

# RNANALYTICS

CE-TDA technology for lipid nanoparticle sizing

## White Paper

# Taylor Dispersion Analysis for Particle Sizing of Lipid Nanoparticles

*A mass-weighted, separation-based approach for robust LNP characterization*

### Executive abstract

RNAnalytics has validated a CE–TDA workflow for research-stage lipid nanoparticle sizing that resolves multimodal populations more transparently than intensity-weighted light scattering. The technology combines controlled capillary transport, Taylor–Aris dispersion physics, dynamic capillary surface conditioning, and software-guided peak modeling to generate fit-for-purpose hydrodynamic size descriptors for formulation development, comparability, and stability trending.



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**RNAnalytics Advanced Research GmbH**

Technology overview for website download

## Why LNP sizing needs a different analytical lens

Lipid nanoparticles are inherently heterogeneous systems. During formulation development, researchers need to distinguish the main nanoparticle population from small excipient-derived species, partially formed structures, and emerging aggregates. Traditional Dynamic Light Scattering (DLS) is fast and useful, but its signal is intensity-weighted, which means larger particles can dominate the reported average and mask smaller or co-existing populations.

CE–TDA addresses this limitation by combining capillary transport with Taylor–Aris dispersion. Instead of relying on scattering intensity, the method derives an apparent hydrodynamic diameter from diffusion-driven peak broadening under defined flow conditions. This creates a measurement that is better suited for trend-based comparison of complex LNP samples.

### Core technology principle

In the RNAalytics workflow, a defined sample plug is introduced into a capillary electrophoresis instrument operated in pressure-driven mode. As the plug travels through the capillary, laminar flow and radial diffusion broaden the signal in a predictable way. The resulting Taylorgram is fitted to extract the diffusion coefficient, which is then converted into an apparent hydrodynamic diameter via the Stokes–Einstein relationship.

### What makes the approach different

Aspect	Conventional DLS	RNAalytics CE–TDA
Signal basis	Intensity-weighted scattering	Dispersion-based, analyte/mass-weighted sizing
Complex populations	Large species can dominate the mean	Peak-resolved view supports population separation
Method role	Rapid orthogonal check	Comparability, trend detection, and development analytics
Output	Single average often emphasized	Model-based cluster statistics with fit-quality context

## Controlling the capillary environment

A critical insight from the validation work is that LNPs can strongly interact with bare fused silica surfaces. Without surface control, adsorption distorts peak shape and undermines reproducibility. RNAalytics therefore optimized a dynamic coating strategy that suppresses particle–wall interactions and stabilizes migration behavior.

For demanding DNA-loaded LNP samples, reproducible analysis was achieved only when a continuous polymer-replenishment coating was maintained in the background electrolyte. This step is central to transforming CE–TDA from an attractive concept into a practical and reliable analytical method.

## Integrated software and data workflow

The technology is paired with an RNAalytics software environment that structures the workflow from data import to audit-ready reporting. Users upload detector traces and metadata, apply a predefined Taylor analysis pipeline, review peak assignments in a human-in-the-loop step, and compare runs across batches or stability time points.

Key processing stages include mild smoothing, reproducible peak detection, statistically guided region selection, Gaussian peak decomposition, clustering of valid components, and reporting of the main LNP population as a method-defined descriptor. This architecture reduces operator-driven variability while preserving scientific review and traceability.

## Operational workflow

- Import instrument output and register method metadata.
- Run the Taylor analysis pipeline with validated settings for peak detection and fitting.
- Review components, reject artifacts, and confirm the final model.
- Export a structured report with plots, fit statistics, and reportable size values.

## Validation highlights

The validation program was designed for fit-for-purpose use in research and process development. Rather than positioning the method as a GMP release assay, the goal was to demonstrate precision, robustness, and reliable trend detection under defined operating conditions.

## What was demonstrated

- Robust separation of the main LNP population from small excipient or micellar species and from larger aggregates.
- High model fit quality across the relevant LNP size window, supporting stable extraction of hydrodynamic size descriptors.
- Operational robustness against reasonable changes in pressure and processing parameters.
- Orthogonal plausibility versus DLS and reference particle measurements, while preserving the distinct analytical value of a mass-weighted method.
- Successful detergent-mediated LNP rupture workflows that establish the analytical basis for future encapsulation-efficiency assays.

## Recommended use cases

RNAalytics positions CE–TDA as a characterization technology for teams working on RNA delivery systems, formulation screening, manufacturing changes, and stability programs. The method is particularly valuable when relative shifts in population structure matter more than a single broad average.

Use case	Decision supported
Formulation screening	Compare candidate recipes and identify cleaner main populations.
Process transfer or scale-up	Check whether the particle profile remains comparable after a manufacturing change.
Stability trending	Track shifts in the main population, appearance of small species, or aggregate growth over time.
Analytical workflow benchmarking	Evaluate coatings, buffers, and software settings in a structured way.

## Scope, positioning, and roadmap

The current validation supports non-GMP development use. Reported hydrodynamic diameters are method-defined descriptors generated under specified capillary, buffer, coating, and software conditions. The method is therefore suited to internal comparison and trend analysis, not to absolute size assignment against certified reference standards or QC release testing.

### What comes next

- Expansion of the full encapsulation-efficiency workflow after validated particle break-up and cargo release.
- Further standardization of kit components, surface-conditioning reagents, and system-suitability controls.
- Transfer of the workflow into increasingly productized, compliance-ready software and kit formats.
- Future extension toward stronger reference-material strategies and, where needed, more formal quality environments.

### Bottom line

RNAnalytics CE–TDA provides a high-value orthogonal technology for LNP teams that need more than a single intensity-weighted average. By combining controlled capillary chemistry, validated data processing, and audit-friendly reporting, the platform enables clearer nanoparticle sizing decisions throughout development.

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