Supporting Information

Electro-Mechanical Signatures for DNA Sequencing through a Mechano-Sensitive Nanopore

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S.1 Molecular structure of DNA bases

The molecular representations of DNA nucleotides (A, C, G and T) are illustrated in Figure S1. The interaction of each nucleotide with the MscL pore depends on the structure and type of the atoms of each base. These interactions involve both VdW and Coulombic forces which are parameterized by the Lennard-Jones parameters (σ and ε) and the partial charges on each atom (tabulated in Table 1 and Table 2). The Lennard-Jones interaction energy is highest for oxygen atoms (ε_O=0.210), therefore, bases containing these protruding oxygen atoms exhibit stronger VdW interactions with the atoms of the pore. As shown in Figure S1, base T has two oxygen atoms while base A does not contain any oxygen atoms which are consistent with the interaction forces calculated in the main article. The other Lennard-Jones parameter σ, which is representative of the size of an atom, plays an important role in the ionic current blockade.

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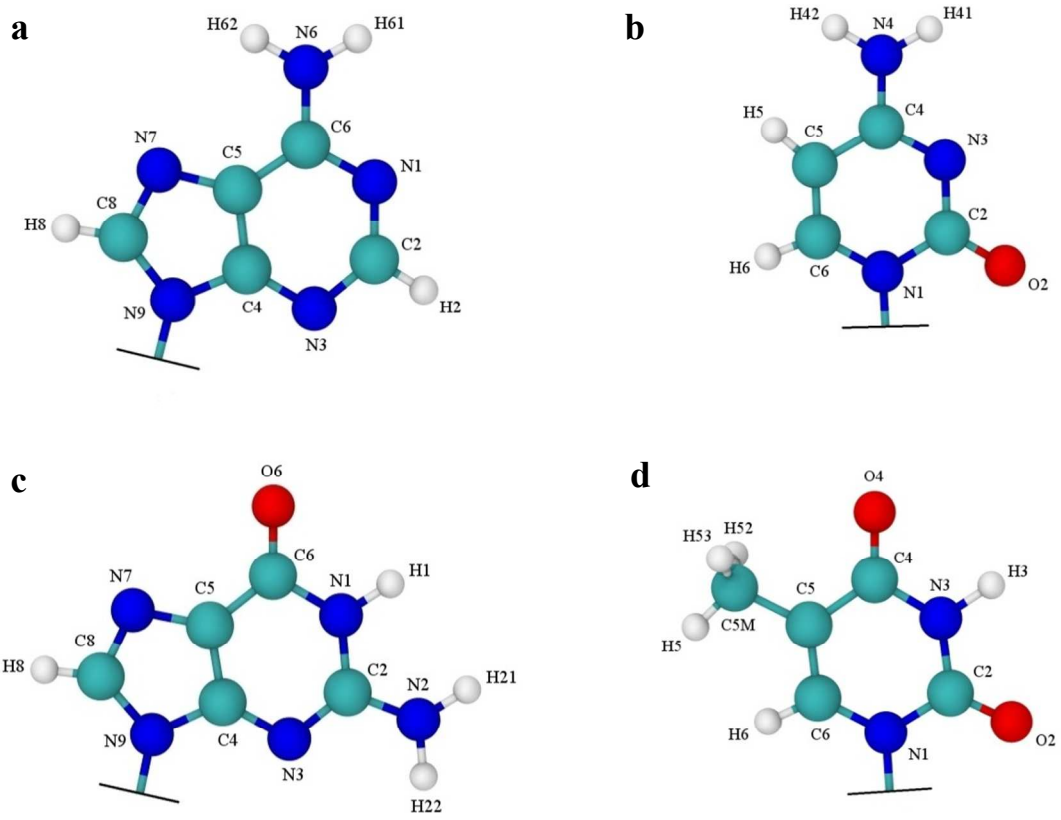

Figure S1. Representation of DNA bases with their atom types (white: hydrogen atoms, blue: nitrogen atoms, cyan: carbon atoms and red: oxygen atoms). **a|** Base A. **b|** Base C. **c|** Base G. **d|** Base T.

Atom	σ (Å)	ε (kcal/mol)
O	2.96	0.210
N	3.25	0.170
C in C=O	3.75	0.105
All C (not in C=O)	3.50	0.080
H bonded to N	0.00	0.000
H Bonded to C	2.50	0.050

Table 1 Lennard-Jones parameters for atoms of bases.

Base A atom	Charge (e)	Base C atom	Charge (e)	Base G atom	Charge (e)	Base T atom	Charge (e)
N1	-0.6710	N1	-0.8420	N1	-0.6710	N1	-0.8680
C2	0.3434	C2	0.9470	H1	0.4050	C2	1.0340
H2	0.1610	O2	-0.6190	C2	0.9748	O2	-0.6040
N3	-0.6360	N3	-0.721	N2	-0.9560	N3	-0.1850
C4	0.6380	C4	0.6740	H21	0.3990	H3	0.4250
C5	0.0860	N4	-0.9240	H22	0.4170	C4	0.8270
C6	0.6510	H41	0.3940	N3	-0.7200	O4	-0.5880
N6	-0.7800	H42	0.4110	C4	0.6480	C5	-0.185
H61	0.3280	C5	-0.3830	C5	-0.0290	C5M	-0.1100
H62	0.3370	H5	0.2160	C6	0.8300	H5	0.0700
N7	-0.5877	C6	0.1950	O6	-0.5950	H52	0.0700
C8	0.3510	H6	0.2400	N7	0.5090	H53	0.0700
H8	0.1820			C8	0.2730	C6	0.1500
N9	-0.7430			H8	0.2220	H6	0.2400
				N9	-0.8240		

Table 2 Partial charges on atoms of DNA bases.

S.2 Ionic current in MspA and MscL

To understand the effect of pore elasticity on the ionic current signals we acquired in MscL, we compared the ionic current signals obtained from translocation of ssDNAs in MspA and MscL pores (Figure S2). In the main text, we already computed the time averaged ionic current for 4 different nucleotides in MscL. Here, using the same simulation approach already explained in the Methods section of the main manuscript, we simulated the translocation of 4 ssDNA (PolydA(60), PolydT(60), PolydG(60) and PolydC(60)) through MspA. The only difference between MscL and MspA simulations is the type of protein. For MspA, we used the crystallography data with the PDB code:1UUN. The snapshots of the initial simulation of PolydA through MspA and MscL are shown in Figure S2.

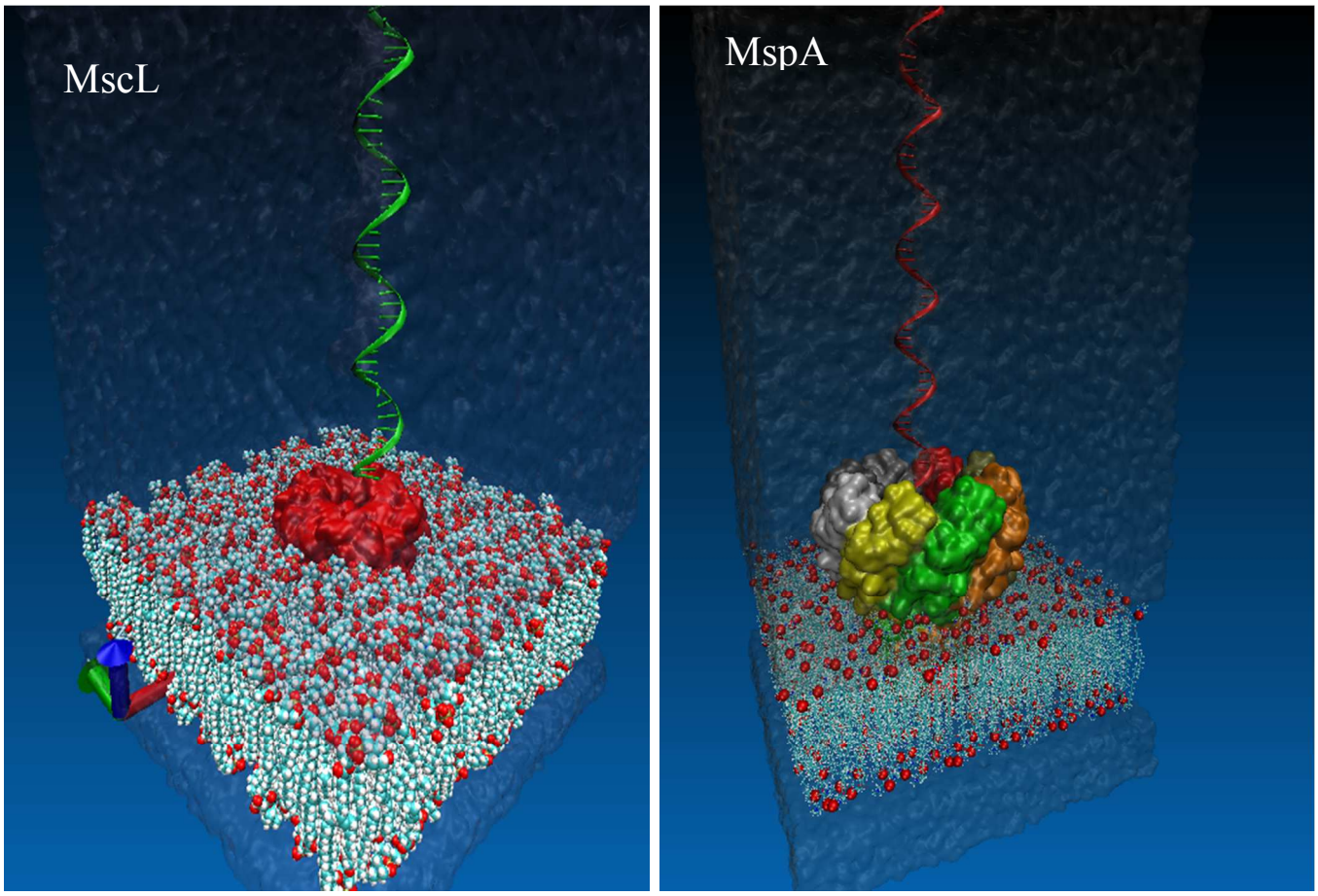

Figure S2. Snapshots of simulation set up Left) MscL and Right) MspA.

The transmembrane bias of 0.5 V is applied in all cases. The average ionic current for bases A, C, G, and T through MspA and MscL are shown in Figure S3. The level of currents for MspA is lower than the one in MscL. Also the order of currents for 4 bases is different in the two pores.

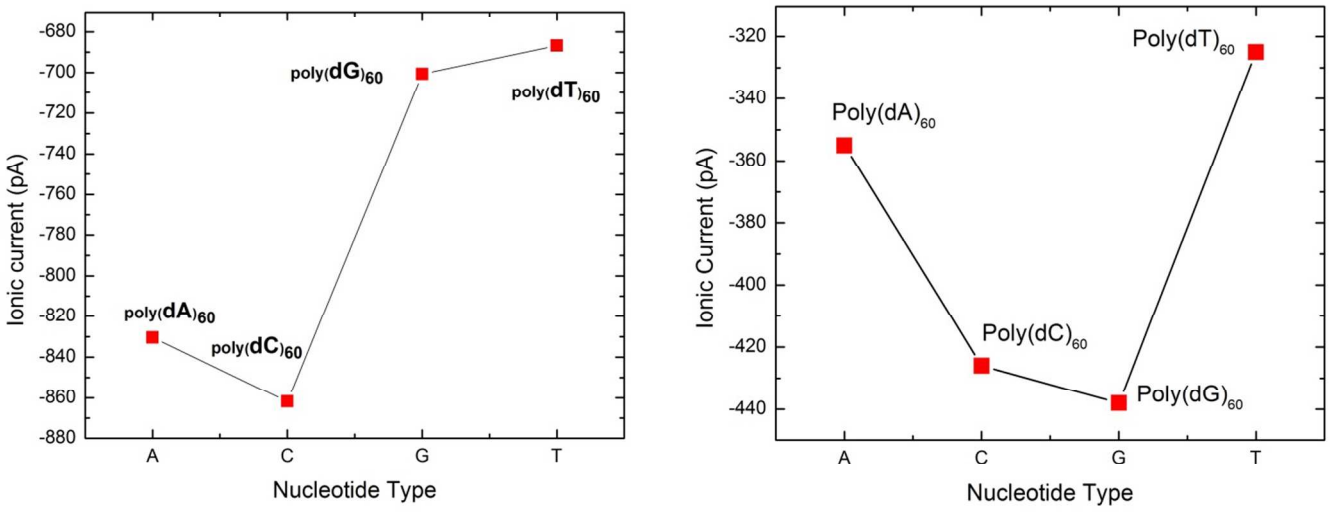

Figure S3. Averaged ionic current for Poly(dA)$_{60}$, Poly(dC)$_{60}$, Poly(dT)$_{60}$ and Poly(dG)$_{60}$ for Left) MscL and Right) MspA

The maximum and minimum current difference, ΔI, is 113.1 pA and 189.2 pA for MspA and MscL, respectively. The signal strength is higher for MscL compared to MspA.

S.3 Signal to Noise (SNR) calculation

SNR is defined as[1]

$$SNR = \frac{|\Delta I|}{I_{noise,RMS}} \tag{S.3.1}$$

where $|\Delta I|$ is the absolute current change due to protein translocation and $I_{noise,RMS}$ is the root-mean-square current noise. It is noteworthy that $I_{noise,RMS}$ equals the square root of the integral of the high-frequency current power spectral densities, which is defined as:

$$I_{noise,RMS} = \left(\int_0^{BW} S_I df \right)^{\frac{1}{2}} \tag{S.3.2}$$

where BW is the bandwidth and S_I is the power spectral density. The current power spectral density (S_I) is defined as:

$$S_I = \int_0^{\infty} < I(t) \cdot I(0) > \cos(\omega t) dt \tag{S.3.3}$$

where $I(t)$ is the instantaneous ionic current.

References

1. Dekker, C. Solid-State Nanopores. *Nat. Nanotechnol.* **2007,** *2*, 209-215.