzA) sequences display hole transport behavior more similar to that of poly( $zA$ ) than poly(G) sequences.

Kawai et al. reported that replacing the  $A_5$  sequence in  $GA_5G$  with  $zA_5$  results in enhancement of the G-to-G transport rate by a factor of  $>10^3$ .<sup>13</sup> They attributed this increase to closer spacing of the HOMO energy levels of G and  $zA$  vs G and A, which would result in faster hole injection from G into the poly( $zA$ ) vs poly(A) bridge. Investigations of purine oxidation potentials by Thorp and co-workers indicated that the oxidation potentials of G and  $zA$  are essentially the same (Chart 1a).<sup>20</sup> The necessity of thermal detrapping of the hole on G for transport across  $A_5$ , but not across  $zA_5$ , can account in part for the very large rate acceleration observed by Kawai et al.<sup>13</sup> However, much faster  $zA$ -to- $zA$  vs A-to-A hole transport is also important. It is important to note that our experimental design does not involve endergonic hole injection and thus permits direct measurements of poly(G) and poly( $zA$ ) charge traversal times, from which hopping rate constants can be obtained for the longer purine blocks.

A plausible explanation for fast  $zA$ -tract hole transport is suggested by the higher mobility reported for poly(purines) in organic solvents<sup>7</sup> and by a recent study of duplexes possessing a 7-deazaguanine ( $zG$ ) $\rightarrow$ G substitution.<sup>16</sup> A single  $zG$  substitution results in increased conformational mobility and decreased major groove hydration, both of which might lower the activation energy for hole migration. These results are consistent with a recent theoretical study which finds that charge transport is coupled to solvent fluctuations.<sup>21</sup> Experiments designed to further explore the effects of duplex conformational mobility and hydration on hole transport dynamics are in progress.

## ■ ASSOCIATED CONTENT

Supporting Information. Characterization of conjugates ( $m/z$  values, UV,  $T_M$ , and CD), transient absorption, and plots showing time-dependent band intensity ratios. This material is available free of charge via the Internet at <http://pubs.acs.org>.

## ■ AUTHOR INFORMATION

### Corresponding Author

fdl@northwestern.edu; m-wasielewski@northwestern.edu

## ■ ACKNOWLEDGMENT

We thank Josh Vura-Weis for helpful discussions. This work was supported by the Chemical Sciences, Geosciences, and Biosciences Division, Office of Basic Energy Sciences, DOE under grants no. DE-FG02-96ER14604 (F.D.L.) and DE-FG02-99ER14999 (M.R.W.).

## ■ REFERENCES

- (a) Schuster, G. B., Ed. *Long-Range Charge Transfer in DNA, I and II*; Springer: Berlin, 2004; Vol. 236, p 237. (b) Wagenknecht, H. A. *Charge Transfer in DNA*; Wiley-VCH: Weinheim, 2005. (c) Genereux, J. C.; Barton, J. K. *Chem. Rev.* **2010**, *110*, 1642.
- (a) Schuster, G. B. *Acc. Chem. Res.* **2000**, *33*, 253. (b) Giese, B. *Acc. Chem. Res.* **2000**, *33*, 631.
- (a) Barnett, R. N.; Cleveland, C. L.; Joy, A.; Landman, U.; Schuster, G. B. *Science* **2001**, *294*, 567. (b) Basko, D. M.; Conwell, E. M. *Phys. Rev. Lett.* **2002**, *88*, 98102.
- (a) Voityuk, A. A. *J. Phys. Chem. B* **2005**, *109*, 10793. (b) Kravec, S. M.; Kinz-Thompson, C. D.; Conwell, E. M. *J. Phys. Chem. B* **2011**, *115*, 6166. (c) Burin, A. L.; Uskov, D. B. *J. Chem. Phys.* **2008**, *129*.
- Conron, S. M. M.; Thazhathveetil, A. K.; Wasielewski, M. R.; Burin, A. L.; Lewis, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 14388.
- Senthilkumar, K.; Grozema, F. C.; Guerra, C. F.; Bickelhaupt, F. M.; Lewis, F. D.; Berlin, Y. A.; Ratner, M. A.; Siebbeles, L. D. A. *J. Am. Chem. Soc.* **2005**, *127*, 14894.
- Yamagami, R.; Kobayashi, K.; Saeki, A.; Seki, S.; Tagawa, S. *J. Am. Chem. Soc.* **2006**, *128*, 2212.
- Miyasaka, H.; Khan, S. R.; Itaya, A. *J. Phys. Chem. A* **2002**, *106*, 2192.
- (a) van de Craats, A. M.; Warman, J. M. *Adv. Mater.* **2001**, *13*, 130. (b) van de Craats, A. M.; Warman, J. M.; de Haas, M. P.; Adam, D.; Simmerer, J.; Haarer, D.; Schuhmacher, P. *Adv. Mater.* **1996**, *8*, 823.
- Lewis, F. D.; Daublain, P.; Cohen, B.; Vura-Weis, J.; Shafirovich, V.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2007**, *129*, 15130.
- Vura-Weis, J.; Wasielewski, M. R.; Thazhathveetil, A. K.; Lewis, F. D. *J. Am. Chem. Soc.* **2009**, *131*, 9722.
- Blaustein, G. S.; Lewis, F. D.; Burin, A. L. *J. Phys. Chem. B* **2010**, *114*, 6732.
- Kawai, K.; Kodera, H.; Osakada, Y.; Majima, T. *Nature Chem.* **2009**, *1*, 156.
- Lewis, F. D.; Wu, Y.; Zhang, L.; Zuo, X.; Hayes, R. T.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2004**, *126*, 8206.
- Lewis, F. D.; Zhu, H.; Daublain, P.; Cohen, B.; Wasielewski, M. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 7982.
- Ganguly, M.; Wang, F.; Kaushik, M.; Stone, M. P.; Marky, L. A.; Gold, B. *Nucleic Acids Res.* **2007**, *35*, 6181.
- Ganguly, M.; Wang, R. W.; Marky, L. A.; Gold, B. *J. Phys. Chem. B* **2010**, *114*, 7656.
- Lewis, F. D.; Zhu, H.; Daublain, P.; Fiebig, T.; Raytchev, M.; Wang, Q.; Shafirovich, V. *J. Am. Chem. Soc.* **2006**, *128*, 791.
- (a) Bar-Haim, A.; Klafter, J. *J. Chem. Phys.* **1998**, *109*, 5187. (b) Kehr, K. W. *Czech. J. Phys.* **1998**, *48*, 449.
- (a) Baik, M. H.; Silverman, J. S.; Yang, I. V.; Ropp, P. A.; Szalai, V. A.; Yang, W. T.; Thorp, H. H. *J. Phys. Chem. B* **2001**, *105*, 6437. (b) Tibodeau, J. D.; Thorp, H. H. *Inorg. Chem.* **2004**, *43*, 408.
- Gutierrez, R.; Caetano, R.; Woiczikowski, P. B.; Kubar, T.; Elstner, M.; Cuniberti, G. *New J. Phys.* **2010**, *12*.