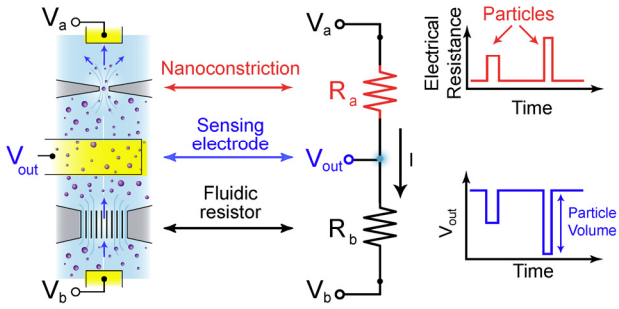
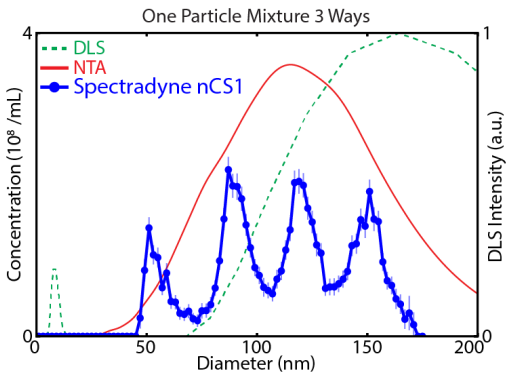
Microfluidic Resistive Pulse Sensing

The Spectradyne nCS1™ employs a novel implementation of the resistive pulse sensing (RPS) method to count and size nanoparticles quickly and with high resolution. The nCS1™ uses unique disposable microfluidic cartridges to implement Spectradyne's microfluidic version of RPS, which we term MRPS. By using state-of-the-art microfluidic fabrication technology, we have shrunk the critical nanoparticle sensing constriction used in traditional RPS by a factor of 100 or so, from a few tens of microns in diameter to a few hundred nanometers. This allows us to detect much smaller particles using microfluidic RPS.



The microfluidic RPS cartridge includes ports for voltage bias V_a and V_b, a microfluidic nanoconstriction R_a and a fluidic resistor R_b. The voltage bias causes a current I to flow, setting the voltage V_{out} of the sense electrode. Particles flowing through the nanoconstriction change the nanoconstriction resistance in time (top right), thereby causing measurable changes in the sense voltage V_{out}. These changes are proportional to particle volume, so each particle's volume is measured individually.

A schematic of a microfluidic cartridge is shown to the right. The microfluidic cartridges include a 3 $\mu\ell$ reservoir for the analyte, on-board filters, ports for voltage-biasing the analyte, a sense electrode, a fluid resistor and the critical RPS nanoconstriction, through which nanoparticles flow one at a time. The analyte, which could be blood serum, diluted or full-strength phosphate-buffered saline, or any conducting fluid, is electrically biased by the voltage-bias electrodes, causing an electrical current to flow through the analyte, the fluidic resistor and the nanoconstriction. When a particle suspended in analyte flows through the nanoconstriction, it changes the electrical resistance of the constriction by occluding part of the current, by an amount proportional to the ratio of the nanoparticle volume to that of the nanoconstriction. Individual particles thus give changes in the sense voltage proportional to their volume, allowing them to be counted and sized. The much smaller nanoconstrictions available in Spectradyne LLC's microfluidic cartridges allow much smaller particles to be detected.



Measurement of four different polystyrene bead diameters in a single sample, with the nCS1™, compared to NTA and DLS.

The RPS method offers much higher resolution than do methods that rely on optical techniques, such as dynamic light scattering (DLS) and nanoparticle tracking analysis (NTA). In the figure to the left, we compare measurements of a mixture of different diameter polystyrene beads measured with the nCS1™ with measurements of the same sample with NTA and DLS. The two optical techniques fail to resolve the four different particle diameters, and further give the incorrect concentration of particles.

The nCS1™ offers sizing precision of ±3%, with measurement rates up to 10,000 particles/s. Only 3 $\mu\ell$ of analyte is required per measurement, and the disposable microfluidic cartridges mean that there is no possibility of sample cross-contamination. The cartridges further cover a wide range of particle diameters, from 40 nm up to 1 μm.

In summary, the nCS1's unique implementation of microfluidic resistive pulse sensing demonstrates a disposable format, ultralow volume, and higher resolution measurement of particle size and concentration than do NTA or DLS methods.

email: info@spectradynellc.com