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Frequency-dependent electrical characteristics of DNA using molecular dynamics simulation

Makoto Ikeda[1,3], **Kazuo Nakazato**[2], **Hiroshi Mizuta**[2], **Martin Green**[1], **David Hasko**[1] **and Haroon Ahmed**[1]

[1] Microelectronics Research Centre, Cavendish Laboratory, University of Cambridge, Madingley Road, Cambridge CB3 0HE, UK
[2] Hitachi Cambridge Laboratory, Hitachi Europe Ltd., Madingley Road, Cambridge CB3 0HE, UK

E-mail: ikeda@silicon.u-tokyo.ac.jp

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Abstract
Research on DNA has been widely carried out as a promising material for nanoelectronics, medicine development and disease diagnosis, using experiment, simulation and theory. We have carried out molecular dynamics simulation coupled with the linear response theory, based on the time-correlation function of an observable, in order to extract the frequency-dependent electrical characteristics of DNA. We observe a dielectric relaxation at around 50 MHz in the case of octamers-DNA, which corresponds to a delta-relaxation. We also observe dielectric relaxation in the case of mixtures of DNA, water molecules and ions, given by the superposition of the individual dielectric relaxations of the DNA and the bulk-like water, at frequencies of about 50 MHz and 10 GHz, respectively.

1. Introduction

Research on DNA has been widely carried out as a promising material for nanoelectronics, medicine development and disease diagnosis, using experiment, simulation and theory. With the completion of the human genome project, a new era of opportunity is brought to molecular biology and genetics. New detection methods for DNA are required, in order to enable devices to collect data at high throughput and in real time. For this purpose, several new techniques have been proposed, such as using cantilevers for the detection of steric forces caused by the hybridization of target DNA with probe DNA immobilized onto a surface [1–15]. For label-free detection, it is essential to know the precise electrical characteristics of DNA. Many experimental results and theoretical calculations on the conductivity of DNA have been published, showing a wide variety of behaviour, from insulating to metallic conduction. Despite this, the conductivity of DNA remains a matter for investigation [16–36].

In this paper, we describe a technique to calculate the electrical characteristics of DNA, which can be applied to label-free DNA detection. We have employed linear response theory in a molecular dynamics simulation, to extract the frequency-dependent electrical characteristics.

In the next section, we describe the linear response theory. In section 3, we describe the molecular dynamics simulation and the simulated systems. In section 4, we describe the results for the frequency-dependent electrical characteristics of DNA.

2. Linear response theory

Linear response theory defines a linear relationship between the macroscopic characteristics and the microscopic observables, in quasi-equilibrated and uniform systems [37–40].

For the explanation of dielectric phenomena, linear response theory deals with the response of a macroscopic system to an applied external electric field. On the macroscopic level, linear response theory assumes a linear relationship between the applied external field $\boldsymbol{E}_0(\omega)$ and the ensemble average of an observable $\langle \boldsymbol{O}(\omega)\rangle$:

$$\langle \boldsymbol{O}(\omega)\rangle = \chi_{OP}(\omega)\boldsymbol{E}_0(\omega).$$

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[3] Address for correspondence: VLSI Design and Education Centre, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan.

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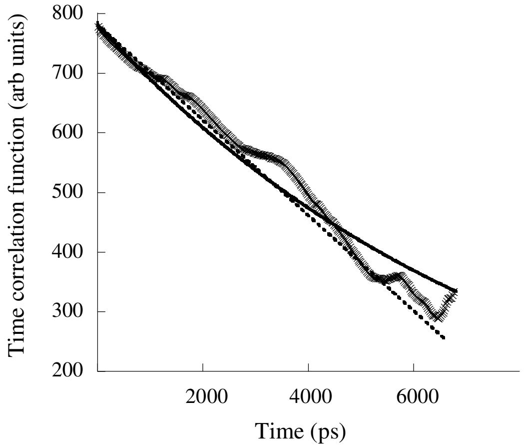

Figure 1. The simulated time-correlation function $\langle M(0)M(t)\rangle$ of a DNA molecule (crosses) and linear-type (dashed line) and exponential-type (continuous curve) approximation curves.

$\chi_{OP}(\omega)$ is the complex generalized susceptibility, which describes the coupling of the observable $\boldsymbol{O}(t)$ to the polarization $\boldsymbol{P}(t)$ of the system. According to linear response theory, the generalized susceptibility for an observable $\boldsymbol{O}(t)$ is defined as

$$\chi_{OP}(\omega) = 1/3kT[\langle \boldsymbol{O}(0)\boldsymbol{M}(0)\rangle - \mathrm{j}\omega\langle \boldsymbol{O}(0)\boldsymbol{M}(t)\rangle_\omega + \langle \boldsymbol{O}(0)\boldsymbol{J}(t)\rangle_\omega]$$

where $\boldsymbol{M}(t) = \Sigma q_i \boldsymbol{r}_i(t)$ is the dipole moment due to charges q_i and displacement $\boldsymbol{r}_i(t)$; and $\boldsymbol{J}(t) = \Sigma q_i \boldsymbol{v}_i(t)$ is the ion current due to charges q_i moving with velocity $\boldsymbol{v}_i(t)$. $\langle \boldsymbol{A}(0)\boldsymbol{B}(t)\rangle$ denotes a time-correlation function of the time-dependent quantities $\boldsymbol{A}(t)$ and $\boldsymbol{B}(t)$, and $\langle \boldsymbol{A}(0)\boldsymbol{B}(t)\rangle_\omega$ denotes a Laplace transform of the time-correlation function. The above equations use a general observable $\boldsymbol{O}(t)$, which can be specified as the polarization of the molecules $\boldsymbol{P}(t) = 1/V\boldsymbol{M}(t)$ or as the current density of the ions $\boldsymbol{I}(t) = 1/V\boldsymbol{J}(t)$, where V is the simulation volume, giving

$$\langle \boldsymbol{P}(\omega)\rangle = \chi_{PP}(\omega)\boldsymbol{E}_0(\omega)$$

with

$$\chi_{PP}(\omega) = 1/3VkT[\langle \boldsymbol{M}(0)\boldsymbol{M}(0)\rangle - \mathrm{j}\omega\langle \boldsymbol{M}(0)\boldsymbol{M}(t)\rangle_\omega + \langle \boldsymbol{M}(0)\boldsymbol{J}(t)\rangle_\omega]$$

and

$$\langle \boldsymbol{I}(\omega)\rangle = \chi_{iP}(\omega)\boldsymbol{E}_0(\omega)$$

with

$$\chi_{iP}(\omega) = 1/3VkT[-\mathrm{j}\omega\langle \boldsymbol{J}(0)\boldsymbol{M}(t)\rangle_\omega + \langle \boldsymbol{J}(0)\boldsymbol{J}(t)\rangle\omega].$$

The phenomenological equations of matter, $\boldsymbol{P}(\omega) = (\varepsilon(\omega) - 1)\boldsymbol{E}(\omega)/4\pi$ and $\boldsymbol{I}(\omega) = \sigma(\omega)\boldsymbol{E}(\omega)$, define the dielectric constant $\varepsilon(\omega)$ and the conductivity $\sigma(\omega)$. Both involve the Maxwell field $\boldsymbol{E}(\omega)$, which is the electric field acting inside a macroscopic piece of matter. In the case of the ideal Ewald summation, where the cut-off radius r_c and decay parameter η are both infinite, the Maxwell field is equal to the externally applied electric field $\boldsymbol{E}_0(\omega)$, and the dielectric constant and conductivity can be expressed as $\varepsilon(\omega) = 1 + 4\pi\chi_{PP}(\omega)$ and $\sigma(\omega) = \chi_{iP}(\omega)$. Note that the conductivity $\sigma(\omega)$, in this case, is independent of the dielectric constant, represented by the susceptibility $\chi_{PP}(\omega)$.

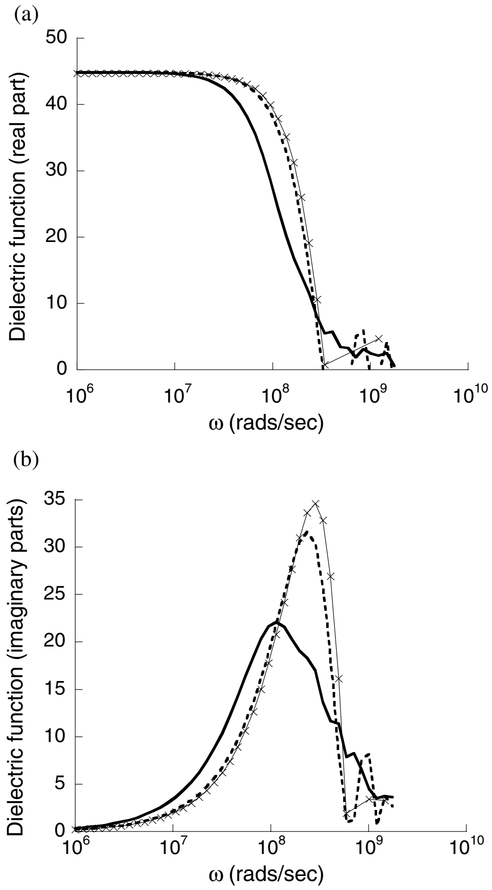

Figure 2. The frequency-dependent dielectric function: (a) real part and (b) imaginary part and linear-type (dashed curve) and exponential-type (continuous curve) approximation curves.

3. Molecular dynamics simulation

Molecular dynamics simulation has been widely used for studying molecular structures. In this work, we use TINKER from Washington University, which employs a smooth particle-mesh Ewald summation method.

We used octamer randomly generated ds/ss-DNA d[GTAGCAAA] in this simulation. The simulation system size corresponds to a DNA surface density of 9.6 molecules nm^{-2}, and a few layers of water molecules occupy the gaps between adjacent DNA molecules. Each DNA backbone requires 14 Na^+ counter-ions, and two Na^+ ions with two Cl^- ions corresponding to a 0.1 M saline solution, similar to many DNA buffer solutions. A summary of the simulation is listed in table 1.

4. Simulation results

Figure 1 shows the time-correlation function of a DNA molecule. A linear-type approximation describes the behaviour well, $F_{lin}(\omega) = C_{0l} + C_{1l}\exp(\frac{-t}{\tau_{1l}}) + C_{2l}t$, as does an exponential-type approximation, $F_{\exp}(\omega) = C_{0e}\exp(\frac{-t}{\tau_{1e}}) + C_{1e}\exp(\frac{-t}{\tau_{2e}})$, where $C_{0l}, C_{1l}, C_{2l}, \tau_{1l}, C_{0e}, C_{1e}, \tau_{1e}$ and τ_{2e}, are respectively 781.4, 3.6, −0.08, 0.8, 781.4, 3.6, 8000 and 0.8 ps. The frequency-dependent dielectric behaviour is shown in figure 2. Figure 3 shows the time-correlation function

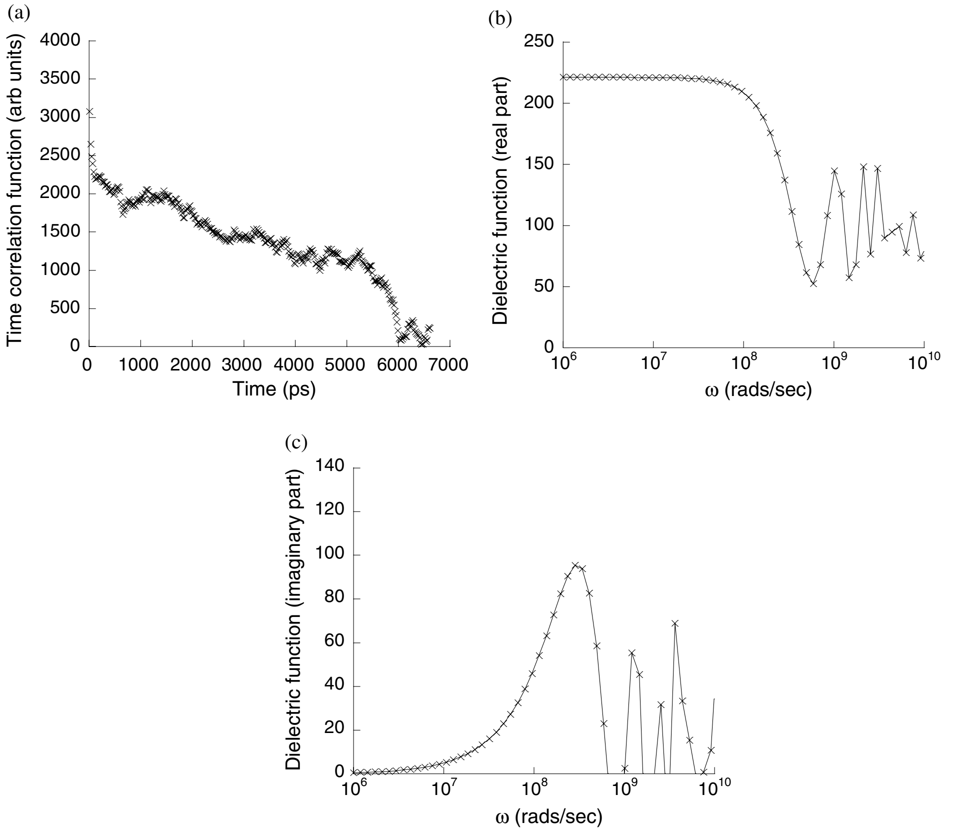

Figure 3. (a) The simulated time-correlation function $\langle M(0)M(t)\rangle$ and (b), (c) the real and imaginary parts of the dielectric function for a mixture of DNA and water molecules.

Table 1. Simulation set-up.

Force field	Lennard-Jones 12–6 potential (amber 94 parameter set)
System size	$3.107 \times 3.107 \times 4.350$ nm^3
Molecules	Octamer random sequence ds-DNA, 1239 water molecules, 16 Na$^+$, 2 Cl$^-$, total 4244 atoms
Temperature	298 K
Time step	1 fs
Cut-offs	Lennard-Jones, 0.9 nm; Ewald, 0.9 nm
Simulation period	600 ps for equilibrium, 7.3 ns for correlation function

and the dielectric behaviour for a mixture of DNA and water molecules. Figure 4 shows the time-correlation function and the dielectric behaviour for water molecules only.

Figure 3 shows that the characteristic frequency of the DNA is between 18 and 27 MHz, which is consistent with the δ-relaxation expected in the range 1 MHz–1 GHz, due to the orientational change of strongly bound water, or due to short scale relaxations of the DNA chain. On the other hand, the characteristic frequency of water molecules, as seen in figure 4, is nearly the same as that of bulk water, which means that the few layers of water molecules present still demonstrate bulklike characteristics. The characteristic frequency of the molecule mixture seems to be a superposition of those due to DNA and water individually.

It has been reported that there are at least three kinds of relaxation for DNA [41].

(1) *α-relaxation.* Less than a few kHz. A large dielectric increment whose characteristic frequency is dependent on the size of the DNA molecule. Relaxation seems to reflect the migrations of counter-ions along the entire length of the DNA molecule.
(2) *δ-relaxation.* 1 MHz–1 GHz. A smaller molecular weight independent dielectric increment. This has been attributed to orientational change of strongly bound water, or the short scale relaxations of the DNA chain.
(3) *γ-relaxation.* 1 GHz or above. Reorientation of dipolar water molecules.

Recently published DNA measurements using a 35-mer of poly-T and poly-G DNA in nanogap junctions demonstrate similar dielectric decay characteristics to those simulated here [42]. The characteristic frequency from these experimental results differs markedly from the simulated results. Such a difference may be caused by the length and surface density of the DNA used or differences in the geometry, in the extent of the simulated region and time or in the relaxation mechanism.

5. Conclusions

In this work, we demonstrate the possibility of extracting the electrical characteristics of DNA using molecular dynamics simulation combined with linear response theory. Results show agreement with previously reported measurements on the δ-relaxation frequency of DNA and water molecules, and the latter show similar characteristics to of bulk water.

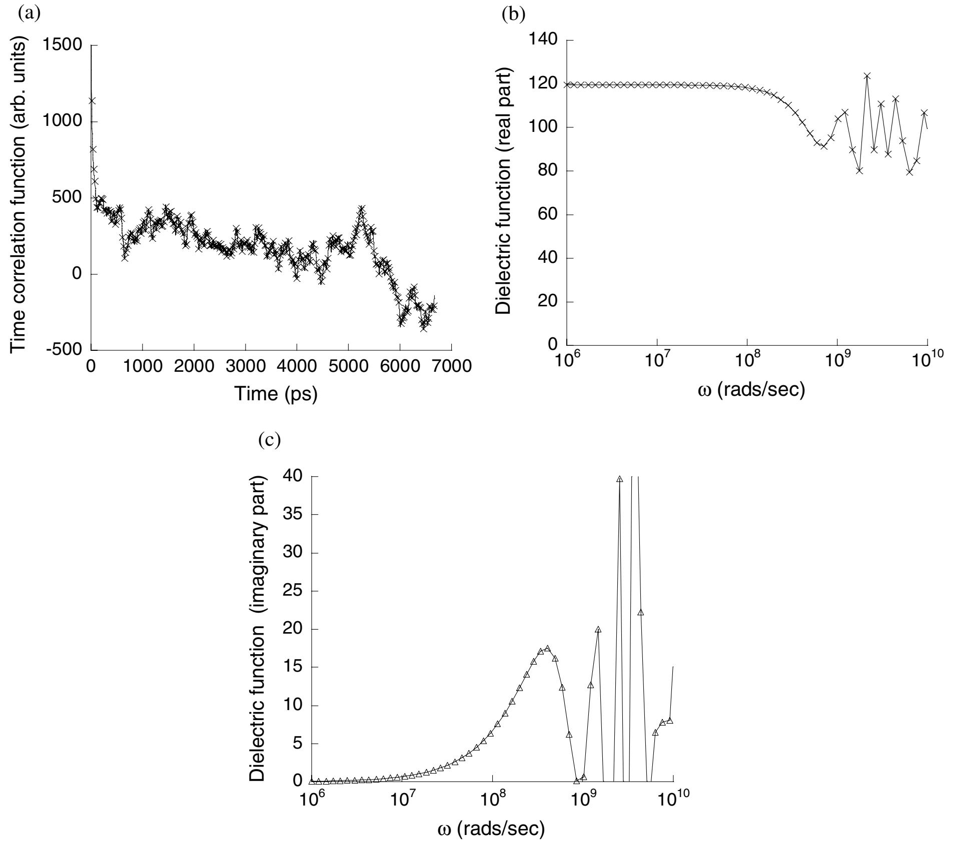

Figure 4. (a) The simulated time-correlation function $\langle M(0)M(t)\rangle$ and (b), (c) the real and imaginary parts of the dielectric function for water molecules only.

The simulation system in this work is not large enough to obtain precise characteristics; however, some agreement with experimental results is obtained.

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