

Virus titer measurements with Spectradyne's nCS1

The nCS1 difference for virus characterization:

- **Accurate virus concentration**
- **Results in minutes**
- **No tissue culture**
- **Only 3µL sample required**

Viruses and VLPs: the importance of titer

Viral titers are critical assays for researchers involved in vaccine development, studying infectious diseases, as well as in cell and gene therapies. There are two general types of assays used: infectivity assays such as plaque or focus forming assays and chemical/physical assays that measure specific virion components, such as ELISA and PCR techniques. These common techniques are labor-intensive and can take anywhere from hours to days to perform.

There is a real need, particularly when trying to monitor during processing/concentration steps of virus production, to be able to quickly measure viral titer. Spectradyne's nCS1 fills this need perfectly, by delivering direct titer measures in 3-5 minutes. Figure 1 shows the repeatability of nCS1 viral titer measurements of human adenovirus, while Figure 2 graphically illustrates how rapid measurements during the purification process helps to quantify the efficacy of purification steps.

A modern implementation of proven technology

Spectradyne's nCS1™ instrument (Figure 3) accurately measures the concentration and size of viruses and virus-like particles (VLPs) using Microfluidic Resistive Pulse Sensing (MRPS, a.k.a. the *Coulter Principle*), a proven technique that is considered the gold standard for whole blood measurements. The RPS technique has been updated using Spectradyne's patented nanoparticle analyzer (NPA) technology. The heart of the technology is the microfluidic cartridge (Figure 3), which allows the electrical detection of viruses/VLPs as they pass one by one through a nanoconstriction.

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Virus titer in *minutes*, not hours or days:

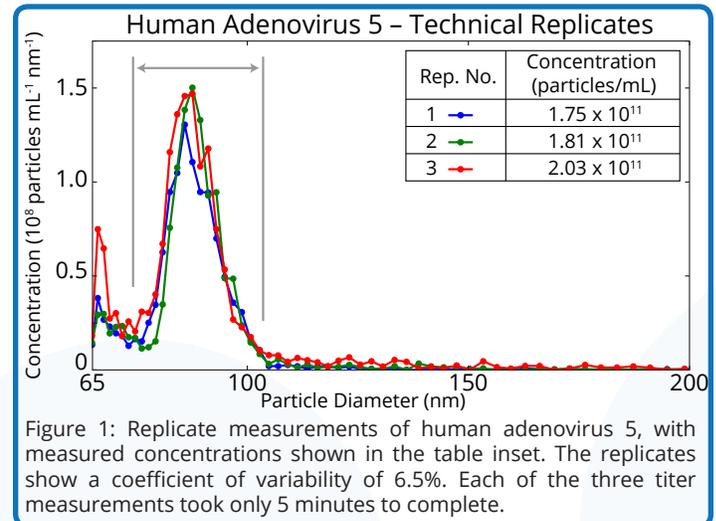


Figure 1: Replicate measurements of human adenovirus 5, with measured concentrations shown in the table inset. The replicates show a coefficient of variability of 6.5%. Each of the three titer measurements took only 5 minutes to complete.

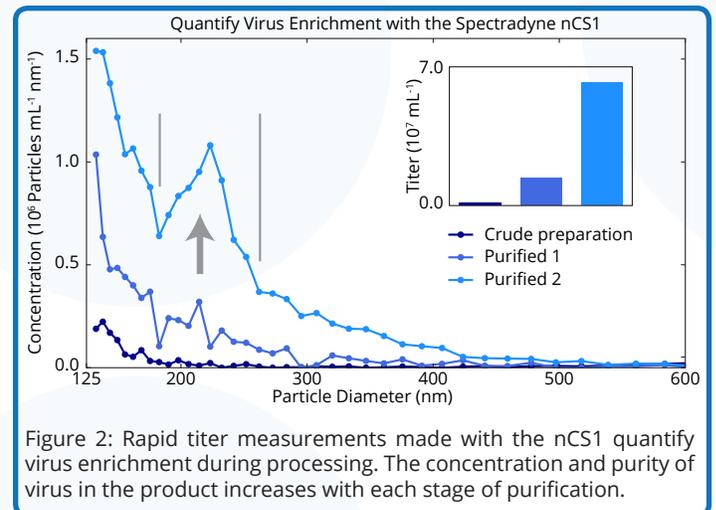


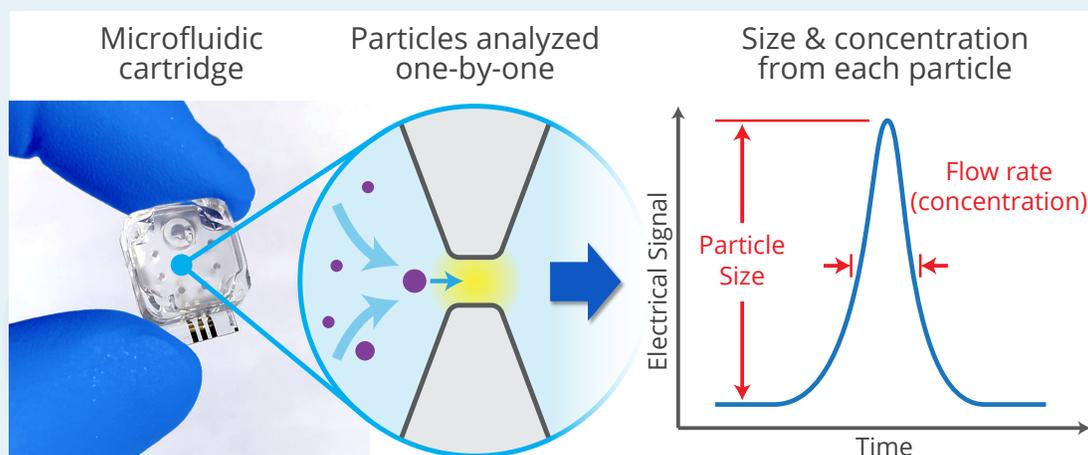
Figure 2: Rapid titer measurements made with the nCS1 quantify virus enrichment during processing. The concentration and purity of virus in the product increases with each stage of purification.

Spectradyne nCS1 and microfluidic cartridges



Figure 3: The Spectradyne nCS1 occupies a small bench top footprint, approximately 1.5 sq ft (left). Only 3 µL of analyte is required for analysis using a disposable microfluidic cartridge (right), which prevents contamination between measurements and eliminates cleaning requirements.

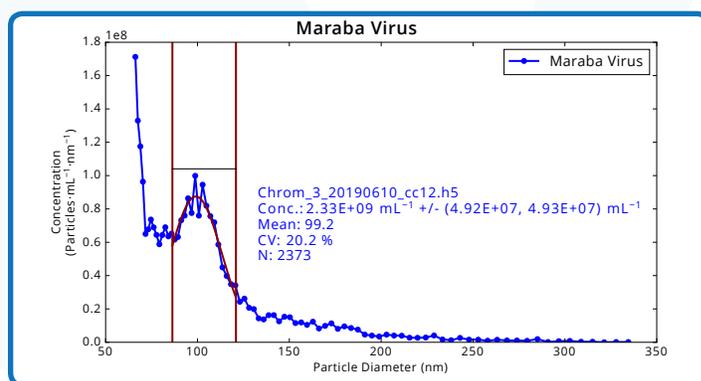
How it works:



How Microfluidic Resistive Pulse Sensing (MRPS) works: Particles in fluid pass through a nanoscale constriction (NC) as shown on left side. A voltage is applied continuously across the two sides of the NC. As particles pass through the NC, the output signal changes in proportion to the volume of the particle. Particles are measured individually, with no dependence on particle material.

No assumption of virus shape required:

The figure on the right shows nCS1 measurement of maraba virus. Maraba is a cylindrical virus: TEM imagery of this sample showed a cylinder of diameter = 65nm and length of 180nm. By calculating the volume of the cylinder, and converting to Equivalent Spherical Diameter (ESD), we were able to correctly predict the nCS1 measured mean diameter of ~100nm. MRPS measures particle *volume* directly, unlike optical techniques which must assume spherical particles.



See what you've been missing!

Contact Spectradyne today and ask for a complimentary sample analysis:
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Spectradyne nCS1 specifications

Technology	Microfluidic Resistive Pulse Sensing (MRPS)
Acceptable particle types	All materials (e.g. transparent/opaque, conducting/insulating, etc.)
Particle size range	50nm to 10,000nm
Sizing/Concentration precision	Sizing < $\pm 7\%$, Concentration < $\pm 20\%$ (particles/ml)
Measurable concentration range	10^4 to 10^{12} particles/ml (sample dependent)
Sample size required	3 μL
Maximum particle detection rate	$\approx 10,000$ particles/sec (sample dependent)
Instrument Control Interface	USB to Windows 10 computer
Data analysis software	Proprietary signal extraction method, real-time signal display, real-time concentration display, multiple filtering methods, multi-dimensional data display, PDF report export
Physical characteristics	13" W x 15" L x 15" H (33 cm W x 38 cm L x 38 cm H)
Electrical	Standard 120/220V, 50/60 Hz AC