Supplemental Information

Interpreting the conductance blockades of DNA translocations through solid-state nanopores

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S1. Employing the conductance model to analyze other experimental results The simple model presented in the main text utilizes free parameters that can be adjusted to predict the expected saturation conductance change, ΔG, for a wide range of experimental conditions. We have identified three previous works that report a voltage dependence for ΔG using dsDNA[1-3]. In Fig. S-1, we employ our model to predict an expected conductance change associated with the conditions used in each of these in order to verify the utility of the approach. Note that we use only the model describing translocation events (see Fig. 2 in the main text) and assume all counterions are stripped away (see main text).

First, we consider the work of Kowalczyk, *et al.*[1], who presented high-ionic strength measurements in multiple different solvents. From the materials description, we take SS-nanopore diameter, d_p, as 21 nm and effective membrane thickness L_{eff}=6.7 nm. Recall that we use the experimentally-determined[4] convention $L_{eff}=L/3$, where L is initial membrane thickness (20 nm in this case). In Fig. S-1, we show data for 1 M KCl (a), 1 M NaCl (b), and 1 M LiCl (c) overlaid with the ΔG resulting from our model (dashed lines), taking into consideration the electrophoretic mobilities of the three different cations. We find that the prediction matches very closely the ΔG measured at high voltage, which we take to be at or near the saturation of the curves.

A second example, published by Yang, *et al.*[3], is presented in a similar way in Fig. S-1d. Here, d_p=24.7 nm, L_{eff}=14.2 nm, and a solvent condition of 1 M KCl is used for the model, which results in a prediction (dashed line) that matches the experimental results within error.

Finally, we consider the results of Skinner, *et al.*[2], for which conditions of d_p=10 nm, L_{eff}=6.7 nm, and a 1 M KCl solvent are used. In this case, we find significant difference between the prediction (dashed line) and the apparent saturation level of the ΔG. However, we note that the authors characterize the group of SS-nanopores used in these experiments as, "approximately 10 nm in diameter"[2], implying that some deviation from this value may be present in the specific device used to collect this data. For comparison, we also plot the value predicted for the same experimental conditions, but with d_p=15 nm (solid line) and find significantly better agreement.

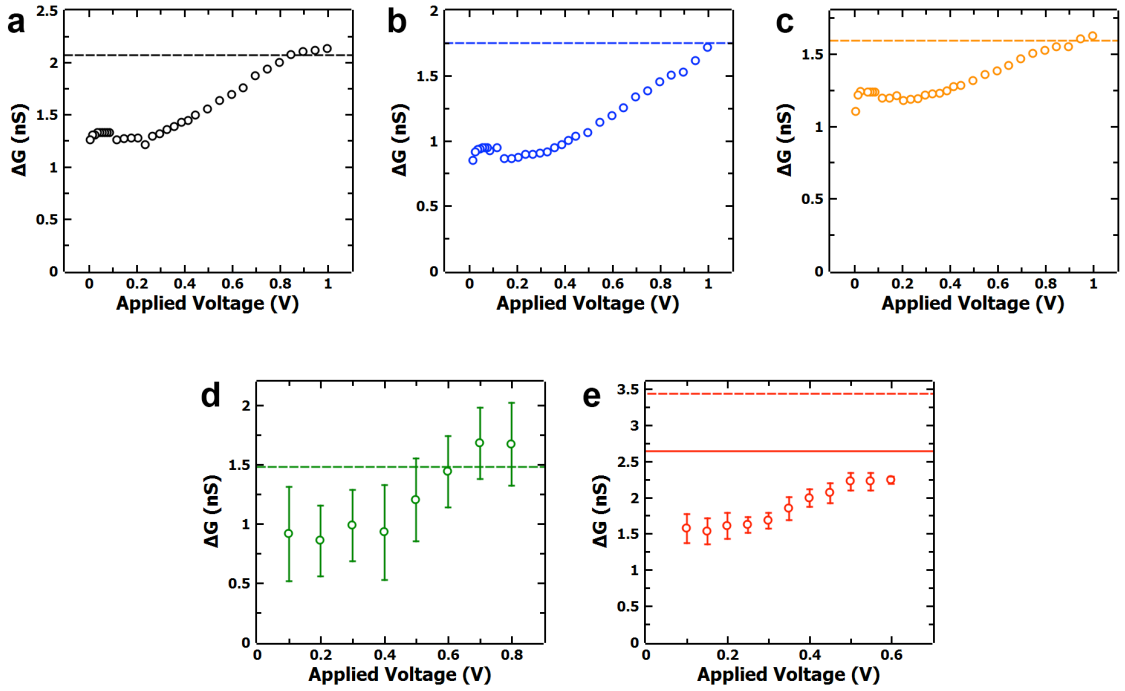

Figure S-1. Application of model to other published results Voltage-dependence of *ΔG* for dsDNA from Supplementary Reference 1 (a: 1 M KCl, b: 1 M NaCl, and c: 1 M LiCl), Supplementary Reference 2 (d), and Supplementary Reference 3 (e). Dashed lines represent the predictions of (saturated) *ΔG* from our model, considering the experimental conditions listed in the respective reports. The solid line in (e) represents the model result considering a nanopore diameter of 15 nm (see text).

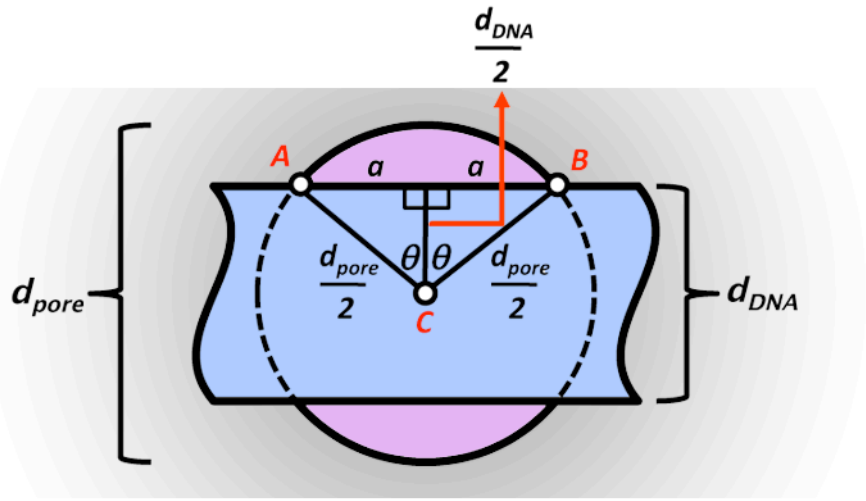

Figure S-2. Geometric model of lateral blocking of SS-nanopore Schematic of dsDNA (blue) laying laterally across a SS-nanopore (gray). The areas shaded in purple represent the remaining accessible area of the blocked nanopore.

S2. Geometric expression of DNA blocking a SS-nanopore laterally The unoccluded area of the laterally-blocked SS-nanopore are two segments of the circular pore, defined by the intersection of the dsDNA with the pore circumference (purple shaded regions in Fig. S-2). The area of one such segment, A_{seg}, can be expressed geometrically as

$$A_{seg} = A_{arc} - 2A_T, \qquad \text{Eq. S-1}$$

where A_{arc} is the area of the arc ABC and A_T is the area of the two right triangles defined by the same three points (blue regions in Fig. S-2). In terms of the known experimental quantities (nanopore diameter, d_p, and dsDNA diameter, d_{DNA}), A_{arc} can be written as

$$A_{arc} = \frac{d_p^2}{4}\theta = \frac{d_p^2}{4}\left(\cos^{-1}\left(\frac{d_{DNA}}{d_p}\right)\right). \qquad \text{Eq. S-2}$$

Line segment a at the base of the two right triangles is defined as $\frac{1}{2}(d_p^2 - d_{DNA}^2)^{\frac{1}{2}}$, and so A_T can be expressed as

$$A_T = \frac{1}{8} d_{DNA}\left(d_p^2 - d_{DNA}^2\right)^{1/2}. \qquad \text{Eq. S-3}$$

Approximating the unblocked pore as a circular region of area A_p^* and diameter d_p^*, we can therefore write

$$A_p^* = \frac{\pi}{4} d_p^{*2} = 2A_{seg} = \frac{d_p^2}{2}\cos^{-1}\left(\frac{d_{DNA}}{d_p}\right) - \frac{1}{2} d_{DNA}\left(d_p^2 - d_{DNA}^2\right)^{1/2}, \qquad \text{Eq. S-4}$$

and therefore

$$d_p^* = \sqrt{\frac{2}{\pi}\left(d_p^2 \cos^{-1}\left(\frac{d_{DNA}}{d_p}\right) - d_{DNA}\left(d_p^2 - d_{DNA}^2\right)^{1/2}\right)}. \qquad \text{Eq. S-5}$$

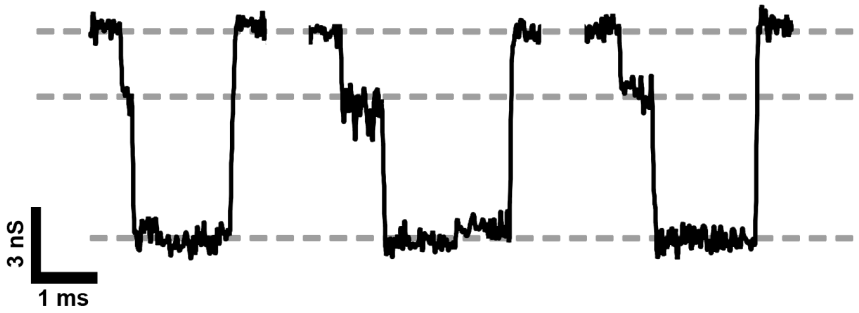

Figure S-3. Two-level events recorded at 50 mV Individual conductance blockade events consisting of a first level at about -2.5 nS and a second level at about -8 nS recorded at the lowest investigated applied voltage. These three events are the only two-level examples observed among 92 total events. Traces are low-pass filtered at 10 kHz.

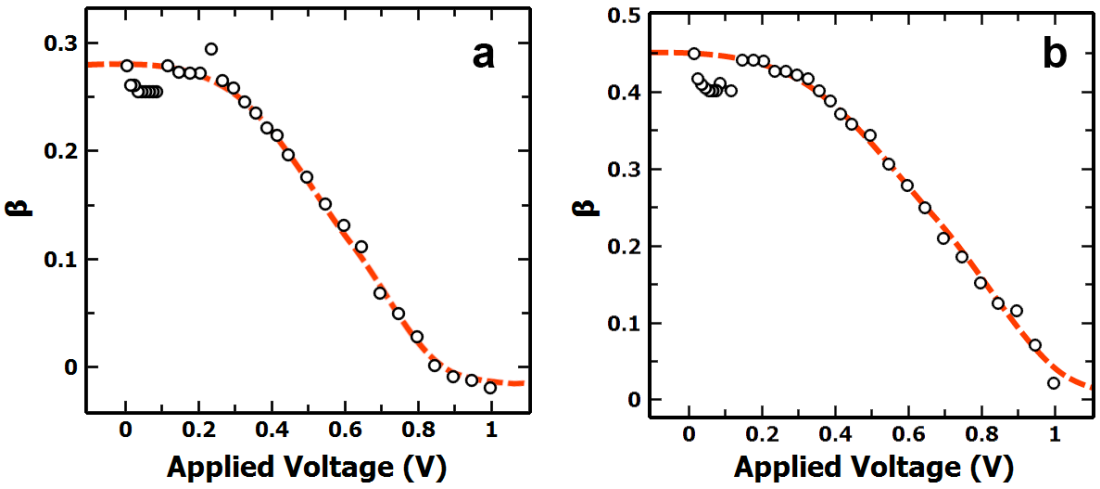

Figure S-4. Estimation of counterion screening of dsDNA in zero field Fractional counterion ion screening factor β vs. applied voltage for both the 1 M KCl data (a) and the 1 M NaCl data (b) from Supplementary Reference 1. β was adjusted in our model to account for the shifting ΔG in the data, yielding a sigmoidal relation. The low-voltage limit appears to fall around 0.28 for 1 M KCl, indicating that 72% of the dsDNA charge is screened by counterions in the absence of electric field. For 1 M NaCl, the low-voltage limit fall at about 0.45, indicating a screening of 55% in zero field. This agrees well with the NaCl data from the main text (Fig. 4), which yields 45% screening. The difference could root from the lower ionic strength used in our experiments (900 mM) compared to these data. The dashed lines are guides to the eye.

S3. Analysis of conductance blockade levels for small-diameter SS-nanopores Recent work by Wanunu, *et al*.[5]and van den Hout, *et al*.[6] explored the conductance signal resulting from measurements on dsDNA with SS-nanopores of diameter ~2-5 nm. Both reported the unexpected observation of multiple, discrete populations of ΔG and speculated that they originated from spurious (non-translocative) interactions with the pore.

Because our model can account for multiple different ΔG levels (translocative and interactions with one access region), we attempted to use it to analyze the results from both groups. In Fig. S-5, we plot all data from the two papers (Fig. 6 from Supplementary Reference 5 and Fig. S4 from Supplementary Reference 6) using the convention from those reports that defines I_B as the relative current blockade ($I_B = I_{blocked}/I_0$, where $I_{blocked}$ is the ionic current during the blockade and I_0 is the open pore ionic current). All data were taken on comparable devices and follow the same trends. In their initial reports, both groups attributed the low-level current blockade (green population in Fig. S-5) to pore occlusion using basic geometric models. However, the high-level population (red population) was not easily identified. Using the experimental conditions given in the two reports, we find that our models for translocation (solid line) and access region interactions (dashed line) yield trends that are in excellent agreement both data populations (Fig. S-5), assuming β=0.11 (i.e. 89% of dsDNA charge is screened by counterions; see Eqs. 9 & 10 from the main text). Considering that a voltage of 300 mV was used in these measurments and that the saturating blockade level usually does not occur until considerably higher applied voltage (c.f. Fig. S-1), this value of β is reasonable. We predict that similar measurements taken at higher voltage would yield

similar results as reported by the two groups, but both populations would be shifted to lower I_B (that is, larger ΔG).

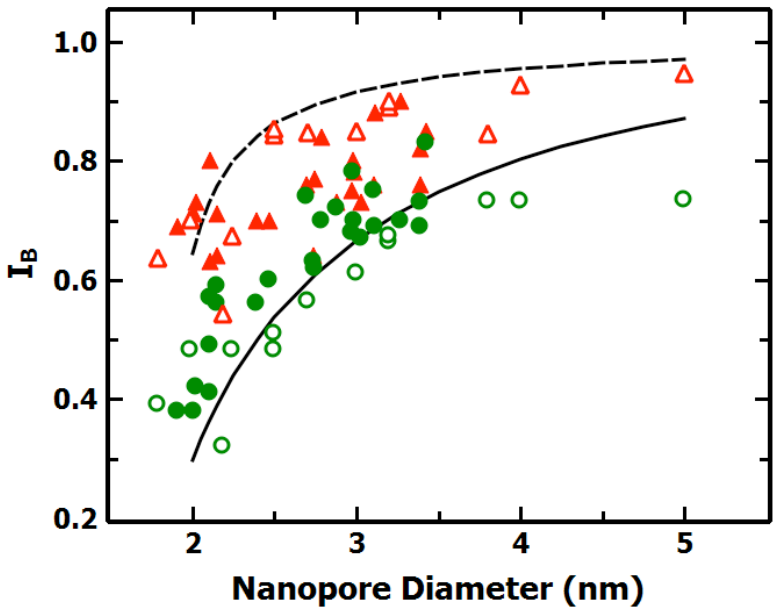

Figure S-5. Interpretation of published small-diameter SS-nanopore data Plotted data points are from Supplementary Reference 5 (solid symbols) and Supplementary Reference 6 (hollow symbols) recorded at 300 mV. Green circles represent the low-current level population and red triangles represent the high-current level population. The dashed and solid lines are predictions from our presented model using the experimental parameters given in the respective references and assuming β=0.11.

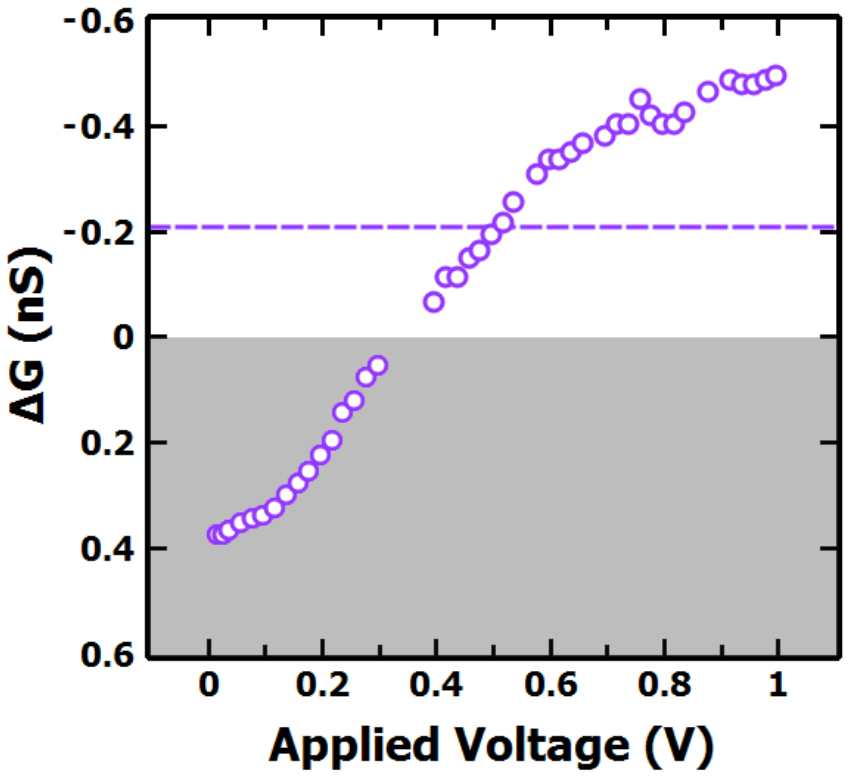

Figure S-6. Application of model to measurements in low ionic strength solvent Plotted are data for 0.1 M KCl from Supplementary Reference 1. The shaded region represents conductance *increases*. The dashed line is the value predicted from our model for β=0. While there is some quantitative disagreement with the experimental saturation level (~0.5 nS), we note that adjustment of β upward does result in the predicted ΔG decreasing to zero and then switching to conductance increases (negative ΔG). Thus the model does capture a major qualitative feature of the low-ionic strength data.

Supplementary References

1. Kowalczyk, S. W.; Dekker, C., Salt and Voltage Dependence of the Conductance Blockade Induced by Translocation of DNA and RecA Filaments Through Solid-state Nanopores. In *Nanopores for Bioanalytical Applications*, Edel, J.; Albrecht, T., Eds. Royal Society of Chemistry: 2012.
2. Skinner, G. M.; van den Hout, M.; Broekmans, O.; Dekker, C.; Dekker, N. H. *Nano Letters* **2009,** 9, (8), 2953-2960.
3. Yang, J.; Ferranti, D. C.; Stern, L. A.; Sanford, C. A.; Huang, J.; Ren, Z.; Qin, L.-C.; Hall, A. R. *Nanotechnology* **2011,** 22, (28).
4. Wanunu, M.; Dadosh, T.; Ray, V.; Jin, J.; McReynolds, L.; Drndic, M. *Nature Nanotechnology* **2010,** 5, (11), 807-814.
5. Wanunu, M.; Sutin, J.; McNally, B.; Chow, A.; Meller, A. *Biophysical Journal* **2008,** 95, (10), 4716-4725.
6. van den Hout, M.; Krudde, V.; Janssen, X. J. A.; Dekker, N. H. *Biophysical Journal* **2010,** 99, (11), 3840-3848.