

Consideration	TRPS (Tunable Resistive Pulse Sensing)	DLS (Dynamic Light Scattering)	NTA (Nanoparticle Tracking Analysis)
Measurement Principle	Measures individual particles via resistive pulse sensing; size is directly proportional to blockade magnitude.	Measures ensemble size distributions via light scattering; calculates hydrodynamic diameter based on assumptions.	Tracks individual particle motion under Brownian motion to calculate hydrodynamic diameter.
Particle Size Range	40 nm to 11 µm, size-dependent on nanopore selection.	1 nm to ~10 µm, less reliable for multimodal or large particles.	~10–2000 nm, depending on sample and settings.
Concentration Range	High precision, even at low concentrations; calibrated with standard particles.	Struggles with high-concentration samples.	Accurate within mid-concentration ranges; tends to overestimate particle concentrations. <sup>1,2,3</sup>
Single-Particle Data	Yes, with size, concentration, and zeta potential.	No, only ensemble data.	Yes, but without zeta potential.
Zeta Potential	Measures zeta potential per particle.	Ensemble zeta potential only.	Not available.
Resolution Capabilities	Excellent for resolving subpopulations in heterogeneous samples.	Limited; cannot resolve a multimodal sample	Moderate; resolution of multimodal samples is relatively limited.
Ease of Use	Moderate; requires technical expertise to set up.	Easy; minimal sample prep and training required.	Moderate; more user-friendly than TRPS, less than DLS.
Data Analysis	Detailed; high-resolution data per particle. Automated data processing with user-friendly data visualisation interface.	Simplistic; intensity-weighted average results.	Tracks and sizes particles individually; requires advanced data analysis.
Key Advantages	High resolution; zeta potential; single-particle data.	Fast; easy to use; affordable.	Combines tracking and sizing; moderate detail.
Key Limitations	Different sized nanopores are needed to cover entire size range; requires more time to master.	Less precise for heterogeneous samples. Accurate knowledge of optical properties of particles and dispersant is required.	Size accuracy affected by Brownian motion uncertainty; sensitivity adjustments can be challenging. No zeta potential; high cost.

<sup>1</sup>Vestad, B., Llorente, A., Neurauter, A., Phuyal, S., Kierulf, B., Kierulf, P., Skotland, T., Sandvig, K., Haug, K. B. F., & Øvstebø, R. (2017). Size and concentration analyses of extracellular vesicles by nanoparticle tracking analysis: a variation study. *Journal of Extracellular Vesicles*, 6(1). <https://doi.org/10.1080/20013078.2017.1344087>

<sup>2</sup>Bachurski, D., Schuldner, M., Nguyen, P. H., Malz, A., Reiners, K. S., Grenzi, P. C., Babatz, F., Schauss, A. C., Hansen, H. P., Hallek, M., & Pogge von Strandmann, E. (2019). Extracellular vesicle measurements with nanoparticle tracking analysis - An accuracy and repeatability comparison between NanoSight NS300 and ZetaView. *Journal of Extracellular Vesicles*, 8(1). <https://doi.org/10.1080/20013078.2019.1596016>

<sup>3</sup>Vogel, R., Savage, J., Muzard, J., Camera, G. della, Vella, G., Law, A., Marchioni, M., Mehn, D., Geiss, O., Peacock, B., Aubert, D., Calzolari, L., Caputo, F., & Prina-Mello, A. (2021). Measuring particle concentration of multimodal synthetic reference materials and extracellular vesicles with orthogonal techniques: Who is up to the challenge? *Journal of Extracellular Vesicles*, 10(3), e12052. <https://doi.org/10.1002/JEV2.12052>