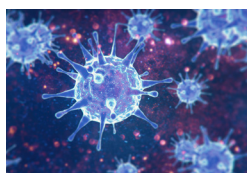




Optimizing the Analysis of Viral Vectors with SEC-MALS

AUGUST 2020

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Quantifying Viral Vector Attributes with Light Scattering

Michelle Chen



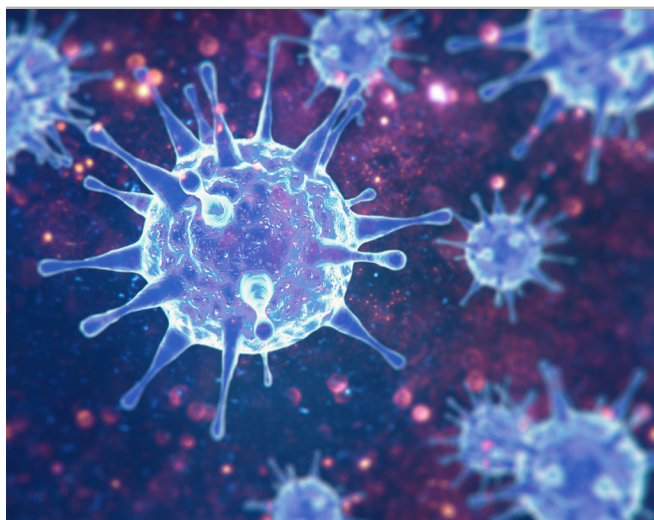
Integrated Analytical Platforms for Viral Vectors

Interview with Peng Wang



SEC-MALS Method for Characterizing mRNA Biophysical Attributes

Pam Wang, Rama Akula, Michelle Chen, and Kristine Legaspi



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Quantifying Viral Vector Attributes with Light Scattering

Michelle Chen

Light scattering combined with methods for size-based separation constitutes a set of powerful techniques for the analysis of viral vectors.

Overview

Over billions of years, viruses have evolved to be extremely effective at entering host cells and hijacking the cellular machinery to replicate, often causing infection and disease. In recent years, however, scientists have learned how to take advantage of the virus's ability to get into cells, to aid in gene therapy by replacing the virus's own genes with therapeutic genes.

In gene therapy, a virus capsid is used as a delivery mechanism to transport therapeutic agents inside patients' cells with the hope of curing genetic disorders, treating chronic diseases, or fighting cancer. To ensure the safety

and efficacy of a viral vector-based gene therapy, it is crucial to identify, characterize, understand, and monitor critical quality attributes (CQAs) such as particle size, concentration, the payload (e.g., ratio of empty to full capsids), and degree of aggregation.

Light scattering offers a direct physical means of measuring several of the necessary quantities. Measurements can take two forms. In the first, known as *multi-angle light scattering* (MALS), the scattered light intensity is measured as a function of angle over a time scale of roughly one second. MALS can provide a measure of the molar mass of the molecule or nanostructure independently of shape. It also determines the radius of gyration, a mass-averaged radius. The second form of light scattering is *dynamic light scattering* (DLS), in which the intensity fluctuations of scattered light



are measured on a microsecond time scale. DLS provides a direct measure of the translational diffusion coefficient, which is then used to calculate the hydrodynamic radius.

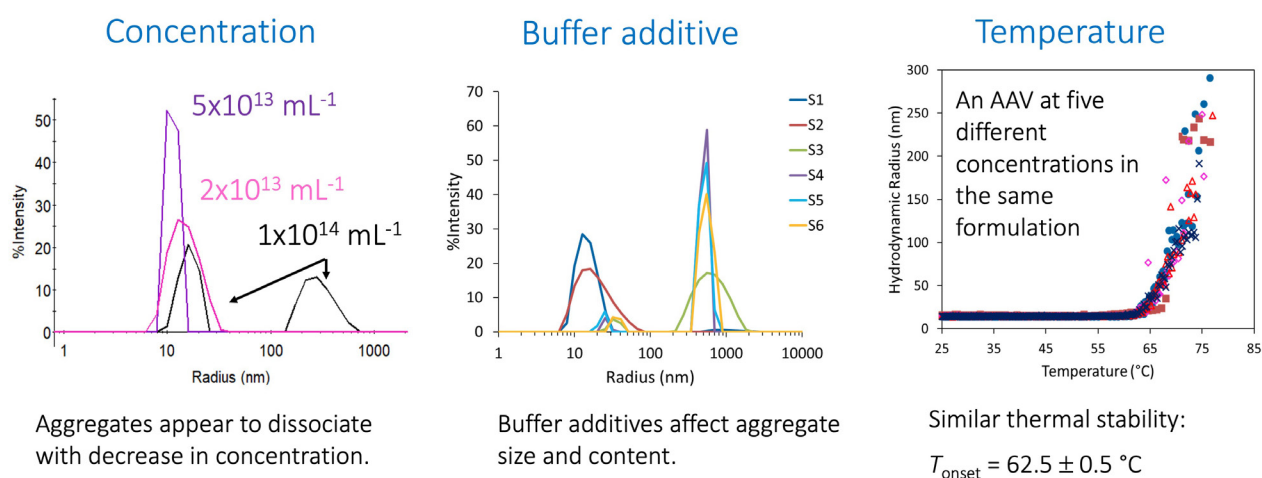
Dynamic Light Scattering

DLS is very useful as a screening tool. Using a small sample amount, it can determine size distribution, aggregation, and particle concentration, and it is also useful for stability screening. Measurements are nondestructive and often take less than 30 seconds per sample. The DynaPro NanoStar is a commercially available DLS instrument that uses as little as 1 μL of sample in a quartz cuvette or 4 μL in a disposable

cuvette. The DynaPro automated plate reader measures DLS with sample volumes down to 25 μL in a 384-well plate and 5 μL when reading a 1,536-well plate.

Some possible DLS screenings that can be performed are presented in **Figure 1**. The samples in this example are adeno-associated viruses (AAVs). In the first example (left), concentration-dependent sample aggregation was studied. The sample was found to have substantial aggregation at a concentration of $1 \times 10^{14} \text{ mL}^{-1}$. A dilution study determined that these aggregates were reversible and disappeared at lower concentrations. In a second study (middle), several buffer additives

Figure 1: Stability screening with the DynaPro Plate Reader





were screened to determine which ones were responsible for initiating aggregation. Last, the sample was screened for temperature stability. In this case, all samples showed the onset of aggregate formation at about the same temperature, regardless of concentration or buffer components.

DLS is a fast screening tool for size distributions, stability, and particle concentration. It can be used in process development or as an at-line manufacturing check. Because it is a direct physical measurement, it can usually be used without further method development.

There is a maximum particle radius for reliable concentration determination of 160–175 nm, depending on the instrument. The measurable concentration range is 10^{11} to 10^{15} particles per milliliter for AAVs and particles of similar size; the upper and lower limits both decrease for larger particles. The commercial software, DYNAMICS, performs concentration

analysis according to a solid sphere model, which works well with viruses and nanoparticles. The two primary sources of the inaccuracy of reported particle concentration are user-supplied particle refractive index and instrument-determined size.

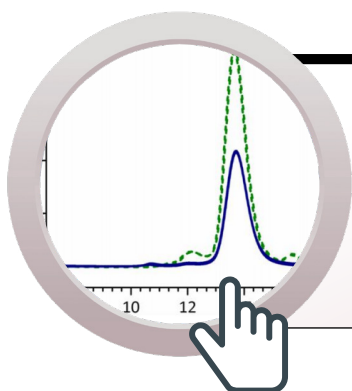
These limitations of DLS are offset by the speed, ease of analysis, small sample quantity required for a measurement, and minimal set-up time. Commercial systems such as the Wyatt DynaPro series feature a secure database system that is compliant with FDA regulations for data integrity and record keeping. This feature is important for using DLS in production and quality control.

SEC-MALS

MALS is an information-rich technique that can be made even more powerful when coupled to a means of particle separation based on size such as size-exclusion chromatography (SEC). In SEC, the sample flows through a bed of porous beads with a specific range of pore size. Sufficiently small particles

can diffuse into and out of the pores. The more time spent in the pores, the longer a particle will take to elute out of the column. Larger particles cannot access the pores and thus remain in the flow stream to migrate out first. The combination technique

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AAV critical quality attribute analysis by SEC-MALS

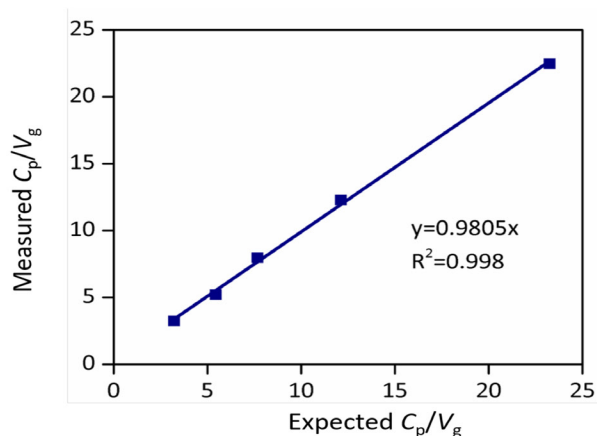


of SEC-MALS is a powerful way to characterize small viruses as well as proteins, polymers and polypeptides. When coupled with UV and refractive index (RI) detection to characterize proteins, SEC-MALS can provide information on conjugation, oligomeric state, molecular weight, aggregation, structure, reversible association, and UV extinction coefficient. SEC-MALS systems have been well validated and used in QC environments for other biological materials such as PEGylated and glycosylated proteins, as well as polysaccharides.

We have developed a robust yet versatile SEC-MALS method for AAV

samples. In a single assay, the AAV particle concentration, capsid content, and degree of aggregation can be determined without calibration. AAVs are essentially conjugates of DNA and protein, and hence are amenable to SEC-MALS-UV-RI conjugate analysis. Conjugate analysis reveals the molecular weight and the mass concentration of both the protein capsids and the DNA separately, leading to the determination of the empty:full capsid ratio. **Figure 2** shows measurements of multiple samples with varying empty:full capsid ratios. This is equivalent to performing both ELISA and qPCR in a single run. The only assumption in particle concentration

Figure 2: Calibration-free quantitation



C_p : capsid particle concentration
(total AAV)

V_g : viral genome particle concentration
(full AAV alone)

- Excellent agreement with theoretical value on capsid content.
- Excellent correlation with AUC data, confirms SEC-MALS is viable & orthogonal method.



analysis is that there is 100% recovery from the SEC column. This assumption has been shown to be generally safe to make using our optimized SEC method. Because SEC elution order is based on size, it is also possible to evaluate and quantify the degree of aggregation in the sample. All these analyses have now been implemented in a new module called “Viral Vector Analysis” in Wyatt’s ASTRA software.

Additional analyses can include measurement of the radius of gyration (R_g) and the hydrodynamic radius (R_h). The ratio of R_g to R_h is the shape factor for the molecule, and can be used to gain insights on shape and structure. SEC-MALS also detects and identifies the impurities like free protein and DNA molecules.

To ensure the accuracy and precision of the analysis, SEC separation must be optimized. The separation should be reproducible with aggregates and fragments well resolved from the main peak. There should be minimal peak

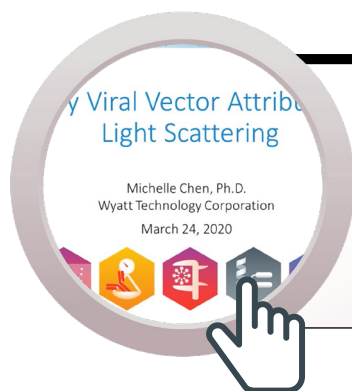
tailing and the blank runs should have no unidentified peaks. The SEC-MALS method does not require calibration, but a system suitability check is recommended using appropriate standards such as bovine serum albumin (BSA) and/or immunoglobulin G (IgG). Both molecular weight and mass recovery values should be within the expected range.

In addition to assumed good column recovery, the SEC-MALS analysis cannot distinguish between capsids with a partial genome from a mixture of empty and full capsids. The presence of the partial AAV, however, will only affect the accuracy, not the precision, of the capsid content measurement. The determination of the total AAV particle concentration will not be impacted by the presence of the partial AAV either.

The SEC-MALS method offers many benefits in measuring these three major AAV COAs within one single run. It requires minimal sample

preparation, is reagent- and label-free and non-destructive, and turn-key systems are available with minimal set-up time. It can be fully automated with each assay taking just 5–30 minutes. The sensitivity of detection

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Quantifying Viral Vector Attributes with Light Scattering



is on the order of 10^{11} particles/mL. In addition, the sample parameters included in the method are applicable to almost all serotypes, so there is minimal guesswork involved.

FFF-MALS and FFF-DLS

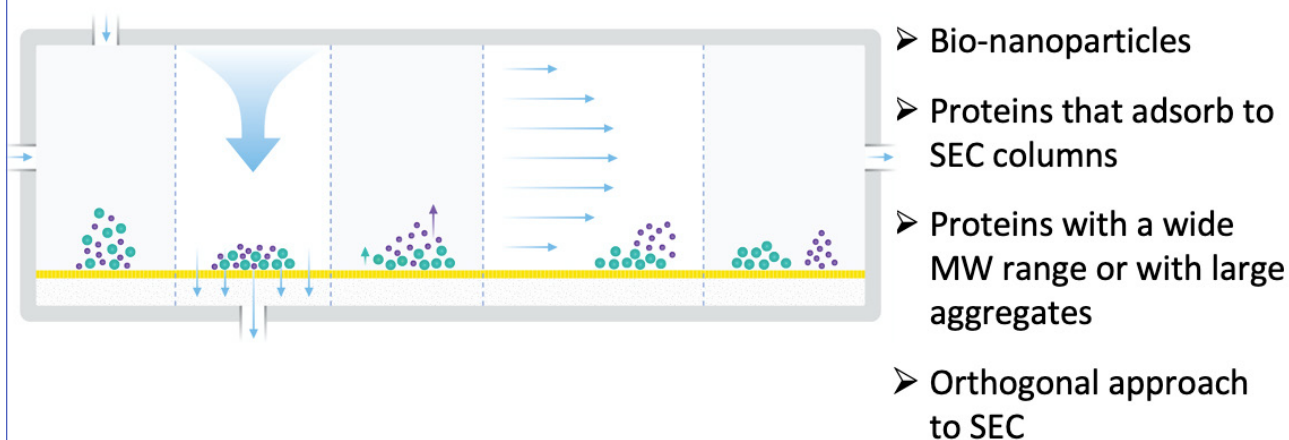
Above a certain particle size, stationary phase availability and mass-transfer limitations prevent adequate separation in SEC. This is where field-flow fractionation (FFF) can take over as the tool of choice for separating nanoparticles, including larger viruses like adenovirus and lentivirus, as well as large aggregates of AAVs. When combined with MALS, FFF determines size distribution with high resolution and

provides characterization similar to SEC-MALS.

Like SEC, the separation in FFF is driven by hydrodynamic size. However, there are differences that make it a good orthogonal approach to SEC. FFF is based on physical forces applied to the particles rather than interaction with a stationary phase. It can be used for proteins that have a tendency to adsorb to SEC columns. It is also better aimed at particles and molecules that are too large to be analyzed easily by SEC, or have a molecular weight range that is too large for separation on a single SEC column.

The typical layout for flow FFF

Figure 3: Alternative separation technique: FFF





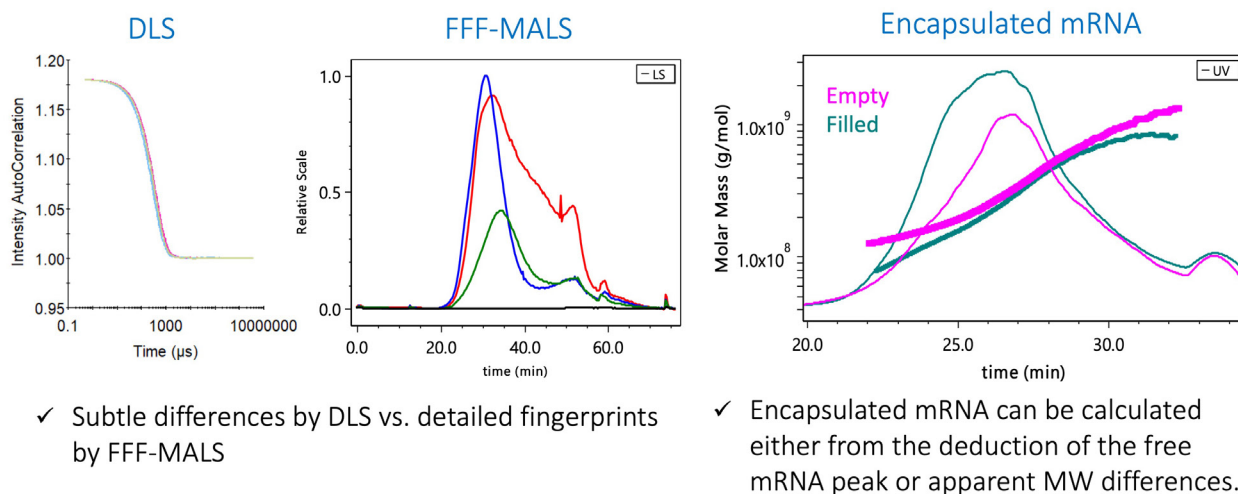
can be seen in **Figure 3**. A net downward flow, known as “cross flow,” concentrates particles against the membrane along the bottom of the channel. Particle diffusion works against this concentration. Smaller, faster-diffusing particles, therefore, reach further upward into the channel. A second longitudinal flow transports the particles along the channel. Because of the parabolic flow profile, particles that diffuse further upward into the channel experience a higher average lateral flow and are swept out of the channel more quickly. The elution order is reversed from SEC, with small particles coming out first.

FFF is highly tunable to cover a wide range of particle sizes and can produce near-baseline resolution of particles with a 15% size difference.

To quantify AAV aggregation, FFF is recommended to confirm the results from SEC, as the SEC column may remove part of the AAV aggregates either by column filtration or shearing degradation. In addition to AAV and large viral vectors, FFF-MALS has been applied to the analysis of lipid nanoparticles and extracellular vesicles.

An example of lipid nanoparticles (LNPs) is shown in **Figure 4**. Three samples of LNPs were first

Figure 4: LNP: DLS vs. FFF-MALS



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screened by DLS. As can be seen in **Figure 4**, the differences are quite subtle. With FFF-MALS, a far more detailed fingerprint for each sample is apparent. When further combined with UV absorption and dRI detectors, it becomes possible to quantify the encapsulated mRNA, either by observing apparent differences in molecular weights of lipids and mRNA or by direct measurement of the free mRNA peak.

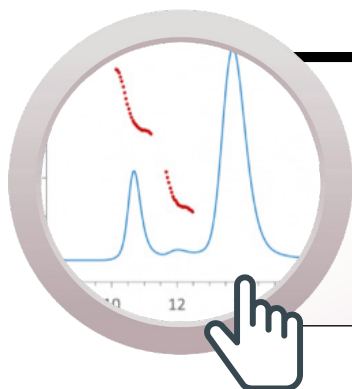
Conclusion

The two light-scattering methods, MALS and DLS, provide essential capabilities for the quantitation and evaluation of viral vectors and other nanoparticles like liposomes, LNPs, and extracellular vesicles. Important

parameters, such as aggregation, encapsulation, and concentration can be determined. When combined with size-based separations, such as SEC or FFF, light scattering becomes even more powerful for determining fundamental quality parameters. Covering different size regimes and chemistries, SEC and FFF are complementary, and one can often be substituted when the other is not applicable. Both SEC and FFF are supported by the Eclipse FFF system, allowing an easy switch between these two modes of separation.

Michelle Chen, PhD, is Vice President of Analytical Services at Wyatt Technology Corporation.

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Quantifying AAV
aggregation and
quality attributes by
FFF-MALS



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Integrated Analytical Platforms for Viral Vectors

Interview with Peng Wang

Challenges with analytics and processes for gene vectors.

Cell and gene therapy is a promising field, but developing analytical methods and manufacturing processes can be a challenge. *LCGC* sat down with Peng Wang, PhD, Scientist at R&D Lonza Houston, to discuss the challenges that arise when creating analytics and processes for gene vectors; the pros and cons of using multi-angle light scattering (MALS), ion-exchange chromatography (IEX)-MALS, and size-exclusion chromatography (SEC)-MALS; and more. Lonza Pharma & Biotech provides contract development and manufacturing services for pharmaceutical and biotechnology companies. The firm's expertise covers the development of basic biomolecules through formulation and process

development to manufacturing the final drug product.

LCGC: How does Lonza's internal R&D contribute to meeting its business objectives as a contract development and manufacturing organization (CDMO) and meeting the needs of its customers?

Wang: As a leading pharmaceutical CDMO, our role is to continuously innovate, improve, optimize, and re-invent processes and platforms for good manufacturing practices (GMPs). R&D activities play a big part, particularly in the cell and gene therapy space, which requires innovations for these promising therapies to be manufactured at a commercial scale robustly, consistently, and in high quality. We work closely with the process development team to understand and anticipate customers' future needs. We conceptualize, develop, test, and experiment in our R&D labs to establish the customized platforms



and technologies that can address these needs. Once we have established and demonstrated a platform, it is handed over to the process development team, which can readily start using it for customer development activities.

LCGC: What are the specific challenges that you encounter developing analytics and processes for gene vectors? How do they differ for different types of vectors?

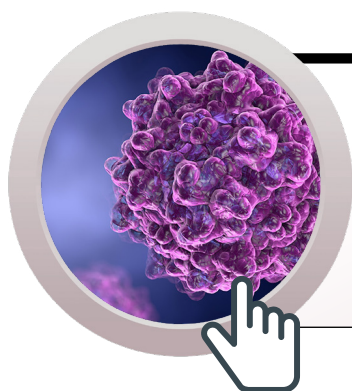
Wang: Due to the structural complexity of viral vectors, we encounter multiple challenges during analytics and process development on a daily basis. The most obvious one is the relatively low titer of viral-vector production. It requires analytical methods with higher sensitivity and resolution in a complex sample matrix. The second challenge is the heterogeneity of viral vectors; once you improve the resolution of your analytical method, you can encounter variants of your product; identifying the variants is time-consuming and requires additional methods to fully characterize them.

In general, the development of analytics and manufacturing processes for various viral vectors share similar challenges, but the requirements are slightly different. For example, the Lentiviral vectors for gene therapy, which are used to transfect T-cells with genes to express the chimeric antigen receptors, are considered to be intermediate products; on the other hand, AAV vectors are the final products for gene therapy. Additionally, based on the differences of biophysical properties between the Lentiviral vector and AAV viral vector, the analytics and process methods are developed accordingly.

LCGC: How does multi-angle light scattering (MALS) fit into your analytical platform? Which application or applications have you found most beneficial or promising?

Wang: MALS has been heavily used to characterize large polymers at the levels of tertiary and quaternary structures. It fits well for characterizing large biological products such as viral vectors. We are using it to characterize our AAV in-process samples in the format of size-exclusion chromatography (SEC)-MALS. Identifying and quantifying aggregates in our viral-vector products are the most beneficial application

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AAV quantitation and stability analysis by batch DLS



of MALS. Determining the full:empty ratio of AAV vectors is a promising application that could be implemented in the format of SEC-MALS and ion-exchange chromatography (IEX)-MALS.

LCGC: SEC-MALS is utilized quite widely in biopharmaceutical analytical labs, but it is far less common to see MALS coupled to IEX. What benefits and challenges do you see in IEX-MALS?

Wang: IEX-MALS is beneficial for determining the full:empty ratio of AAV viral vectors since IEX-HPLC is able to resolve AAV full and empty peaks. The refractive index (RI) detector that is usually used together with MALS and UV to perform these analyses is highly sensitive to salt concentration, however. To obtain the most accurate results, the experimental configuration and method must be carefully optimized.

LCGC: Based on your current experience with MALS, what are your expectations for moving it forward to process development and quality control?

Wang: We are delighted to see that Wyatt is working on developing methods for the determination of full and empty AAV capsids using the SEC-MALS system. New software for the data analysis in this regard will be beneficial. We are also expecting Wyatt will develop methods for Lentivirus, for example, using the field-flow

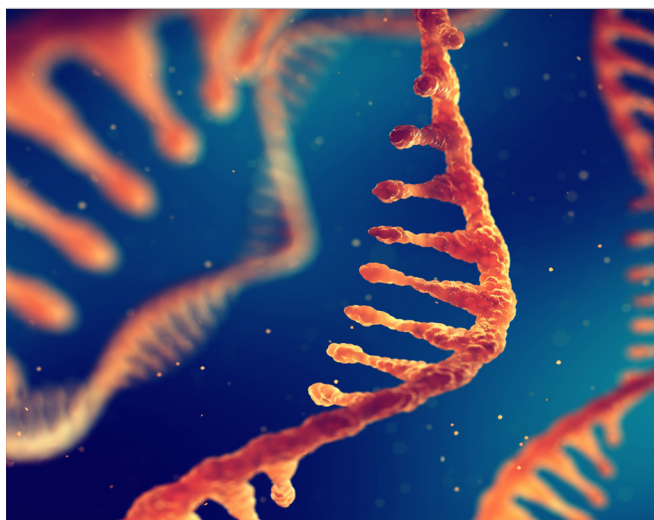
“Identifying and quantifying aggregates in our viral-vector products are the most beneficial application of MALS. Determining the full:empty ratio of AAV vectors is a promising application that could be implemented in the format of SEC-MALS and ion-exchange chromatography (IEX)-MALS.”

Peng Wang, PhD,
Scientist at R&D Lonza Houston

fractionation (FFF)-MALS system, for both process development and quality control.

LCGC: What is the principal value of MALS in gene vector R&D, process, and quality control?

Wang: The principal value of MALS in R&D, process, and quality control for viral vectors is the capacity to assess multiple critical quality attributes (CQAs) in one experiment. The well-established MALS technology coupled with various separation methods will be beneficial for not only purified samples but also in-process samples.



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SEC-MALS Method for Characterizing mRNA Biophysical Attributes

Pam Wang, Rama Akula, Michelle
Chen, and Kristine Legaspi

Summary

An SEC-MALS method incorporating DAWN and Optilab detectors is developed to quantify a number of biophysical attributes of mRNA. These attributes include molecular weight, percentage of aggregates, R_g , R_h , and R_g/R_h . This method can be readily adopted to further study how these attributes are being affected by mRNA preparation, formulation and storage conditions.

Introduction

RNA therapeutics is a rapidly growing field that encompasses a wide variety of biologically inspired molecules. Messenger ribonucleic acid (mRNA) is a transient biopolymer responsible for converting genetic information stored in DNA into functional proteins (1).

Over the past decade, mRNA has emerged as an increasingly desirable alternative to traditional protein-based

therapies; mRNA molecules with the appropriate sequence, synthetic modifications, and delivery vehicle are much more likely to lead to the production of properly folded and post-translationally modified proteins within the human body. Furthermore, unlike DNA-based gene therapy, mRNA drugs pose minimal risks of genome integration and reduce long-term safety concerns. Considering these benefits, mRNA has the potential to revolutionize the biologicals industry, providing a versatile platform for vaccine development, immuno-oncology, and protein replacement therapies (2).

Despite its apparent advantages, mRNA therapeutic development is in its early stages, and clinical success will rely heavily on the elucidation of mRNA attributes using high-quality analytical tools. Given the intrinsic dynamics of RNA molecules, 3D structural



information is particularly difficult to obtain. Therefore, complementary techniques that can provide insight into size, oligomeric state, and conformation would be invaluable for understanding the biochemical and biophysical properties of mRNA.

High-performance size-exclusion chromatography (SEC) has been widely used in protein research and protein therapeutic development with applications including purification and molecular weight (MW) estimation, and aggregation quantification. Its application can be further extended to include accurate MW determination and shape estimation when light scattering (LS) detectors, namely multi-angle light scattering (MALS) and online dynamic light scattering (DLS), are added (3).

Commonly used in protein analysis, characterization by SEC-MALS is particularly important for RNA molecules, especially the large RNA molecules like mRNA. The SEC-MALS

method can provide biophysical and structural information that are otherwise difficult to obtain given the large size and high charge density of mRNA.

In order to develop an mRNA molecule into a drug product, properties like MW, size, and conformation need to be well characterized and monitored throughout the development cycle. In this note, we will discuss the use of an SEC-MALS method for comprehensive mRNA characterization, employing two commonly used tool constructs: RNA for human erythropoietin (EPO), a hormone that plays a key role in the production of red blood cells; and firefly luciferase (fLuc), a bioluminescent protein whose expression levels can be easily quantified *in vivo* (4).

Materials and Methods

EPO and *fLuc* mRNA were synthesized by *in vitro* transcription. The purified mRNA products were quantified by UV absorbance. SEC was carried out on an Agilent 1260 HPLC system with a Wyatt WTC050S5 column using PBS (50 mM

phosphate, 50 mM NaCl, and 250 ppm NaN_3 at pH 6.8) as the mobile phase. A relatively high flow rate of 0.8 mL/min was used here to shorten run time and increase assay throughput.

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FFF-MALS-DLS nanoDDs key publications

publications on the characterization of
and gene delivery systems by FFF-MALS

lists key publications using AFA-MALS
characterization of nanoparticle drug delivery
systems, including nanoparticles for delivery
of proteins, DNA, RNA and other ther-

apeutic products: methodology, val-
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laboratory.eu/en/PPP/PCC/ELN/1222.pdf) (rev 3-6-2013/10/2016)

- Mechanism and kinetics of
soluble "green lip" for
a novel release



Figure 1: Chromatograms of *fLUC* (blue) and *EPO* (green) mRNA obtained from 90°LS (solid) and UV at 260 nm (dashed).

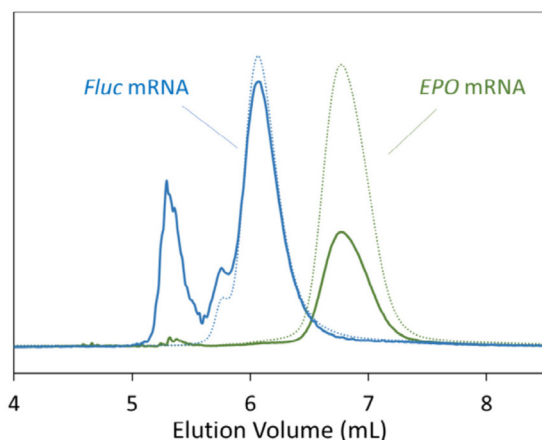


Table 1: Summary of measured attributes of *EPO* and *fLUC* mRNA.

	MW [kDa]	Agg ^a [%]	R_g [nm]	R_h [nm]	R_g/R_h	ϵ^b
<i>EPO</i>	272 ± 1	4.8	15 ± 1	12+/-1	1.2	22.8
<i>fLuc</i>	622 ± 1	2.6	20 ± 1	17+/-1	1.2	22.4

^a Agg is the percentage of aggregate by weight

^b ϵ is the extinction coefficient at 260 nm in mL·mg⁻¹·cm⁻¹

Results and Discussion

Small amounts of large MW species were observed in both *EPO* and *fLuc* mRNA samples, adequately separated from the main population, as seen in the UV and light scattering (LS) chromatograms presented in **Figure 1**. Since LS intensity is proportional to the product of concentration and MW, the LS signal is particularly useful for detecting small quantities of large MW species, compared to UV or refractive index (RI) detection.

Using the hardware configuration detailed in the Materials and Methods section, we can simultaneously measure MW and two types of radius:

- radius of gyration (R_g), using the MALS detector, and
- hydrodynamic radius (R_h), using the online DLS detector.

The properties that are measured, including MW, R_g , R_h , R_g/R_h , and UV extinction coefficient at 260 nm of the main peak, as well as percentage of aggregate, are summarized in **Table 1**. It should be noted that the method is highly reproducible, and all of the attributes were measured within a single SEC-MALS experiment, requiring less than 15 minutes.

The MW values of the main peak of each mRNA determined from MALS-RI analysis are in near-perfect agreement with the theoretical values for *EPO* and *fLuc* mRNA (273 kDa and 619 kDa, respectively). The results confirm that

The effluent was detected by a variable UV detector at 260 nm for mRNA molecules and 280 nm for proteins, followed by a DAWN® MALS detector equipped with a WyattQELS™ embedded DLS module, and an Optilab® differential refractive index (RI) detector. ASTRA® software was used for HPLC control, data collection, and data analysis. A dn/dc value of 0.172 mL/g was used for mRNAs and 0.185 mL/g was used for proteins.



Figure 2: Molar mass of *fLuc* mRNA (blue), EPO mRNA (green) and thyroglobulin (red) samples, superimposed on UV chromatograms acquired at 260 nm.

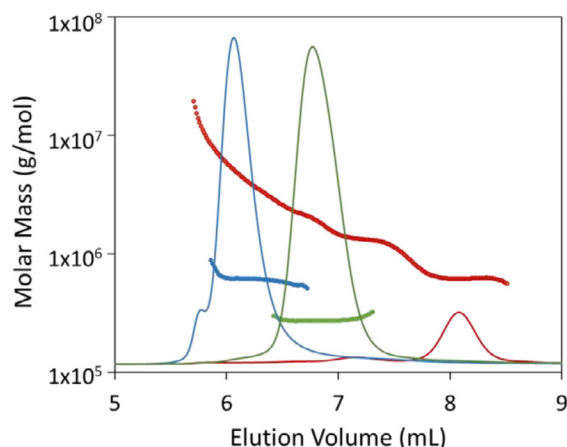
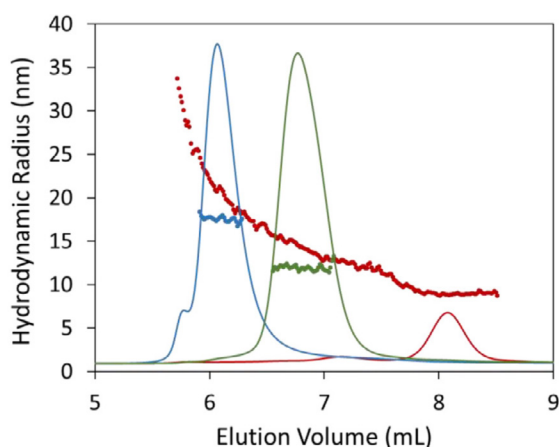


Figure 3: Hydrodynamic radius (R_h) from online DLS for *fLuc* mRNA (blue), EPO mRNA (green) and thyroglobulin (red) are plotted against elution volume, superimposed on UV chromatograms at 260 nm.



the mRNAs used in this study remained intact throughout the production, storage, and transportation.

This level of detail provided by SEC-MALS cannot be revealed by the traditional SEC-UV method of column calibration. Column calibration using globular protein standards typically overestimates the molar mass of RNA molecules by a factor of a few times due to the drastic difference in compactness between a globular protein and an RNA molecule (5). Even if polynucleotides of various lengths are used as the calibration standards, the calibration method can provide, at its best, a rough approximation of the actual molar mass of the RNA molecules, given the low resolution of the SEC separation.

The online MALS detector, on the other hand, permits the accurate molar mass measurement of both mRNAs and proteins, regardless of their compactness and potential non-ideal column interaction. **Figure 2** presents chromatograms and molar masses from MALS of the two mRNAs studied here plus a protein, thyroglobulin, and the aggregates of all three. The *fLuc* mRNA has a similar molar mass as thyroglobulin yet it eluted at a much earlier elution volume due to its less compact conformation. It is also seen from **Figure 2** that the molar mass across the main peak of the mRNA samples is constant, suggesting the main population in both samples is a pure monomer.

**Table 1:** Summary of measured attributes of *EPO* and *fLUC* mRNA.

	MW [kDa]	Agg ^a [%]	R_g [nm]	R_h [nm]	R_g/R_h	ϵ^b
<i>EPO</i>	272 ± 1	4.8	15 ± 1	12+/-1	1.2	22.8
<i>fLuc</i>	622 ± 1	2.6	20 ± 1	17+/-1	1.2	22.4

^a Agg is the percentage of aggregate by weight^b ϵ is the extinction coefficient at 260 nm in mL·mg⁻¹·cm⁻¹

In addition to molar mass, online LS detectors can measure other biophysical properties like size and conformation which may impact delivery strategy. Hydrodynamic radii of the two mRNAs and thyroglobulin versus elution volume are depicted in **Figure 3**.

Both R_g and R_h are insightful as their ratio is correlated to the conformation of a macromolecule. EPO and fLuc mRNA monomer showed an $R_g : R_h$ ratio of approximately 1.2 (see **Table 1**), consistent with a random coil conformation. A random coil structure is much less compact than the globular conformation typical of proteins which has an $R_g : R_h$ ratio of 0.77.

Conclusions

The SEC-MALS method reported in this note provides a convenient and quick, yet powerful tool for measuring the biophysical attributes of mRNA molecules. The method can also be used to study the effects of different

ions, ionic strength, pH, and other buffer conditions on mRNA biophysical properties and stability. These attributes are crucial in understanding any large RNA molecules, especially when developed as a therapeutic product.

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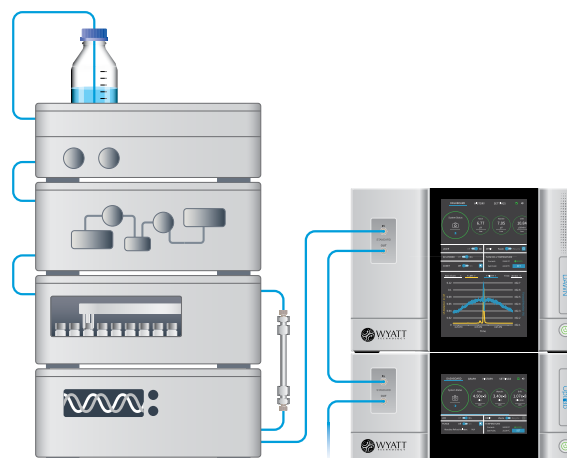
Pam Wang, PhD, and Rama Akula are affiliated with Moderna Therapeutics.
Michelle Chen, PhD, and Kristine Legaspi are affiliated with Wyatt Technology Corporation.

Solutions for Viral Vector Characterization

Analyze AAV attributes with SEC-MALS-DLS

Size-exclusion chromatography combined with multi-angle and dynamic light scattering (SEC-MALS-DLS) is a standard tool for biophysical characterization of biopharmaceuticals. Recent developments have highlighted its importance for adeno-associated viruses as vectors in gene therapy, where SEC-MALS-DLS determines multiple critical quality attributes, simultaneously.

SEC-MALS-DLS combines size-based separation, using standard HPLC equipment, with independent determination of molar mass and size by a DAWN® light scattering instrument. In combination with UV absorbance data, the system characterizes key CQAs: aggregation, relative capsid content and AAV physical titer.



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To learn more about Wyatt's unique solutions for AAV characterization visit wyatt.com/GeneTherapy

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