From Single Droplet to Plume: Probing SMIs

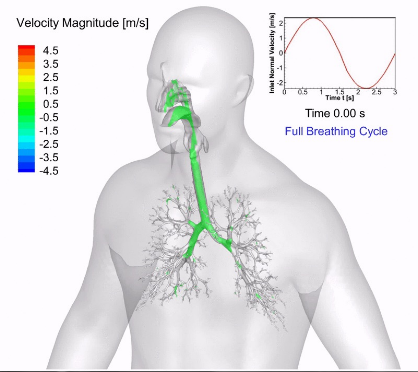
Dan Hardy

SMI.London
28 June 2023

Context

Deposition is determined by particle size, but size time changes over time.

- Simulating gas flow in the lung is possible



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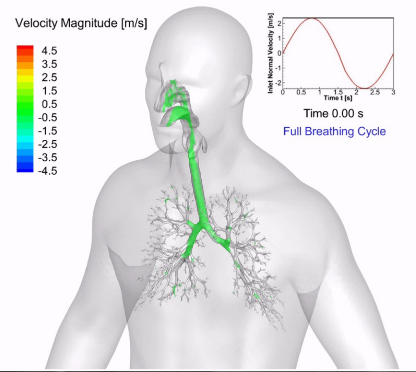
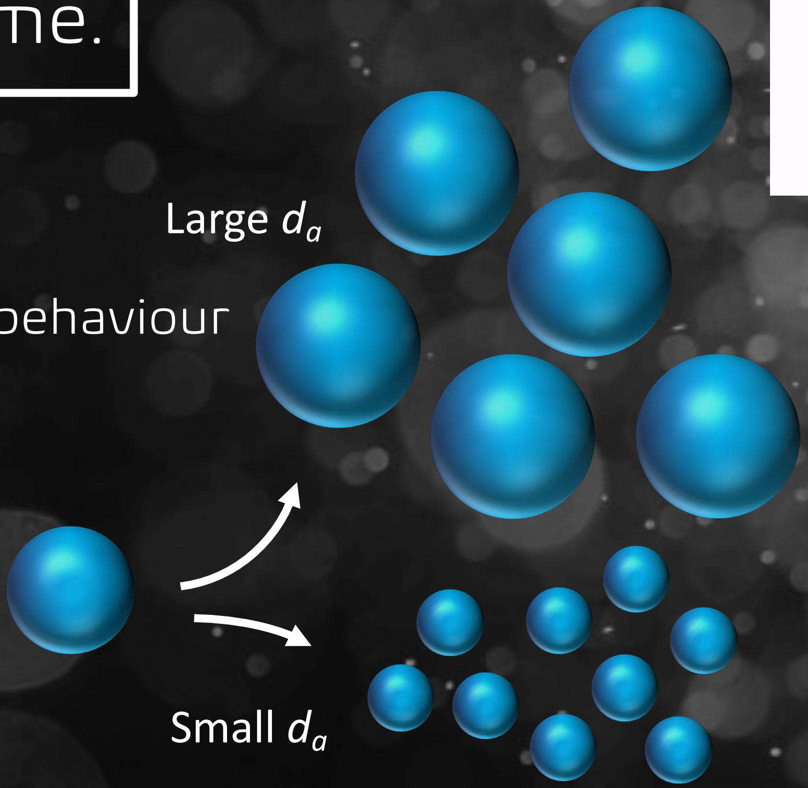
- Thus, formulation optimisation is difficult





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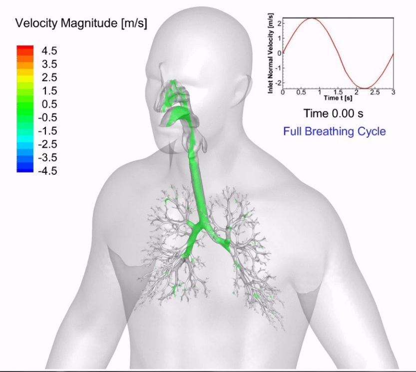
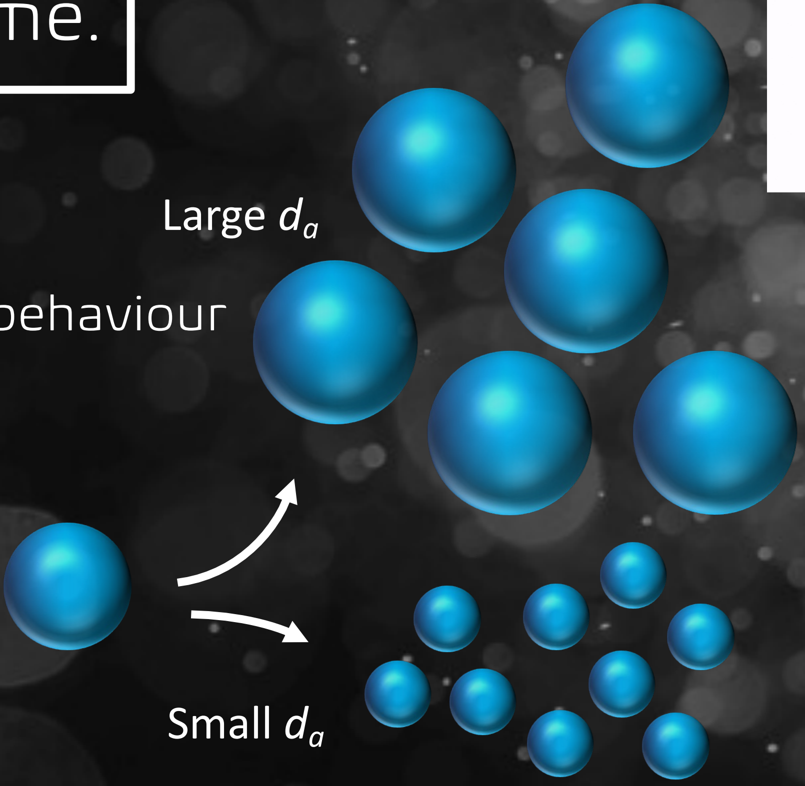
Controlling size is key to optimising deposition.





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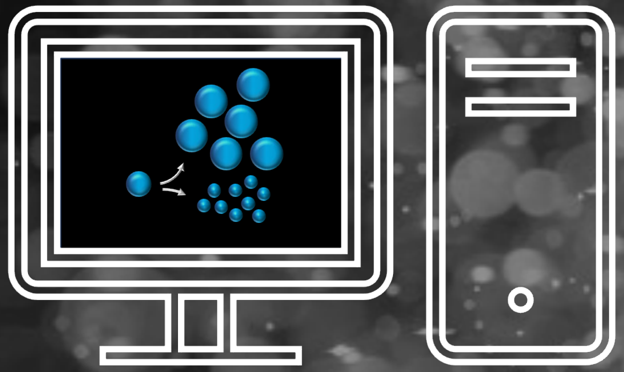
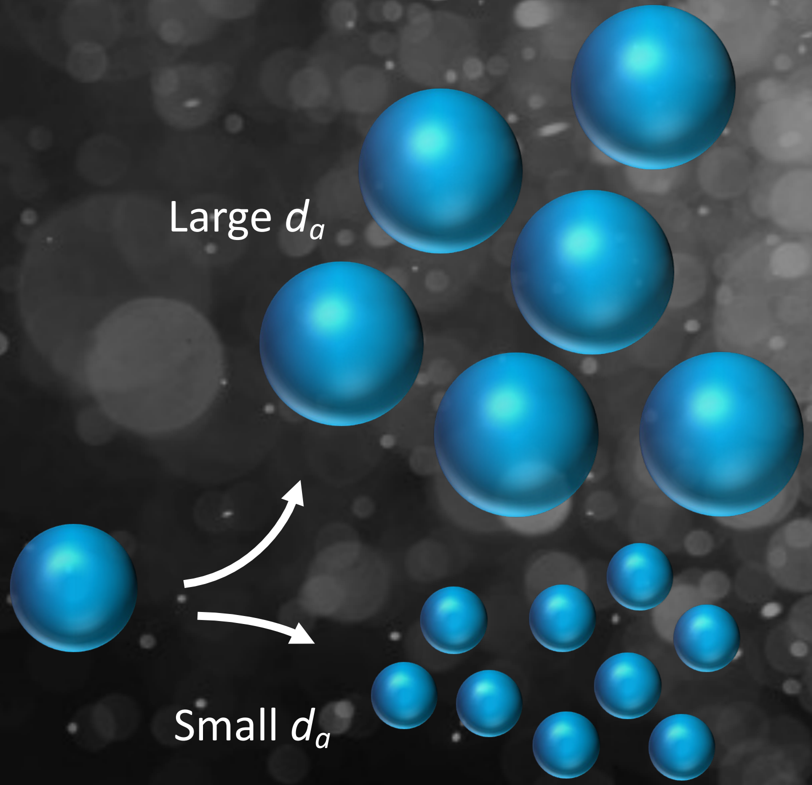
Formulation development can be accelerated using in-silico approaches





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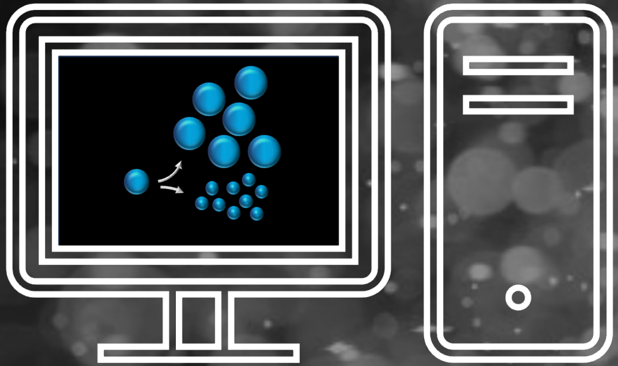
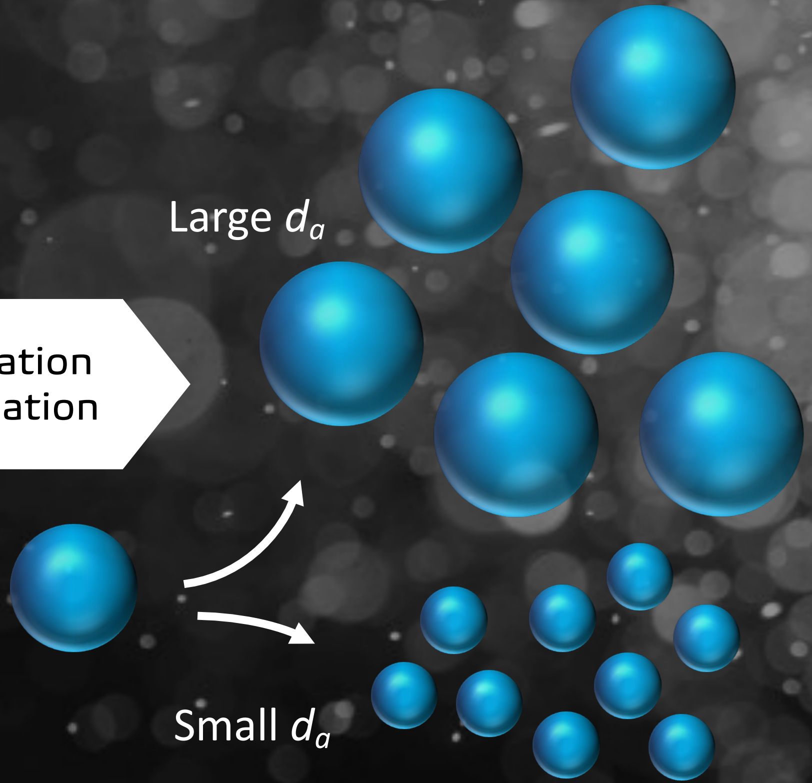


Accurate Droplet Simulations

Filtration Simulations

→ Coupled Model → Digital Impactor Studies → Regional Deposition Predictions → Formulation Optimisation



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Current state of the art

Bristol Aerosol Research Centre (BARC)

University of BRISTOL

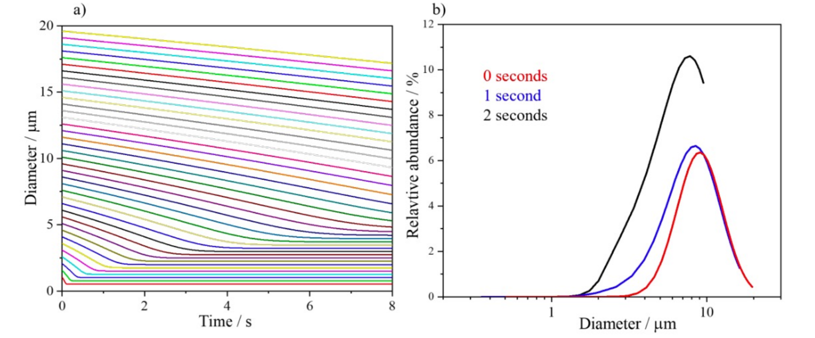

Figure 4.15. a) Multiple Respimat droplets simulated using the cascade impactor simulator, initial diameter ranging from 0.1 to 20 µm. b) Size distribution as a function of time, inferred from the droplet dynamics in a) and the impactor stage sizes. Relative abundance is equal to the relative number of particles at each size bin width.

- Evaporative models (Kulmala)
- Evolving size distributions introduced

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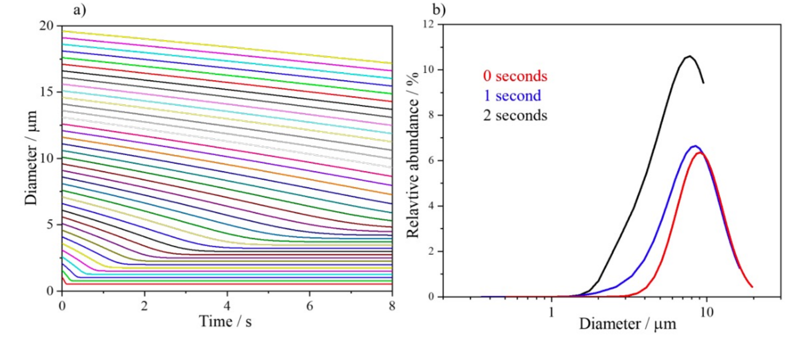
https://research-information.bris.ac.uk/ws/portalfiles/portal/319819894/Natalie_Armstrong_Green_Thesis_2022.pdf

Current state of the art

Bristol Aerosol Research Centre (BARC)

- Evaporative models (Kulmala)
- Evolving size distributions introduced
- First simulations of impactors

University of BRISTOL



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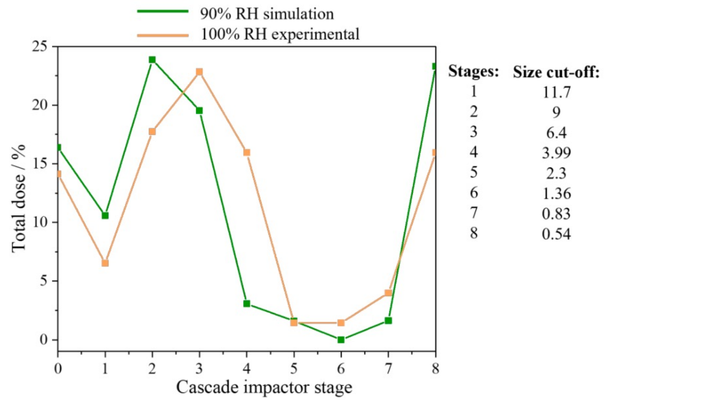

Figure 4.17. Simulated cascade impactor measurements compared with data collected on an NGI, at 90% and 100% RH, respectively.

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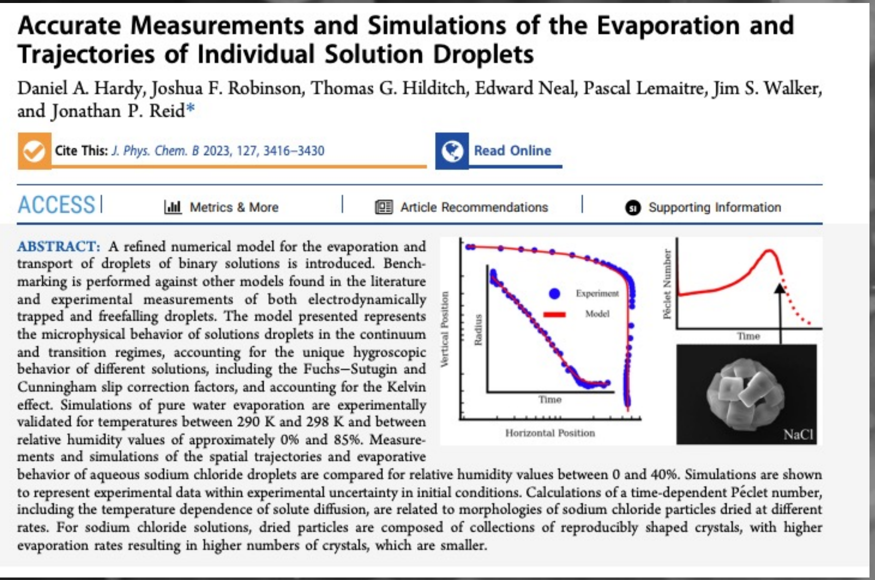
Our Approach

- Improved SADKAT model engine
- Simulate full size distributions



Accurate Measurements and Simulations of the Evaporation and Trajectories of Individual Solution Droplets

Daniel A. Hardy, Joshua F. Robinson, Thomas G. Hilditch, Edward Neal, Pascal Lemaitre, Jim S. Walker, and Jonathan P. Reid*

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ABSTRACT: A refined numerical model for the evaporation and transport of droplets of binary solutions is introduced. Benchmarking is performed against other models found in the literature and experimental measurements of both electrodynamically trapped and freefalling droplets. The model presented represents the microphysical behavior of solutions droplets in the continuum and transition regimes, accounting for the unique hygroscopic behavior of different solutions, including the Fuchs−Sutugin and Cunningham slip correction factors, and accounting for the Kelvin effect. Simulations of pure water evaporation are experimentally validated for temperatures between 290 K and 298 K and between relative humidity values of approximately 0% and 85%. Measurements and simulations of the spatial trajectories and evaporative behavior of aqueous sodium chloride droplets are compared for relative humidity values between 0 and 40%. Simulations are shown to represent experimental data within experimental uncertainty in initial conditions. Calculations of a time-dependent Péclet number, including the temperature dependence of solute diffusion, are related to morphologies of sodium chloride particles dried at different rates. For sodium chloride solutions, dried particles are composed of collections of reproducibly shaped crystals, with higher evaporation rates resulting in higher numbers of crystals, which are smaller.

Our Approach

- Improved SADKAT model engine
- Simulate full size distributions
- Virtual impactors
  - Device agnostic formulation optimisation

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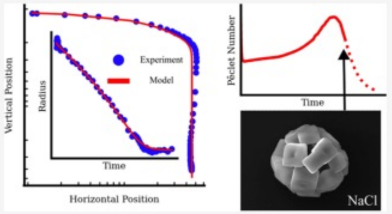

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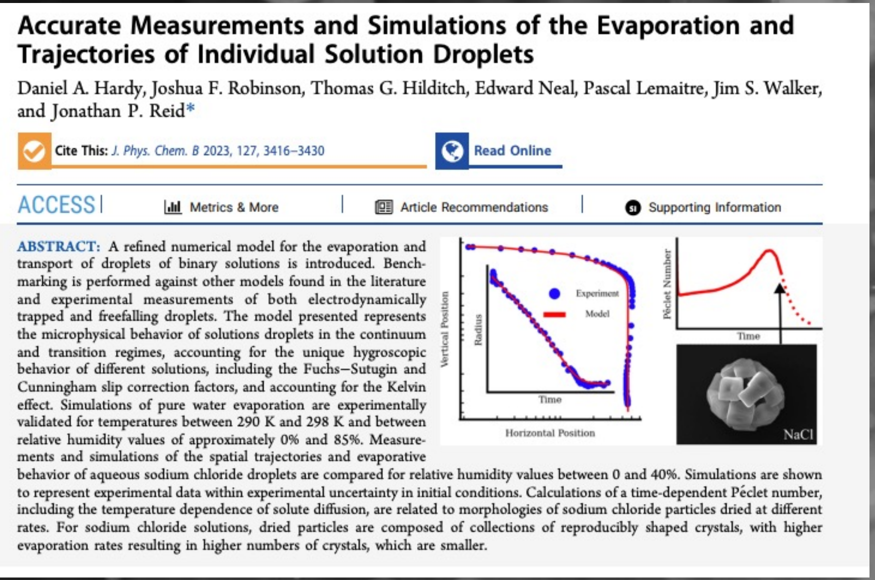
- Virtual impactors
  - Device agnostic formulation optimisation
- Moving towards modelling inhalation
  - Regional deposition
  - Physiological conditions



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Simulating Single Droplets

We simulate droplets at the single-particle scale and then expand up to the emergent distribution properties

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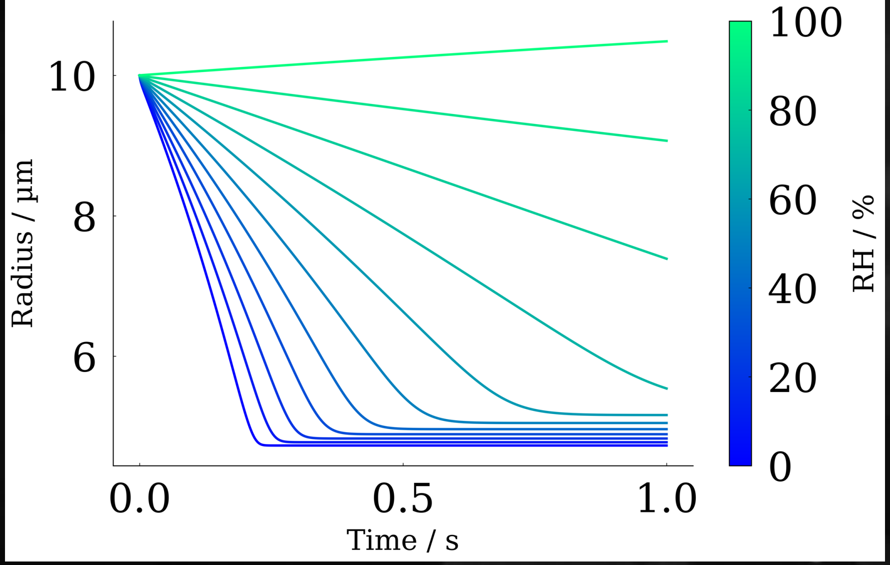
Applicable Across:

- RH
- Temperature



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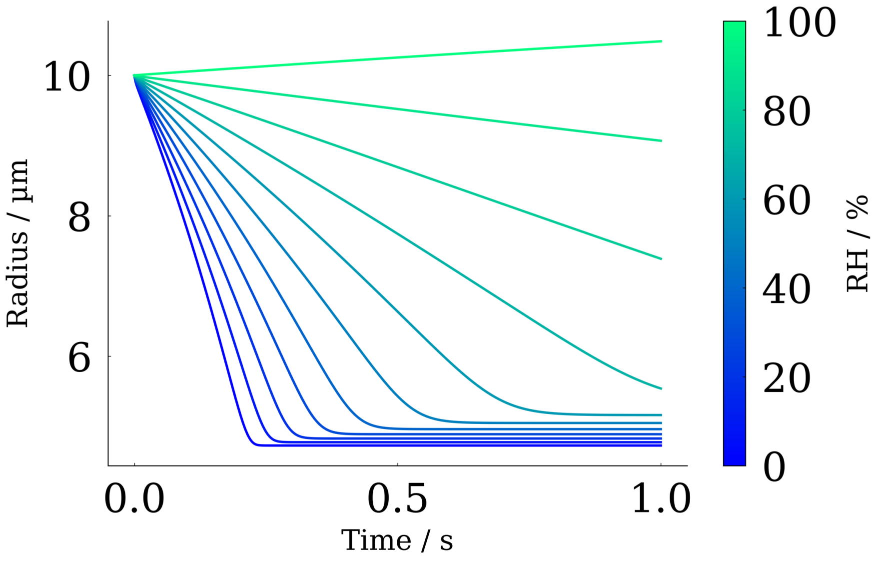

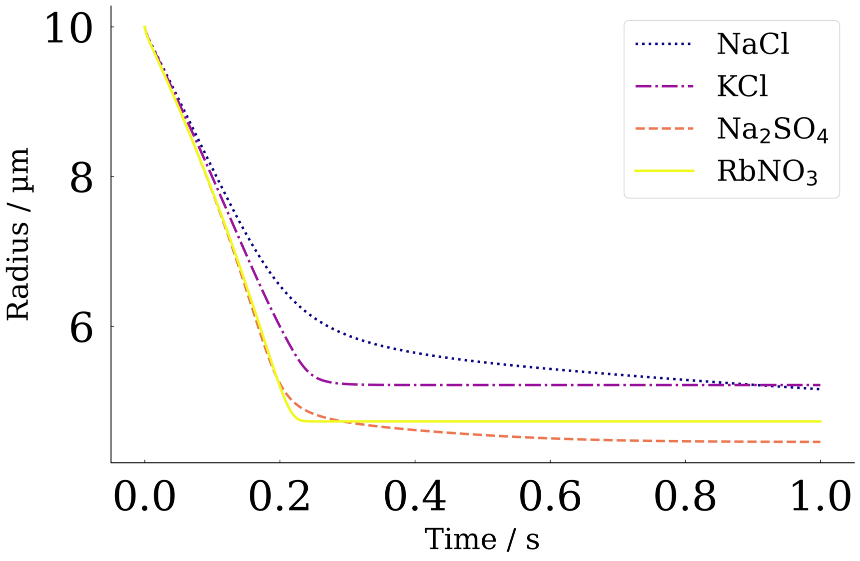

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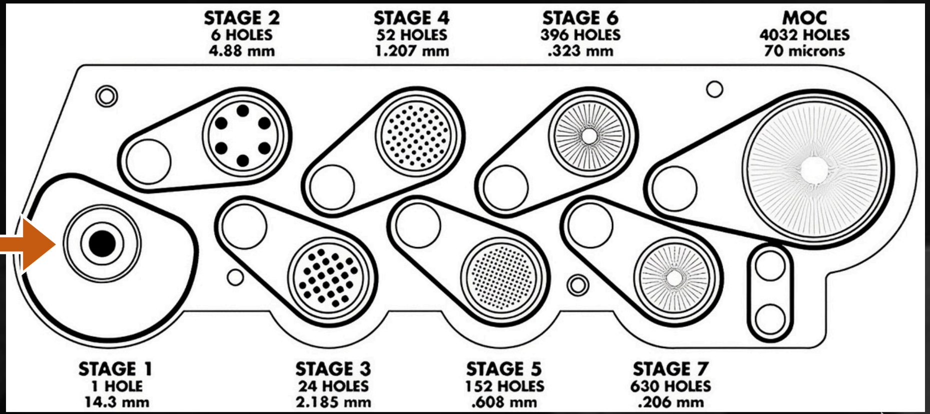
Size Distribution

Complex impaction in throat

Distribution after throat → input to virtual impactor



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https://aaqr.org/articles/aaqr-22-11-pui-0436

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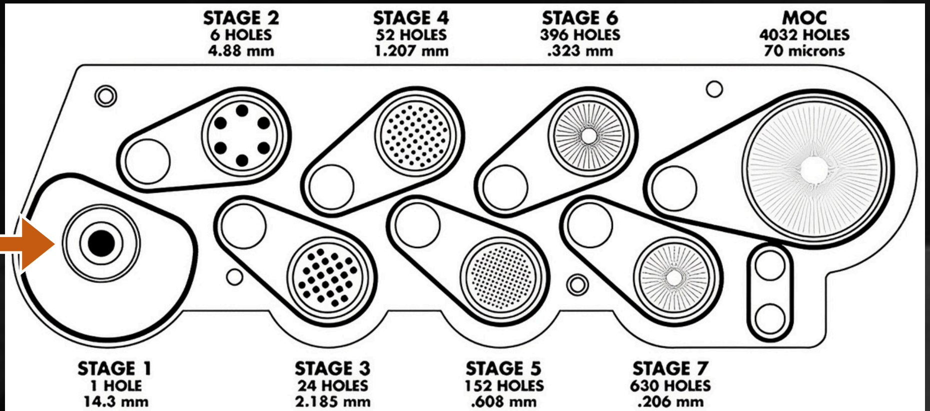


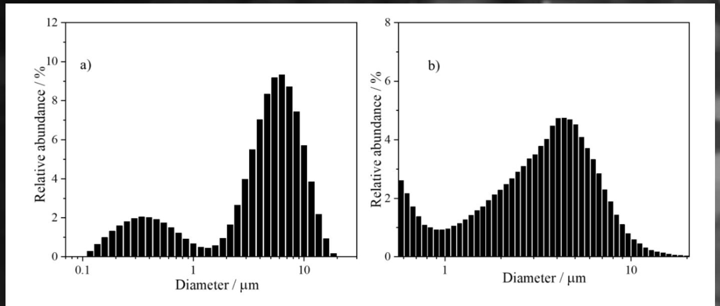
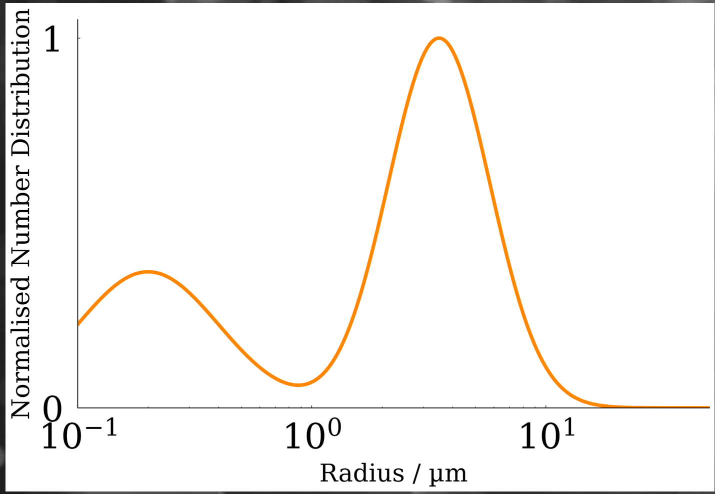


Figure 4.16. a) Size distribution of Respimat collect at Bath University by Ganley et al. in ambient conditions. b) Size distribution of Respimat collected at BARC in below ambient conditions. The graphs were used to determine the radial size range inputted into the cascade impact, 0.06 to 9 µm.



Example Distribution

Any Distribution Possible

https://aaqr.org/articles/aaqr-22-11-pui-0436

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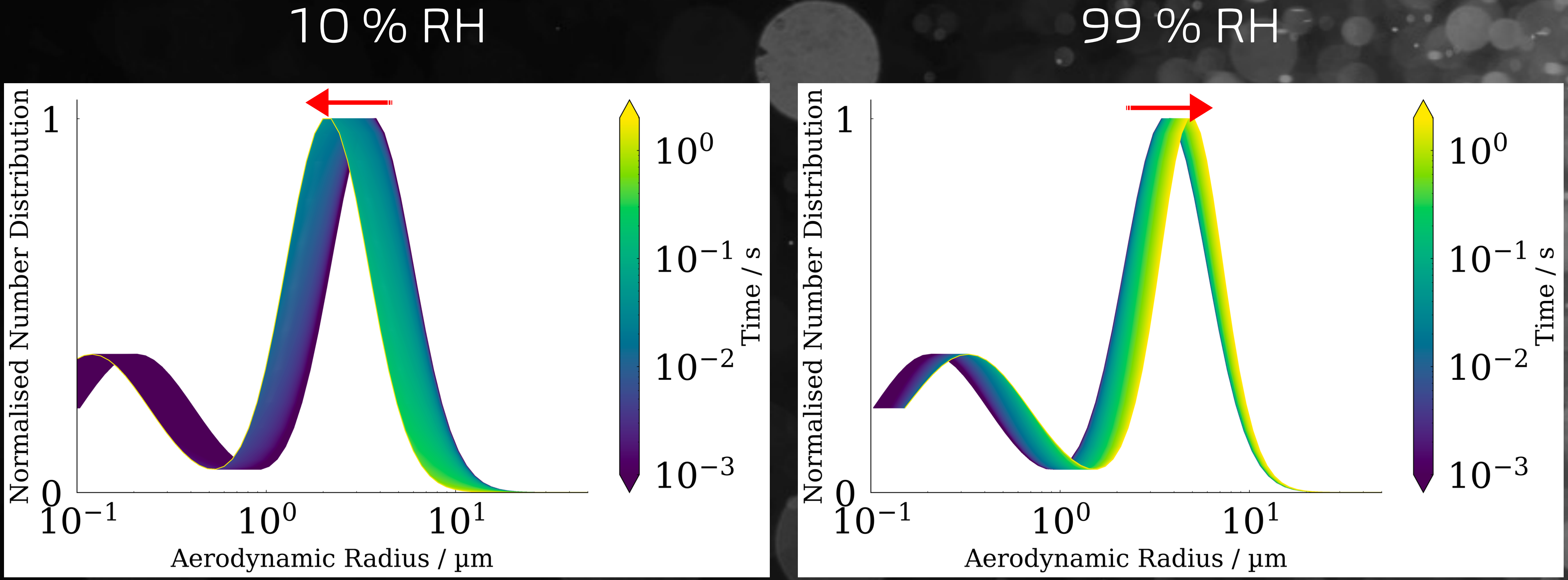
Evolving Size Distributions



Speed of evaporation / condensation depends upon size

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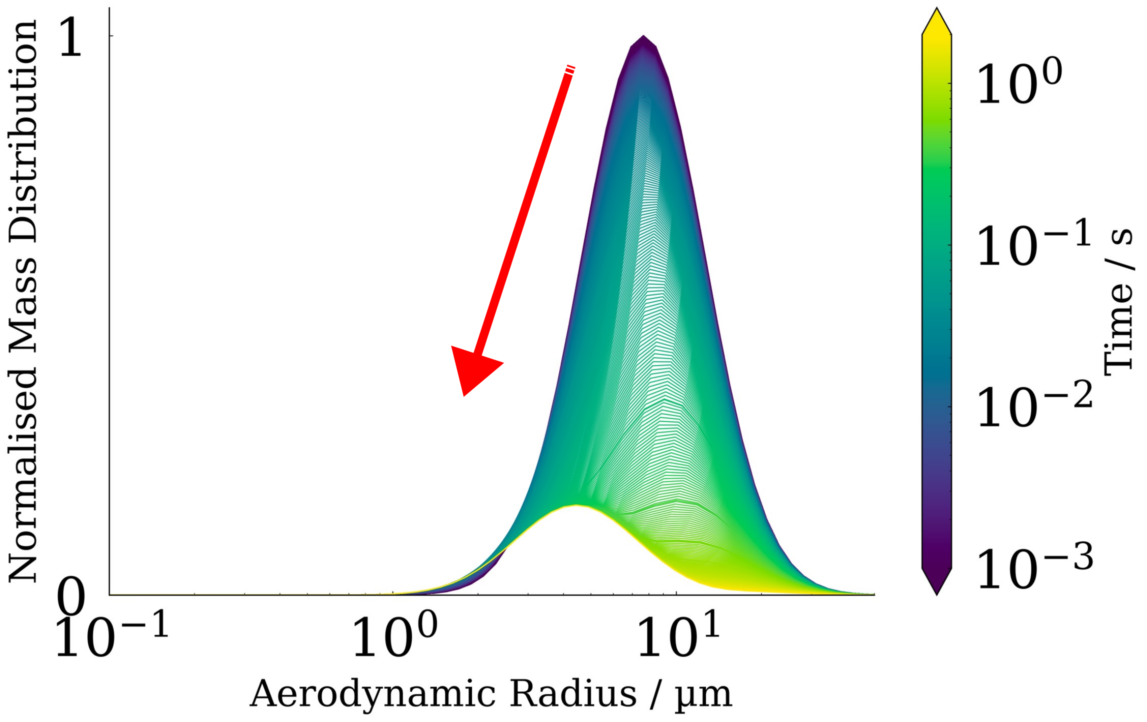
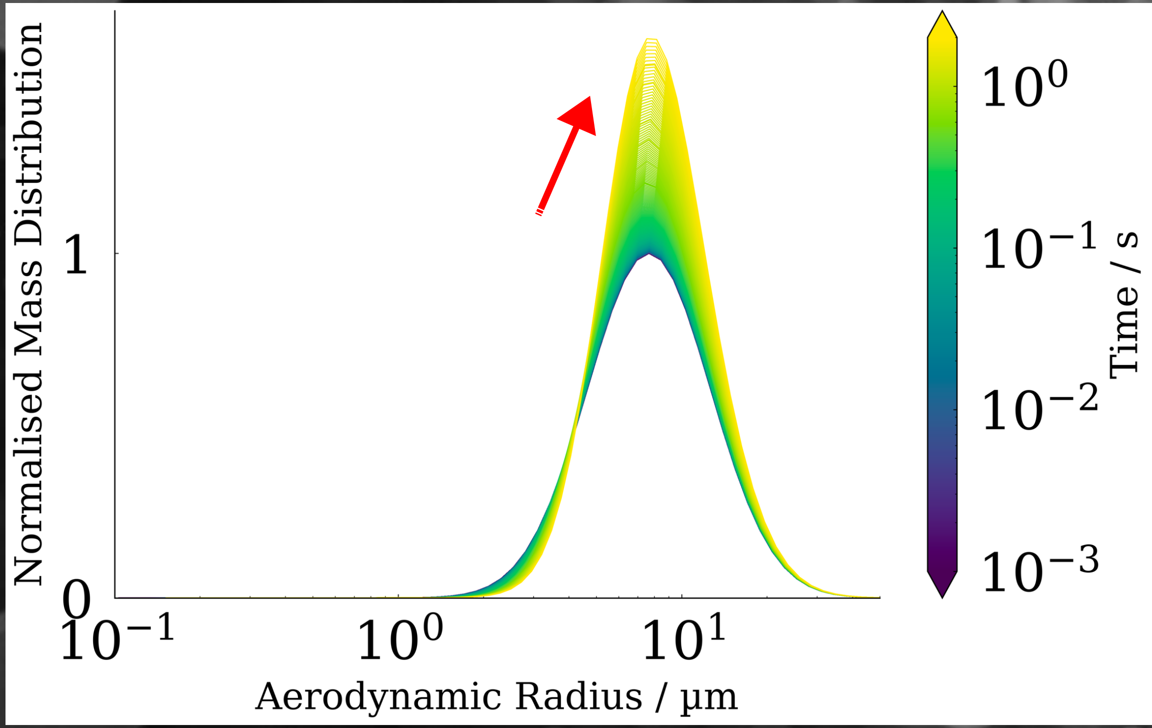
Aqueous NaCl solution, 0.1 MFS, 298 K

Evolving Size Distributions

10 % RH



99 % RH



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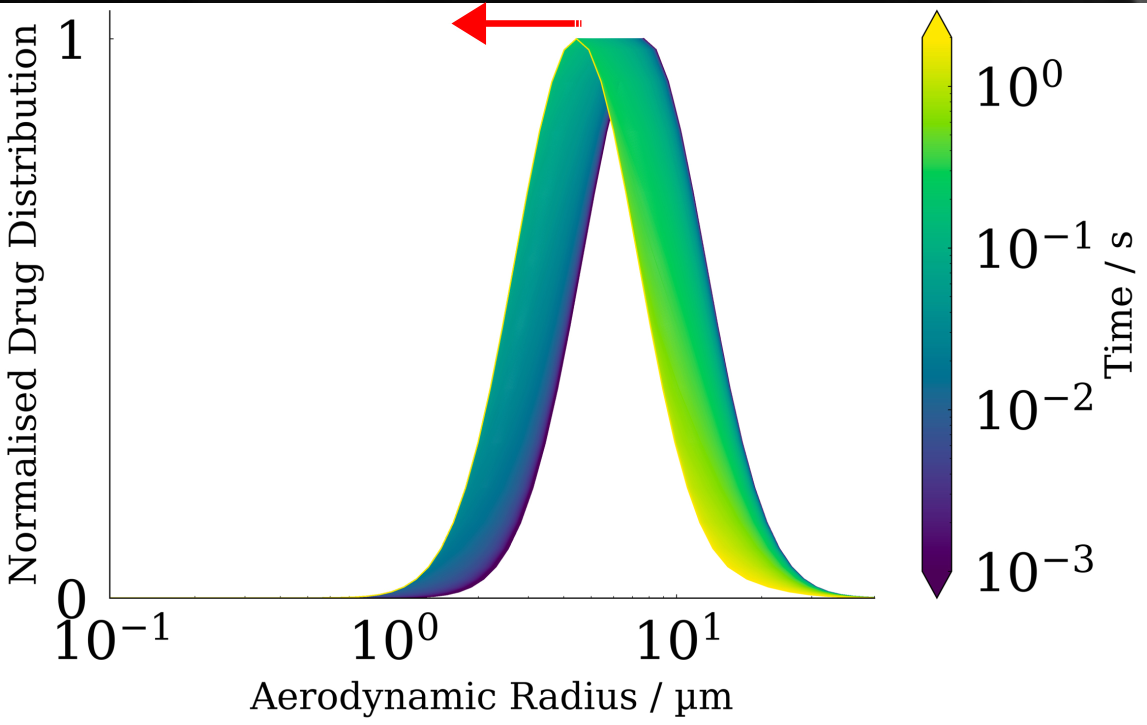

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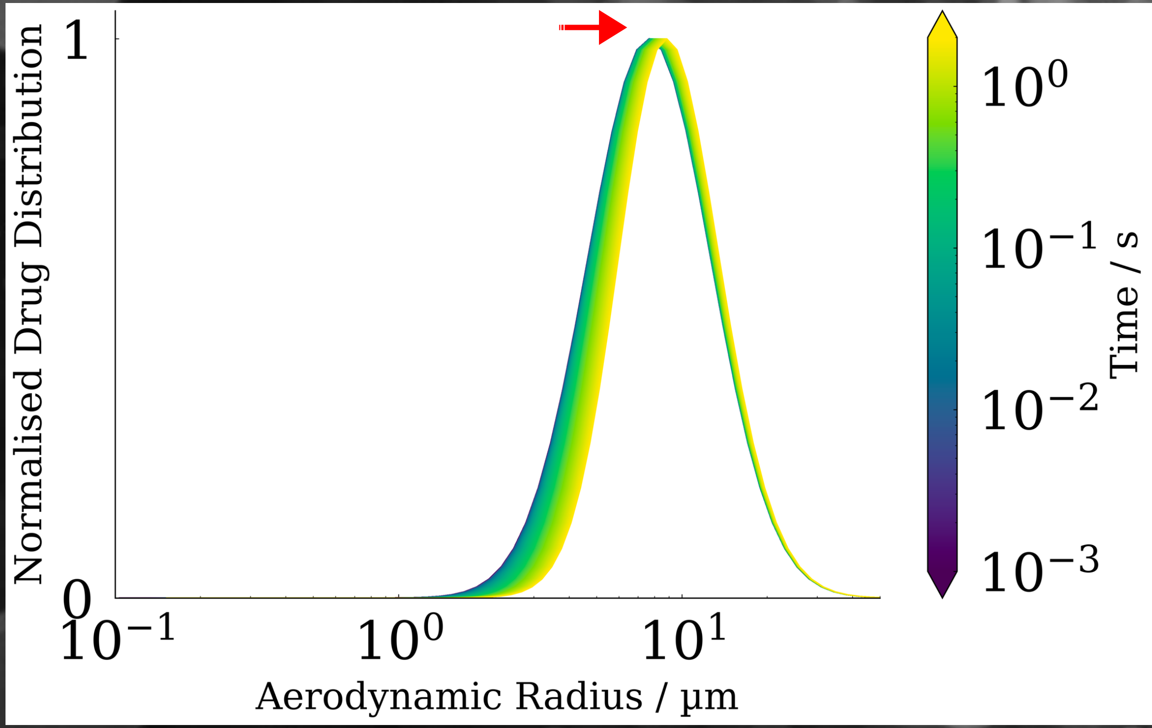

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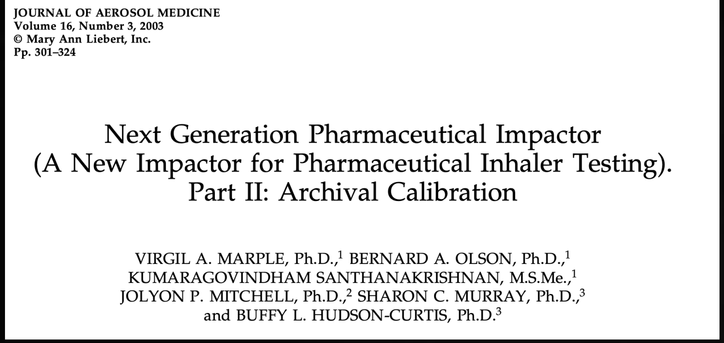
Aqueous NaCl solution, 0.1 MFS, 298 K

Filtering a distribution


JOURNAL OF AEROSOL MEDICINE
Volume 16, Number 3, 2003
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Pp. 301–324

Next Generation Pharmaceutical Impactor
(A New Impactor for Pharmaceutical Inhaler Testing).
Part II: Archival Calibration

VIRGIL A. MARPLE, Ph.D.,[1] BERNARD A. OLSON, Ph.D.,[1]
KUMARAGOVINDHAM SANTHANAKRISHNAN, M.S.Me.,[1]
JOLYON P. MITCHELL, Ph.D.,[2] SHARON C. MURRAY, Ph.D.,[3]
and BUFFY L. HUDSON-CURTIS, Ph.D.[3]

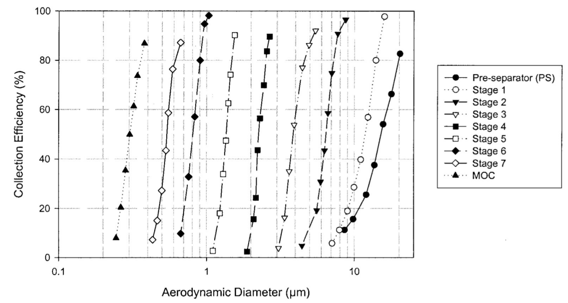
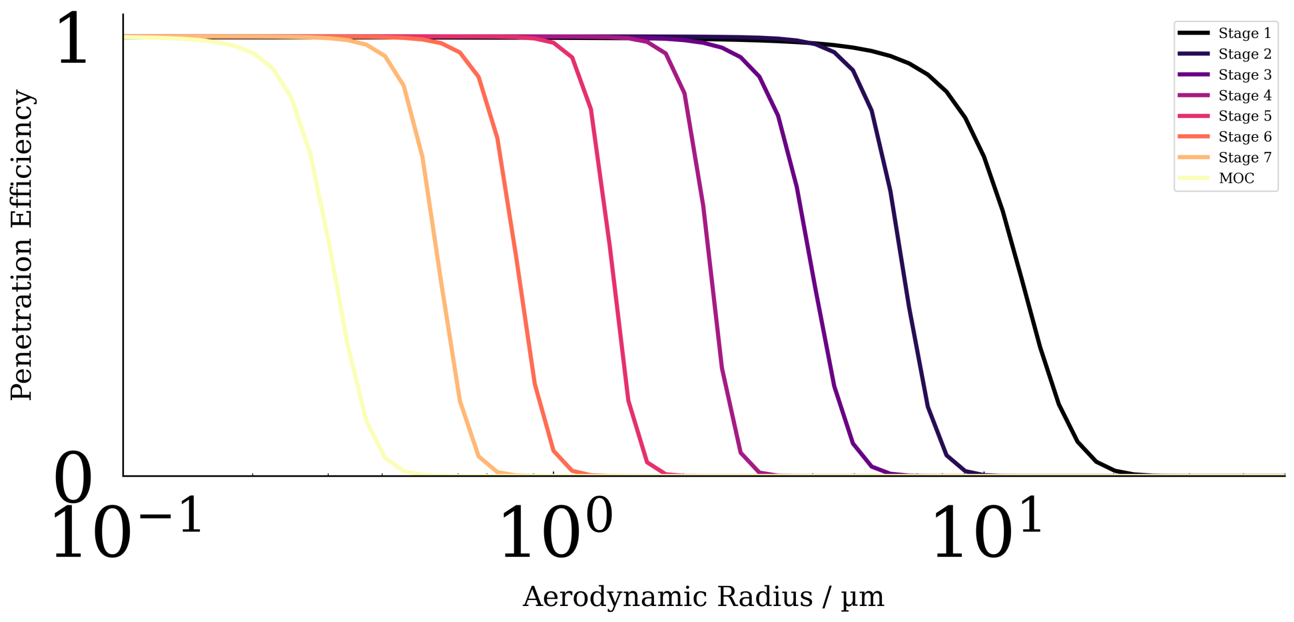
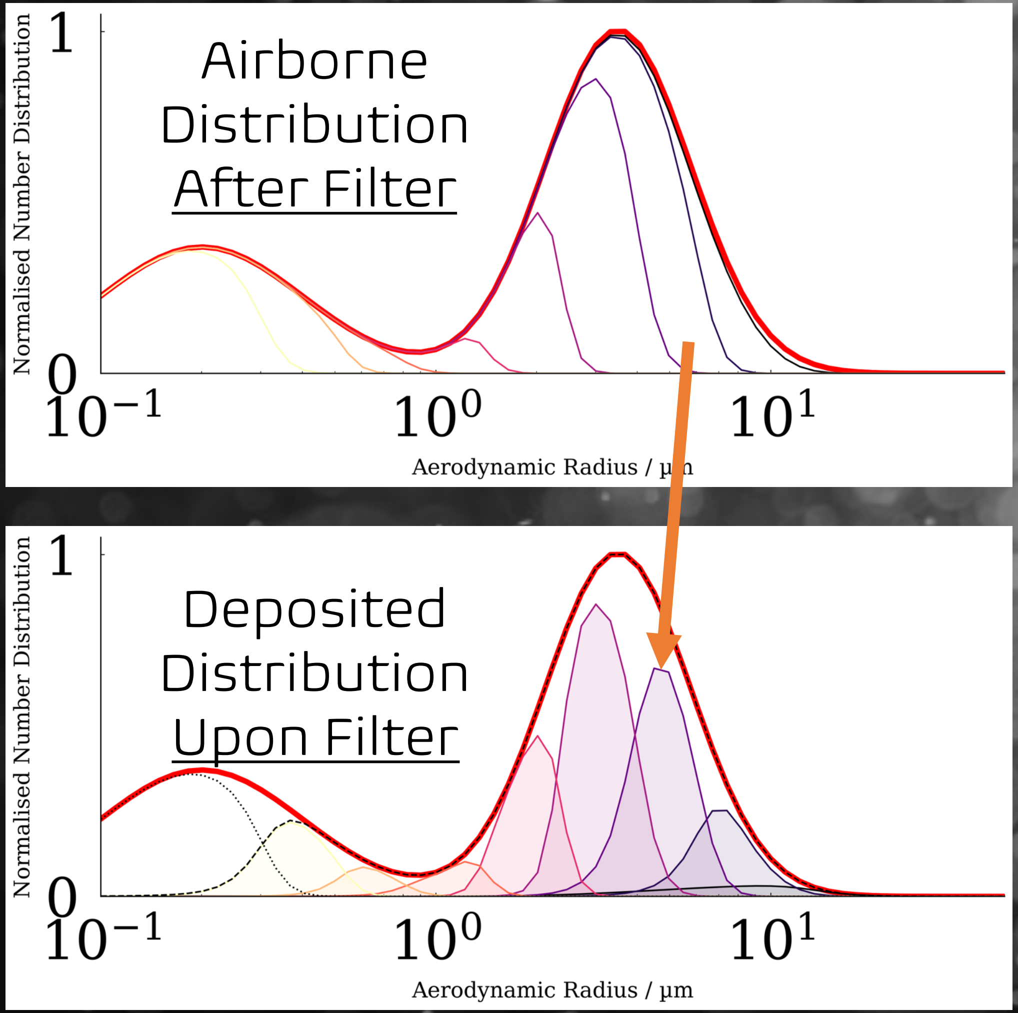


FIG. 7. Calibration of the archival NGI at 30-L/min inlet flow rate.





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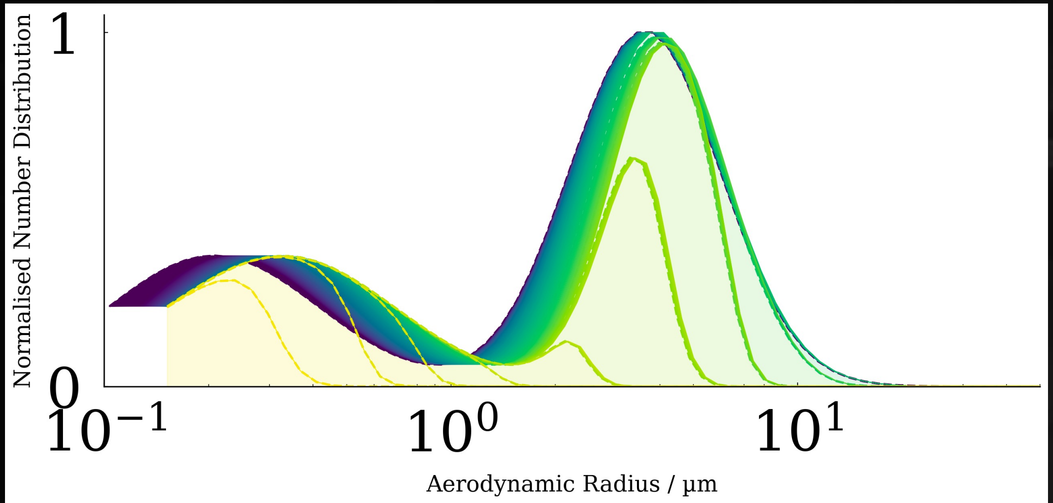
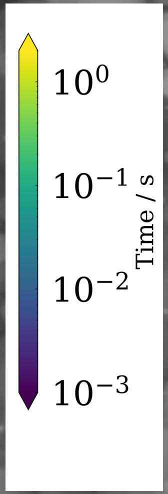
Coupling Droplet Evolution & Filtration





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RH = 99 %, NGI flow rate 60 $Lmin^{-1}$

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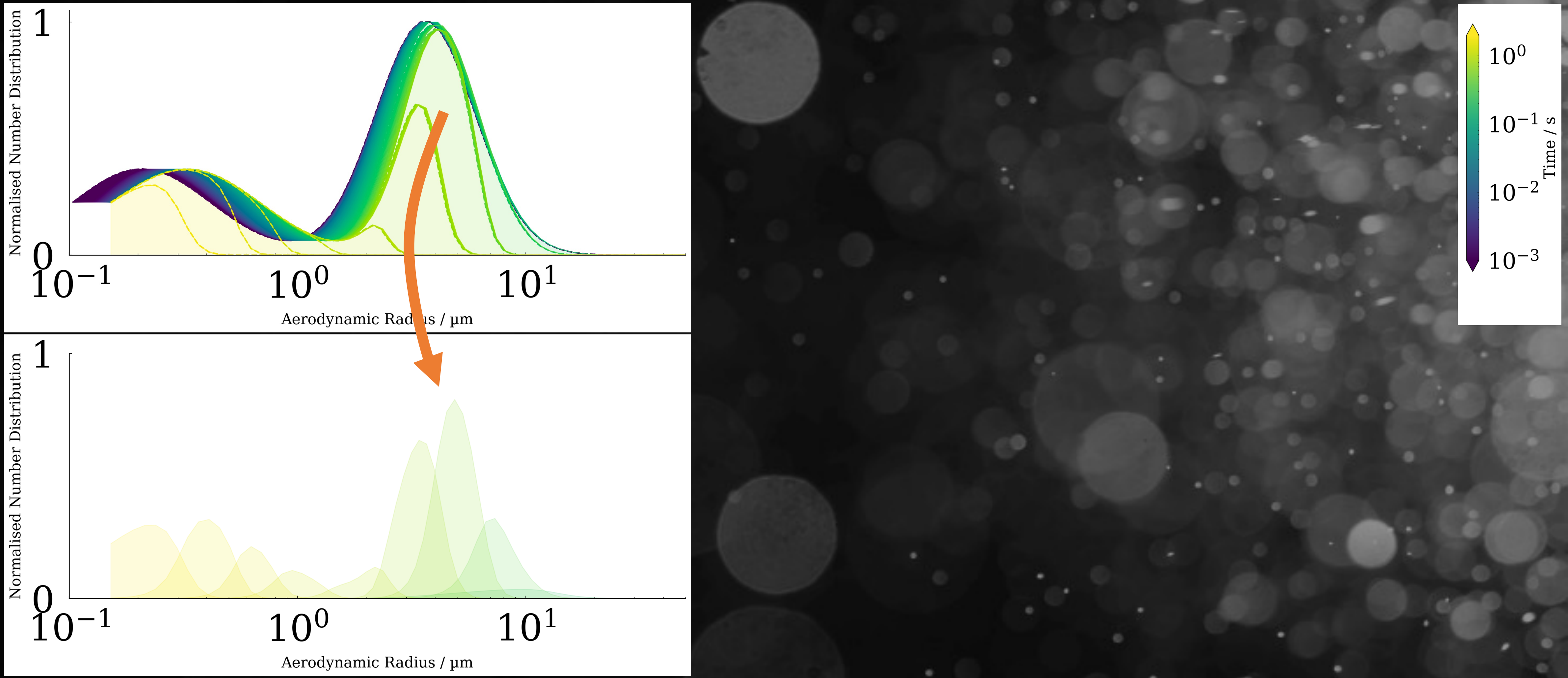

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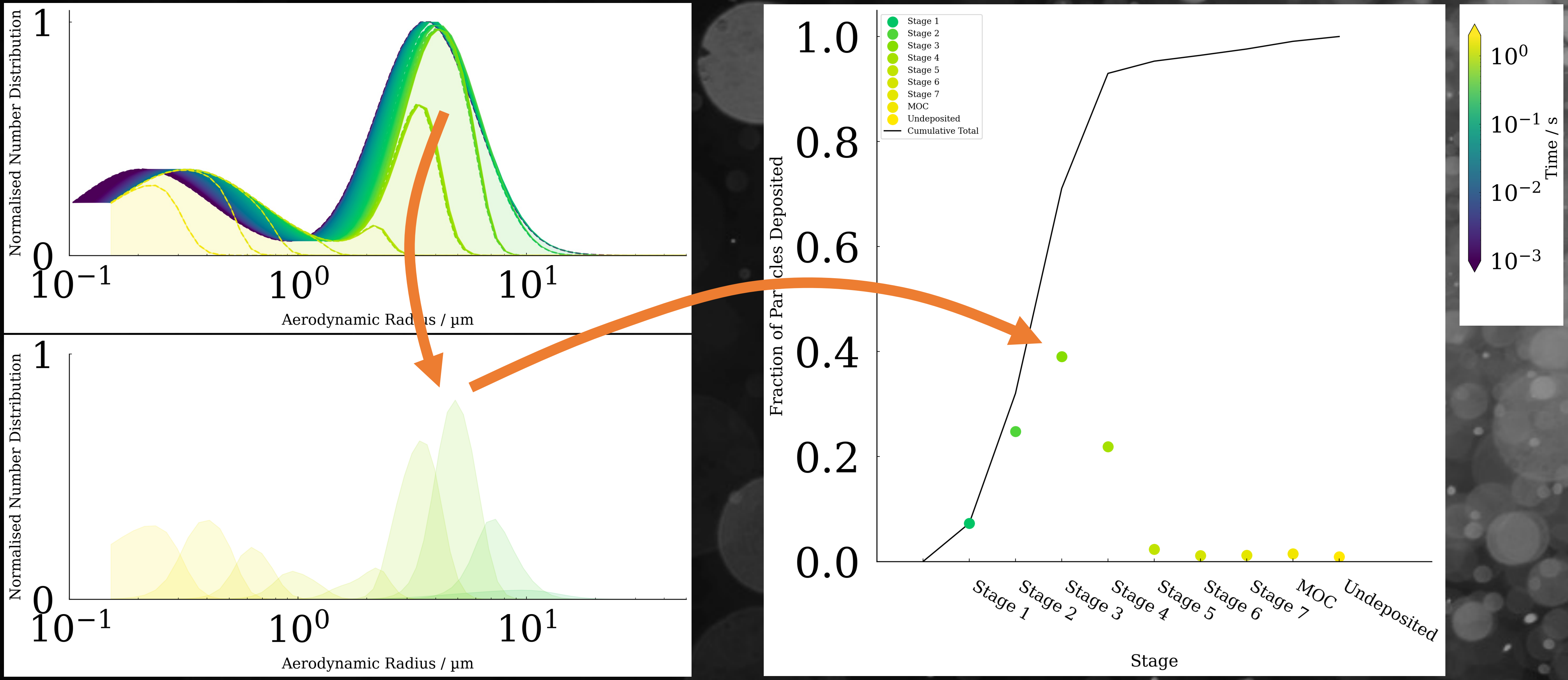

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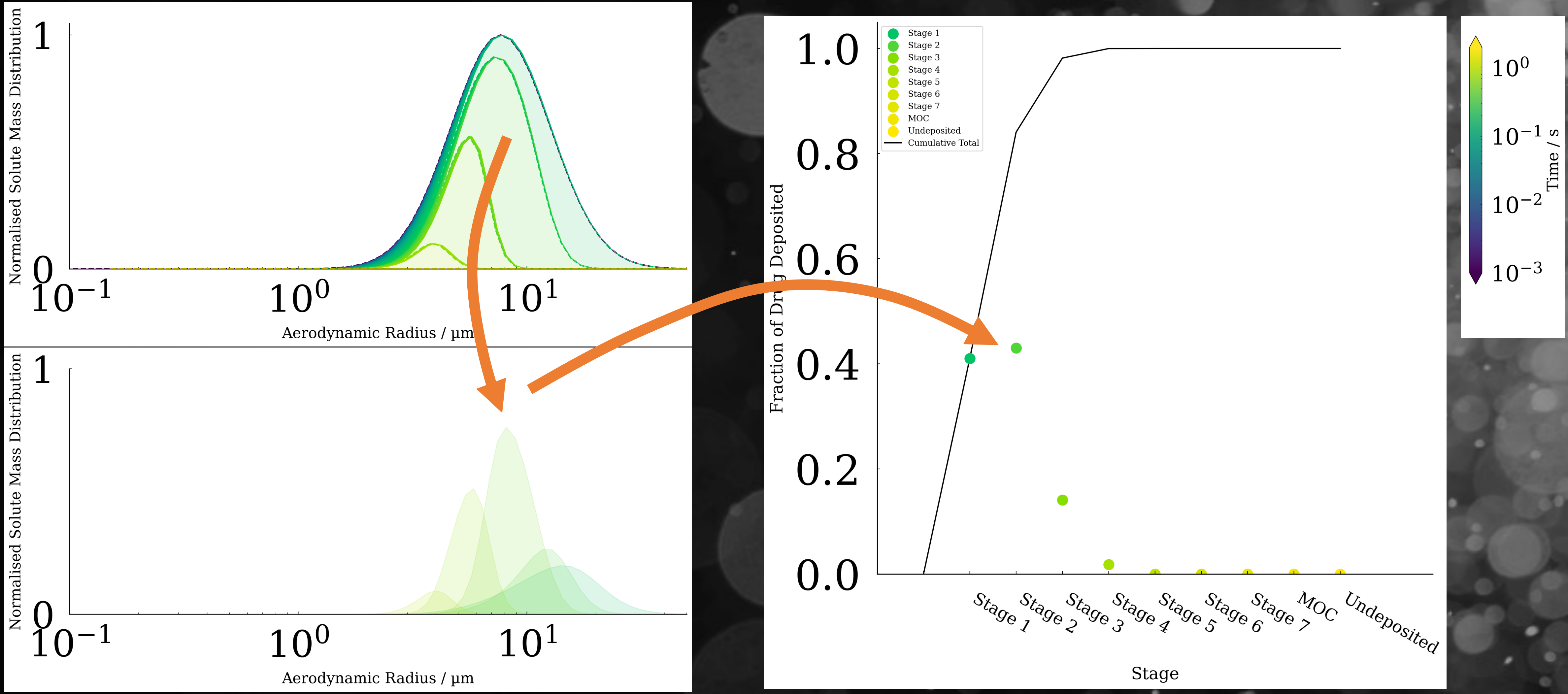

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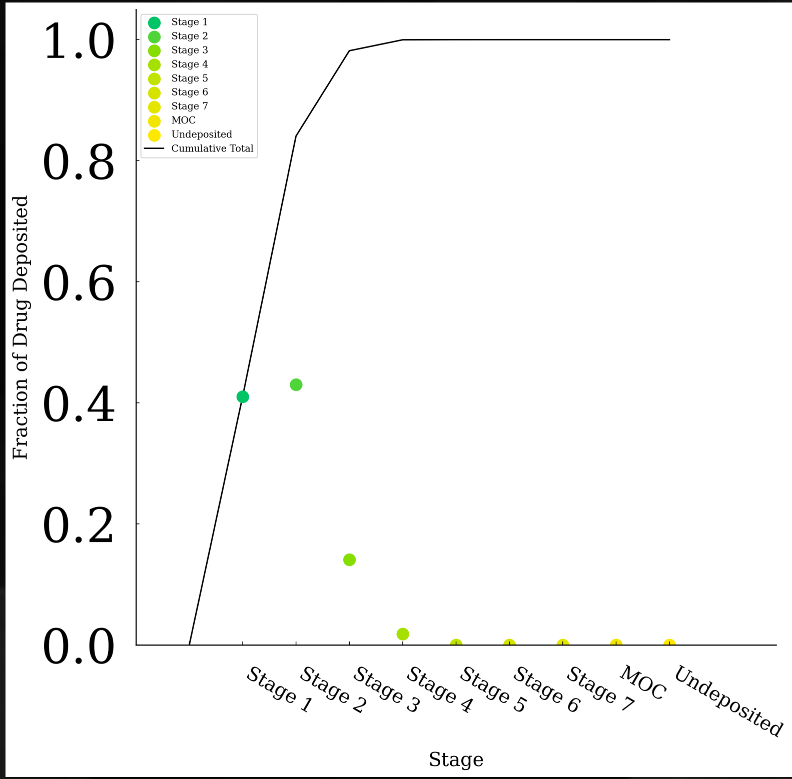
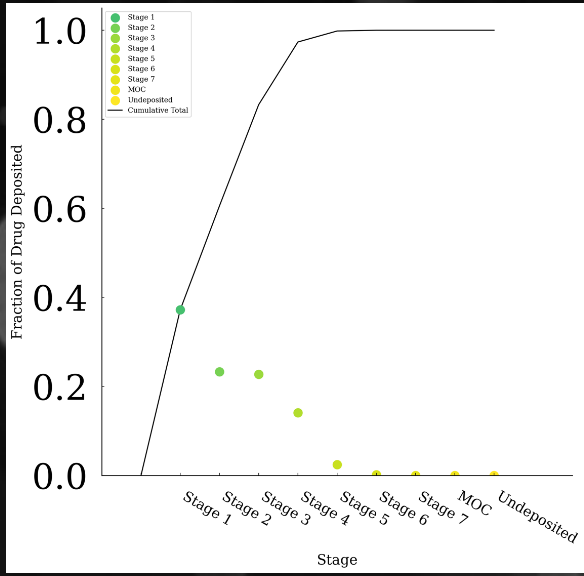
RH = 99 %, NGI flow rate 60 Lmin^{-1}

Controlling Deposition

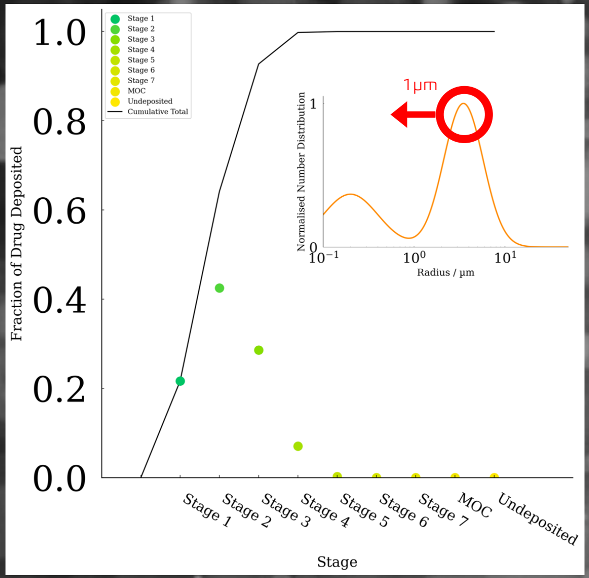
Reference: NaCl at 99 % RH



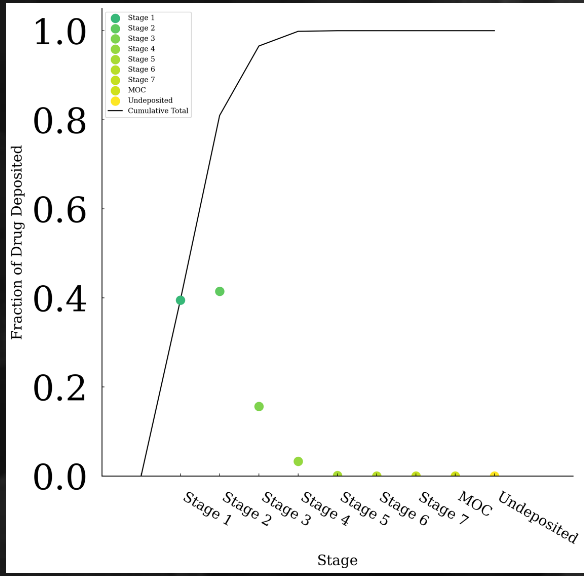
NGI at 10 % RH



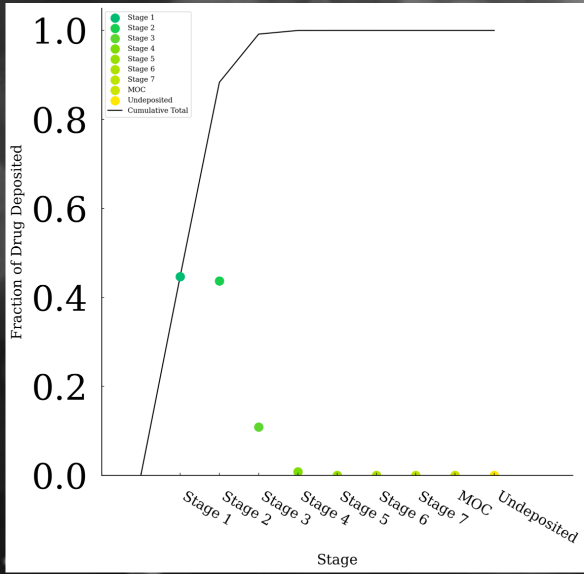
Peak at 2.5 μm



Less Hygroscopic



Higher Concentration



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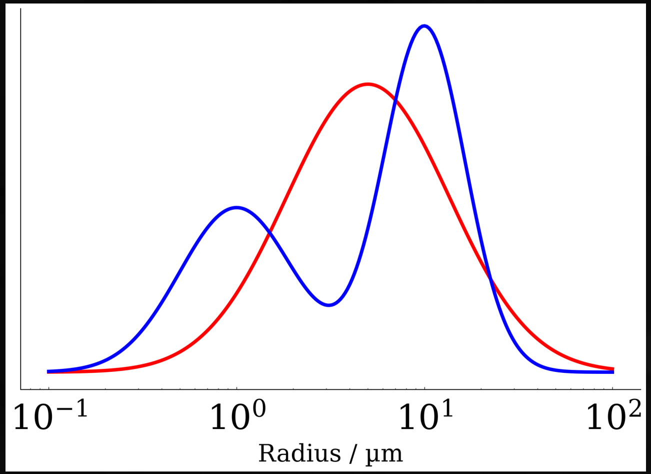
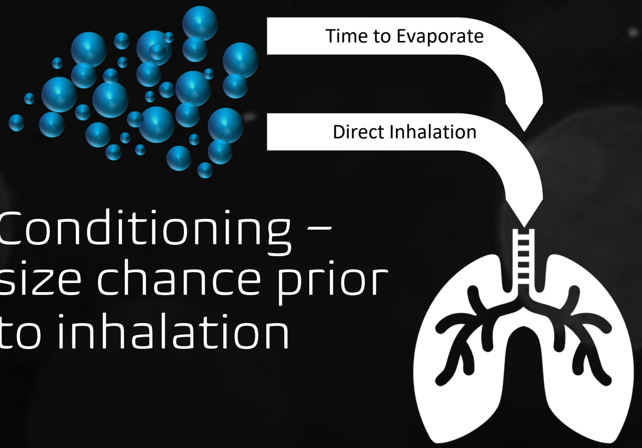
Tool Box: Controlling Deposition

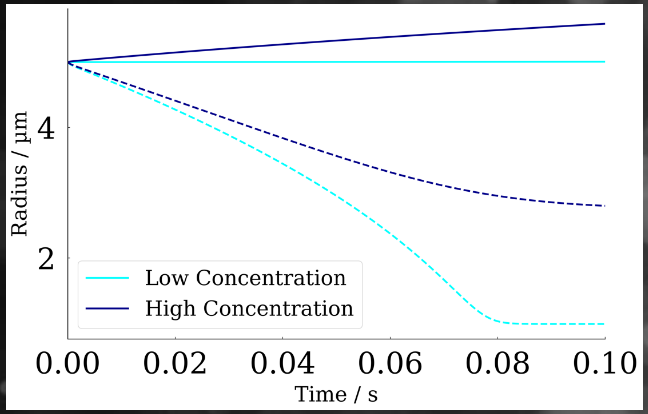
- Initial size distribution



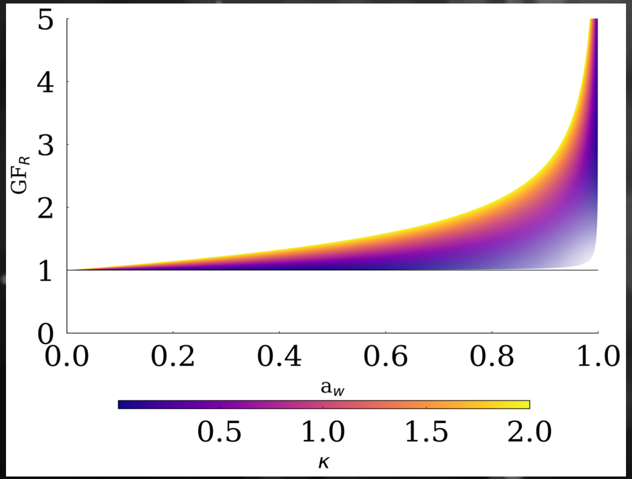


- Conditioning – size chance prior to inhalation

- Solute Concentration



- Hygroscopicity



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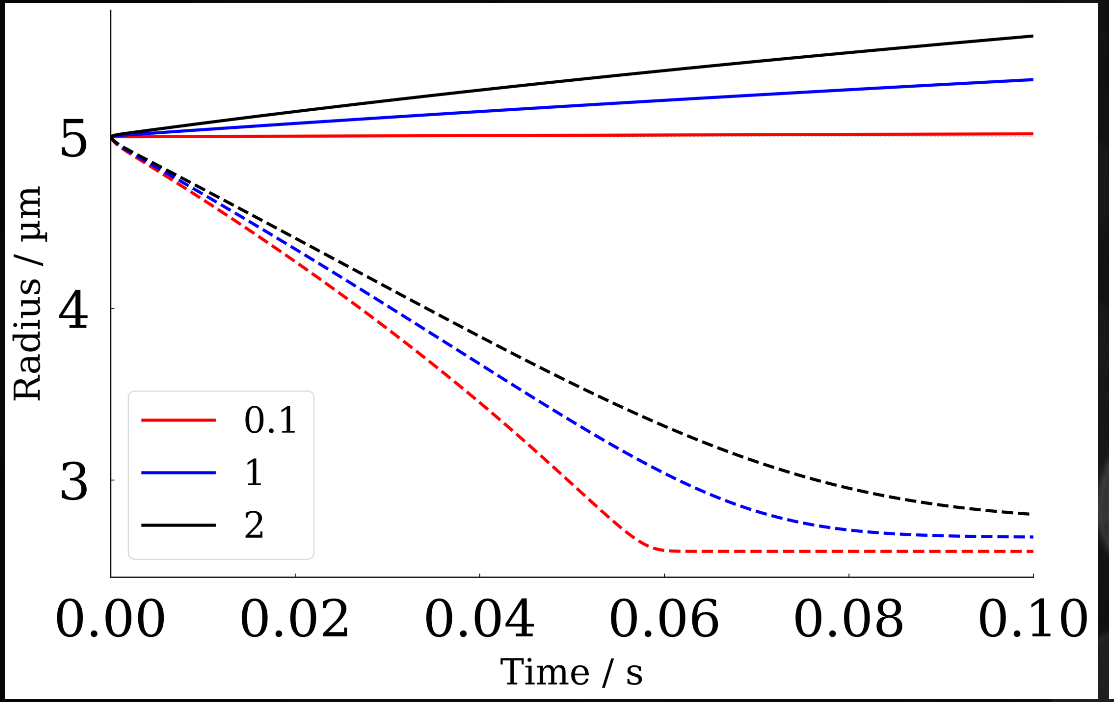
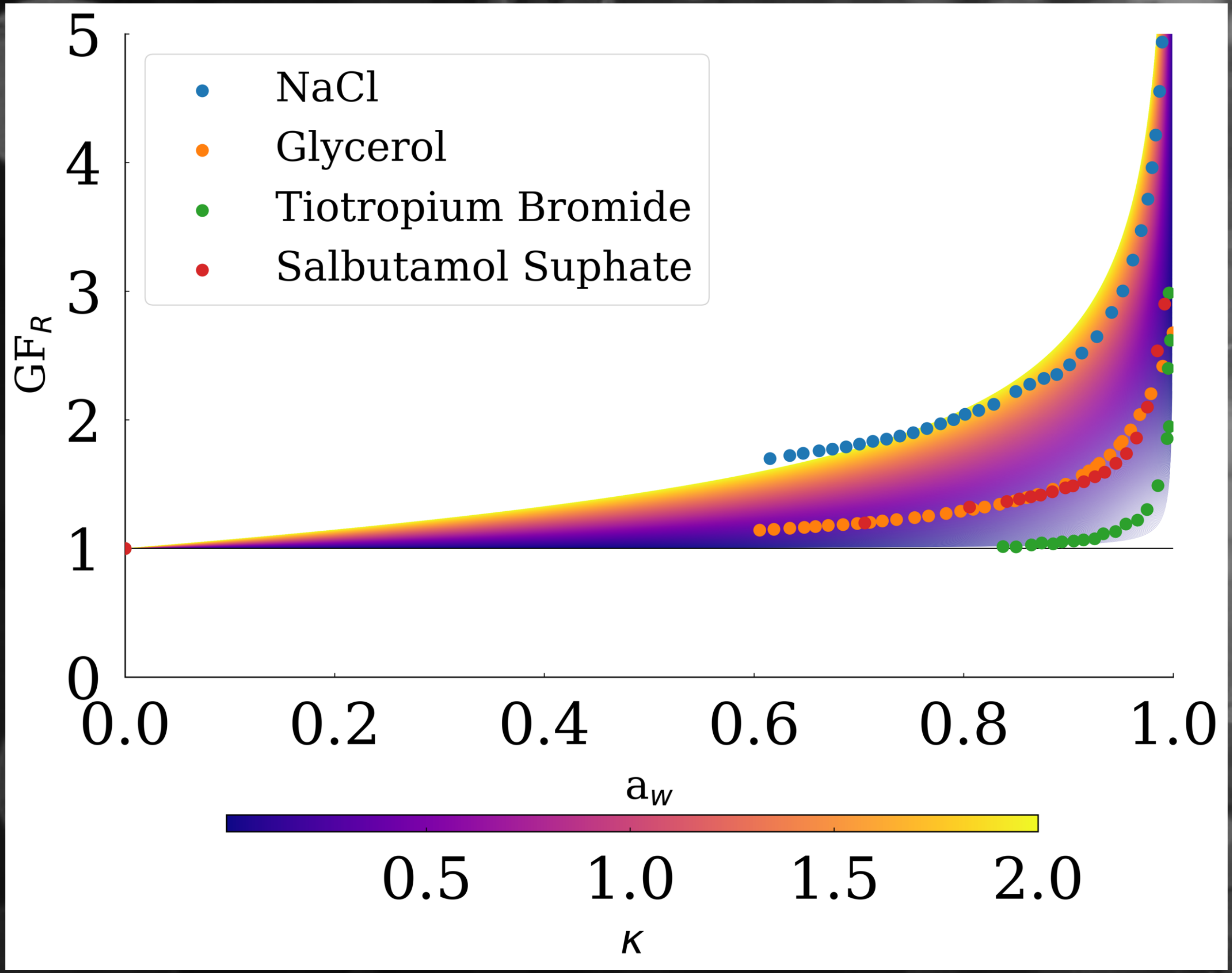
Hygroscopicity is important

- Determines equilibrium size and rate of size change





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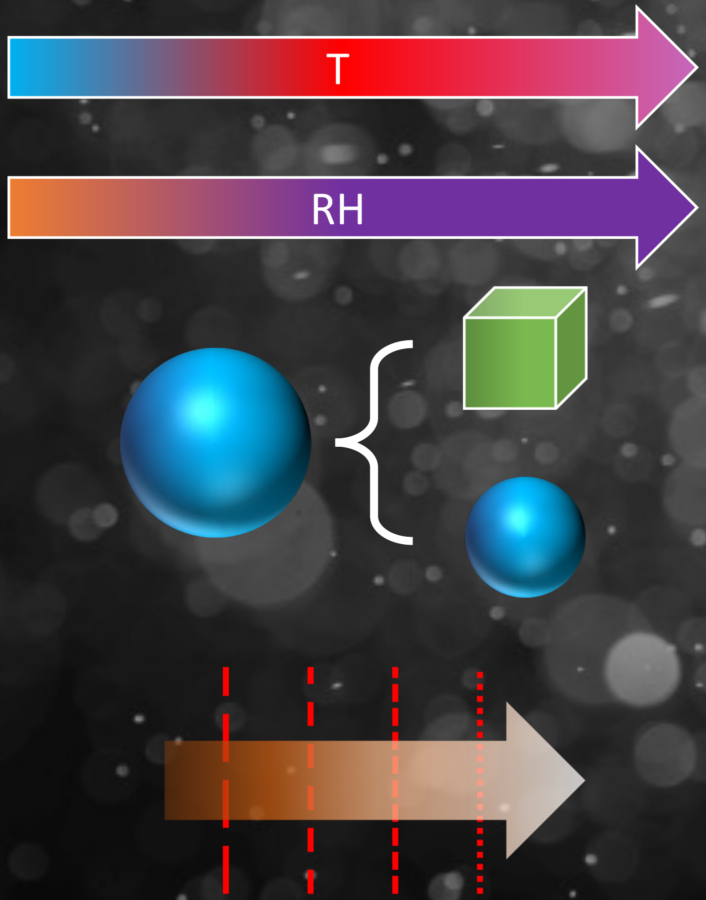
Time Resolved Behaviour is Important

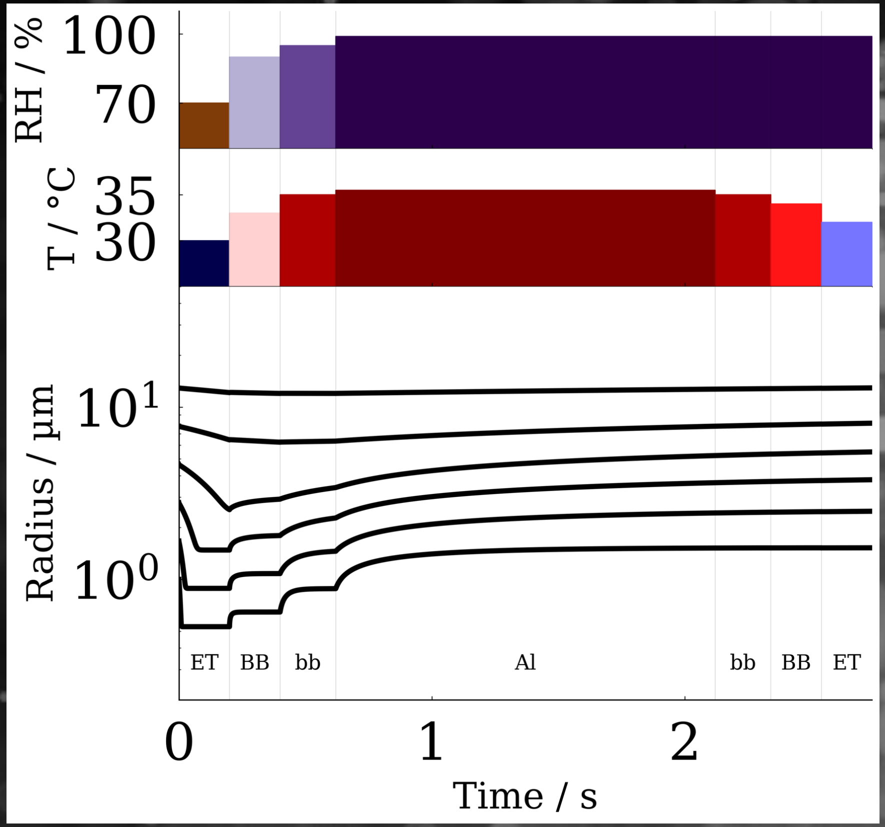
During inhalation dynamic processes occur

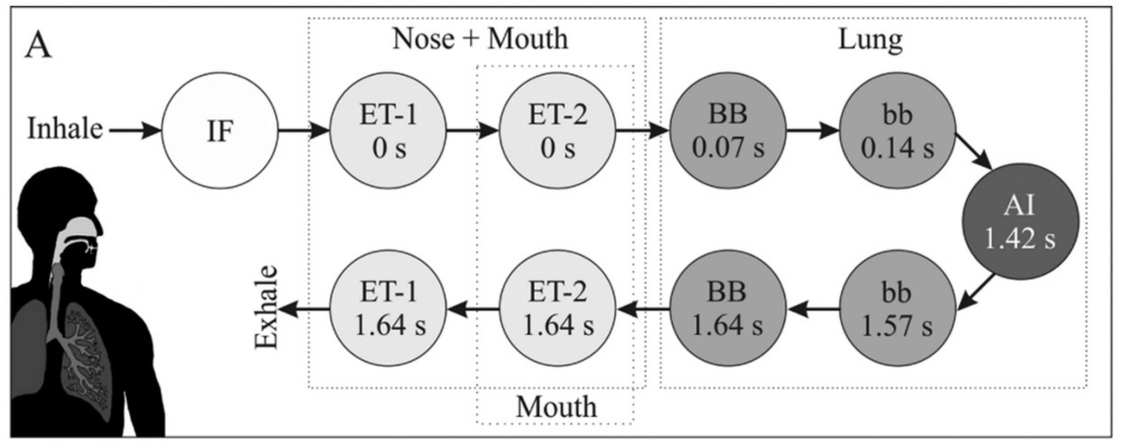
- Droplet Environment
  - Temperature & Relative Humidity (RH)
- Droplet State
  - Size, temperature, density
  - Solidification or dissolution
- Filtration Events
  - Passage though the lung and regional deposition

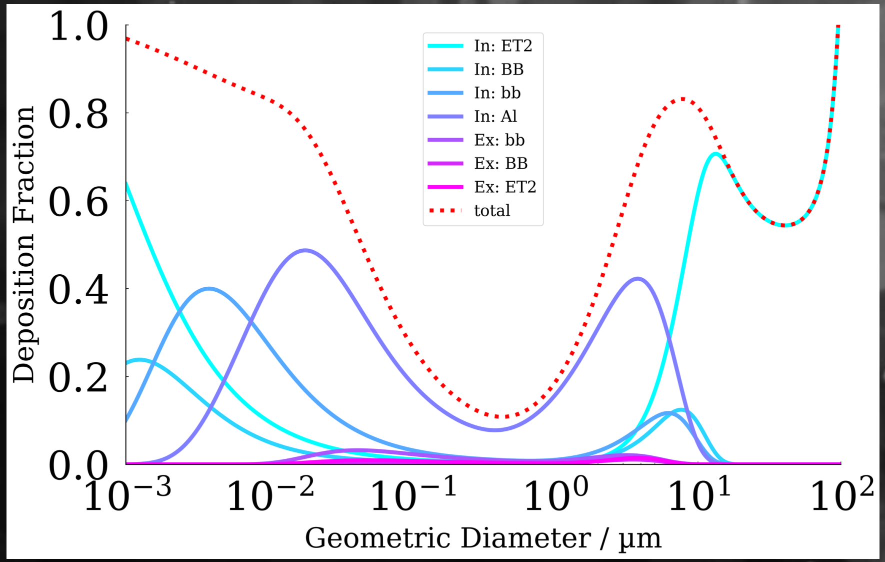


Next Steps

- Simulate physiological conditions
- Combine with ICRP deposition model







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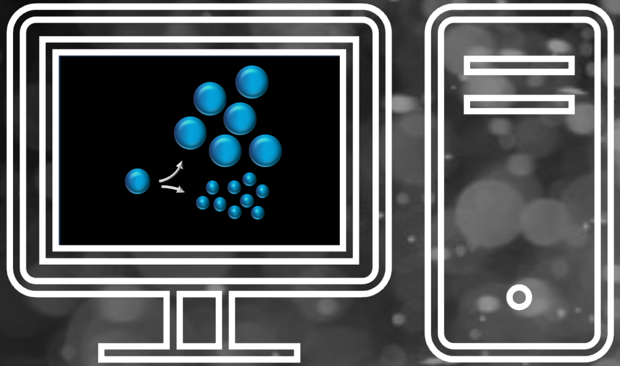
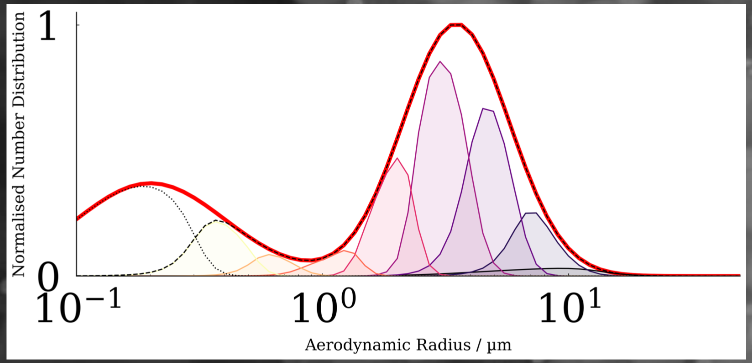
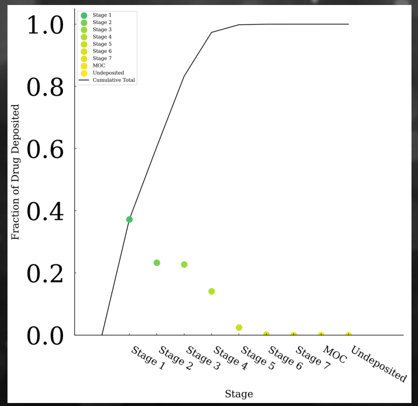
Conclusions



- Accurate simulations of population size change are possible



- Virtual impactors enable accelerated formulation testing
- Enabling formulation engineering for optimised deposition



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Questions

Thank you for your attention

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