Stepwise oscillatory circuits of a DNA molecule

Kunming Xu

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Abstract A DNA molecule is characterized by a stepwise oscillatory circuit where every base pair is a capacitor, every phosphate bridge is an inductance, and every deoxyribose is a charge router. The circuitry accounts for DNA conductivity through both short and long distances in good agreement with experimental evidence that has led to the identification of the so-called super-exchange and multiple-step hopping mechanisms. However, in contrast to the haphazard hopping and super-exchanging events, the circuitry is a well-defined charge transport mechanism reflecting the great reliability of the genetic substance in delivering electrons. Stepwise oscillatory charge transport through a nucleotide sequence that directly modulates the oscillation frequency may have significant biological implications.

Keywords DNA • Conductivity • Oscillatory circuit • Electric capacitor

1 Introduction

Long after the chemical structure of DNA has been elucidated, the electrical property of the double helix remains a puzzle. Previous studies by direct measurements of electric current in DNA fibers have produced various conclusions from no conductivity [1, 2], semi-conductivity [3], good conductivity [4], to superconductivity of a DNA molecule [5]. By appending a photo-oxidant to one end of a DNA duplex and measuring the oxidative damage of a guanine doublet site at various distances, recent biochemical studies of DNA charge transfer have provided more convincing results. It has been established that very fast charge transport can take place over a short distance (~ 37 Å), and a slower transport may propagate over a long distance (~ 200 Å) [6–14]. The results have led to two hypotheses of charge transport mechanisms in DNA, one indicating super-exchange, or tunneling,

K. Xu (✉)

State Key Laboratory of Marine Environmental Science, Environmental Science Research Center,
Xiamen University, Xiamen 361005, China
e-mail: kunmingx@xmu.edu.cn

through the sugar phosphate bridge between the bound charge donor and acceptor for the short distance and the other suggesting charge hopping between discrete bases through the DNA π -stack over long distances. Although both mechanisms are widely regarded, they are incompatible and rather ill-defined, giving the impression of loose or uncertain charge transfer along a DNA molecule. As genetic substance, DNA must possess well-defined electrical behavior. In this paper, we show a DNA double helix as a stepwise LC oscillatory circuit, in line with the experimental evidence. We demonstrate that a DNA molecule maintains an electron transport mechanism through both strands that matches the fidelity and reliability of its chemical structure.

2 DNA circuit model

The circuit model regards each base pair as an electric capacitor because it is composed of two heterocyclic amines placed at a semi-conductive distance, capable of storing opposite charges. The hydrogen bonds between the base pairs deliver electric pulses but prohibit direct current between them, which is a typical characteristic of electric capacitors. In the double helix, the phosphate bridges are twisted physically like both strands of a rope under torsion. The wound phosphate bridge can be treated as an electric inductance, capable of storing energy as well. The rigid structures of the Watson–Crick pairs and of the pentose sugars help in forcing the torsion onto the phosphate bridges mechanically. Charge transport through the strands, like electric current through a coiled wire, constitutes a typical characteristic of electric inductances. Hence, DNA structure can be modeled as a circuit composed of multiple oscillatory LC circuits (Fig. 1).

The deoxyribose is a key electric element in the circuit, which serves as a switch at the juncture (Fig. 2). It has been stated that a chiral carbon center may transfer electrons toward a selective pathway due to its asymmetric polarizations [15]. Three chiral carbons in a deoxyribose direct electric charges in a selective course. Specifically, as electrons enter $C4'$ from $C5'$, they will be routed through the ether bond by the chirality of $C4'$ because an oxygen atom is more electronegative than carbon in drawing the electron, and thereafter, the electrons must build up to a threshold potential to escape oxygen attraction. In this way, the ether bond delivers electric pulses through itself. When the electrons arrive at $C1'$, they will be directed to the N -glycosyl linkage, which is more electronegative than carbon, hence

Fig. 1 DNA double strands (a) along with stepwise oscillatory circuits (b, c), where the *dashed arrows* indicate electric current directions and the deoxyriboses are represented by electric switches

Fig. 2 Chemical structure of a deoxyribose (a) and its electric switch property (b) where *dashed arrows* indicate electric current directions. Positive holes at the nucleotide base are routed to C5' (c) while electrons at the nucleotide base are routed to C3' (d)

charging the nitrogenous base; after electrons overflow out of the base toward C1', they will be transferred via C2' to C3', which in turn directs the electrons toward the oxygen atom connecting the phosphate and then through the phosphate bridge. Direct charge flow between C3' and C4' is choked by both chiral carbons. Positive holes are transported in the reverse direction as indicated by the dashed arrows. Thus, the role of a deoxyribose is an electric switch. Depending on whether the nucleotide base is positively charged or negatively charged, the switch connects C1' to C5' or otherwise connects C1' to C3', respectively. The anti-parallel alignment of the pentose sugars on both strands determines that electric current forms a stepwise closed loop between every two adjacent base pairs.

Suppose in the closed circuit (Fig. 1b) charges stored in capacitor C_1 are transported through the phosphate inductances L_1 and L_2 to reach capacitor C_2 under the routing of the deoxyriboses. The anti-parallel alignment of the pentose sugars on both strands determines that positive charges transfer along the strand in the direction of $3' \rightarrow 5'$, while negative charges transfer along the strand in the direction of $5' \rightarrow 3'$. Electric current forms a closed circuit so that by Kirchhoff's loop rule, we have a voltage drop relationship of

$$\frac{Q_1}{C_1} = IR_1 + L_1 \frac{dI}{dt} + \frac{Q_2}{C_2} + IR_2 + L_2 \frac{dI}{dt}, \quad (1)$$

where I is electric current around the circuit unit, Q_1 and Q_2 are charges stored in base pair capacitances C_1 and C_2 , respectively, and R_1 and R_2 are representative resistors along the path. Let

$$R_1 + R_2 = R, \quad (2)$$

$$L_1 + L_2 = L, \quad (3)$$

$$\frac{1}{C_1} + \frac{1}{C_2} = \frac{1}{C}, \quad (4)$$

$$Q_1 + Q_2 = Q_0, \quad (5)$$

then upon differentiation on both sides, Eq. 1 becomes

$$L \frac{d^2 I}{dt^2} + R \frac{dI}{dt} + \frac{I}{C} = 0. \quad (6)$$

This second-order differential equation is a damped harmonic oscillator. Depending on the relative values of L , R , and C , the system may be over-damped, critically damped, under-damped, or simple harmonic. When $R^2 < 4L/C$, the circuit property falls into the two latter categories with a current function of

$$I = I_0 e^{-\frac{R}{2L}t} \cos(\omega t), \quad (7)$$

where I_0 is the initial current and ω is the angular velocity of the oscillation with a value of

$$\omega = \sqrt{\frac{1}{LC} - \frac{R^2}{4L^2}}. \quad (8)$$

The circuit system transfers electric charges from a base pair to another in stepwise oscillatory processes, i.e., from capacitor C_1 to C_2 (Fig. 1b) and then from capacitor C_2 to C_3 (Fig. 1c) along the double helix. Simple as it is, this model is in line with experimental evidence [6–13] so far established concerning DNA conductivity and reconciles both super-exchange and multi-step hopping mechanisms.

3 Model discussion and predictions

It has been reported that the rate of electron transfer over a short distance decreases exponentially with increasing distance [7–10]. Such a phenomenon corresponds to the under-damped condition of the circuit system due to the relatively low ($R^2 < 4L/C$) resistance response of DNA backbones to the artificial introduction of voltage drops between base pairs in the experiments. However, when R is considerable, the exponential signal of electric current prevails over the sinusoidal cycle in Eq. 7 and vanishes within a few oscillatory cycles. Since the distance between the base pairs of B-DNA is a fixed value of 3.4 Å and each stepwise oscillatory cycle transports a certain amount of charges for that distance, we may replace the time variable in Eq. 7 with a distance variable Δr . Considering that electric current is a measure of electron transfer rate k , Eq. 7 is equivalent to the Marcus correlation [16, 17]

$$k \propto e^{-\beta \Delta r} \quad (9)$$

where β values between 0.1 and 1.4 Å⁻¹ have been estimated for the double helix [7–10]. The dramatic difference can be ascribed to the uncertainty of measuring the resistance R , which is sensitive to various experimental conditions. The presence of considerable R value along the circuit is because the phosphate bridges are under persistent high voltage drop induced artificially in experiments so that inductances partially manifest as resistances in the circuit. Based on frequency value of 10⁻¹⁰ s⁻¹ measured by Fukui et al. [7], we simulate the under-damped oscillation with parameters of $C = 0.02$ pF, $L = 0.01$ μH, and $R = 100\Omega$ in Eq. 8. Assuming three radical cations are initially generated to trigger charge migration from a base pair to another through the stepwise oscillatory cycles, the current function of Eq. 7 is calculated to be

$$I = 5.2e^{-0.005t} \cos(0.068t), \quad (10)$$

where electric current is in units of nanoamperes, and time is in units of picoseconds (Fig. 3). Supposing, at $t = 0$, capacitor C_1 carries charges in the polarity as shown in Fig. 1b, the deoxyribose switches (S_1 to S_4) will route the charges in the dashed arrow direction. After

Fig. 3 Model predictions for charge transfer of DNA circuit by fast stepwise under-damped oscillations in vitro (*black curve*) in contrast to slower stepwise simple harmonic oscillations in vivo (*gray curve*) where each cycle spans $3.4 \text{ \AA}$ in distance

one oscillatory cycle at $t = 92 \text{ ps}$, the charges reach capacitor C_2 so that switches S_3 and S_4 change their connections. The charges at capacitor C_2 will then be transferred to capacitor C_3 in the next step (Fig. 1c). The amplitude of the electric current along the double helix decreases exponentially with each oscillatory cycle in the under-damped situation (Fig. 3). Because each oscillatory cycle takes 92 ps for charges to migrate $3.4 \text{ \AA}$ along DNA strands, the β value in Eq. 9 is $0.14 \text{ \AA}^{-1}$ in this case.

In vivo, we believe that natural electron transport from a base pair to another should incur trivial electric resistance. Even if there exists certain electric resistance along the strands, the thermal energy produced by resistors would immediately be absorbed by both energy storage components of the base pair capacitor and the phosphate inductance. Hence, electric resistance can be neglected. Letting $C = 0.02 \text{ pF}$, $L = 0.05 \text{ \mu H}$, and $R = 5 \text{ \Omega}$, the circuit declines into a series of LC oscillators that transfer charges step by step along the strands harmonically at a slower pace. The frequency of the harmonic oscillation is slower than that of the under-damped oscillation as can be predicted from the ω formula under the relatively high value of inductance and trivial resistance. It takes about 200 ps for electrons to transfer from a base pair to the next. However, the amplitude of the electric current remains almost the same in each oscillatory cycle. A comparison of under-damped oscillation and simple harmonic oscillation can be found in Fig. 3.

In the stepwise LC circuits, electric current is defined as positive when a base pair capacitor is being charged and negative when discharged in the next cycle down the chain. The stepwise oscillations agree with the evidence that has supported a hopping mechanism through the base π -stack [6–14], but electric current through the sugar phosphate bridges is more reliable than the haphazard migration by hopping across the base rungs. Charges stored in capacitor C_1 are transported through both strands to capacitor C_2 and will continue to move toward C_3 in a similar sinusoidal manner but at a lagging phase of π in the cycle. During these processes, positive holes move in the $3' \rightarrow 5'$ direction on one strand while electrons flow in the $5' \rightarrow 3'$ direction on the other strand in good synchronization. The mechanisms for charge transport through long and short distances are the same. It takes more oscillation cycles for charges to be transported through longer sequences of base pairs. Without considering the effect of sequence dependence, traveling time is proportional to distance.

The stepwise oscillatory LC circuits show that a DNA fiber can be considered as a special case of an AC conductor. Oscillatory frequencies in the range 10^7 to 10^{11} s^{-1} have been reported [18–20]. Single strands have been observed to be less conductive than double

strands [2], which agrees with the circuit model prediction because only double strands constitute closed circuits in each grid, allowing for proper conduction. It has been pointed out that the intensity of the torsion may influence the charge transport through the double helix [7, 21]. However, we may attribute this effect to inductance change in the circuit rather than the variation of π -stack overlap for hopping.

We shall go one step further to discuss the biological implication of the circuitry. From Eq. 8, we know that ω is codetermined by inductance L and capacitance C when R is negligible. Assuming constant inductance for all nucleotides, the harmonic frequency would be determined by two neighboring capacitance values in the closed circuit, such as C_1 and C_2 , which are specific to the base pairs. This is perhaps the most subtle part of the story, for it indicates that charge transfer rate is sequence dependent [8–10, 22]. Because nucleotide bases have ionization potentials in the order of $G < A < C < T$ and electron affinities in the order of $C < T < G < A$ (disregarding negative sign) [23], it takes the least amount of energy to charge a G/C base pair in the polarity of $+G/C-$ and requires the highest amount of energy to charge a $+T/A-$ capacitor. This means that the capacitances of the base pairs are in the order of $+G/C- > +A/T- > +C/G- > +T/A-$ polarities. Thus, there are four distinct capacitance values depending on the base pair and polarity. Since ω is determined by two neighboring capacitances in series, it may take eight possible values. It is predicted that charge transport along the strands will produce various frequencies, reflecting the identity of the bases. In other words, the pattern of charge transport is precisely controlled by the gene sequence. The $+G/C-$ capacitor has a higher capacitance than the other base pairs and carries a higher amount of charges in experiments, whereas $+T/A-$ has a lower capacitance than the other base pairs and is the limiting step or bottleneck in charge transfer along the DNA strands [11, 17]. However, at long $(+T/A-)_n$ sequences, the size of the bottleneck remains the same, so that the sequence distance dependence vanishes [17]. Because $+G/C-$ has a relatively high capacitance, it is easy to trap charges, so it is likely to become the end point of a charge transport [11, 17]. In this regard, the circuit model prediction agrees with experimental results completely.

Oscillatory current through the double helix is likely to have physiological significance. For example, if a base pair is mismatched at a certain position, then the oscillatory rhythms would be broken. Proofreading enzymes that scan the DNA sequence continually might easily locate the trouble point by the abnormal electric signal [24]. Furthermore, biomolecules are inherently unstable. Only a constant flow of energy prevents them from being disorganized. It stands to reason that the incessant charge vibrations in the genetic substance are vital for living organisms to maintain the integrity of the gene sequence.

From an organic chemistry perspective, the base pair is capable of storing a considerable amount of charges in either polarity by at least two conceivable mechanisms. First, both pyrimidine and purine are heterocyclic rings composed of carbon and nitrogen atoms. On the one hand, nitrogen is more electronegative than carbon for attracting a higher electron density in covalent bonds with carbon. On the other hand, the nitrogen atom has lone pair electrons to share with carbon under electron deficiency. The combination imparts great flexibility to the nucleotide bases for either holding or releasing electrons. Second, the heterocyclic rings are aromatic, and possess diamagnetic ring current. In the circuit, aromatic ring current may reduce the charge saturation of the nitrogenous base in the same way that wind induces low pressure in the air and, as a result, increase the electric capacitance of the base pair. Both properties enable a base pair to be a good bipolar capacitor. The recognition of a base pair as a valid capacitor provides a clear insight into the electrical properties of DNA.

To summarize, the electron transport mechanism in DNA is of paramount importance to understanding the biological function of the genetic substance. Based on the identification of chemical structures as electric elements, we describe an electron transport mechanism in DNA by a reliable and well-structured oscillatory circuit that distinguishes a DNA molecule from messy condensed matter. This alternative view is supported by the established experimental evidence for super-exchange and hopping mechanisms. The *LC* oscillatory circuit is robust and classical in physics, yet quite revolutionary in chemistry and biology. This interdisciplinary analysis produces a result of general interest in biological physics and may have potential influence in molecular electronics.

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