Theoretical electrical conductivity of hydrogen-bonded benzamide-derived molecules and single DNA bases

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Abstract A benzamide molecule is used as a “reader” molecule to form hydrogen bonds with five single DNA bases, i.e., four normal single DNA bases A,T,C,G and one for 5methylC. The whole molecule is then attached to the gold surface so that a meta-molecule junction is formed. We calculate the transmission function and conductance for the five metal–molecule systems, with the implementation of density functional theory-based non-equilibrium Green function method. Our results show that each DNA base exhibits a unique conductance and most of them are on the pS level. The distinguishable conductance of each DNA base provides a way for the fast sequencing of DNA. We also investigate the dependence of conductivity of such a metal–molecule system on the hydrogen bond length between the “reader” molecule and DNA base, which shows that conductance follows an exponential decay as the hydrogen bond length increases, i.e., the conductivity is highly sensitive to the change in hydrogen bond length.

Keywords Hydrogen-bonded • Benzamide • Conductance • DNA sequencing

1 Introduction

DNA sequencing techniques are very important tools that benefit many scientific fields such as biology and biomedical science, genetics, biotechnology, and molecular biology [1]. Long before the launch of the Human Genome Project, a wealth of sequence information was already being obtained from the Sanger sequencing method [2]. However, as the sequencing needs grow faster and faster, the time and cost it takes for the Sanger method rises to be a big barrier and this leads directly to the demand for new sequencing technology that is much faster and cheaper than the Sanger method.

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The electron transport properties of DNA open a new way of sequencing the human genome of a specific individual [3–6] and research on charge transfer in DNA through quantum tunneling raises much interest because of potential applications with molecular wire in mesoscopic electronic devices [7] or especially in sequencing technology [5]. In Porath et al. [8] double-stranded poly-guanine-poly-cytosine DNA molecules are connected to two metal electrodes and current is measured to find out that DNA actually transfers charge in the same way as silicon-based semiconductor does, and conductance of a single DNA molecule in aqueous solutions was also investigated [9], results showed that conductance decreases with length much slower along DNA than in alkanes and peptides. Large amount of studies on conduction of DNA reveal that the I-V(Current-Voltage) characteristic of DNA could open a new way in sequencing technology.

A good starting point in studying I-V characteristic of DNA is identifying the single DNA base by finding the difference in conductivity of different single DNA bases. On the theoretical side, the conductivity of a molecule is related to its transport property and the transport mechanism is mainly about tunneling over short distances and hopping over long distances [10]. On the experimental side, to measure the current across DNA, people start to construct circuits in which DNA molecules are attached to two metal electrodes at each end and then obtain current through the junction by applying a small voltage bias. Good contact between DNA molecules and metal electrodes must be made in order to receive steady and reliable current signals. Lots of theoretical and experimental research results have been summarized in Endres et al. [11].

Hydrogen bond as a contact bridge between molecules rises with lots of interest in electron tunneling studies. Ohshiro and Umezawa [12] has shown that hydrogen bonds can facilitate electron tunneling so that tunneling current decays more slowly when it is formed between a Watson–Crick complementary base pair compared to a non-complementary base pair. Also, the electron-tunneling property of different base pairs (G-C, A-T, G-T, and 2AA-T) has been investigated by Lee et al. [13] with methods of complex band structure and Green's function scattering theory for I-V characteristics, showing that as more hydrogen bonds are formed between the DNA bases, higher conductance can be observed, and the decay factor for a unit cell of base pair will increase as the hydrogen bond distance increases with a linear relationship. Experiments on DNA sequence through hydrogen-bonded electron tunneling have been performed [14–18].

In this paper, we will deal with a 'biocircuit' including electrode, molecule, and DNA base, as shown in Fig. 1.

In Fig. 1a, the two identical 'reader' molecules are attached on both electrodes, respectively. Then in Fig. 1b we add the DNA base into the gap of the two identical 'reader' molecules. Here the 'reader' molecule has some special structure and properties which are able to form several hydrogen bonds as good contact with each single DNA base, and with metal electrodes (here we use gold slabs) achieved by the thiol linker part (HS-) in the 'reader' molecule. Therefore, each single base forms hydrogen bonds on either side so that a complete junction is formed. Starting from this structure, we explore the electronic transport properties by adding a small voltage bias and perform quantum chemistry calculations to find the current and then the conductance.

2 Structures of biocircuit formation and attachment to gold

A good structure of molecule used as a reader in DNA sequence needs to meet at least three requirements. First, it should be able to form a stable and strong metal–molecule junction.

Fig. 1 A pair of metallic slabs with schematic diagram of “reader” molecule used to read a DNA base. A pair of readers with **a** no DNA and **b** with a DNA base hydrogen bonded to the reader

Second, it can form hydrogen bonding to the DNA base in order to “read” the DNA bases. Third, it should contain one or more ring-like structures to improve the conductivity since the ring-like structure contains pi-bonds, which have better electron transport properties.

In order to form a tight metal–molecule junction, we include the sulfur atom into the ‘reader’ molecule since sulfur binds strongly to gold, acting as a molecular “solder” for gold electrodes. Simulations of an alkanethiol being pulled off of a gold surface showed gold atoms being pulled off of the surface by the sulfur rather than a simple break of the gold–sulfur bond [19]. Therefore we use ‘HS-’ as the left part of ‘reader’ molecule where the H atom will pump off when attached to the gold surface. For the middle part, as we know that π bond contributes more to conductivity than σ bond does (typical values of decay factor for π -bond linked-ring system is $0.2\text{--}0.5\text{\AA}^{-1}$ [20, 21], while for σ -bonded system alkane chain is $0.79\text{\AA}^{-1}$ [22]), we will choose benzene ring, which has six π bonds. For the right part, it should be able to form hydrogen bonds with DNA base. We then tentatively choose ‘-CONH₂’, which can form two or even three hydrogen bonds with the DNA base. Putting all of the three parts together, we finally have the structure of the ‘reader’ molecule, which is ‘HS-C₆H₄-CONH₂’, named as the benzamide reader. The optimized geometry is shown in Fig. 2 (optimization is performed through density functional theory (DFT) calculation in a vacuum, using quantum chemistry package NWChem [23] with exchange-correlation potential PW91 [24] and basis 6-31 G**(xperdew91, perdew91). The DNA bases are optimized in the same way). Next, we attach two identical benzamide readers to the left and right sides of the DNA base by forming hydrogen bonds between them, which is shown in Fig. 3. The ‘-CONH₂’ part in the reader plays a key role in such a connection, where the two H’s can form hydrogen bonds with O or N in DNA base while

Fig. 2 Reader molecule optimized in PW91

Fig. 3 Molecular junction gold-reader-DNA base-reader-gold. The molecule between two gold electrodes is formed by two identical 'reader' molecules and one DNA base. Weak hydrogen bonds are formed between 'reader' molecules and DNA base, and strong S-Au bonds are formed between 'reader' molecules and gold surfaces. We use six gold layers in calculation instead of only two shown here. **a** gold-reader-base A-reader-gold, **b** gold-reader-base C-reader-gold, **c** gold-reader-base 5methylC-reader-gold, **d** gold-reader-base G-reader-gold, **e** gold-reader-base T-reader-gold

the O can form hydrogen bonds with H's in DNA base. The hydrogen bond length here depends on the separation of electrodes and the binding scheme and will then be discussed in the following section.

Finally, we attach the reader molecule to the gold electrodes so that each sulfur contacts the gold surfaces in hollow by forming S-Au bonds (Fig. 3). The distance between sulfur and gold surface is 1.95 Å and the actual size of gold layers is $N_{Au,x} \times N_{Au,y} \times N_{Au,z} = 6 \times 6 \times 6$ (CZ), which is large enough to minimize the size effect. We choose the separation between two electrodes to be 25 Å because hydrogen bonds at this distance can be well formed between the reader molecules and DNA bases. If the separation is too large, no hydrogen bonds can be formed. If the separation is too small, the DNA base may stack on the reader molecule, which would be more complicate than the hydrogen binding issue. The gold-reader-DNA base-reader-gold system is made periodic in three dimensions in our later DFT calculations.

3 Energy levels

Conductivity of a molecule is an important signature of energy level from which we can obtain rough information about electronic structure. Here we are more interested in finding out how energy levels are shifted when we bring the isolated molecules together to form a combined hydrogen-bonded molecule. The isolated molecules are two identical reader molecules, and one DNA base molecule, while the combined molecule is reader-base-reader. To illustrate the energy shift, we choose A base as an example (with the combined molecule abbreviate as RAR). The DFT calculation is performed in siesta code [25] using local density approximation (LDA) functional and double-zeta polarization (DZP) basis for all the elements but single-zeta polarization (SZP) for gold. The result is shown in Fig. 4. The plot shows energy levels especially the HOMO/LUMO (highest occupied molecular orbitals/lowest unoccupied molecular orbitals) shift dramatically when the DNA base is connected to the reader molecule. The energy gap between the HOMO and LUMO significantly shrinks, so that they move closer to the Fermi level (of metal–molecule system) and then improve the conductivity [26]. To carry out quantitative analysis on the shift in energy level, we need to calculate the project amplitude of connected system onto isolated system to extract the information hidden in Fig. 4.

Fig. 4 The energy levels near the HOMO and LUMO for isolated reader molecule, isolated DNA molecules and the connected molecules reader-DNA base-reader. H and L represent the HOMO and LUMO respectively. The HOMO-LUMO gap is reduced when connecting the reader molecules and DNA base together

3.1 Project amplitude

We consider the connected system reader-base-reader as full system and the separate left/right reader or DNA base as isolated system. Let ψ_i be the i -th eigenstate of full system, ϕ_j be the j -th eigenstate of isolated system and $\{\phi_\alpha\}$ be the atomic orbitals used to expand the eigenstate of full system and isolated system, i.e.,

$$\psi_i = \sum_{\alpha} a_{\alpha i} \phi_{\alpha}, \quad \phi_j = \sum_{\alpha} b_{\alpha j} \phi_{\alpha} \quad (1)$$

where $a_{\alpha i}$, $b_{\alpha j}$ are the expansion coefficients for full system and isolated system, respectively. The projected amplitude is then

$$A_j(i) = \langle \phi_j | \psi_i \rangle = \sum_{\alpha\beta} b_{\beta j}^* a_{\alpha i} S_{\alpha\beta} \quad (2)$$

here $S_{\alpha\beta}$ is overlap matrix for non-orthogonal atomic basis. The sign of project amplitude indicates the node and antinode information. In Fig. 5, we show the projection relation of HOMO/HOMO-1/HOMO-2 and LUMO/LUMO+1/LUMO+2 between connected system and isolated system with reader-A base-reader (abbreviated as RAR) as an example. We are interested in the states that have energy around HOMO/LUMO because they are more relevant to electron transport properties. Results for other DNA bases are very similar. From Fig. 5 we can see that the eigenstate of the connected system is highly localized. For the HOMO part, the eigenstate corresponding to the HOMO level is mainly localized on the right reader and contributed its HOMO, while the eigenstate of HOMO-1 is mainly localized on the A base also contributed by the HOMO, and HOMO-2 localized on the right reader again contributed by the HOMO-1. For the LUMO part, both the LUMO and LUMO+1 of connected system are localized on left reader and contributed by its LUMO, LUMO+1, respectively, while LUMO+2 is localized on the right reader, contributed by the LUMO. Since the more localized the state is the less conductive the corresponding connected system will be, we may expect the molecular junction gold-reader-A base-reader-gold to have a very small conductance given that the interaction between the molecule and the gold electrode does not change such a localized property significantly, which is actually true for the system we consider here.

Fig. 5 Patterns between eigenstates of RAR and that of isolated parts including left reader, A base, and right reader with percentage the project amplitude square

3.2 Projected density of states

The projected amplitude clarifies the relationship between the eigenstate of the connected system and eigenstate of the isolated system, however it does not tell anything about the contribution to each eigenstate of connected system from every species in the system. To calculate the projected density of states on the k -th specie of left reader, right reader or DNA base, we using the following formula

$$\rho^{k \text{ spec}}(E) = \text{Re} \left[\frac{i}{\pi} \sum_j \sum_{i \in k \text{ spec}} \sum_l \frac{|\langle \phi_l^i | \psi_j \rangle|^2}{E - \epsilon_j + i\eta} \right] \quad (3)$$

where η is the broadening factor with value 0.1 (eV), ϵ_j is the j -th eigenvalue of full system and ϕ_l^i is the l -th atomic orbital of i -th atom, which belongs to species k . We therefore find the projected density of states onto hydrogen, carbon, nitrogen, oxygen, and sulfur in the left/right reader and DNA base separately, an example for R-A-R system is shown in Fig. 6, where the energy is directly from the output of Siesta without being shifted. It can be observed that the LUMO of connected system is mostly from the LUMO of the left reader, more precisely from the oxygen (blue line), which is consistent with our projected amplitude calculation (98% on left reader), while the right reader and A base contributes very little except for those LUMO states with energies 1.4 eV above the LUMO. The LUMO+1 of connected system is completely contributed by the left reader, mostly from carbon (red line) (100% in projected amplitude calculation). For LUMO+2 of the connected system, the plot shows it is mainly from the LUMO of the right reader contributed by the sulfur (orange line), the small amplitude is due to the average of projected density of states per atom. For the HOMO part, it has a very different behavior compared to the LUMO part from the plot. The HOMO and HOMO−1 of connected system are from the HOMO of the right reader (mostly from oxygen) and HOMO of A base (mostly from nitrogen), respectively, though not obvious in the plot as the energy level for HOMO and HOMO−1 are too close. Instead it can be easily viewed from the projected amplitude (89% for both HOMO and HOMO−1). The HOMO−2 is also very close to HOMO, being contributed

Fig. 6 Average projected density of states per atom for reader-A base-reader system, onto hydrogen, carbon, nitrogen, oxygen, and sulfur for each part represented by black, red, green, blue, and orange lines

Fig. 7 Projected density of states for gold-reader-A base-reader-gold system, onto hydrogen, carbon, nitrogen, oxygen, and sulfur for each part represented by *black, red, green, blue, and orange* lines while for the gold part the *black line* represents projected density on left gold, and the *red line* for right gold. The HOMO and LUMO are also shown

by HOMO–1 of the right reader and mainly from the sulfur with 98% in projected amplitude.

To see how density of states changes when attached the molecule to gold surface, we recalculate the projected density of states including gold slabs on left/right gold, left/right reader and A base. The plot is shown in Fig. 7, from which we can see that the average projected density of states on the sulfur in left reader molecule changes significantly when including the gold electrode. Besides, the sharp spikes in Fig. 6 have been broadened in Fig. 7 due to the strong Au–S bonding between the left reader and gold electrode. The same occurs to the right reader, but not as significant as left reader, indicating a weaker interaction between the right reader and gold than that between the left reader and gold. Such an unsymmetrical effect arises from the asymmetric structure of reader–base–reader. It can also be observed from the projected density on oxygen (blue line), where the highest spike of oxygen in left reader has a noticeable shift to the right but little occurs on oxygen in right reader.

4 I-V calculation and conductance

From the previous qualitative analysis, the eigenstates of the gold–reader–DNA base–reader–gold system are mainly localized, indicating a small conductance. In order to perform a quantitative analysis, the I–V calculation on such a molecule–gold junction is necessary. Under the small voltage bias, the relation between the voltage and current can be expected to be linear so that the slope is the conductance. In the following, we first briefly introduce the ballistic transport theory, then discuss the transmission function, and finally obtain the conductance.

4.1 Theory

The Hamiltonian of a molecular junction contains four parts: the left electrode, the bridged molecule (reader and DNA base), the right electrode, and couplings between the electrodes and molecule, represented by H_L , H_M , H_R and $V = H_{LM} + H_{RM}$ if the coupling between the

left electrode and right electrode H_{LR} can be neglected, which is true in most cases. Thus, the Hamiltonian can be expressed as

$$H = H_L + H_M + H_R + H_{LM} + H_{RM} \quad (4)$$

Expanded in localized basis set $\{\phi_\mu(\mathbf{r} - \mathbf{R}_i)\}$ with μ the index of basis and i the index of nuclei, which is implemented in Siesta code, the total Hamiltonian becomes a matrix.

$$H = \begin{bmatrix} H_{LL} & H_{LM} & 0 \\ H_{ML} & H_{MM} & H_{MR} \\ 0 & H_{RM} & H_{RR} \end{bmatrix} \quad (5)$$

with $H_{\mu\nu} \equiv \langle \phi_\mu | H | \phi_\nu \rangle$. The basis set $\{\phi_\mu(r - R_i)\}$ is not orthogonal in general, so that the overlap $S_{\mu\nu} \equiv \langle \phi_\mu | \phi_\nu \rangle \neq 0$. The Green's function corresponding to the total Hamiltonian is therefore

$$G = (ES - H)^{-1} = \begin{bmatrix} ES_{LL} - H_{LL} & ES_{LM} - H_{LM} & 0 \\ ES_{ML} - H_{ML} & ES_{MM} - H_{MM} & ES_{MR} - H_{MR} \\ 0 & ES_{RM} - H_{RM} & ES_{RR} - H_{RR} \end{bmatrix}. \quad (6)$$

The most important part of G is from the bridged molecule,

$$G_{MM} = ((ES - H)^{-1})_{MM} = (ES_{MM} - H_{MM} - \Sigma_L(E) - \Sigma_R(E))^{-1}, \quad (7)$$

where $\Sigma_L(E)$, $\Sigma_R(E)$ are the self energies that incorporate the couplings between the bridged molecule and the left/right electrodes, respectively, and they can be shown as

$$\Sigma_{L(R)}(E) = ((E - s_{L(R)})S_{L(R)M} - H_{L(R)M})^+ G_{L(R)}^0(E)((E - s_{L(R)})S_{LM} - H_{LM}). \quad (8)$$

Here, $S_{L(R)M}$ is the overlap between left contact and the molecule and the energy shift $s_L = eV/2$, $s_R = -eV/2$ due to the bias voltage V . $G_{L(R)}^0(E)$ is the retarded Green's function for the isolated left(right) semi-infinite electrode which can be written as

$$G_{L(R)}^0(E) = ((E + i\eta)S_{LL(RR)} - H_{LL})^{-1} \quad (9)$$

with η a small positive value acting as the lifetime broadening.

The ballistic transport theory is based on Fermi-golden rule with the transition rate from left gold-reader contact to right reader-gold contact as

$$\Gamma_{L \rightarrow R} = \frac{2\pi}{\hbar} |T_{RL}|^2 \delta(E_L - E_R) \quad (10)$$

here $T = V + VGV$ is the transition matrix or scattering matrix [27]. The net current thus can be determined according to the formula

$$I = 2e \sum_{LR} \Gamma_{L \rightarrow R} (f(E_L - \mu_L) - f(E_R - \mu_R)), \quad (11)$$

where the factor 2 is from the spin (we assume the electron with spin up or down has the equal contribution to the current) and the Fermi-Dirac distribution function $f(E) = (1 + e^{E/kT})^{-1}$. Further simplification gives the more compact form [22]

$$I = \frac{2e}{h} \int_{\mu_R}^{\mu_L} T(E) dE, \quad (12)$$

with chemical potential of left and right electrode $\mu_L = E_F + \frac{eV}{2}$, $\mu_R = E_F - \frac{eV}{2}$. The transmission function $T(E) = \text{tr}(\Gamma_L G_M \Gamma_R G_M^+)$ with $\Gamma_{L(R)} = i(\Sigma_{L(R)} - \Sigma_{L(R)}^+)$ the spectral

density of states. Provided with the Hamiltonian and overlap matrix for the molecular junction from which the couplings between left, right contacts and the molecule can be extracted, we can find the current according to (12) as well as the conductance and transmission function $T(E)$.

In the following calculation, we applied periodic boundary condition in three dimensions to the molecular junction so that each supercell has the structure gold-reader-DNA base-reader-gold with three-layer gold slabs ($6 \times 6 \times 3$ in XYZ) on either side in the z-direction, i.e., six layers of gold between any two neighbor bridged molecules. The total number of atoms in the supercell is therefore 263 atoms for DNA A base connection, similar for other bases (261, 264, 263, 264 atoms for DNA C, G, T, 5meC base connection, respectively). The calculation can be divided into three steps. We first optimize the molecular junction in the quantum chemistry package NWChem 5.1 [23] with 6-311G basis set using the perdw exchange-correlation functional since it was shown to be most suitable for dealing with hydrogen bonds. Second, we perform DFT calculation for the optimized structure in Siesta Code, implementing LDA functional, basis SZP for gold and DZP for all the rest elements. The output is the Hamiltonian and overlap matrix for the metal–molecule system. Third, we calculate the Green function, the transmission function, and then the conductance in the code developed by Otto Sankey at ASU by extracting the Hamiltonian and overlap matrix from the output file of the second step.

4.2 Transmission plot and fermi level alignment

As an integral kernel for current, the transmission function $T(E)$ tells the transport properties for electrons with energy E . Besides, the combination of the transmission function and Fermi level alignment can roughly tell the conductivity by observing the relative position between the HOMO, LUMO of bridged molecule, and the Fermi level of the metal–molecule system [26]. The Fermi level here is defined as $(E_{\text{HOMO}} + E_{\text{LUMO}})/2$ with E_{HOMO} and E_{LUMO} the highest occupied and lowest unoccupied energy levels of the supercell containing left/right gold slabs, reader molecules, and DNA base. The HOMO-LUMO gap, however, refers only to the bridged molecule, i.e., the energy difference between the HOMO and LUMO of reader-DNA base-reader system.

The transmission plots for each connection with A, T, C, G and 5methylC base are shown in Fig. 8. Roughly speaking, the closer the Fermi level to HOMO or LUMO, the larger the conductance. Comparing the relative gap between Fermi level and HOMO or LUMO of each case in Fig. 8 to the experimental conductance values in Table 1, we find that the order of gap size and experimental values match fairly well.

4.3 Conductance

Once we find the transmission function $T(E)$, current and conductance can be obtained easily from (12). To check whether the conductance is sensitively dependent on the gold–gold distance, we try 24 Å and 26 Å besides 25 Å the final results of conductance for each connection of DNA base A, C, 5methylC, G and T are shown in Table 1 including the experimental results, which are taken from [16]. We observe that the conductance decreases as the gold–gold distance increases for each case but with different decay factors. Although the conductances from the calculation are about one order of magnitude off compared to the ones from the experiment, we find that both the theoretical and experimental conductances have the same relative order in magnitude for each base. This is consistent with the order of HOMO-LUMO gap (except for 24 Å case). The discrepancy in conductance between the

Fig. 8 The plots of natural logarithm of transmission function $T(E)$ with energy E for molecules **a** reader-A base-reader. **b** reader-C base-reader. **c** reader-5methylC-reader. **d** reader-G base-reader. **e** reader-T base-reader

theoretical calculation and the experimental measurement is due to water effect, since our calculations were done in gas phase while the experiment was performed in solution phase. The water around the bridged molecule may alter the connection of reader-DNA-reader, such as the hydrogen bonding between the reader and the DNA base, newly introduced hydrogen bonding between the water molecules and the reader or DNA base, the hydrogen bonding between water molecules themselves. Molecular dynamics is able to show these effects on metal–molecule–metal junction in the presence of water and the calculation

Table 1 Conductance from I-V calculation for each connection case with different gold-to-gold distance

Structure	Cal G(pS)(24Å)	G(pS)(25Å)	G(pS)(26Å)	H-L gap(25Å)	Expt G(pS)
RAR	14.54	4.83	0.28	0.81	27
RCR	15.09	8.03	1.74	0.57	65.2
R5methylR	9.48	5.97	1.12	0.76	37
RGR	14.28	6.20	1.34	0.75	40
RTR	0.58	0.03	0.02	1.01	no signal

The first column is calculated conductance with gold-to-gold distance equal to 24Å, the second column is for 25Å, the third column is for 26Å, the forth column is the gap between fermi level and HOMO or LUMO (the smaller one), the fifth column is experimental value for conductance. The order of experiment value matches that of HOMO-LUMO gap value and the calculated value (except for 24Å). Unit of conductance (G) is in pS (10^{-12} Siemens)

of conductance corresponding to such a complicate system will be the task of our future research.

We note that conductance depends on the gold–gold distance, since different distance corresponds to different connecting structure or even different hydrogen bond length. Also, we notice that base T case always gives a very low conductance regardless of which gold–gold distance we choose, and this is confirmed by the experiment result as no signal comes up in experiment [17].

5 How energy levels and conductivity change with hydrogen bond length

Though the hydrogen bond is weak, it is crucial for acting as a bridge between reader molecule and DNA bases. Therefore it would be natural to ask how actually the hydrogen bond strength can affect the electronic structure such as energy levels and consequently the conductivity of the molecular junction. The hydrogen bond strength depends on many factors, including the bond length and angle, the temperature and pressure of its surroundings. In a practical experiment, the temperature and pressure are usually fixed at room temperature and atmosphere pressure. Besides, it has been shown that small deviations in the bond angle can have a relatively minor effect up to 20° [28] (our molecular dynamic simulation in water shows that the deviations of hydrogen bond angle are less than 20°). In contrast, the hydrogen bond strength sensitively depends on the hydrogen bond length and more exactly, it decays exponentially when increasing the hydrogen bond length [29]. Therefore, to simplify the discussion, we only focus on the main contribution to the hydrogen bond strength, i.e., the hydrogen bond length in this paper.

In the previous section, we fix the hydrogen bond length, but the experiment is usually performed in solution, so that hydrogen bond length varies from time to time, sometimes even broken and then reformed, producing a significant effect on conductivity of molecular system. Therefore, it is interesting to find out how energy levels and conductivity depend on hydrogen bond length. To do this, we select the structure of R-R (reader-reader) and R-A-R (reader-A base-reader in Fig. 11a) as examples.

The optimized structure for R-R case is shown in Fig. 9a and its energy levels are shown in Fig. 9b, we increase the two hydrogen bond lengths from 1.83Å to 2.15Å gradually. Calculations are performed for each structure in Siesta code and results show that energy levels of R-R have little dependence on the changes in hydrogen bond length (see Fig. 9c). We also check other bases and there are no exceptions. This is actually what we have

Fig. 9 **a** Reader–reader connected structure in vacuum. **b** Energy levels for the reader and reader–reader connection (with hydrogen bond length is 1.83 Å) together with fermi level of the system with gold. **c** Energy levels for different hydrogen bond length, which is 1.83, 1.86, 1.89, 1.92, 1.95, 1.98, 2.01, 2.05, 2.15 Å

expected since the hydrogen bonds between reader and base are so weak that they act as a very small perturbation to the full Hamiltonian. In the R-A-R case (Fig. 11a), we work in two parts: the first part is to fix the right hydrogen bond length (1.83 Å) and increase the left two hydrogen bond length from 1.83 Å to 2.15 Å. We stop at 2.15 Å in order to keep the accuracy of the calculation. The reason lies in that the Siesta code we have used in the calculation implements the linear combination of atomic orbitals (LCAO) method so that it works best if the hydrogen bond length is not too long (in fact, we have tested the longer hydrogen bond length up to 3.00 Å but with no obvious deviations observed in the pattern of energy levels/conductivity versus shifts in hydrogen bond). Similar to the previous case, the plot shows little dependence of energy levels on the shifts (see in Fig. 10a). The second part is to fix the left two hydrogen bond lengths (1.83 Å) and increase the right hydrogen bond length from 1.83 Å to 2.15 Å. Again, we find that the energy levels have little dependence on the shifts in hydrogen bond length on right part (Fig. 10b).

As we are more interested in the effect of hydrogen bond length on the conductivity of the molecular junctions, we performed the DFT/conductance calculations for each structure with shifted hydrogen bond length. To better illustrate the dependence of conductance on the shifts in hydrogen bond length, we plot the natural log of dimensionless conductance $\ln(G/G_0)$ with the shift by noticing that $G \simeq G_0 e^{-\beta_H(L_0 + \Delta L)}$ [30, 31] so that $\ln(G/G_0) = -\beta_H L_0 - \beta_H \Delta L$. Here, G represents the conductance of the gold-reader-base-reader-gold system. $G_0 = 77 \mu S$ is the quantum conductance. L_0 and ΔL are the equilibrium hydrogen

Fig. 10 The plot of energy levels with the shift in hydrogen bond length. **a** shift the two hydrogen bonds between the left reader and A base. **b** shift the only hydrogen bond between right reader and A base

bond length and its shift. The $\beta_H = -\frac{d \ln(G/G_0)}{dL}$ is the decay factor characterizing how fast the conductance decreases/increases when increasing/decreasing the hydrogen bond length.

By making the plot $\ln(G/G_0)$ versus ΔL we find that the natural log of dimensionless conductance G/G_0 obviously decreases linearly when increasing the hydrogen bond length in the R-R case (Fig. 10a), despite that the energy levels are hardly affected as we increase hydrogen bond length. This is consistent with the results obtained in [13]. The decay factor β_H is $3.82 \text{ \AA}^{-1}$, much larger than the one obtained from the molecule system with only a covalent bond, which is less than $1 \text{ \AA}^{-1}$. This may help us understand the role of hydrogen bonds in electron transport.

Similar to the R-R case, the conductance in R-A-R case is also linearly dependent on the shift in hydrogen bond length for both the N---H($d_{eq} = 1.85 \text{ \AA}$) and O---H($d_{eq} = 1.83 \text{ \AA}$) hydrogen bonds, but with even larger decay factors. The decay factor β_H is $4.35 \text{ \AA}^{-1}$ for N---H part and $6.48 \text{ \AA}^{-1}$ for O---H part. The linearity between the natural log of dimensionless conductance and shift in hydrogen bond length shows that the conductance decays exponentially as the hydrogen bond length increases, while the large decay factor implies that such a decay is very rapid. This actually singles out the variation of hydrogen bond length as the dominant part in determining the conductance when considering the fluctuation of molecular junctions in water solution (Fig. 11).

6 Dependence of DNA conductivity on connecting structure and number of hydrogen bonds formed between reader molecule and bases

Given the structure of a ‘reader’ molecule, we usually have different ways to connect it to DNA bases by forming several hydrogen bonds between them since there are several parts in each DNA base that contain either an H atom, O atom, or N atom that is able to form hydrogen bonds with the O atom or H atom in the reader molecule. Here we will show the conductance of several different connecting structures for DNA single base A to see how sensitively DNA conductivity depends on connecting structure between molecules and DNA bases.

The three structures are shown in (Fig. 12). The first one (Fig. 12a) is the structure we used before, while in the second one (Fig. 12b), there are some rearrangements in hydrogen bond formation but with the same number of hydrogen bonds as in the first one. For the third

Fig. 11 Plots showing the linearity between the natural log of dimensionless conductance and the shift in hydrogen bond length for **a** the R-R case, **b** N-H hydrogen bond in the R-A-R case, **c** O-H hydrogen bond in the R-A-R case

Fig. 12 Different connecting structures between reader molecule and single DNA base A. All of them have the same gold-gold distance 25 Å. **a** The structure we used before. **b** New connection between reader and base A with a change on the left side. **c** New connection between reader and base A with a change on the right side

Table 2 Conductance of different connecting structures (corresponding to (a), (b), and (c) shown in Fig. 12) between reader molecule and single DNA base A

Structure	RAR(a)	RAR(b)	RAR(c)
G(pS)(25A)	14.54	0.69	115.25
G(pS)(26A)	21.29	0.56	14.20

All of them have the same gold–gold distance 25 Å

one (Fig. 12c), about two hydrogen bonds are formed between the right reader and DNA base A instead of just one in the first one. After building up the structures, we tether them to gold slabs in the same way as we did before. By performing an I-V calculation for each, we finally obtain the conductance results and present them in (Table 2). The conductance of the second one drops a lot while the third one rises a lot compared to the first one. The drop in conductance for the second one is probably because the hydrogen bond of N-H---N is much weaker than O---H-N. There are two O---H-N bonds in the first one, but one O---H-N bond and one N-H---N bond in the second one. Larger conductance obtained in the third structure may lie in that about one more N---H-N bond is added in the connection, which seems to show more hydrogen bonds may provide more channels for charge transfer and then larger conductance. From above, we can see that the conductance of the whole molecule junction including reader, DNA bases, and gold slabs does depend heavily on how hydrogen bonds are formed between reader molecule and DNA bases.

7 Dependence of DNA conductivity on the contact angle between molecule and gold surface

When we attach a reader molecule to the gold surface, we have no reason to let them be perpendicular with each other and there may be some arbitrary contact angles between molecule and gold surface depending on how people control them in the experiment. At this time, we test the conductance at a few different contact angles from 50 degrees to 90 degrees for every 10 degrees. The structures are shown in Fig. 13. After the I-V calculation, we find the conductance for each case in (Table 3). Results show that the conductance does not change much when decreasing from 90 to 50 degrees, and this is easy to be understood since the contact angle will not affect the chemical bonds and inner electronic structure significantly. Therefore, we can ignore its effect when dealing with this ‘biocircuit’ system in solution despite how the contact angle changes due to the solvent.

Fig. 13 The reader-DNA base-reader molecule can be attached to the gold surface at different contact angles, where the angle is measured between the gold surface and the plane of reader molecule. We only shown the structure with contact angle 50 degrees. The separation between two gold surfaces is 25 Å

Table 3 Conductance of different contact angles between reader molecule and gold surface

Contact angle	50	60	70	80	90
G(pS)(25Å)	20.16	13.40	16.04	13.92	14.54

8 Conclusions

We have chosen the benzamide molecule as a ‘reader’ to form hydrogen bonds with DNA bases on both sides and then attach the ‘HS-’ part in reader molecule to the gold surface so as to form a complete molecule–metal junction. Under zero bias voltage, we calculate the transmission function $T(E)$ and it roughly gives the order of conductivity of each DNA bases, which is consistent with the experiment conductance values. The full I-V calculation is followed by the transmission function and the conductance for each connecting system is found in pS level, while the order in conductivity for the five systems matches the experimental results (except for the 24Å case), although the value of conductance in calculation is off by one order, which is not quite important since we are more interested in sequencing the DNA and the relative order of conductance for each DNA base. Our results also show that the conductance depends sensitively on the distance between two inner gold surfaces, because different distances between the gold may lead to different hydrogen bond lengths and different connecting schemes between ‘reader’ and DNA base.

The hydrogen bond length plays a very important role in electronic structures and conductance, and we have found that the conductance decreases significantly when increasing the hydrogen bond length, though the energy level of the molecule shows little change. More specifically, the natural log of conductance decreases linearly with the increment in hydrogen bond length within suitable range so that the decay factor is a constant, and is much larger than the one found in the two-base pair system. This implies that the conductance in our molecular junctions depends very sensitively on the hydrogen bonds formed between reader molecules and DNA bases.

Our work reveals some important properties of conductivity in our molecular junctions which contain gold slabs, reader molecules, and DNA bases without solvent considered. In future research, we will add water molecules into the system and perform a more thorough investigation about quantum tunneling characteristics of molecule–metal junctions.

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