Spectradyne®
Particle Analysis

Liposomes & Lipid Nanoparticle (LNPs) Measurements with Spectradyne's nCS1

A Modern Implementation of Proven Technology

Spectradyne's nCS1™ instrument (Fig.1) accurately measures the concentration and size of liposomes and lipid nanoparticles (LNPs) 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 (Fig.1), which allows the electrical detection of liposomes/LNPs as they pass one by one through a nanoconstriction.

The nCS1 Difference for LNP Characterization:

- **Accurate concentration & size**
- **Fast & easy to use**
- **Only 3µL sample required**
- **Truly orthogonal to optical techniques**
- **Any polydispersity!**

LNPs: A New Frontier for DP Delivery:

Liposomes and LNPs are being increasingly used today as efficient delivery mechanisms for many drug products (DPs). The recent success of Pfizer and Moderna's COVID-19 vaccines, based on delivering messenger RNA (mRNA) payloads with LNP delivery, has sparked significant enthusiasm in particular for mRNA-based therapies.

SInce mRNA itself is very delicate and easily destroyed inside the body, the potential of mRNA use had been held back by finding an appropriate delivery mechanism. Early solutions using liposomes have recently been supplanted mostly by LNPs. This has only been made possible by newer LNP formulations which use multiple different lipids to "tune" the particles for delivery to specific target areas of the body.

Measuring the size and concentration of LNPs is of critical importance: size can make a difference on where the DP is delivered, and concentration directly reflects dosage.

Spectradyne nCS1 and Microfluidic Cartridges

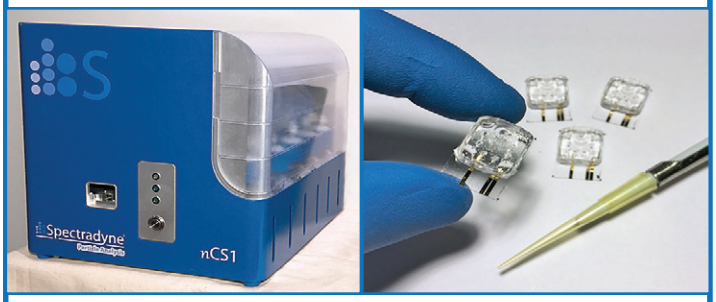

Figure 1: The Spectradyne nCS1 occupies a small bench top footprint, approximately 1.5 sq ft (left). Only 3 µL of analyte is required for analysis using a disposable microfluidic cartridge (right), which prevents contamination between measurements and eliminates cleaning requirements.

Superior accuracy and Detail versus DLS:

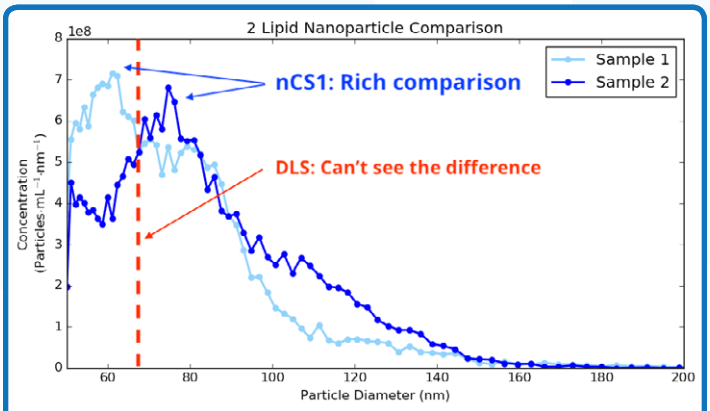

Figure 2: Two LNP samples measured using the nCS1 and DLS. The DLS measurement indicates *no difference* (other than PDI) between the two samples, while the nCS1 shows critical differences in the mean sizes, distribution and concentrations of the two samples.

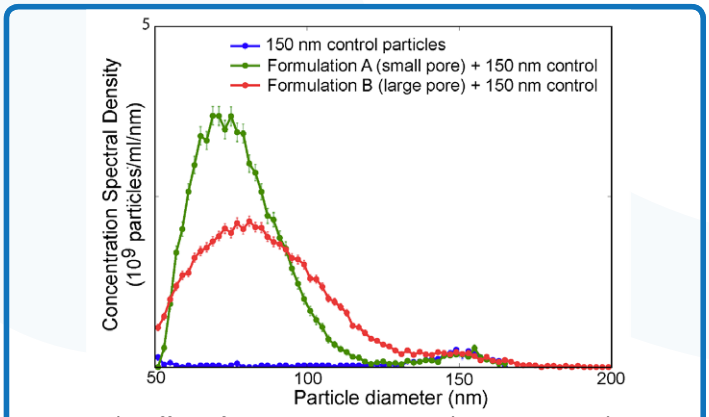

Figure 3: The effect of extrusion pore size on liposome size. The same formulation is extruded through a small and large pore, showing dramatic differences in particle size distribution, not detectable using DLS. In-measurement 150nm controls verify the measurements.

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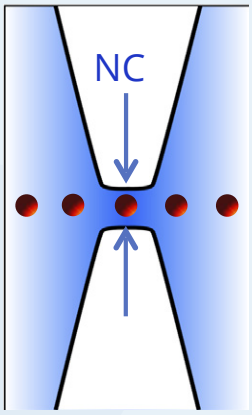
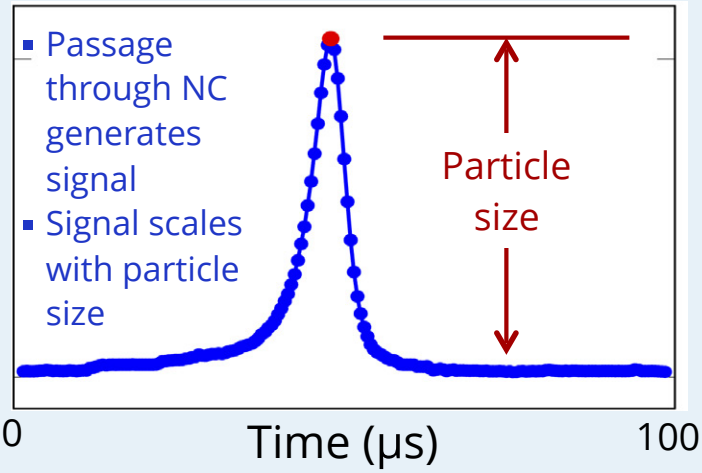
How it Works:

- Nanoscale constriction (NC)
- Electrical detection
- **Individual particles**

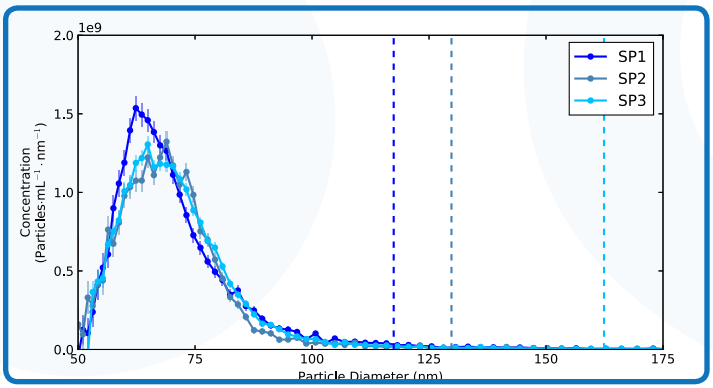




How Microfluidic Resistive Pulse Sensing (MRPS) works: Particles in fluid pass through a nanoscale constriction (NC) as shown on left side. A voltage is applied continuously across the two sides of the NC. As particles pass through the NC, the output signal changes in proportion to the volume of the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

Don't Settle for Misleading DLS Data!

The figure on the right and table below show 3 replicate batches of LNP made using the same recipe, measured by both DLS (dotted lines) and nCS1 (curves). The DLS data is extremely misleading, showing how just a few large particles can totally skew the results to larger sizes.



Sample	DLS Z-Avg	DLS PDI	nCS1 Mode
SP1	117.5nm	0.31	62.5nm
SP2	129.8nm	0.35	68.7nm
SP3	162.4nm	0,31	71.2nm

See what you've been missing!

Contact Spectradyne today and ask for a complimentary sample analysis:
Spectradyne LLC, 2601 Cherry Ave., Suite 140, Signal Hill, CA 90755
(424) 271-9262 www.nanoparticleanalyzer.com

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 < ±3%, Concentration < ±10% (particles/ml)
Measurable Concentration Range	10^4 to 10^{12} particles/ml (sample dependent)
Sample Size Required	3 µL
Maximum Particle Detection Rate	≈ 10,000 particles/sec (sample dependent)
Instrument Control Interface	USB to Windows 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 (33 cm W x 38 cm L)
Electrical	Standard 120/220V, 50/60 Hz AC