Nanoelectronics Tools for DNA Sequencing

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Direct sequencing of the human genome using electronic measurements is potentially orders of magnitude faster than existing methods. The proportionally lower cost enables this technology to be used in everyday clinical practice for genome-based medical treatments. This tutorial will discuss challenges, controversies and open problems in this approach, as well as promising routes to their solution.

The possibility of genome sequencing by measuring the transverse conductivity upon applied electric bias while a single or double stranded DNA is translocated through a nanogap or nanopore between metallic or CNT electrodes has recently been a subject of great interest [1] on the theoretical approaches and results, and significant experimental activities . The theoretical studies show that the dc transverse conductance of a nucleotide is sensitive to its location, orientation, and geometric shape. The variation in the conductance due to the geometry of the molecule relative to the electrodes can overwhelm the difference between different types of nucleotides. This makes the reliability issue the major obstacle for DNA sequencing using the dc conductance measurement. Molecular eigen-levels of the DNA nucleotides, are quite far (~2 eV) from the Fermi energy of gold electrodes at 0 K. As a consequence, the electronic transport between the electrodes is dominantly a non-resonant tunneling, strongly dependent on the geometry conformations of a nucleotide in the inter-electrode gap, that is difficult to control since it is dependent on aqueous/electrolytic environment, thermal conditions, and the effects of the applied transverse as well as longitudinal (translocating) electric fields. Simultaneously, the tunneling electrons are insensitive to the energetically distant electronic structure of a nucleotide, which is reflected in a weak and a difficult-to-calibrate dependence of the conducting current of a DNA base as it is instantaneously positioned in the gap. At transversal voltage biases low enough to both prevent electric breakdown and allow translocation of the negatively charged DNA strand through the gap, low values of the nonresonant tunneling current, typically of the order of pA-to-sub-pA, yield poor signal-to-noise ratio, further weakening chances for reasonable certainty in the genome sequencing with such a device. Thus, in spite of tremendous progress in understanding the problems, a targeted fully distinguishable difference between the DNA bases by electron transport is not established yet either theoretically or experimentally. More advanced theories and precise gap measurements are needed to resolve these issues.

Control of geometry during the DNA translocation through a nanogap/nanopore is the essential predecessor for achieving the sequencing of the DNA bases from electrical conductance measurements. The sensitivity of quantum transport on the interface geometry is not limited to the transversal DNA measurements; it is a universal effect that makes measurement in a single molecule particularly difficult. An attractive idea is development of a quadrupole Paul type nanotrap/nanofilter which provides opportunity for isolation, trapping, localization and control of the DNA motion during translocation, as the predecessor for the sequencing. The discovery of a quasi-resonant tunneling regime, based on H-bonding, that results in several orders of magnitude increase in the transverse tunneling current using nitrogen doped carbon nanotube electrodes, may lead to a significant increase of the signal-to-noise ratio in the electronically based DNA sequencing. A number of other recent studies and approaches to the problems of the DNA control and electronic detection will be also presented and discussed.

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[1] D. Branton at al, Nature Biotechnology 26, 1146 - 1153 (2008) | doi:10.1038/nbt.1495