Optical-Electro Readout of Single Molecular Metastable States in Confined Spaces

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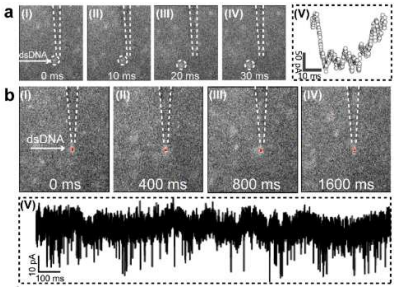
Nanopores act as excellent single-molecule sensors to rapidly acquire information of single molecules from the significant statistics. Plenty of pervious experimental and theoretical nanopore researches illustrated diverse single molecules motions and behaviours based statistical analysis and modelling.[1,2] However, the challenge still remains in resolving and classification of each single molecules signals to uncover the precise motion behind the electrical response. Here, we employ a simultaneous electro-optical readout approach to interrogate each single molecule behaviours in confined spaces. By virtue of the high performance EMCCD and the ultralow current amplifier, it could be easily achieved to record synchronous images of fluorescent dye-labelled dsDNA with current signatures of each single molecule interacting with the quartz nanopore in real-time.[3] Different frfom conventional cognition for electrical read-outs, our results show that bumping events could contribute significant voltage-dependent current oscillation with a long dwell time, which usually hardly discriminates from the translocation events in conventional electric readouts (Figure 1a). By real-time tracking the single-molecule motion, we further observed a cluster of distinct signals in several hundred microseconds originates from only one molecule repeatable blocked at the tip of the quartz nanopore instead of corresponding successive molecules translocation events (Figure 1b). The result suggests that the DNA molecule undergoes complex conformation transitions at the tip of the nanopore to overcome the translocation barrier. By utilizing this simultaneous electro-optical readout strategy, around 5 types of different single molecule conformations could be distinguished from the current signals and the fluorescent images. This method paves a new path for nanopore sensing of individual single molecules motion which could also provide the visible evidence for further investigation.



References

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