Development of Single-Molecule Tunnel-current based Electrical Identification of DNA/RNA nucleotides

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Single-molecule electrical genome sequencer is one of the important technologies for a realization of personal medicine. We have been proposed a tunneling-current based identification as a candidates for a single-molecule DNA/RNA sequencing. This methodology is based on sequentially reading the tunneling-current across individual single-nucleotides in the sequence, resulting in a high-speed electrical discrimination of the individual nucleotides without chemical probes and PCR amplifications. In this study, we report on a read of DNA / RNA sequence by the tunnel-current intensity during translocating through nanogap-electrode. When the molecules passed between the nanoelectrodes separated by a sub-nanometer gap, the tunneling-current through the molecules was in-creased, relative to that in the absence of molecules. The current intensity is closely related to the individual electronic conductance. We measured the extent of the electron-tunneling by using nanofabricated, mechanically controllable break junction (nano-MCBJ).

We investigated the conductance values of single base molecules of DNA and RNA, and determined the conduct-ance values for four deoxyribonucleoside monophosphates (dAMP, dCMP, dGMP, dTMP) and four ribonucleoside monophosphates (rAMP, rCMP, rGMP, rUMP). The magnitude of the peak conductance of four nucleotides was found to be in the following order: dGMP > dAMP > dCMP > dTMP, and rGMP > rAMP > rCMP > rUMP. This conductance values is due to the individual molecular energy level. In addition, the methyl cytosine, methyl adenine monophosphate were also measured, and each of the relative conductance values to the dGMP conductance was determined. Calculations based on density functional theory indicated that the order based on the highest occupied molecular orbital (HOMO) energy was similar to our experimental results. Note that this order corresponds to the order of the relative G values, suggesting that our single-molecule electrical detection method can identify molecular species based on characteristic energy levels, particularly the HOMO energy level.We also applied this single-molecule electrical identification method to base-typing of microRNA in oligonucleotides. Based on the electrical conductivity for single-nucleotides, we identified the

base-type in the sample oligonucleotides. We can read the fragment of sample nucleotide passing through the sensing electrode. On the basis of a reconstruction of the read fragment sequences, we successfully determined a sample RNA sequence. This single-molecule electrical sequencing using nano-gap device can be used to randomly identify sequences of single base DNA/RNA molecules.

References

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[2] Tsutsui M, Matsubara K, Ohshiro T, Furuhashi M, Taniguchi M, Kawai T. Electrical detection of single methylcytosines in a DNA oligomer. J Am Chem Soc. 2011 Jun 15;133(23):9124-8.

Figures

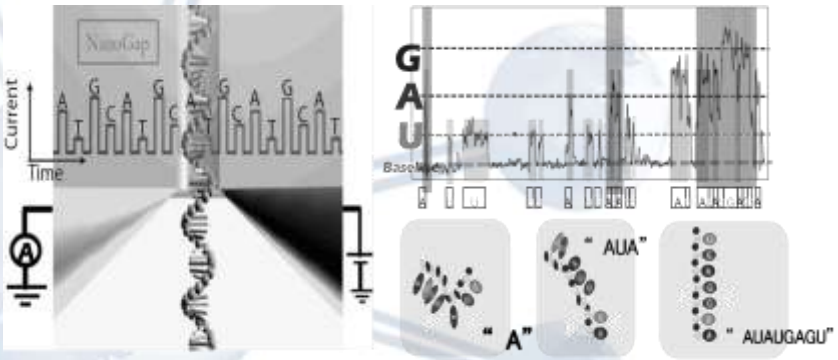

Figure 1. Schematics of Tunnel-Current Measurements(left), I-t profiles for UGAGGUA nucleotide (right)