Aerosol Plume Dynamics at Different Relative Humidity

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Background

- Inhalable medications are highly dependent on size. 0.5-5 µm is considered the optimal size range for drug deposition in the lung [1].
- Current models do not provide an accurate representation of the drug deposition profile.
- Size of the drug particle may change in vivo due to various factors including hygroscopic growth.
- Size distribution is often measured in the bulk phase.
- Change in relative humidity (RH) during actuation.
- Ambient RH ~30%-40%. Deep lung RH ~99%.
- Need to understand the aerosol dynamics at high RH.

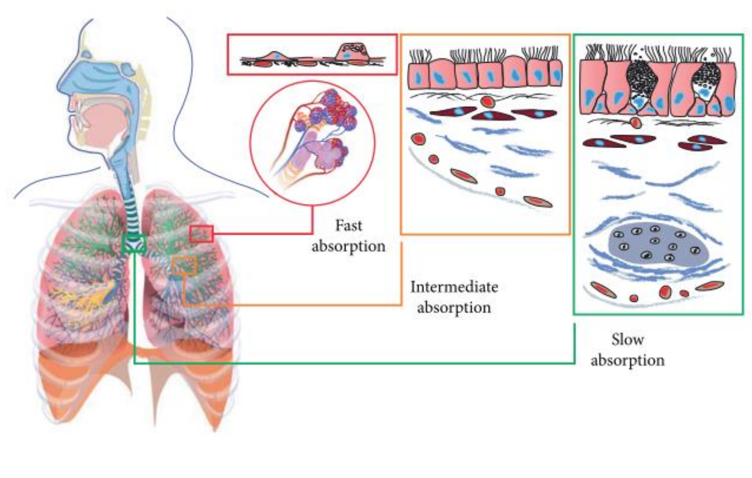

Figure 1 – Schematic diagram illustrating pulmonary absorption kinetics [1]

Aim

- To reconcile the size-changing dynamics of a plume of pharmaceutical aerosol emitted into a controlled environment with single droplet hygroscopic growth and kinetics measurements.

Method

Dual Aerodynamic Particle Sizer (APS)

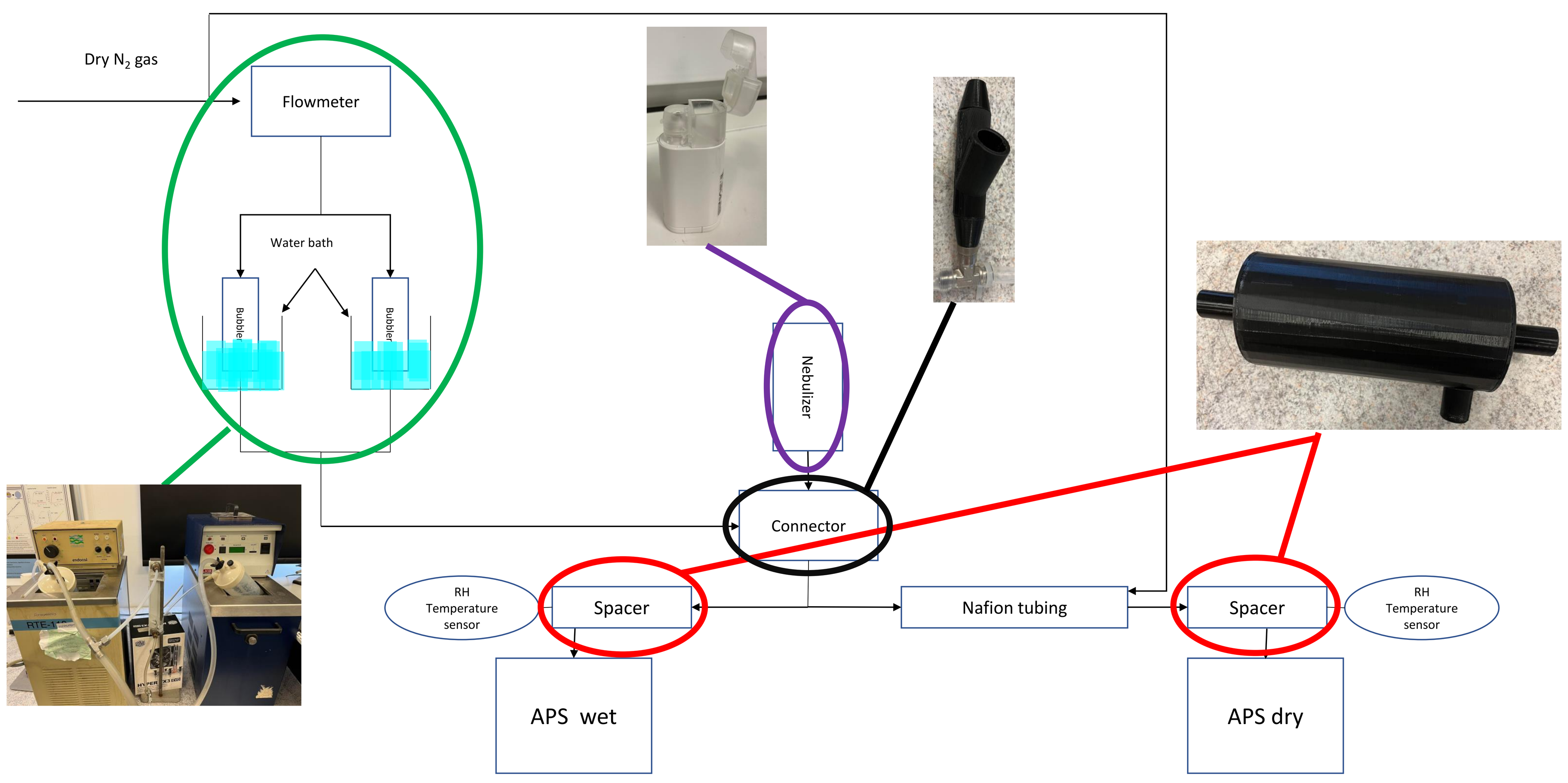

Figure 2 – Schematic diagram of the dual APS set up

Formulation

- Salt (NaCl)
- Respimat (Ipratropium bromide)

3D Printing

- Connector – to join the actuated mist with the wet flow
- Spacer – 1L volume, printed separately (caps, cylinder)

Comparative Kinetic Electrodynamic Balance (CK-EDB)

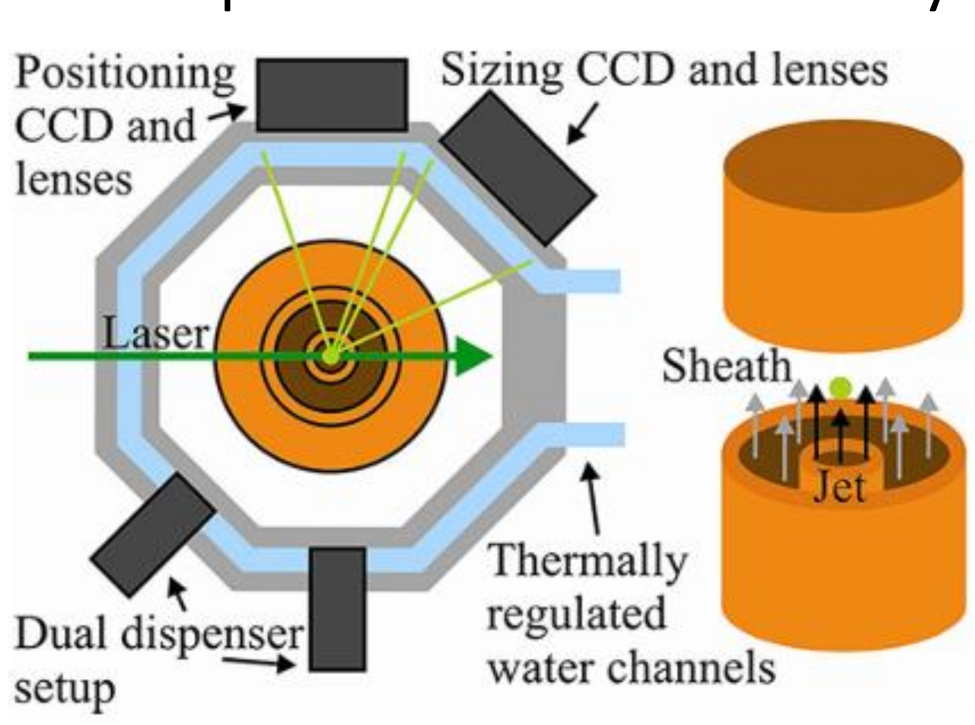

Figure 3 – Schematic of a CK-EDB with dual dispensers [2].

- Single droplet levitation
- Controlled temperature and RH
- Change in radius over time
- Phase function

E-AIM

- Aerosol thermodynamic model
- Fixed temperature (298.15K)
- Model for common compounds (e.g., NaCl)
- Calculate the radial growth factor from the data

Software

- OriginLab
- Aerosol Instrument Manager
- LabView
- Python

Results

- Every time the APS has been modified; the size distributions are checked.
- Figure 2 shows an example of the size distribution data (OriginLab) from an APS before and after the addition of the connector.

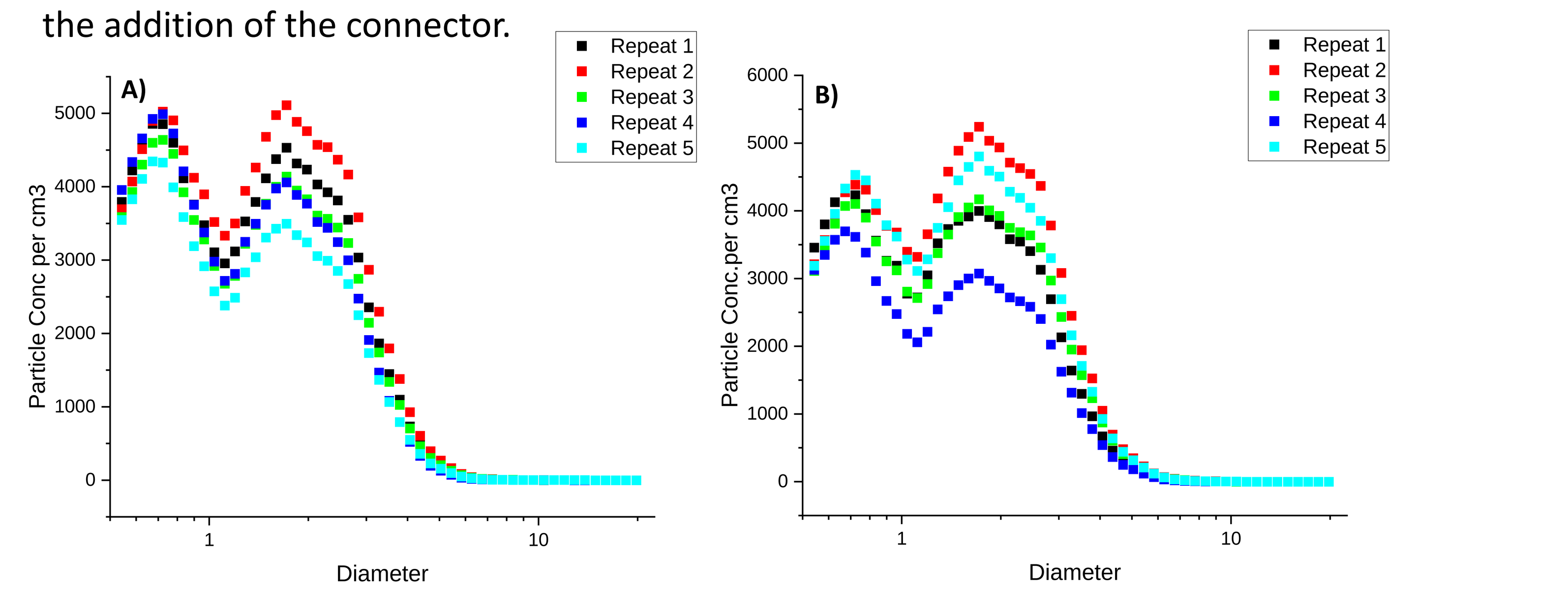

Figure 4 – APS data of 0.03 mfs NaCl at 5L/min flowrate, constant temperature and RH, A) with a connector, B) without a connector.

- Figure 3 shows another example of the size distribution data (Python) from APS with and without a Nafion dryer attached.

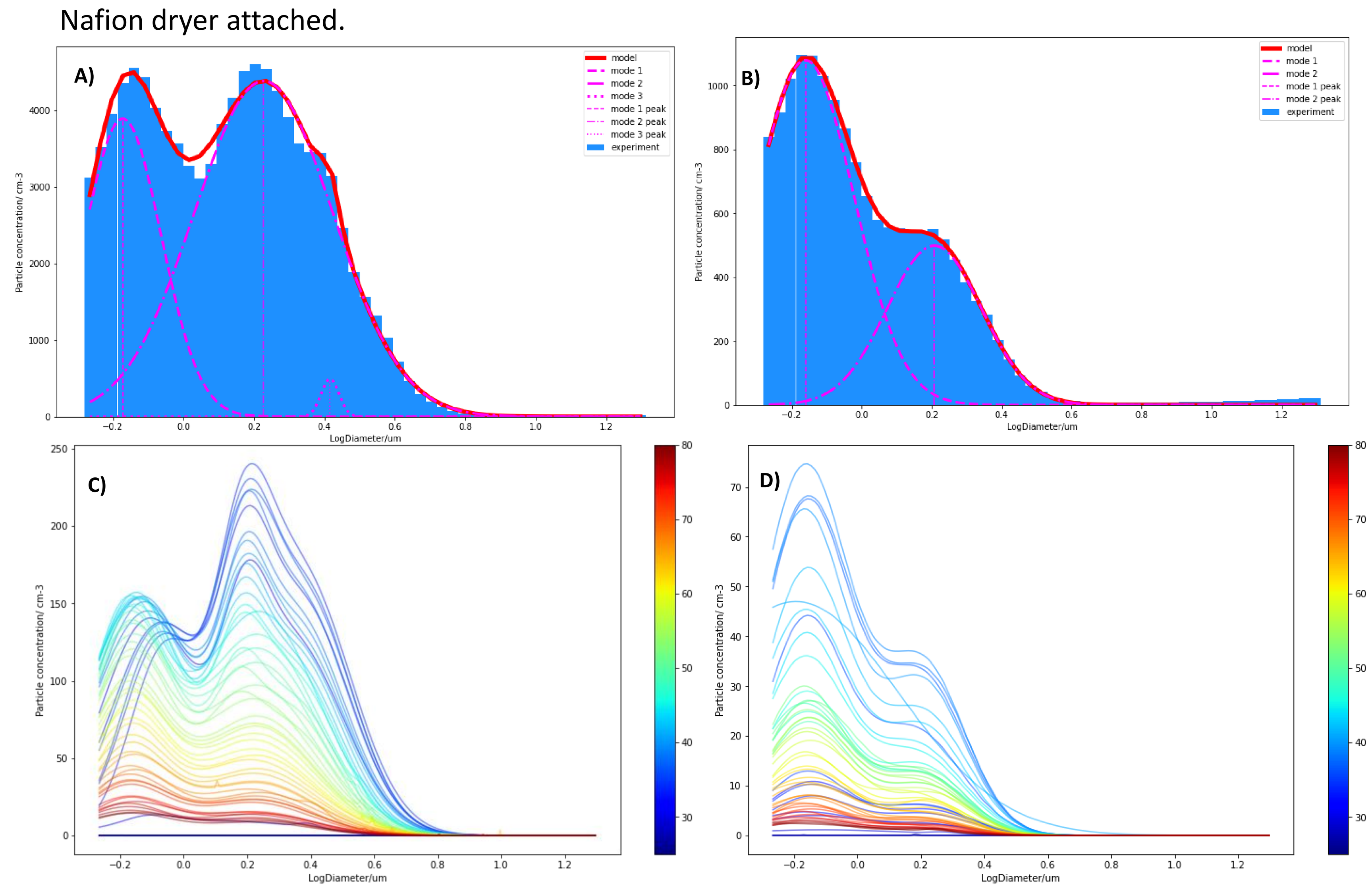

Figure 5 – APS data of the overall size distribution of 0.03 mfs NaCl at 5L/min flowrate, constant temperature, A) without a Nafion dryer (RH=70%) or B) with a Nafion dryer (RH=34%). C) and D) show the size distribution of A) and B) per second, respectively.

- Mode 2 of different RHs can be compared in Figure 3.
- The quotient should reflect the growth factor.
- For commonly used compounds (e.g., salt), the result can be compared with the radial growth factor curve from E-AIM data (Figure 4).
- Current APS results show divergence from the E-AIM data.
- Calibration of the APS is needed to ensure the reliability of the results.
- Further improvement of the Python program to obtain an accurate mode 2 value is essential.

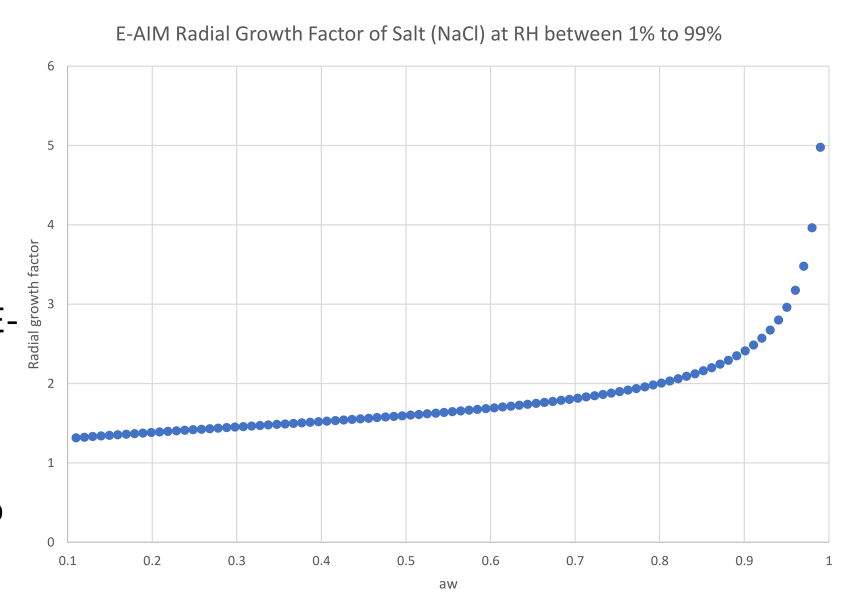

Figure 6 – Radial growth factor curve of salt obtained from E-AIM

Calibration

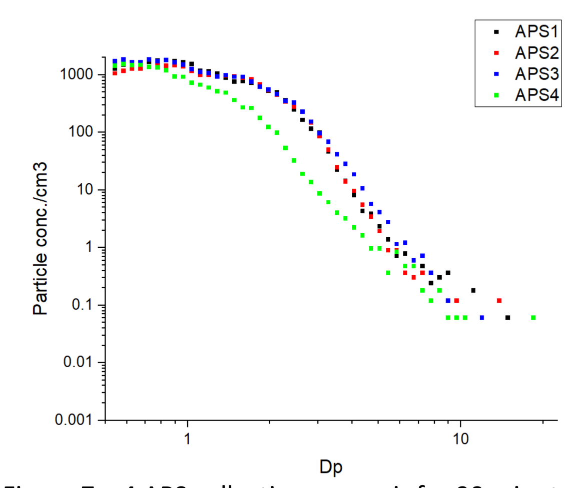

Figure 7 – 4 APS collecting room air for 90 minutes.

As shown in Figure 5, APS 4 is likely to be contaminated and needs to be serviced and recalibrated.

Further development

- Mass flow controller – faster RH change
- Unify the length of the actuation
- Minimize inter-dose variation
- Next Generation Impactor data comparison
- Reduce sampling frequency
- Different formulations
  - Ipratropium bromide, salbutamol
  - Ethanol based formulations, HFA-152a

Reference

[1]Borghardt, J. M., Kloft, C., & Sharma, A. (2018). Inhaled Therapy in Respiratory Disease: The Complex Interplay of Pulmonary Kinetic Processes. *Canadian Respiratory Journal*. https://doi.org/10.1155/2018/2732017

[2] Davies, J. F., Haddrell, A. E., Rickards, A. M. J., & Reid, J. P. (2013). Simultaneous analysis of the equilibrium hygroscopicity and water transport kinetics of liquid aerosol. *Analytical Chemistry*, *85*(12), 5819–5826. https://doi.org/10.1021/ac4005502

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