Dependence of the electrical conductivity of DNA on the double helical structure

Aoi Inomata[1], Takeshi Shimomura[2], Seiji Heike, Masaaki Fujimori[3], Tomihiro Hashizume[3,4], and Kohzo Ito[1]

[1]Graduate School of Frontier Sciences, The University of Tokyo, 5-1-5 Kashiwanoha, Kashiwa-shi, Chiba 277-8561, inomata@molle.k.u-tokyo.ac.jp,
[2]Graduate School of Engineering, Tokyo University of Agriculture and Technology, Koganei-shi, Tokyo 184-8588,
[3]Advanced Research Laboratory, Hitachi, Ltd., Hatoyama, Saitama 350-0395,
[4]Department of Physics, Tokyo Institute of Technology, 2-12-1 Oh-okayama, Meguro, Tokyo 152-8551

DNA, known as a biological material with self-assembled double helical structure, has attracted much attention to its conductivity. Interaction between p_z orbitals of parallel stacked base pairs would lead to conduction path along the helical axis. We measured the electrical conductivity of DNA molecules of various base sequences. Fine electrodes for the measurements with the gap of 100-200 nm are fabricated by using optical and AFM lithographies. Circular dichroism (CD) spectra showed that the sample DNA molecules took A-, B-, intermediate or irregular form depending on the base sequences. Some DNA molecules expected in B-form with parallel base pair planes tended to show higher conductivity, but others in A-form or any other forms had insulating properties.
Key Words: DNA, fine electrodes, electrical conductivity measurements, double helix conformation

INTRODUCTION

Prospects for application of DNA in molecular electronics has attracted much interest from researchers [1, 2] since it is generally accepted that the planar stacking of adjacent base pairs should make electron transfer along the axis of the double helix [3]. The specific binding ability and self-assembling property of DNA would be very useful for selective wiring between molecular devices. Regarding the electrical properties of DNA, short-range charge transfer in DNA had been experimentally confirmed by several research groups [4, 5, 6]. However, the band structure of DNA has not been elucidated yet. Previous reports about the long-range electrical conductivity of DNA were much controversial: insulating [7-9], semiconducting [10–15], and even metallic properties were reported [16]. This uncertainty of the conductivity of DNA would be partly because of the disparity in the experimental conditions. Numerous numbers of parameters could affect the electrical properties: base pair sequence, length of molecules, conformation of helices, ionic environment or humidity around DNA, etc. But the most critical factor for the conductivity of DNA has not been determined yet. In this study, we particularly focused on the two parameters: sequence and conformation. The base pair sequence would influence the electronic state in DNA because the ionization potentials of four kinds of bases are different [17]. Especially the content of guanine(G) would have influence on the charge generation in DNA molecules because it has the lowest ionization potential among the four kinds of bases. Oxidation of guanine leads to generation of positive holes. Structure of double-helix, that is, A-form or B-form of right-handed helix, would affect the hybridization of atomic p_z orbitals of the stacked base pairs. In A-DNA, the base-pair planes are largely inclined to the helical axis, while those in B-DNA are perpendicular to the helical axis. Thus p_z orbitals of atoms in neighboring base pairs would overlap better in B-DNA [2, 18]. Here, we report electrical conductivity measurements using fine electrodes for DNA with ordered base sequences. With a focus on the two factors mentioned above, base pair sequences and conformation of the helices, we attempted to compare the conductivity of DNA with four types of base sequences: Poly(dG) • Poly(dC), Poly(dG-dC) • Poly(dG-dC), Poly(dA) • Poly(dT), and Poly(dA-dT) • Poly(dA-dT). In the former two DNAs, all the base pairs contain guanines, whereas the latter two have no guanines. There were some reports that conformation of double-stranded DNA would strongly depends on its base pair sequence [19], as well as on humidity and counterions around it. Prior to electrical conductivity measurements, we performed CD spectrum analysis on aqueous buffer solutions of the sample DNA molecules to examine the conformation. CD spectrum of DNA reflects the stacking of the nucleotide bases, and make it possible to distinguish A-form from B-form [20, 21]. In this report, we show the CD spectra of the four types of DNA, and *I-V* characteristics of them except for Poly(dG-dC) • Poly(dG-dC). By comparing the results with the case of λDNA [22], we discuss the correlation between the two factors mentioned above and the electrical properties of DNA.

EXPERIMENT

Materials: Four types of DNA molecules were under investigation; Poly(dG)•Poly(dC) and Poly(dA)•Poly(dT) are double-stranded(ds) complexes of two homopolymers, whereas Poly(dG-dC) • Poly(dG-dC) and Poly(dA-dT) • Poly(dA-dT) consist of alternating copolymers. All the

DNA samples in solid form were purchased from Amersham Biosciences Corp. The approximate average length of Poly(dG) • Poly(dC) is 2.91 μm (8,560 base pairs, bp). Poly(dG-dC) • Poly(dG-dC) and Poly(dA-dT) • Poly(dA-dT) has a length of 0.345 μm (1,014 bp) and 1.20 μm (3,523 bp) on average, respectively. Length of Poly(dA) • Poly(dT) is undescribed. Each DNA sample was dissolved in TE buffer (10 mM Tris-HCl and 1 mM EDTA in distilled water, pH 8.0) to the concentration of 30-70 μg/ml. The base pair content of each sample was determined from the value of absorbance at 260 nm.

CD spectrum analysis: To obtain the information about the conformation of the DNA duplexes, we measured CD spectra of the samples. CD spectra were recorded with a CD spectrometer (JASCO J-820) with the integrating of ten times.

Electrical conductivity measurements: Platinum fine electrodes for the electrical conductivity measurements were prepared by using the optical and AFM lithography on SiO$_2$/Si substrates. A gap of two adjacent fine electrodes was from 100 to 200 nm in length. Further details about the fabrication of the electrodes have appeared in a previous report [23]. The sample DNA molecules were put on the substrate by the molecular combing method [24]: 30 μl of DNA solution was dropped onto the substrate, and shortly afterwards, sucked at the speed of 0.5 μl/s. Control of the dropping and suction of the DNA solution was kept by using a contact angle meter, OCA20 (Data Physics Instruments GmbH). DNA molecules on the substrate were observed with Multimode AFM (Nanoscope IIIa, Veeco Instruments Inc.) in tapping mode. The electrical conductivity measurements were performed in vacuum (below 10^{-5} torr) at room temperature using Cryogenic Probing Station (Nagase Electronic Equipment Service) and KEITHLEY model 236 Source-Measure Unit (Keithley Instruments, Inc.).

RESULTS AND DISCUSSION

CD spectra of the sample DNA solutions in the wavelength range of 200-300 nm appear in Fig. 1. The CD spectrum of Poly(dG) • Poly(dC) (Fig. 1 curve (a)) had a local minimal value around 290 nm, a large positive peak near 260 nm, and negative peak around 210 nm; it appeared analogous to that of A-DNA or A-RNA [25, 26]. Fig. 1 curve (d) is the CD spectrum of Poly(dA-dT) • Poly(dA-dT) which has approximately equal positive and negative peaks centered around 260 nm and a positive peak in the range of 210-230 nm; it is similar to the spectrum of B-DNA [27]. In contrast, the conformation of Poly(dG-dC) • Poly(dG-dC) (Fig. 1 curve (b)) and Poly(dA) • Poly(dT) (Fig. 1 curve (c)) could not be identified by the CD spectra since they indicated intermediate characteristics of those of A- and B-DNA. Poly(dG-dC) • Poly(dG-dC) and Poly(dA) • Poly(dT) may take irregular forms which are different from standard A- or B-form.

Figure 2 shows an AFM image of Poly(dG) • Poly(dC) placed on the substrate. A fiber of DNA molecules branching into two parts at the contact point with electrode 2; Parts of the fiber between electrodes 2-3 and 3-4 were 3.1-3.3 nm in height, while two branches between electrodes 1 and 2 had heights of 1.6-1.8 nm.
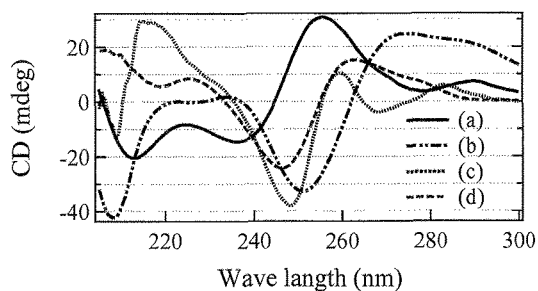

Fig. 1 Circular dichroism spectra in the range of 200-300 nm for (a) Poly(dG) • Poly(dC), (b) Poly(dG-dC) • Poly(dG-dC), (c) Poly(dA) • Poly(dT), and (d)Poly(dA-dT) • Poly(dA-dT).

A ds-DNA has a diameter of about 2 nm, and observation with AFM would show a height of less than 2 nm [11]. Thus the observed fiber was expected to consist of several ds-DNA molecules. The whole length of the bundle was over 3 μm, longer than that of a single molecule of double-stranded Poly(dG) • Poly(dC). The length of the parts of the fiber, bridging the gap of electrodes 2-3 and 3-4, were 280 nm and 320 nm, respectively. Between electrodes 1 and 2, one branch of the fiber extending from electrodes 2 seemed to contact electrode 1, but the other did not. The former one bridged electrodes 1-2 over 260 nm.

Poly(dA) • Poly(dT) and Poly(dA-dT) • Poly(dA-dT) were aligned on the substrates in the same way. It was observed that two Poly(dA) • Poly(dT) molecules were stretched between two adjacent fine electrodes (data not shown). One fiber was 2.5 nm and the other 1.8 nm in height. The former seemed to be a fiber of several DNA molecules, while the latter could be a single molecule of ds-DNA.
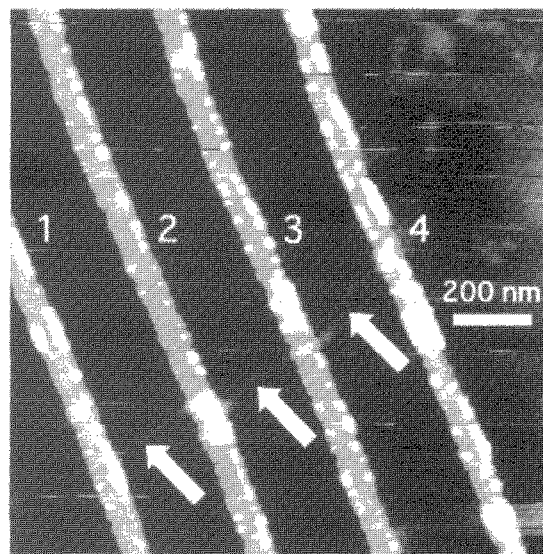

Fig. 2 AFM image of Poly(dG) • Poly(dC) molecules on Pt fine electrodes. The electrodes are numbered 1-4 from the left. Arrows indicate linear structures connecting the electrodes.

The fibers did not run parallel to the electrodes; The lengths of the part of the fibers between the electrodes ranged from 300 to 400 nm. A fiber consisting of several Poly(dA-dT) • Poly(dA-dT) molecules was also found to cross two electrodes (Fig. 3). The heights of the fiber ranged from 2.0 to 2.4 nm, and the lengths of the electrode gap was about 200 nm.
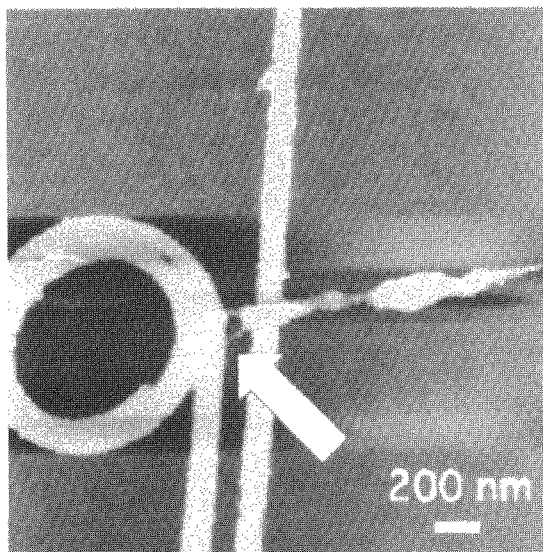

Fig. 3 AFM image of a Poly(dA-dT) • Poly(dA-dT) fiber   on Pt fine electrodes.

Figure 4 shows the current-voltage (*I-V*) characteristics of Poly(dG) • Poly(dC). For electrodes 1-2 and 2-3 (Fig. 3 curve (a) and (b)), the value of the detected electrical current ranged less than 1 pA; much the same order of the background level. Between electrodes 3-4, a fraction of significant current (several picoamperes) was detected, and the electrical resistance was determined to be about 300 GΩ. These results represented that Poly(dG) • Poly(dC) has rather low conductivity. It contradicts the expectation of high conductivity associated with its guanine-rich sequence. There are also some contradictory previous reports to our results. For example, higher conductance of Poly(dG) • Poly(dC) than Poly(dA) • Poly(dT) in low temperatures had been reported [14]. In our experiment, the conformation of Poly(dG) • Poly(dC), which was expected to be A-form, could be a hinderance for the electrical conduction through the whole molecule.

For Poly(dA) • Poly(dT), no significant electrical current was detected (>10 TΩ, Fig. 5). In contrast with the above two samples, Poly(dA-dT) • Poly(dA-dT) yielded much higher conductivity (Fig. 6). Nearly Ohmic behavior was observed with the electrical resistance of 20 GΩ from linear fitting.

The *I-V* measurements for Poly(dG) • Poly(dC) and Poly(dA) • Poly(dT) demonstrated the insulating characteristics. And CD spectrum analysis of the aqueous solutions of these two DNA molecules showed different spectra from that of regular B-form. In contrast, Poly(dA-dT) • Poly(dA-dT), of which CD spectrum was similar to that of standard B-form, was
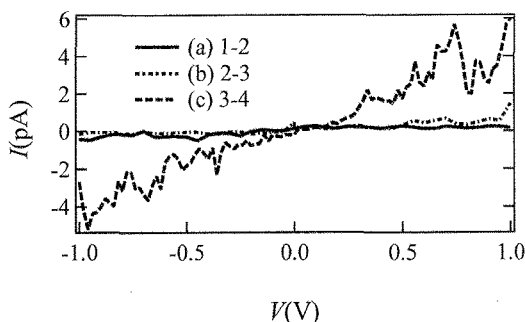

V(V)

Fig. 4 *I-V* characteristics of Poly(dG) • Poly(dC) between electrodes (a) 1-2, (b) 2-3, and (c) 3-4. Curve (a) and (b) indicate less electrical current than 1 pA. The electrical resistance determined from the gradient of curve (c) is about 300 GΩ.
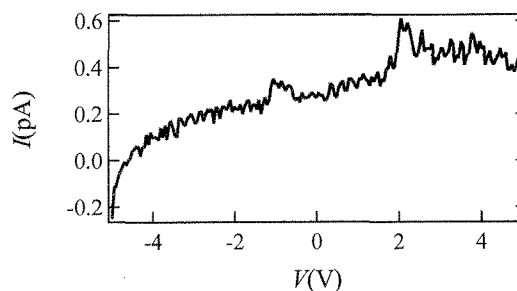

V(V)

Fig. 5 *I-V* characteristics of Poly(dA) • Poly(dT). Insulating behavior was observed.
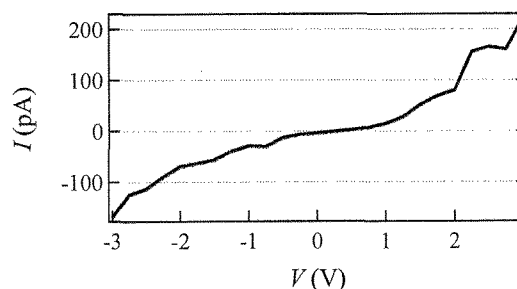

V (V)

Fig. 6 *I-V* characteristics of Poly(dA-dT) • Poly(dA-dT). Rather high conductivity was obtained.

indicative of rather high conductivity. These results imply that conformation of the DNA double helix has a greater influence on the electrical conductivity of DNA than the content of Guanine.

In addition, we refer to our previous experiments on λDNA reported elsewhere [22]. λDNA with irregular base sequence took B-form in aqueous solution (CD spectra had not been shown in the paper). *I-V* measurements showed that λDNA was capable of both conducting and insulating parts. In that case, contact resistance between the λDNA and electrodes or conformational transition from B- to A- form might have led the reduction in conductivity.

In conclusion, DNA molecules with B-form associated with parallel base pair stacking are capable of high electrical conductivity.   In further studies,   *I-V* measurements for Poly(dG-dC) • Poly(dG-dC) and other different kinds of DNA are presently underway.

Additionally, conformational analysis of DNA on the surface of a substrate, not in aqueous solution, would be sufficient proof of our model.

REFERENCES

[1] C. Dekker, M. Ratner, *Phys. World*, **14**, 29-33 (2001).
[2] R. G. Endres, D. L. Cox, R. R. P. Singh, *Rev. Mod. Phys.*, **76**, 195-214 (2004).
[3] D. D. Eley, D. I. Spivey, *Trans. Faraday. Soc.*, **58**, 411-415 (1962).
[4] B. Giese, J. Amaudrut, A.-K. Köhler, M. Spormann, S. Wessely, *Nature*, **412**, 318-320 (2001).
[5] P. T. Henderson, D. Jones, G. Hampikian, Y. Kan, G. B. Schuster, *Proc. Natl. Acad. Sci. U.S.A.* **96**, 8353-8358 (1999).
[6] F. D. Lewis, X. Y. Liu, J. Q. Liu, S. E. Miller, R. T. Hayes, M. R. Wasielewski, *Nature* **406**, 51-53 (2000).
[7] A. J. Storm, J. van Noort, S. de Vries, C. Dekker, *Appl. Phys. Lett.*, **79**, 3881-3883 (2001).
[8] E. Braun, Y. Eichen, U. Sivan, *Nature*, **391**, 775-778 (1998).
[9] P. J. de Pablo, F. Moreno-Herrero, J. Colchero. J. G. Herrero, P. Herrero, A. M. Baró, P. Ordejón, J. M. Soler, E. Artacho, *Phys. Rev. Lett.*, **85**, 4992-4995 (2000).
[10] D. Porath, A. Bezryadin, S. de Vries, C. Dekker, *Nature*, **403**, 635-638 (2000).
[11] L. Cai, H. Tabata, T. Kawai, *Appl. Phys. Lett.*, **77**, 3105-3106 (2000).
[12] P. Tran, B. Alavi, G. Gruner, *Phys. Rev Lett.*, **85**, 1564-1567 (2000).
[13] A. Rakitin, P. Aich, C. Papadopoulos, Y. Kobzar, A. S. Vedeneev, J. S. Lee, J. M. Xu, *Phys. Rev. Lett.*, **86**, 3670-3673 (2001).
[14] K. -H. Yoo, D. H. Ha, J. -O. Lee, J. W. Park, J. Kim, J. J. Kim, H. -Y. Lee, T. Kawai, H. Y. Choi, *Phys. Rev. Lett.*, **87**, 198102 (2001).
[15] H. -W. Fink, C. Schönenberger, *Nature*, **398**, 407-410 (1999).
[16] A. Y. Kasumov, M.Kociak, S. Guéron, B. Reulelt, V. T.Volkov, D. V. Klinov, H. Bouchiat, *Science*, **291**, 280-282 (2001).
[17] H. Sugiyama, I. Saito, *J. Am. Chem. Soc.*, **118**, 7063-7068 (1996).
[18] R. G. Endres, D. L. Cox, R. R. P. Singh, e-print cond-mat/0201404 (2002).
[19] A. G. W. Leslie, S. Arnott, *J. Mol. Biol.*, **143**, 49-72 (1980).
[20] M. J. B. Tunis-Schneider, M. F. Maestre, *J. Mol. Biol.*, **52**, 521-541 (1970).
[21] V. A. Bloomfield, D. M. Crothers, and I. Tinoco, Jr., "Nucleic Acids: structures, properties, and functions", University Science Books, Sausalito, California (2000) pp. 190-196.
[22] A. Inomata, T. Shimomura, S. Heike, M. Fujimori, T. Hashizume, K. Ito, submitted.
[23] T. Akai, T. Abe, T. Shimomura, M. Kato, M. Ishibashi, S. Heike, B. -K. Choi, T. Hashizume, K. Ito, *Jpn. J. Appl. Phys.*, **42**, 4764-4766 (2003).
[24] A. Bensimon, A. Simon, A. Chiffaudel, V. Croquette, F. Heslot, D. Bensimon, *Science*, **65**, 2096-2098 (1994).
[25] D. M. Gray, J. –J. Liu, R. L. Ratliff, F. S. Allen, *Biopolymers*, **20**, 1337-1382 (1981).
[26] C. A. Sprecher, W. A. Baase, W. C. Johnson, Jr., *Biopolymers*, **18**, 1009-1019 (1979).
[27] D. M. Gray, F. D. Hamilton, M. R. Vaughn, *Biopolymers*, **17**, 85-106 (1978).