Supplementary Material (ESI) for Chemical Communications

Nanopore DNA sensors based on dendrimer-modified nanopipettes

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Experimental Details.

Instrumentation. Quartz nanopipettes with inner diameter ~50 nm were produced using a laser-based pipet puller (Sutter Instrument P-2000) by pulling quartz capillaries(Q100-70-7.5, Sutter Instrument). The pulling parameters were as follows: HEAT = 700; FIL = 3; VEL = 40; DEL = 175; PUL = 190. A Keithley 6487 picoammeter/voltage source (Keithley Instruments Inc.) was used for the measurement of current-voltage curves. Ag/AgCl electrodes, one in the bath and the other inside the nanopipette, were used as the working and reference electrodes, respectively. A Faraday cage was used for the measurements. Nanopipette diameters could be characterized using scanning electron microscopy or the current-voltage response and Equation 1. Nanopipettes with small diameters could be reproducibly prepared under these conditions, typically giving pipettes with current-voltage responses ± 10 %.

Materials. All oligonucleotides used in this paper were purchased from Integrated DNA Technologies. Experiments were conducted on multiple sequences to confirm the generality of sensor response. Examples of sequences used in the Figure 2 of the paper are shown below.

Probe	3'-CTT GTC ATA GTT GTT-5'
PolyT	3'-TTT TTT TTT TTT TTT-5'
Mismatch	5'- GAA AAG TAT CAA CAA-5'
Complement	5'- GAA CAG TAT CAA CAA-5'

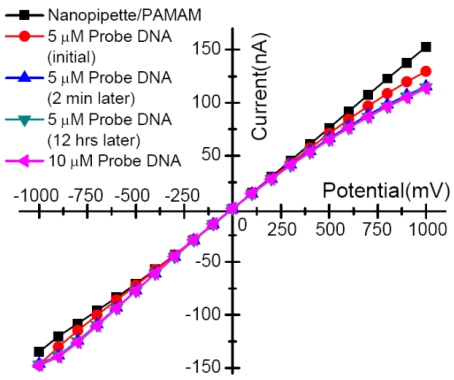
Triethoxysilylbutyraldehyde (90%, Gelest Inc.) and G4-PAMAM dendrimer (1, 4-diaminobutane core, generation 4, Sigma-Aldrich) were used as received. MilliQ water was used throughout the experiments. All experiments were done in 50 mM KCl, 50mM phosphate buffer (PBS).

Preparation of nanopipettes modified with G4-PAMAM.
Quartz capillaries were cleaned in piranha solution prepared by mixing 3:1 concentrated sulfuric acid with hydrogen peroxide (30%) for 1 day before pulling. *Caution: The piranha solution is a highly energetic oxidizer. It reacts very violently with organic materials.* The freshly pulled nanopipette was further treated with 30% HNO_3 for 1 day. The nanopipette then was washed with water and ethanol, respectively. The nanopipette

was then filled with a solution of 0.9 mL ethanol, 50 µL triethoxsilylbutyraldehyde and 50 µL acetate buffer (0.1 M, pH 4.7). After keeping the solution in the nanopipette for 20hrs, the nanopipette was washed with first with ethanol and then with borate buffer (50 mM, pH 9.2). This produced a nanopipette tip which was functionalized with an aldehyde-terminated silane. The nanopipette was filled with a solution of 2 mL borate buffer (50mM, pH 9.2), 10 µL G-4 PAMAM solution (30% in methanol) and excess $NaCNBH_3$. After 12 hrs, the nanopipette was washed and filled with PBS buffer. Surface modification was followed by measuring current-voltage responses, as shown in Figure 3 of the paper.

pH dependence of the current rectification effect.
Solutions containing 50 mM KCl and 50 mM PBS buffer at several different pH values (pH 9.0, pH 7.5 and pH 6.5) were used to measure the effect of protonation on the observed current-voltage response. Both the external bath solution and the solution inside the nanopipette were exchanged to measure these responses. The pH was verified with PC 510 Bench pH/Conductivity Meter(Oakton Instruments).

Response of the nanopipette to probe DNA, polyT, complement and mismatch DNA.
Nanopipettes and bath solutions were first filled with 50mM PBS buffer at pH 5.8. The Probe DNA was adsorbed to the surface of the G4-PAMAM modified nanopipette by adding aliquots of the probe DNA to the external bath solution. The current-voltage response was monitored until a constant response was obtained (Supplementary Figure 1). Typical total probe DNA concentrations were 3-5 µM, and constant responses could often be obtained within several minutes, and most always within 1-2 hrs. The solution in



Supplementary Figure 1.

the external bath and nanopipette were then changed with fresh PBS buffer was added. PolyT sequences were then added to the bath at concentrations indicated. The current-voltage response before and after adding polyT sequences were compared. Again, the current-voltage response typically changed within several minutes. After that, the mismatch DNA sequence was added to the bath and the procedure repeated. Finally, the complementary DNA was added to the bath and the procedure repeated.