EXPLORATION OF A NEW DNA SEQUENCING METHODS VIA SINGLE-WALLED CARBON NANOTUBE

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Introduction

The genetic code is embedded in DNA sequence. Accordingly numerous researchers focus on investigating the sequencing methods. The Sanger method[1] based on PCR amplification has succeeded in the recent sequencing of human genome. Establishing the base sequence of individual DNA without the PCR technique evolves great challenges in biotechnology. Attribute to high strength and unique physics property, low-dimensional carbon structures are widely used in bio-technology. Recent researches indicate that the carbon nanotube and graphene have great potential to sequence the individual DNA[2-3].

In this work, the single-walled carbon nanotube (SWNT) is used to detect the DNA sequence information basing on van der Waals interaction. Single strand DNA (ssDNA) is pulled out of the SWNT. The pulling force fluctuates around a plateau. The amplitudes of fluctuations relate to the nucleotide type, and the radius of the SWNT. One may determine the base type of the ssDNA by the distinction of the amplitude. Moreover, the force plateau can be reduced by charging the SWNT, letting the measuring range down, and promoting the measuring precision.

Method

The molecular simulation is performed by software GROMACS[4-5]. The single strand DNA (ssDNA) is depicted by GROMOS-96 force field[6]. The bond interaction among carbon nanotube is described a Morse bond, a harmonic cosine angle, and a cosine torsional potential[7]. The non-bond interaction is portrayed by Lenard-Jones (L-J) potential. Furthermore the L-J parameters of the atoms among the DNA-SWNT system not mentioned in reference 6 and 7 are determined by geometrical average[8].

The Berendsen method[9] is used to maintain the temperature at the room temperature (300K). The ssDNA with 15 homogeneous bases is centered in a uncapped (15, 15) or (20, 20) SWNT, with length of 18.3nm. Four serials of simulation are carried out to investigate the distinction among homopolymers of dA (deoxyadenylate), dC (deoxycytidylate), and dT (deoxythymidylate), respectively.

Three steps of simulation are carried out. The first two are energy minimization and relaxation. The third simulates the pulling out process. Two atoms at each end of the SWNT are restrained at their initial positions in the last two steps. In the pulling process, a dummy atom is linked to 3' end of the ssDNA through a spring, with elasticity constant of K = 20000 kJ/(mol • nm). *Via* pulling the dummy atom in the 5'-3' direction of ssDNA, the biomolecule is drawn out from the SWNT.

Results

The process of pulling a piece of ssDNA out of a carbon nanotube is similar to the process of dragging a string of carts stepping up a hillside on a smoothing ground. Fig. 1a and b illustrate these two processes. The smoothing ground never hinders the carts moving. The pulling force drawn at the right side is only related to the weight of the cart climbing the hillside, and the cargo in it. The cargo is loaded every other carts, leading to the pulling force fluctuates around a plateau. The height of plateau is related to the average weight of the carts and the cargoes in length. The amplitude of the fluctuation is related to the weight of the cargo. The tiny energy barrier of SWNT resembling the smoothing ground, hardly hinder the ssDNA moving in it. When the ssDNA comes out of the outlet of the SWNT, the van der waals interaction between DNA and SWNT resembles the gravity, the backbone resembles the string of carts, and the bases hanging on the backbone resembles the cargo in the carts. As analysis of the carts stepping up the hillside, the pulling force of the ssDNA fluctuates around a plateau, as shown in fig. 1c.

The different bases have different vdW interaction energies with the SWNT. At the same time the vdW energy also influenced by the geometry of the carbon nanotubes, as listed in the table 1. Higher curvature leads to higher vdW energy. The vdW energies of dG and dC are the largest and the tiniest both in (15, 15) and (20, 20) SWNT. Due to the geometry confine, the purines which has larger area, hardly adhere closely to the SWNT with small radius, leading to the vdW energies between nucleotide of purines tend smaller comparative with pyrimidines. Therefore the vdW energies emerge different magnitude order between dA/dT and (15, 15)/(20, 20) SWNT.

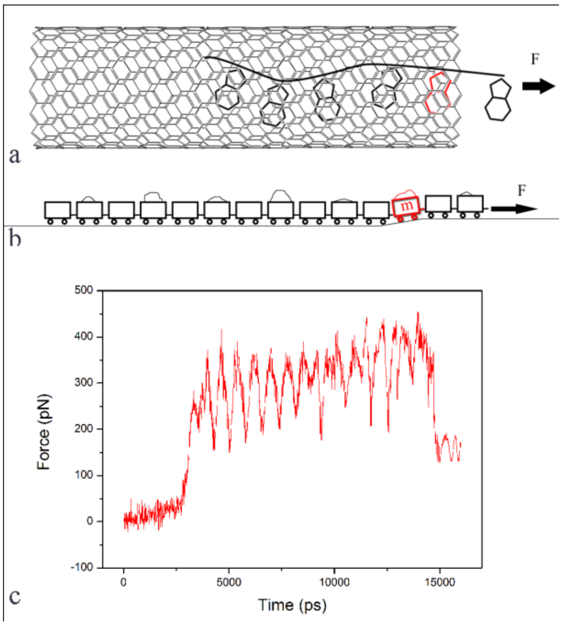

Fig. 1 The schematic of pulling a ssDNA out of a SWNT (a) and dragging a string of carts up a hillside (b), and the ssDNA with dT pulling force history (c).

The distinct energies lead to different fluctuation amplitude of the pulling force, shown as fig. 2. Combining these fluctuation amplitude magnitude results, one may get the sequence information. The smallest amplitude of pulling force from both kind of SWNT indicates the dC nucleotide, the largest amplitude from (15, 15) SWNT indicates the dT nucleotide, the largest amplitude from (20, 20) SWNT indicates the dG nucleotide, and the last one indicates the dA nucleotide.

Table 1. vdW energy between DNA and SWNT

	dA	dG	dC	dT
(15, 15)	-60.0	-66.7	-51.1	-62.3
(20, 20)	-58.6	-65.0	-47.0	-58.4

Negative charging SWNT lowers the force plateau, due to the ssDNA is negative electrification. DNA and SWNT with like charges repel each other, counterpoising the vdW attracting force. As shown in fig. 3, favorable quantity of electricity of the SWNT reduce the force plateau to about 0 pN, letting the measuring range down, and promoting the measuring precision.

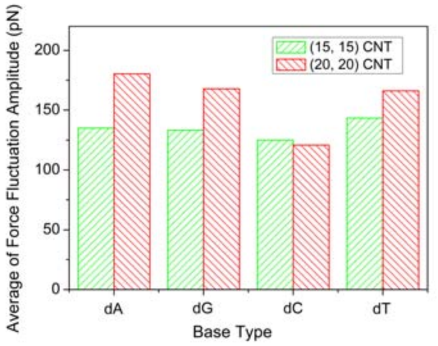

Fig. 2 The average fluctuation amplitude of pulling force

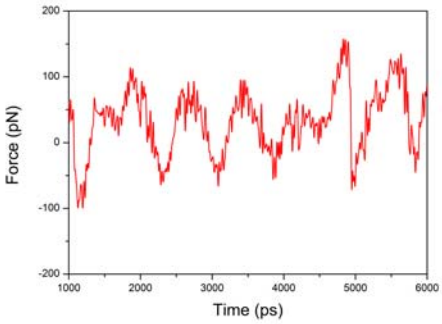

Fig. 3 The ssDNA pulling force history in a charged SWNT. 6000 atoms on (15, 15) SWNT are charged by 1 electron charge.

Conclusion

Different nucleotides have different vdW energy to SWNT. And the radius of SWNT influence the vdW energy between nucleotide and nanotube. The SWNT has great potential to sequence ssDNA by pulling out the ssDNA.

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