

High-throughput low-cost DNA sequencing has emerged as one of the challenges of the post-genomic era. Here we present the proof of concept for a new single-molecule platform that allows for DNA identification and sequencing. In contrast with most present methods, our scheme is not based on the detection of the fluorescence of incorporated nucleotides, but rather on the measurement of a DNA hairpin length. By cyclically modulating the force pulling on small magnetic beads tethered by a hairpin to a surface, one can unzip and rezip the molecule. In the presence of complementary oligonucleotides in solution, reziping may be transiently interrupted by the hybrids they form with the hairpin. By measuring the extension of the blocked hairpin, one can determine the position of the hybrid along the molecule with nearly single base precision. Our approach, well adapted to a high-throughput scheme, can be used to identify a DNA fragment of known sequence among a sample of various fragments and to sequence an unknown DNA fragment by hybridization or ligation