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Fast DNA sequencing with nanopore-embedded graphene electrodes

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1. Introduction:

Over the past years there have been great advances in the fabrication of nanopores and their use for molecular recognition and genome analysis [1,2]. The recent proposal of using nanopore-embedded graphene nanoelectrodes for electrically sequencing DNA is particularly attractive since it predicts to achieve single-base resolution [3], which is very challenging for metal nanoelectrodes technically. However, there has been no direct simulation study of the proposal. In this paper, we report a theoretical study of DNA sequencing using graphene nanoelectrodes. The methodology and findings demonstrates several advantages of the proposed approach, which may lead to some important applications in genome sequencing.

2. Device structure

Fig.1 gives a schematic view of nanopore-based DNA sequencing: a single-stranded (s-s) DNA molecule is being driven electrophoretically through a nanopore under longitudinal electrical field E_x, while the transverse tunneling conductance G is kept records of for sequencing. Fig.2 shows the cross-section of a nanopore with graphene nanoelectrodes in the *y-z* plain. The nanopore is built in a SiN-graphene-SiN sandwich structure: a graphene layer works as transverse electrodes in the middle of nanopore, while two 4~6 *nm* SiN membranes lie at two ends insulating the electrodes from the solution environment. Here four electrodes are defined to provide more flexibility for conductance measurement. The inner diameter of nanopore is 1.1 *nm*, wide enough for the passing through of a s-s DNA molecule, meanwhile narrow enough for measurable transverse tunneling conductance. Fig. 3 gives a snapshot of the translocation of DNA through the nanopore in *KCl* solution.

3. Modeling and simulation methods

Table 1 presents the simulation flowchart and some key formula and software used. First, translocation of s-s DNA through nanopore is simulated with NAMD [4], a classical molecular dynamics (MD) package using Amber force-field parameters [5]. Then the real-time atomic configuration is extracted from MD trajectory files, and the corresponding real-time electronic structure of DNA during the DNA translocation is calculated within extended Hückel model using YAeHOP [6]. Finally, characteristic resonance levels (A, T, C, G) are picked out for each kind of nucleotide, and the corresponding transverse tunneling currents are calculated with Landauer-Büttiker formalism and nonequilibrium Green's function technique [7].

4. Electronic signatures of nucleotides

Fig. 4 plots the transverse transmission spectrum, nucleotide densities of states (DOS) and their projections on base atoms of poly$(dX)_{30}$ (X=A,T,C,G) at one typical snapshot during the translocation. The resonance levels which can be used as electronic signatures of different nucleotides are characterized as α, β and γ in the figure. First, these local densities of states (LDOS) of nucleotides are made up by base atoms but not by backbone atoms and thus can serve for sequencing; second, the resonance transmission observed in this figure indicates that the transverse electrical properties are determined by these resonance levels of nucleotides; last but not the least, each nucleotide has its characteristic resonance levels, making unique electronic signatures as seen in transverse transmission and conductance spectrums. Fig. 5 and Fig. 6 plot the fluctuations of γ level of guanine during the translocation and the distribution of transverse electrical currents near that level. It shows that the differences between electrical currents of different homogeneous polynucleotides are of order, thus making different nucleotide identified. Fig. 7 demonstrates that at other resonance level, the selectivity may be not so good. It is worth mentioning that the selectivity achieved in Fig.5-7 is much greater than previous approaches. Finally, a comparison between approach using nanopore-embedded graphene nanoelectrodes and that using gold nanoelectrodes is presented Table 2. Single-base resolution could not be obtained for the latter case once there are two or more residues close enough to nanoelectrodes and conducting simultaneously as seen in Fig.8. In summary, sequencing with graphene nanoelectrodes can achieve single-base resolution and are more feasible technically despite weaker conductance measurability.

5.Conclusions

We set up model and perform simulation of DNA sequencing with nanopore-embedded graphene nanoelectrodes. Simulation results show that compared to sequencing with gold nanoelectrodes, much improved discrimination of different nucleotides and single-base resolution are achieved. The achieved results can provide a design guide for future realization of nanopore-based electrical DNA sequencing.

References: [1] M. Zwolak and M. Di Ventra, Rev. Mod. Phys. **80**, 141 (2008). [2] D. Branton et al, Nature Bio., vol. 26, pp. 1146, 2008. [3] H. Postma, Nano Lett. **10**, 420 (2010). [4] L. Kale, J. Comput. Phys., vol. 151, pp. 283, 1999. [5] W. Cornell et al, J. Am. Chem. Soc., vol. 117, pp. 5179, 1995. [6] G. Landrum, Ph. D. dissertation, Cornell Univ., 1997. [7] M. Di Ventra, Electrical Transport in Nanoscale Systems, Cambridge Univ. Press, 2008.

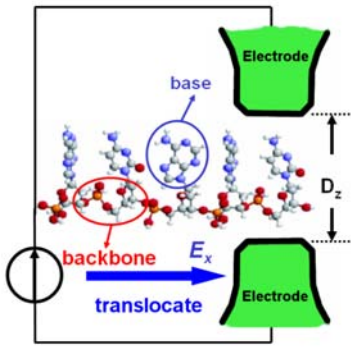

Fig.1 Schematic view of a single-strand DNA translocating through a nanopore under electrical field, while transverse conductance is recorded for sequencing.

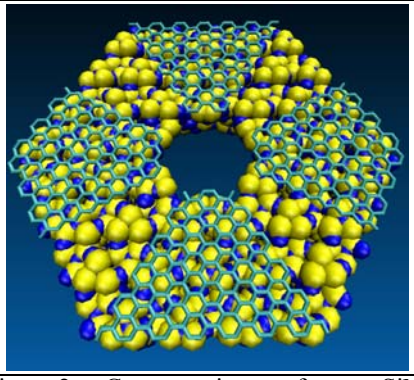

Fig. 2 Cross-section of a SiN-graphene-SiN nanopore in *y-z* plain: Si Atom (yellow), N (blue), C (cyan). Here four electrodes are defined.

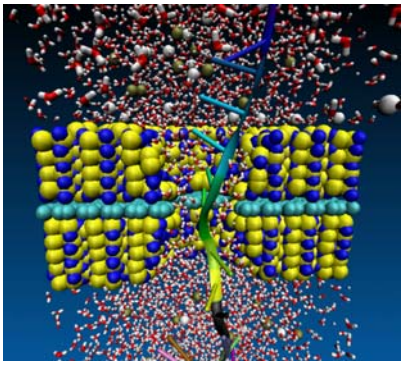

Fig. 3 a snapshot of a single-strand DNA molecule translocating through the graphene-embedded nanopore: K (brown), Cl (grey), H_2O (licorice)

➢Translocation through nanopore
Molecular Dynamics simulation:
$-\nabla V = m\vec{a}$
$V = V_{bond} + V_{angle} + V_{dihedral} + V_{improper} + V_{vdw} + V_{es}$
(Tool: NAMD + VMD)

Real-time atomic configuration

➢Electronic structure during translocation
Extended Hückel Model:
$H_{ij} = kS_{ij}(H_i + H_j)/2$ (Tool: YAEHMOP)

Characteristic resonance levels

➢Real-time transverse conductance
Landauer-Büttiker Formalism:
$I_{ij} = \frac{q^2}{hkT}\int d\varepsilon T_{ij}(\varepsilon)[f(\varepsilon,\mu_i) - f(\varepsilon,\mu_j)]$
$T_{ij}(\varepsilon) = Tr[\Gamma_i G^r \Gamma_j G^a]$ (Tool: NEGF)

Table 1: Simulation flowchart and key formula and software used in simulation.

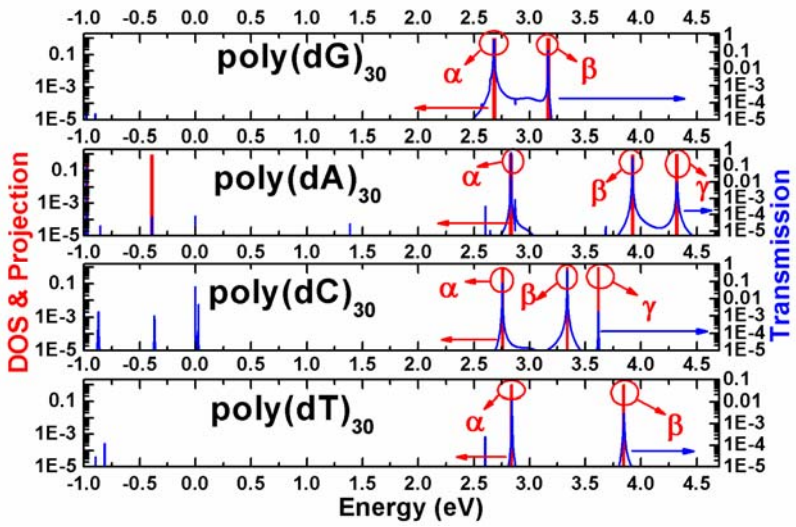

Fig. 4. Resonance levels (red lines) and transverse transmission spectrum (blue lines) of poly(dX)$_{30}$ (X=A, T, C, G) near the Fermi energy at some typical snapshots during the translocation.

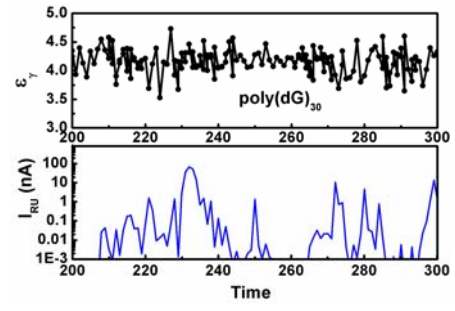

Fig.5. real-time fluctuations of $[\varepsilon_\gamma]_{guanine}$ and the corresponding transverse tunneling currents at $V_0=[\varepsilon_\gamma]_{guanine}$.

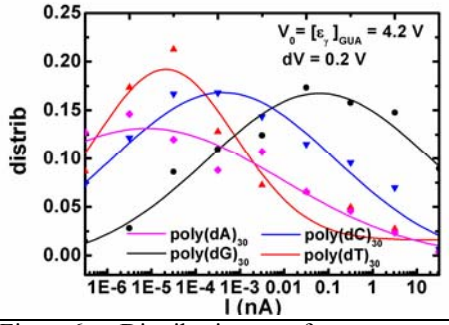

Fig. 6. Distributions of transverse tunneling currents of poly(dX)$_{30}$ (X=A, T, C, G) at $V_0=[\varepsilon_\gamma]_{guanine}$.

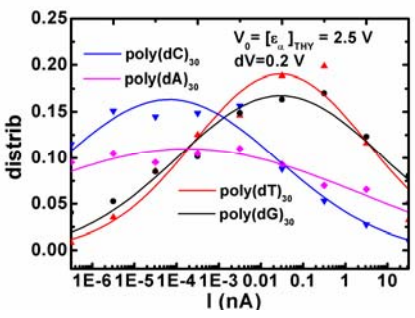

Fig. 7. Distributions of transverse tunneling currents of poly(dX)$_{30}$ (X=A, T, C, G) at $[\varepsilon_\alpha]_{thymine}$.

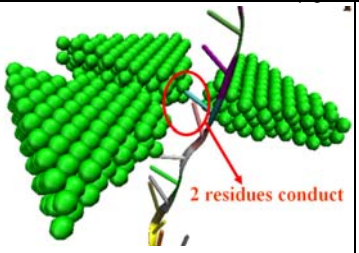

Fig. 8. A schematic view of sequencing with gold- embedded nanopore. The two residues conducting simultaneously are characterized.

embedded electrodes	Error rate (Single-base Resolution)	G_{max} (Conductance measurability)	Process feasibity
Graphene	**< 10%**	**~0.1 nA**	√
Gold	**> 30%**	**~10 nA**	**Difficult**

Table 2: A comparison between DNA sequencing with graphene-embedded nanoelectrodes and that with gold-embedded nanoelectrodes.