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Nanapore Sequencing with MSPA[1]

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Nanopore sequencing is the simplest concept of converting the sequence of a single DNA molecule directly into an electronic signal. We introduced the protein pore MspA. derived from Mycobacterium smegmatis, to nanpore sequencing [1]. MspA has a single, narrow (-1.2nm) and short (<1nm) constriction, ideal to identify single nucleotides. Compared to solid state devices, MspA is reproducible with sub-nanometer precision and is engineerable using genetic mutations. DNA moves through the pore at rates exceeding 1nt/microsec. too fast to observe the passage of each nucleotide. However, when DNA is held with double stranded DNA sections or an avidin anchor, single nucleotides resident in MspA's constriction can be identified with highly resolved current differences. We have provided proof of principle of a nanopore sequencing method [2] in which we use DNA modified by inserting double stranded DNA-sections between every nucleotide. The double stranded sections are designed to halt translocation for long enough to sequentially read the sequence of the original DNA molecule. Prospects and developments to sequence unmodified native DNA using MspA will be discussed.

[1] T.Z. Butler, et al, PNAS 105 20647 (2008)
[2] I.M. Derrington, et al, PNAS 107 16060 (2010).

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