Charge transfer and charge transport on the double helix

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We present a short review of various experiments that measure charge transfer and charge transport in DNA. Some general comments are made on the possible connection between various *'chemistry-style'* charge transfer experiments that probe fluorescence quenching and remote oxidative damage and *'phys-s-style'* measurements that measure transport properties as defined typically in the solid-state. We then describe measurements performed by our group on the millimeter wave response of DNA. By measuring over a wide range of humidity conditions and comparing the response of single strand DNA and double strand DNA, we show that the appreciable AC conductivity of DNA is not due to photon assisted hopping between localized states, but instead due to dissipation from dipole motion in the surrounding water helix.

1 Overview The electrical conductivity of DNA has been a topic of much recent interest and controversy [1]. Measurements from different groups have reached a variety of conclusions about the nature of charge transfer and transport along the double helix. Although there has been a flurry of recent activity, the subject has long history. Eley and Spivey in 1962 [2] were the first to note that the unique structure of DNA with $\pi-\pi$ orbital stacking separated by 3.4 Å resembled high mobility aromatic crystals and suggested it as efficient structure for electron transfer.

Charge transfer is one of the most fundamental chemical processes, driving such disparate reactions as corrosion and photosynthesis. The semi-classical Marcus [3] theory predicts a charge transfer efficiency in large molecules that falls off as $e^{-\beta r}$ with $\beta \approx 1.5$ Å^{-1}. These considerations seemed borne out by two decades of experiments on proteins and other σ-bonded network bridges between photoexcited metal complexes and electron acceptors. Hence, initial experiments [4] probing the π-bond stack of DNA that showed the possibility of longer range charge transfer were surprising. In these first experiments, fluorescent molecules bound to calf thymus DNA were quenched by the addition of electron acceptors to the strands. They suggested a transfer efficiency $e^{-\beta r}$ with $\beta \approx 0.2$ Å. The expectations of Eley and Spivey not-withstanding this was counter to the prevailing paradigm of transfer efficiency $\beta \approx 1.5$ Å from the Marcus theory. Such long range mobile electrons raised the possibility of interesting electronic effects on the double helix. Transfer along this supposed π-way was referred to as wire-like. This work prompted many other experiments to be done, both within the chemistry community and within the solid-state physics community the latter attempting to measure the transport properties of DNA directly. The activity has lead to new theories, such as polaron transport [5] and conformational gating [6], regarding charge transfer and transport in molecular stacks and biological systems.

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Additional experiments showed that the value of β obtained seemed to depend on the details of the strand sequences and donor-acceptor complex used. In the initial experiments Murphy et al. [4] tethered a ruthenium intercalator to end of a single DNA strand and a rhodium intercalator to a complementary stand. When annealed, ruthenium luminescence was completely quenched by the rhodium intercalator positioned almost 40 Å down the π-stack. With the organic intercalator ethidium [7] as the photoexcited donor and rhodium as the acceptor similar quenching behavior was shown over distances of 20 to 30 Å. However other organic donor-acceptor complexes showed $\beta \approx 1$ Å^{-1} [8]. Lewis et al. [9], using stilbene as fluorescence at the end of an A–T chain, systematically moved a G–C pair (functioning as an acceptor) away from the stilbene. They found that quenching rate decreased quickly until about 4 separating A–T's and then more slowly after that.

So-called 'chemistry-at-a-distance' by electron transfer was shown by radical induced strand cleavage. Meggers et al. [10] formed a highly oxidizing radical guanine cation at one end of a DNA strand that had a GGG unit on the other end. The GGG unit is purported to have a lower ionization potential than a single G and hence can accept the hole which neutralizes the radical G. The strand was then treated to cleave at the resulting oxidation site. The length dependence of the electron transfer could be found by varying the number of intervening bridge states and performing electrophoresis to find the number and lengths of cleaved strands. The measurements showed exquisite sensitivity to intervening T–A bases. The efficiency was found to be determined by the longest bottleneck i.e. the longest hopping T–A step.

Strong evidence that the charge transfer was truly happening through base–base hopping via the π–π overlap was given by measurements that probed changes in oxidized guanine damage yield with response to base perturbations [11, 12]. Overall the efficacy of charge transfer through the mismatch was found to correlate with how well bases in the mismatch were stacked. This gave strong evidence that charges are transferred through the π–π stack directly.

These measurements, taken as a whole, gave an emerging picture where a hole has its lowest energy on the G–C sites and for short distances moves from one G–C pair to the next by coherent tunnelling through the A–T sites. The overall motion from the donor to the acceptor site is an incoherent hopping mechanism i.e. the charged carrier is localized on G–C sites along the path. For longer distances between G–C base pairs the picture was that thermal hopping onto A–T bridges becomes the dominant charge-transfer mechanism which gave the weaker distance dependence above four separating A–T pairs of Lewis et al. [9]. Under such circumstances β becomes a poor parametrization of the transfer efficiency as the distance dependence is no longer exponential. Such a picture has been supported from the quantum-mechanical computation models of Burin, Berlin, and Ratner [13].

These 'chemistry-style' experiments give convincing evidence that electron or holes can delocalize over a number of base pairs and that the extent of the delocalization is governed by strand sequence among other aspects. Although such experiments have motivated the direct measure of transport properties via DC and AC techniques, the information gained from luminescence quenching measurements and the like is not directly related to their conductivity i.e. the ability to behave as a molecular wire. Although the descriptor 'wire-like' has been applied to sequences where a small β has been found, such terminology is misleading.

Luminesce quenching is an excited state property. Under appreciated by the solid state community working in this field is the relatively large energy scale (≈ 2 eV) of the typical redox potentials for a luminence quenching reaction (stilbene*/stilbene: 1.75 eV and Rh-complex + 3/Rh-complex + 2: 2 eV). In solid-state physics jargon these are very high energy electron–hole excitations. Perhaps a good solid-state analog of this phenomenon is the luminescence quenching of fluorescent atoms doped into semiconductors, as for instance in Si : Er or ZnSe : Cu [14–16]. In erbium doped silicon a photoexcited electron–hole pair is captured by an impurity level on Er. Decay of this level imparts energy to the 4f Er^{+3} system, which then decays and emits a fluorescent photon. Such a fluorescence can be quenched by detrapping of the captured electron pair on the Er level into the conduction band. In this case, the detrapping is into an orbital which is completely invisible to DC transport. Such an experiment tells us only that there is finite overlap between the localized level and some further extended states. We learn nothing directly applicable to the material's ability to conduct electricity. Likewise

luminescence quenching in DNA can be viewed as the detrapping of a hole into the HOMO orbital, whereupon even weak orbital overlap allows it to make its way to the acceptor under the influence of the driving redox potential. Charge transfer experiments confirm delocalization of hole over a few bases, but we learn little about materials ability to behave as wire. In this regard these charge transfer experiments merely reflect the strong effects of disorder in 1-D i.e. the localization of all states. A small β is not synonymous with 'wire-like' behavior.

Although there is relative agreement among chemists regarding the charge transfer properties of DNA, the physics community has not reached a similar detente with respect to measurements of its direct charge transport properties. DNA has been reported to be metallic [17], semiconducting [18], insulating [19, 20], and even a proximity effect induced superconductor [21]. However, questions have been raised in many papers with regards to length effects, the role played by electrical contacts, and the manner in which electrostatic damage, mechanical deformation by substrate–molecule interaction, and residual salt concentrations and other contaminants may have affected these results. Some recent measurements, where care was taken to both establish a direct chemical bond between λ-DNA and Au electrodes and also control the excess ion concentration, have given compelling evidence that the DC resistivity of the DNA double helix over long length scales ($< 10\,\mu$m) is very high indeed ($\rho > 10^6\,\Omega$ cm) [22]. These results were consistent with earlier work that found flat I–V characteristics and vanishingly small conductances [20], but contrast with other studies that found a substantial DC conductance that was interpreted in terms of small polaron hopping [5]. DC measurements that show DNA to be a good insulator are also in apparent contradiction with recent contactless AC measurements that have shown appreciable conductivity at microwave and far-infrared frequencies [23, 24] the magnitude of which approaches that of a well–doped semiconductor [25].

In previous finite frequency studies, the AC conductivity in DNA was found to be well parameterized as a power-law in ω [23, 24]. Such a dependence can be a general hallmark of AC conductivity in disordered systems with photon assisted hopping between random localized states [26] and led to the reasonable interpretation that intrinsic disorder, counterion fluctuations, and possibly other sources created a small number of electronic states on the base pair sequences in which charge conduction could occur. However, such a scenario would lead to thermally activated hopping conduction between these localized states and is thus inconsistent with a very low DC conductivity [22]. To the end of resolving some of these matters, we have extended our previous AC conductivity experiments in the millimeter wave range to a wide range of humidity conditions. We have shown that the appreciable AC conductivity of DNA in the microwave and far infrared regime should not be viewed as some sort of hopping between localized states and is instead likely due to dissipation in the dipole response of the water molecules in the surrounding hydration layer.

2 Experimental details Double stranded DNA films were obtained by vacuum drying of 7 mM PBS solution containing 20 mg/ml sodium salt DNA extracted from calf thymus and salmon testes (Sigma D1501 and D1626). In order to improve the DNA/salt mass ratio we used a high concentration of DNA, but it was found that the limit was 20 mg/ml. Higher concentrations makes it difficult for DNA fibers to dissolve and the solution becomes too viscous, which prevents producing the flat uniform films which are of paramount importance for the quasi-optical resonant technique. It was found that as long as the excess salt mass fraction is kept between 2–5% the final results were not significantly affected. Single stranded DNA films were prepared from the same original solution as the double stranded ones. The solution was heated to 95 °C for 30 minutes and the quickly cooled to 4 °C. We checked the conformational state of both double-strand DNA (dsDNA) and single-strand DNA (ssDNA) by fluorescent microscope measurements. Films, when dry, were 20 to 30 microns thick and were made on top of 1 mm thick sapphire windows. Immediately after solution deposition onto the sapphire substrates the air inside the viscous solution was expelled by vacuum centrifuging at 500 g, otherwise the evaporation process causes the formation of air bubbles that destroy the film uniformity.

The AC conductivity was measured in the millimeter spectral range. Backward wave oscillators (BWO) in a quasi-optical setup (100 GHz–1 THz) were employed as coherent sources in a transmission configuration. This frequency range, although difficult to access experimentally, is particularly
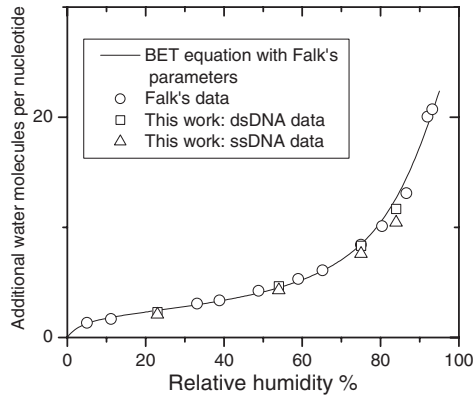
Fig. 1 Adsorbtion of water molecules per nucleotide as a function of humidity. The data represented by the open circles is taken from Falk et al. [28].

relevant as it corresponds to the approximate expected time scale for relaxation processes in room temperature liquids (0.1–10 ps). Importantly, it is also below the energy range where one expects to have appreciable structural excitations. The technique and analysis are well established [27].

3 Results   We measured samples at room temperature at several fixed humidity levels. They were maintained in a hermetically sealed environment with a saturated salt solution [28] that kept moisture levels constant. The mass of the DNA films and changes in thickness were tracked by separate measurements within a controlled environment for each sample in a glove box. The total number of water molecules per nucleotide A can be correlated to the relative humidity x ($x = 0 - 1$) through the so-called Branauer–Emmett–Teller (BET) equation [29]

$$A = \frac{BCx}{(1 - x)(1 - x + Cx)} . \qquad (1)$$

The constant B denotes the maximum number of water molecules in the first layer sites. Mobile water molecules within the double helix can be characterized as 2 types according to the statistical formulation of the BET equation by Hill [30]. The first are those within the initial hydration layer, which are directly attached to DNA and have a characteristic binding energy ϵ_1. Water molecules of the second and all other layers can be approximated as having a binding energy ϵ_L. To a good approximation this ϵ_L can be taken to be that of bulk water. These parameters enter into the BET equation through the expression for C which equals $De\left(\frac{\epsilon_1 - \epsilon_L}{kT}\right)$
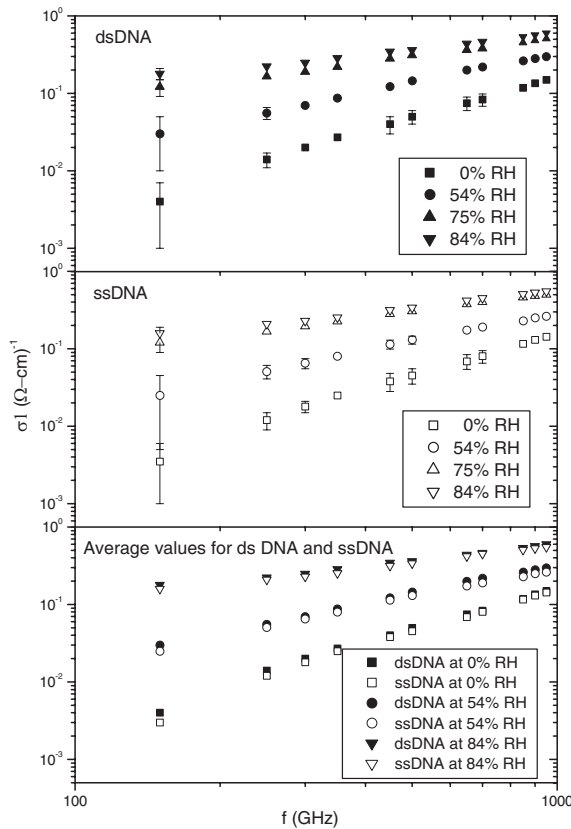
Fig. 2 AC conductivity of calf thymus DNA at different relative humidity levels. a) Double stranded DNA, b) single stranded DNA. c) A comparison of conductivity between single and double stranded DNA.

where D is related to the partition function of water. Also we should note that there is, in actuality, a structural 0-th layer of water molecules, containing 2.5−3 water molecules per nucleotide that cannot be removed from the helix under typical conditions [31].

Falk et al.'s [28] first established that the adsorption of mobile water layers of DNA can be modelled by distinguishing 2 different types of water parameters by use of the BET equation to describe the hydration of sodium and lithium DNA salts. They found good agreement between experimental data and theory with constants $B = 2.2$ and $C = 20$. We performed a similar hydration study of our dsDNA and ssDNA films; as shown in Fig. 1 the hydration of our films is perfectly consistent with the results of Falk. Moreover, we found no appreciable difference in the hydration between dsDNA and ssDNA.

In Fig. 2 data is presented for the extracted $\sigma_1(\omega)$ of both dsDNA and ssDNA thin films. In both cases, the conductivity is an increasing function of frequency. Since the conductivity also increases with humidity, one may wish to try to separate the relative contributions of charge motion along the DNA backbone from that of the surrounding water molecules.

First, one can consider that there should be two main effects of hydration in our dsDNA films. There is the hydration itself, where water molecules are added in layers. Additionally, the conformational state of dsDNA changes as a function of adsorbed water. Although water molecules can certainly contribute to the increase in conductivity, at high humidities there is the possibility that some of the conduction might be due to an increase in electron transfer along the dsDNA helix in the ordered B form. However since such an effect would be much reduced in disordered and denaturalized single strand DNA and since Fig. 2 shows that to within the experimental uncertainty the conductivity of dsDNA and ssDNA in the millimeter wave range is indistinguishable, it is most natural to suggest that water is the major contribution to the AC conductivity. From this comparison of dsDNA and ssDNA, we find no evidence for charge conduction along the DNA between bases.

4 Discussion In Fig. 3 we plot the conductivity σ_1 of the DNA films normalized by the expected volume fraction of water molecules including both the hydration layers plus the structural water. Although this normalization reduces the spread in the thin film conductivity at the lowest frequencies it does not reduce it to zero, showing that if the observed conductivity comes from water, the character of its contribution changes as a function of humidity.

The complex dielectric constant of bulk water has been shown to be well described by a biexponential Debye relaxation model [32−34], where the first relaxation process [32], characterized by a time scale $\tau_D = 8.5$ ps, corresponds to the collective motion of tetrahedral water clusters, and the second from faster single molecular rotations [35] with a time scale $\tau_F = 170$ fs. For bulk water, the contribution of each relaxation process is determined by the static dielectric constant $\epsilon_S(T) \approx 80$, $\epsilon_1 = 5.2$,
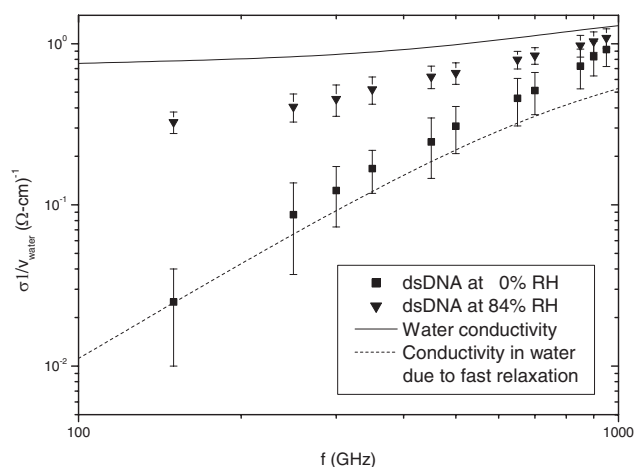

Fig. 3 Conductivity of dsDNA and ssDNA films normalized by the volume fraction of all water molecules (structural plus hydration layer). For clarity, only 0% and 84% humidities are shown. The solid line represents the conductivity of pure water as modelled by the biexponential Debye model using the parameters of Ronne et al. The dashed line shows just the contribution from single water molecule relaxation.

and the dielectric constant at high frequencies $\epsilon_\infty = 3.3$.

$$\widehat{\epsilon}(w) = \epsilon_\infty + \frac{\epsilon_S - \epsilon_1}{1 + i\omega\tau_D} + \frac{\epsilon_1 - \epsilon_\infty}{1 + i\omega\tau_F} \qquad (2)$$

Eq. 2 gives us insight into the conduction and loss processes occurring in the water layers. For high hydration levels, where multiple water layers exist around the dipole helix, the relaxation losses may approach those of bulk water. The above equation can be compared, using the independently known values [32] for τ_D, ϵ_S, τ_F and ϵ_1, to the experimental data normalized to the expected volume fraction of the water. The conductivity of well hydrated DNA is seen to approach that of bulk water.

One expects that the contribution to the loss of cluster relaxation processes to decrease as the number of water layers decreases. As the structural water is not tetrahedrally coordinated, it is reasonable that first term of Eq. 2, which is due to the collective motion of water clusters, cannot contribute at low humidity. Remarkably, the 0% humidity conductivity appears to be described by a model that only includes the fast single molecule rotation of bulk water. This is notable because such behavior is at odds with many systems that find longer average relaxation times in thin adsorbed gas layers than in the corresponding bulk systems [36].

In Fig. 3, along with the experimental data at two representative humidity levels, two theoretical curves for 0% and 100% humidity are plotted. With the only two assumptions being that at 0% humidity, the sole relaxational losses come from singly coordinated water molecules in the structural water layer and that it is only at higher humidity levels where the collective losses can gradually play a greater role, the theoretical curves provide a very good bound to the data over almost all of the measured frequency range.

The only large difference between the experiment and theory is the high frequency data at low humidity, where the model underestimates the conductivity. There are a number of possibilities for these discrepancies. It may be that at higher frequencies for low hydration samples, the weak restoring force from charge-dipole interaction in the structural water layer becomes more significant and our biexponential Debye model is less applicable. Alternatively, it is possible that at very low relative humidities for the ionic phosphate groups on the DNA backbone to form stable dihydrates which may give their own contribution to relaxation losses through their additional degree of freedom [28]. We should also note that one advantage of working in the millimeter spectral range is the known weak contribution of ionic conduction in this regime [37]. The motion of the surrounding relatively large mass counterions only becomes appreciable at lower frequencies [38].

5 Conclusion In conclusion, we have found that the considerable AC conductivity of DNA can be attributed largely to relaxational losses of the surrounding water dipoles. The AC conductivity of ssDNA and dsDNA was found to be identical to within the experimental error. As ssDNA has significantly different base−base orbital overlap than dsDNA, this indicates the absence of charge conduction along the DNA backbone itself. The conclusion that the observed conductivity derives from the water layer is supported by the fact that, over much of the range, it can be well described by a biexponential Debye model, where the only free parameter is the relative contributions of single water molecule and tetrahedral water cluster relaxation modes.

References

[1] C. Dekker and M. Ratner, Physics World **14**, 29 (2001).
[2] D. D. Eley and D. I. Spivey, Trans. Faraday Soc. **58**, 411 (1962).
[3] R. A. Marcus and N. Sutin, BioChim. BioPhys. Acta **811**, 265 (1985).
[4] C. J. Murphy, M. R. Arkin, Y. Jenkins, N. D. Ghatlia, S. H. Bossmann, N. J. Turro, and J. K. Barton, Science **262**, 1025 (1993).

[5] Yoo et al., Phys. Rev. Lett. **87**, 198102 (2002).

[6] R. Bruinsma, G. Grüner, M. R. D Orsogna, and J. Rudnick, Phys. Rev. Lett. **85**, 4393 (2000).

[7] S. O. Kelley and J. K. Barton, Science **273**, 475 (1996).

[8] A. M. Brun and A. Harriman, J. Am. Chem. Soc. **116**, 10383 (1994).

[9] F. D. Lewis, T. Wu, Y. Zhang, R. L. Letsinger, S. R. Greeneld, and M. R.Wasielewski, Science **277**, 673 (1997).

[10] E. Meggers, M. E. Michel-Beyerle, and B. Giese, J. Am. Chem. Soc. **120**, 12950 (1998).

[11] P. K. Bhattacharyaa and J. K. Barton, J. Am. Chem. Soc. **123**, 8649 (2001).

[12] M. A. Rosen, L. Shapiro, and D. J. Patel, Biochemistry **31**, 4015 (1992).

[13] Y. A. Berlin, A. L. Burin, and M. A. Ratner, J. Phys. Chem. A **104**, 443 (2000).

[14] Jung H. Shin et al., App. Phys. Lett. **68**, 997 (1996).

[15] F. Priolo et al., J. App. Phys. **49**, 16313 (1994).

[16] J. F. Suyver et al., App. Phys. Lett. **79**, 4222 (2001).

[17] H. W. Fink and C. Schonenberger, Nature **398**, 407 (1999).

[18] D. Porath et al., Nature **403**, 635 (2000).

[19] E. Braun et al., Nature **391**, 775 (1998).

[20] P. J. de Pablo et al., Phys. Rev. Lett. **85**, 4992 (2000).

[21] A. Y. Kasumov et al., Science **291**, 280 (2001).

[22] Zhang et al., Phys. Rev. Lett. **89**, 198102 (2002).

[23] P. Tran, B. Alavi, and G. Grüner, Phys. Rev. Lett. **85**, 1564 (2000).

[24] E. Helgren et al., cond-mat/0111299.

[25] E. Helgren, N. P. Armitage, and G. Grüner, Phys. Rev. Lett. **89**, 246601 (2002).

[26] A. L. Efros and B. I. Shklovskii, J. Physics C **8**, L49 (1975).

[27] A. Schwartz et al., Rev. Sci. Instrum. **66**, 2943 (1995).

[28] M. Falk, K. Hartman, and R. Lord, J. Am. Chem. Soc. **84**, 3843 (1962).

[29] S. Braunauer, P. Emmett, and E. Teller, J. Am. Chem. Soc. **80**, 309 (1938).

[30] T. L. Hill, J. Chem. Phys. **14**, 263 (1946).

[31] N. Tao and S. Lindsay, Biopolymers **28**, 1019 (1989).

[32] C. Ronne et al., J. Chem. Phys. **107**, 5319 (1997)

[33] J. Kindt and C. Schmuttenmaer, J. Phys. Chem. **100**, 10373 (1996).

[34] J. Barthel and R. Buchner, Pure Appl. Chem. **63**, 1473 (1991).

[35] N. Agmon, J. Phys. Chem. **100**, 1072 (1996).

[36] G. P. Singh et al., Phys. Rev. Lett. **47**, 685 (1981).

[37] J. D. Jackson, Classical Electrodynamics, 2nd ed. (John Wiley and Sons, New York, 1975), p. 291.

[38] Z. Kutnjak et al., Phys. Rev. Lett. **90**, 98101 (2003). Kutnjak et al. have observed an extension of the region of apparent power-law conductivity to frequencies below that of the lower relaxation time. Within our interpretation this is reasonably attributed to counterion motion.