Characteristic Length Scale of Electric Transport Properties of Genomes

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A tight-binding model together with a novel statistical method are used to investigate the relation between the sequence-dependent electric transport properties and the sequences of protein-coding regions of complete genomes. A correlation parameter $\Omega$ is defined to analyze the relation. For some particular propagation length $w_{\text{max}}$, the transport behaviors of the coding and non-coding sequences are very different and the correlation reaches its maximal value $\Omega_{\text{max}}$. $w_{\text{max}}$ and $\Omega_{\text{max}}$ are characteristic values for each species. The possible reason of the difference between the features of transport properties in the coding and non-coding regions is the mechanism of DNA damage repair processes together with the natural selection.

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The conductance of DNA molecules is one of the central problems of biophysics because it plays a critical role in the biological systems. For example, it is postulated that there may be proteins which can locate the DNA damage by detecting the long-range electron migration properties\textsuperscript{1, 2}. And for the interest of applications, DNA is one of the most promising candidates which may serve as the building block of molecular electronics because of its sequence-dependent and self-assembly properties.

There have been many experimental results on the conductance of DNA from different measurements for the last few years. Yet the results are still highly controversial\textsuperscript{3}. The experimental results almost cover all possibilities, ranged from insulating\textsuperscript{4}, semiconducting\textsuperscript{5}, Ohmic\textsuperscript{6, 7}, and even induced superconductivity\textsuperscript{8}. The diversity comes from the methods of the measurements and the preparation of DNA samples. One of the critical factors influencing the results is the contact of the DNA and electrodes\textsuperscript{4, 9, 10, 11}. The different nucleotide sequences of the DNA molecules used in the experiments also diversify the results because the transport properties are sequence-dependent.

Aside from the electrical properties, the statistical features of the symbolic sequences of DNA have also been studied intensely during the past years\textsuperscript{12, 13, 14, 15, 16, 17}. The previous works are mainly focused on the correlations and linguistic properties of the symbols A, T, C, and G, which represent the four kinds of bases adenine, thymine, cytosine, and guanine of the nucleotides, respectively. The analyses also give some eccentric results. For example, the statistical behavior of the intron-free coding sequences is similar to random sequences while the intron-rich or junk sequences have long-range correlations. One should note that the root of these statistical properties of the symbolic sequences are the results of evolution, and the underlying driving forces are the principles of physics and chemistry. On the other direction, the correlation of sequences will influence the physical and chemical properties, such as the electric and mechanical properties of DNA\textsuperscript{18}. Thus it is reasonable to conjecture that the sequence-dependent electric properties can play critical roles during the evolution process in nature by some ways such as the DNA damage repair processes\textsuperscript{12, 14}. In this Letter, the relation between electric transport properties and the gene-coding/non-coding parts of genomic sequences will be discussed.

The simplest effective tight-binding Hamiltonian for a hole propagating in the DNA chain can be written as\textsuperscript{19, 20}

$$H = \sum_n \epsilon_n c_n^\dagger c_n + \sum_n t_{n,n+1} (c_n^\dagger c_{n+1} + H.C.)$$ (1)

where each lattice point represents a nucleotide base of the chain. $c_n^\dagger$ ($c_n$) is the creation (destruction) operator of a hole at the $n-$th site. $\epsilon_n$ is the potential energy at the $n-$th site, which is determined by the ionization potential of the corresponding nucleotide. $\epsilon_n$ equals to 8.24 eV, 9.14 eV, 8.87 eV, and 7.75 eV for $n = A$, $T$, $C$, and $G$, respectively\textsuperscript{21}. The DNA molecule is assumed to be connected between two semi-infinite electrodes with energy $\epsilon_m = \epsilon_G = 7.75$ eV. The hopping integral $t_{n,n+1} = t_m = 1$ eV for electrodes and $t_{n,n+1} = t_{\text{DNA}}$ for nucleotides. $t_{\text{DNA}}$ is assumed to be nucleotide-independent here for simplicity. Typical value of $t_{\text{DNA}} = 0.1 \sim 0.4$ eV from the first-principle calculation\textsuperscript{21, 22}. To reduce the back scattering effect at the contacts, larger $t_{\text{DNA}}$ (up to 1 eV) is also used in this study\textsuperscript{19}. Note that $n \in (-\infty, 1]$ and $n \in [N+1, \infty)$ are for electrodes and $n \in [2, N]$ are for nucleotides.

The eigenstates of the Hamiltonian $|\Psi\rangle = \sum_n a_n |n\rangle$ ($|n\rangle$ represents the state that the hole is located in the $n-$th site) can be solved exactly by using the transfer matrix method:

$$\begin{pmatrix} a_{N+2} \\ a_{N+1} \end{pmatrix} = M_{N+1} M_N \cdots M_1 \begin{pmatrix} a_1 \\ a_0 \end{pmatrix} \equiv P(N) \begin{pmatrix} a_1 \\ a_0 \end{pmatrix}$$ (2)
where
\[ M_n = \left( \begin{array}{cc}
\frac{E - \epsilon_n}{\epsilon_{n+1} - \epsilon_n} & -\frac{\epsilon_n - \epsilon_{n-1}}{\epsilon_{n+1} - \epsilon_n} \\
1 & 0
\end{array} \right) \tag{3}\]

\( E \) is the energy of the injected hole. In electrodes, the

\[ T(E) = \frac{4 - (E - \epsilon_n)^2}{\sum_{i,j=1,2} P_{ij}^2 + 2 - (E - \epsilon_n)^2 P_{11} P_{22} + (E - \epsilon_n)(P_{11} - P_{22})(P_{12} - P_{21})} \tag{4}\]

The transmission of several sequences of complete genomes \( S = (s_1, s_2, \ldots, s_{N_{tot}}) \) is studied (\( s_i = A, T, C, \text{ or } G \)). Since the total length \( N_{tot} \) of the complete genome is usually much longer than the distance which holes can migrate along the DNA chain even for the smallest \( N_{tot} \) for viruses, we won’t measure the transmission through the whole chain but only shorter segments instead. A “window” with width \( w \) is defined to extract a segment \( S_{i,w} = (s_i, s_{i+1}, \ldots, s_{i+w-1}) \) for \( 1 \leq i \leq N_w = N_{tot} - w + 1 \) from \( S \). Starting from \( i = 1 \) and sliding the window, we can get the “transmission sequence” \( T_w(E, i) \) of \( S_{i,w} \) for all \( i \), which depends on the energy of the injected hole \( E \), the starting position of the segment \( i \), and the propagation length \( w \). For further analysis of the whole genome sequences, \( T_w(E, i) \) is integrated in an energy interval \([E, E + \Delta E] \):

\[ \overline{T}_w(E, \Delta E, i) = \int_{E}^{E+\Delta E} T_w(E', i) dE' \tag{5} \]

In the remaining of the Letter, the transmission is integrated for the whole bandwidth, that is, \( E = 5.75 \text{ eV} \) and \( \Delta E = 4 \text{ eV} \). And these two values will be omitted in the related formulas for short. 300 base pairs at the two ends of the DNA chain will be omitted in the following analysis because the telomere sequences at the terminals usually have larger transmission (due to the periodicity) and will dominate some of the average properties. Thus \( N_w = N_{tot} - w + 1 - 2 \times 300 \).

The averaged transmission \( T_w^{\text{ave}} = \frac{1}{N_{tot}} \sum_i \overline{T}_w(i) \) versus propagation length \( w \) is plotted in Fig. 1 for the third chromosome of Saccharomyces cerevisiae (bakery yeast, accession number = NC.001135 for GenBank [24], simplified as Y3 for short) with several values of \( t_{DNA}/t_0 \). \( T_w^{\text{ave}} \) decreases exponentially with increasing \( w \), which is consistent with the localization picture. The curves can be fitted by the function \( T_w^{\text{ave}} = a e^{-w/w_0} \). The inset of Fig. 1 shows the averaged localization length \( w_0 \) for each \( t_{DNA} \). Note this is an averaged result of the complete genome, and the possibility of high conductance of some particular segments is not ruled out. Other important features are that \( T_w(i) \) decreases faster for smaller \( t_{DNA} \), and \( w_0 \)

is nearly proportional to \( t_{DNA} \). The reason is that the back scattering is stronger for smaller \( t_{DNA} \). Although smaller \( t_{DNA} \) (≤ 0.4 eV) values are more physical, the signal revealing the intrinsic properties of the sequences may be smeared out by the strong back scattering. \( T_w^{\text{ave}} \) for a random sequence R3 with \( t_{DNA} = 1.0, 0.9, 0.8 \) and 0.4 eV, respectively. (Inset) Localization length \( w_0 \) of Y3 (full circles) and R3 (open circles) for each \( t_{DNA} \) (see text).

Since the transport properties are related to the DNA damage repair mechanism, there could be correlation between the locations of genes and the corresponding integrated transmission \( \overline{T}_w(i) \). In Fig. 2 \( \overline{T}_{240}(i) \) and the coding regions are compared for part of the sequence of Y3. It seems that most of the sharp peaks of \( \overline{T}_{240}(i) \) are located in the protein-coding region.

To check this correlation in a more quantitative way,
both $\Omega_{\text{max}}$ can move more freely in the coding regions. As strong positive overlap implies that the holes can move the coding regions have larger conductance. On the other hand, $\Omega(w)$ for acinetobacter sp. ADP1, Deinococcus radiodurans R1 chromosome II, and chlamydia trachomatis D/UW-3/CX are negative, which means the coding regions have smaller conductance. ($\Omega_{\text{max}}$, $w_{\text{max}}$) for these genomes are summarized in TABLE II.

In Fig. 4 $\Omega(w)$ for Y3 is shown for different $t_{\text{DNA}}$. For $t_{\text{DNA}} = 1$ eV, there is a maximum at $w_{\text{max}} = 240$ with $\Omega_{\text{max}} = 0.103$. Note that $\Omega_{\text{max}}$ denotes the maximal absolute value of $\Omega(w)$ and can be positive or negative. The strong positive overlap implies that the holes can move more freely in the coding regions. As $t_{\text{DNA}}$ decreases, both $\Omega_{\text{max}}$ and $w_{\text{max}}$ decrease. For $t_{\text{DNA}} \leq 0.5$ eV, the overlap becomes negative which means the electronic conductance is poorer at the coding regions. The dependence of $\Omega_{\text{max}}$ and $w_{\text{max}}$ on $t_{\text{DNA}}$ are shown in the inset of Fig. 4. Although the values of $w_{\text{max}}$ and $\Omega_{\text{max}}$ vary with $t_{\text{DNA}}$, $G(i)$ and $T_w(i)$ are correlatad in general.

Several $\Omega(w)$ with $t_{\text{DNA}} = 1$ eV for different genomes are shown in Fig. 4. It can be seen that there is maximal positive or negative overlap $\Omega_{\text{max}}$ at some “characteristic migration length” $w_{\text{max}}$ for each genome. $\Omega(w)$ for yeast chromosomes III, VIII and X, and Ureaplasma parvum serovar 3 str. ATCC 700970 are positive, which means the coding regions are positive, which means the coding regions have larger conductance. On the other hand, $\Omega(w)$ for acinetobacter sp. ADP1, Deinococcus radiodurans R1 chromosome II, and chlamydia trachomatis D/UW-3/CX are negative, which means the coding regions have smaller conductance. ($\Omega_{\text{max}}$, $w_{\text{max}}$) for these genomes are summarized in TABLE II.

To ensure that $\Omega(w)$ shown above are physically and biologically meaningful, we compare the results with random sequences. Ten sequences generated by the same way as R3 are analyzed and the averaged $\Omega(w)$ (overlap with the $g(i)$ of Y3) are shown in Fig. 4 (open circles with error bars). It is clear that its overlap is about one order of magnitude smaller then the real sequences. So $\Omega_{\text{max}}$ and $w_{\text{max}}$ are not artifacts, but intrinsic properties of
In summary, with a new method combining the transfer matrix approach and symbolic sequence analysis, the correlation between the transport properties and the positions of genes is studied for complete genomes. There are two characteristic values $\Omega_{\text{max}}$ and $w_{\text{max}}$ for each genome. These two values can provide information for taxonomy or the mechanism of evolution.

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**TABLE I: $\Omega_{\text{max}}$ and $w_{\text{max}}$ for the genomes studied in Fig 4**

| Genome                          | Access No.   | $w_{\text{max}}$ | $\Omega_{\text{max}}$ |
|---------------------------------|--------------|------------------|-----------------------|
| Yeast III                       | NC.001135    | 240              | 0.103                 |
| Yeast VIII                      | NC.001140    | 200              | 0.077                 |
| Yeast X                         | NC.001142    | 170              | 0.085                 |
| Ureaplasma parvum serovar 3 str.| NC.002162    | 130              | 0.041                 |
| Deinococcus radiodurans R1      | NC.001264    | 80               | -0.149                |
| chlamydia trachomatis           | NC.000117    | 50               | -0.075                |
| D/UW-3/CX                       | had to be finer-grained by introducing the more realistic interactions like the base-dependent hopping \cite{27}, the sequence dependent potentials \cite{28}, and the charge-charge interactions.