Dynamics of binding and translocation of short nucleotides in the aerolysin pore: evidence for multiple interaction sites

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Polymer interactions with pore-forming membrane proteins, as evidenced by the resulting block of ionic current, are of two types: (1) the threading of an extended polymer chain of which only a small length interacts with the pore at a time (2) a binding reaction, where the polymer enters the pore entirely and interacts as a particle. Threading typically occurs in dilute aqueous electrolyte solutions (e.g. KCl < 1 M), requires long and charged molecules and is the basis of nanopore sequencing (e.g. of DNA). In contrast, the binding reaction typically occurs with short, neutral polymer molecules, requires high salinity (e.g. KCl 3-4 M) and enables the high-resolution discrimination of polymer masses[1].

The aerolysin nanopore has recently been shown to strongly interact with short adenine oligonucleotides (A3-A10) and this interaction allows mass discrimination on the basis of the depth of block of ionic current induced by the binding of the analyte[2], suggesting a binding-type interaction. Using low-noise high-bandwidth current recording, we have identified strong dynamics of this interaction between DC and 50 kHz and detected short visits to deeper blocked states preceding and following the principal, mass-dependent state (termed pre- and post-blocks). Statistical analysis indicates that the probability of post- but not pre-blocks decreases with (1) oligomer length and (2) transmembrane voltage. We interpret this finding in terms of a combined translocation and binding interaction, probably involving several binding sites for DNA in the pore.

(1) Robertsonet al. Proc. Natl. Acad. Sci. U S A 2007, 104, 8207–8211.

(2) Cao et al. Nature Nanotechnology 2016, 1–7.