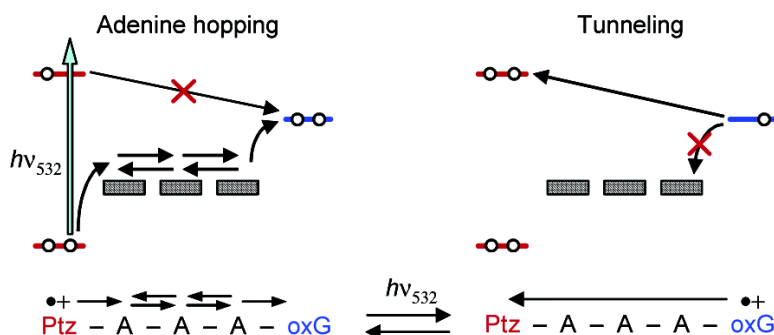


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Kinetics of Weak Distance-Dependent Hole Transfer in DNA by Adenine-Hopping Mechanism

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One-electron oxidation of DNA leads to formation of the radical cation of guanine ($G^{\bullet+}$), with the lowest oxidation potential among the four bases, and a hole has been demonstrated to migrate through DNA by hopping between Gs.¹ From the transient absorption measurements, the distance dependence parameter β in eq 1 of single-step hole transfer in DNA has been determined as 0.6 \AA^{-1} .^{2,3}

$$\ln k \propto -\beta \Delta r \quad (1)$$

On the other hand, strand cleavage experiments revealed the occurrence of the weak distance-dependent long-range hole transfer over a distance of 200 \AA which requires the hole transfer between Gs separated by long A–T sequences.⁴ Recently, Giese et al. explained this weak distance dependence by a mechanism in which hole transfer is mediated by thermally induced hole-hopping between the second most easily oxidized base adenine (A-hopping).⁵ Thus, the hole transfer in DNA has been demonstrated to occur by the two different mechanisms, G-hopping (super exchange between Gs across the intervening A–T bridge) and A-hopping (charge is carried by the bridge base A as $A^{\bullet+}$). The rate constants of hole transfer by G-hopping across one A–T base pair have been determined by Lewis et al. to be in the range of 10^6 – 10^8 s^{-1} .⁶ Considering the low efficient endothermic oxidation of A by $G^{\bullet+}$ and the weak distance dependence of A-hopping, it was suggested that once after the generation of $A^{\bullet+}$ the hopping between A proceeds fast.⁷ However, there are no direct time-resolved measurements especially addressing the kinetics of hole transfer by A-hopping in DNA. In this study, the kinetics of hole transfer by the A-hopping mechanism was investigated by the combined pulse radiolysis–laser flash photolysis method,⁸ and the weak distance dependent hole transfer with the hole transfer rates faster than 10^8 s^{-1} over the distance range of 7 – 22 \AA was demonstrated.

For the measurement of the hole transfer rates in DNA, it is desirable to generate the hole selectively, without generation of radical anion, in DNA. For this purpose, pulse radiolysis serves as a suitable method. We have previously reported the pulse radiolysis of pyrene (Py)-^{3,9} and phenothiazine (Ptz)-conjugated¹⁰ oligodeoxynucleotides (ODNs), in which hole transfer in DNA was monitored by the transient absorption of $Py^{\bullet+}$ and $Ptz^{\bullet+}$, respectively. However, pulse radiolysis is disadvantageous in that it cannot be used to measure the kinetics in the time scale of $< 1 \text{ \mu s}$ because of the time taken for the collisional process for the generation of a hole in DNA. Here, to avoid this difficulty, we employed the pulse radiolysis–laser flash photolysis of Ptz-conjugated ODN. After the generation of $Ptz^{\bullet+}$ with a maximum absorption peak at 520 nm during the pulse radiolysis,¹¹ $Ptz^{\bullet+}$ was irradiated with a 532-nm laser flash with a delay time of 50 \mu s to produce $Ptz^{\bullet+}$ in the excited state ($Ptz^{\bullet+*}$). Since the driving force for the one-electron oxidation of A by $Ptz^{\bullet+*}$ is enough large,^{12,13} $A^{\bullet+}$ will be mainly produced when A is the nearest base to the $Ptz^{\bullet+*}$. Thus, pulse radiolysis–laser flash photolysis of Ptz-G-ODNn and Ptz-oxG-ODNn leads

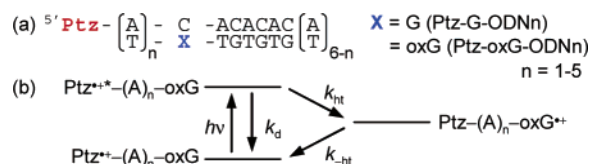


Figure 1. (a) Sequences of Ptz-G-ODNn and Ptz-oxG-ODNn, and (b) kinetic scheme for forward (k_{ht}) and backward (k_{-ht}) hole transfer.

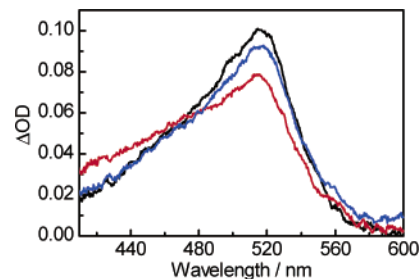


Figure 2. Transient absorption spectra of Ptz-oxG-ODN1 obtained at 45 \mu s (black), 55 \mu s (red), and 500 \mu s (blue) after the electron pulse during pulse radiolysis–laser flash photolysis. The 532 nm laser flash was delayed by 50 \mu s relative to the electron pulse.

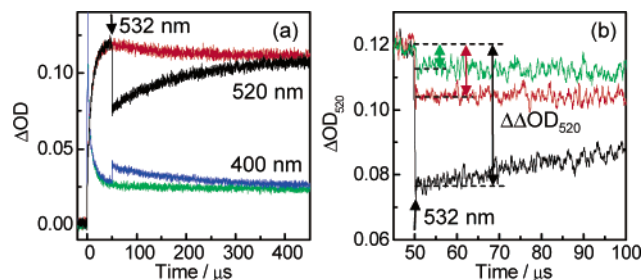


Figure 3. (a) Time profiles of transient absorptions monitored at 520 nm (black, red: without laser flash) and 400 nm (blue, green: without laser flash) during the pulse radiolysis–laser flash photolysis of Ptz-oxG-ODN1. The delay time of the laser flash was 50 \mu s after the electron pulse. (b) Bleaching of $Ptz^{\bullet+}$ monitored at 520 nm upon the laser flash for Ptz-oxG-ODNn (black, $n = 1$; red, $n = 3$; green, $n = 5$).

to the selective injection of a hole at A nearest to Ptz, and the hole transfer from $A^{\bullet+}$ across $(A)_n$ -bridge to the hole acceptor G or 8-oxo-7,8-dihydroguanine (oxG) was investigated (Figure 1).¹⁴

In the case of Ptz-G-ODNn, little change of the transient absorption of $Ptz^{\bullet+}$ was observed upon the irradiation of the 532-nm laser flash. Therefore, the generation of $A^{\bullet+}$ and backward hole transfer seem to occur within the laser flash duration (5 ns) when the hole acceptor is G. Of special interest, irradiation of $Ptz^{\bullet+}$ in Ptz-oxG-ODN1 with a laser flash caused a decrease in ΔOD of $Ptz^{\bullet+}$, and a formation of broad absorption around 400 nm immediately after the flash (Figures 2 and 3a). The new absorption band was assigned to $oxG^{\bullet+}$ or $oxG(-H^{\bullet+}):C(+H^{\bullet+})^+$,¹⁵ demonstrating the hole transfer from $Ptz^{\bullet+*}$ to oxG (forward hole transfer)

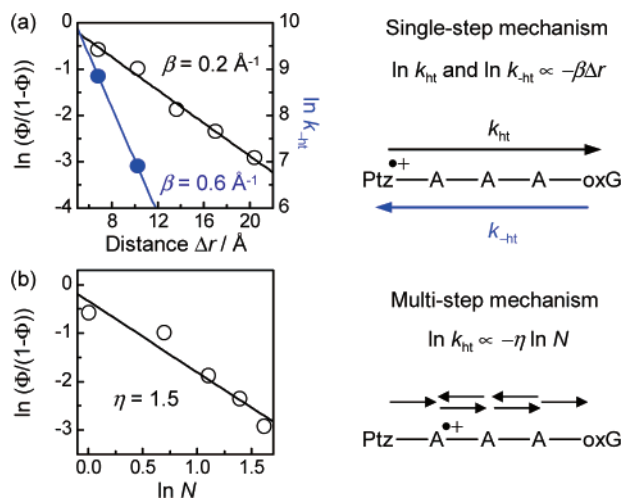


Figure 4. Dependence of the forward and backward hole transfer rates (○ and ●, respectively) (a) on the distance between Ptz and oxG (Δr), and (b) on the number on hopping steps (N).

within the laser flash duration, that is the forward hole transfer proceeds faster than 10^8 s^{-1} . The spectrum of Ptz^{•+} was recovered in the time scale of $\sim 500 \mu\text{s}$ concomitant with the decay of oxG^{•+}, according to the backward hole transfer from oxG^{•+} to Ptz. Bleaching of the transient absorption at 520 nm assigned to Ptz^{•+} upon the laser flash ($\Delta\Delta\text{OD}_{520}$) only slightly decreased as the distance between the Ptz and oxG increased, demonstrating the weak influence of the distance on the forward hole transfer rate. In contrast, backward hole transfer from oxG^{•+} to Ptz was strongly distance dependent, and when Ptz and oxG^{•+} are separated by more than three A–T base pairs, no backward hole transfer was observed in the present experimental time scale. Thus, different distance dependence was observed in the forward and backward hole transfer in Ptz-oxG-ODNn.

The relative rate for the forward hole transfer (k_{ht}) follows eq 2 where Φ and k_{d} designate the yield of the forward hole transfer ($\Phi = \Delta\Delta\text{OD}_{520}/\Delta\text{OD}_{520 \text{ before laser}}$) and rate of deactivation of Ptz^{•+}, respectively. Then, $\ln k_{\text{ht}}$ can be described by eq 3.

$$\Phi = k_{\text{ht}}/(k_{\text{ht}} + k_{\text{d}}) \quad (2)$$

$$\ln k_{\text{ht}} = \ln(\Phi/(1 - \Phi)) + \text{const.} \quad (3)$$

The rate of the backward hole transfer ($k_{-\text{ht}}$) was directly determined from the recovery of Ptz^{•+}. Figure 4a shows the semilog plot of $\Phi/(1 - \Phi)$ and $k_{-\text{ht}}$ against the distance between the Ptz and oxG (Δr). From the slope of the plot, values of 0.2 and 0.6 \AA^{-1} were obtained for the distance dependence of k_{ht} and $k_{-\text{ht}}$, respectively. The β value of 0.6 \AA^{-1} obtained for the backward hole transfer is consistent with the single-step charge transfer in DNA. In contrast, the value of 0.2 \AA^{-1} for the forward hole transfer is significantly smaller than the reported β values for the single-step charge-transfer process.¹⁶

The distance dependence of the charge transfer by hopping mechanism can be described in the simplest way by eq 4 in which η is a proportional factor and N is the number of hopping steps.¹⁷

$$\ln k \propto -\eta \ln N \quad (4)$$

In the case of random walk, η takes the value between $1 \leq \eta \leq 2$. A plot of $\ln(\Phi/(1 - \Phi))$ against $\ln N$ gave a straight line and a η -value of 1.5 (Figure 4b). Thus, the forward hole transfer was demonstrated to proceed by A-hopping rather than a single-step super exchange mechanism.

In the present study, two different processes for the hole transfer across the identical (A)_n-bridge in DNA have been demonstrated. Since Ptz^{•+} oxidizes A, Ptz^{•+} injects a hole at A nearest to Ptz, and the forward hole transfer proceeds by the A-hopping mechanism. Whereas, oxG^{•+} cannot oxidize A, resulting in the hole transfer by single-step super exchange mechanism across (A)_n-bridge. These results clearly show that the mechanism of hole transfer in DNA strongly depends on the redox nature of the oxidant, whether it produces only G^{•+} or both A^{•+} and G^{•+}. Hence, the fast hole transfer rates reported in previous literature¹⁸ may be explained by the hole transfer by A-hopping mechanism which has been revealed to proceed faster than 10^8 s^{-1} , over the distance range of 7–22 Å. Such a fast hole transfer may help to separate the hole and radical anion of the photosensitizer (S^{•-}) during the photosensitized one-electron oxidation of DNA, making the chance for G^{•+} and S^{•-} to react with water or O₂.

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References

- (1) (a) Meggers, E.; Michel-Beyerle, M. E.; Giese, B. *J. Am. Chem. Soc.* **1998**, *120*, 12950. (b) Nakatani, K.; Dohno, C.; Saito, I. *J. Am. Chem. Soc.* **1999**, *121*, 10854.
- (2) (a) Lewis, F. D.; Wu, T. F.; Zhang, Y. F.; Letsinger, R. L.; Greenfield, S. R.; Wasielewski, M. R. *Science* **1997**, *277*, 673. (b) Wan, C. Z.; Fiebig, T.; Schiemann, O.; Barton, J. K.; Zewail, A. H. *Proc. Natl. Acad. Sci. U.S.A.* **2000**, *97*, 14052.
- (3) Kawai, K.; Takada, T.; Tojo, S.; Ichinose, N.; Majima, T. *J. Am. Chem. Soc.* **2001**, *123*, 12688.
- (4) (a) Henderson, P. T.; Jones, D.; Hampikian, G.; Kan, Y. Z.; Schuster, G. B. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 8353. (b) Nunez, M. E.; Hall, D. B.; Barton, J. K. *Chem. Biol.* **1999**, *6*, 85.
- (5) Giese, B.; Amaudrut, J.; Kohler, A. K.; Spormann, M.; Wessely, S. *Nature* **2001**, *412*, 318.
- (6) Lewis, F. D.; Liu, X. Y.; Liu, J. Q.; Miller, S. E.; Hayes, R. T.; Wasielewski, M. R. *Nature* **2000**, *406*, 51.
- (7) (a) Kendrick, T.; Giese, B. *Chem. Commun.* **2002**, 2016. (b) Giese, B.; Biland, A. *Chem. Commun.* **2002**, 667. (c) Giese, B.; Spichty, M. *ChemPhysChem* **2000**, *1*, 195.
- (8) The details of the experimental setup of the combined pulse radiolysis–laser flash photolysis method were described in the previous paper: Ishida, A.; Fukui, M.; Ogawa, H.; Tojo, S.; Majima, T.; Takamuku, S. *J. Phys. Chem.* **1995**, *99*, 10808.
- (9) (a) Kawai, K.; Miyamoto, K.; Tojo, S.; Majima, T. *J. Am. Chem. Soc.* **2003**, *124*, 912. (b) Kawai, K.; Takada, T.; Tojo, S.; Majima, T. *Tetrahedron Lett.* **2002**, *43*, 8083.
- (10) Kawai, K.; Takada, T.; Tojo, S.; Majima, T. *Tetrahedron Lett.* **2002**, *43*, 89.
- (11) Holes were generated in Ptz-conjugated ODN by the oxidation with TIOH⁺ which was generated during the pulse radiolysis (28 MeV, 8 ns) of N₂O-saturated ($\sim 22 \text{ mM}$) aqueous solution containing $1 \text{ mM Ti}_2\text{SO}_4$, $20 \text{ mM pH } 7.0 \text{ Na phosphate buffer}$, and 0.1 mM ODN (strand concentrated) (ref 10).
- (12) The energy of Ptz^{•+} in the excited state was estimated to be higher than 2 eV from the edge of the absorption peak of Ptz^{•+} at the longer-wavelength side. Using the reduction potential of Ptz ($E_{\text{ox}} = 0.76 \text{ V vs NHE}$ in CH₃CN, ref 10), reduction potential of Ptz^{•+} was estimated to be $\sim 2.8 \text{ eV}$. Thus, hole transfer from Ptz^{•+} to A ($E_{\text{ox}} = 1.42 \text{ V vs NHE}$ in H₂O, ref 13a; $E_{\text{ox}} = 1.96 \text{ V vs NHE}$ in CH₃CN, ref 13b) will be exergonic.
- (13) (a) Steenken, S.; Jovanovic, S. V. *J. Am. Chem. Soc.* **1997**, *119*, 617. (b) Seidel, C. A. M.; Schulz, A.; Sauer, M. H. M. *J. Phys. Chem.* **1996**, *100*, 5541.
- (14) Hole injection is the general mechanism for the decay of radical cations in the excited state. Shkrob, I. A.; Sauer, M. C.; Liu, A. D.; Crowell, R. A.; Trifunac, A. D. *J. Phys. Chem. B* **1998**, *102*, 4976.
- (15) Shafirovich, V.; Cadet, J.; Gasparutto, D.; Dourandin, A.; Huang, W. D.; Geacintov, N. E. *J. Phys. Chem. B* **2001**, *105*, 586.
- (16) Lewis, F. D.; Wu, Y. *J. Photochem. Photobiol. C* **2001**, *2*, 1.
- (17) (a) Jortner, J.; Bixon, M.; Langenbacher, T.; Michel-Beyerle, M. E. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 12759. (b) Giese, B.; Wessely, S.; Spormann, M.; Lindemann, U.; Meggers, E.; Michel-Beyerle, M. E. *Angew. Chem., Int. Ed.* **1999**, *38*, 996. (c) Behrens, C.; Burgdorf, L. T.; Schwogler, A.; Carell, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1763.
- (18) Pascaly, M.; Yoo, J.; Barton, J. K. *J. Am. Chem. Soc.* **2002**, *124*, 9083.

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