

表面電荷揺らぎ防止によるソリッドナノポアの低周波ノイズ低減法

Low-frequency noise reduction with solid-state nanopores by preventing surface charge fluctuation

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To realize DNA sequencing with solid-state nanopore, reduction of an ionic current noise is an important issue. Especially, low-frequency noise causes a serious problem for reducing read accuracy of DNA sequencing. The low-frequency noise consists of binary current fluctuations, and the noise is similar to the blockade current. To maximize the signal-to-noise ratio in DNA translocation, any baseline current fluctuations should be minimized. Ever since the discovery of the noise, its origins have been heavily debated, but it has not yet clarified. An effective method for the noise reduction is not also established. One of the convincing explanation includes surface charge fluctuations such as the transitions between the association and dissociation of a proton (H^+) on a nanopore wall surface. Hoogerheide, D. P. *et al.* suggests that the noise is due to the surface charge fluctuations on silicon oxide group: $SiO^- + H^+ \rightleftharpoons SiOH$. They measured the noise over broad pH ranges, and the pH-dependence roughly matches with the theoretical predications [1].

In this research, we identify a new origin of the noise due to the following exchange reaction of metal ions (M^+) contained in solution (Fig. 1(a)): $SiOM + H^+ \rightleftharpoons SiOH + M^+$. We hypothesized the charge fluctuations are dependent on the equilibrium constants of M . With various cations ($M = Li, Na, K, Rb, Cs, Mg, Ca$), its low-frequency noise coefficient $C_{lf} = S(1 \text{ Hz})/I^2$, which is the magnitude of the low-frequency noise, was compared. C_{lf} is the largest at Cs, and its current consists of large multi-level noise due to the complex binary fluctuation (Fig. 1(b)). The order of C_{lf} ($Li < Na < K < Rb < Cs$) follows the theoretical one estimated from their equilibrium constants (Fig. 1(c)). We calculated from C_{lf} equilibrium selectivity coefficients K_M ($M = Li, Na, K, Rb$) which was determined with Cs as a reference cation. Surprisingly, K_M almost matches with the reference values. This result supports the validity of our proposed hypothesis.

To reduce the low-frequency noise, we developed a new procedure preventing the absorption of Cs. First, a nanopore was fabricated with 1 mol/L $CaCl_2$ solution via controlled dielectric breakdown, and Ca absorbed on the cation-exchange spot. Second, the solution was replaced with 1 mol/L $CsCl$. Cs cannot absorb on the spot because the adsorption affinity of Ca is higher than that of Cs (Fig. 2(a, b)). C_{lf} was measured under 1 mol/L $CsCl$ solution using some nanopores which are fabricated with various cations (Fig. 2(c)). C_{lf} was largely reduced from $\sim 10^{-3}$ to $\sim 10^{-5}$ with divalent cation (Mg and Ca) whose affinity to silicon oxide group is larger than that of Cs. From these experiments, we verified the new hypothesis and established a noise reduction method by pre-wetting a nanopore with a solution containing divalent cations.

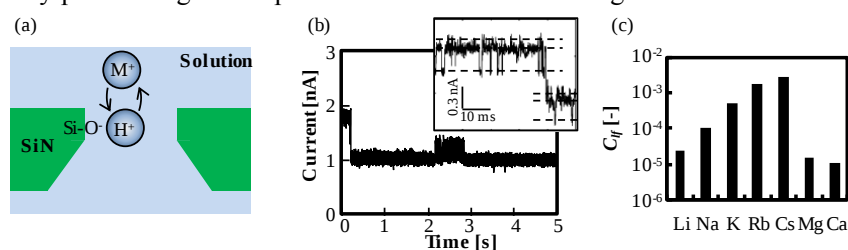


Figure 1. (a) Low-frequency noise model due to cation-exchange reaction. (b) Current trace of a nanopore fabricated with 1 mol/L $CsCl$ solution. Enlarged view shows multi-level noise (inset). (c) C_{lf} of nanopores with 1 mol/L MCl solutions including various cations ($M = Li, Na, K, Rb, Cs, Mg, Ca$).

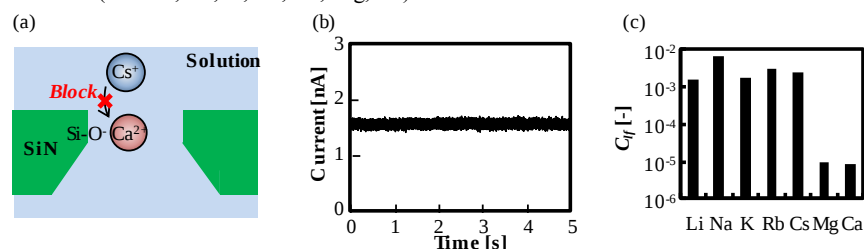


Figure 2. (a) Divalent cation-based nanopore fabrication for reducing noise. (b) Current trace of a nanopore fabricated with 1 mol/L $CaCl_2$ solution. The data was measured under 1 mol/L $CsCl$ solution. (c) C_{lf} of nanopores with 1 mol/L MCl solutions including various cations ($M = Li, Na, K, Rb, Cs, Mg, Ca$). All data were measured under 1 mol/L $CsCl$ solution.

References

- [1] Hoogerheide, D. P. *et al.*, *Phys. Rev. Lett.* 102(25), 256804 (2009).