SUPPLEMENTARY INFORMATION

Microscopic Detection Analysis of Single Molecules in MoS_2 Membrane Nanopores

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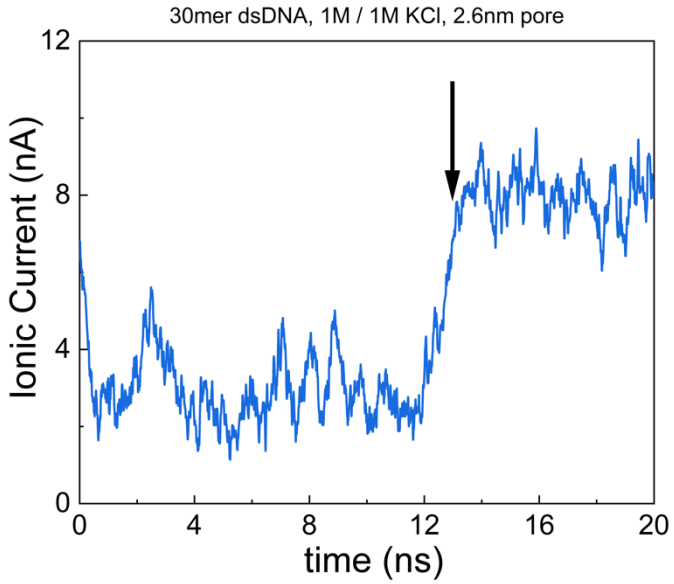
S1. Molecular Dynamics Simulation List

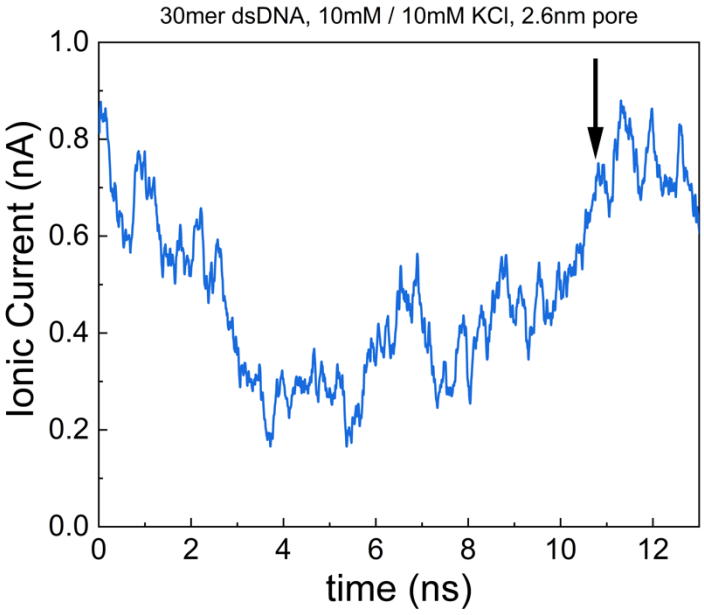
Descriptions / Simulations	Trans-membrane Voltage (V)	Simulation Box Dimensions (X x Y x Z) (nm)	Nanopore Diameter (nm)	Ionic Solution Concentration	Biomolecule translocated	Total number of atoms	Total translocation Time (ns)	No. of Runs
Sim 1	1	9 x 9 x 22	2.6	1 M KCl	dsDNA (30bp)	~163,500	~12.50	3
Sim 2	1	9 x 9 x 22	2.6	10 mM KCl	dsDNA (30bp)	167,149	10.62	1
Sim 3	1	9 x 9 x 22	5.2	1 M KCl	dsDNA (30bp)	163,960	11.73	1
Sim 4	1	9 x 9 x 22	5.2	10 mM KCl	dsDNA (30bp)	167,716	8.28	1
Sim 5	Artificially translocated	9 x 9 x 14	5.2	10 mM KCl	Zif268 protein-DNA complex	-	7.86	1

Supplementary Table 1: Description of simulated systems

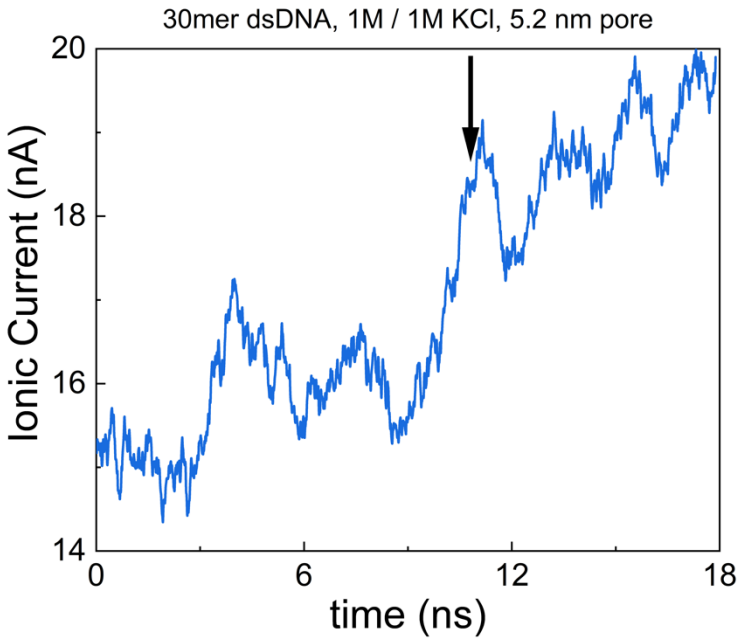
S2. Ionic Signal as a Function of Time during DNA Translocations



Supplementary Figure 1: Plot of ionic current versus time for a 30-mer dsDNA translocating through a 2.6 nm diameter MoS_2 nanopore in a **1 M KCl** solution. The black arrow indicates the time when dsDNA exits the nanopore.



Supplementary Figure 2: Plot of ionic current versus time for a 30-mer dsDNA translocating through a 2.6 nm diameter MoS_2 nanopore in a **10 mM KCl** solution. The black arrow indicates the time when dsDNA exits the nanopore.

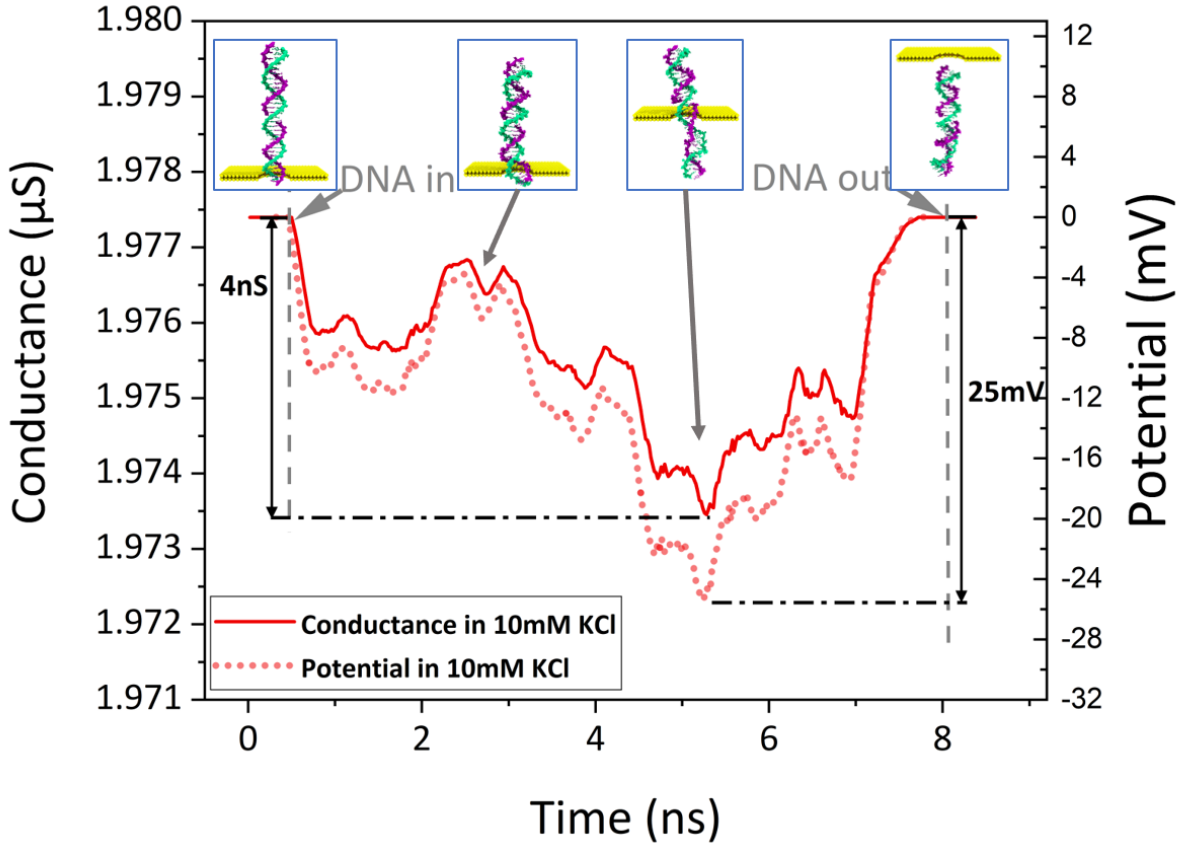


Supplementary Figure 3: Plot of ionic current versus time for a 30-mer dsDNA translocating through a 5.2 nm diameter MoS_2 nanopore in a **1 M KCl** solution. The black arrow indicates the time when dsDNA exits the nanopore.

S3. Notes on Molecular Dynamics Simulation

For 5.2 nm diameter system, the total number of ions in the system (comprising of a total of 167,716 atoms) modeled for MD simulations in 10 mM case is 77. No clear distinction is observed between the blocking current and the open-pore current in this case, which is due to (i) the extremely low ion count (ii) the large pore diameter compared to the diameter of the dsDNA molecule (iii) the applied voltage bias of 1 V.

S4. Additional Information on Transverse Conductance Trace



Supplementary Figure 4: Potential and transverse conductance variation during a 30bp dsDNA translocation through a 2.6 nm MoS_2 nanopore in uniform 10 mM KCl and 1 M KCl solutions: the conductance in 10 mM KCl shows a clear signal of translocation which agrees well with the experimental results displayed in 4(d). Inset: the DNA strand position in the simulation box. at the four frames corresponding to i) the beginning of translocation, ii) the first dip in the conductance trace, iii) the major dip, and iv) the end of translocation.

S5. Comment on Form Factor

We wish to point out that if indeed the form factor varies by 5% in the relative pore location (y_0/L_y), it still represents an absolute variation of 25 nm, which is within experimental resolution. The precision in spatial location of nanopore is in order of tens of nanometers (see Section S6). The variation of the form factor across the nanoribbon is due to the confined nature of the electron wave functions, which induces peaks and nodes along the y-direction. When the pore is positioned close to one of peaks (nodes), its presence will influence electron transport in the nanoribbon to a greater (less) extent. Moreover, we also show on fig.2 the form factor sensitivity on the carrier concentration in the nanoribbon, which could in principle be controlled by a membrane back gate as proposed early.[1]

S6. Comment on Experimental Precision of Pore Drilling

In order to minimize the electron irradiation of the MoS2 FET devices in fabrication, alignment and optimization of the imaging conditions were performed several microns away from the FET. The time of nanopore fabrication and imaging process is as short as possible. Then the nanopore was drilled in the area that has least PMMA contamination. With aforementioned procedures, the precision in spatial location of nanopore is in order of tens of nanometers.

S7. Comment on Noise Behavior

Experimentally, the level of noise and baseline fluctuations are significant due to various sources such as capacitive noise, noise from the electrolyte, noise from the electrode and electrolyte interface, *etc*. While the current traces shown in figure 4d is recorded at low salt concentration conditions (10mM/1M KCl), we have observed the increase of the standard deviation in the ionic current as the concentration of KCl solution increases. For instance, the former varies from 0.5 nA to 0.8 nA when the latter increases from 10mM/1M to 1M/1M condition, which is in agreement with previous report[2] and is associated with the low-frequency $1/f$ noise.

Alternatively, the standard deviation in the transverse current decreases substantially as the ionic concentration increases. For instance, the former is observed to decrease from 8.6 nA to 3.1 nA as the latter varies from 10mM/1M to 1M/1M condition. For more details see SI Figure 9 and 10 in Graf *et al.*[3]

In practice, the ionic and the transverse current signals are passed through noise filters such as low-pass filter (to remove high-frequency noise), whitening filter (to remove the Gaussian noise), etc. before carrying on further signal processing analysis to detect the translocated biomolecule. Similarly, in our model, the transverse current signals have already passed through a $1/f$ noise prefilter (where all high-frequency noise from experimental sources

removed), so it contains information only about the dsDNA fluctuations and the electrolyte ion distribution in the pore.

(1) Girdhar, A.; Sathe, C.; Schulten, K.; Leburton, J.-P. Graphene Quantum Point Contact Transistor for DNA Sensing. *Proc. Natl. Acad. Sci.* **2013**, *110* (42), 16748–16753.

(2) Smeets, R. M. M.; Keyser, U. F.; Dekker, N. H.; Dekker, C. Noise in Solid-State Nanopores. **2008**, *105* (2), 417–421.

(3) Graf, M.; Lihter, M.; Altus, D.; Marion, S.; Radenovic, A. Transverse Detection of DNA Using a MoS 2 Nanopore. *Nano Lett.* **2019**, *19* (12), 9075–9083.