

Optimizing LNP-RNA Formulations: Key Insights into Size, Zeta Potential, and Stability

Will Penny, PhD, Wyatt Technology, LLC



Abstract

The microfluidic formulation of RNA-containing lipid nanoparticles (LNP-RNA) is a widely utilized approach for developing and producing non-viral gene delivery systems. A critical challenge in this process is optimizing lipid selection and formulation conditions to achieve targeted particle sizes and surface potential. This study highlights the application of the DLS/SLS/ELS instrument for rapid characterization of LNP-RNA therapeutics, focusing on size, polydispersity, and zeta potential. Results demonstrate the impact of production methods on LNP formulations, colloidal stability across various buffer conditions, and structural changes following freeze-thaw cycles. These findings underscore the importance of precise characterization for optimizing LNP-RNA formulations and ensuring their stability and efficacy.

The **DynaPro™ ZetaStar™** instrument combines dynamic, static and electrophoretic light scattering (DLS/SLS/ELS) all in one platform.

Particle Concentration	Charge and Isoelectric Point
Thermal Denaturation	Size and Polydispersity
k_D and A_2	Molar Mass
Viscosity	Turbidity

Features

Designed for Casual and Expert users

DYNAMICS Touch™ software intuitively guides with virtually no training. Measure particle concentration, size, and zeta potential in **less than 2 minutes with 65 μ L**.

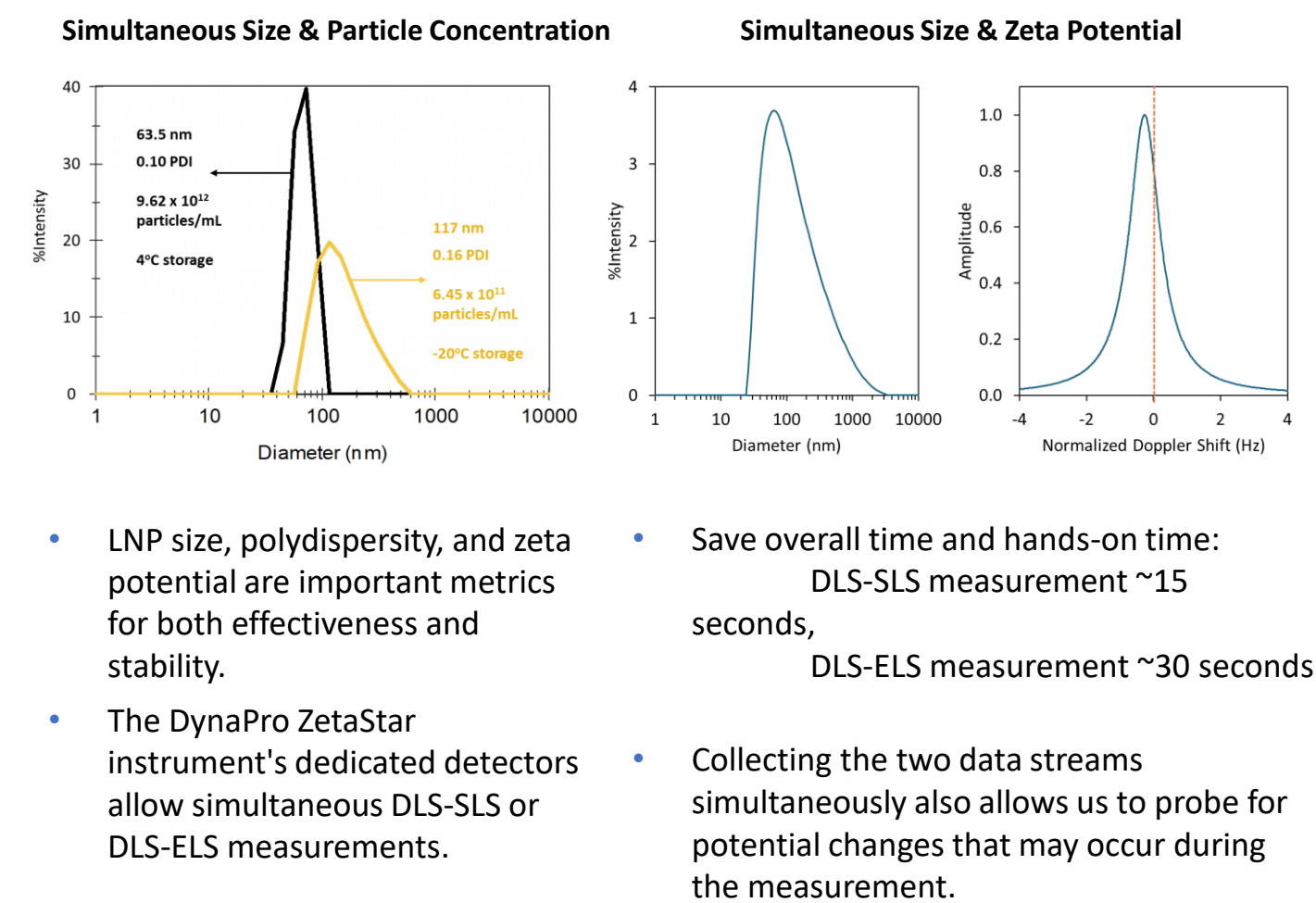
Hands-free automation

Combine the DynaPro ZetaStar instrument with an autosampler for **unattended measurements of dozens of samples**; probe stability with automated temperature ramps.

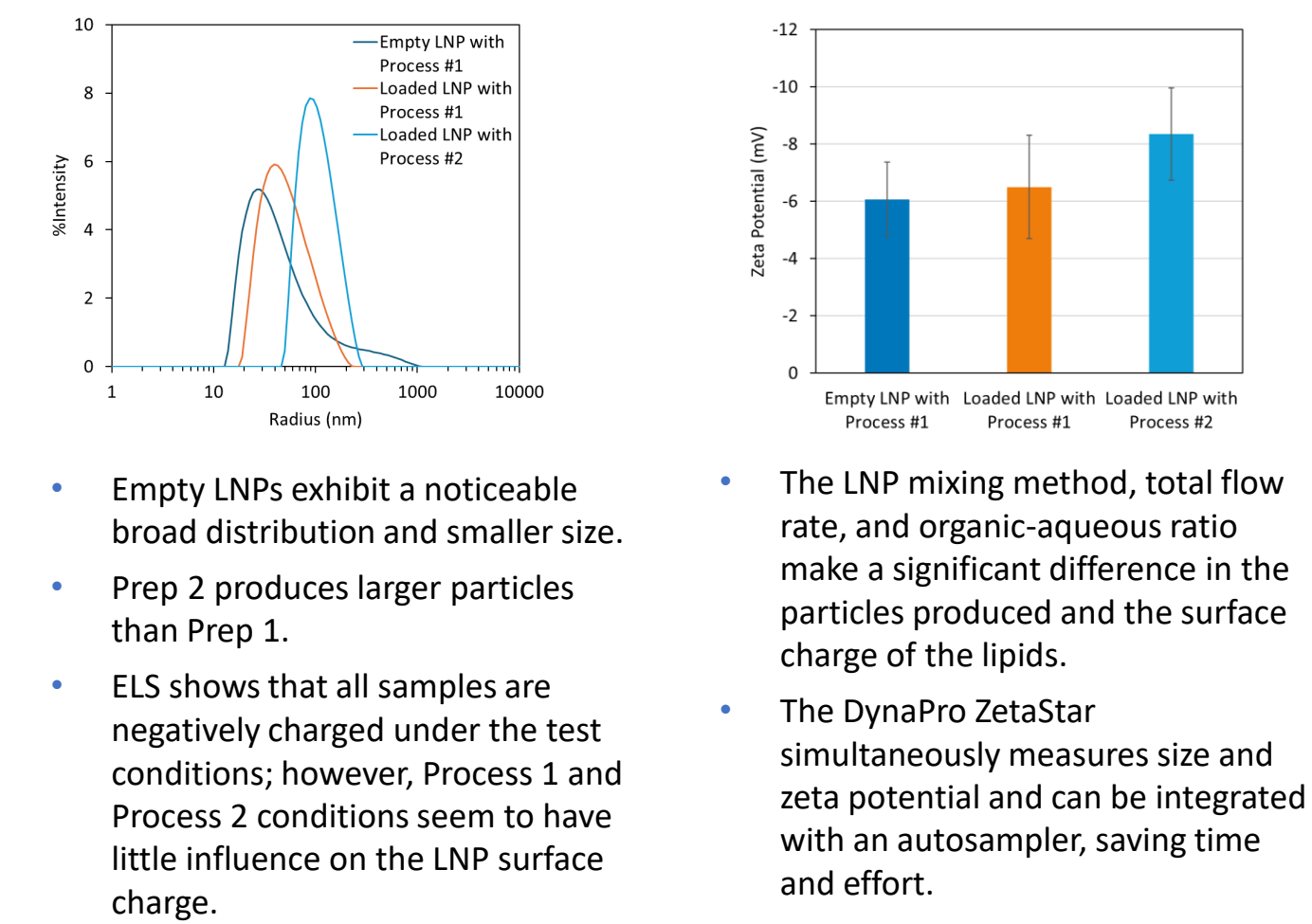
ELS in native buffer.

The ZetaStar instrument was designed for biopharma applications and with the addition of the ATLAS™ pressurization accessory, excels in high salt buffers. **Obtain size and zeta potential in formulation buffer without dilution.**

Rapid quality check



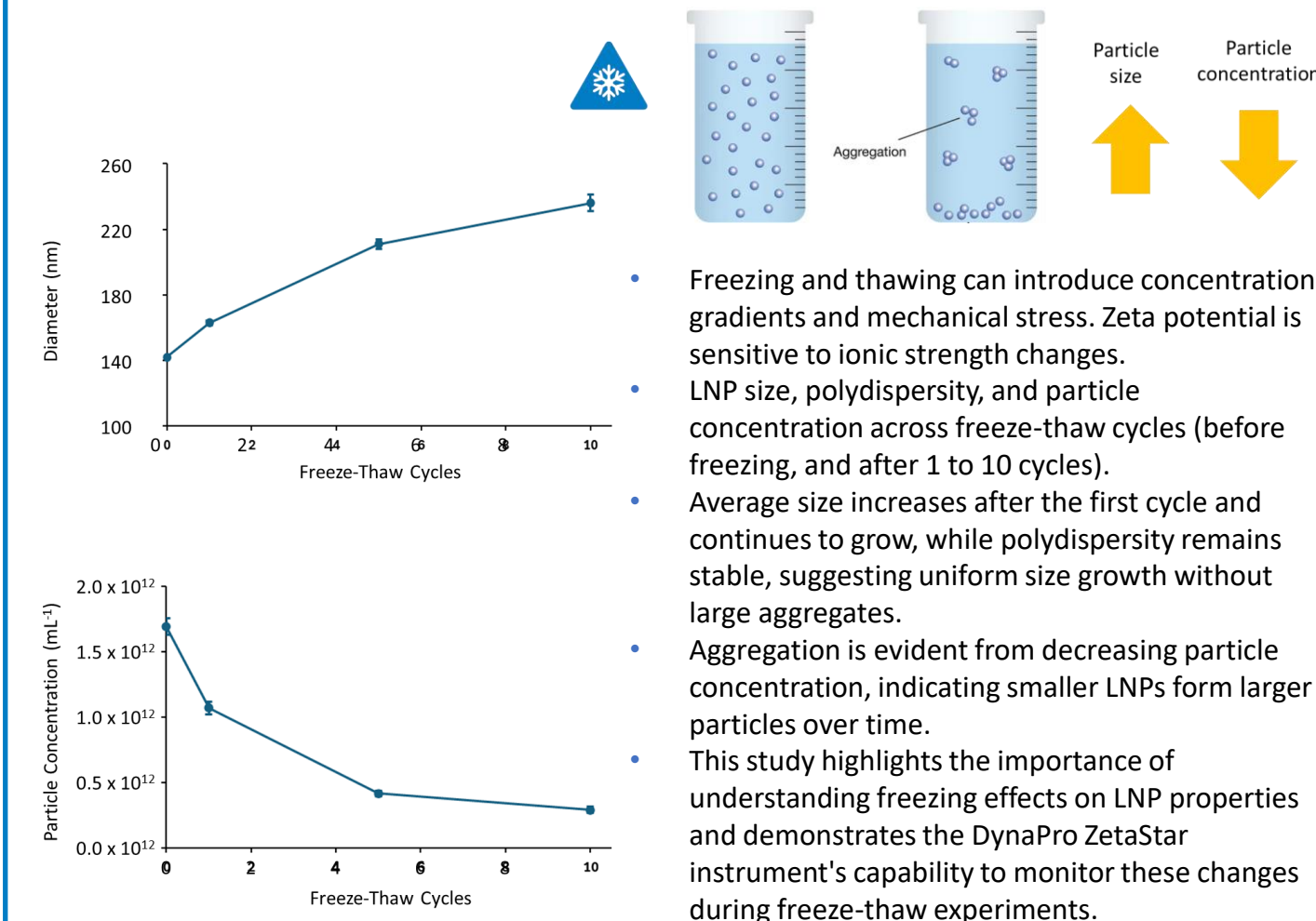
Mixing Process Repeatability Assessment



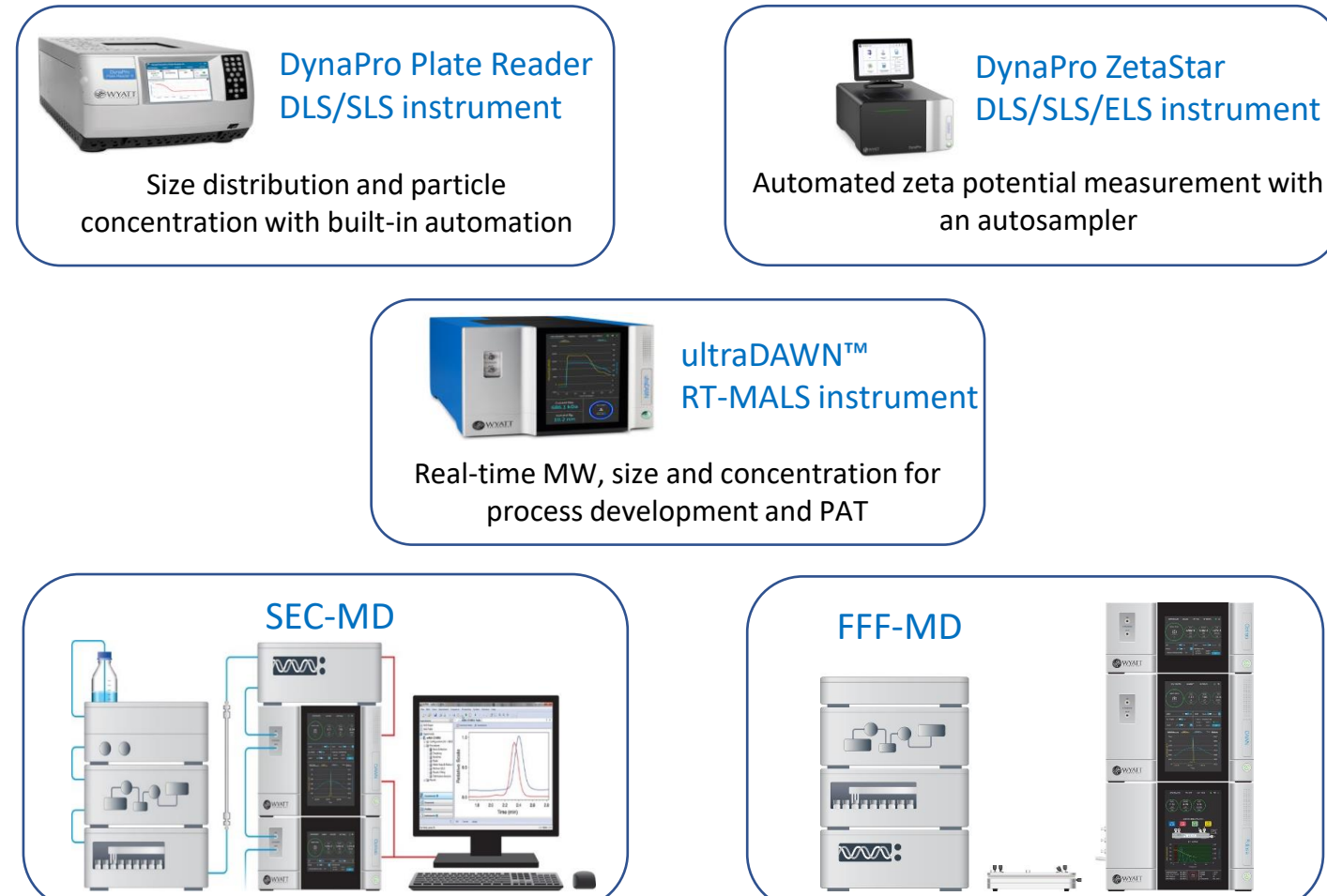
Zeta Potential Measurement in Buffer Formulation



Freeze Thaw Stability



Wyatt Solutions for LNP analysis



Conclusion

- The DynaPro ZetaStar instrument provides a streamlined approach for rapid screening of LNP formulation and process conditions. It measures LNP-RNA size, size distribution, zeta potential, and particle concentration.
- The DynaPro ZetaStar instrument is a simple, powerful, and versatile tool that can also determine molar mass, turbidity, interactions, and thermal behavior for macromolecules like polymers, proteins, or nucleic acids.
- For more detailed studies, separation-based techniques such as SEC-MALS and/or FFF-MALS are recommended.



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