Sensing single molecule penetration into nanopores: pushing the time resolution to the diffusion limit

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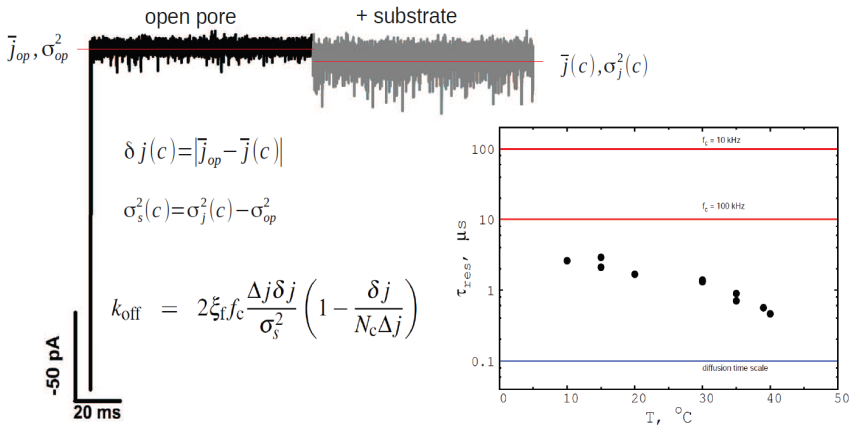
To quantify small molecule penetration into and eventually permeation through nanopores we applied an improved excess-noise analysis of the ion current fluctuation caused by entering molecules in the single-channel electrophysiology experiment. The kinetic parameters of substrate entry and leave are derived from a Markov-state model by analyzing the substrate concentration dependence of the average ion current and its variance. Including filter corrections allows one to detect the transition rates beyond the cutoff frequency, f_c , of the instrumental ion-current filter. As an application of the method, we performed the analysis of the single-channel ion current in the presence of meropenem, an antibiotic of the carbapenem family, interacting with OmpF, the major general outer membrane channel of Escherichia coli bacteria. At 40 °C, we observed the correlation time of the channel gating process of about 500 nanoseconds – more than two orders of magnitude smaller than f^{-1}_c and close to the diffusion limit of few hundred nanoseconds. We also have established theoretical limit conditions under which the substrate-induced channel blockages can be detected and suggest that sub-microsecond-scale gating kinetic parameters are accessible with existing experimental equipments. This analysis opens up the way to detect the weak affinity substrate binding to nanopore, expanding the use of the single-channel electrophysiology to less specific systems and for the time-scales accessible in the all-atom simulations.



References

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