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

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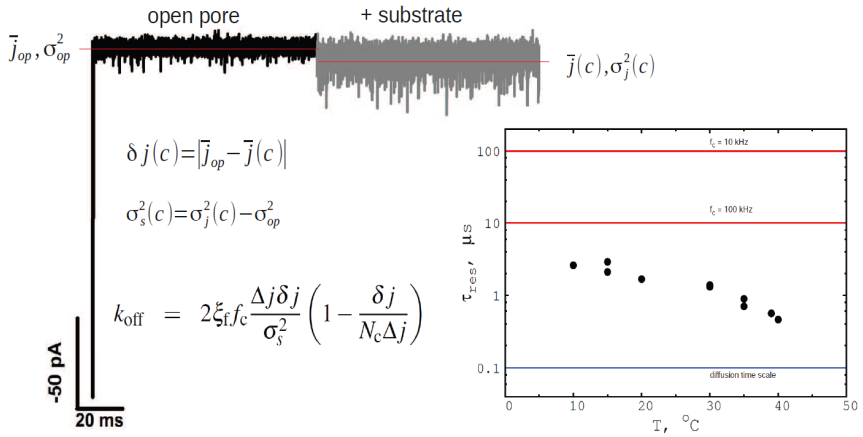
To quantify small molecule penetration into and eventually permeation through nanopores we applied an improved excess-noise analysis of the ion current fluctuation caused by entering molecules. The kinetic parameters of substrate entry and leave are derived from a two-state Markov model analyzing the 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 an analysis of the single-channel ion current 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 a correlation time of the channel gating process of about 500 nanoseconds – more than two orders of magnitude smaller than f_c^{-1} 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.



References

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