

Rapid Long-Distance Hole Transfer through Consecutive Adenine Sequence

Tadao Takada, Kiyohiko Kawai, Mamoru Fujitsuka, and Tetsuro Majima*

The Institute of Scientific and Industrial Research (SANKEN), Osaka University, Mihogaoka 8-1, Ibaraki, Osaka, Japan

Received June 13, 2006; E-mail: majima@sanken.osaka-u.ac.jp

Charge transfer through the DNA π -stack has been the focus of considerable interest because of its potential importance to DNA oxidative damage, its application to DNA-based sensors, and the general interest in understanding electron-transfer chemistry through π -stacked arrays.^{1,2} Recent kinetic investigations based on the time-resolved measurements and biochemical analysis have shown that a hole can migrate over long distances along a DNA π -stack,^{1,3,4} but hole transfer does not occur rapidly although the rates are sequence-dependent.⁵ This is because a long-range hole transfer proceeds mainly via hopping between neighboring G bases (G-hopping) through a superexchange type of mechanism.⁶ So far, the rate of G-hopping in a GAG sequence, which is the fastest sequence for single-step hole transfer, is determined to be 10^7 – 10^8 s⁻¹.^{4,7} In this process, a hole is largely localized on each G base, and the electronic state of each G is not strongly coupled with another neighboring G because intervening AT base pairs behave like a potential barrier which originate from the difference in oxidation potential between G and A ($E_{ox} = 1.29$ V vs NHE for G, and 1.42 V for A).⁸ Since each hopping step is a slower process, hole transfer over long distances (>100 Å) through G-hopping occurs in the micro- to millisecond time scale.⁹ This slower G-hopping process for hole transport as compared with conjugated polymer¹⁰ may limit the application of DNA as a molecular wire. In this context, it is essential to develop the concept to construct the rapid and efficient hole transport system on DNA.¹¹

Recently, it has been suggested by Giese et al. that the hole transfer occurs via thermally induced hopping of positive charges between A bases (A-hopping) when two G sites are separated by more than four AT base pairs.¹² Furthermore, recent kinetic investigations for A-hopping carried out in our laboratory have shown that the hole transfer via A-hopping is weakly distance dependent and each A-hopping occurs faster than 10^{10} s⁻¹.¹³ These characteristics of the A-hopping process may serve to establish the efficient and rapid hole transfer in DNA over long distances. Here, we report the rapid and efficient long-distance hole transfer through consecutive A bases.

The long-distance hole transfer process through consecutive A bases is schematically shown in Scheme 1. Previously, we established a donor–acceptor system to observe the hole transfer process, in which the naphthalimide (NI) and phenothiazine (PTZ, $E_{ox} = 0.76$ V vs NHE), as a sensitizer to induce the photoinduced electron transfer with A and a probe molecule for trapping and monitoring hole, respectively, are attached at each end of the duplex.^{9,14} The dynamics of the hole transfer through long-A was evaluated by observing the transient absorption of the NI radical anion (NI^{•-}) and PTZ radical cation (PTZ^{•+}) produced after the 355-nm laser-pulse excitation.

To prove that the hole transfer can occur rapidly through consecutive A bases over long distances, we designed DNA consisting of a long A repeat sequence (Table 1). A GG doublet was introduced at the near PTZ site for the appropriate hybridization

Scheme 1. Mechanistic Scheme of Long-Distance Hole Transfer through Consecutive A Bases via an A-Hopping Process

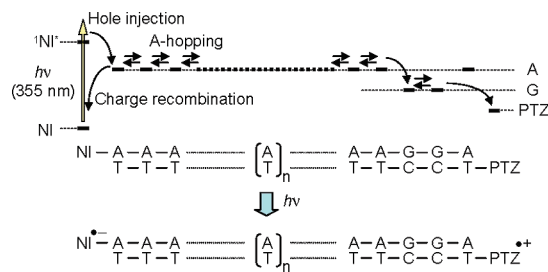


Table 1. DNA Sequences, Hole Injection Yields (Φ_{inj}), and Ratios of Absorption Monitored at 400 and 520 nm after the Laser Flash Excitation

DNA	sequence	Φ_{inj}^a (%)	$\Delta A_{520}/\Delta A_{400}^b$ (%)
N-A ₁₀ -P	NI-A ₁₀ -GGA-3' 3'-T ₁₀ -CCT-PTZ	0.64 ± 0.05	36 ± 3
N-A ₁₅ -P	NI-A ₁₅ -GGA-3' 3'-T ₁₅ -CCT-PTZ	0.47 ± 0.07	31 ± 5
N-A ₂₀ -P	NI-A ₂₀ -GGA-3' 3'-T ₂₀ -CCT-PTZ	0.40 ± 0.04	27 ± 3
N-A ₂₅ -P	NI-A ₂₅ -GGA-3' 3'-T ₂₅ -CCT-PTZ	0.36 ± 0.08	29 ± 1
N-A ₃₀ -P	NI-A ₃₀ -GGA-3' 3'-T ₃₀ -CCT-PTZ	0.34 ± 0.06	31 ± 3
N-AT ₁₀ -P	NI-(AT) ₁₀ -GGA-3' 3'-(TA) ₁₀ -CCT-PTZ	0.12 ± 0.03	39 ± 8
N-GG-P	NI-A ₉ -GG-A ₉ -GGA-3' 3'-T ₉ -CC-T ₉ -CCT-PTZ	0.72 ± 0.06	16 ± 3
N-Am-P	NI-A ₁₀ -A-A ₉ -GGA-3' 3'-T ₁₀ -A-T ₉ -CCT-PTZ	0.50 ± 0.03	21 ± 2
N-A ₂₀	NI-A ₂₀ -GGA-3' 3'-T ₂₀ -CCT	0.37 ± 0.06	18 ± 4

^a Quantum yields of hole injection obtained from the absorption of NI^{•-} monitored at 400 nm by using benzophenone in the triplet state as an actinometer. ^b Ratios in the transient absorption at 400 nm for NI^{•-} against that at 520 nm for PTZ^{•+} obtained at 100 ns after laser flash excitation. From the extinction coefficient of two transient species, the ratio is around 30% when a hole injected into DNA migrates to the PTZ-site.

of DNA. Each 5'-end of synthetic DNA is modified with NI and PTZ, respectively.⁹ Transient absorption spectra for N-A₂₀-P and N-A₂₀ at 100 ns observed after the 355 nm laser-pulse excitation are shown in Figure 1a. The strong absorption band with a peak at 400 nm and a somewhat broad absorption around 520 nm can be assigned to NI^{•-} and PTZ^{•+}, respectively, from previous reports.⁹ The transient absorption spectrum obtained for N-A₂₀-P shows that a hole was injected into the DNA by charge separation between NI^{•-} and A and migrated to the opposite end of the DNA to generate PTZ^{•+}. A similar strong absorption at 400 nm assigned to NI^{•-} was also seen for N-A₂₀ irrespective of the absence of PTZ, showing that a hole was trapped at the GG site as shown in Scheme 1.¹⁵ Time profiles monitored at 400 and 520 nm for N-A₂₀-P are shown

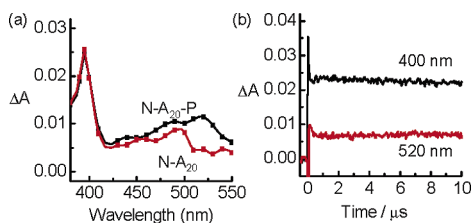


Figure 1. (a) Transient absorption spectra for N-A₂₀-P and N-A₂₀ at 100 ns after the 355 nm laser pulse excitation. (b) Time profiles for N-A₂₀-P monitored at 400 and 520 nm. Sample contained 100 μM DNA, 20 mM Na phosphate buffer (pH 7.0), and 100 mM NaCl.

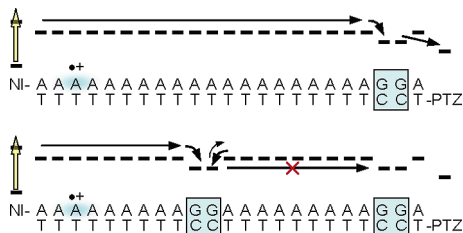


Figure 2. Schematic illustration of rapid hole transfer through a consecutive A sequence.

in Figure 1b. The formation of PTZ⁺⁺ was observed within the laser-pulse duration (20 mJ/pulse, fwhm = 8 ns), which means that a hole transfer from A next to NI to PTZ occurred faster than the rate constants of 10⁸ s⁻¹. Previous computational studies demonstrated that a hole on a nucleobase can partially delocalize onto an adjacent base.¹⁶ Rapid long-distance hole transfer can be rationalized by considering the expanded hole delocalization onto the adjacent A base facilitating the hopping process.

To investigate systematically the distance dependence of the long-distance hole transfer through consecutive A bases, a series of DNA in which NI and PTZ are separated by different numbers of A bases were constructed (N-A_n-P, *n* = 10, 15, 20, 25, and 30). Quantum yields of hole injection into DNA (Φ_{inj}) and the ratio of the absorption of NI^{•+} at 400 nm against that of PTZ⁺⁺ at 520 nm ($\Delta A_{520}/\Delta A_{400}$) for N-A_n-P series are shown in Table 1. From the $\Delta A_{520}/\Delta A_{400}$ values, we confirmed that the long-distance hole transfer occurred for all sequences. Of special interests, rapid formation of PTZ⁺⁺ within laser pulse duration (>10⁸ s⁻¹) was observed even in the case of A₃₀ where the distance between NI and PTZ is longer than 100 Å. As expected from the A-hopping mechanism, the Φ_{inj} values were slightly dependent on the number of A bases, confirming that a hole injected into DNA migrated to PTZ via a multistep hopping process.¹⁷ Extremely rapid long-distance hole transfer could be explained by the direct stacking between A bases, leading to the hole delocalization to the adjacent A as mentioned above. Consistent with this interpretation, a considerable decrease in the yields of the charge-separated state was seen when the repeat A sequence for N-A₂₀-P was changed to the alternating AT sequence (N-AT₁₀-P). In addition, given that A^{•+} as a hole carrier does not have a strong acidic proton such as a NI-proton of G^{•+}, the absence of the deprotonation process may contribute to the rapid hole transfer between A bases.^{12,18}

When a GG doublet was introduced in the middle of DNA strands (N-GG-P), PTZ⁺⁺ was not produced in our experimental time scale (~500 μs), showing that a hole trapped at proximal GG sites cannot migrate to a distal GG site. Figure 2 shows the hole transfer process over a long A sequence in the presence and absence of a GG doublet. Although it has been shown that the hole transfer

between Gs through the thermally induced A-hopping process proceeds when two Gs are separated by more than four AT base pairs, our results show that the hole transfer via the thermal hopping from G to the bridging A is considered to be inefficient and occurs in the millisecond time scale. A similar effect was observed for DNA containing an AA mismatch at the middle of the DNA (N-Am-P). Although the AA mismatch did not diminish the hole injection efficiency drastically compared with the same sequence possessing no mismatch, the hole transfer to PTZ was prevented. Considering that the NI^{•+} in this sequence persisted for several hundred microseconds, an injected hole was considered to be trapped around an AA mismatch site because of a local structural perturbation.

In summary, we clearly showed the rapid long-distance hole transfer through consecutive A bases via A-hopping on the basis of the time-resolved measurements for DNA modified with NI and PTZ. Once a hole resides on an A base, the hole transfer over a long A sequence occurs rapidly and efficiently. This can be explained by considering that the long-distance hole transfer proceeds via a multistep mechanism and each hopping step between As is rapid because of the direct stacking due to hole delocalization. Our results suggest that the oxidation potential and surface stacking area of hole carriers are important factors for designing and realizing a DNA molecular wire.

Acknowledgment. This work has been partly supported by a Grant-in-Aid for Scientific Research (Project 17105005, Priority Area (417), 21st Century COE Research, and others) from the Ministry of Education, Culture, Sports, Science and Technology (MEXT) of Japanese Government.

References

- (1) Delaney, S.; Barton, J. K. *J. Org. Chem.* **2003**, *68*, 6475.
- (2) Lewis, F. D.; Letsinger, R. L.; Wasielewski, M. R. *Acc. Chem. Res.* **2001**, *34*, 159.
- (3) (a) Williams, T. T.; Odom, D. T.; Barton, J. K. *J. Am. Chem. Soc.* **2000**, *122*, 9048. (b) Yoo, J.; Delaney, S.; Stemp, E. D.; Barton, J. K. *J. Am. Chem. Soc.* **2003**, *125*, 6640. (c) Kelley, S. O.; Barton, J. K. *Science* **1999**, *283*, 375. (d) Henderson, P. T.; Jones, D.; Hampikian, G.; Kan, Y.; Schuster, G. B. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 8353.
- (4) Lewis, F. D.; Liu, J. Q.; Zuo, X. B.; Hayes, R. T.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2003**, *125*, 4850.
- (5) Lewis, F. D.; Liu, X.; Wu, Y.; Zuo, X. *J. Am. Chem. Soc.* **2003**, *125*, 12729.
- (6) Meggers, E.; Michel-Beyerle, M. E.; Giese, B. *J. Am. Chem. Soc.* **1998**, *120*, 12950.
- (7) (a) Lewis, F. D.; Liu, X. Y.; Liu, J. Q.; Miller, S. E.; Hayes, R. T.; Wasielewski, M. R. *Nature* **2000**, *406*, 51. (b) Kawai, K.; Osakada, Y.; Takada, T.; Fujitsuka, M.; Majima, T. *J. Am. Chem. Soc.* **2004**, *126*, 12843.
- (8) Steenken, S.; Jovanovic, S. V. *J. Am. Chem. Soc.* **1997**, *119*, 617.
- (9) Takada, T.; Kawai, K.; Fujitsuka, M.; Majima, T. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 14002.
- (10) Davis, W. B.; Svec, W. A.; Ratner, M. A.; Wasielewski, M. R. *Nature* **1998**, *396*, 60.
- (11) Okamoto, A.; Tanaka, K.; Saito, I. *J. Am. Chem. Soc.* **2003**, *125*, 5066.
- (12) (a) Giese, B.; Amaudrut, J.; Kohler, A. K.; Spormann, M.; Wessely, S. *Nature* **2001**, *412*, 318. (b) Kendrick, T.; Giese, B. *Chem. Commun.* **2002**, 2016.
- (13) (a) Kawai, K.; Takada, T.; Tojo, S.; Majima, T. *J. Am. Chem. Soc.* **2003**, *125*, 6842. (b) Takada, T.; Kawai, K.; Cai, X. C.; Sugimoto, A.; Fujitsuka, M.; Majima, T. *J. Am. Chem. Soc.* **2004**, *126*, 1125.
- (14) Tierney, M. T.; Grinstaff, M. W. *J. Org. Chem.* **2000**, *65*, 5355.
- (15) Thermodynamic equilibrium between G and GG (ΔG_{th}) was determined to be about 50 mV. Lewis, F. D.; Liu, X. Y.; Liu, J. Q.; Hayes, R. T.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2000**, *122*, 12037.
- (16) Conwell, E. M.; Basko, D. M. *J. Am. Chem. Soc.* **2001**, *123*, 11441.
- (17) Charge separation yields are quite low since the initial charge recombination process between the NI radical anion and neighboring A radical cation is rapid. (ref 13b).
- (18) Takada, T.; Kawai, K.; Fujitsuka, M.; Majima, T. *Chem. Eur. J.* **2005**, *11*, 3835.

JA0641554