

Polarons in DNA: Transition from Guanine to Adenine Transport

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Experiments on hole transport in DNA have been interpreted as showing that a hole introduced onto a guanine (G) followed by a series of adenines (As) in a DNA duplex travels through the first three As by tunneling and then, with thermal energy, makes the transition onto the bridge of As. It has been widely believed that, once on the bridge, the hole is localized on a single A and proceeds by hopping between As. In the experiments, the holes on the A bridge diffuse, with little attenuation, until trapped by a GGG sequence. Recently, it has been discovered by Bixon and Jortner that the model of tunneling followed by hopping between As cannot account for the very weak dependence on bridge size of the relative chemical yields and the ratios of the rates for the two processes. In earlier calculations, we have shown that interaction with water results in the hole becoming a polaron spread over approximately four As. According to these calculations, the energy of the hole on the polaron is decreased so much that it is lower than that of the hole on G and even that of GGG. Estimates of energy fluctuations, due to fluctuations in the environment and conformational changes of the DNA, find them to be large enough so that GGG, and even G, can still act as hole traps, but trapping on the former is still very much more likely because of its lower energy.

Introduction

A hole introduced onto a guanine (G) in a DNA duplex can tunnel to another G that is separated from it by no more than three adenine/thymine (A/T) pairs.¹ Each A/T the holes traverse causes their number to be attenuated by approximately a factor of 8.¹ If the initial G is followed by more than three A/Ts, then further transport takes place by means of the As.² Because the As have higher energy than Gs, it was suggested that, after tunneling through three A/Ts, a hole hops onto the bridge of As by means of thermal energy.² The A transport differs in entailing relatively little attenuation as the number of As traversed increases.

Different models have been set up to describe the A transport. Berlin et al. suggested that while on the A bridge the holes travel in a tight-binding band.³ They did calculations for a situation in which the series of As following the initial G is interrupted by another G separated by L As from the initial G. For L less than a critical value L_{cr} , the holes tunnel through the L As. For $L > L_{cr}$, the As are assumed to form a tight-binding band of width $4t$, t being the transfer integral, into which the holes are thermally excited. They then move ballistically or by diffusive motion, with the second G and any succeeding isolated Gs acting as traps out of which the holes can be thermally activated. That results in a hopping rate proportional to $\exp(-g_G/kT)$, where g_G is the trap depth, the energy difference between the trap and the band edge. With the parameter values not well-known, Berlin et al. calculated L_{cr} for different values

of the various parameters, including several different values of t . For $t = 0.1$ eV, larger than the value calculated later by various groups,^{4,5} they obtained $L_{cr} = 3$, in agreement with experiment. (For $0.1 < t \leq 0.4$ eV, they obtained $L_{cr} = 4$.) However, with $t = 0.1$ eV and the other parameters chosen, the trap depth g_G was $12kT$, which would make the rate at which holes leave the traps vanishingly small. Also for $t = 0.1$ – 0.4 eV, the width of the tight-binding band is 0.4 – 1.6 eV, distinctly greater than has been found in any of the calculations of DNA band structure.⁶

The problem of hole transport between Gs separated by an AT sequence was also addressed formally within an “adiabatic” model. In this model, it was suggested that the barrier between Gs was overcome due to fluctuations of molecular geometry in the local water environment.⁷

The idea that has been most widely accepted is that in the A transport the hole is localized to a single A and travels by hopping between adjacent As.^{2,8} The transport on As has been referred to as thermally induced hopping (TIH). However, a recent study of the kinetics of the transport processes has shown that the model of superexchange tunneling followed by TIH cannot account for the very weak dependence on bridge size, $(A)_L$, of the relative chemical yields and the ratios of the rates for the two processes.⁹ Discussing this problem, Bixon and Jortner note that the experimental observations could be accounted for if the back-recombination from $(A)_L^+$ to G were switched off.⁹ They suggest that this might be accomplished by fast configurational relaxation accompanying the thermally activated hole injection from G^+ to the $(A)_L$ bridge. Such a gating mechanism, which they suggest, might be due to a drastic reduction of the G–A electronic coupling arising from thermal fluctuations. That suggestion has been explored further by Voityuk et al.¹⁰ They find evidence that the fluctuations facilitate

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hole transfer from G^+ to A, but the effect is much too small to account for the discrepancy noted in ref 9.

Another possible gating mechanism suggested by Bixon and Jortner is hole trapping via proton transfer in the A^+-T Watson-Crick pair.⁹ The latter is not a possibility, however, because the process of a proton in A^+ going over to T has very little driving force.¹¹ Proton transfer between G^+ and cytosine (C) is much more likely,¹¹ but that can only increase the back-transfer rate. In any case, proton transfer between G^+ and C is not expected to have much effect on the back-transfer of holes. Although it has been shown that protonation occurs in DNA,¹² the calculations of Steenken¹¹ and Li et al.¹³ indicate that the stabilization of the hole is a small effect, ~ 0.02 eV or less. The contribution to the energy difference between G^+ and A appears negligible.

We suggest that the difficulty cited above with the TIH model stems from the assumption that the hole wave functions are localized on a single base. A number of theoretical calculations have found the hole wave function to be delocalized over as many as three or four sites (bases), forming a large polaron.^{14,6b} In what follows, we discuss some effects of extended polarons and how their introduction can explain the crossover from tunneling to another transport mechanism, which we identify as drift of large polarons. We show that this polaron formation hinders back-recombination and makes it possible to account for the experimental results of Giese et al.^{1,2} Other examples of hindered recombination involving a sequence of many As have been seen in recent experiments of a group at Osaka; these will be discussed also.

Some Effects of Large Polarons

Evidence for the polaron model comes from the good agreement of the energy differences it predicts between hole traps G and GG, Δ_{G-GG} , and between G and GGG, Δ_{G-GGG} , the Gs in all cases surrounded by As, with the energy differences measured for these cases by Lewis et al.¹⁵ Note that the effect of solvation is expected to more or less cancel out because it is differences that are being measured. Calculations of these energy differences by Voityuk et al.¹⁶ on the assumption that the hole wave functions are localized to a single site gave poor agreement with experiment.^{17,18} For our initial calculations of the energy differences, we used the SSH Hamiltonian, in which the transfer integral t varies linearly with the spacing between neighboring bases about a mean value t_0 .¹⁹ With t_0 taken as 0.2 or 0.3 eV in our original calculations, a value of ~ 0.2 eV for the energy difference Δ_{A-G} between a hole on A and one on G was found to give very good agreement with the experimental results of Lewis et al.¹⁵

Subsequently, we recalculated the energy differences Δ_{G-GG} and Δ_{G-GGG} , incorporating the results of later investigations that found t to be smaller and varying exponentially rather than linearly with departures from uniform spacing of the bases.⁴ Adopting one of the results of ref 4, we replaced the linear variation of t with displacement characteristic of the SSH Hamiltonian by $t = t_0 \exp[-2.0(R - 3.38)]$, where R is the interbase spacing in Å. Again, taking Δ_{A-G} as 0.2 eV, we found that we could fit the experimental results of ref 15 quite well with $t_0 = 0.075$ eV,¹⁸ a value close to what has been obtained in recent calculations. However, using the same parameters in calculations for a sequence with all bases the same, all As, we found the extent of the wave function to be much larger, ~ 15 sites. The smaller extent of the polaron, ~ 4 or 5 sites in refs 18 and 17, respectively, is due to the low energy of the Gs that they contain.

An excess charge on DNA also creates a strong polarization in the surrounding medium, water and ions, this polarization traveling with the charge. Thus, the excess charge is a polaron even if only solvation is taken into account. To determine the properties of this polaron, calculations were carried out for a series of As with surrounding water, but the coupling to the lattice displacements was not included. A Hamiltonian was set up to represent the change in hole energy due to the polarization of the surrounding water and ions.²⁰ The effect of the environment was incorporated by considering the DNA molecule to be placed inside a cylindrical cavity corresponding to the interior of the double helix, with the water and ions outside. The potential was found by solving Laplace's equation with appropriate boundary conditions. The result is a polaron width of approximately four bases, the width and binding energy being insensitive to the transfer integral.²⁰ Inclusion of the coupling of the charge to the lattice displacements did not change the width.²⁰ The contribution to the polaron binding energy from the environment was found to be 0.5 eV, almost 10 times that from the chain distortion.²⁰ Thus, a hole on a sequence of As forms a polaron almost entirely due to solvation.

In one of the definitive experiments of Giese et al.,² a hole was introduced at a G followed by a sequence of L As and a GGG trap. A logarithmic plot of the ratio of the holes reaching GGG to those trapped on G, denoted P_{GGG}/P_G , vs L shows a steep decline up to $L = 3$, clearly attributable to tunneling. For $L > 3$, the steep decline is followed by an almost horizontal line out to the last of the As at $L = 16$.² The latter behavior indicates a transport mechanism that depends weakly on chain length. As noted earlier, that mechanism has been widely considered to be hopping of a localized hole between bases, but it cannot account for the observations.

A stability analysis was carried out for a hole on a chain with a G and a GGG separated by L As.²¹ The questions addressed were whether a hole initially in the G well would end up in the global minimum, the GGG well, and if it did, would it have arrived there by tunneling or propagation on the bridge. With the SSH Hamiltonian and the parameters of ref 17, it was found that for $L \leq 4$ a hole initially in the G trap would tunnel from G to GGG.²¹ For $L > 4$, it was concluded that, having hopped onto the bridge of As, the hole would propagate as a polaron on the bridge until it was captured by the GGG trap.²¹ With the parameters of ref 17, the polaron, as discussed above, occupies approximately five sites. Significantly, free propagation on the bridge occurs when L is greater than or equal to the width of the polaron. The crossover between tunneling and propagation on the bridge occurs at $L = 4$, just below the width of the polaron. For the present case where the polaron is mainly due to solvation, our calculations, as noted above, gave a polaron width close to four As. According to the above considerations, this would correspond to a crossover at $L = 3$, in agreement with what is found experimentally.

With this picture of the polaron, it is possible to account for the change from the initial rapid decrease of P_{GGG}/P_G with L , indicating tunneling, to the very slow decrease after the crossover. Once there are at least four As following the G and the polaron is formed, the energy relations are changed. We suggest that, because of the lowering of the hole energy in the polaron, a G is no longer an effective hole trap. We noted earlier that the binding energy calculated for the polaron due to water is 0.5 eV, i.e., the energy level of the hole in the polaron lies 0.5 eV below the energy level of the hole on a single A on the bridge. For an isolated G in water, the hole energy has been measured as 0.4 eV lower than the hole energy on an isolated

A in water.²² If that were still the case for G and A on a DNA chain, then the energy of a hole on the polaron would be 0.1 eV lower than its energy on G. If the energy difference between a hole on G and one on A in the DNA chain were only 0.2 eV, as suggested by our calculations^{17,18} and by Bixon and Jortner,⁸ then the energy of the hole on the polaron would be 0.3 eV lower than that on G. In either case, a G could no longer compete with the polaron for the hole.

Because a hole on GGG is lower in energy than a hole on G by 0.077 eV,¹⁵ if the energy difference between a hole on G and a hole on A were 0.4 eV, then the energy of a hole on GGG would still be $\sim kT$ higher than its energy on the polaron. If the energy difference were only 0.2 eV, then the energy of the hole on GGG would be ~ 0.2 eV higher than on the polaron. In either case, the size of environmental fluctuations found by Voityuk et al.,¹⁰ with the standard deviations of the G value being approximately 0.3–0.4 eV, is large enough to allow holes to transfer from the polaron to GGG, where they could interact with water and end up as contributions to P_{GGG} . Of course, fluctuations of this magnitude could result in some holes going from the polaron into the G trap. However, the exponential dependence of the probabilities on the ratio of the energy difference to kT makes the probability of the holes ending up in the GGG trap very much larger.

Other Studies of Motion along Adenines

A number of experiments have been carried out by Kawai et al.²³ and Takada et al.²⁴ to study the kinetics of hole motion along a series of As. Typically, the source of the hole was a molecule with an excited state having high enough reduction potential to ionize A. The acceptor molecule was conjugated to a DNA with a series of As following the acceptor. After excitation by a laser flash, the formation and decay of the acceptor excited state were monitored by observing its transient absorption. In one set of experiments, there were four to eight As between the acceptor and a donor molecule. The charge separation was found to occur very rapidly. The number of holes arriving at the donor decreased only slightly as the number of As increased. In another experiment, where the acceptor was separated from a G by six A/T pairs, Takada et al. found that the transient absorption of the acceptor persisted over several hundred microseconds.²⁴ The long-lived charge separation can be attributed to slow charge recombination; its rate decreased exponentially with increasing number of As, indicating that it proceeded by tunneling.²⁴ However, a long-lived separation of charge requires first that many holes be able to avoid rapid back-recombination. Since there were four or more As between the acceptor and donor or trap in these experiments, this avoidance can be attributed to polaron formation on the As, just as in the Giese experiments.

In another set of experiments, Kawai et al. studied propagation of a similarly photoinduced hole through samples with different numbers of As, one to five, following the excited acceptor.²³ If the hole were localized on a single base and transfer took place by diffusive hopping, then the transfer rate k should be related to the number L of hopping steps, equal to the number of As in the sample, by²⁵

$$\ln k \propto -\eta \ln L$$

where η is a parameter whose value lies between 1 and 2. Thus, if the hole motion were simply hopping between adjacent As, then a plot of $\ln k$ versus $\ln L$ should yield a straight line through the values obtained for L from 1 to 5 with a slope between 1 and 2. The data for $\ln k$ versus $\ln L$ obtained by Kawai et al.

(Figure 4b of ref 23) have been fitted to a straight line with a slope of 1.5, which Kawai et al. take as verification that they are observing localized hole hopping between adjacent As for all values of L . However, there is considerable scatter of the data, particularly for the first three points, and no error bars are supplied.

Consider what the plot of $\ln k$ versus $\ln L$ should be if the propagating entity for large L were an all-A polaron. For $L = 1-3$, the plot should be the same as that for localized holes hopping because a polaron would not be formed for such a short sequence. For $L = 4$ and beyond, the plot should differ. When L is large enough so that the polaron wave function does not overlap GGG, after formation the polaron can travel freely on the bridge. In its motion, the polaron wave function shifts, one A at a time, in the direction of motion. An example of such drift is shown in ref 26 for the case where the interaction with the lattice vibrations is what determines the properties of the polaron. In that reference, an electric field is accelerating the polaron, but this is not necessary; it can drift with only thermal energy. Thus, the polaron motion is also a random walk in one dimension, and the change in position in each step is also likely to be a single A. However, the slope of $\ln k$ versus $\ln L$ should be different from that for hopping by localized holes. Although there is not clear evidence for a change in slope at $L = 3$ in ref 23, it is noteworthy that in a later paper by the same group, where there were four to eight As between the acceptor and donor molecules, the log of the charge separation was found to vary linearly with $\ln L$, with a slope of 1.7²⁴ rather than the 1.5 obtained in ref 23 for fewer As. Further experiments on samples with $L = 1-8$ should be undertaken to distinguish between the two models.

Conclusion

In summary, we propose that underlying the transition from G to A transport in the experiments of Giese et al.^{1,2} is the formation of a hole polaron on the bridge of As, $(A)_L$, for $L = 4$, its binding energy provided almost entirely by polarization of the surrounding water. This has the consequences that (1) propagation of holes on the bridge is by motion of this four A polaron rather than TIH of single-site polarons. Motion of this polaron is expected to be a 1D random walk. (2) Back-recombination of the holes is largely avoided for $L \geq 4$ because formation of the polaron lowers the hole energy level to the extent that G is no longer an effective hole trap. Even trapping by GGG may require energy fluctuations that lower the hole energy level on GGG relative to that on the polaron. (3) Crossover between superexchange tunneling and polaron motion takes place at $L = 3$ because the polaron is formed for $L = 4$. Similar statements apply to the situation where the hole originates from an acceptor that can ionize a G or an A (however, in the case where an A is ionized directly tunneling does not take place) and is trapped by a donor at the end of the bridge.

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