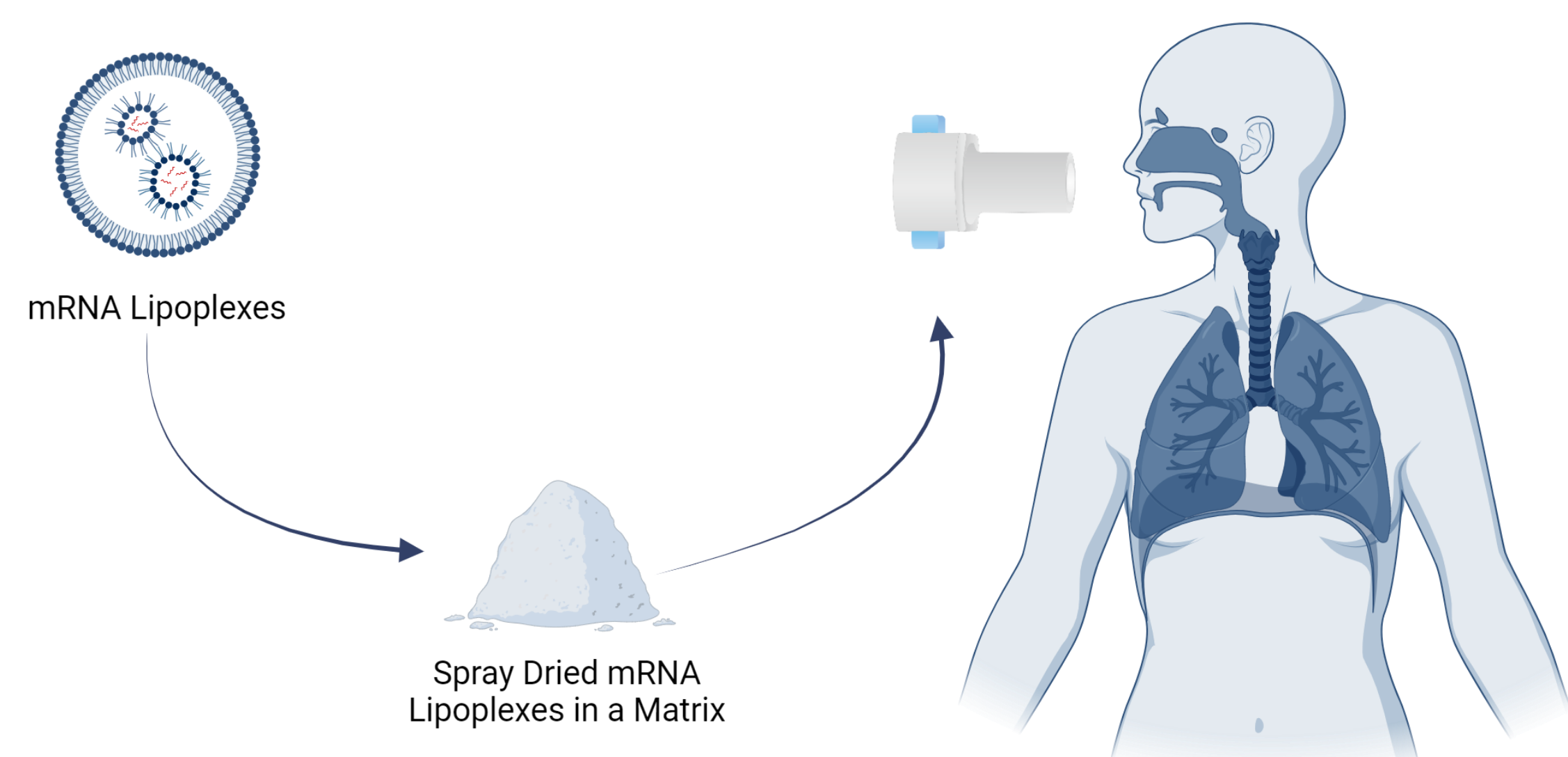


Optimising the Aerodynamic Performance of
Spray Dried mRNA Lipoplexes
in Mannitol or Lactose MatrixJana Schembera^{1*}, Ricarda Leister², Constanze Müller², Regina Scherließ¹¹Department of Pharmaceutics and Biopharmaceutics, Kiel University, Germany²Meggle GmbH & Co. KG, Wasserburg am Inn, Germany

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Objective:

Formulation of an Inhalable Dry Powder
Platform for mRNA Therapeutics

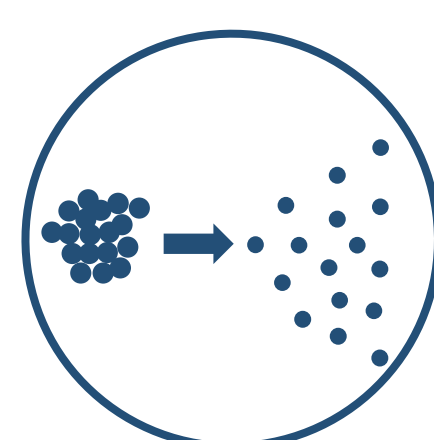
- Many respiratory pathogens enter the body through the respiratory tract
→ The lungs and the mucosal immune system are promising targets for therapeutic interventions
- Liquid vaccines face the risk of chemical degradation and physical instability
→ Solid formulations can secure stability without challenging storage conditions. Since spray drying offers continuous manufacturing with high production capacity, we chose spray drying as production technique.

Previous Work:

- Spray drying at an outlet temperature of 50°C in mannitol matrix
→ efficient transfection
- Aerodynamic assessment of the formulation exhibited a FPF (fine particle fraction, aerodynamic diameter < 5 µm) of 35% and a powder residue of 22% in the capsules.

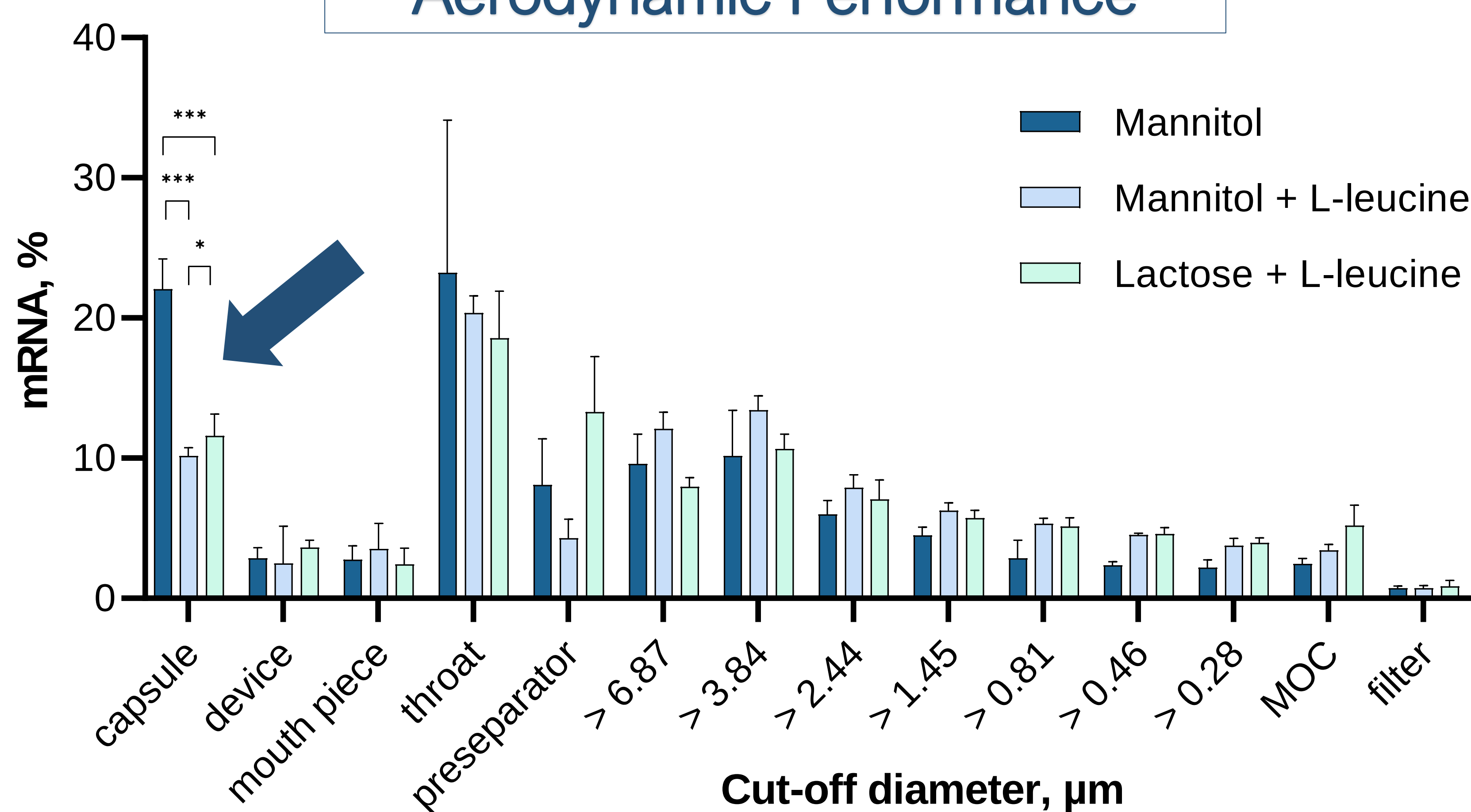
→ Optimisation of Aerodynamic Performance and Increasing Detachment by Co-Spray Drying with L-leucine

Hypothesis:

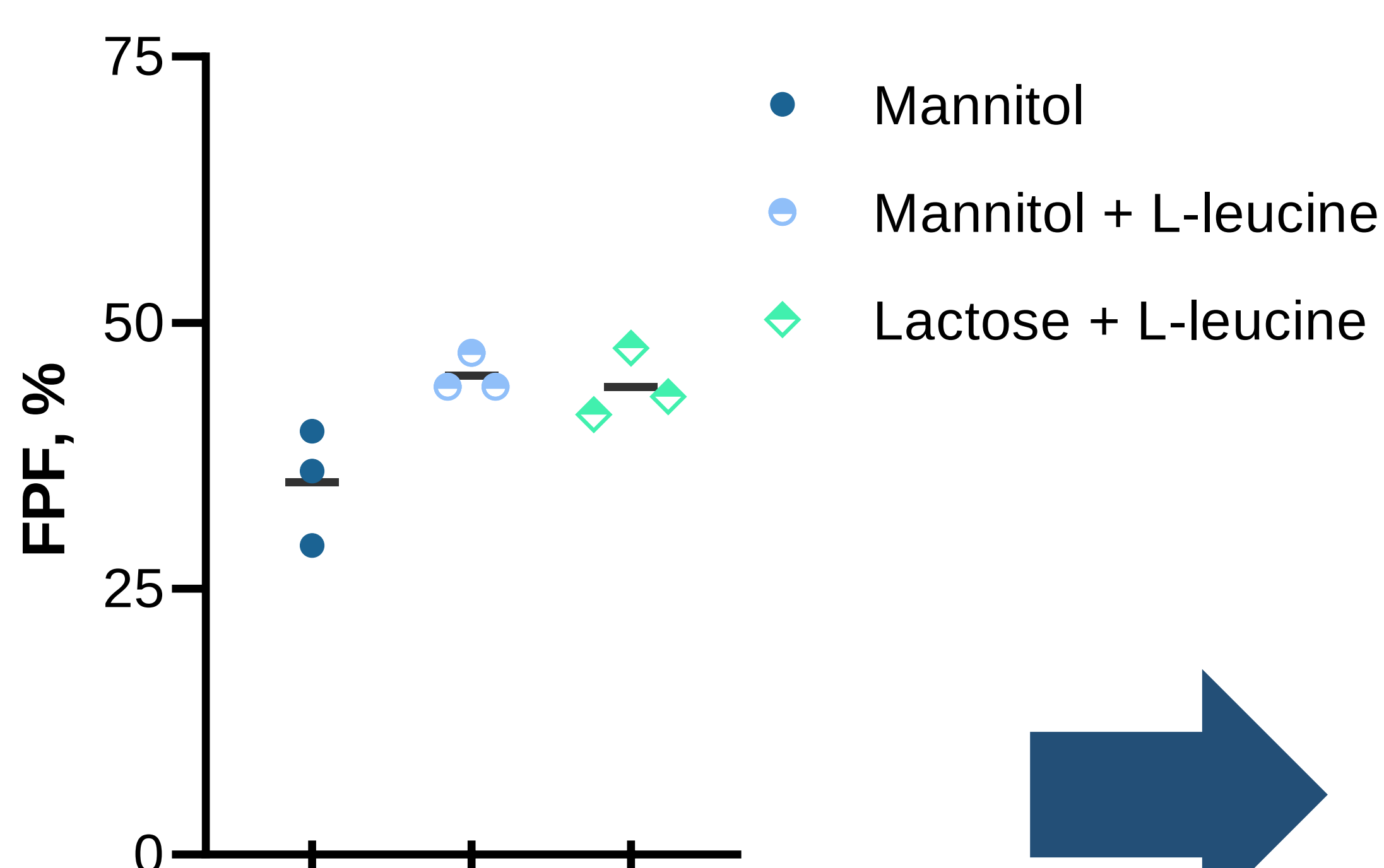
Surface Hydrophobicity ↑
Electrostatic Interactions ↓FPF ↑
Dispersibility ↑
Capsule Residue ↓

Results:

Aerodynamic Performance

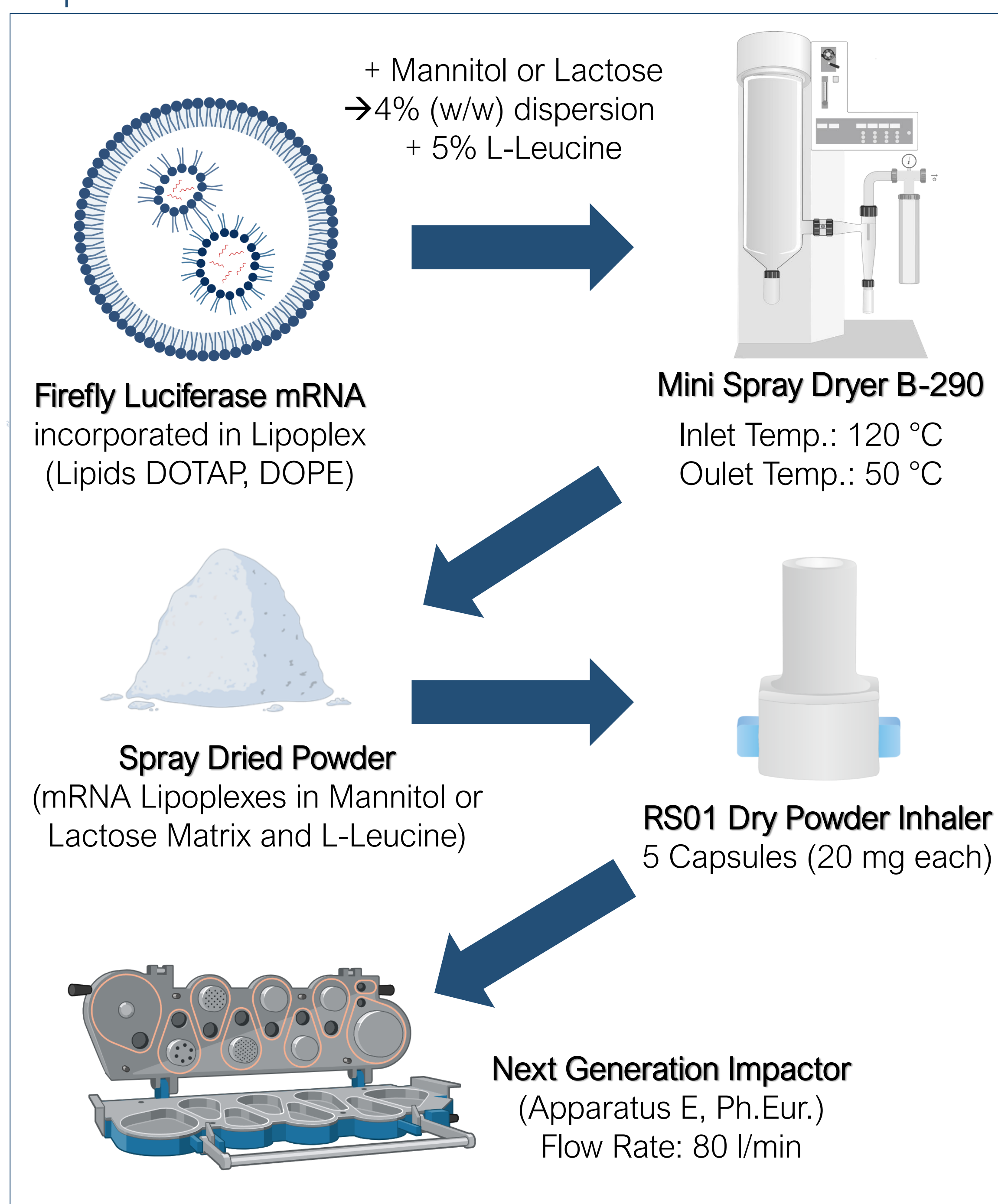


Deposition profiles of the spray dried formulation in mannitol matrix, with or without the addition of L-leucine and in lactose matrix with L-leucine, error bars show standard deviation of 3 NGI measurements *p < 0.05; ***p < 0.001.



Fine particle fraction (FPF) of the spray dried formulations. Symbols represent individual values and lines show mean of 3 NGI measurements.

Experimental:



Residue in the capsules and fine particle fraction (FPF) of the spray dried formulations with mannitol or lactose matrix after the addition of L-leucine (+) in comparison to the spray dried mannitol-based formulation without L-leucine (-).

Matrix	L-leucine	Capsule Residue, %	FPF, %
Mannitol	-	22	35
	+	10	45
Lactose	+	12	44

Conclusion:

Co-spray drying with L-leucine achieved for both matrices:

- Significant reduction of powder residue in the capsules
 - Considerably higher fine particle fraction (FPF)
- by increasing surface hydrophobicity and thereby reducing electrostatic interactions

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DRUG DELIVERY TO THE LUNGS

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