

Strong localization of positive charge in DNA from a charge-balance theory

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Microscopic mechanisms of positive charge transfer in DNA remain unclear. A quantum state of electron hole in DNA is determined by the competition of a pi-stacking interaction b smearing the charge between different base pairs and interaction λ with the local environment, which attempts to trap the charge. To determine which interaction dominates, we investigate charge quantum states in various $(GC)_n$ sequences choosing DNA parameters such as to satisfy experimental data for the balance of charge-transfer rates $G^+ \leftrightarrow G_n^+$; $n=2,3$ [Lewis *et al.*, *Nature (London)* **406**, 51 (2000)]. We show that experimental data can be consistent with theory only under an assumption of $b \ll \lambda$, which implies that charge is typically localized within a single G base. Consequently any DNA sequence, including the stack of identical base pairs, behaves more like an insulating material than a molecular conductor.

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Positive charge transfer in DNA is being extensively investigated since its experimental discovery.¹ Charge transfer in DNA can be responsible for the oxidative DNA damage¹⁻⁵ and is possibly important for DNA repair.^{6,7} Also an ability of DNA to promote long distant charge transfer can be used in molecular electronics.⁸ However the microscopic mechanism of charge transfer is not well understood yet. We hope that the present work may shed some light on this challenging problem.

DNA contains two different types of base pairs (AT and GC) forming quasirandom sequences. The lowest ionization potential is attributed to a GC pair (essentially G base⁹). Since the electron transfer integral b between adjacent bases does not exceed $AT-GC$ ionization potential difference $b \leq \Delta \sim 0.5$ eV, the quantum state of charge in a frozen environment will be localized near some G base and its localization length is comparable to the interbase distance.¹⁰ Interaction with fluctuating environment may change the localization, inducing charge hopping between adjacent quantum states localized at spatially separated G sites. According to experimental studies^{4,5} and a theoretical model,^{11,12} the sequence-dependent charge transfer in DNA can be represented as a series of charge hops between adjacent G bases serving as centers of localized states. An addition of AT pair between adjacent GC pairs dramatically reduces the charge hopping rate;^{4,11,12} consequently, the optimum base sequence for efficient charge transfer consists of identical base pairs. In this Brief Report, we study the quantum state of positive charge in different sequences of identical GC base pairs.

The thermal energy at room temperature is very small compared to other characteristic energies so that the system of charge coupled to environment spends most of its time in the ground state. Therefore, the spatial size of the hole state is determined by the competition of charge delocalization via the pi-stacking interaction of heterocyclic groups of adjacent bases and the localization due to environment polarization around the charge. Charge delocalization energy can be characterized by the effective electron transfer integral b and the localization energy is given by the medium reorganization energy $\lambda/2$.¹³⁻¹⁷ Delocalization of charge over k base pairs

leads to the gain in the energy $E_{\text{del}} \sim -2b + b/k^2$, while the reorganization energy scales with the size of charge wave function as $E_{\text{loc}} \sim -\lambda/(2k)$ (see, e.g., in Ref. 13). Optimization of the total energy with respect to the number of sites k provides an estimate of the size of the ground-state wave function $k \sim 2b/\lambda$. While at zero temperature the hole is localized, at finite temperature it can hop to different states because of its interaction with the fluctuating environment. In the translationally invariant system $[(GC)_n$ or $(AT)_n]$, the potential barrier Δ , separating two configurations, can be estimated as the energy price for increasing the size of the wave function by one more site $k \rightarrow k+1$ compared to its optimum size. If $b \ll \lambda$ then Δ is given by one half of the reorganization energy $\Delta \approx \lambda/4 \gg k_B T$, while in the opposite limit Δ can be very small $\Delta \sim \lambda^4/(128b^3)$ and quickly becomes negligible at moderately large b/λ .

It is important to determine actual relationship between b and λ in DNA. Indeed, in the regime $b \gg \lambda$ a DNA molecule made of identical base pairs would behave as a one-dimensional conductor, while in the opposite limit DNA always acts as an insulator. Estimates existing in literature^{9,13-18} do not allow one to resolve the problem because there is a large controversy between different approximations. In particular, various estimates for the electron transfer integral b range from 0.05 (Ref. 16) to 0.5 eV (Ref. 9) and nearly all calculations of b do not take into account the possible effect of vibrational rearrangements.¹⁹ The estimates for the reorganization energy λ using the continuous medium approach range from 0.25 (Ref. 17) to more than 1 eV (Ref. 13), mostly due to the uncertainty in the value of water dielectric constant in the vicinity of the DNA molecule. Therefore based on different approaches, contradictory conclusions were made about the character of charge state. Some theoretical models predict existence of propagating intermediate size polaron,^{9,17,18} while other theories describe quantum state of charge as a small radius polaron essentially localized within a single base.¹⁶

To resolve this problem, we suggest an alternative method of studying the charge quantum state within the DNA molecule using experimental data sensitive to the relationship of two key parameters of the theory b and λ . Namely, we ex-

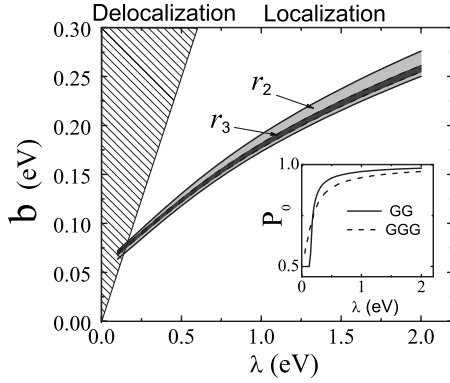
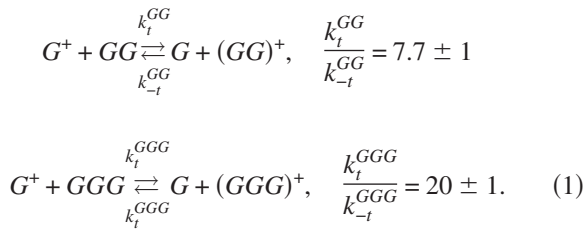


FIG. 1. The domains consistent with the experimental ratios of reaction rates in Eq. (1); dark gray for GGG and light gray for GG . Inset shows the fraction of the quantum charge state belonging to the central site (P_0) vs the reorganization energy λ .

plot the rate constants for the balance of charge-transfer rates between different $(GC)_n$ complexes measured by Lewis *et al.*,²⁰



In the thermal equilibrium, these ratios are directly determined by ratios of base pair partition functions,

$$r_2 = \frac{k_t^{GG}}{k_{-t}^{GG}} = \frac{Z_{2+}Z_1}{Z_2Z_{1+}}, \quad r_3 = \frac{k_t^{GGG}}{k_{-t}^{GGG}} = \frac{Z_{3+}Z_1}{Z_2Z_{3+}}, \quad (2)$$

where Z_{n+} is the partition function of G_n sequence containing a single electron hole, while Z_n is the partition function for the same base sequence without the charge. Since G and G_n complexes are separated by an AT bridge, we can ignore their interactions in calculations of partition functions.

Both ratios in Eq. (1) depend on two parameters b and λ and the thermal energy at room temperature $k_B T \sim 0.026$ eV. Below we calculate both ratios using tight-binding model for G_n complexes and standard linear-response theory for charge interaction with environment.^{14,21} The theory allows one to determine the domain of parameters λ and b satisfying experimental data in Eq. (1). We demonstrate that any choice of λ and b , satisfying Eq. (1), corresponds to the regime $b \ll \lambda$ where the hole in its ground state is localized essentially in a single G base (see Fig. 1).

The chain of n GC base pairs can be described by the tight-binding Hamiltonian coupled to the classical environment represented by coordinates X_i , where $i=1, \dots, n$ (one coordinate for each DNA site),

$$\hat{H} = \hat{H}_0 + \hat{V}_{\text{int}}, \quad \hat{H}_0 = -b \sum_{i=1}^{n-1} (c_i^+ c_{i+1} + c_{i+1}^+ c_i),$$

$$\hat{V}_{\text{int}} = \frac{1}{2\lambda} \sum_{i=1}^n X_i^2 - \sum_{i=1}^n X_i c_i^+ c_i. \quad (3)$$

Here c_i and c_i^+ are operators of creation and annihilation of electron hole in a site i . Classical coordinates X_i describing the polar environment are directly coupled to the local charge density $n_i = c_i^+ c_i$. We neglect the $G-C$ interstrand coupling since it is about one order of magnitude smaller than $G-G$ intrastrand coupling¹⁶ and because of the large difference of $G-C$ ionization potentials.⁹ The solvent energy is expressed as a bilinear form with respect to solvent coordinates.²¹ We assume that only classical degrees of freedom with quantum excitation energy comparable to or less than the thermal energy are retained in Eq. (3), while high-energy modes are integrated out. This may lead to the renormalization of parameters in the system Hamiltonian Eq. (3) as compared to direct quantum chemistry calculations without the effect of vibrational reorganization (see, e.g., in Refs. 19 and 22). Full quantitative description of such renormalization may be a challenging task; however, in this present Brief Report, we use an alternative approach: parameters λ and b are determined using experimental data. We do not include off-diagonal terms $X_i X_j$, where $i \neq j$ in the V_{int} . This is justified because they are smaller than the diagonal ones.¹⁵ It can also be shown that for G_2 sequence, the problem including off-diagonal terms can be reduced to the diagonal model in Eq. (3) with the replacement of the single-site reorganization energy λ by the reorganization energy for charge transfer between adjacent sites. For GGG sequence, a similar replacement removing off-diagonal terms remains a good approximation.²³ Note that the addition of A or T bases, surrounding G_n sequences, leads only to small changes in our results because of the large difference in ionization potential energy of A and G bases compared with the electron transfer integral.²³

We assume the electron transfer integral b to be independent of the environment fluctuations. Fluctuations of the electron transfer integral were treated as less significant compared to fluctuations in local site energies because the change in the site energy by more than the thermal energy strongly modifies the tunneling rate, while the change in the electron transfer integral requires the energy fluctuation comparable to the energy $\delta E \sim \hbar/\tau$, where τ is the tunneling time for the electron transition. This energy δE can be comparable to the barrier height, which is much larger than the thermal energy (see Ref. 23 for more details).

We study the ratios of charge-transfer rates in Eq. (2). Each partition function is given by $Z_n = \int dX_1 \dots dX_n \text{Tr} e^{-\beta H_n}$, where H_n is G_n Hamiltonian in Eq. (3); trace is taken only over the states with the single hole (Z_{n+}) or no hole (Z_n) and $\beta = 1/(k_B T)$. If there is no charge, calculation is reduced to multiple evaluation of a Gaussian integral leading to $Z_n = c^n$, where $c = \sqrt{2\pi\lambda/\beta}$. For the sequences containing a hole, an analytical expression can be obtained only for $n=1$ ($Z_{1+} = ce^{\beta\lambda/2}$). For $n=2, 3$ one can perform analytical integration over a ‘‘center of mass’’ coordinate $X_1 + \dots + X_n$ coupled to the conserving operator of the total number of particles $c_1^+ c_1 + \dots + c_n^+ c_n = 1$. For instance, the expression for $(GG)^+$ partition function reads

$$Z_{2+} = (\sqrt{2}c)e^{\beta\lambda/4} \int_{-\infty}^{+\infty} du e^{-\beta u^2/4\lambda} \cosh\left(\beta\sqrt{\frac{u^2}{4} + b^2}\right). \quad (4)$$

We performed numerical evaluations of ratios in Eq. (2) to find the domains of parameters b and λ satisfying Eq. (1) and show these domains in Fig. 1. The upper and lower boundaries of each domain are determined by maximum and minimum values of the ratios r_2 and r_3 [Eq. (2)] within the experimental error, which are 8.7 and 6.7 for GG and 21 and 19 for GGG correspondingly. The domains for GG and GGG base sequences are completely consistent with each other. The best result for the relation between parameters λ and b is given by the “dark” domain for GGG . This relation is sufficient to consider the localization of the hole wave function in G_n aggregates.

Since the thermal energy $k_B T \approx 0.026$ eV is smaller than other characteristic energies of the system [remember that the minimum estimate for the reorganization energy is $\lambda \sim 0.25$ eV (Ref. 17)], we can characterize the wave function using the system ground state at coordinates X_i minimizing the ground-state energy. In the relevant domain of parameters in Fig. 1 ($\lambda > 0.25$), the ground-state wave function has a maximum at one of G bases (left or right ones for the GG sequence and the central one for a GGG sequence). We characterize localization by the quantum probability P_0 for the particle to be located on one site. One can show that $P_0 = X_i/\lambda$, where i is the localization site.²³

For the GG sequence the expression for the hole ground-state energy at arbitrary coordinates X_1 ; X_2 reads $E_2 = \frac{X_1^2 + X_2^2}{2\lambda} - \frac{X_1 + X_2}{2} - \sqrt{\frac{(X_1 - X_2)^2}{4} + b^2}$. In the regime of interest $2b < \lambda$ (see Fig. 1), the minimum of energy is given by

$$E_{2\min} = -\lambda/2 - b^2/\lambda, \quad (5)$$

and it is realized at $X_1 = \lambda/2 \pm \sqrt{(\lambda/2)^2 - b^2} = \lambda - X_2$. Accordingly $P_0 = \frac{X_1}{\lambda} = \frac{\lambda + \sqrt{\lambda^2 - 4b^2}}{2\lambda}$. Note that if $2\lambda < b$, the ground-state wave function is symmetric in the minimum $X_1 = X_2 = \lambda/2$ and the energy of this state is given by

$$E_{2\text{symm}} = -\lambda/4 - b. \quad (6)$$

In the case of $2b < \lambda$, this symmetric state is the transition state [saddle point in the energy function $E_2(X_1, X_2)$] between the energy minima centered in the first and the second G 's.

For the GGG complex the probability of residing in the central site was evaluated numerically. Both probabilities P_0 , calculated for the ratio $r_2 = 7.7$ [Eq. (2)], are shown in the inset in Fig. 1. It is clear that for both GG and GGG sequences the hole is essentially localized on a single G site. At the minimum value of $\lambda \sim 0.25$ eV, we have 85% and 78% for the probabilities to find the particle in that site for GG and GGG sequences, respectively. As the reorganization energy increases to 1 eV, these probabilities increase to 96% and 94%, respectively. Thus we arrive at the important conclusion that wave functions of a hole are essentially localized in the single G site for G_n sequences. This conclusion differs from predictions in Refs. 7, 17, and 18 where the polaron of an intermediate range arise in description of the quantum state of the hole.

A remarkable consistency between GG and GGG data in Fig. 1 is not accidental and it can be explained by the strong localization of charge wave functions. In the regime of strong localization the partition function Z_{n+} for $n \geq 2$ consists of n contributions from n energy minima, corresponding to charge wave function centered consecutively on n G sites with coordinates X realizing the corresponding energy minimum $X_i \approx \lambda \gg X_k$; $k \neq i$ for the state centered at site i . Since in the zero-order approximation in b/λ (each quantum state is localized at one site), one can neglect the difference in pre-exponential factors for the case of $b=0$ and approximate the partial i th contribution to the partition function as $Z_n^i = c^n e^{-\beta E_i}$, where E_i is the energy of the ground state for coordinates X realizing the local minimum. First-order correction to $E_i^{(0)} = -\lambda/2$ is important because it is multiplied by the large factor β . For two states at the edges of G_n sequences this correction is $E_1 = E_n \approx -\lambda/2 - b^2/\lambda$ [Eq. (5)]. This is not surprising because contributions of non-neighboring sites are negligible due to the strong localization of charge. For $n-2$ remaining states, the correction to the energy is doubled because contributions from two neighbors add up so that $E_i^{(1)} = -\lambda/2 - 2b^2/\lambda$; $1 < i < n$. Consequently, we can approximate the ratio r_n [cf. Eq. (2)] as

$$r_n = Z_{n+} Z_1 / (Z_n Z_{1+}) \approx 2e^{\beta b^2/\lambda} + (n-2)e^{2\beta b^2/\lambda}. \quad (7)$$

Particularly, one has $[Z_{3+} Z_1 / (Z_3 Z_{1+}) \approx [Z_{2+} Z_1 / (Z_2 Z_{1+}) + \{[Z_{2+} Z_1 / (2Z_2 Z_{1+})]^2\}]$, which is satisfied for the observed ratios within the accuracy of the experiment. This explains the consistency of domains for GG and GGG (Fig. 1). One can also predict that ratios r_n form arithmetic series. Particularly for the balance between G and G_4 sequence, we predict the ratio $r_4 = 2r_3 - r_2 = 32.3$. This estimate agrees with our numerical calculations for the G_4^+ partition function.

In summary, we considered the quantum state of the positive charge (hole) in poly- G -poly- C base sequence. It appears that the agreement with the experimental data for the ratios r_n [Eq. (2)] for $n=2,3$ can be achieved only under an assumption of strong localization of charge within almost a single G base. The charge in DNA then behaves as a small polaron with the size less than the interbase distance. Based on our theory, we predict that ratios of charge transfer form the arithmetic series $r_n = 7.7 + 12.3(n-2)$. However, we are not able to identify more accurately the electron transfer integral b and the reorganization energy λ using experimental data only for the ratios of charge transfer.

We can suggest finding these parameters by measuring the temperature dependence of the charge-transfer rate through poly- G -poly- C base sequence. We expect that this temperature dependence will be described by the Arrhenius law with the activation energy determined by the difference between the energy of transitional state of $(GG)^+$ base pair [Eq. (6)] and the energy of the ground state of $(GG)^+$ [Eq. (5)] $E_A = \lambda/4 - b + b^2/\lambda$, corresponding to adiabatic regime (for example, see Refs. 23 and 24). Since complimentary relationship between b and λ is determined by the phase diagram in Fig. 1, this information will be sufficient to find both parameters.

We believe that the strong localization of charge is because the DNA under consideration is in its native environ-

ment (highly polar solvent, i. e., water) trapping the charge. For dry DNA (Ref. 8), its structure and ionization potentials are subjects to major changes.²⁵ The consideration of dry DNA is beyond the scope of this Brief Report.

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