10MHz measurements on solid-state nanopores made using controlled breakdown

Introduction

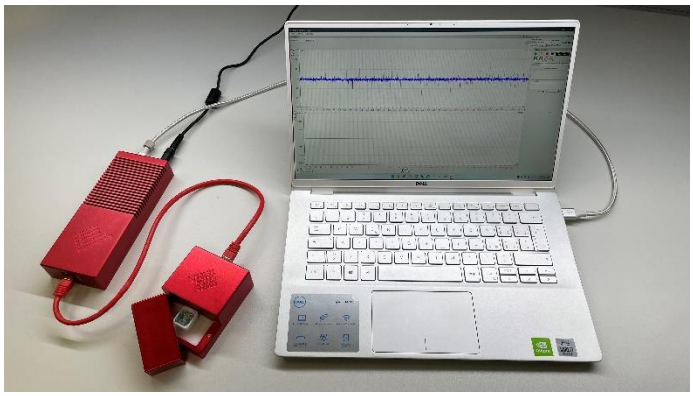

Figure 1: The 10Mhz amplifier from Elements srl in operation

Northern Nanopore Instruments (NNi) tested the new 10MHz amplifier from Elements srl for suitability with solid-state nanopore biosensing applications. Overall, the system performs very well both with solid-state nanopore device architectures optimized to reduced high-frequency noise (i.e. with low capacitive load value) as well as a regular nanopore chips. The system is compact and portable, and remarkably robust to a range of capacitive loads and performs well across the full spectrum of nanopore measurements attempted. While the noise performance is on par and in some cases better than other low-noise current amplifiers on the market, the full 10 MHz bandwidth and 40 Msps sampling rate, combined with ±100nA of dynamic range, is what sets this instrument apart from others as it offers an unprecedented opportunity to study details of fast biomolecular translocations using the entire range of solid-state nanopore chips.

Methods

The nanopores were fabricated using a Spark-E2 from Northern Nanopore Instruments (NNi) in 1 M KCl pH 8 (10.6 S/m) and enlarged and measured in 3.6 M LiCl pH 8 (16.5 S/m), both buffered with 10 mM HEPES. Nanopores were made in both standard 10 nm thick SiNx membranes without capacitance optimization, and membranes painted with PDMS to reduce the capacitance. Experiments were performed in standard NNi flow cells using a simple custom adapter to connect to the amplifier. Nanopore noise was tested at the full 10 MHz bandwidth. Double-stranded DNA (1000 bp NoLimits DNA Fragments) was subsequently added to the pore and DNA translocations measured at the full bandwidth. Data was collected using Elements 10 MHz amplifier control software at 40 Msps sampling and analyzed using NNi Nanolyzer.

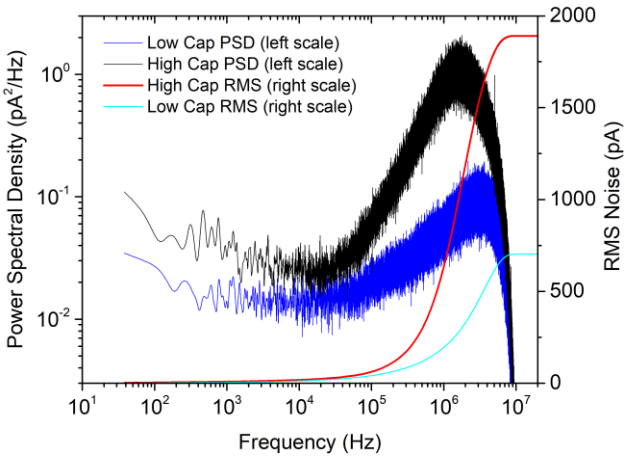

Figure 2: The power spectrum of (black curve) a typical high-capacitance solid-state nanopore chip with a 10MHz 8-pole low-pass Bessel filter applied; (blue curve) a capacitance-optimized nanopore chip with the same filter applied. Red and cyan curves are plotted on the right axis and correspond to the RMS noise for the black and blue curves respectively.

Results

Figure 1 shows the power spectrum of a two nanopore chips: a SiN_x membrane chip with SiO_2 capacitance reducing underlayer (10-100pF) with a 5.4 nm diameter solid-state nanopore measured at 10 MHz bandwidth, and a heavily capacitance-optimized chip (1-10pF) measured in the same conditions, but without a pore. For reference, the blockage caused by linear passage of dsDNA in these conditions is about 1200 pA. Typical SiN_x chips without capacitance optimization show too much noise to be measured with the amplifier practically, though remarkably, the electronics remain stable even with high capacitance chips.

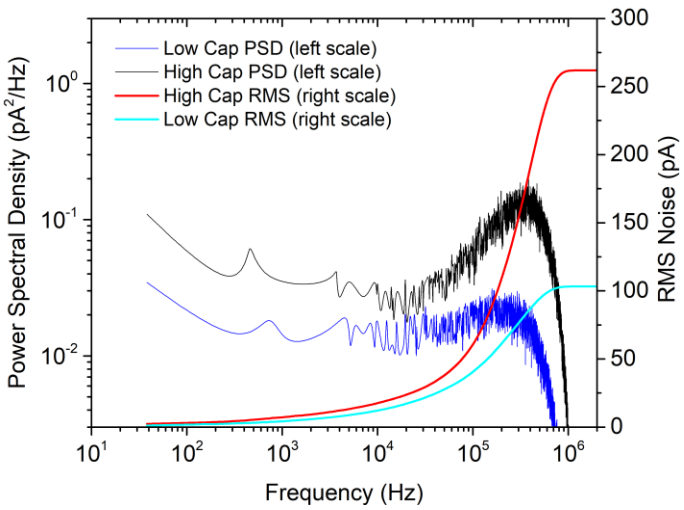

Figure 3: The power spectrum of (black curve) a typical high-capacitance solid-state nanopore chip with a 1MHz 8-pole low-pass Bessel filter applied; (blue curve) a capacitance-optimized nanopore chip with the same filter applied. Red and cyan curves are plotted on the right axis and correspond to the RMS noise for the black and blue curves respectively.

Filtering at 1 MHz, as shown in Figure 2, brings RMS noise down by nearly an order of magnitude in both cases.

If we define the maximum usable bandwidth as that where the signal-to-noise ratio for dsDNA translocating the nanopore is equal to 3, then the maximum usable bandwidth in the case of the former nanopore chip is 1.5Mhz while the maximum usable bandwidth for the capacitance optimized chip is an impressive 5.5 MHz.

Conclusions

Even though the full 10MHz bandwidth is not usable for solid-state nanopores, the additional data afforded by the sampling leads to high-quality fits and resolution of rise time features that would otherwise be difficult or impossible to accurately extract. To utilize the full bandwidth, chip architecture optimization is required to reduce the capacitance to the <1 pF range.

On top of having a large bandwidth, this amplifier also has 200 nA of dynamic range, allowing for operation with large (>10nm) pores in high salt concentration. The extra sampling rate of 40 MHz results in high quality downstream data fitting and allows Nanolyzer to accurately capture features of the translocation that would be too fast to confidently fit with sparser sampling. An example of a simple fit is included in Figure 3. While dsDNA affords little by way of structural features to fit, the clear resolution of the rise times suggests that features as fast as 1 microsecond are likely resolvable with minor work to optimize the chip capacitance.

Something to keep in mind when using this higher bandwidth is the volume of data collected, at approximately 540 GB/hr. This means you will burn through hard drives very quickly and analysis is slower, but this is a small price to pay for additional fit quality and the bandwidth required to pick out fine features of translocating biomolecules. Note that one can expect a linear slowdown in Nanolyzer's event fitting with sampling rate.

Overall, we are very impressed with this amplifier, which performs well when paired with solid-state nanopore fabricated using NNi's controlled breakdown methods and suite of nanopore tools. The 10 MHz amplifier from Elements srl is an impressive piece of hardware which opens new biomolecular measurement possibilities, and we look forward to seeing the results of research it enables going forward.

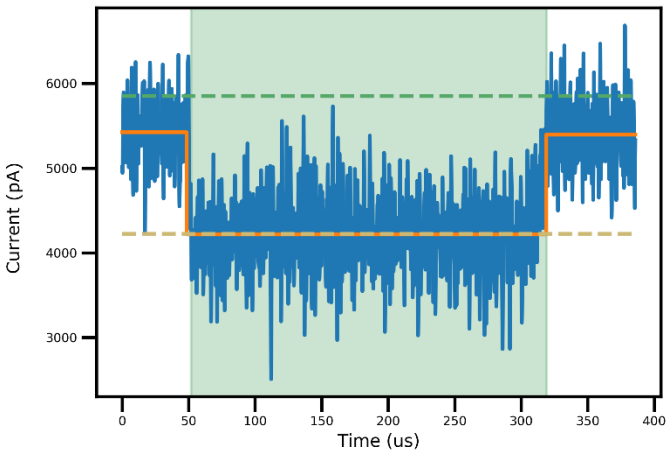

Figure 4: dsDNA translocating a high capacitance nanopore at 1.5MHz bandwidth, showing high rise time resolution and good quality fitting using NNi Nanolyzer.