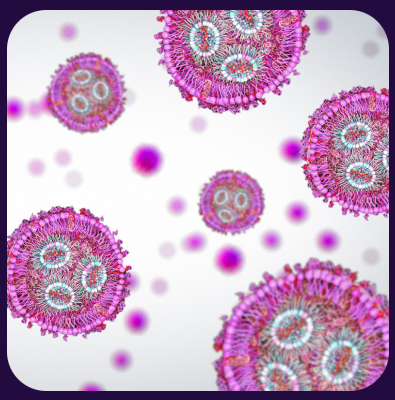
THE EXOID

VERSATILITY IN PARTICLE MEASUREMENT

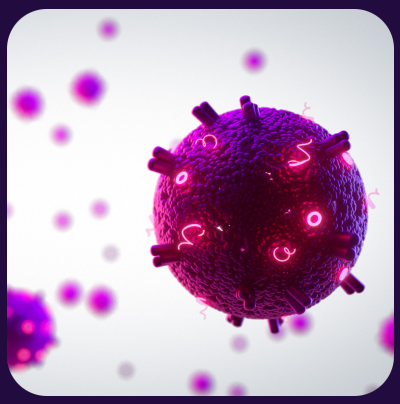
IZON

MEET THE EXOID: VERSATILE, HIGH-RESOLUTION PARTICLE CHARACTERISATION

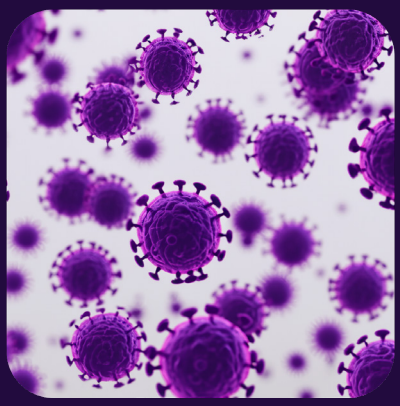
The Exoid is Izon's latest instrument for measuring the physical characteristics of nanoparticles in solution using Tunable Resistive Pulse Sensing. The uniquely high-resolution data that can be obtained using the Exoid enables you to compare your samples with confidence. Either size and concentration, or size and zeta potential can be measured concurrently.



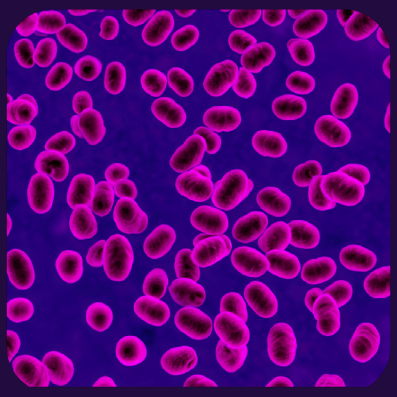
Analyse liposomes and lipid nanoparticles



Measure extracellular vesicles



Investigate viruses and virus-like particles



Measure whole bacteria and more

THE EXOID USES TUNABLE RESISTIVE PULSE SENSING TO PROVIDE SINGLE-PARTICLE MEASUREMENTS

Why Choose Tunable Resistive Pulse Sensing?

TRPS is a single-particle measurement technique which, compared to ensemble techniques, provides superior resolution and data collection capabilities.

While ensemble techniques (such as Dynamic Light Scattering (DLS) and Nanoparticle Tracking Analysis (NTA) for particle sizing, and Electrophoretic Light Scattering (ELS)/Phase Analysis Light Scattering (PALS) for zeta potential) estimate what is going on at a population level, they do not measure individual particles. This leads to substantial data loss and limits your ability to compare your samples in-depth (Figure 1).

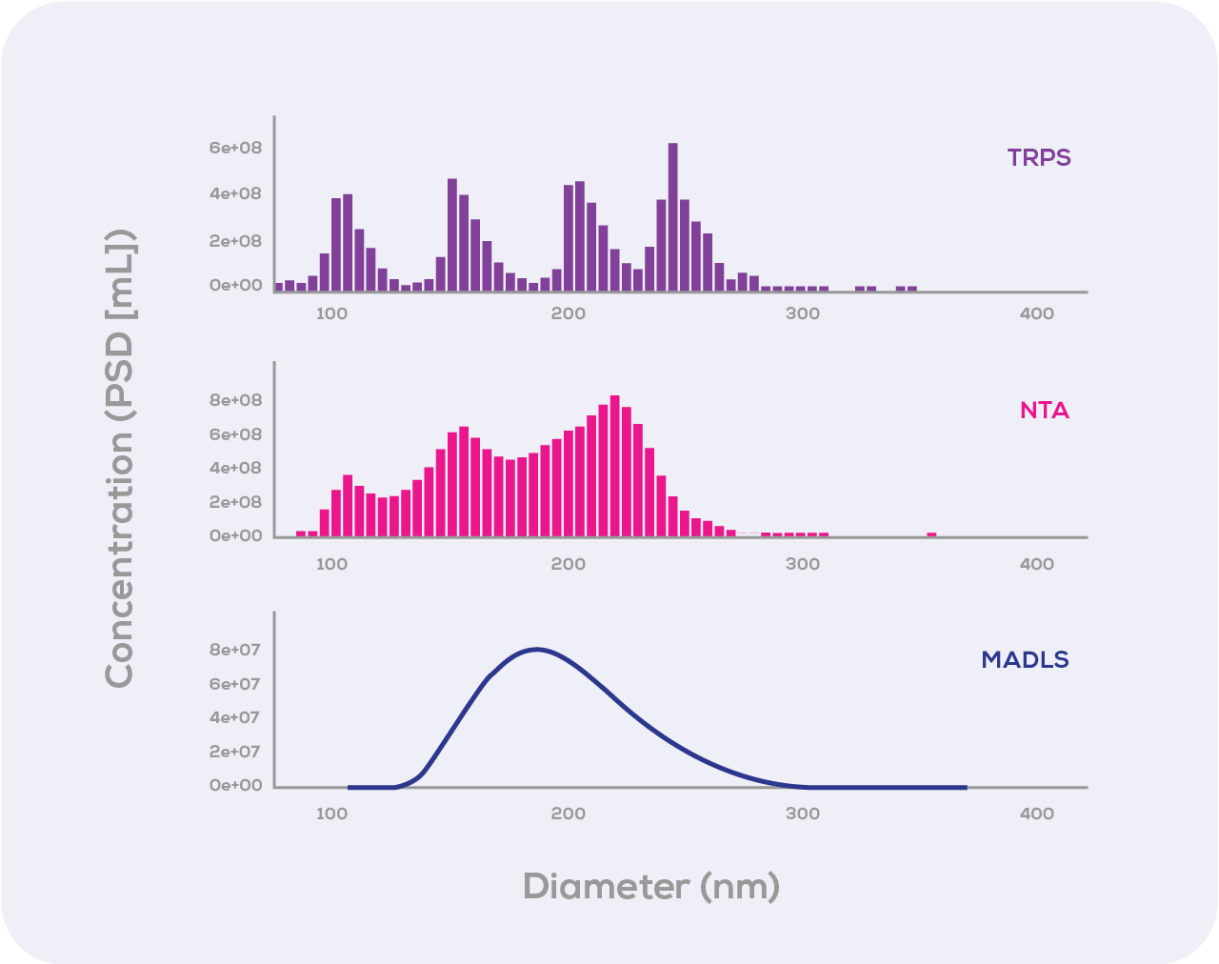


Figure 1: Tunable Resistive Pulse Sensing (TRPS), Nanoparticle Tracking Analysis (NTA) and Multi-angle Dynamic Light Scattering (MADLS) measurements of a quadrimodal sample (CPN100/CPN150/CPN200/CPN240 at 25/25/25/25). TRPS, NTA and MADLS measurements were averaged over 3 runs. TRPS identifies all four subpopulations clearly. NTA was able to identify that multiple subpopulations were present. MADLS was not able to identify any subpopulations.

Tunable Resistive Pulse Sensing: A True Single-Particle Technique

TRPS is a true single-particle measurement technique that provides far greater resolution over ensemble techniques:

- Reproducibility is enabled through the use of standardised NIST-traceable calibration particles.
- Automated data processing is achieved via a user-friendly data visualisation interface.
- Unlike other techniques, TRPS measurements do not rely on prior knowledge of the optical properties of particles or dispersant.
- Parameters are adjusted to maximise the signal-to-noise ratio and are monitored during calibration and sample measurement to ensure high-quality data.

Measure Size and Concentration, or Size and Zeta Potential

Figure 2: The Exoid's clean, user-friendly interface.

APPLICATIONS OF TRPS

The Exoid utilises TRPS which can measure particles in an electrolyte solution (such as PBS) within the size range of 40 nm to 11 µm. This wide particle size range lends TRPS to the analysis of a variety of particle types, as shown in the literature over the years.

Analysis of Liposomes and Lipid Nanoparticles (LNPs) for Vaccine and Therapeutic Development

Both liposomes and more complex LNPs such as solid lipid nanoparticles and nanostructured lipid carriers can be analysed using TRPS. This has been shown both in the literature[1] and through our own in-house data. The Exoid is a powerful tool for detecting even small changes in the size of LNPs, such as those from fresh to freeze-thawed mRNA-loaded LNPs (Figure 3). This is particularly important in the identification of aggregates and other signs of sub-optimal stability. Recording and monitoring the size, concentration and zeta potential of LNPs is not just valuable for development, but for nanomedicine regulatory compliance.

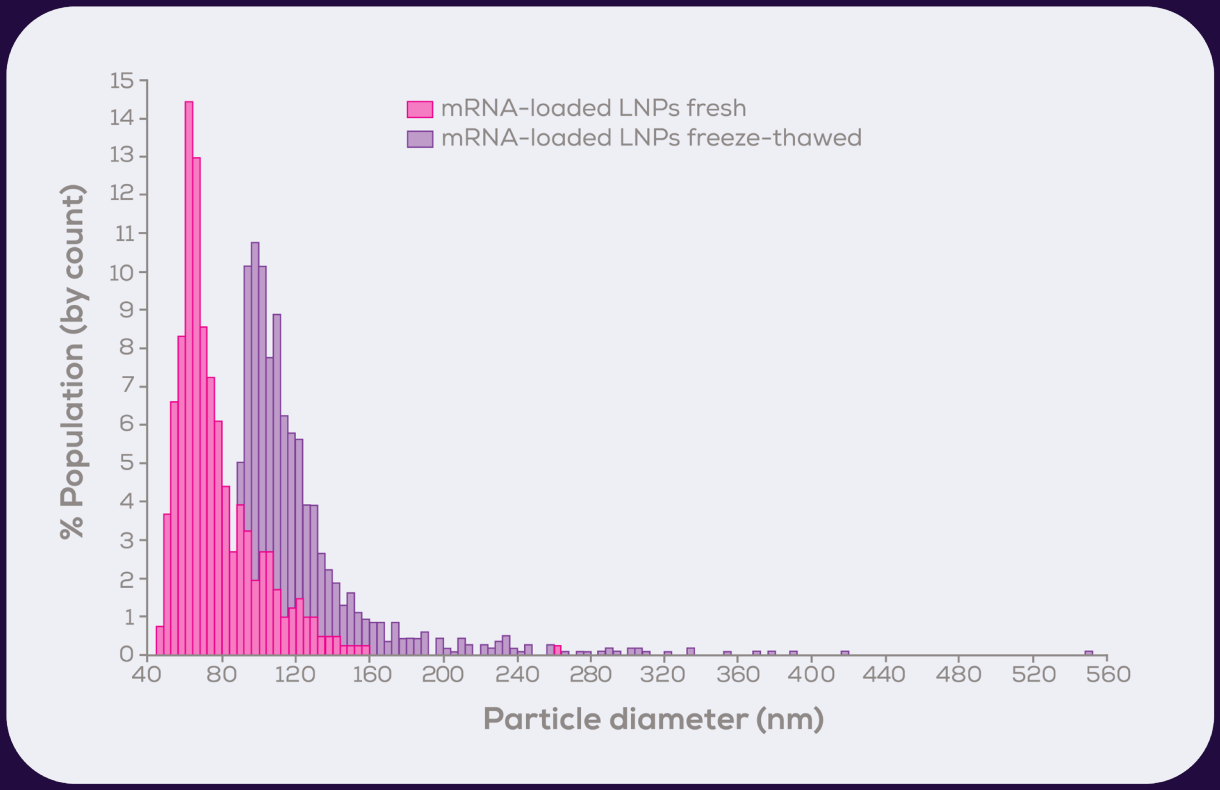


Figure 3: The impact of freeze-thaw on lipid nanoparticle (LNP) size as measured using Tunable Resistive Pulse Sensing (TRPS). Lipid nanoparticles containing mRNA were assessed by TRPS on the Exoid for particle size both fresh and after 2 rounds of freeze-thaw. The shift to the right indicates an increase in size from freeze-thaw, likely indicating some degree of aggregation.

Extracellular Vesicle Characterisation for Fundamental Research and Diagnostic and Therapeutic Development

Extracellular vesicles (EVs) is a blanket term for membrane bilayer vesicles produced and secreted by cells. EV types are differentiated from one another by their biogenesis, and include exosomes, microvesicles (also called microparticles), oncosomes and many others. Different types of EVs can overlap within any given size range. Nevertheless, the size and concentration of EVs are important and even required parameters to be collected for any EV research and publications. Without the concentration, dosing cannot be determined for functional studies. Without sizing, how do you know which size range of EVs you have isolated? Zeta potential is also important, as it has been shown to differ with disease/physiological changes and with factors such as storage.[2,3]

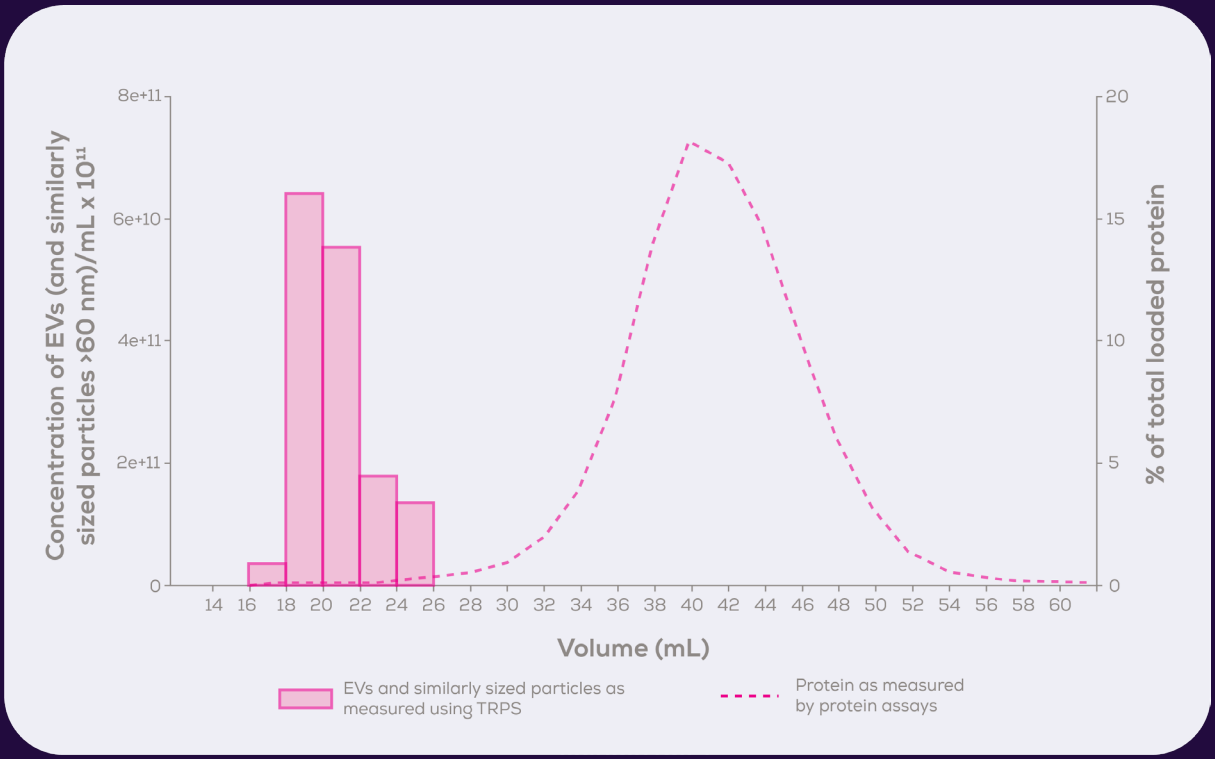


Figure 4: Tunable Resistive Pulse Sensing (TRPS) for the sizing of extracellular vesicles (EVs) and similarly sized particles. EVs and particles of similar size were measured by TRPS on the Exoid to allow for the localisation of EVs within the isolate volume of the qEV2 Gen 2/ 35 nm columns. Protein was measured by bicinchoninic acid (BCA) assay.

Analysis of Viruses and Viral-like Particles

One of the most important parameters in experimental studies on viruses is dosage. Multiplicity of infection is the number of viral particles added to a cell culture vessel per cell. Similar dosing quantification is needed for *in vivo* studies. This is important as it allows for the impact of viral exposure level to be investigated. This means that measuring the precise concentration of virions in your sample is very important. For this, researchers have turned to TRPS to give them accurate viral titres and even viral size distributions.[4,5] Others have used TRPS to measure the concentration of viral particles in environmental samples.[6] Or even the size, zeta potential and concentration of viral-like particles.[7]

Analysis of Bacteria and Bacterial EVs

The EVs produced by bacteria are frequently measured using TRPS[8], but so are the size and concentration of bacteria themselves.[9] This offers a much more accurate concentration measurement as compared to optical density measurements, as individual bacteria are counted rather than making an estimate. TRPS also critically allows for the sizing of the bacteria, which can give critical information about the viability and state of the bacteria.

Alternative Uses of TRPS

TRPS is predominantly used for analysing cell-derived or therapeutic particles. However, its application has expanded into other research areas. For instance, in microfluidics research, a study utilised TRPS to measure carboxylate-modified fluorescent polystyrene submicrometer particles, allowing for a more precise determination of their position within a microchannel.[10] When comparing different analytical techniques for nanoplastic measurement, TRPS was uniquely able to discern particle sizes that eluded many other methods. These instances, although exceptions, underscore the versatility of TRPS beyond its conventional uses.[11]

How Does TRPS Work?

Nanoparticle suspensions are complex and often polydisperse. Characterising them fully requires a tunable system which allows you to customise the measurement for your sample.

TRPS is based upon the Coulter principle and the use of a tunable, stretchable nanopore – i.e. a crucible with an aperture (hole) in the centre (Figure 5). Nanopores are consumable items and come in a variety of sizes to suit your measurement needs.

Figure 5: Tunable, stretchable nanopores used in Tunable Resistive Pulse Sensing.

Your sample is placed into an upper fluid cell, after which particles pass through the nanopore into the lower fluid cell. The nanopore has an electrical current running through it, meaning that a blockade is created by each particle that passes through the nanopore one by one by virtue of either one or both of the current (i.e., attracting particles on the basis of charge) or pressure.

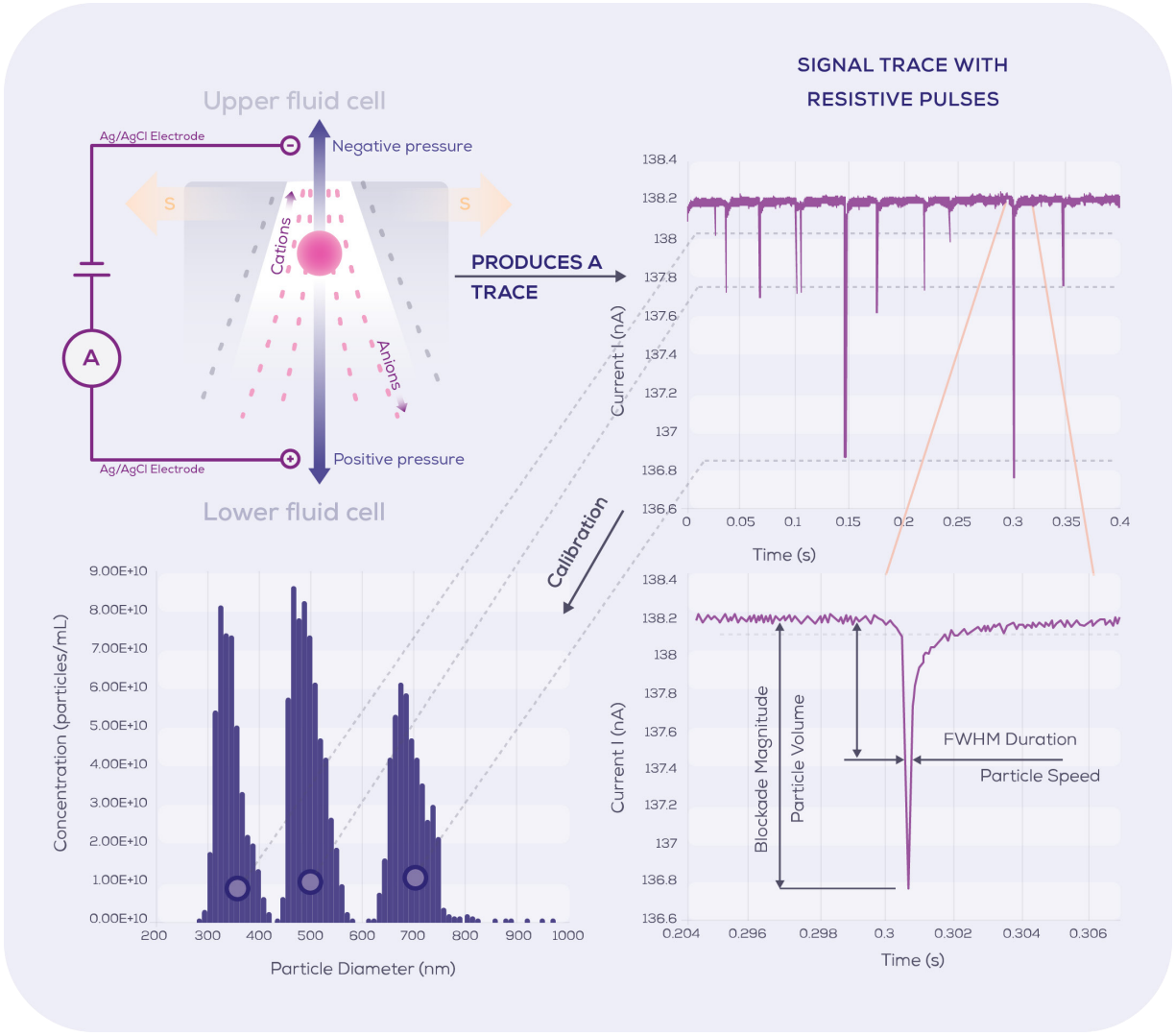


Figure 6: Schematic diagram of Tunable Resistive Pulse Sensing (TRPS). Top left: The nanopore is stretched "S" to optimise the nanopore size to the particle size range within your sample. The applied pressure is tuned to adjust (or even reverse) fluid flow through the nanopore. Voltage can be tuned to attract particles of different surface charge or polarity through the nanopore, and optimise the signal-to-noise ratio of the system. Top right: The resulting trace produces blockade parameters which can be studied to obtain measurements on a single-particle basis (bottom left). Bottom right: From each blockade, the size (via blockade magnitude) and zeta potential (via blockade duration) of the particle can be measured, while concentration is derived from blockade frequency.

Particle size and concentration can be measured for particles in the size range of 40 nm to 11 µm, while size and zeta potential can be measured for particles in the size range of 40 – 2000 nm. Detailed specifications of the Exoid are shown in Figure 7.

Figure 7: Detailed specifications for the Exoid

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