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Microchip Electrophoresis System MultiNA™ II MCE-301

Application News

Rapid and Simple Analysis of LNP-Encapsulated mRNA Using a Microchip Electrophoresis System

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User Benefits

- Automates gel preparation, sample application, and data acquisition for nucleic acid electrophoresis.
- Enables rapid and simple measurement of LNP-encapsulated mRNA samples without purification.
- Provides highly sensitive mRNA analysis.

■ Introduction

Recently, medical technology utilizing mRNA has advanced rapidly. In addition to infectious disease vaccines, mRNA is gaining attention in fields such as cancer vaccines and gene therapy. Since mRNA is a large, negatively charged molecule with poor cell membrane permeability, delivery technology is essential for efficient transport into cells. Currently, Lipid Nanoparticles (LNPs) are primarily used as Drug Delivery Systems (DDS). This technology protects mRNA from extracellular degradation and enables efficient intracellular transport.

LNP-encapsulated mRNA (mRNA-LNP) formulations are expected to serve as treatments for various diseases; however, quality control in their manufacturing and storage has become a critical challenge. The quality of mRNA-LNP formulations directly impacts their safety, efficacy, and stability. Therefore, establishing appropriate analytical methods for quality evaluation is essential for improving product reliability and ensuring compliance with regulatory standards.

Methods for confirming mRNA purity include agarose gel electrophoresis and capillary electrophoresis; however, these can be disadvantageous due to the time required for preparation and analysis, or insufficient resolution. In contrast, the Microchip Electrophoresis System MultiNA™ II (Fig. 1) automates the entire process from gel preparation to sample loading and data analysis. It enables rapid analysis with a migration time of approximately 100 seconds per sample. This application presents an example of simple and rapid analysis of mRNA-LNP using the MultiNA II without the need for pretreatment.

Fig. 1 Microchip Electrophoresis System MultiNA™ II MCE-301

■ Sample and Pretreatment

The RNA Kit (P/N: 292-27913-91) was used for electrophoresis. Samples were prepared by mixing equal volumes of the sample and the RNA marker solution included in the kit. The mixture was then heated at 70˚C for 5 minutes and cooled at 4˚C for 5 minutes, in accordance with the draft guidelines (Analytical Procedures for Quality of mRNA Vaccines and Therapeutics, Draft Guidelines: 3rd Edition). Analytical procedures are shown in Fig. 2, and analytical conditions are listed in Table 1.

SYBR Green II (P/N: S-7564) was used as the fluorescent dye, and RNA 6000 Ladder (P/N: AM7152) was used as the size standard. The size standard was diluted 6-fold with THE RNA Storage Solution (P/N: AM7001). After adding an equal volume of the RNA marker solution, the mixture was heated at 70˚C for 5 minutes and cooled at 4˚C for 5 minutes.

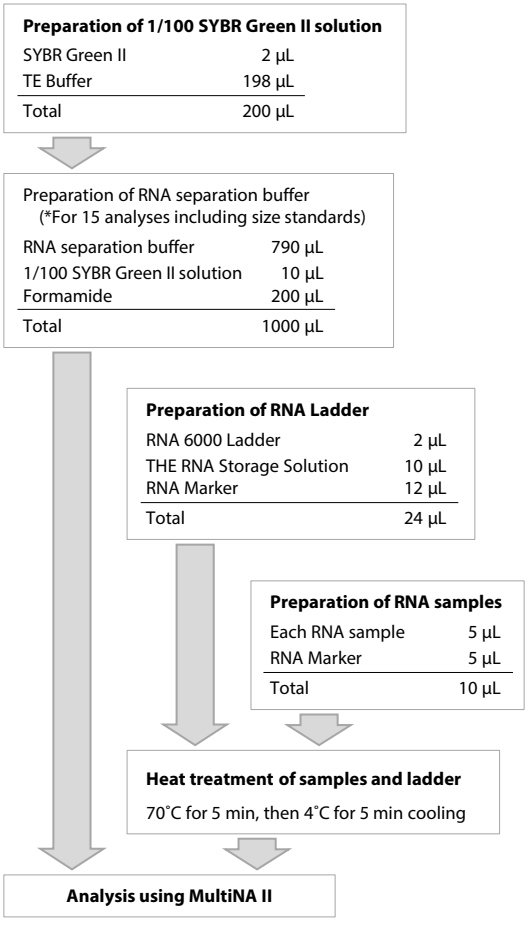

Fig. 2 Analytical workflow for mRNA-LNP using MultiNA II

Table 1 Analytical Conditions for mRNA

System	: MultiNA II
Reagent Kit	: RNA kit (P/N: 292-27913-91)
Fluorescent Dye	: SYBR Green II (P/N: S-7564)
Size Standard (Size Marker)	: RNA 6000 Ladder (P/N: AM7152)
Dilution Solvent	: THE RNA Storage Solution (P/N: AM7001)

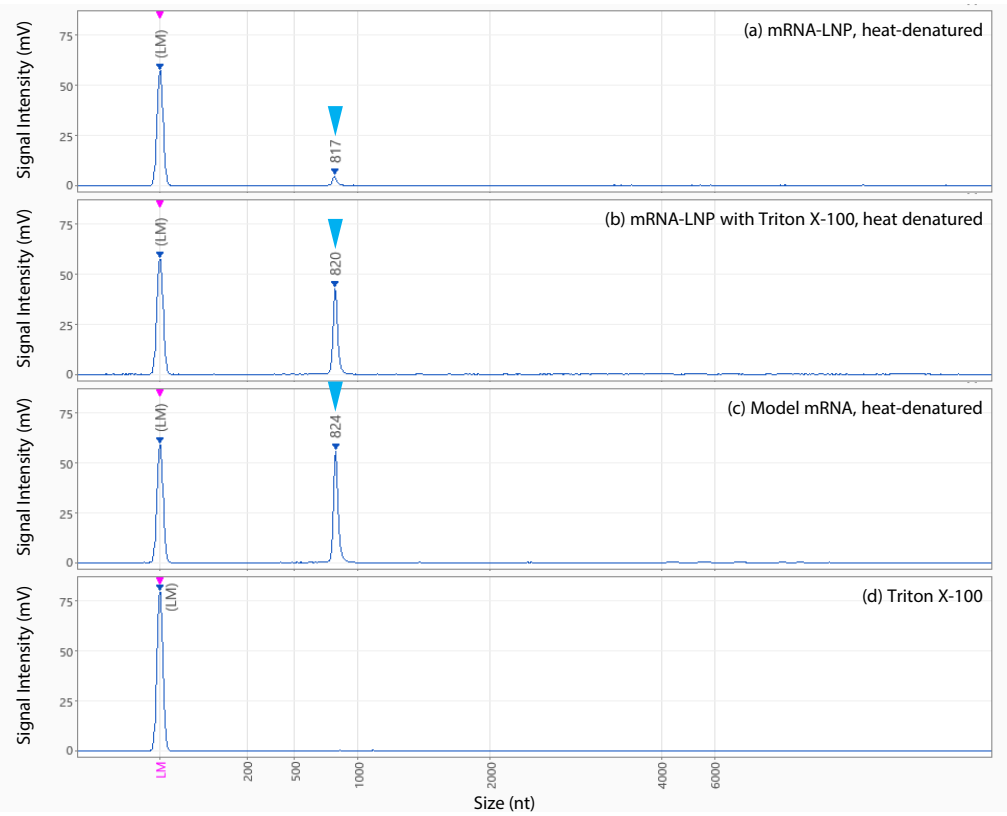

Fig. 3 Microchip electrophoresis results of mRNA-LNP

■ Electrophoresis Results using MultiNA II

Microchip electrophoresis was performed on mRNA samples and mRNA-LNP. The resulting electropherograms (waveform data) are shown in Fig. 3. The blue triangles in the figure indicate the mRNA peaks. From top to bottom, the results represent (a) an mRNA-LNP solution subjected to heat treatment (70˚C, 5 minutes), (b) an mRNA-LNP solution with Triton X-100 added (final concentration 0.1%) followed by heat treatment, (c) an mRNA sample solution, and (d) a 0.1% Triton X-100 solution. The mRNA concentrations for (a) through (c) were adjusted to 10 ng/µL.

In the mRNA-LNP solution without surfactant (a), only a minimal peak appeared, making it difficult to confirm the concentration. It was observed that heat treatment alone did not significantly release mRNA from the LNPs. Therefore, following the draft guidelines for mRNA quality evaluation issued by the USP, Triton X-100 was added, and electrophoresis was conducted after heat treatment (b). As a result, the RNA peak was clearly identified, and the estimated size was equivalent to the model mRNA sample. Furthermore, short RNA fragments suspected to be degradation products were not detected.

■ Conclusion

This application demonstrates the simple and rapid analysis of mRNA-LNP size, concentration, and purity using the Microchip Electrophoresis System MultiNA II. The MultiNA II automates the entire process from gel preparation to sample loading and data analysis for mRNA sample evaluation. In accordance with the USP draft guidelines, it was confirmed that mRNA-LNP detection is possible by adding Triton X-100 as a surfactant and applying heat treatment, without the need for lipid removal. This method enables the simple and rapid evaluation of mRNA-LNP, which is expected to contribute to improving the efficiency of mRNA pharmaceutical development.

<Acknowledgments>

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<Reference>

Analytical Procedures for Quality of mRNA Vaccines and Therapeutics, Draft Guidelines: 3rd Edition

01-00840-EN First Edition: Mar. 2026

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