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Sequence-dependent ion current modulations in biological and synthetic nanopores[1]

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The possibility of DNA sequence detection by measuring the blockade ionic current in nanopores has been the driving force for the spectacular development of the nanopore research field. Nevertheless, fifteen years after the first measurements, the molecular mechanism(s) of ion current modulation by the sequence of DNA nucleotides remains elusive. Here, we report the results of extensive all-atom molecular dynamics and Brownian dynamics simulations of three nanopore systems: a biological nanopore MspA, a solid-state nanopore and a graphene nanopore, aimed at elucidating the microscopic mechanism of the ion current modulation. In the case of solid-state and graphene nanopores, we determined the effect of sequence convolution on the ionic current value by simulating the ionic current blockades produced by all 64 permutations of the DNA nucleotide triplets. In the case of MspA, we determined the effect of the sequence, the global orientation, and the conformation of a DNA strand on the distribution of the ion current blockades. Based on the results of our simulations, we suggest possible routes for increasing the resolution of DNA sequence detection by measuring the nanopore ionic current and describe the inherit limitations of the method.

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