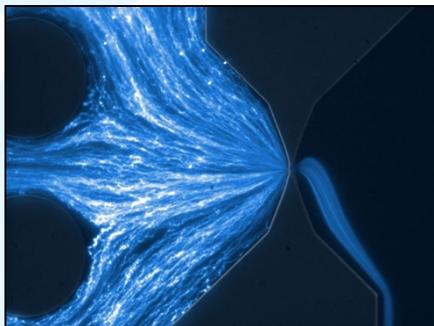


Microfluidic Resistive Pulse Sensing (MRPS) Cartridge Features

Resistive Pulse Sensing (RPS) technology, also known as the Coulter principle, is a widely deployed metrology capable of robust measurements of cells and other particles in the size range of microns to tens of microns. Submicron particle mixtures, however, are difficult to measure reliably with conventional RPS implementations, which typically consist simply of a small pore separating two large fluid vessels. This difficulty arises



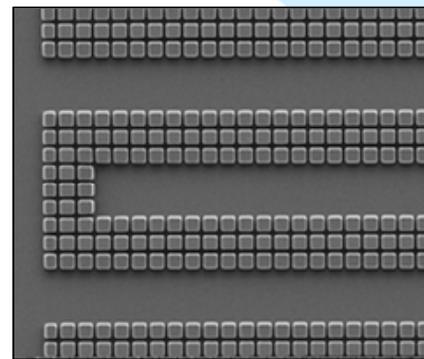
because the pore size must be scaled down in size to detect nanoparticles, and without significant further modifications to the implementation, the frequency of blockages of the nanopore increases prohibitively.



Spectradyne has overcome this limitation with its Microfluidic RPS (MRPS) approach. In the MRPS architecture, micro- and nano-fluidic features are patterned into a plastic block, which is then attached to a glass substrate with electrodes. This assembly, or cartridge, is shown above. By employing state-of-the-art nanofabrication techniques, high-precision complex fluidics are readily designed into the cartridge. As an example, a micrograph of fluorescent nanoparticles flowing through a representative MRPS nanoconstriction is shown above left.

Four key benefits are readily achieved in the MRPS architecture:

- 1) An extremely small sample volume of only a few microliters is required for analysis. This can result in significant cost savings, and permit new experiments that cannot be performed with conventional metrologies.
- 2) A network of embedded filters comprising thousands of parallel channels are integrated into the cartridge upstream of the nanoconstriction. The SEM image at right shows a section of these filter channels, which significantly reduce the chance of large particles blocking the nanoconstriction.
- 3) A bypass channel is designed into the cartridge to allow for fluid to be diverted away from the nanoconstriction. Thus, in the unlikely event of a blockage, fluid flow can be reversed through the nanoconstriction and the blockage can be removed permanently.
- 4) Cartridge dimensions are highly repeatable, enabling factory calibration. Sizing and concentration measurements are therefore robust and do not depend on operator skill.



RPS has been a popular, reliable metrology for large particles for decades. Spectradyne's MRPS implementation brings the benefits of RPS—individual particle detection, high resolution size and concentration measurements, ability to measure particles of all transparencies—to the nano scale in a robust, easy-to-use package.