The Electron Transfer Path Between Cytochrome C and Single-walled Carbon Manotubes Based on Quantum Mechanics

Xin-xin WANG, Ying-xue XU, Yin-jie LIAO, Shi-jie ZHOU, Bing ZHANG

ABSTRACT

By analyzing the shortest path between cytochrome c (Cytc) and single-walled carbon nanotubes (SWNTs), the study investigated electron transfer mechanism. By simplifying the snapshots model of SWNT(10, 10)-(Cytc) at 10 ns, the charge density of the simplified model was calculated by using quantum mechanics simulation and the charge density image was drawn. On the basis, the study discussed and verified the electron transfer mechanism and paths between Cytc and SWNTs at the optimal localization. The result revealed that the electrons were transferred to Cytc protein from the surfaces of SWNTs through Cys18.

INTRODUCTION

As a water-soluble redox protein containing heme, cytochrome c (Cytc) appears in cytoplasm between mitochondrial inner and outer membranes. Cytc is used for transferring electrons between reductase and oxidase of Cytc (physiological function), and is a research hotspot in the fields of proteolysis and drug delivery for a long term. Due to the unique electron transfer function, Cytc has been concerned in various fields in recent years including bionic electronic devices and widely used for modifying electrode surface to strengthen the efficiencies of electron transfer of biosensors or biofuel cells. However, the interactive effect between Cytc and the surfaces of single-walled carbon nanotubes (SWNTs) is scarcely reported in molecular scale, for example, the possible paths of electron transfer between Cytc and SWNTs. The study investigated the electron transfer paths and mechanism between SWNTs and Cytc through theoretical simulation. In this way, the research attempted to provide theoretical guidance and experimental basis for reasonably designing new biosensors and photoelectric converters with high efficiency and low costs.
Models and methods

Dynamic research has been carried out on the localization of Cytc on the surfaces of SWNTs. On the basis, the study considered the stable dynamic snapshot of Cytc protein on the surface of SWNT (10, 10) in 0 localization system as the initial equilibrium state for the dynamics simulation of the structure. After doing this, the poly-cyclic planes of heme in Cytc were always perpendicular to the surfaces of SWNTs. During the simulation based on quantum mechanics, it was necessary to keep the heme planes always perpendicular to the surfaces of SWNTs in the model. In order to guarantee this, heme, two amino acids (HID19 and Lys99) coordinated with Fe, MET100 and THR101 were intercepted as a part of Cytc guaranteeing heme planes perpendicular to the surfaces of SWNTs. To properly reduce the computation amount, the 6-nm-long SWNT was intercepted on the precondition of not influencing the calculation result and it was guaranteed that heme planes were exactly in the middle part of SWNTs, as shown in Figure 1.

![Figure 1. A snapshot of TSWNT(10,10)-cytc at 10000ps.](image)

The experiment was conducted by employing the density functional based tight binding (DFTB) and the package – green density functional tight-binding (gDFTB) that combined with the non-equilibrium Green's function. The force field parameters of sulfur element are not included in the total force field parameters during structural optimization. Therefore, in order to guarantee the smooth simulation and not to exert influences on the interactive effect between heme and SWNTs, the sulfur elements in cysteine Cys15 and Cys18 were replaced with oxygen elements. It meant that the C-S bonds formed by sulfur in Cys15 and Cys18 and C in heme were replaced with C-O bonds. During the optimization, the convergences of energies and forces were limited to 0.05 kal/mol and 0.5 kcal/mol*Å, respectively. The smearing parameter was set as 0.005 Ha to further calculate charge distributions by employing electrondensity and the self-consistent convergence was limited to 105 eeV/Å.
Speculation of electron transfer paths between Cytc and SWNTs

As displayed in Figure 2, the heme on the poly-cyclic heme surface was still perpendicular to the tangent plane of SWNTs during the simulation by using DFTB method. It implied that the optimal localization of poly-cyclic surface of heme occurs when heme surface was perpendicular to the hydrophobic surface whatever the surface was a flat or an arched plane. The distance between HID19 and the surface of SWNTs always kept at the lowest level and the average distance was far lower than 14 Å in the simulation. Therefore, it can be speculated that the electron transfer between SWNTs and Cytc was mainly achieved through electron tunneling effect.

Figure 2. The snapshot at the end of the model optimization.

While studying the localization of Cytc on the surfaces of SWNTs, it can be speculated through previous dynamic researches that heme planes in SWNT(6, 5)-Cytc, SWNT(7, 6)-Cytc, SWNT(8, 7)-Cytc and SWNT(10, 10)-Cytc systems all rotated in a counterclockwise direction by small angles of 19.6°, 16.8°, 10.8° and 11.4°, respectively. It was found that the counterclockwise rotation was mainly favorable for the double bonds of CAC=CBC inclining to the surfaces of SWNTs. Heme was the primary part for electron transfer inside Cytc and a large electron delocalization system was formed by combining poly-cyclic conjugated plane of heme and double bonds of CAC=CBC. Therefore, the closer the double bonds to the surfaces of SWNTs, the more favorable the electron transfer between the two parties was. In the four stable localization systems, the initial and final distances between CAC=CBC of heme and the surfaces of SWNTs are displayed in Table 1. Thus, it can be inferred that the possible path of electron transfer appeared as SWNTs-CAC=CBC (double bonds)-poly-cyclic plane-Fe when Cytc directly reacted with SWNTs.
TABLE 1. COMPARISON OF THE DISTANCES BETWEEN THE HEME CAC = CBC AND THE SURFACE OF THE SWNTS BEFORE AND AFTER THE MD SIMULATIONS.

<table>
<thead>
<tr>
<th>Angle</th>
<th>0°</th>
<th>45°</th>
<th>90°</th>
<th>135°</th>
</tr>
</thead>
<tbody>
<tr>
<td>System</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SWNT(6,5)</td>
<td>4.300</td>
<td>3.961</td>
<td>4.729</td>
<td>6.187</td>
</tr>
<tr>
<td></td>
<td>3.387</td>
<td>2.961</td>
<td>7.148</td>
<td>3.604</td>
</tr>
<tr>
<td>SWNT(7,6)</td>
<td>4.112</td>
<td>4.012</td>
<td>3.699</td>
<td>3.357</td>
</tr>
<tr>
<td></td>
<td>3.124</td>
<td>3.218</td>
<td>7.542</td>
<td>2.842</td>
</tr>
<tr>
<td>SWNT(8,7)</td>
<td>3.390</td>
<td>3.992</td>
<td>3.468</td>
<td>3.326</td>
</tr>
<tr>
<td></td>
<td>4.852</td>
<td>2.711</td>
<td>2.909</td>
<td>3.325</td>
</tr>
<tr>
<td>SWNT(10,10)</td>
<td>3.559</td>
<td>4.659</td>
<td>4.339</td>
<td>3.885</td>
</tr>
<tr>
<td></td>
<td>3.057</td>
<td>2.669</td>
<td>4.525</td>
<td>2.456</td>
</tr>
</tbody>
</table>

Results and analysis

Figure 3 shows the electron densities of the model in the simulation. As shown in the figure, the part on HID19 which was closest to the surface of SWNTs shows the darkest color and the largest electron density, implying the part has the most powerful capacity for absorbing positive charges. Besides, the figure reveals that the electron density of the HID10 surface was coincided with that of the surface of SWNTs, thus probably forming a coherent electronic path. On this basis, the electron transfer path between Cytc and the surfaces of SWNTs is revealed: electrons tunnel to the amino acid HID10 from the surfaces of SWNTs through tunneling effect, showing the electron transfer path as SWNT-HID19-LYS99-Fe.

Figure 3. Optimized electron density schematic diagram.
According to the aforementioned method applied in the simplified model, the parts of models of SWNT(6,5)-Cytc, SWNT(7,6)-Cytc and SWNT(8,7)-Cytc at 10000 ps were taken as the initial models. By doing so, it not only guarantees the complete interaction between heme and the surfaces of SWNTs but also save the calculation time. As shown in Figure 4, the heme planes in Cytc are still perpendicular to the surfaces of SWNTs and the HID19 has the closest distance to the surface of SWNTs in the three models. It can be speculated that the electron transfer mechanism and paths of SWNT(6,5)-Cytc, SWNT(7,6)-Cytc and SWNT(8,7)-Cytc are similar to those of SWNT(10,10)-Cytc. The electrons transfer to HID19 after passing through the potential barrier from the surfaces of SWNTs by virtue of the electron tunneling effect and the electron transfer paths are all displayed as SWNT-HID19-LYS99-Fe.

![Figure 4. Simplified model of SWNT(8,7)-Cytc, SWNT(7,6)-Cytc and SWNT(6,5)-Cytc.](image)

**CONCLUSIONS**

The study systematically investigated the direct electron transfer mechanism between SWNTs and Cytc. On this basis, the electron densities on the surfaces of models were calculated by using DFTB method and the electron transfer paths revealed.

(1) Heme plane in the SWNT(10,10)-Cytc system was still perpendicular to the surface of SWNTs. The distance between SWNTs and HID19 in Cytc was far lower than 14 Å and electrons were transferred between them through electron tunneling effect.

(2) The study calculated the electron density and drew electron density image by using DFTB method. Afterwards, it was found that the electron density on the surface of SWNTs was coincided with that of the HID19, thus forming a coherent charge density path. The coincident part of the electron densities of HID19 and the surface of SWNTs was the darkest in the whole electron density image, implying the largest electron density. Thus, the electron transfer path was revealed.

(3) By comparing SWNT(6,5)-Cytc, SWNT(7,6)-Cytc and SWNT(8,7)-Cytc with SWNT(10,10)-Cytc, it can be found that heme planes in the models of the three systems were still perpendicular to the surfaces of SWNTs under stable molecular mechanics. Afterwards, HID19 had the closest distance to the whole Cytc after the simulation equilibrium. Therefore, it was speculated that the electron transfer mechanisms and paths of the other three systems were the same as those of SWNT(10,10)-Cytc.
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REFERENCES