Transforming Nanoparticle Analysis:
What Light Scattering Techniques Reveals About LNPs & Liposomes

Will Penny

Sr. Sales Manager, Bio

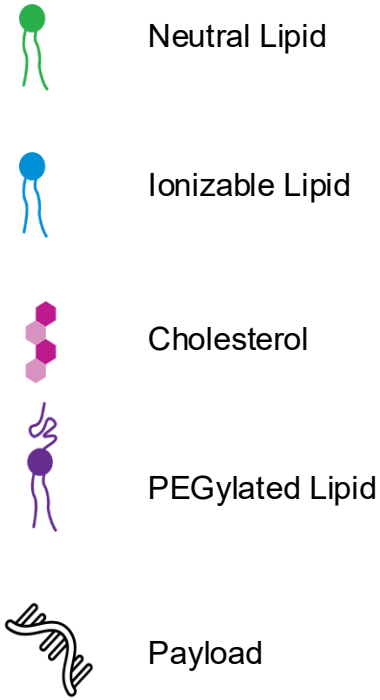
Waters | Wyatt Technology

LNP-mediated therapies

- LNPs are a new class of delivery vehicles.
- First US and EU approvals in 2018.

  Alnylam® Pfizer moderna
- Multiple drug products in development:
  - siRNA
  - mRNA
  - Cas mRNA + sgRNA
  - DNA
  - protein
  - small molecules
- Quality attributes are evolving.
- Second-generation targets are more challenging. Many outstanding questions.

Optimizing LNP formulation is a challenge



Permutations:

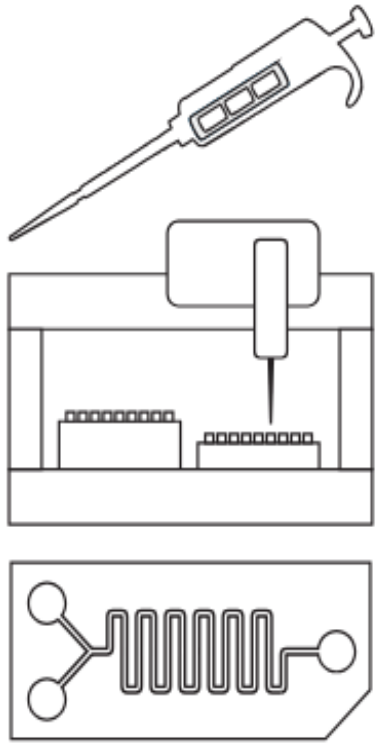
Choice of payload

Choice of lipids

- Neutral
- Ionizable
- Cholesterol
- PEGylated

Relative concentration

Total concentration



Permutations:

Mixing Methods

Speed

TFR

Scale-up

Hundreds of samples may be generated in early stages.
High-throughput solutions are critical for efficient sample analysis.

Waters |Wyatt LNP Characterization Solutions

Non-exhaustive

High-Throughput Screening → Zeta Potential Optimization → MAQ & Detailed Characterization

DynaPro™ Plate Reader High Throughput DLS/SLS Instrument

- Size/ radius (QC)
- Aggregation content
- Freeze-thaw stability
- Structure
- Polydispersity (QC)

DynaPro ZetaStar™ DLS/SLS/ELS Instrument

- Size/radius (QC)
- Aggregation content
- Structure
- Charge/Zeta Potential
- Polydispersity (QC)

Digest

Intact & Digest

Waters LC-MS

QDa detector

BioAccord™ MS

Lipid Composition & ratio

Modifications – Lipids and mRNA

Low level impurities

Size Exclusion or Eclipse™ FFF system

MALS

RI

UV

Size distribution

Payload concentration

Size-based payload distribution

Encapsulation efficiency

Morphology

Lipid concentration

Aggregation

Waters |Wyatt LNP Characterization Solutions

Non-exhaustive

High-Throughput Screening

Hundreds of samples

DynaPro™ Plate Reader High Throughput DLS/SLS Instrument

- Size/ radius (QC)
- Aggregation content
- Freeze-thaw stability
- Structure
- Polydispersity (QC)

Zeta Potential Optimization

DynaPro ZetaStar™ DLS/SLS/ELS Instrument

- Size/radius (QC)
- Aggregation content
- Structure
- Charge/Zeta Potential
- Polydispersity (QC)

MAQ & Detailed Characterization

Digest

Waters LC-MS

QDa detector

BioAccord™ MS

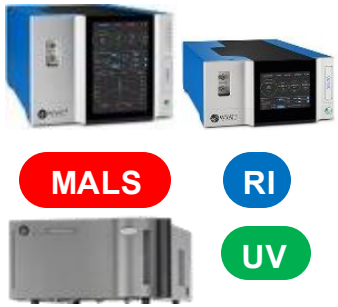
Lipid Composition & ratio

Modifications – Lipids and mRNA

Low level impurities

Intact & Digest

Size Exclusion or Eclipse™ FFF system



Size distribution

Payload concentration

Size-based payload distribution

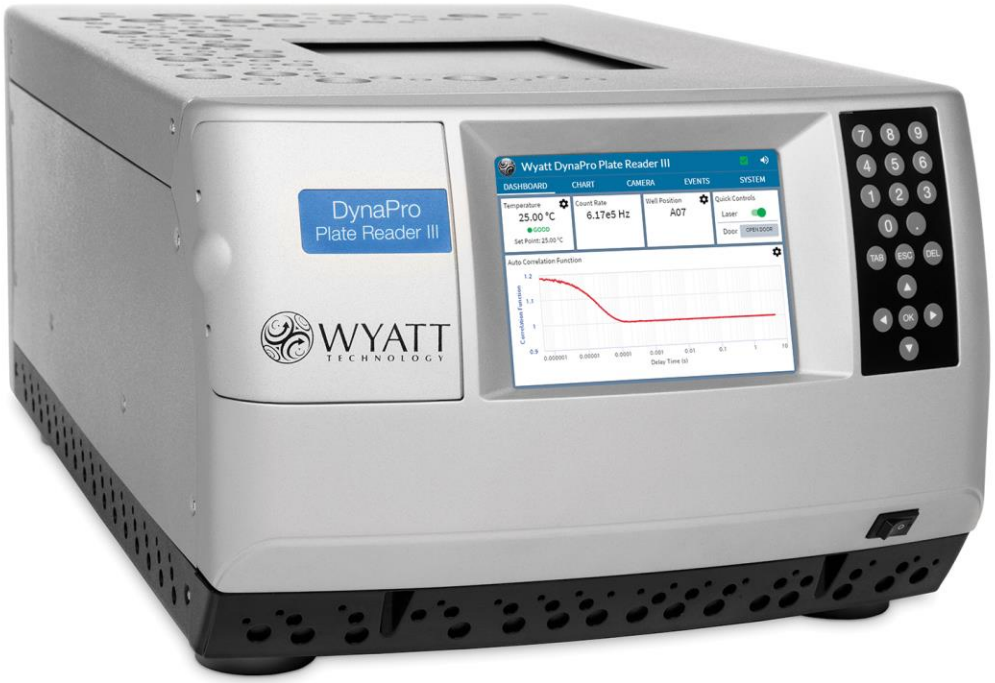
Encapsulation efficiency

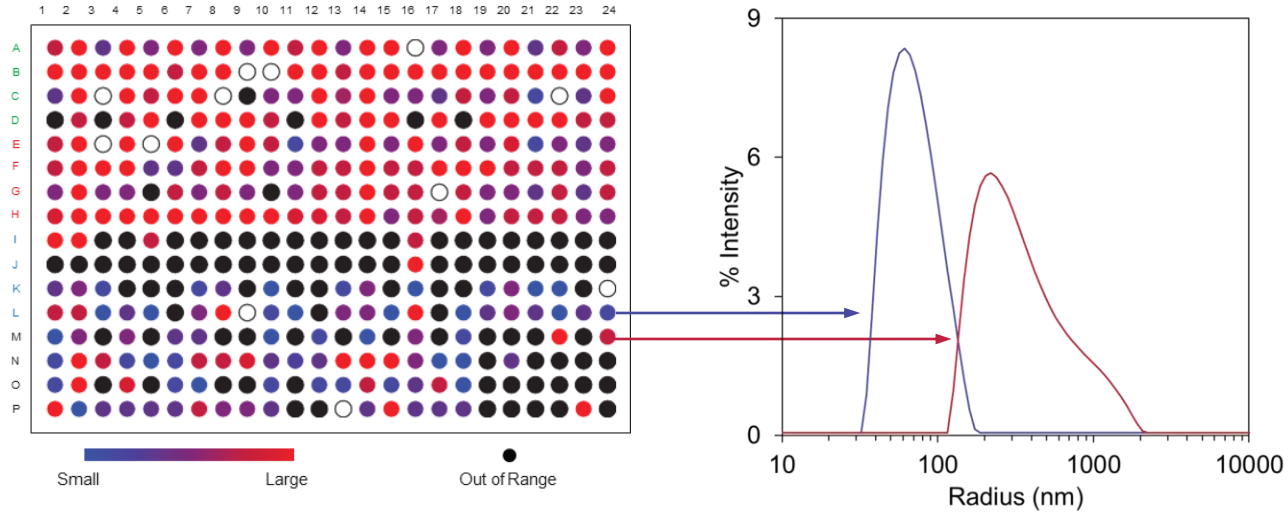
Morphology

Lipid concentration

Aggregation

High-throughput LNP formulation screening

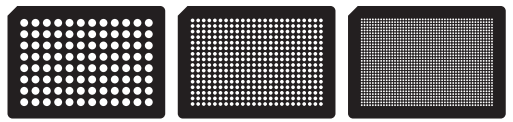




DynaPro Plate Reader

High-throughput DLS/SLS instrument

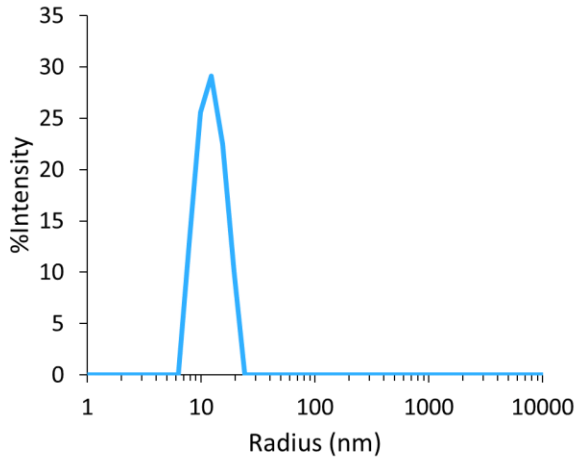
- Automation friendly
- Size and Polydispersity
- Particle concentration
- Degradation



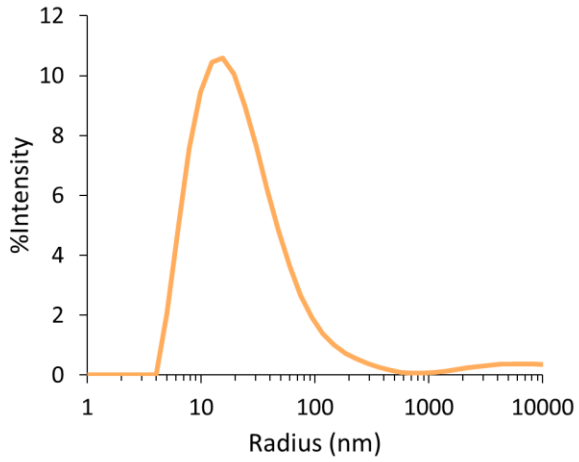
Compatible with industry-standard
96, 384, 1536 well plates

Strength of DLS measurement

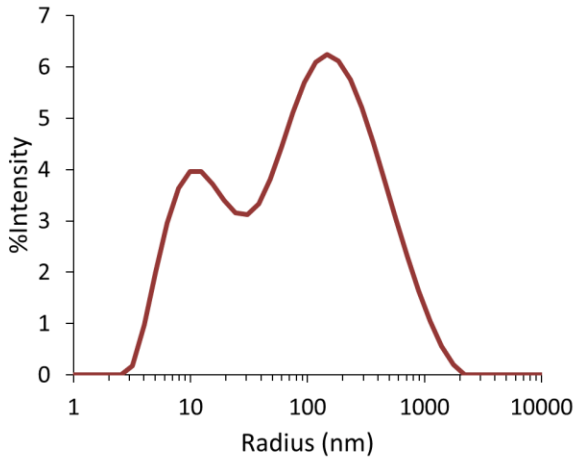
- **<u>Fast</u> and sensitive assessment of aggregation**



Sample appears to be in good shape



Some self association happened



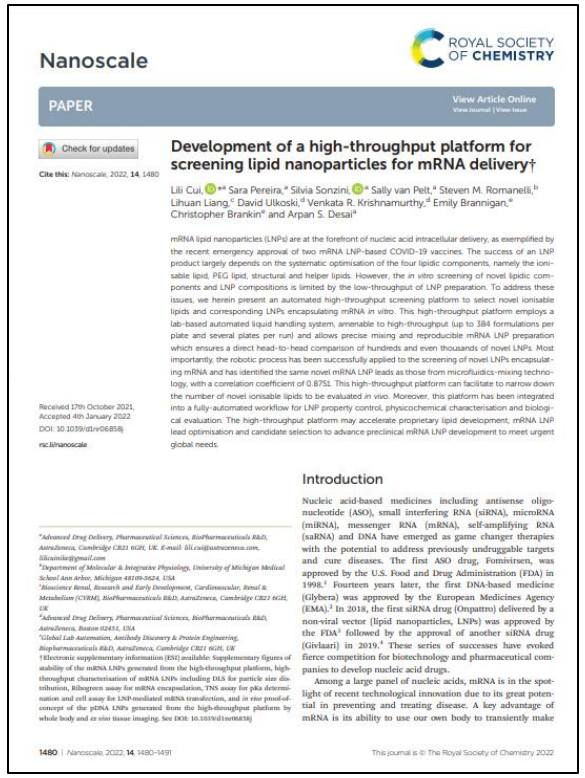
Sample contains larger aggregates.

Rapid check on sample quality

Get result in <1min and minimal volume use

Case Study: Industry-standard plates for HT LNP screening

"Development of a high-throughput platform for screening lipid nanoparticles for mRNA delivery"
Collaboration: AstraZeneca & U.Michigan



Nanoscale

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online

Check for updates

Cite this: Nanoscale, 2022, 14, 1480

Development of a high-throughput platform for screening lipid nanoparticles for mRNA delivery†

Lili Cui, Sara Pereira, Silvia Sonzini, Sally van Pelt, Steven M. Romanelli, Lihuan Liang, David Ulkoski, Venkata R. Krishnamurthy, Emily Brannigan, Christopher Brankin and Arpan S. Desai

mRNA lipid nanoparticles (LNPs) are at the forefront of nucleic acid intracellular delivery, as exemplified by the recent emergency approval of two mRNA LNP-based COVID-19 vaccines. The success of an LNP product largely depends on the systematic optimisation of the four lipidic components, namely the ionisable lipid, PEG lipid, structural and helper lipids. However, the *in vitro* screening of novel lipidic components and LNP compositions is limited by the low-throughput of LNP preparation. To address these issues, we herein present an automated high-throughput screening platform to select novel ionisable lipids and corresponding LNPs encapsulating mRNA *in vitro*. This high-throughput platform employs a lab-based automated liquid handling system, amenable to high-throughput (up to 384 formulations per plate and several plates per run) and allows precise mixing and reproducible mRNA LNP preparation which ensures a direct head-to-head comparison of hundreds and even thousands of novel LNPs. Most importantly, the robotic process has been successfully applied to the screening of novel LNPs encapsulating mRNA and has identified the same novel mRNA LNP leads as those from microfluidics-mixing technology, with a correlation coefficient of 0.8751. This high-throughput platform can facilitate to narrow down the number of novel ionisable lipids to be evaluated *in vivo*. Moreover, this platform has been integrated into a fully-automated workflow for LNP property control, physicochemical characterisation and biological evaluation. The high-throughput platform may accelerate proprietary lipid development, mRNA LNP lead optimisation and candidate selection to advance preclinical mRNA LNP development to meet urgent global needs.

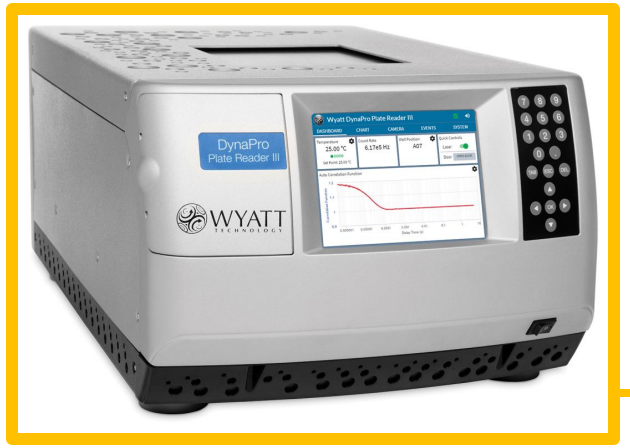
Received 17th October 2021,
Accepted 4th January 2022
DOI: 10.1039/d1nr06858j
rsc.li/nanoscale

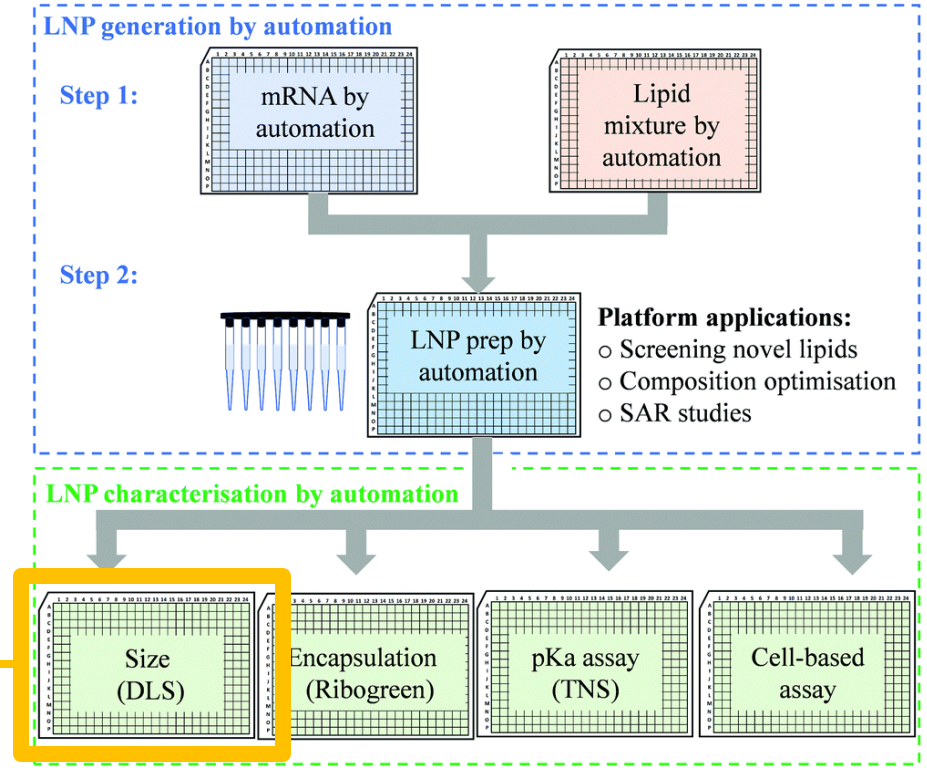
Introduction

Nucleic acid-based medicines including antisense oligonucleotide (ASO), small interfering RNA (siRNA), microRNA (miRNA), messenger RNA (mRNA), self-amplifying RNA (saRNA) and DNA have emerged as game changer therapies with the potential to address previously undruggable targets and cure diseases. The first ASO drug, Fomivirsen, was approved by the U.S. Food and Drug Administration (FDA) in 1998.[1] Fourteen years later, the first DNA-based medicine (Glybera) was approved by the European Medicines Agency (EMA).[2] In 2018, the first siRNA drug (Onpattro) delivered by a non-viral vector (lipid nanoparticles, LNPs) was approved by the FDA.[3] followed by the approval of another siRNA drug (Givlaari) in 2019.[4] These series of successes have evoked fierce competition for biotechnology and pharmaceutical companies to develop nucleic acid drugs.

Among a large panel of nucleic acids, mRNA is in the spotlight of recent technological innovation due to its great potential in preventing and treating disease. A key advantage of mRNA is its ability to use our own body to transiently make

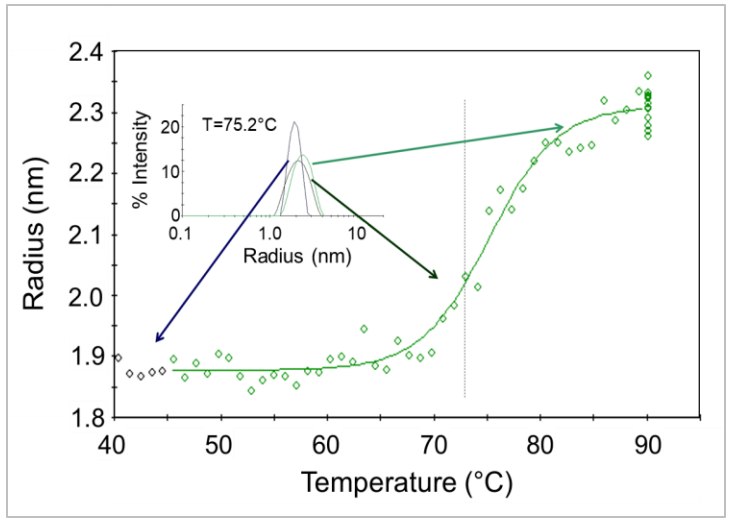
[a]Advanced Drug Delivery, Pharmaceutical Sciences, BioPharmaceuticals R&D, AstraZeneca, Cambridge CB21 6GH, UK. E-mail: lili.cui@astrazeneca.com, lilicuiniko@gmail.com
[b]Department of Molecular & Integrative Physiology, University of Michigan Medical School Ann Arbor, Michigan 48109-5624, USA
[c]Bioscience Renal, Research and Early Development, Cardiovascular, Renal & Metabolism (CVRM), BioPharmaceuticals R&D, AstraZeneca, Cambridge CB21 6GH, UK
[d]Advanced Drug Delivery, Pharmaceutical Sciences, BioPharmaceuticals R&D, AstraZeneca, Boston 02451, USA
[e]Global Lab Automation, Antibody Discovery & Protein Engineering, Biopharmaceuticals R&D, AstraZeneca, Cambridge CB21 6GH, UK
†Electronic supplementary information (ESI) available: Supplementary figures of stability of the mRNA LNPs generated from the high-throughput platform, high-throughput characterisation of mRNA LNPs including DLS for particle size distribution, Ribogreen assay for mRNA encapsulation, TNS assay for pKa determination and cell assay for LNP-mediated mRNA transfection, and *in vivo* proof-of-concept of the pDNA LNPs generated from the high-throughput platform by whole body and *ex vivo* tissue imaging. See DOI: 10.1039/d1nr06858j



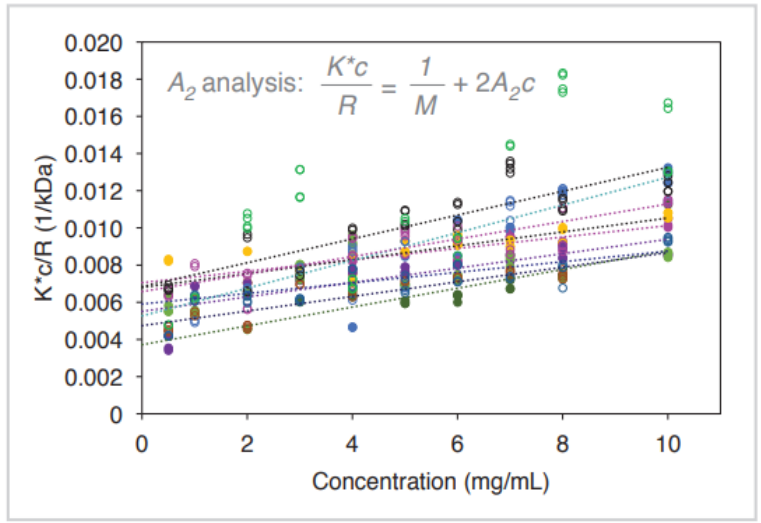


Development of a high-throughput platform for screening lipid nanoparticles for mRNA delivery
Collaboration: AstraZeneca & U.Michigan
https://doi.org/10.1039/D1NR06858J

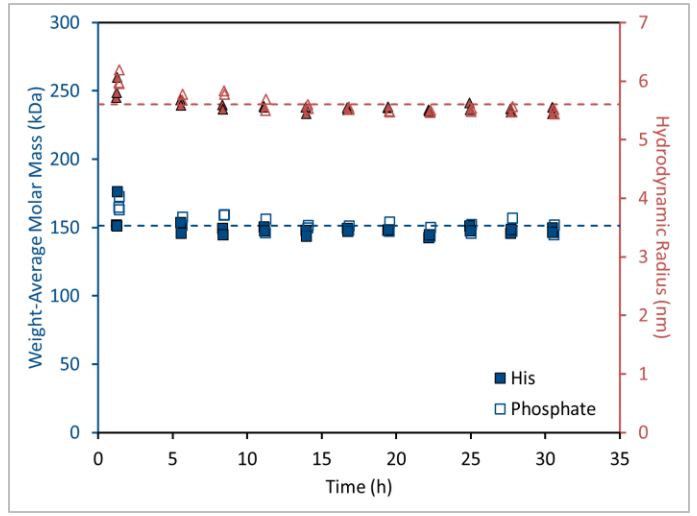
Biophysical characterization with DLS and SLS



Onset of Aggregation
with Thermal ramp



Colloidal stability metrics with
A_2(SLS) and **k_D(DLS)**



Accelerated storage
stability assessment

Applicable in candidate screening and formulation development

Waters |Wyatt LNP Characterization Solutions

Non-exhaustive

High-Throughput Screening → Zeta Potential Optimization → MAQ & Detailed Characterization

DynaPro™ Plate Reader High Throughput DLS/SLS Instrument

- Size/ radius (QC)
- Aggregation content
- Freeze-thaw stability
- Structure
- Polydispersity (QC)

Dozens of samples

DynaPro ZetaStar™ DLS/SLS/ELS Instrument

- Size/radius (QC)
- Aggregation content
- Structure
- Charge/Zeta Potential
- Polydispersity (QC)

Digest

Intact & Digest

Waters LC-MS

QDa detector

BioAccord™ MS

Lipid Composition & ratio

Modifications – Lipids and mRNA

Low level impurities

Size Exclusion or Eclipse™ FFF system

MALS

RI

UV

Size distribution

Payload concentration

Size-based payload distribution

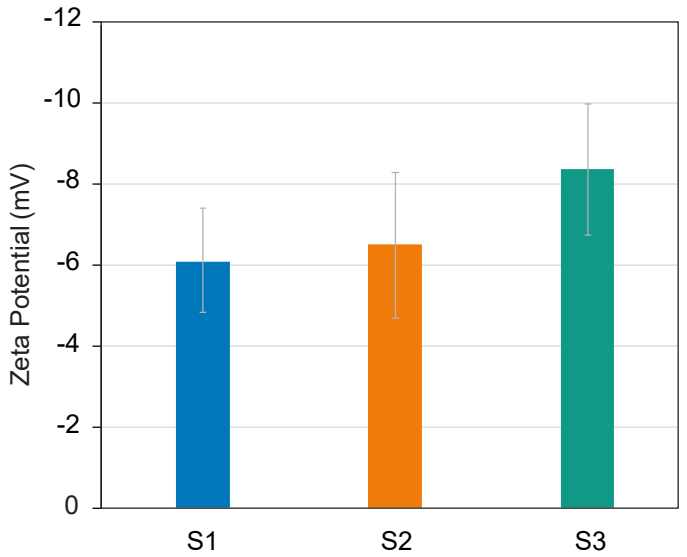
Encapsulation efficiency

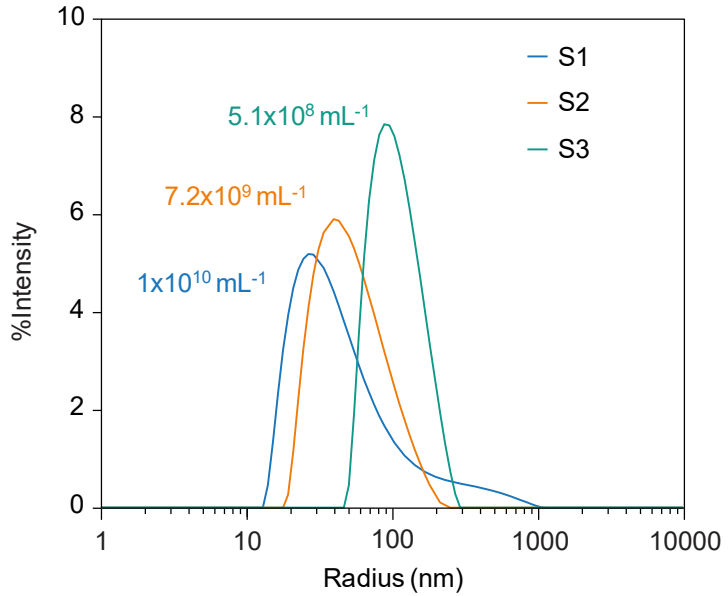
Morphology

Lipid concentration

Aggregation

Walk-up or Automated Zeta Potential LNP screening





DynaPro ZetaStar

walk-up or automated
DLS/SLS/ELS instrument

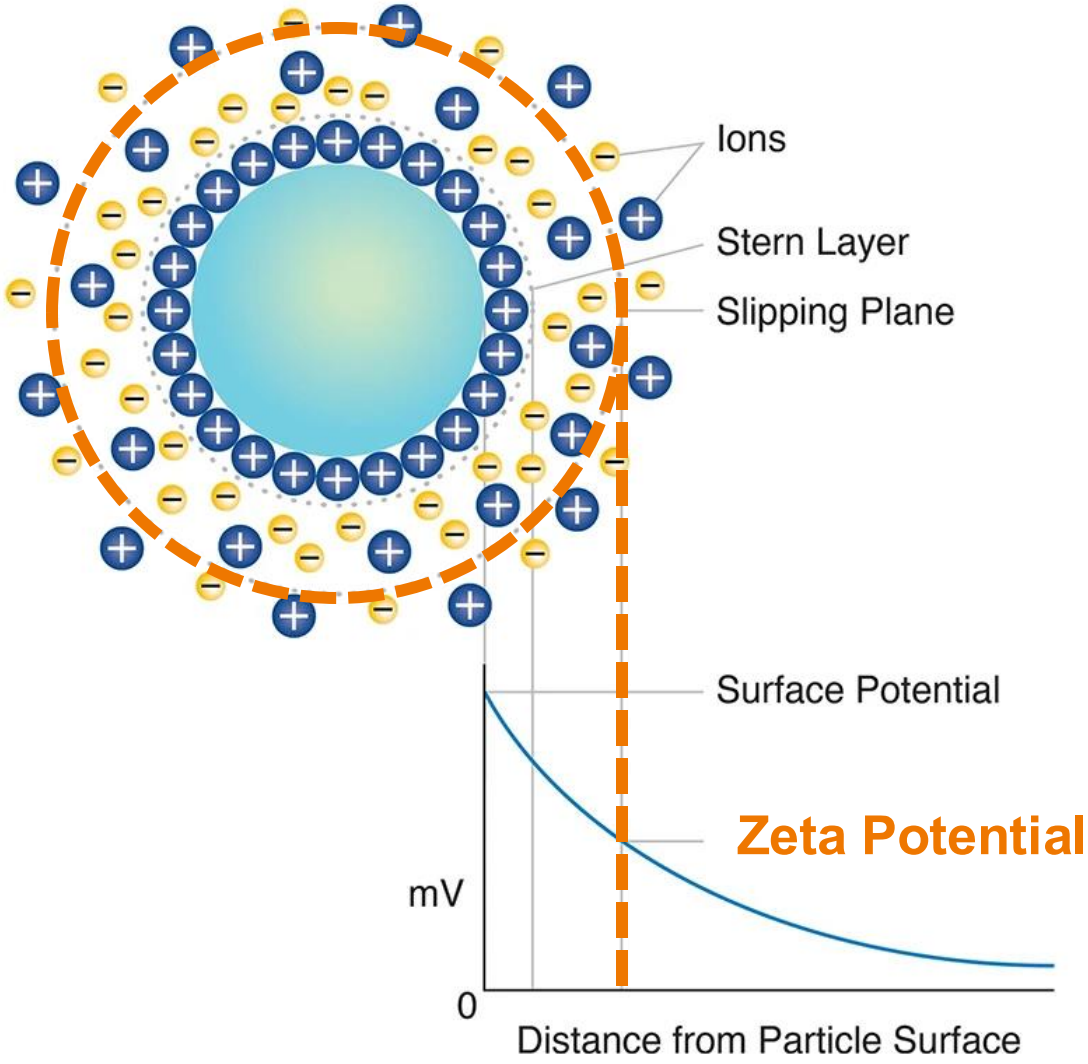
- Zeta Potential
- Size
- Polydispersity
- Particle concentration
- Colloidal stability

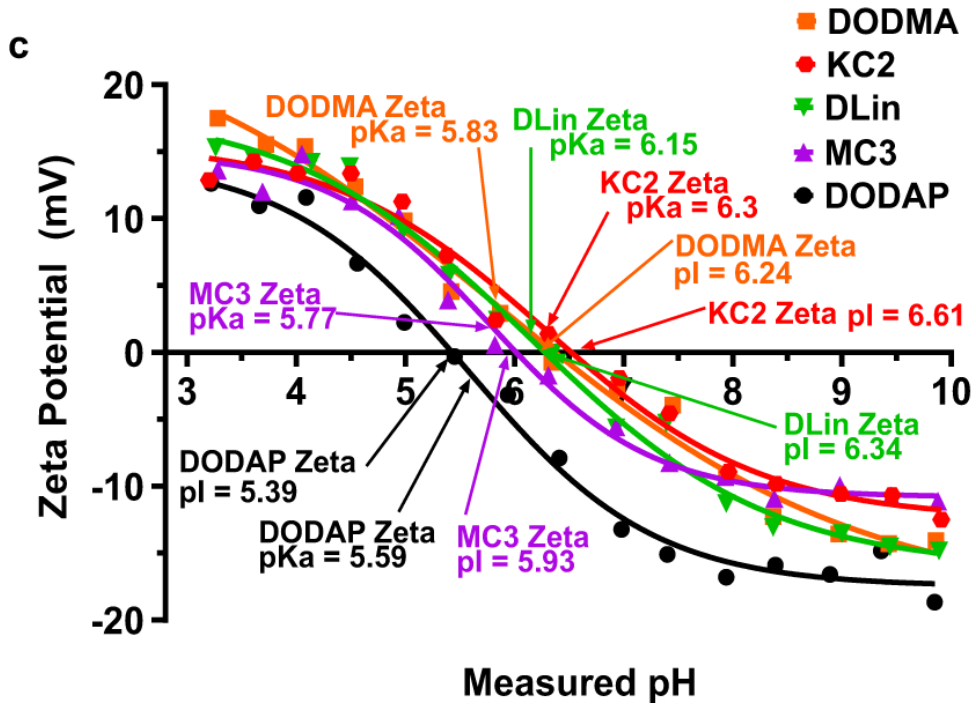
Fast and Simple workflow

ELS in native buffer.

Hands-free automation

LNP electric charge is known to control in vivo distribution and expression of mRNA-LNPs





- Charge and Zeta-Potential depends on ionizable lipid choices and pH
- LNP charge may change between formulation and in vivo

COMMUNICATIONS BIOLOGY | (2021) 4:956
https://doi.org/10.1038/s42003-021-02441-2

Challenges with traditional ELS technology

Staffing challenge

Training new staff following expansion & turnover

Productivity bottlenecks

Not enough staff, access to instruments / instrument downtime, workflow inefficiencies

Boost lab efficiency

Outdated technology, multiple platforms required for obtaining information

Sample challenges

Volume limitations, interest in measuring samples in physiological conditions

DynaPro ZetaStar is a newer generation technology

Traditional ELS & needed improvements:

Better Measurement

Faster Measurement

Less Sample

Less Hands-on-time

Completely redesigned

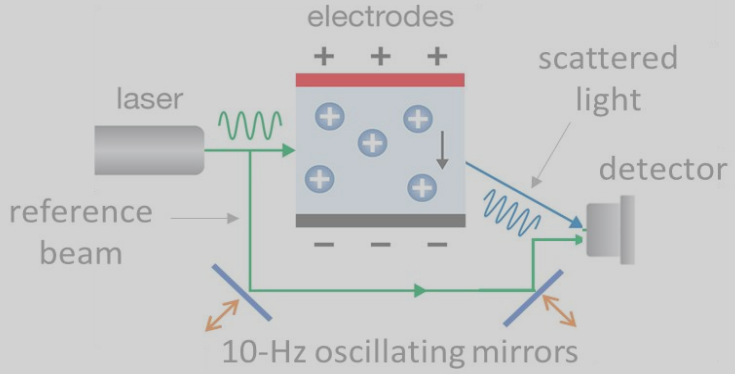
Hardware

User Interface

Workflow

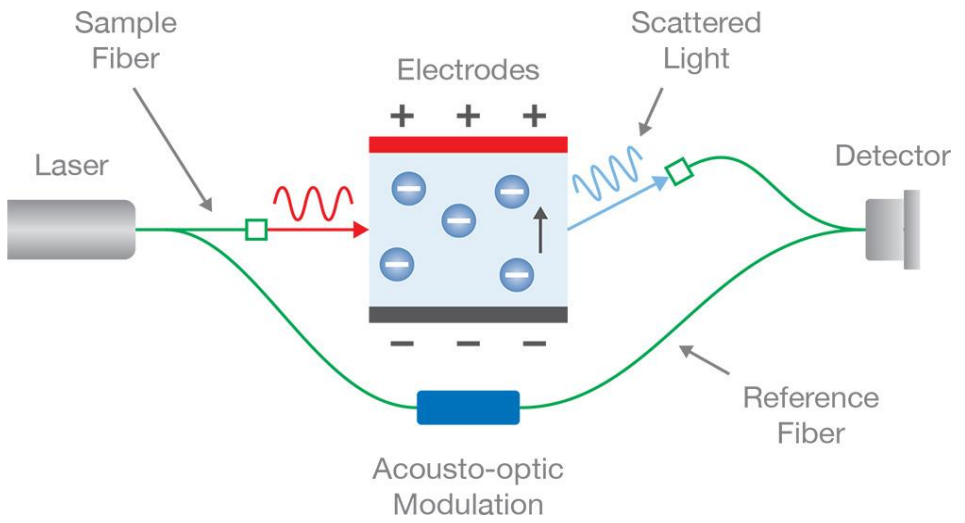
Some changes under the hood: FIDELIS
Robust and more sensitive instrument

Conventional PALS



- Mechanical motion, low frequency → low SNR, slow measurements, fragile samples degrade
- Free space optics: difficult maintenance, factory repair

FIDELIS



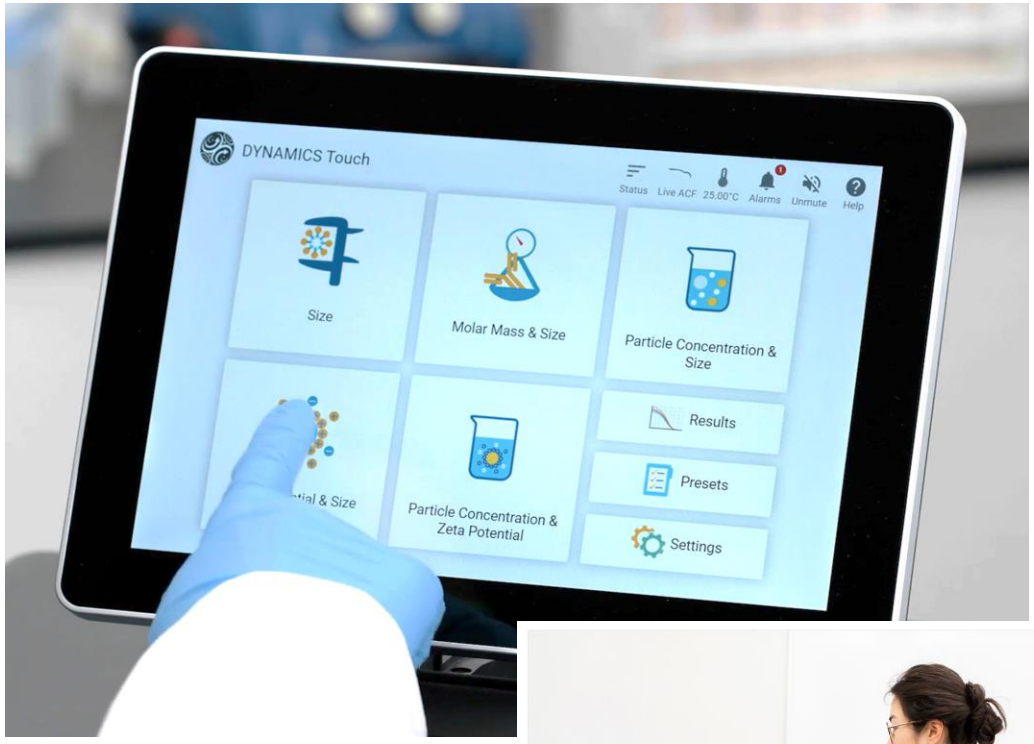
Fiber
Interferometric
Doppler
Electrophoretic
LIght
Scattering

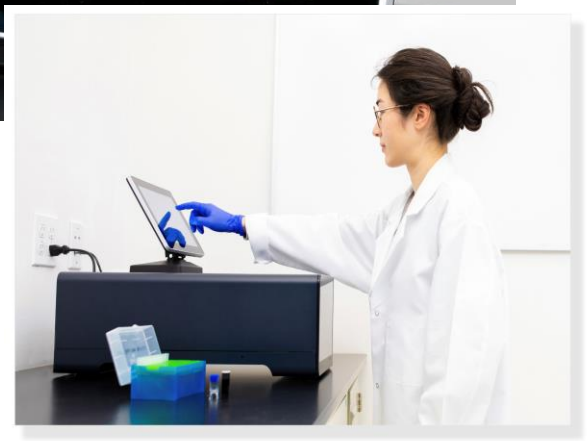
- Solid-state modulator, high frequency → high SNR, fast measurements, no degradation
- Fiber-coupled optics → simple maintenance, field-replaceable modules

Result: Simpler and Faster data collection

As little as:
~30 sec
and 65µL /
sample

Size
Zeta Potential
Polydispersity
Particle Concentration





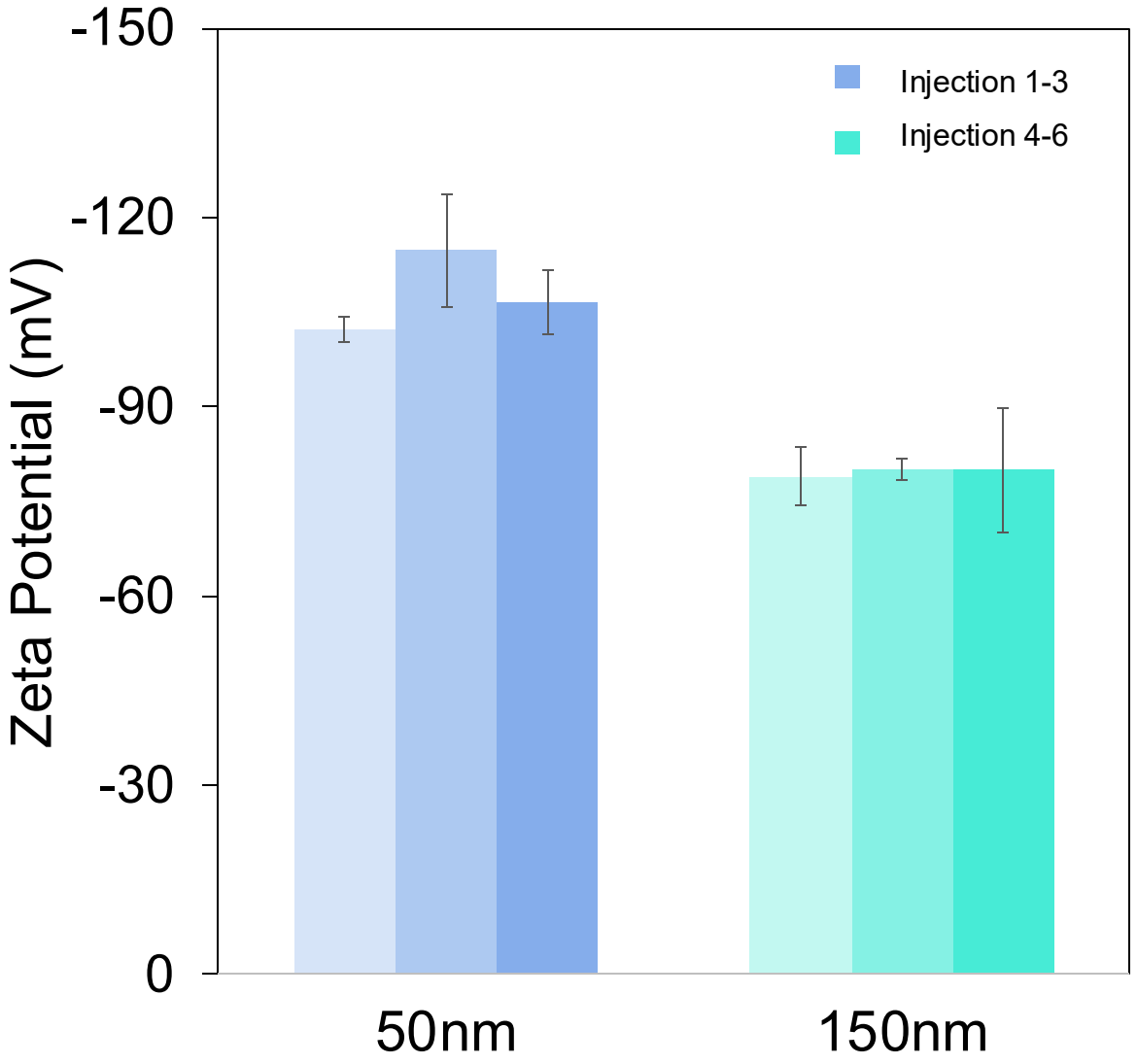
- Flexible walk-up measurements with stand-alone touch interface
- **Simultaneous size and zeta potential**
- **Adaptive ELS** collection mode
  - Less user input and knowledge required
  - No need to change measurement parameters for various sample types
  - Mitigates the chance of sample degradation

Automated Measurements to minimize Hands-on time

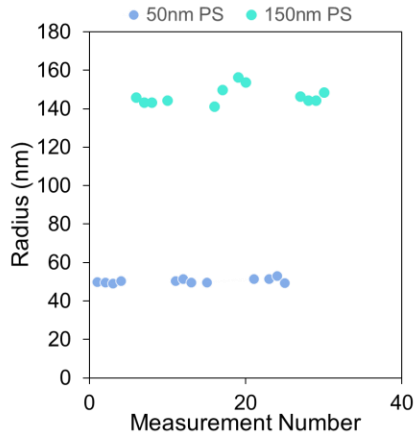
Run dozens to hundreds of samples, effortlessly

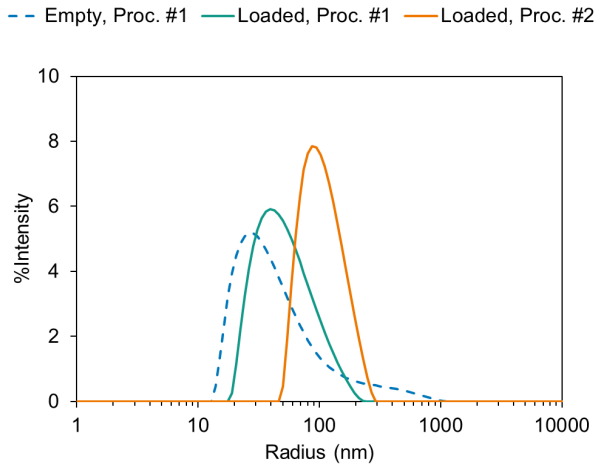
Load autosampler vials or plates, execute method and generate reports

Automate and measure simultaneous size and zeta potential



- The unique combination of the ZetaStar with an autosampler and pump automates sample delivery, creating a powerful, reproducible characterization system
- Adaptive mode utilized for easy method set-up and optimization





Waters |Wyatt LNP Characterization Solutions

Non-exhaustive

High-Throughput Screening → Zeta Potential Optimization → MAQ & Detailed Characterization

DynaPro™ Plate Reader High Throughput DLS/SLS Instrument

- Size/ radius (QC)
- Aggregation content
- Freeze-thaw stability
- Structure
- Polydispersity (QC)

DynaPro ZetaStar™ DLS/SLS/ELS Instrument

- Size/radius (QC)
- Aggregation content
- Structure
- Charge/Zeta Potential
- Polydispersity (QC)

Digest

Intact & Digest

Waters LC-MS

QDa detector

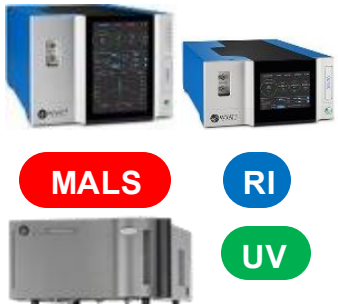
BioAccord™ MS

Lipid Composition & ratio

Modifications – Lipids and mRNA

Low level impurities

Size Exclusion or Eclipse™ FFF system



Size distribution

Payload concentration

Size-based payload distribution

Encapsulation efficiency

Morphology

Lipid concentration

Aggregation

Few samples

Unprecedented detailed LNP characterization

- RNA integrity
- LNP size
- LNP distribution
- LNP number
- Physical stability
- LNP morphology
- Encapsulation efficiency
- mRNA concentration
- Lipid concentration

Obtain high-resolution LNP size, payload, and how these payloads are distributed across the particles within the sample, all in a single experiment.

Optilab™

differential refractive index (dRI) detector

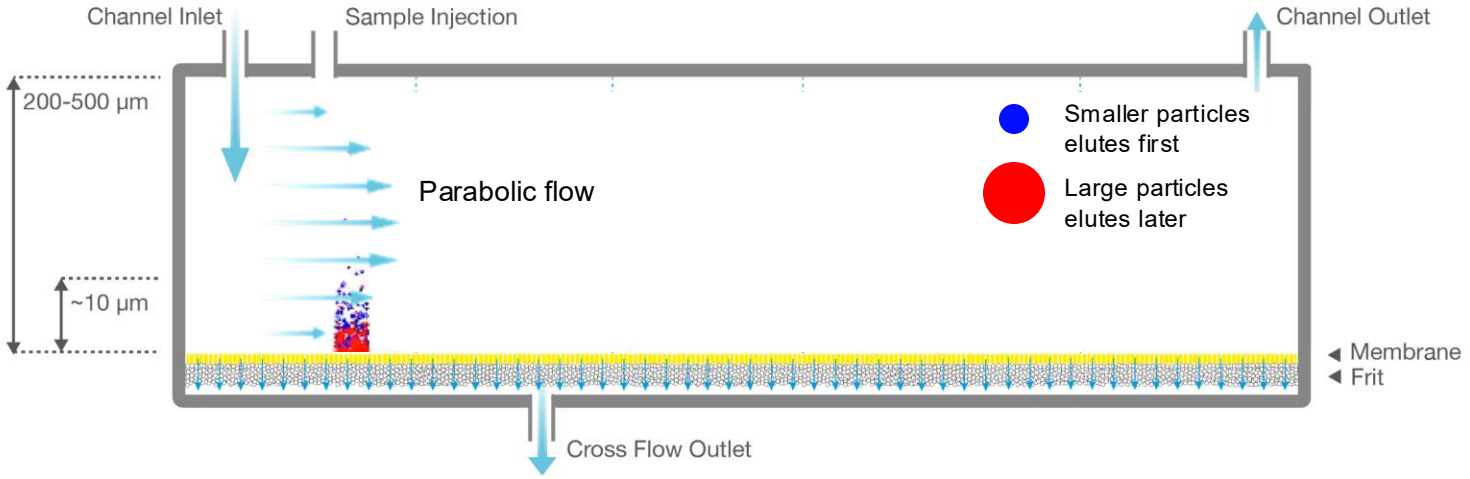
DAWN™

multi-angle light scattering (MALS) photometer

Eclipse

Field Flow Fractionation (FFF) system

FFF separation, alternative to SEC



- FFF **separates based on size**: small particles elutes first.
- **Gentle separation** with **tunable resolution**.
- Multidetector MALS provide **in-depth characterization and quantification.**
- **FDA recognizes FFF** as an orthogonal technique to SEC and AUC.

Eclipse™ FFF system

- LNPs
- Viral Vectors
- Exosomes
- Polymers
- Proteins & Peptides

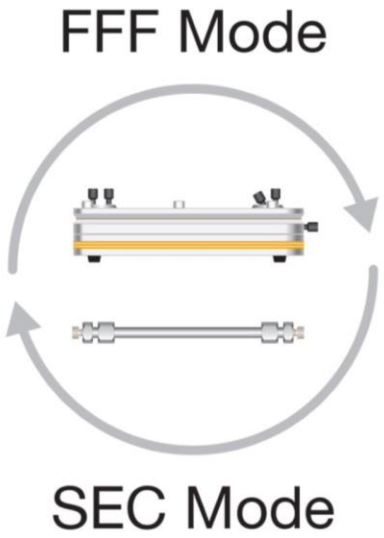
Flexible Channel Selection

Fixed Height Channel

- Robust channel for faster assembly
- Ideal for routine and QC applications
- Temperature regulation module from ambient up to 50°C (all eclipse channel)

Channel	Benefits
Analytical Short	Rapid nano/microgram separations
Analytical Long	Nano/microgram separations
Dispersion Inlet	For aggregation-prone samples
Semi-Prep	Milligram separations coupled to a fraction collector
Mobility EAF4	Separation by size and charge

Benefits of Eclipse FFF-System



- Industry-leading Waters Arc HPLC front-end for maximum accuracy and reliability
- Flexible and convenient channel selection
- SEC switching option enables automated switching between FFF-MALS and SEC-MALS
- Intelligent solvent management system with configurable recycling minimizes solvent consumption

FFF = High Resolution Size Distribution of LNPs

DLS
Fast Screening

Cumulant	R_h [nm]	%PD
Comirnaty™	38 ±1	26 ± 2
Spikevax™	75 ± 1	24 ± 2

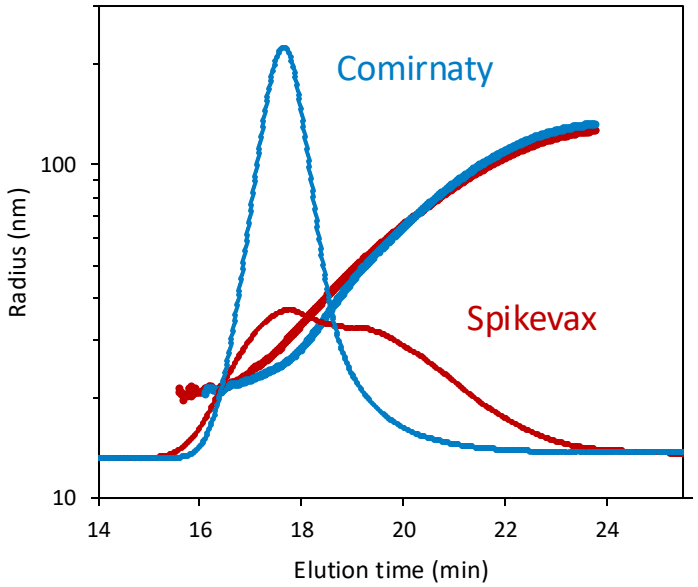
High Resolution Size Distribution Analysis of LNPs

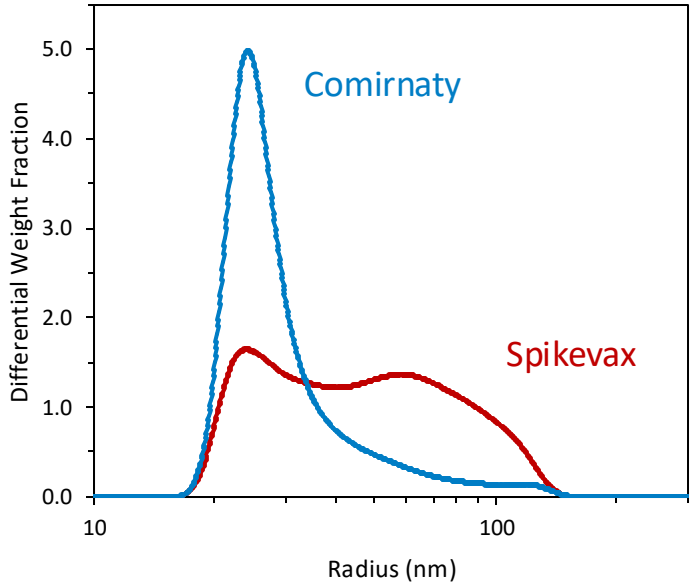
Waters™ | WYATT TECHNOLOGY

DLS
Fast Screening

Cumulant	R_h [nm]	%PD
Comirnaty™	38 ±1	26 ± 2
Spikevax™	75 ± 1	24 ± 2

FFF-MALS
High-resolution size distribution





	R_z [nm]	$Đ = M_w/M_n$	c_{RNA} [mg/mL]
Comirnaty	69.6 ± 0.3	2.6 ± 0.1	0.106
Spikevax	85.8 ± 0.5	5.0 ± 0.1	0.086

Unprecedented detailed LNP characterization

- RNA integrity
- LNP size
- LNP distribution
- LNP number
- Physical stability
- LNP morphology
- Encapsulation efficiency
- mRNA concentration
- Lipid concentration

Obtain high-resolution LNP size, payload, and how these payloads are distributed across the particles within the sample, all in a single experiment.

Optilab™

differential refractive index (dRI) detector

DAWN™

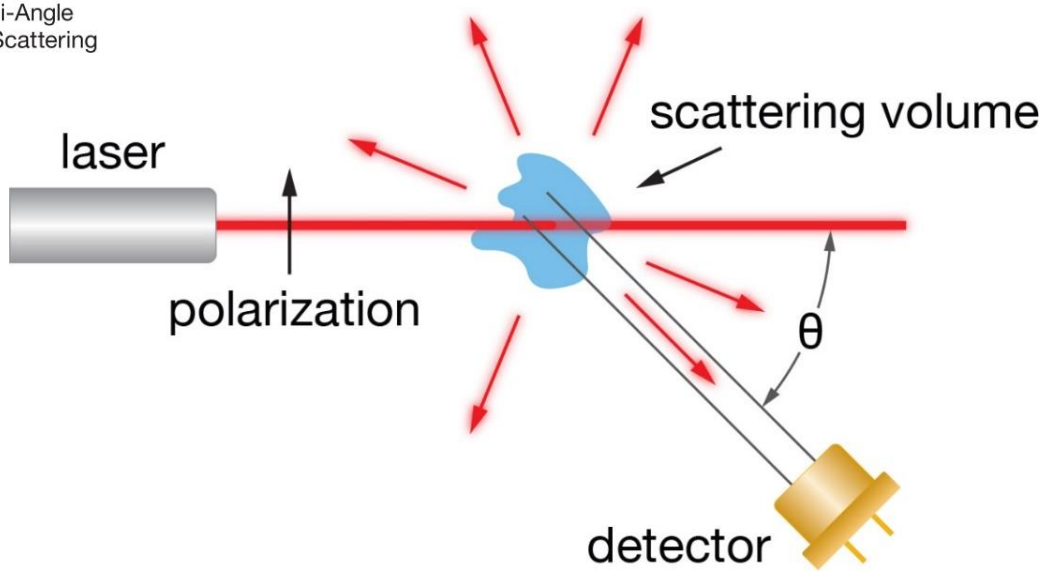
multi-angle light scattering (MALS) photometer

Eclipse

Field Flow Fractionation (FFF) system

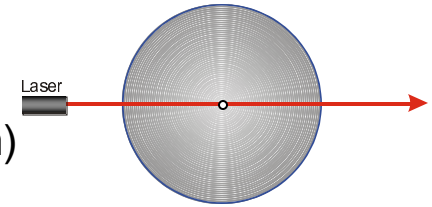
Multi-angle static light scattering (MALS)

Multi-Angle
Light Scattering



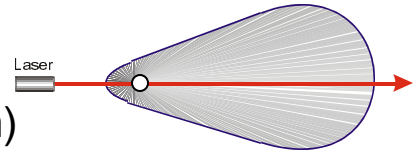
Isotropic scattering

Small
particles
(R < 10 nm)



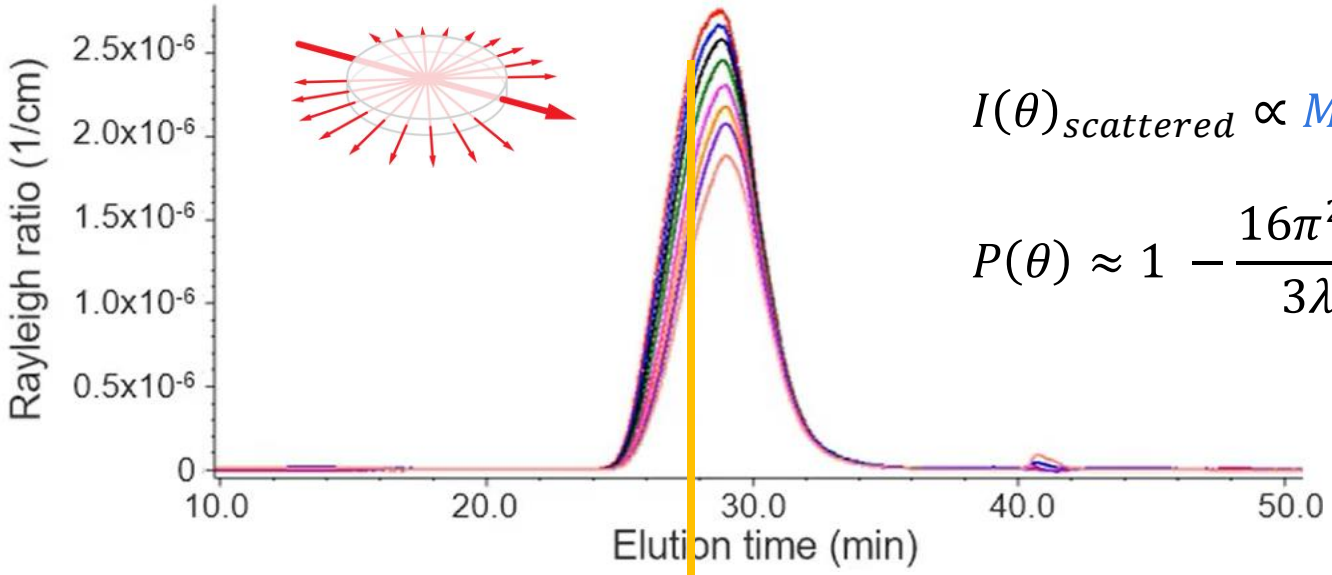
Anisotropic scattering

Large
particles
(R > 10 nm)



Intensity of scattered light provide information on both size and molecular weight

Data in Action

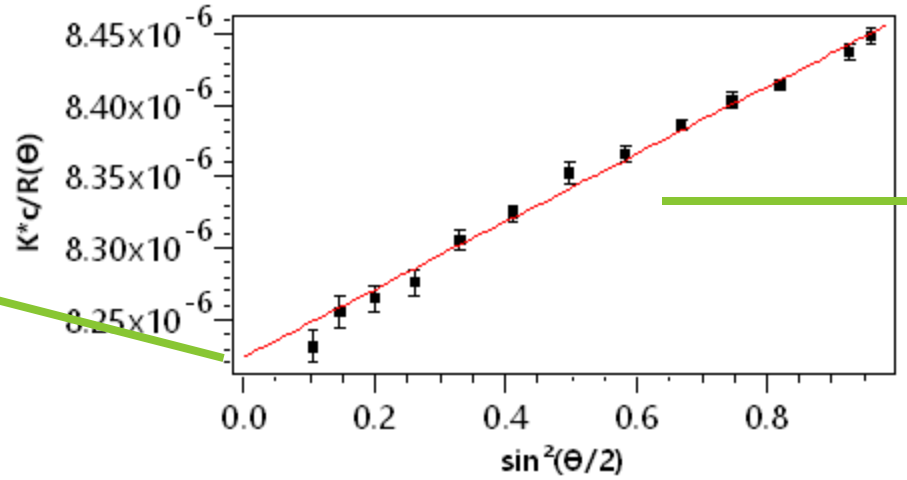


$$I(\theta)_{scattered} \propto M \cdot c \cdot \left(\frac{dn}{dc}\right)^2 P(\theta)$$

$$P(\theta) \approx 1 - \frac{16\pi^2 n_o^2}{3\lambda_0^2} \sin^2\left(\frac{\theta}{2}\right)\langle r_g^2 \rangle + \cdots$$

Zeroth-angle intercept

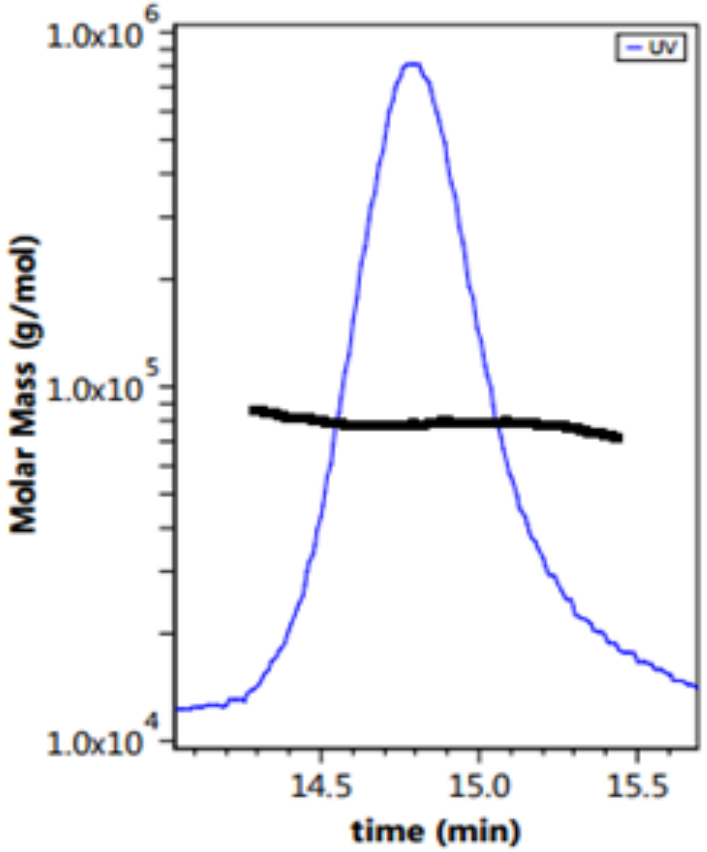
Mw

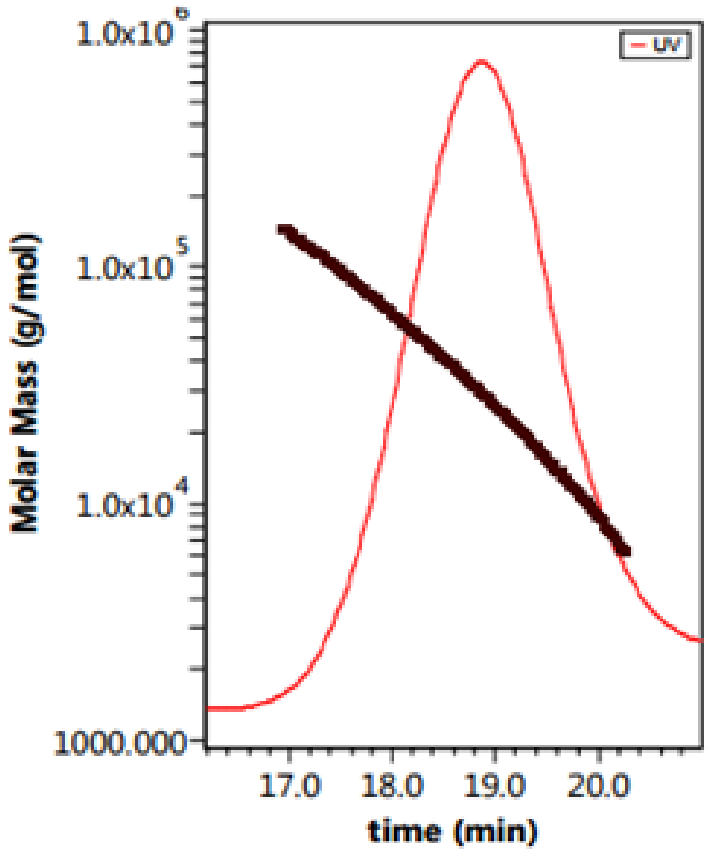


Slope

r_g

SEC-MALS: Provide Mw Details



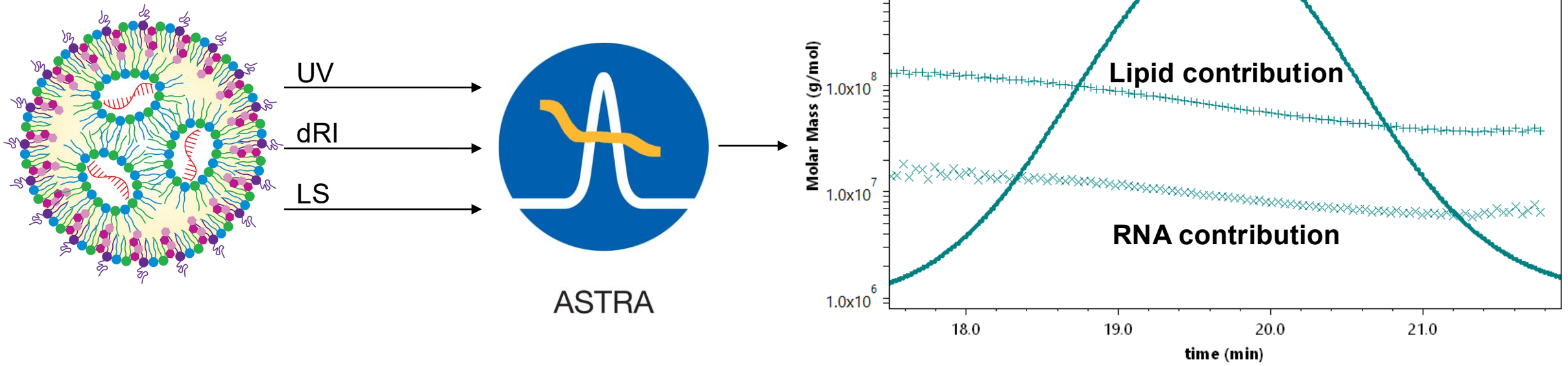


Concentration signal is ambiguous:
is the peak homogeneous or polydisperse?

MALS gives the answer

Software is equally important

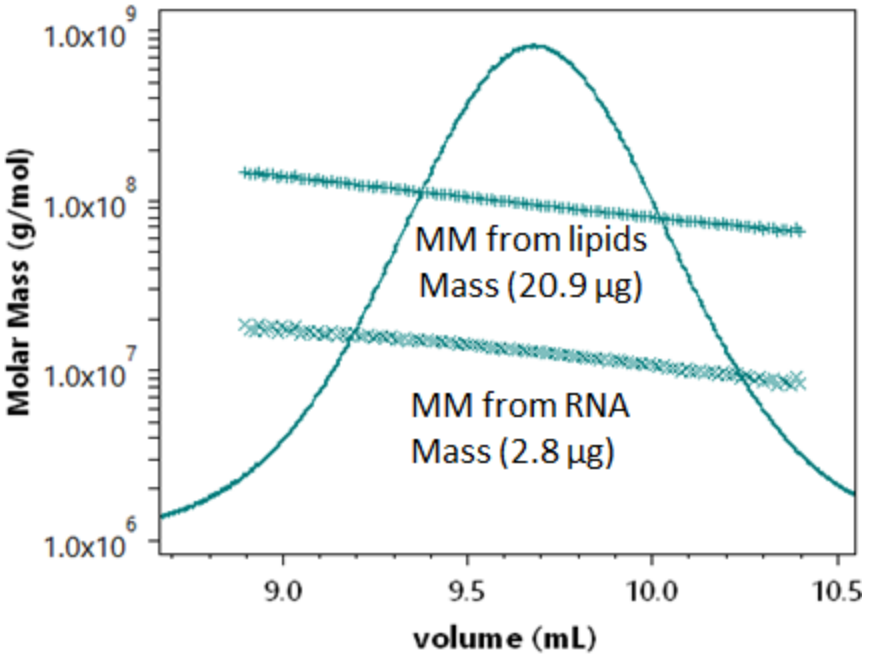
ASTRA™ software LNP Analysis tease out Lipid vs RNA contribution



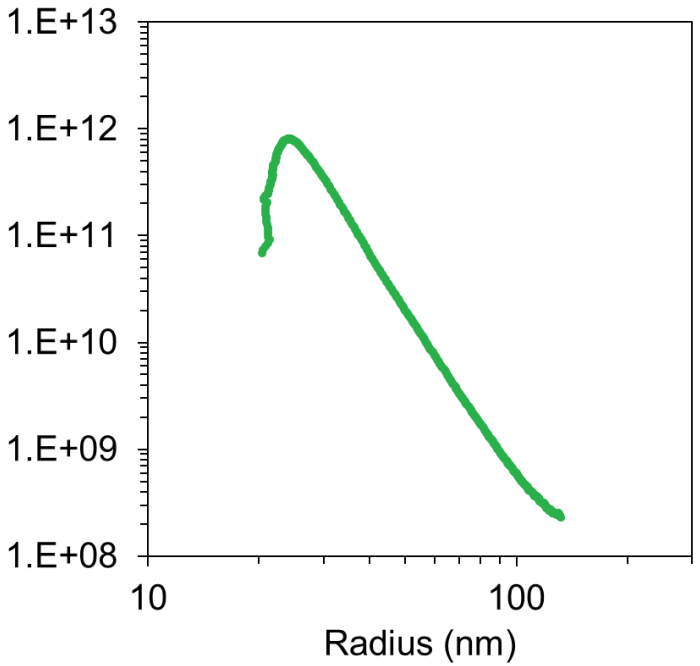
ASTRA software combines signals from multiple detectors to *tease out* the signal contributions from lipid and payload to determine size dependent encapsulation efficiency

Get all the details in a single experiment

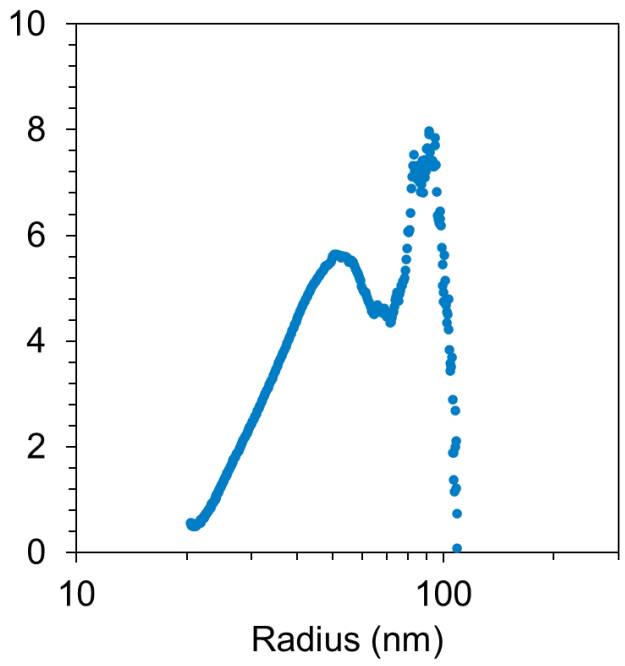
Molar Mass of Lipids and Payload



Particle Concentration



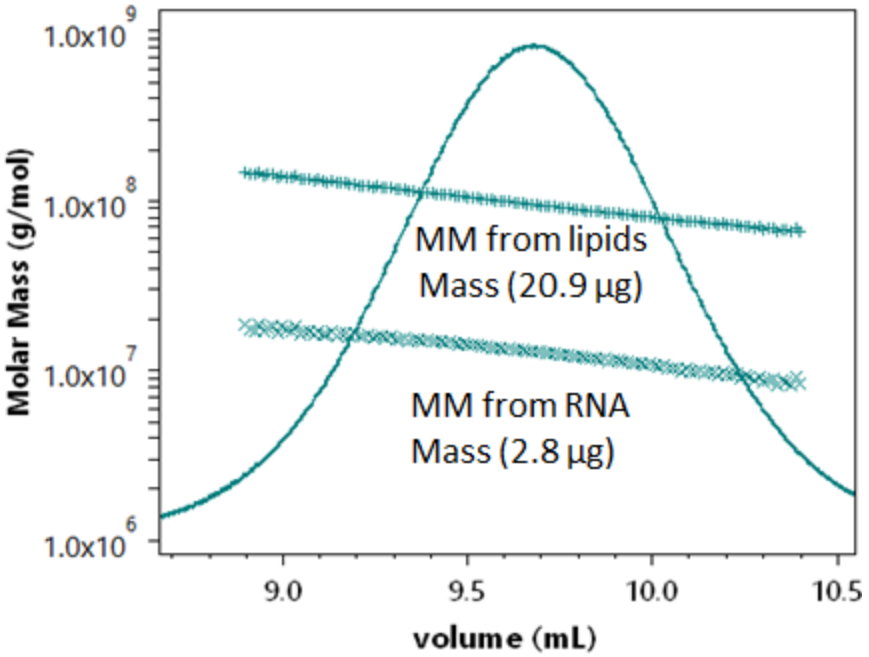
mRNA number



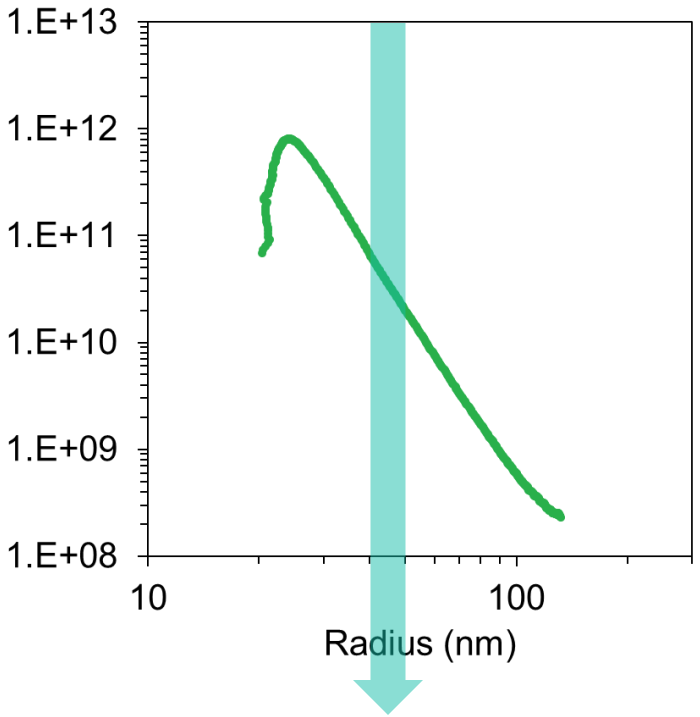
ASTRA software deconstruct the data to provide, in a single physiologically relevant experiment:
Particle Concentration, Size-based Payload distribution, Aggregation, mRNA number, and more

Example:

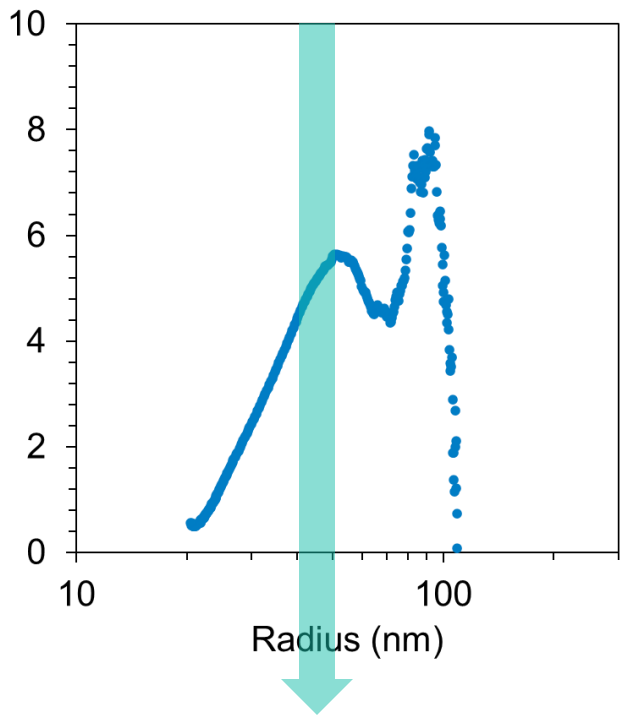
Molar Mass of Lipids and Payload



Particle Concentration



mRNA number



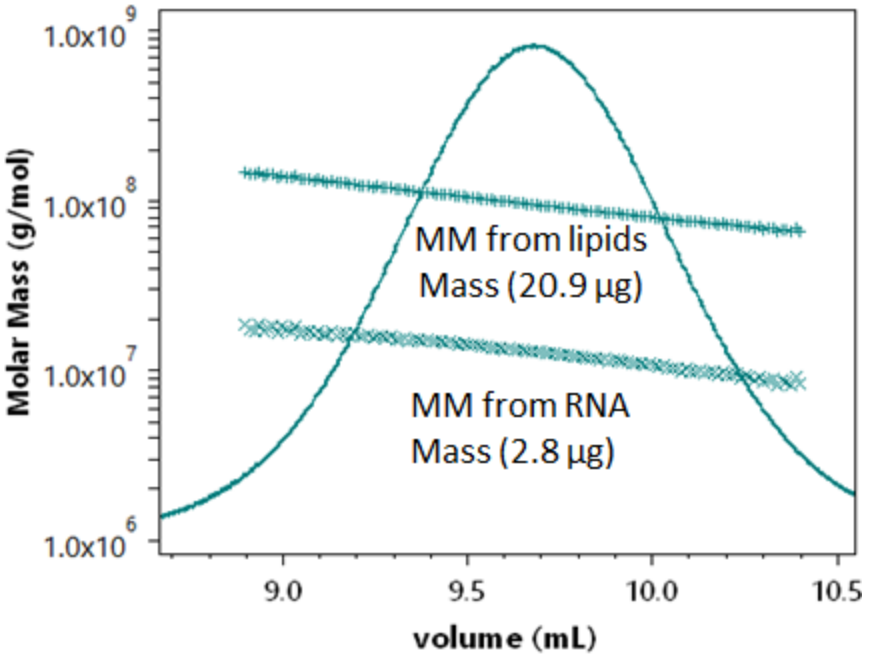
Size range
40-50nm

~$5x10^{10}$
particles/mL

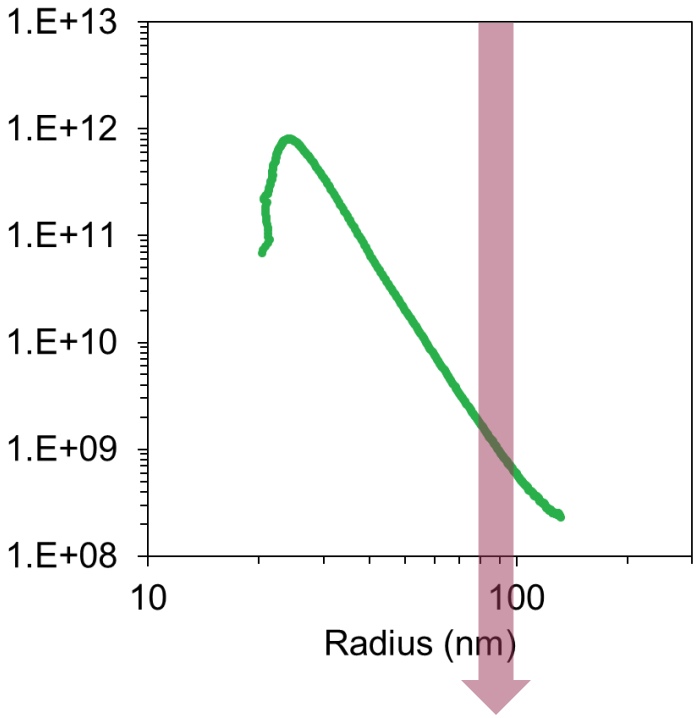
On average,
~5 mRNA / particle

Example:

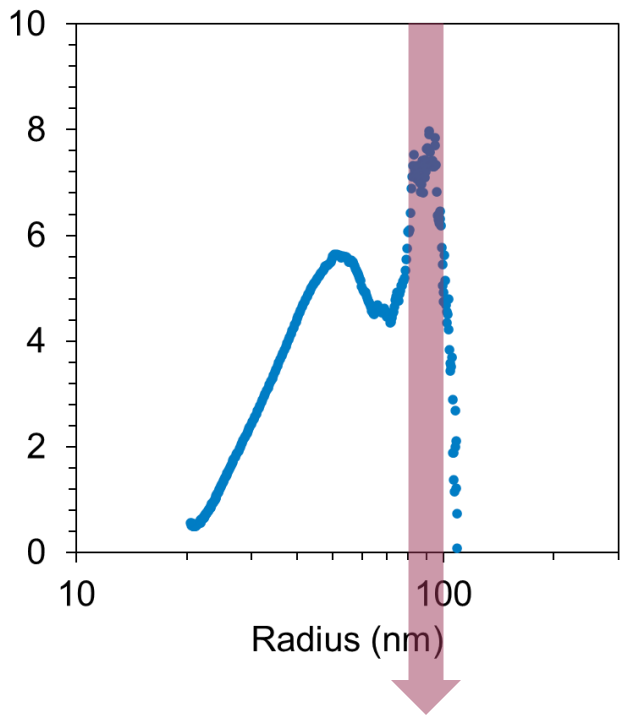
Molar Mass of Lipids and Payload



Particle Concentration



mRNA number

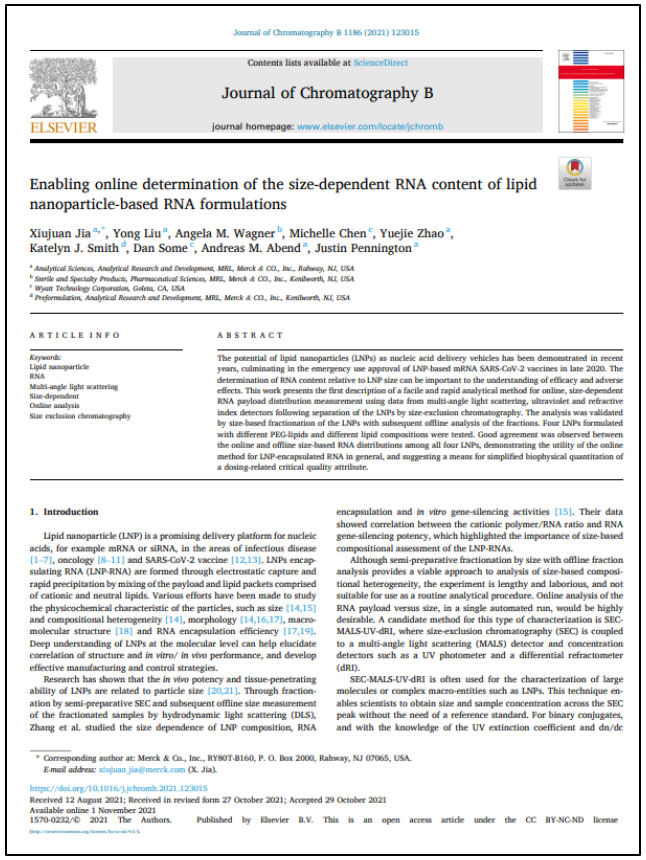


Size range
80-100nm

~1x10^9
particles/mL

On average,
~8 mRNA / particle

Cross-verification - Size-based payload



Journal of Chromatography B 1186 (2021) 123015

Contents lists available at ScienceDirect

Journal of Chromatography B

journal homepage: www.elsevier.com/locate/jchromb

Enabling online determination of the size-dependent RNA content of lipid nanoparticle-based RNA formulations

Xiujuan Jia [a,*], Yong Liu [a], Angela M. Wagner [b], Michelle Chen [c], Yuejie Zhao [a], Katelyn J. Smith [d], Dan Some [c], Andreas M. Abend [a], Justin Pennington [a]

[a] Analytical Sciences, Analytical Research and Development, MRL, Merck & CO., Inc., Rahway, NJ, USA
[b] Sterile and Specialty Products, Pharmaceutical Sciences, MRL, Merck & CO., Inc., Kenilworth, NJ, USA
[c] Wyatt Technology Corporation, Goleta, CA, USA
[d] Preformulation, Analytical Research and Development, MRL, Merck & CO., Inc., Kenilworth, NJ, USA

ARTICLE INFO

Keywords:
Lipid nanoparticle
RNA
Multi-angle light scattering
Size-dependent
Online analysis
Size exclusion chromatography

ABSTRACT

The potential of lipid nanoparticles (LNPs) as nucleic acid delivery vehicles has been demonstrated in recent years, culminating in the emergency use approval of LNP-based mRNA SARS-CoV-2 vaccines in late 2020. The determination of RNA content relative to LNP size can be important to the understanding of efficacy and adverse effects. This work presents the first description of a facile and rapid analytical method for online, size-dependent RNA payload distribution measurement using data from multi-angle light scattering, ultraviolet and refractive index detectors following separation of the LNPs by size-exclusion chromatography. The analysis was validated by size-based fractionation of the LNPs with subsequent offline analysis of the fractions. Four LNPs formulated with different PEG-lipids and different lipid compositions were tested. Good agreement was observed between the online and offline size-based RNA distributions among all four LNPs, demonstrating the utility of the online method for LNP-encapsulated RNA in general, and suggesting a means for simplified biophysical quantitation of a dosing-related critical quality attribute.

1. Introduction

Lipid nanoparticle (LNP) is a promising delivery platform for nucleic acids, for example mRNA or siRNA, in the areas of infectious disease [1–7], oncology [8–11] and SARS-CoV-2 vaccine [12,13]. LNPs encapsulating RNA (LNP-RNA) are formed through electrostatic capture and rapid precipitation by mixing of the payload and lipid packets comprised of cationic and neutral lipids. Various efforts have been made to study the physicochemical characteristic of the particles, such as size [14,15] and compositional heterogeneity [14], morphology [14,16,17], macromolecular structure [18] and RNA encapsulation efficiency [17,19]. Deep understanding of LNPs at the molecular level can help elucidate correlation of structure and *in vitro*/ *in vivo* performance, and develop effective manufacturing and control strategies.

Research has shown that the *in vivo* potency and tissue-penetrating ability of LNPs are related to particle size [20,21]. Through fractionation by semi-preparative SEC and subsequent offline size measurement of the fractionated samples by hydrodynamic light scattering (DLS), Zhang et al. studied the size dependence of LNP composition, RNA encapsulation and *in vitro* gene-silencing activities [15]. Their data showed correlation between the cationic polymer/RNA ratio and RNA gene-silencing potency, which highlighted the importance of size-based compositional assessment of the LNP-RNAs.

Although semi-preparative fractionation by size with offline fraction analysis provides a viable approach to analysis of size-based compositional heterogeneity, the experiment is lengthy and laborious, and not suitable for use as a routine analytical procedure. Online analysis of the RNA payload versus size, in a single automated run, would be highly desirable. A candidate method for this type of characterization is SEC-MALS-UV-dRI, where size-exclusion chromatography (SEC) is coupled to a multi-angle light scattering (MALS) detector and concentration detectors such as a UV photometer and a differential refractometer (dRI).

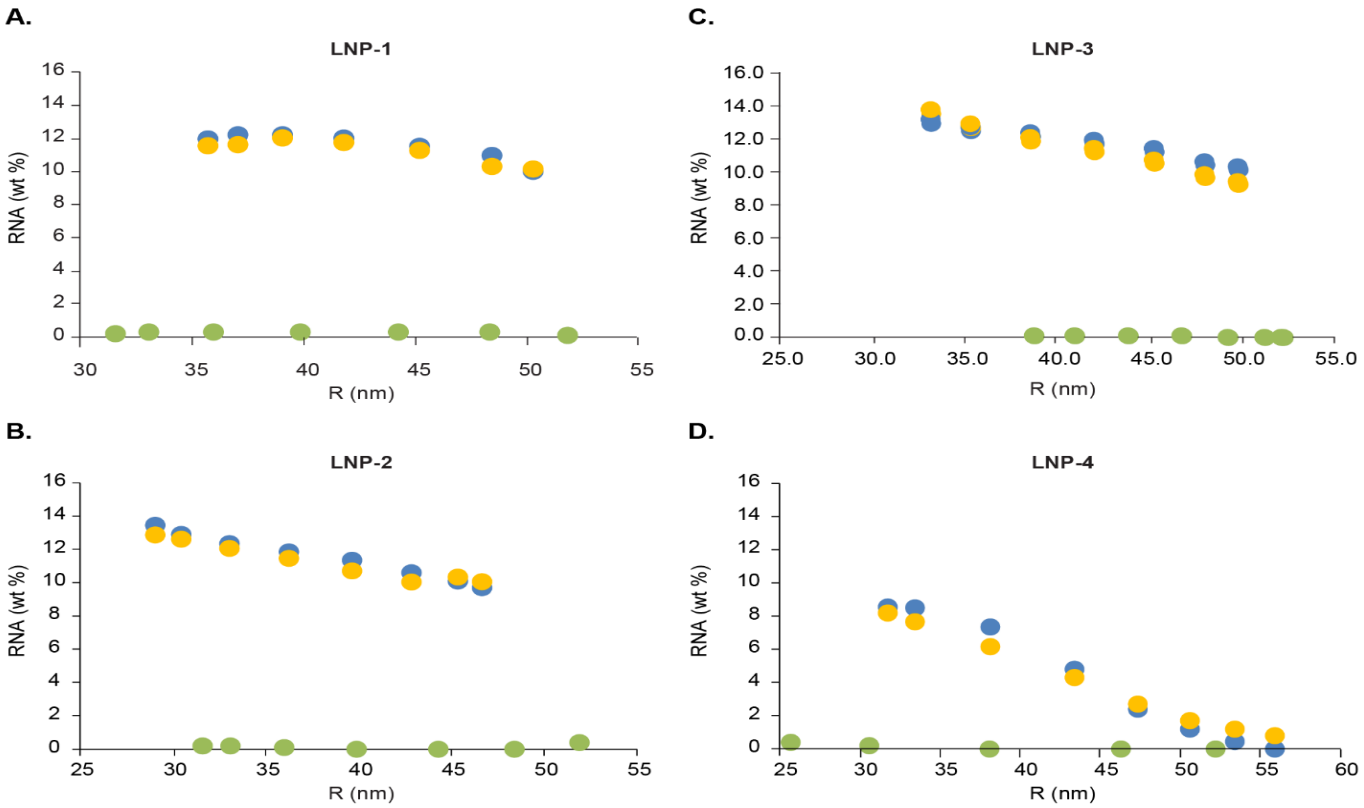
SEC-MALS-UV-dRI is often used for the characterization of large molecules or complex macro-entities such as LNPs. This technique enables scientists to obtain size and sample concentration across the SEC peak without the need of a reference standard. For binary conjugates, and with the knowledge of the UV extinction coefficient and dn/dc

* Corresponding author at: Merck & Co., Inc., RY80T-B160, P. O. Box 2000, Rahway, NJ 07065, USA.
E-mail address: xiujuan.jia@merck.com (X. Jia).

https://doi.org/10.1016/j.jchromb.2021.123015
Received 12 August 2021; Received in revised form 27 October 2021; Accepted 29 October 2021
Available online 1 November 2021

"Enabling online determination of the size-dependent RNA content of lipid nanoparticle-based RNA formulations"
Merck & Co. 2021
https://doi.org/10.1016/j.jchromb.2021.123015

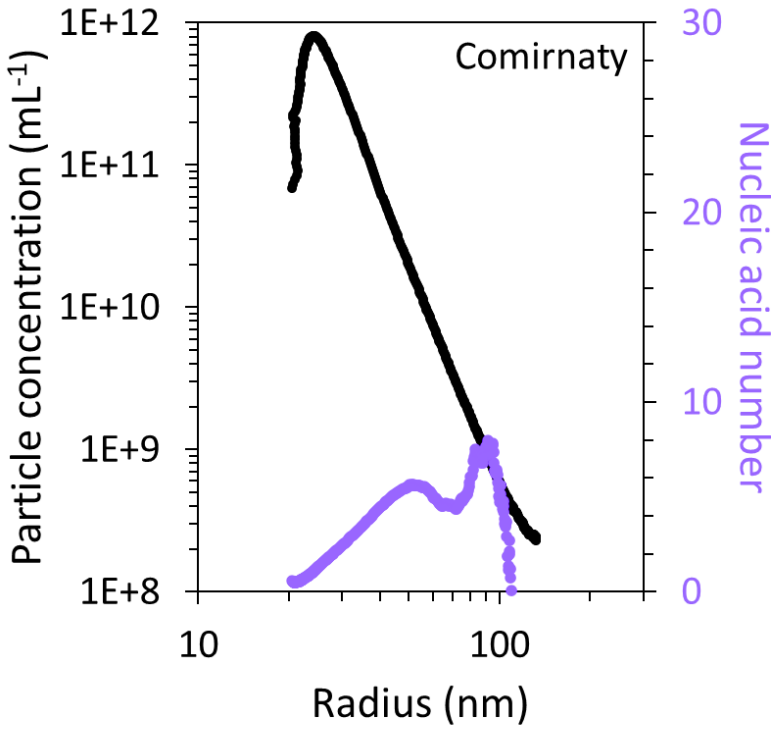
Aliquots collected with fraction collector match!

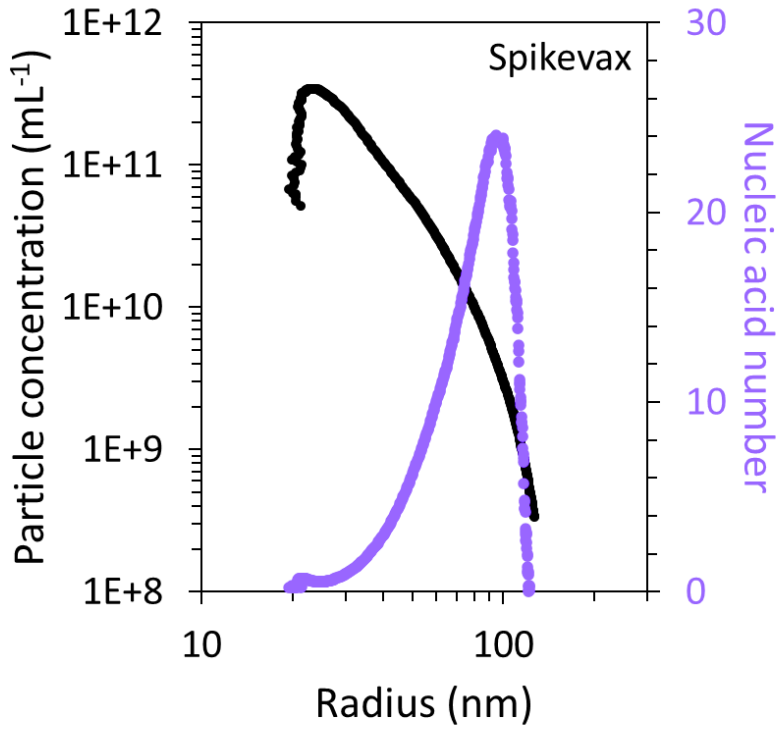


LNP-RNA, RNA wt% (online)
LNP-RNA, RNA wt% (offline)
Empty LNP, RNA wt% (online)

More details in app note:

- Quantify the amounts of LNPs with a specific size and drug substance content.





- The mRNA payload is *not* distributed equally across the different-sized LNPs.

Waters |Wyatt LNP Characterization Solutions

Non-exhaustive

High-Throughput Screening → Zeta Potential Optimization → MAQ & Detailed Characterization

DynaPro Plate Reader
High Throughput DLS/SLS
Instrument

- Size/ radius (QC)
- Aggregation content
- Freeze-thaw stability
- Structure
- Polydispersity (QC)

DynaPro ZetaStar
DLS/SLS/ELS
Instrument

- Size/radius (QC)
- Aggregation content
- Structure
- Charge/Zeta Potential
- Polydispersity (QC)

Digest

Intact & Digest

Waters LC-MS

QDa detector

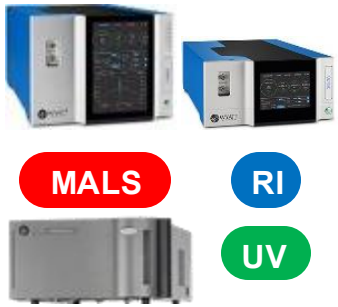
BioAccord MS

Lipid Composition & ratio

Modifications – Lipids and mRNA

Low level impurities

Size Exclusion or Eclipse FFF system



Size distribution

Payload concentration

Size-based payload distribution

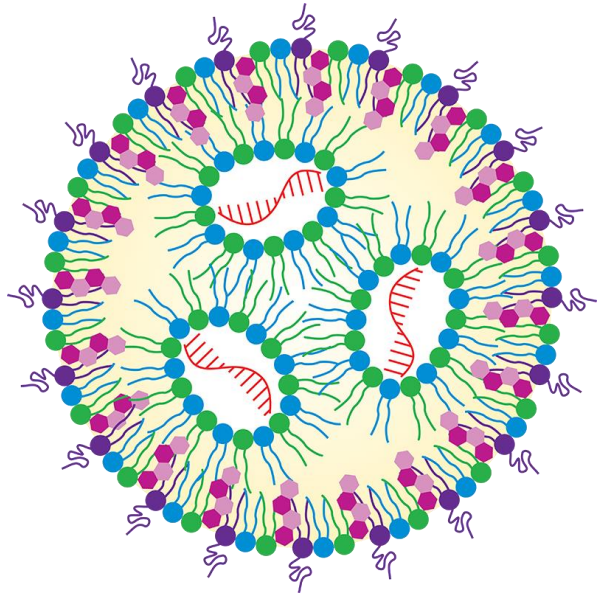
Encapsulation efficiency

Morphology

Lipid concentration

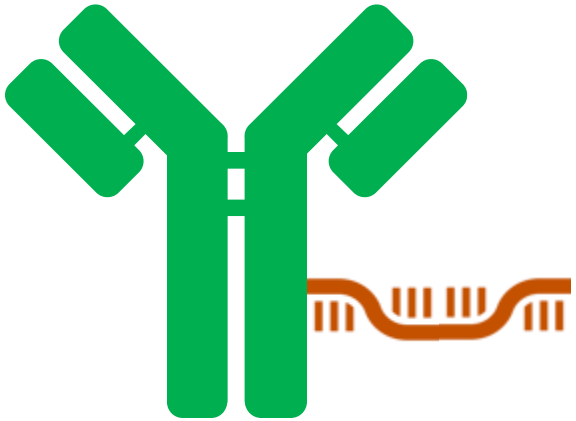
Aggregation

Multi-detector MALS can provide:



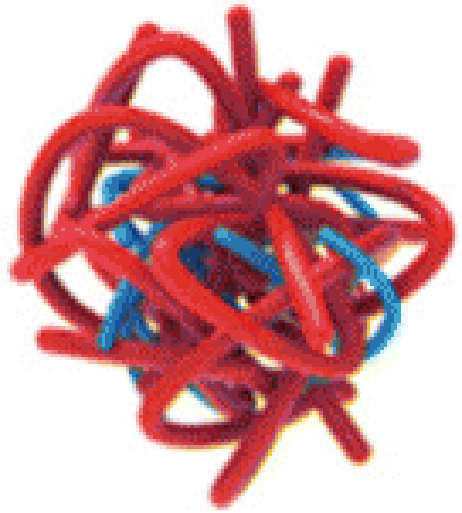
LNPs

Hig-Res Size
Polydispersity
Encapsulation
Size-based payload distribution
Stability



ADCs

Aggregation
Molar mass
Antibody concentration
Payload concentration
Drug-Antibody Ratio
Stability
Variant analysis



Polymeric

Hig-Res Size
Polymer concentration
Payload concentration
Conformation
Molecular weight

Questions