DNA Sequencing Using an Engineered Protein Nanopore

JENS H. GUNDLACH, University of Washington

Inexpensive and fast sequencing of DNA is of paramount importance to medicine, the life sciences and to many other applications. Because of the nanometer diameter of DNA a nanometer-scale reader directly interfaced to macroscopic observables seems particularly attractive. We are working on a new single molecule technique based on a biological pore embedded in a lipid bilayer. When a voltage is applied across the bilayer an ion current is measured that flows through the nanometer opening of the pore. Poly-negatively charged single stranded DNA passes through the pore and reduces the ion current with the remaining ion current being indicative of the nucleotide type in the constriction of the pore. The protein pore that we introduced to the field, MspA, has a shape ideally suited to nanopore sequencing, has robustness comparable to solid state devices, is easily reproduced with sub-nanometer level precision and is engineerable using genetic mutations. I will present proof-of-principle data showing that this technique can lead to a direct very inexpensive and fast sequencing technology. The experimental electronic signatures of the DNA translocation process provide an ideal test bed for molecular dynamics simulations, which in turn allows developing intuition and prediction of nanoscale dynamics.

1Supported by NIH grant 1R01HG005115