Electronic Supplementary Material (ESI) for Nanoscale.

Detection of Methylation on dsDNA using Nanopores in MoS_2 Membrane

Supporting Information

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Supplementary Information Figure S1

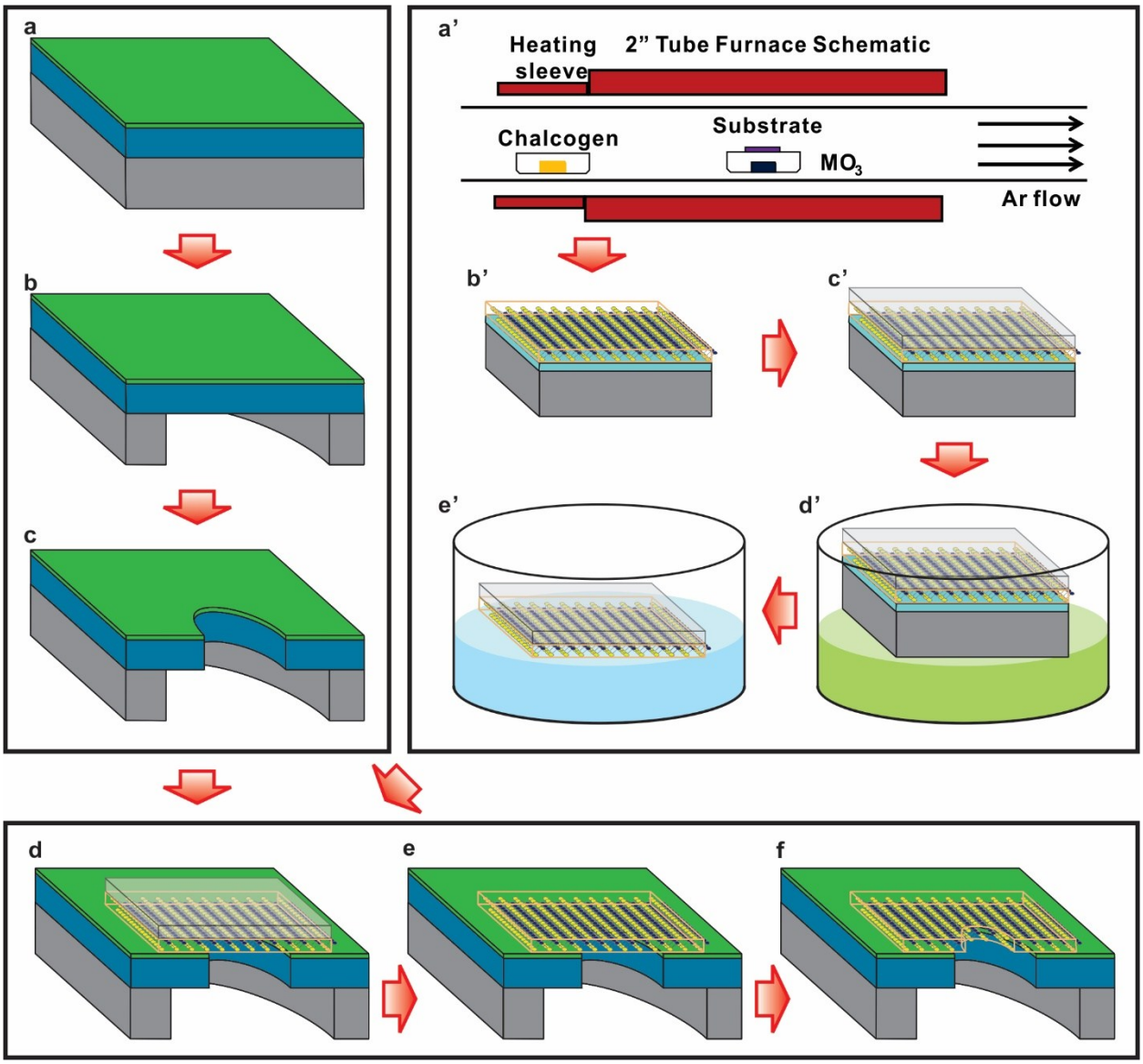

Figure S1. Detailed process of fabricating free-standing MoS_2 membrane nanopore on the supporting substrate. a. Membranes consisting of stacked layers of SiN_x and Al2O3 are fabricated on 300 ± 2 μm thick double-side polished <100> silicon wafers purchased from Silicon Quest international. Before deposition of stacked layers, wafers are piranha cleaned (2:1 H2SO4/H2O2) for 20 min on a 120 °C hotplate. 300 nm of low-stress SiNx is deposited using STS Mesc PECVD system on the silicon substrate at a mixed-frequency recipe (high freqeuncy, 6 s at 13.56 Mhz, platen power of 20 W; and low frequency, 2 s at 380 kHz, platen power of 60W) with precursors SiH4 and NH3 at flow rates of 40 and 55 sccm, respectively, at a platen termperature of 300 °C. Subsequently 20 nm-thick Al_2O_3 was deposited at a paten temperautre of 250 °C via ALD (Cambridge Nanotech) using tetramethyl-aluminum (TMA) and water vapor precursors. b. Optical lithography is used to define 80 μm square windows on the back side of the wafer with the aid of plasma resistant megaposit SPR-220 photoresist and an ABM Flood Exposure (Model 60) tool. The wafer is then placed inside an STS Pegasus ICP DRIC and 80 μm square membranes are suspended using a Bosch etching process. c. 500 to 600 nm holes are sculpted in these membranes using a focused ion beam (FIB, FEI DB235) operated at a beam current of 30 pA. a'. For MoS_2 growth, the substrate is placed face-down over a crucible

containing ~1 mg of MoO_3 powder, and solid sulfur pieces are placed ~26 cm upstream. After evacuating the tube to <1 Torr, the tube is filled to 760 Torr with Ar. The Ar flow is then reduced to 30 sccm for the growth. Synthesis on SiO_2 is done as in Ref. S1, whereas synthesis on sapphire was done in a similar manner as Ref. S2. b'. The MoS_2 film is then removed from the furnace. c'. PMMA (A4 950K) is coated on the MoS_2 film by using spin coater at 3000 rpm follwed by baking at 200 °C for 10 min. After 15 min cooling down, second PMMA layer was coated using the same parameters. d'. PMMA coated MoS_2 film on SiO_2 or Sapphire substrate was then floated on the 1M KOH at 80 °C for 1 hour till MoS_2/PMMA stack delaminates. e' PMMA coated MoS_2 film is detached from the substrate. d. The detached PMMA/ MoS_2 layers are transferred to supporting substrate after rinsing with DIH2O, and dried at room temperature for 2 hours. Subsequently, the substrate is placed on a hot plate at room temperature and ramp to 150 °C for 20 min. e. The PMMA layer was dissolved in acetone for 30 min, rinsed with IPA, washed with DIH2O. Then, the samples are heated in Ar/H2 atmosphere for 1.5 hours at 400 °C. f. A nanopore was drilled on the MoS_2 membrane as dscribed in Methods.

Supplementary Information Figure S2

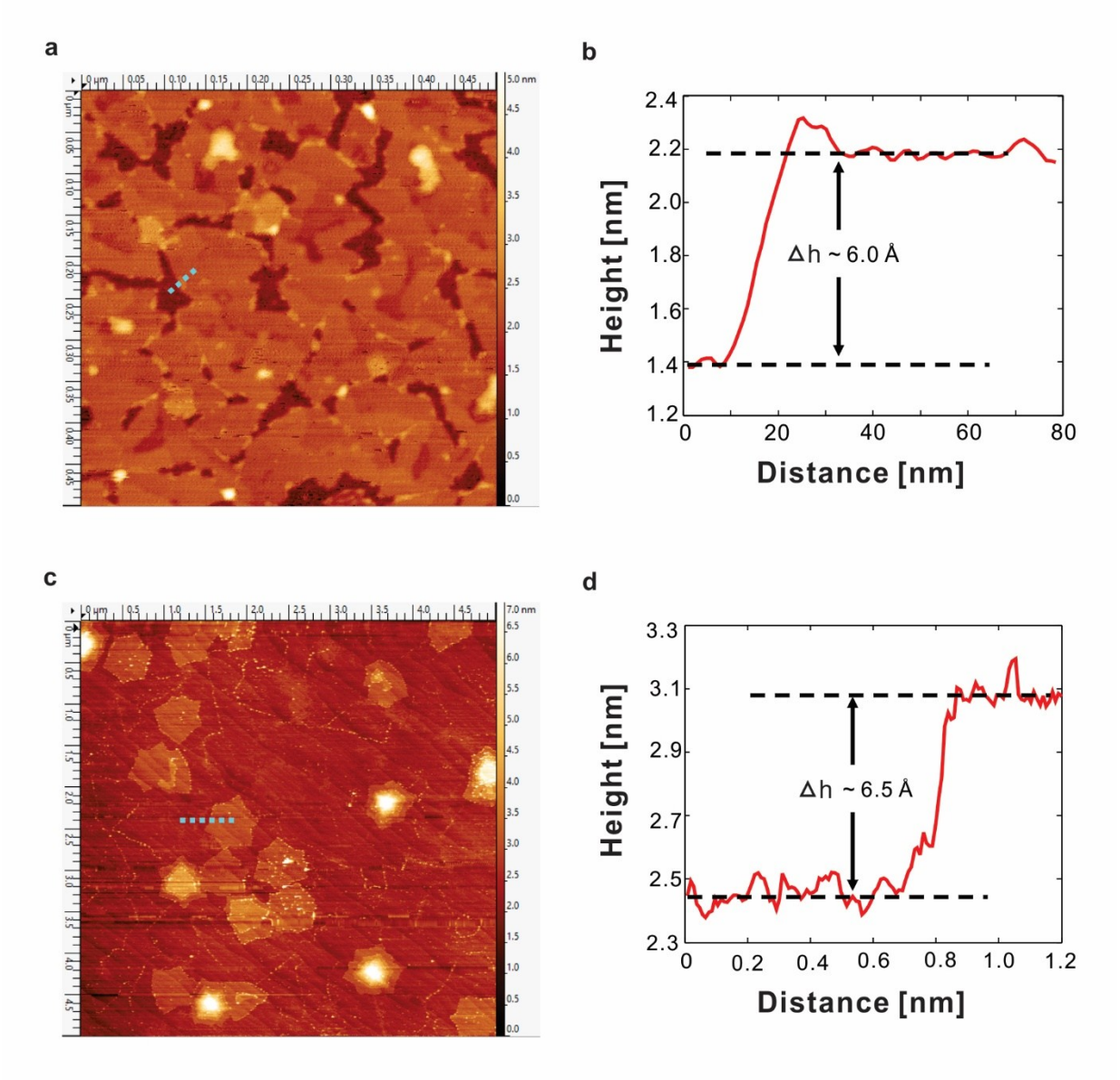

Figure S2. (a) and (b): AFM image and height profile of a subcontinuous MoS_2 growth on sapphire showing the monolayer height of ~6 Å. (c) and (d): AFM image and height profile of a continuous growth on sapphire, showing small overgrowth regions with a 1L-2L height of ~6.5 Å. Also note the ridges in Fig. S2c, which are the terraces of the reconstructed sapphire surface, as in Ref. S2.

Supplementary Information Figure S3

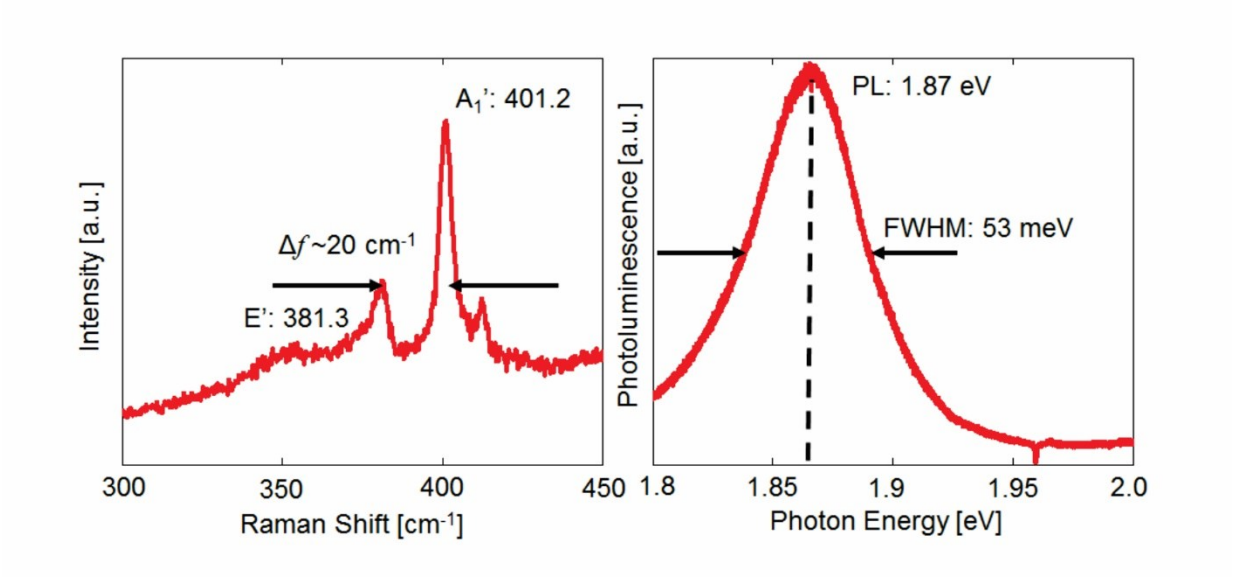

Figure S3. Raman (left) and photoluminescence (right) data for as-grown 1L MoS_2 on sapphire. In the Raman spectrum, the E' and A_1' vibrational modes are near 381 and 401 cm^{-1}, respectively. The PL spectrum has a peak near 1.87 eV and FWHM of 53 meV.

Supplementary Information Figure S4

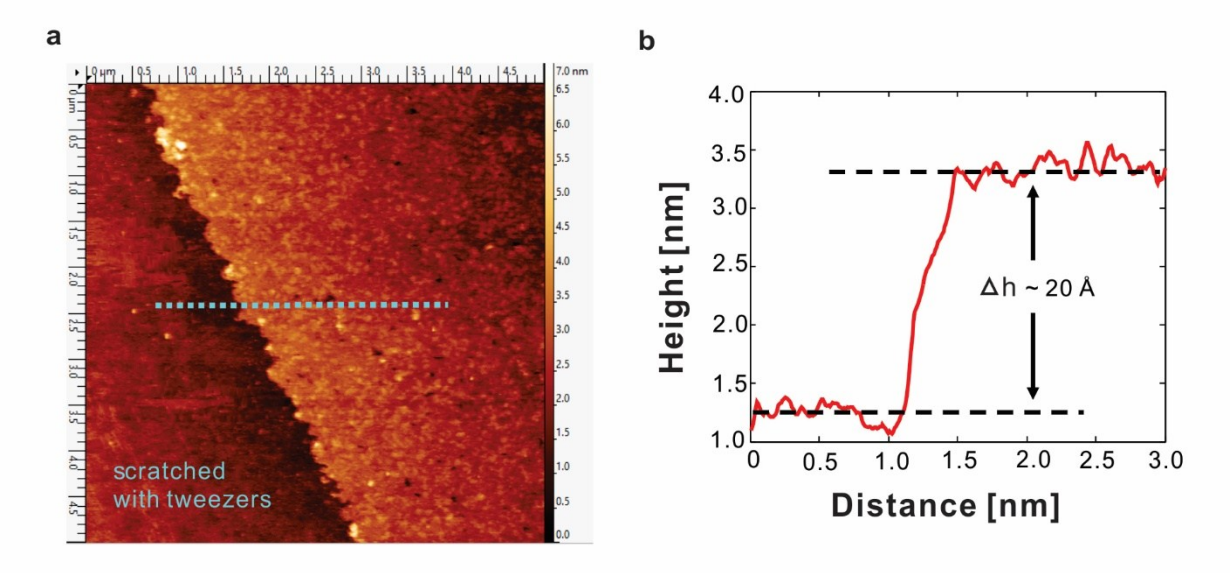

Figure S4. (a) and (b): AFM image and height profile of a continuous growth on SiO_2. The measured step height here is ~20 Å due to the bare surface being made by scratching the MoS_2 away with tweezers.

Supplementary Information Figure S5

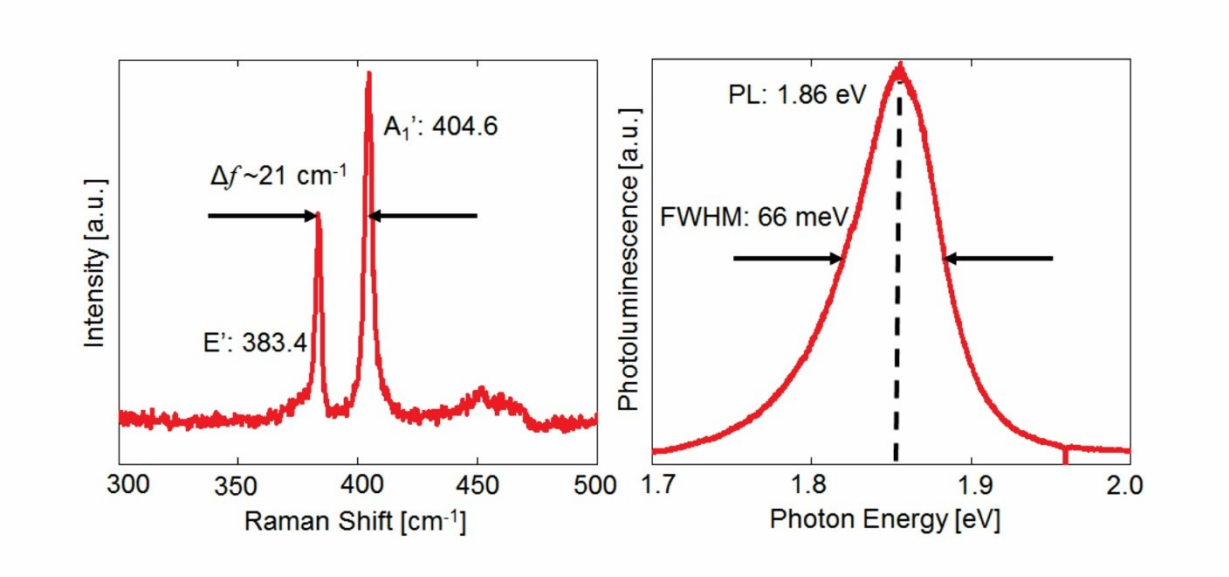

Figure S5. Raman (left) and photoluminescence (right) data for continuous MoS_2 grown on SiO_2. In the Raman spectrum, the E' and A_1' vibrational modes are near 383.5 and 404.5 cm^{-1}, respectively. The PL spectrum has a peak near 1.86 eV and FWHM of 66 meV.

Supplementary Information Figure S6

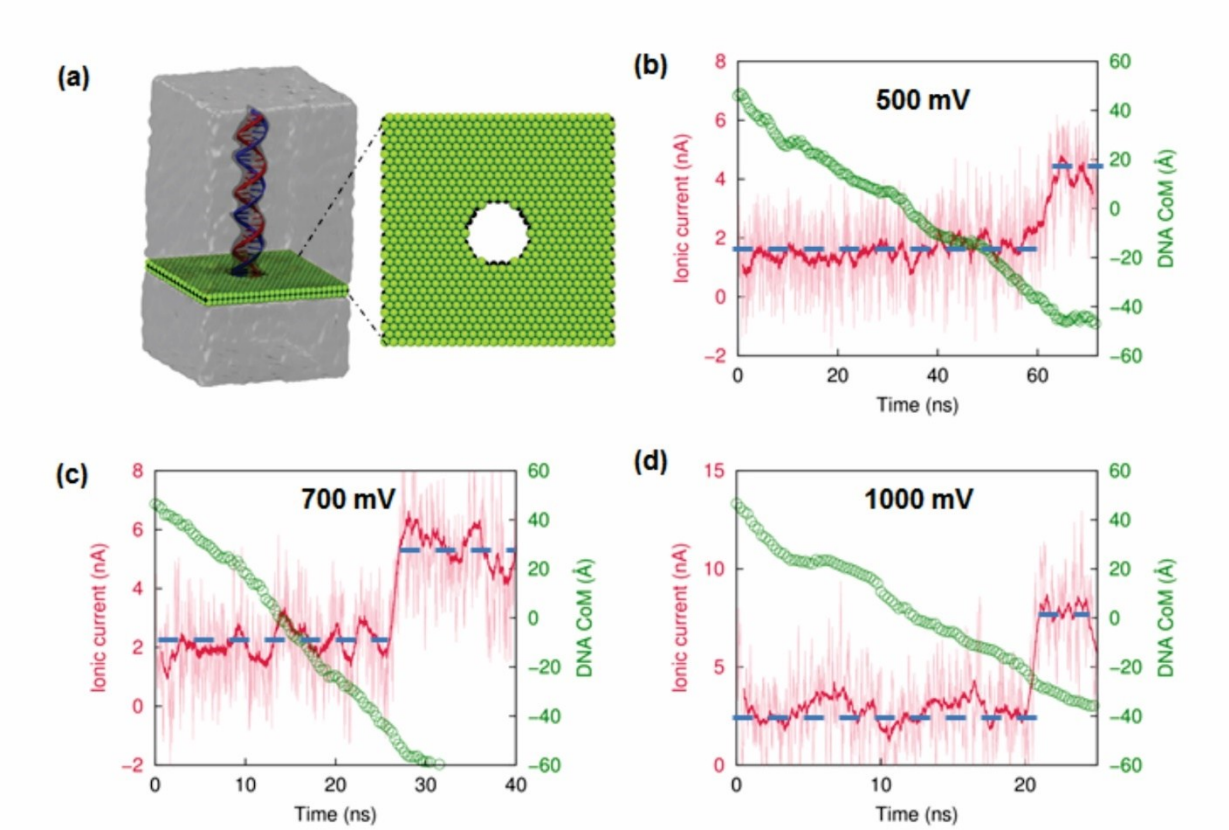

Figure S6. Molecular dynamics simulation of dsDNA translocation through a 2.4 nm diameter MoS_2 nanopore under different voltage biases. (a) Simulation system consisting of a monolayer MoS_2 and a 30 bp long dsDNA strand embedded in a 1 M NaCl solution. (b-c) Recorded ionic current (red) and the center of mass positions of the DNA molecule (green circles) in the direction perpendicular to the MoS_2 membrane when an transmembane voltage 500 (b), 700 (c), 1000 (d) mV was applied to drive the dsDNA translocation through the pore.

To explore the atomic-scale translocation dynamics of a dsDNA through MoS_2 nanopore, we performed three independent molecular dynamics simulations on the system shown in Figure S6a under voltage biases of 500, 700, 1000 mV, respectively. It is found that the recorded ionic current when the pore is occupied by DNA is evidently lower than the open pore current in all the simulations, showing successful detection of DNA translocation (Figure S6c-d), in agreement with our experimental observation.

Supplementary Information Figure S7

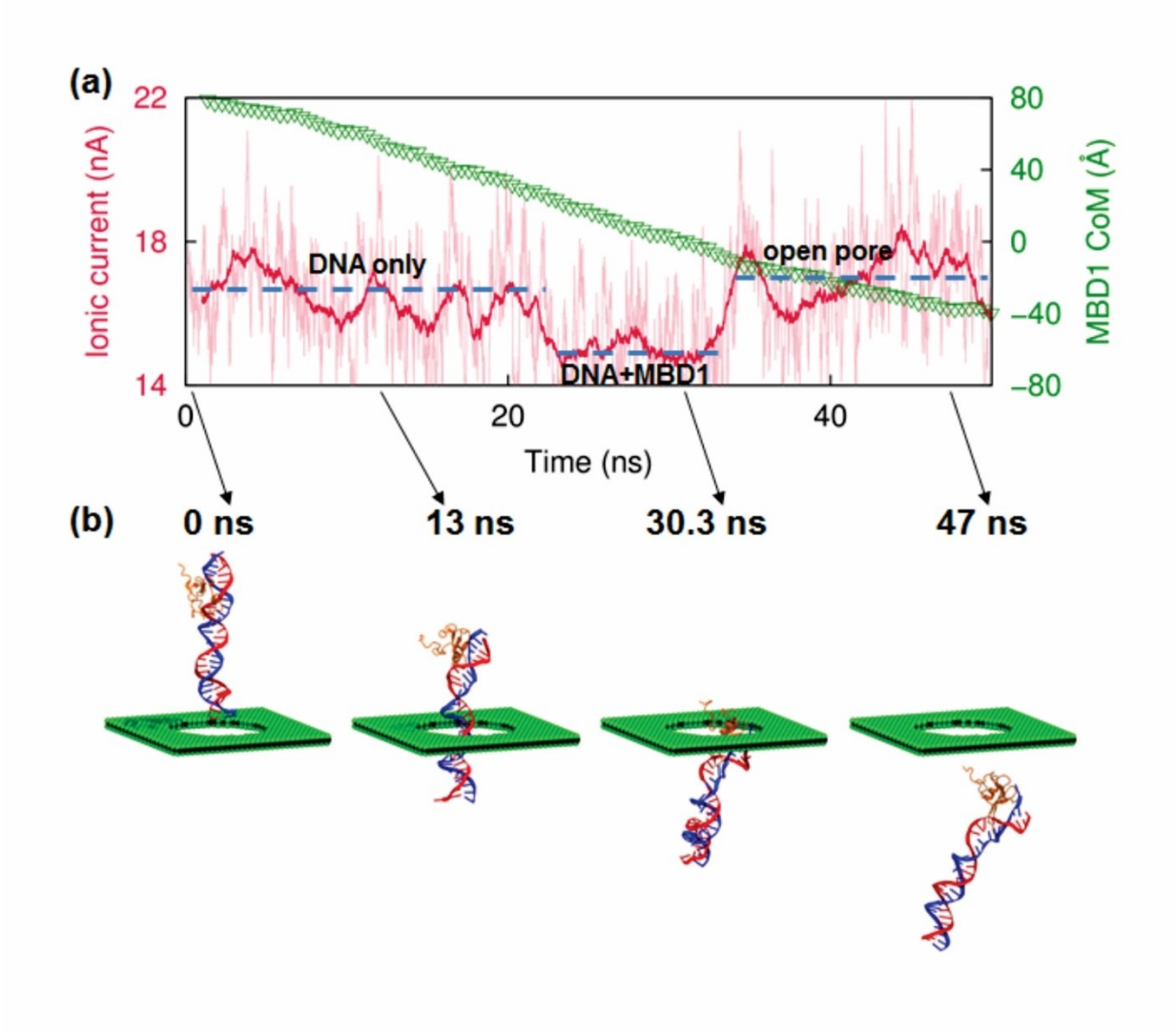

Figure S7. Molecular dynamics simulation of a DNA-MBD1 complex translocation through a 6 nm diameter MoS_2 nanopore under a 500 mV voltage bias. (a) Recorded ionic current (red) and the center of mass position of the MBD1 protein (green triangles) during the translocation of the complex. (b) Snapshots of the MD trajectory at different time instants

We also performed molecular dynamics simulations to study on the atomic-scale the translocation process of a terminal-methDNA/MBD1 complex through a MoS_2 nanopore, as shown in Figure S7. The recoded ionic current exhibits clearly three subsequent levels, ~16.7, ~15 and ~17 nA, induced by the occupation of the pore by DNA only, DNA plus MBD1 protein and nothing (i.e., open pore), respectively. This finding suggests detection of the MBD1 protein and the associated methylation sites.

Supplementary Information Figure S8

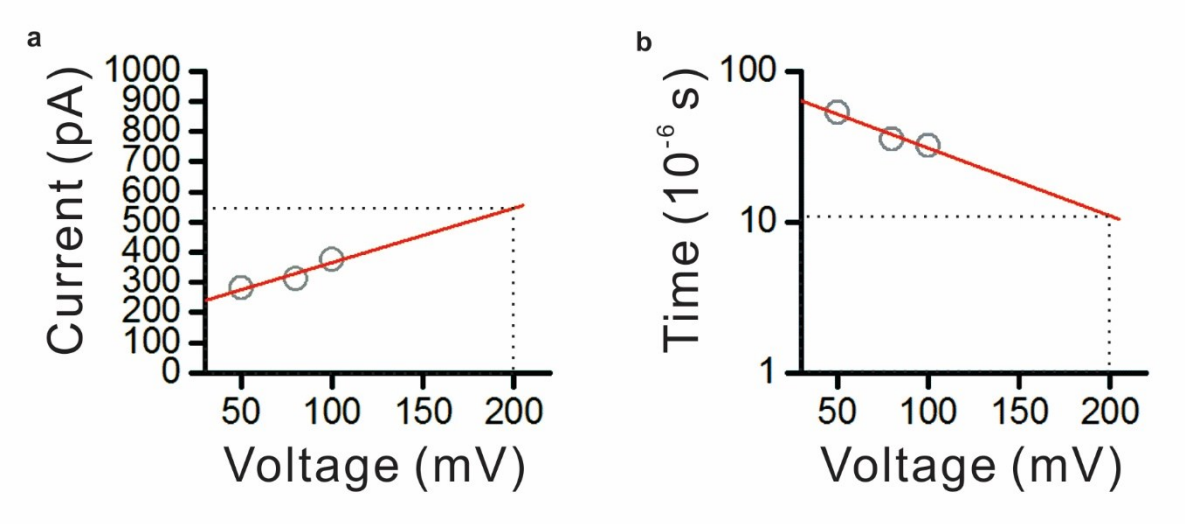

Figure S8. Expected blocked current level and current blockage duration for translocation of 90 bp double-stranded DNA through 7.2 nm MoS_2 nanopore at 200 mV. a. Blocked current at 200 mV was obtained by fitting first-order Polynomial to blocked current values at 50 mV, 80 mV, and 100 mV, and extended the fitting trend to 200 mV. b. Transport duration of 90 bp dsDNA at 200 mV was obtained by fitting Exponential decay function to transport duratin value at 50 mV, 80 mV, and 100 mV, and extended the fitting trend to 200 mV.

Supplementary Information Figure S9

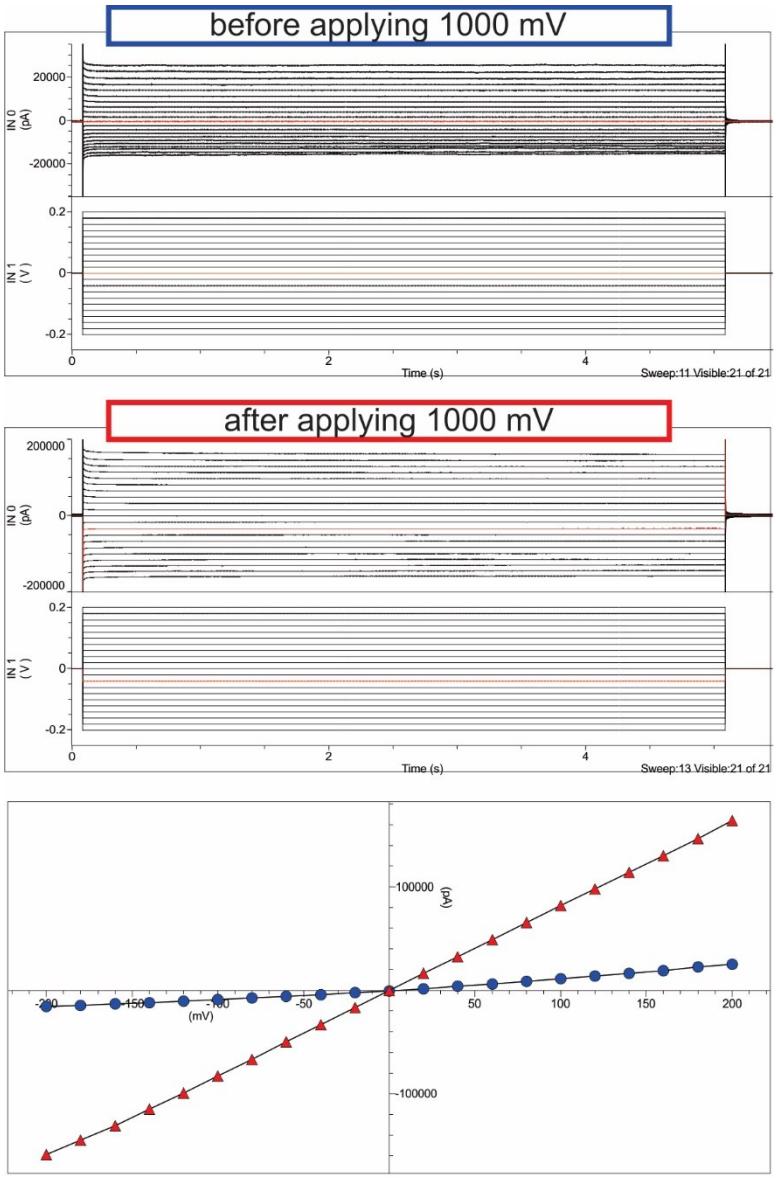

Figure S9. Enlargment of a MoS2 nanopore. The top figure shows the initial IV curve characteristic of a MoS2 nanopore before appying 1000 mV. The middle figure shows the IV curve characteristic of the MoS2 nanopore after exposed at 1000 mV for multiple times. The bottom figure shows the difference of IV characteristic between before and after applying the biased voltage of 1000 mV.

Supplementary References

[S1] K. K. H. Smithe, C. D. English, S. V Suryavanshi, and E. Pop, 2D Mater. **4**, 1 (2017). DOI: 10.1088/2053-1583/4/1/011009.

[S2] D. Dumcenco, D. Ovchinnikov, K. Marinov, P. Lazić, M. Gibertini, N. Marzari, O. L. Sanchez, Y.-C. Kung, D. Krasnozhon, M.-W. Chen, S. Bertolazzi, P. Gillet, A. Fontcuberta i Morral, A. Radenovic, and A. Kis, ACS Nano **9**, 4611 (2015). DOI: 10.1021/acsnano.5b01281.