DNA Conductance

DOI: 10.1002/ange.200601263

Variable-Temperature Measurements of the Single-Molecule Conductance of Double-Stranded DNA**

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There has been much interest in the electrical properties of DNA.[1] Recent studies have shown that it is possible to record the current–voltage characteristics of both single-stranded and double-stranded DNA immobilized between metal electrodes in an ambient or aqueous environment.[2–4] As in the case of organic molecular bridges,[5,6] there is also great value in being able to determine the conductance of DNA over a range of temperatures, since this enables charge-transport mechanisms to be investigated. With this aim, we present here a first study of the effect of temperature on the single-molecule conductance (SMC) of double-stranded oligodeoxynucleotides with homogeneous canonical base-pair sequences (adenine–thymine (AT) and guanine–cytosine (GC)).

Each of the DNA duplexes under study here contains 15 canonical nucleotide pairs, and for brevity they are referred to as "$(dA)_{15}$-$(dT)_{15}$" and "$(dG)_{15}$-$(dC)_{15}$", when treated separately, or as "DNA", when described together. The SMC of $(dA)_{15}$-$(dT)_{15}$ and $(dG)_{15}$-$(dC)_{15}$ have been determined over a range between room temperature to about 70 °C by using recently developed STM-based methods.[4,7] These duplexes have been functionalized at their 3′-ends with trimethylene-thiol (C_3) linkers, which help to covalently attach DNA

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[**] This work was supported by the European Community under contract IST-2001-32152, MINT (Molecular Interconnects for Nanotechnology) and under contract HPRN-CT-2002-00185, SUSANA (Supramolecular Self-Assembly of Interfacial Nanostructures) Research Training Network. Support from the EPSRC under grant EP/C00678X/1 (Mechanisms of Single Molecule Conductance) is also gratefully acknowledged. The work was also supported by a grant from the German National Science Foundation (DFG WE1863/14-1) and through the DASY project of the "Volkswagen Stiftung" foundation.

strands to gold electrodes; the resistance of these linker chains is known to be relatively low, so they should not contribute significantly to the conductance or its temperature dependence.[5] The SMC values determined over this temperature range are 0.51 ± 0.08 nS and 1.2 ± 0.2 nS for $(dA)_{15}$-$(dT)_{15}$ and $(dG)_{15}$-$(dC)_{15}$, respectively (Figure 1d). It is thus evident that $(dG)_{15}$-$(dC)_{15}$ is a better conductor than $(dA)_{15}$-$(dT)_{15}$. Strikingly, along with this, the data do not show (within experimental error) any dependence of the SMC on the temperature, contrary to observations for long homogeneous base sequence DNA in a vacuum.[8] These differences indicate that the medium has a great influence on the temperature dependence of DNA conductance.

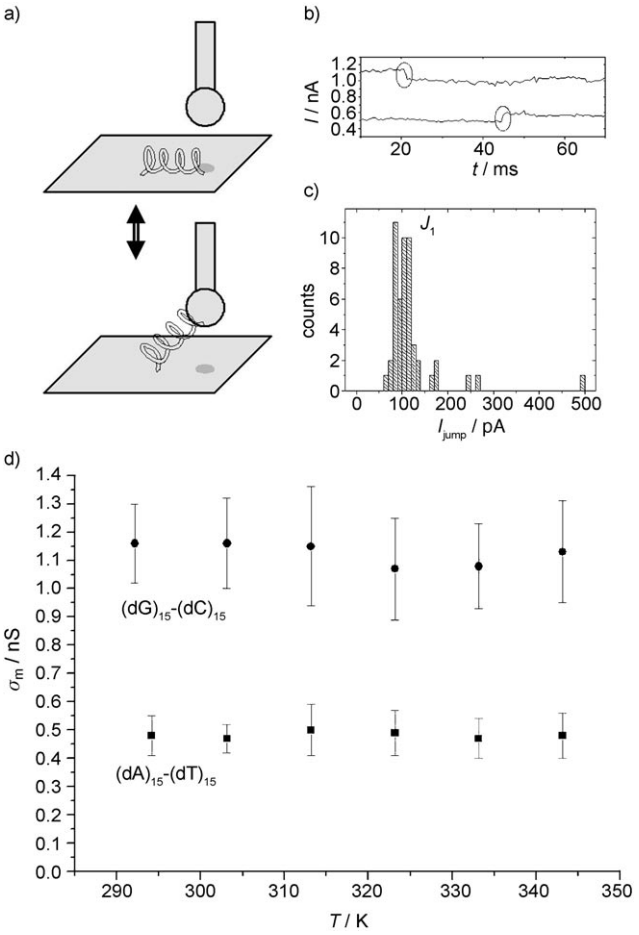

Figure 1. a) The $I(t)$ technique with a fixed gap between the tip and the substrate and a DNA molecule spontaneously bridging the gap. b) Typical $I(t)$ traces. Representative current jumps for this technique are shown in circles. c) The resulting histogram, $J_1 = 102 \pm 16$ pA. All measurements shown are for $(dA)_{15}$-$(dT)_{15}$ at $U_{tip} = 200$ mV in air. d) The SMC as a function of the substrate temperature for both $(dA)_{15}$-$(dT)_{15}$ (■) and $(dG)_{15}$-$(dC)_{15}$ (●). All measurements were performed in air at $U_{tip} = 200$ mV.

The temperature independence recorded here seems to be paradoxical, since there are several theoretically established mechanisms that would predict strong temperature dependence. Firstly, a temperature dependence would be expected for activated charge that hops through DNA in a polaron-like manner. Temperature-dependent conductance may also be expected for DNA in aqueous solutions containing counterions, which are predicted to influence charge transport through a "counterion-gating" mechanism.[9] Moreover, the polaron-like charge transport in DNA is believed to be largely augmented with contributions coming from intramolecular thermal fluctuations.[10,11] Finally, the DNA hydration shell ought to influence the charge transport in a temperature-dependent manner.[12] Thus, our present finding contradicts, at first glance, these theoretical expectations for the temperature dependence of DNA conductance.

In an attempt to explain our surprising experimental result we have carried out a series of DNA conductance calculations by using a completely atomistic approach.[13] With these calculations we can study the influence of the deformations arising from acoustic modes on the valence-band transmission spectrum of $(dA)_{15}$-$(dT)_{15}$ and $(dG)_{15}$-$(dC)_{15}$. On the basis of these data we can ascertain whether the DNA acoustic modes could give rise to the temperature dependence of the conductivity at ambient temperatures. Figure 2a shows that deformation along DNA acoustic modes greatly affects the valence-band transmission for the 26-mer studied in Ref. [2]. The same qualitative conclusion can be drawn for the valence-band transmission in the two 15-mers studied here (Figure 2b and c).

Figure 2b and c show that the area covered by the whole $(dG)_{15}$-$(dC)_{15}$ valence band in the equilibrium conformation is much larger than that of $(dA)_{15}$-$(dT)_{15}$. This area is expected to be approximately proportional to the magnitude of the electrical current flowing through the molecule under study.[14] Closer examination of Figure 2b and c reveals that the DNA acoustic modes significantly suppress the valence-band conduction of $(dG)_{15}$-$(dC)_{15}$, but noticeably improve it for $(dA)_{15}$-$(dT)_{15}$. Even in its improved form the valence-band conduction of $(dA)_{15}$-$(dT)_{15}$ is not as high as that of the $(dG)_{15}$-$(dC)_{15}$ in its equilibrium B-DNA conformation. These results (Figure 2) suggest that DNA valence-band conductance in $(dG)_{15}$-$(dC)_{15}$ is larger than that in $(dA)_{15}$-$(dT)_{15}$, which is in qualitative accordance with the experimentally observed trend (see Figure 1). However, these computations indicate that different acoustic modes for the same sequence give very different valence-band transmission spectra, which might result in a temperature-dependent conductance.

To explain the experimental finding we additionally consider the temperature-dependent population of the acoustic modes through the Debye temperature of the system. By assuming a speed of sound in B-form DNA of 1900 m s^{-1}[15] and a lattice constant of approximately 0.34 nm, the Debye temperature is estimated as 166 K.[16] For this reason, DNA acoustic modes will significantly affect the conductance at low temperatures, but at room and higher temperature this effect will have no noticeable temperature dependence.

In conclusion, we have recorded the SMC of $(dA)_{15}$-$(dT)_{15}$ and $(dG)_{15}$-$(dC)_{15}$ as a function of temperature (from room temperature to about 70 °C). The G-C sequence gives a higher conductance than the equivalent length A-T sequence. This experimental result is consistent with the computations presented here for the valence-band transmission spectra. These computations also predict that the conductance should

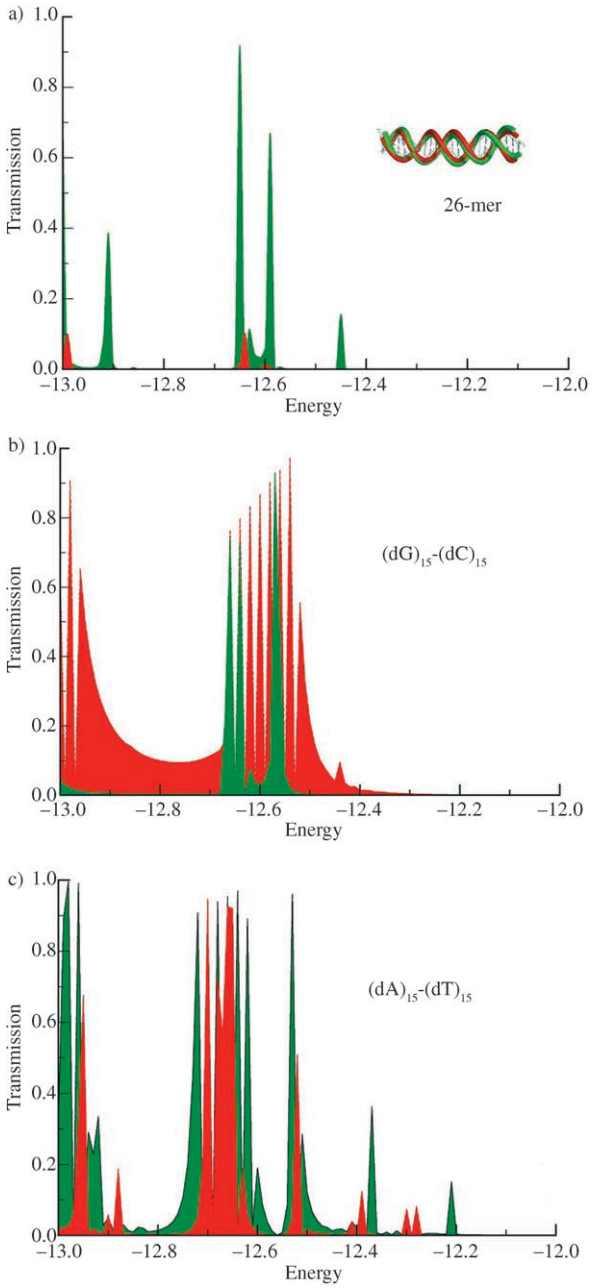

Figure 2. Comparison of the calculated transmission spectra at the upper edge of the valence band for: a) 26-mer duplex studied in Ref. [2] with a trimethylenethiol linker between the 3′-ends and electrodes (inset shows the mode of deformation of the DNA duplex), b) $(dG)_{15}$-$(dC)_{15}$, and c) $(dA)_{15}$-$(dT)_{15}$; the latter two were attached to electrodes directly (without C_3SH linkers) in our calculations. The Fermi level (defined here as halfway between the energies of the highest occupied and lowest unoccupied orbitals at 0 K) is around −12.05 eV for all the graphs. The red spectra correspond to the transmission spectra of the duplexes in their ideal B-DNA conformation, the green ones depict those with deformations along DNA acoustic modes.

be strongly influenced by the acoustic mode. The fact that the Debye temperature of these systems is far below room temperature, means that the contribution from DNA acoustic modes should be essentially temperature-independent, which is in agreement with the experimental observation. Future studies, both theoretical and experimental, of the temperature dependence of DNA conductance and its relationship to other experimental parameters (for example, base sequence, electrolyte concentration, molecular length) are expected to play a key role in establishing DNA conductance mechanisms.

Experimental Section

The experiments were based upon a recently developed technique.[7] The so-called "$I(t)$ technique" is shown schematically in Figure 1a, with temperature control as described by Haiss et al.[5] A gold tip and a gold on glass substrate were employed along with a low coverage of DNA strands. The tunneling current was monitored as a function of time at a fixed tip–substrate separation. Under these conditions events occured in which the DNA strands bridged the gap between the tip and the substrate to form a "molecular wire" (Figure 1b). Examples of both attachment and detachment events for DNA are shown in circles in Figure 1b). These current jumps are associated with current flowing through one or more DNA strands and can be used to calculate the SMC, after statistical analysis of the data. DNA adsorption was achieved by immersion of the gold substrates in aqueous 10 mM sodium phosphate buffer (pH 6.8) with a DNA concentration of ca. 10^{-4} M. The sample was then rinsed with Milli-Q water and gently blown with N_2 to remove excess water. By using these conditions, it was expected that a water film and phosphate counterions would be retained with the DNA sample. Indeed, control experiments at room temperature for fully immersed samples (in an electrochemical STM cell) gave comparable conductance values for a given sequence, thus adding evidence that it is the hydrated sample that is analyzed.

Single-stranded DNA is a much worse conductor than dsDNA and the conductance measured here is consistent with the latter and not the former.[4] Further verification that the double helix was measured in these experiments comes through observation of the frequency of the $I(t)$ jumps. Raising the temperature above the melting temperature (T_M) should show a decreased frequency of such events in the $I(t)$ traces, although the transition should not be sharp since the melting curve is not expected to be sharp.[18] Indeed we saw a much decreased frequency of events with $(dA)_{15}$-$(dT)_{15}$ duplexes bridging the contacts on increasing the temperature from 50 to 70 °C, which is consistent with the melting of the duplex. Such a decrease in the frequency of the current jumps was not observed for a control molecule: nonanedithiol.[5]

The T_M value of $(dG)_{15}$-$(dC)_{15}$ is 76.5 °C, while that of $(dA)_{15}$-$(dT)_{15}$ is 41.9 °C (data supplied by Sigma-Genosys). The highest temperature at which the conductance was measured was 70 ± 2 °C. It may therefore seem paradoxical that molecular conductance for $(dA)_{15}$-$(dT)_{15}$ could still be measured above the quoted melting point. A possible explanation for this observation is that under ambient conditions the electrolyte concentration at the surface is high, since the aqueous film of ambient water/electrolyte is likely to dry at least partially during the temperature ramps. It is well known that a higher ionic strength gives rise to higher melting temperatures.[19]

To compute the conductance behavior of DNA strands, we used a previously established computational method,[13] which employs an all-atom representation for the DNA strands and describes their electronic structure in the framework of an extended Hückel Hamiltonian. To study the influence of DNA acoustic vibrations on its conductive properties, we generated ideal B-DNA conformations for $(dA)_{15}$-$(dT)_{15}$ and $(dG)_{15}$-$(dC)_{15}$, as well as for the DNA duplexes studied elsewhere.[2,3] Deformations were then produced along the three lowest frequency intramolecular vibrational modes for all of these molecules by using an elastic network model.[20] The three vibrations involved are invariant with respect to DNA base composition and sequence, and include bending of DNA double-helical rods

in the two orthogonal directions perpendicular to the rod axis, as well as a combination of helical twisting and longitudinal stretching/squeezing. Thus, we can consider these modes acoustic ones. Finally, we calculated the energy spectra of charge-transmission probabilities as in Ref. [13] for all the equilibrium and deformed B-DNA conformations.

Received: March 31, 2006
Revised: June 2, 2006
Published online: August 7, 2006

Keywords: conducting materials · DNA · scanning probe microscopy · single-molecule studies

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