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Dynamics and efficiency of photoinduced charge transport in DNA: Toward the elusive molecular wire*

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Abstract: Experimental investigations of photoinduced charge transport in synthetic DNA capped hairpins possessing electron acceptor and donor stilbene chromophores at either end have established the mechanism, dynamics, and efficiency of charge transport in DNA. The mechanism for charge transport in repeating A-T base pairs (A-tracts) was found to change from single-step superexchange at short distances to multistep incoherent hole hopping at longer distances. The rate constants for base-to-base hole hopping in longer A- and G-tract sequences are 1.2×10^9 s^{-1} and 4.3×10^9 s^{-1}, respectively, considerably slower than the rate constants associated with molecular wires. Even slower rate constants are observed for alternating or random base sequences such as those encountered in natural DNA. The efficiency of charge separation in capped hairpins with A-tract sequences is also low as a consequence of the competition of hole hopping with charge recombination. Significantly higher efficiencies for charge separation are possible using diblock purine base sequences consisting of two or three adenines followed by a larger number of guanines. The short A-block serves as a molecular rectifier, slowing down charge recombination. More efficient charge separation can also be achieved using non-natural bases or by using the triplet acceptor anthraquinone for hole injection.

Keywords: DNA; electron transfer; hole hopping; photochemistry; superexchange.

INTRODUCTION

The first systematic studies of the dynamics of photoinduced electron transfer in DNA employed synthetic DNA hairpins in which the singlet excited state of a stilbenedicarboxamide hairpin linker (Sa) functions as an electron acceptor and a guanine (G), the most readily oxidized of the natural DNA bases, serves as an electron donor (Figs. 1a,b) [1]. The distance between the Sa acceptor and G donor in these hairpins is determined by the number of intervening A-T base pairs. We proposed that electron transfer occurred via a single-step coherent superexchange process which can be simply described by

$$k_{et} = k_0 e^{-\beta R} \tag{1}$$

in which R is the Sa-G plane-to-plane distance and β is dependent upon the energetics and overlap of the bridging orbitals with D and A. A superexchange mechanism assumes that the A-T base pairs serve as a bridge in a donor-bridge-acceptor (D-B-A) system, but are not oxidized or reduced during the electron-transfer process. Analysis of the multiple exponential decays and band shape changes for the

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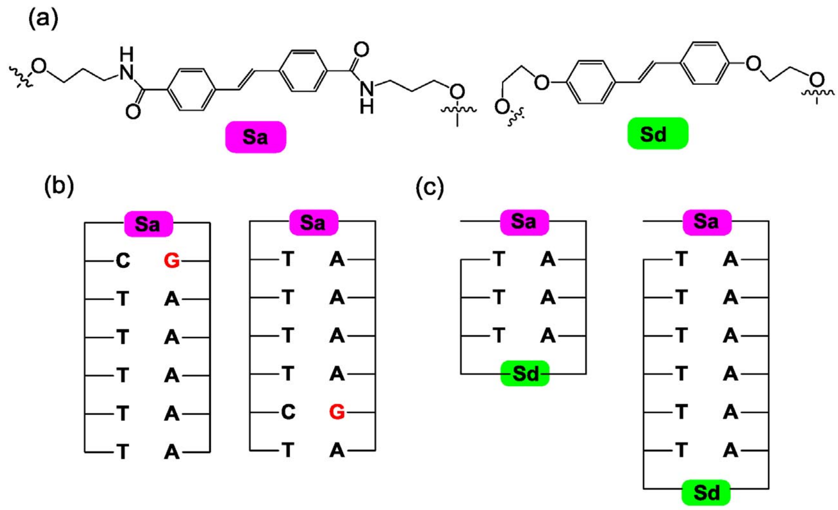

Fig. 1 Structures of (a) the stilbene diamide and diether linkers (Sa and Sd), (b) Sa-linked hairpins having a single G-C base pair in the 1st or 5th base pair position, and (c) Sa/Sd capped hairpins having three and six A-T base pairs.

femtosecond transient absorption spectra of these systems provided values of k_{et} for D-B-A systems with 1-4 bridging A-T base pairs. These measurements were limited to short bridges (≤4 A-T base pairs) because of the low efficiency for charge separation at longer distances. The slopes of plots of $\log(k_{et})$ vs. R yielded values of $\beta = 0.7$ and 1.0 Å^{-1} for charge separation and charge recombination, respectively. These values of β are intermediate between those reported for proteins ($1 < \beta < 1.5$ Å^{-1}) and for conjugated polyenes, which behave as molecular wires ($\beta < 0.1$ Å^{-1}) [2].

Following our initial studies there have been a number of reports of shallow distance dependence for the relative efficiency of strand cleavage at multiple GG or GGG steps separated by varying numbers of base pairs from the point of photochemical charge injection in DNA [3]. Charge transfer in these systems is thought to occur via a multistep incoherent hopping mechanism in which charge is injected into the bridge and hops reversibly between Gs until a chemical reaction cascade leading to strand cleavage occurs. The rate constant for incoherent hopping across a repeating sequence of identical bridging bases separating two shallow trapping sites (e.g., GT_nG) can be described by

$$k_{ct} = k_0 N^{-\eta} \qquad (2)$$

where N is the number of hopping sites and $1 < \eta < 2$. Owing to the shallower distance dependence of k_{ct} in the hopping mechanism than in the tunneling mechanism when $\beta > 0.5$ theoretical analyses of photoinduced charge separation in DNA led to the suggestion that tunneling might be the dominant mechanism at short D-A separations and hopping at longer separations [4]. Experimental support for a change in mechanism was provided by a strand cleavage study by Giese et al. [5]. Whereas strand cleavage studies provided evidence for the occurrence of a hopping mechanism and for the base sequence dependence of the relative efficiency of strand cleavage at different DNA sites, they do not provide either the dynamics or the absolute efficiency (quantum yield) of photoinitiated charge transport.

The development of D-B-A systems in which both D and A have distinct neutral and radical ion spectra has made possible the accurate determination of both charge-transfer rates and quantum yields for the formation of long-lived charge-separated states by means of femtosecond-nanosecond transient absorption spectroscopy [6]. We describe here recent results from our laboratories for capped DNA hairpin systems having Sa as the electron acceptor and stilbenediether (Sd) as the electron donor or hole

trap (Figs. 1a,c). These results permit development and evaluation of criteria for the design of DNA molecular wires [7].

CHARGE TRANSPORT IN HOMOPURINE AND ALTERNATING BASE SEQUENCES

Our initial investigations of the charge separation in a Sa/Sd capped hairpin system employed a variable number of A-T base pairs (an A-tract) as the bridging element [6]. The red-shifted absorption of the neutral Sa vs. Sd permits selective excitation of the former with a 355-nm pulsed laser and resolving the blue-shifted absorption maximum of the $Sd^{+\bullet}$ cation radical (525 nm) from that of $Sa^{-\bullet}$ anion radical (575 nm), as shown in Fig. 2 for the capped hairpin SaA_5Sd. This makes it possible to monitor the time required for charge separation (hole arrival at Sd) as is best done by fitting the rise of the 525/575 nm intensity ratio vs. time [8]. Quantum yields for charge separation are determined by comparing the integrated band intensities with those for the capped hairpin with a single A-T base pair.

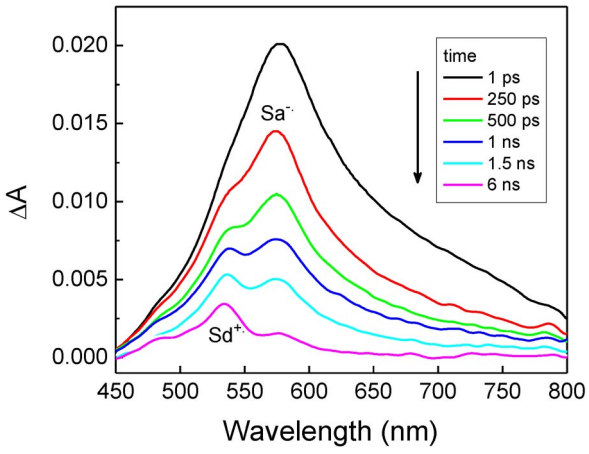

Fig. 2 Transient absorption spectra of a Sa/Sd capped hairpin having five A-T base pairs with delay times of 1 ps to 6 ns following femtosecond laser excitation. Reprinted with permission from *Angew. Chem., Int. Ed.* **45**, 7982 (2006). Copyright © 2006 Wiley-VCH.

Plots of rate constants and quantum yields for A-tract charge transport are shown in Fig. 3a along with data for G-tract and diblock systems (vide infra). The rate constants for A-tract charge transport display bimodal distance dependence, as expected for a change in mechanism from tunneling at short distances to hopping at longer distances. Kinetic modeling of this data by Burin and co-workers provided good agreement between calculated and experimental arrival times and quantum yields with a crossover from tunneling (initiated in the $Sa^{-\bullet}/A^{+\bullet}$ radial ion pair) for A-tracts shorter than 5 base pairs to hopping for longer A-tracts [9]. Alternative mechanisms for charge separation in this system have been proposed, and the precise mechanism of the initial photoinduced charge separation process remains poorly defined [10]. The rate constant for reversible A-to-A hole hopping obtained from kinetic modeling is 1.2×10^9 s^{-1}, much slower than either the value of 50 ps/base pair estimated by Takada et al. [11] or theoretical estimates which predate our experimental work.

The decrease in k_{cs} with distance is accompanied by an approximately parallel decrease in the quantum yield for charge separation Φ_{cs} (Fig. 3b). The distance-dependent decrease is attributed to the competition between reversible hole transport and charge recombination, which occurs mainly from the contact radical ion pair (Fig. 4a). The decay time of an Sa-linked hairpin lacking a G or Sd hole trap

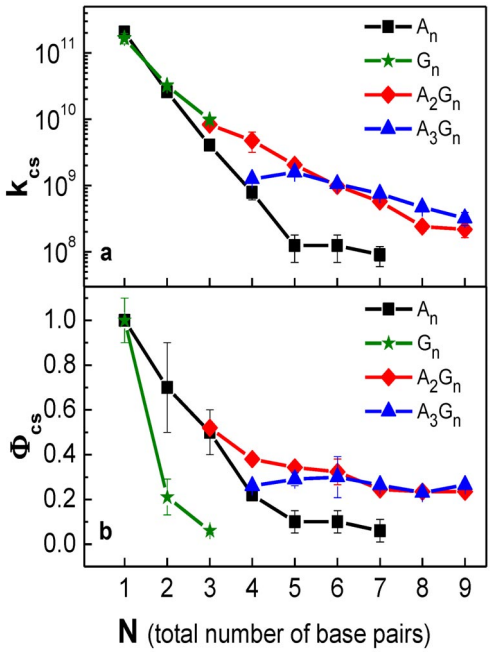

Fig. 3 Rate constants (a) and quantum yields (b) for charge separation in Sa/Sd capped hairpins having intervening A-tracts, G-tracts, or diblock (A_2G_n or A_3G_n) polypurine sequences. Reprinted with permission from *J. Am. Chem. Soc.* **131**, 9722 (2009). Copyright © 2009 American Chemical Society.

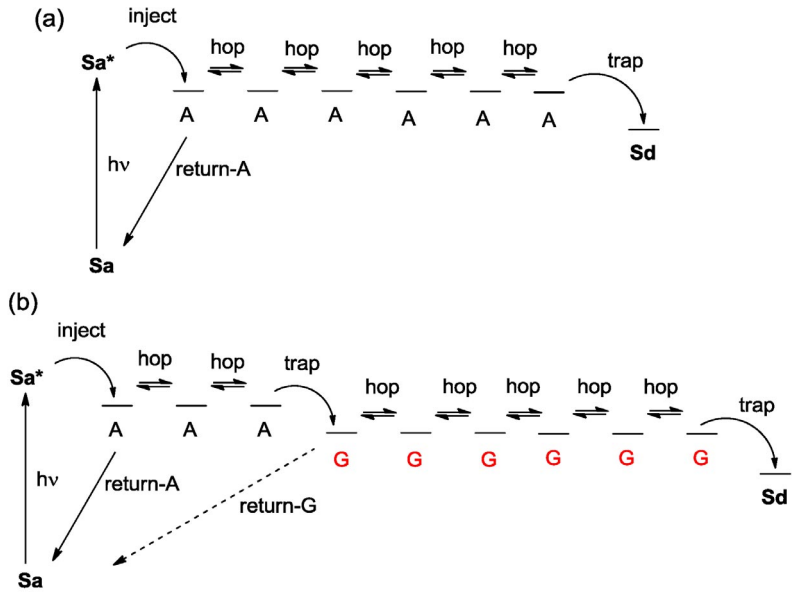

Fig. 4 Simplified hole hopping mechanism for charge separation in Sa/Sd capped hairpins having (a) A_6 or (b) A_3G_6 purine base sequences.

provides a rate constant of 5×10^8 s^{-1} for this process, only slightly slower than the rate constant for A-to-A hole hopping in DNA [12].

The dynamics and efficiency of charge separation in SaG_nSd capped hairpins having a variable number of G-C base pairs were also investigated [13]. Values of k_{cs} and Φ_{cs} for 1–3 G-C base pairs are shown in Fig. 3. Quantum yields are even more strongly distance-dependent than is the case for A-tract bridges, making it impossible to detect the occurrence of charge separation for capped hairpins having four or more G-C base pairs. While arrival times appear to be somewhat faster for short G- vs. A-tract systems, the measured decay time for the $Sa^{-\bullet}G^{+\bullet}$ radical ion pair is 4×10^{10} s^{-1}, two orders of magnitude faster than for the $Sa^{-\bullet}A^{+\bullet}$ radical ion pair [14]. At least part of this difference can be attributed to the larger energy gap for charge recombination for the $Sa^{-\bullet}A^{+\bullet}$ radical ion pair. According to Marcus theory for electron transfer, exergonic electron transfer should display an inverse dependence on energy gap; the larger the energy gap the slower the electron-transfer process.

Comparison of rate constants and quantum yields for charge separation in Sa/Sd capped hairpins having alternating AT base sequences vs. poly(A) sequences showed that hole transport is much slower in the alternating sequences [15]. For example, charge separation across an ATAT sequence occurred with lower efficiency than across a longer A_7 sequence. Similarly, charge separation across an AGAGAG sequence was slower and less efficient than across a A_6 sequence. Rate constants for G-T-G and G-A-G hole transfer have been recently reported by Kawai et al. [16]. The values of 7.0×10^5 s^{-1} and 3.8×10^7 s^{-1}, respectively, are substantially slower than our value for base-to-base hole hopping in A-tracts.

The dynamics and efficiency of charge transport in the SaA_nSd capped hairpins hardly qualify as wire-like behavior. Since the efficiency of charge transport is determined by the competition between hole transport and charge recombination (Fig. 4a), we have concentrated our efforts investigating changes in our capped hairpins, which might either decrease the rate constant for charge recombination or increase the rate constant for hole transport.

CHARGE TRANSPORT IN DIBLOCK AND TRIBLOCK PURINE SEQUENCES

The first indication that placement of G within the A-tract of a SaA_nSd capped hairpin might result in faster and more efficient hole transport was provided by a study in which a single G was placed at various locations within A-tracts consisting of 2–6 base pairs (Figs. 5a,b) [17]. Location of G near Sa (the point of hole injection) results in low values of Φ_{cs} as a result of fast charge recombination in the $Sa^{-\bullet}A_nG^{+\bullet}$ radical ion pair when $n = 0$ or 1. The highest values of Φ_{cs} are realized when G is separated from Sa by two or three A-T base pairs and is located near Sd (the point of hole trapping). The requirement of separation from Sa by two or more AT base pairs is a consequence of the strong distance dependence of charge recombination for the $Sa^{-\bullet}A_nG^{+\bullet}$ radical ion pair [18]. The requirement of separation from Sd by no more than one AT base pairs indicates that tunneling from G to Sa across a single AT base pair is much faster than tunneling across two AT base pairs [19]. The rate constants for hole transport in A_nGA purine systems are faster than those for the corresponding A_{n+2} systems having the same total number of purine bases.

The observation of faster and more efficient charge transport in Sa/Sd capped hairpins having A_nGA vs. A_{n+2} purine bridges when $n = 2$ or 3 led us to examine charge transport in A_mG_n diblock purine systems (Fig. 5c) [13]. Time-dependent 525/575 nm band intensity ratios for the A_2G_n systems ($m = 2$–7) are shown in Fig. 6. Fitting the slow component of the first-order rise of these plots to a single exponential provides values of k_{cs} shown in Fig. 3a along with values for the A_n and A_3G_n systems. Values of Φ_{cs} for the diblock systems A_2G_n and A_3G_n are shown in Fig. 3b. The diblock systems possessing two or more Gs display two noteworthy features: (a) the values of k_{cs} decrease slowly and have a linear dependence of $\log(k_{cs})$ on N and (b) the quantum yields become independent of N, where N is the total number of base pairs separating Sa and Sd.

A simplified hole transport mechanism that accounts for the behavior of the diblock capped hairpins is shown in Fig. 4b. Hole injection into the short A-block generates a contact radical ion pair that can either undergo charge recombination or hole migration to the G-block, where it is trapped. Hole

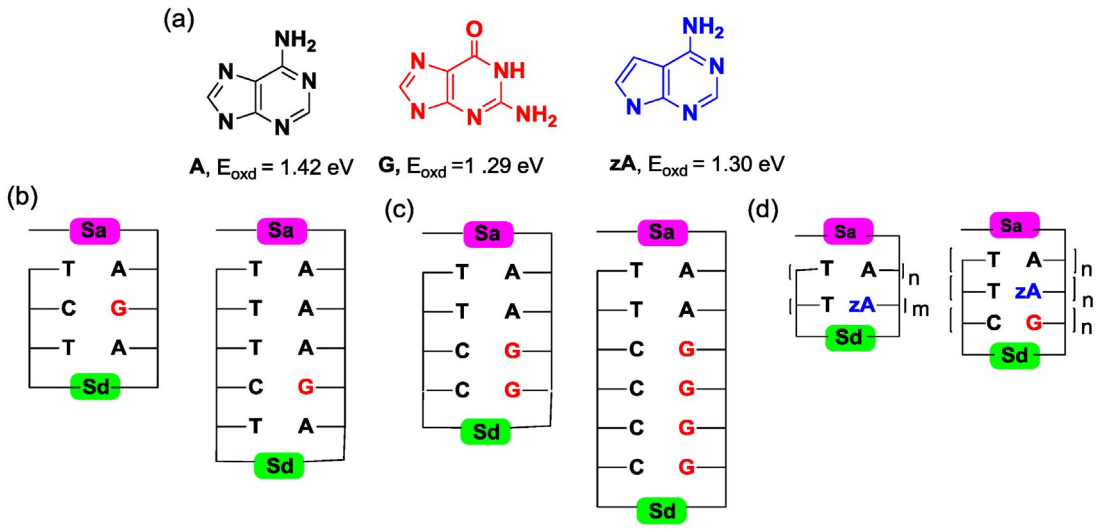

Fig. 5 Structures and oxidation potentials of the purine bases A, G, and zA and Sa/Sd capped hairpins possessing (b) a single G-C base pair, (c) diblock A_2G_n base sequences, and (d) A_nzA_m diblock or $A_nzA_nG_n$ triblock base sequences. Reprinted with permission from *J. Am. Chem. Soc.* **133**, 11485 (2011). Copyright © 2009 American Chemical Society.

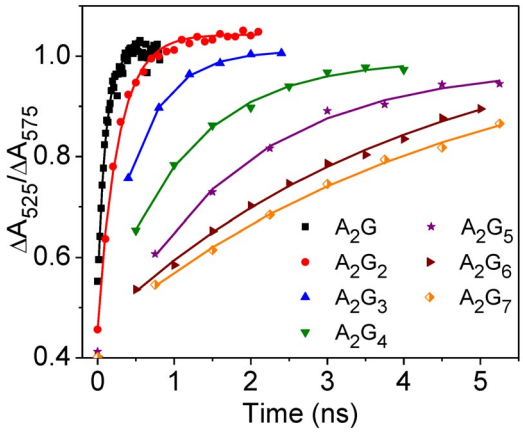

Fig. 6 Time-dependent 525/575 nm band intensity ratios for A_2G_n diblock capped hairpins. Reprinted with permission from *J. Am. Chem. Soc.* **131**, 9722 (2009). Copyright © 2009 American Chemical Society.

hopping in the G-block and trapping by Sd can account for the distance dependence of k_{cs}, and faster hole hopping vs. charge recombination of the $Sa^{-\bullet}/G^{+\bullet}$ charge-separated radical ion pair can account for the lack of dependence of Φ_{cs} on distance (Fig. 3b). Evidently, thermal repopulation of the A-block does not occur on the time scale of our experiments (0–6 ns, Fig. 6).

We subsequently extended this study to diblock systems having much longer G-blocks (m = 13–19) [20]. Values of k_{cs} are slower than those for the shorter G-blocks, requiring the use of a nanosecond laser system. Kinetic modeling of the data for the diblock systems provides a value of $k_{hop} = 4.3 \times 10^9$ s^{-1} for G-to-G hopping, somewhat faster than the value of 1.2×10^9 s^{-1} for A-to-A base hopping. Our data for the arrival times (τ) for the longer diblock systems can also be fit by an unbiased first passage random walk in one dimension (eq. 3)

$$\tau(N) = (1/2k_{hop})N^2 \quad (3)$$

where N is the number of hopping steps. The temperature dependence of k_{cs} for A_3G_{13} provides Årrhenius parameters of E_{act} = 2.8 kcal/mol and A = 7×10^9 s^{-1} for the overall charge-transport process, consistent with weakly activated processes. As was the case for the shorter diblock systems, the efficiency of charge separation is independent of the length of the G-block. We have also investigated charge transport in diblock Sa/Sd capped hairpins possessing a short A-block (2 or 3 A-T base pairs) followed by an alternating GCGC or GAGAG base sequence in place of the G-block. Values of Φ_{cs} for these sequences are lower than those for A_n sequences having the same total number of base pairs and charge separation is too slow to measure on the 6 ns time window of our experiments.

The rise time and efficiency for charge separation in the A_3G_{19} diblock system are ca. 40 ns and 25 %, respectively. These values represent the fastest and most efficient charge separation reported to date for a system possessing >20 base natural pairs. Further progress toward wire-like behavior requires still faster hole transport and more efficient charge separation. Kawai et al. have reported that a significant increase in the rate of hole transport between Gs in the sequence GA_5G is realized by replacing one or more of the A bases with 7-deazaadenine (zA, Fig. 5a) [21]. Faster hole transport was attributed to a better match of the highest occupied molecular orbital (HOMO) level of zA with G than that for A with G. Better matching of energy levels would result in a smaller tunneling barrier or lower activation energy for thermal detrapping.

We have investigated the kinetics and efficiency of charge separation in several diblock Sa/Sd capped hairpins having A_nzA_m sequences and triblock systems having $A_nzA_nG_n$ sequences (Fig. 5c) [22]. The rise time for the A_3zA_6 system is significantly faster than for the A_3G_6 system (0.72 vs. 3.1 ns); however, the value of Φ_{cs} is only slightly larger for the A_3zA_6 system (0.34 vs. 0.27). The values for the triblock system lie in-between those for the two diblock system, indicating that there is no advantage for the triblock vs. the A_nzA_m systems other than the lower cost of the natural bases. The similar values of Φ_{cs} for the A_3zA_6 and A_3G_6 systems are consistent with our previous conclusion that the efficiency of charge separation is largely determined once the hole exits the short A-block. However, the charge-separation time is dependent upon the number of bases in both the A- and G- or zA-block and their hopping rates. The estimated rate constant for zA-to-zA hole hopping is 4.2×10^{10} s^{-1}, an order of magnitude faster than for a G-to-G random walk.

A plausible explanation for this large rate enhancement is that removal of a lone-pair donor from the major groove releases tightly bound water, leading to increased conformational mobility in poly(zA) vs. the A-tract. A further indication that hole mobility is related to DNA conformational mobility is provided by the effect of restricting duplex mobility. Faster charge transport is reported for more flexible peptide nucleic acid (PNA) duplexes [23], whereas slower charge transport is reported for more rigid locked nucleic acid (LNA) duplexes [24]. The small decrease in k_{cs} observed for our Sa/Sd diblock systems upon replacing the G-bock with LNA bases was attributed to decreased electronic coupling in the resulting A-type duplex structure.

A more pronounced decrease in k_{cs} is observed for diblock A_3G_m systems (m = 1–6) in the presence of 100 mM Mg^{2+} vs. Na^+. The crystal structure of a Sd-linked hairpin displays a Mg^{2+} bound inside the minor groove clamped onto two adjacent base pairs of the A-tract [25]. A similar binding geometry in solution presumably would decrease the conformational mobility of the A-tract and hence the hole mobility.

CONCLUSIONS

The Sa/Sd capped hairpins have provided a vehicle for determining the base sequence dependence of the mechanism, efficiency, and dynamics of photoinduced charge separation in DNA. The mechanism for charge separation in systems having more than four or five intervening base pairs is best described as incoherent hopping in which the charge is largely localized on a single base. For shorter intervening

base sequences, the mechanism of charge separation is still undergoing analysis. The efficiency of charge separation over multiple base pairs is substantially increased upon changing from alternating base sequences to homo(adenine). Efficiencies of ca. 25 % are obtained using diblock purine sequences (A_nG_m, where $n = 2$ or 3 and $m \geq 2$). The short initial A-block serves as a rectifier in these systems by slowing return electron transfer once the hole arrives in the G-block. The dynamics of base-to-base hopping are somewhat faster for poly(G) vs. poly(A) sequences (4.3×10^9 s^{-1} vs. 1.2×10^9 s^{-1}). Substantially faster hopping is observed for zA, suggesting the possibility that further increases in dynamics may be possible by redesign of the natural nucleobases or changes in the solvent. Higher efficiencies may also be possible using a triplet acceptor for which competing singlet electron transfer does not result in energy-wasting charge recombination.

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