

Hygroscopic Dynamics of Solution Phase Aerosol on Generation and Inhalation to the Lungs

Nan Zhou¹, Rachael Miles¹, and Jonathan Reid¹

¹University of Bristol, School of Chemistry, Cantock's Cl, Bristol, BS8 1TS

BACKGROUND

- Soft Mist Inhalers (SMIs) deliver bronchodilators for COPD treatment, overcoming limitations of conventional inhalers such as coordination of actuation and environmental impact.
- Drug deposition profile of SMIs is a function of particle size distribution, with an optimal range of 1-5 μm for effective deep lung delivery.
- Hygroscopic growth of aerosol particles, influenced by the transition from ambient to lung relative humidity (RH) is poorly understood.

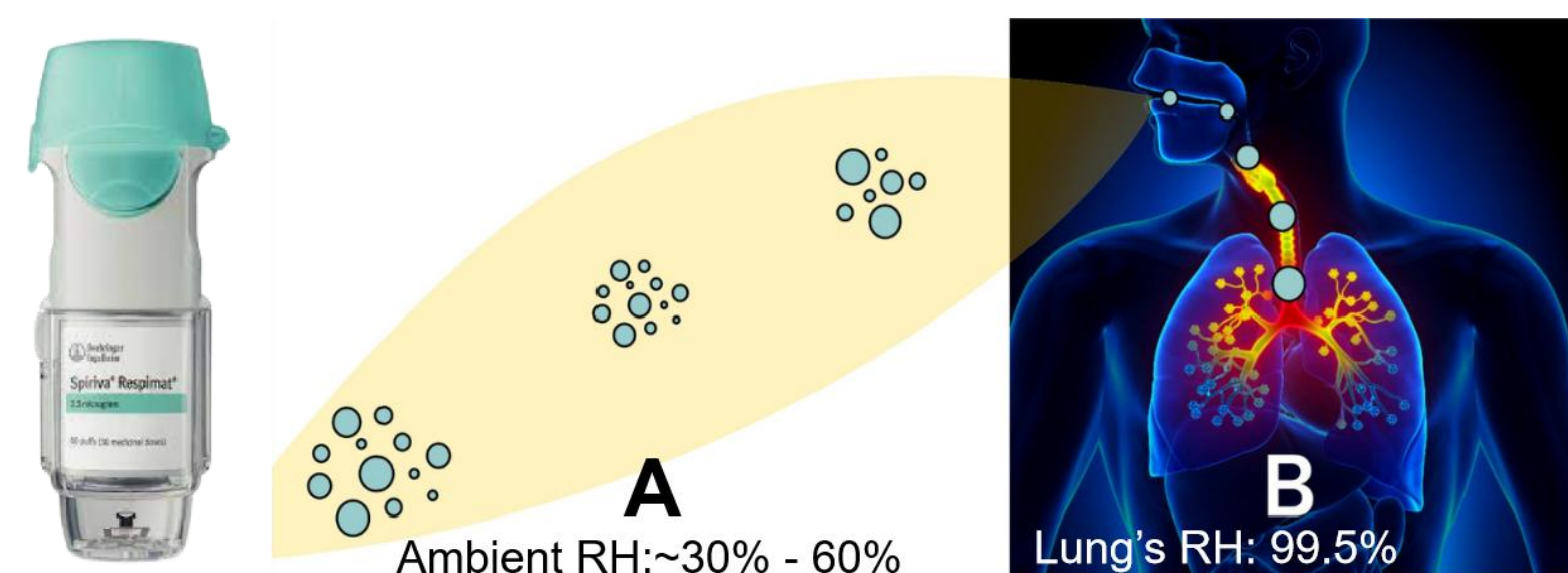


Figure 1: Diagram of droplet dynamics of SMIs on generation and inhalation to the lungs [1]

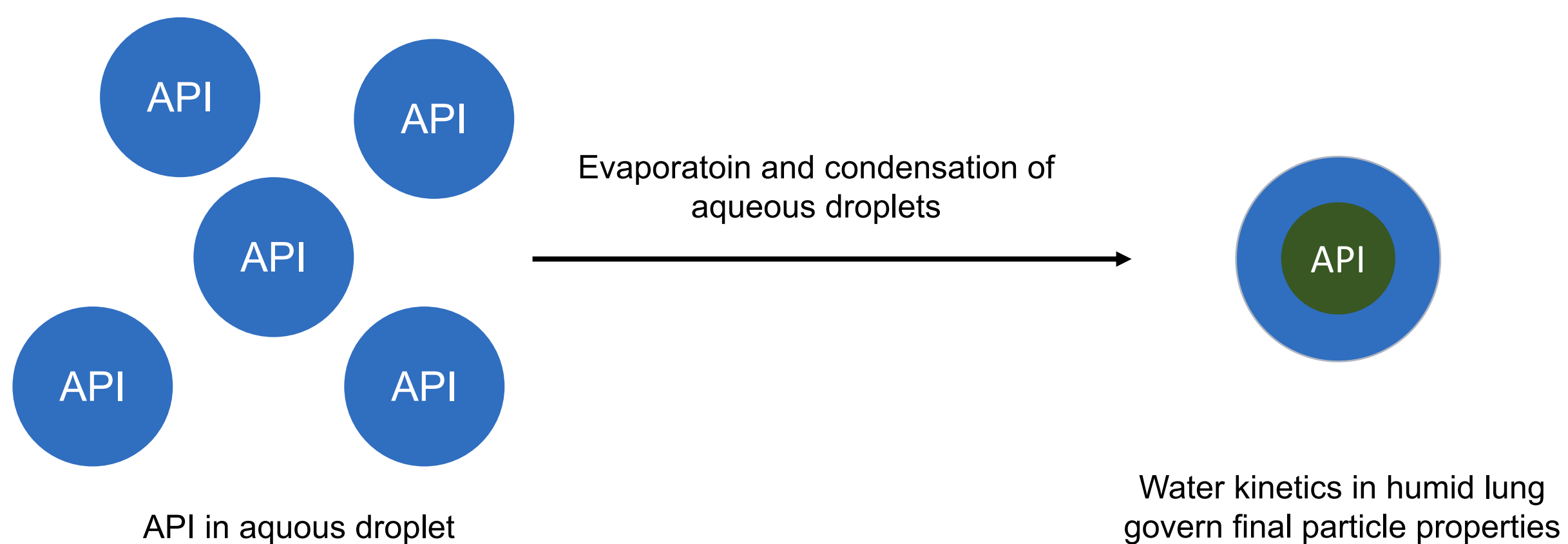


Figure 2: Aqueous aerosol production and dynamic aerosol processes occurring during inhalation of SMIs [2]

AIM

- To explore the impact of hygroscopic growth on particle size dynamics of aerosols from generation to lung deposition employing TAPS and CK-EDB.
- To revise current drug deposition models to include hygroscopic growth dynamics.
- To develop a Next Generation Impactor (NGI) simulator.

METHODS

Tandem Aerodynamic Particle Sizers (TAPS)

- Measuring plume size distribution under varying relative humidity (RH)

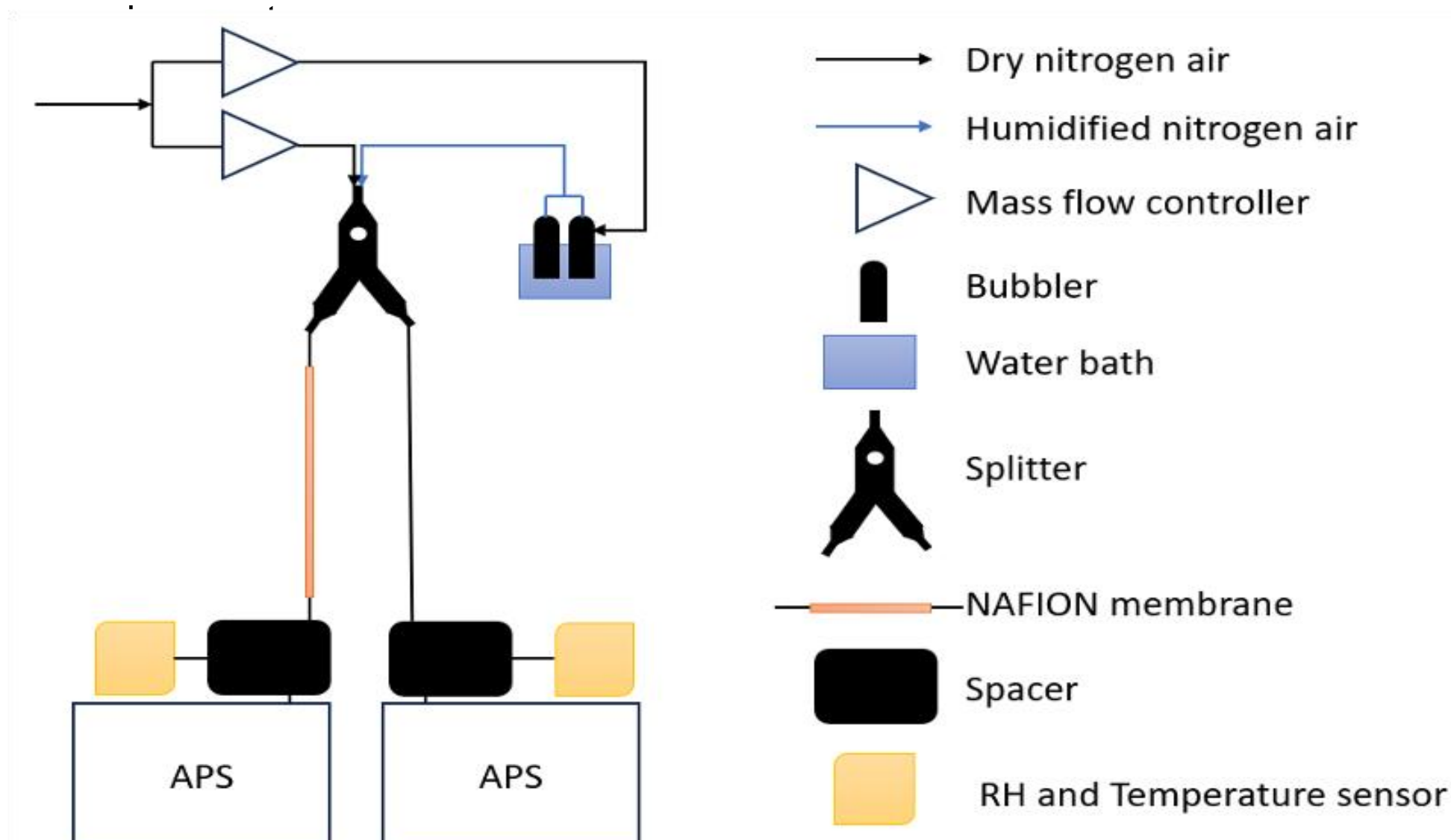


Figure 3: Experimental set up of TAPS [3]

Comparative Kinetics Electrodynamic Balance (CK-EDB)

- Studying hygroscopicity of single droplets to understand individual particle behavior.

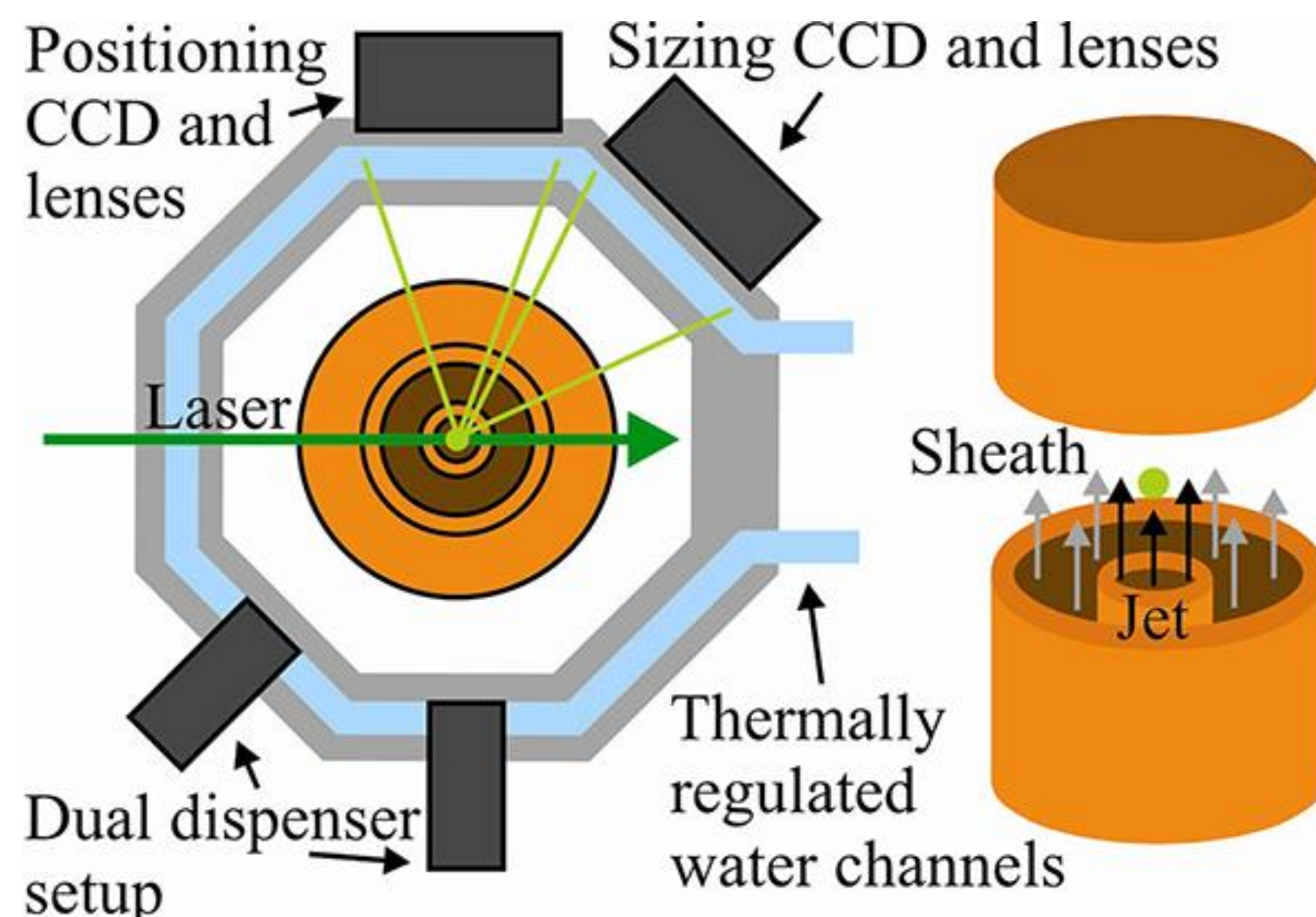


Figure 4: Experimental set up of CK-EDB [4]

MODELS

Models (E-AIM and AIOMFAC)

- Comparing experimental results with theoretical predictions to understand the hygroscopic dynamics of SMIs aerosols.

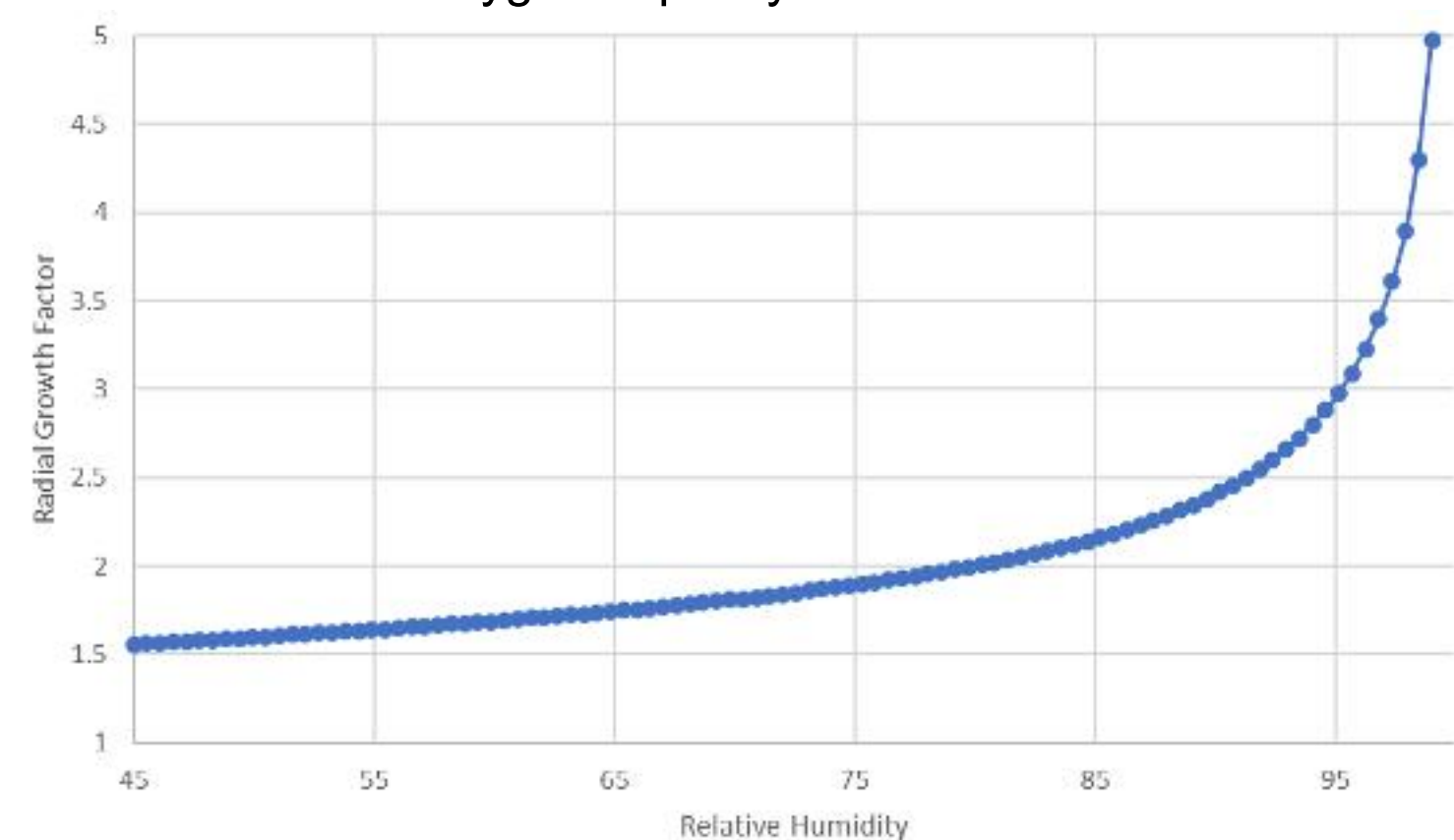


Figure 5: The radial growth factor curve for Sodium Chloride under RH from 45% to 99% determined by E-AIM model [3]

INNOVATION

Responsible Innovation

- Ethical and social consideration** — Potential inequity in access to SMIs across all socioeconomic groups
- Environmental concerns** — Manufacturing process and disposal of SMIs emit carbon dioxide
- Policy implications** — Simplify dosing regimes and prioritize patient education on inhalation techniques
- Scientific innovation** — Deliver biologics for treating systemic diseases

CHALLENGES

- Specific setup of TAPS for SMIs requires a newly designed inlet and tailored splitter to ensure engineering precision and compatibility.
- Testing new APIs for SMIs presents formulation and financial challenges, including selecting appropriate ingredients, rigorous testing, and potential investment. In-house preparation of formulations carries risks, requiring careful implementation planning.

REFERENCES

- 1 JP Reid et al (2019). The Microphysics of Aerosol Particle Transformations on Inhalation
- 2 NC Armstrong Green (2022). Dynamic Response of Hygroscopic Pharmaceutical Aerosol on Inhalation.
- 3 Jiang et al (2023). Drug Delivery to the Lungs, Volume 34.
- 4 Davies, J. F et al (2013). Simultaneous analysis of the equilibrium hygroscopicity and water transport kinetics of liquid aerosol. Analytical Chemistry.