Design and Application of an Adept Aerosol/Vapor Lung-on-Chip and Aerosol/Vapor Delivery Systems

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Introduction

Organ-on-a-chip technology and other micro-physiological systems (MPS) were designed to recreate living tissues or organ microenvironments through precise control of the cells, extracellular matrix, and other micro-environmental factors to investigate physiological or pathological mechanisms. While correcting many of the gaps present in traditional tissue culture with a more physiologically relevant model these systems still suffer from limitations. The inability to administer aerosols to the lung epithelial cells is a specific limitation to current lung-on-a-chip technology. Having the capability to perform testing and analysis on tissues through conventional routes of exposure specific to the organ is paramount in achieving a complete biologically relevant system. There have been numerous mechanisms to create aerosols, however a true commercially available aerosol delivery system has not been successfully executed in organs-on-chips or other MPS. We combined 3D printing technology with microfluidic organ-chip engineering to build a customizable open-top lung-chip specific for the evaluation of aerosol toxicity and efficacy testing. In addition to utilizing the 3D printing technology to design novel lung-chips we also used this technology to design an aerosol delivery chamber specific to the open-top lung-chips. The 3D printing provides customizable, time and cost-effective parts which allowed us to apply this technology to manufacture novel aerosol delivery systems for lung tissue exposures *in vitro*. By producing an aerosol delivery system amenable to a lung-chip, we filled a gap in our current technology by enhancing and expanding our repertoire of testing available to lung microenvironments.

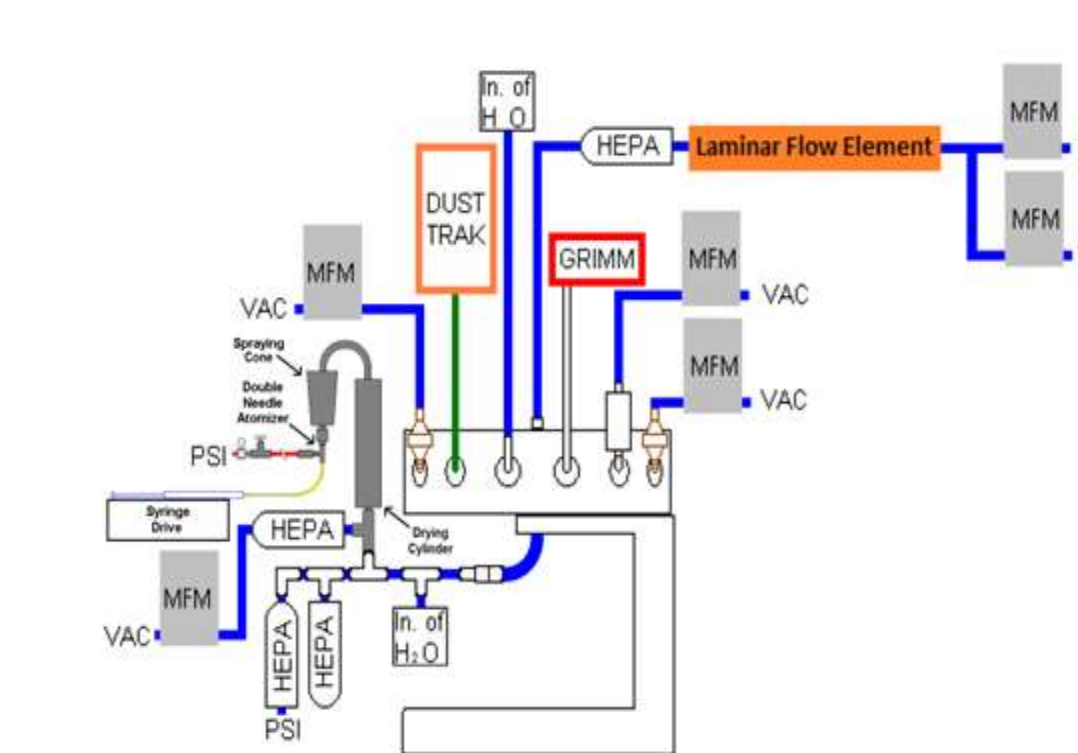**Large Airways** — **Small Airways**
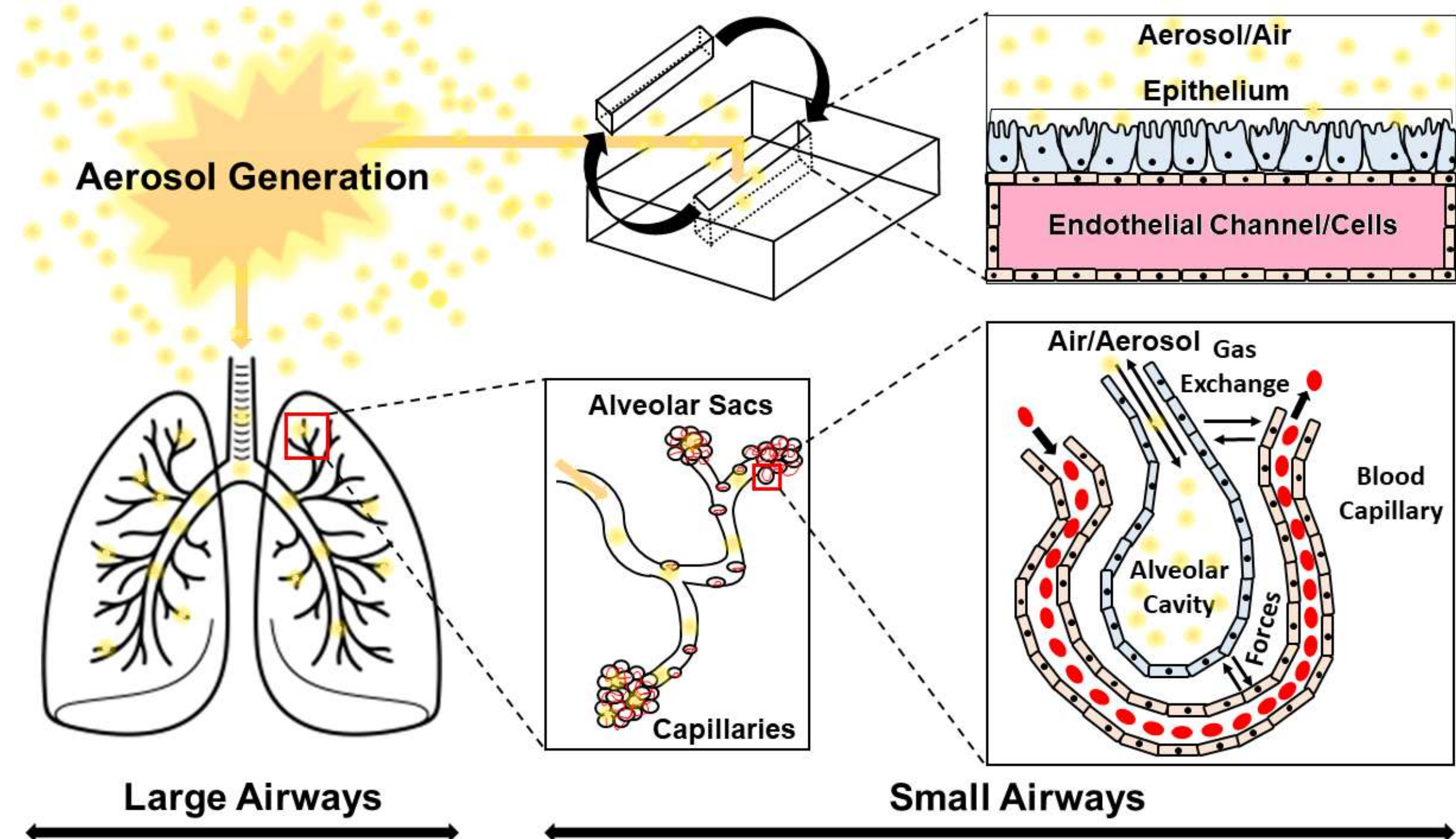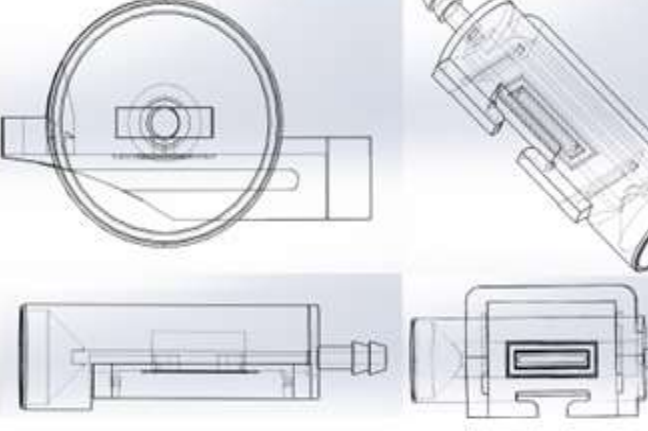
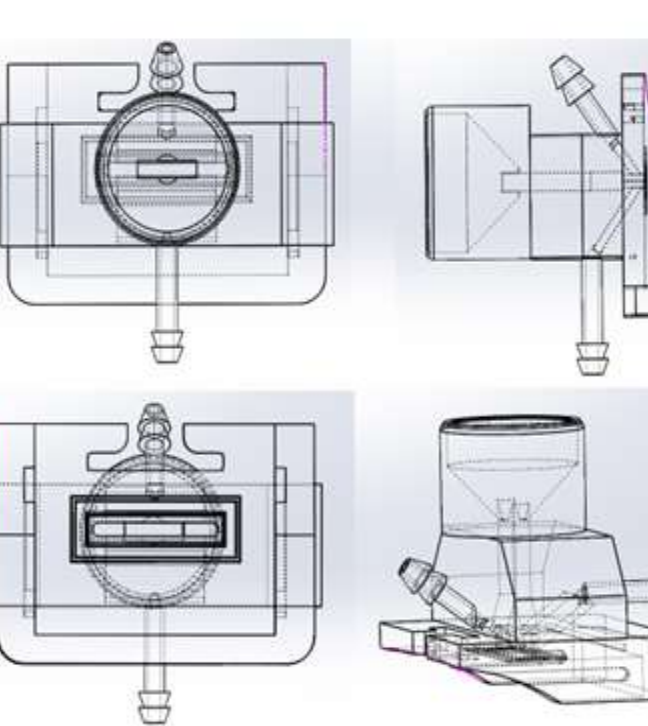## SLA/DLP 3D-Printers
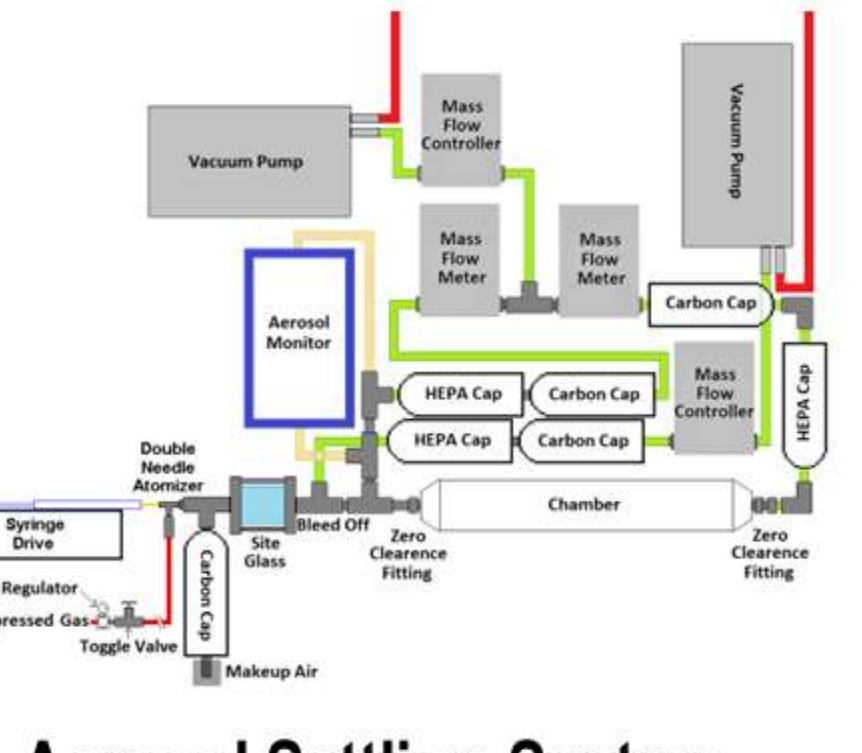

Monochrome LCD

Laser Scanning

Micro SLA

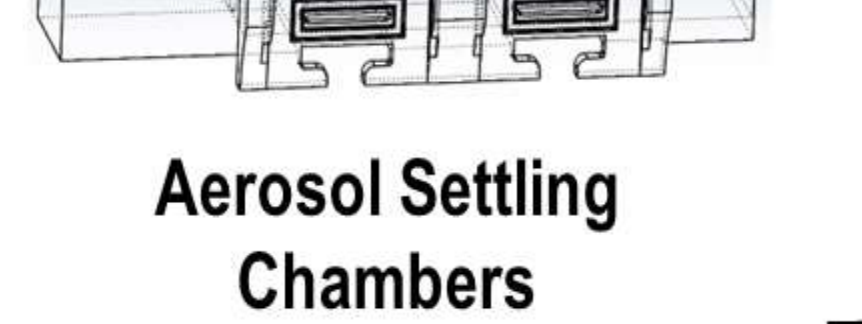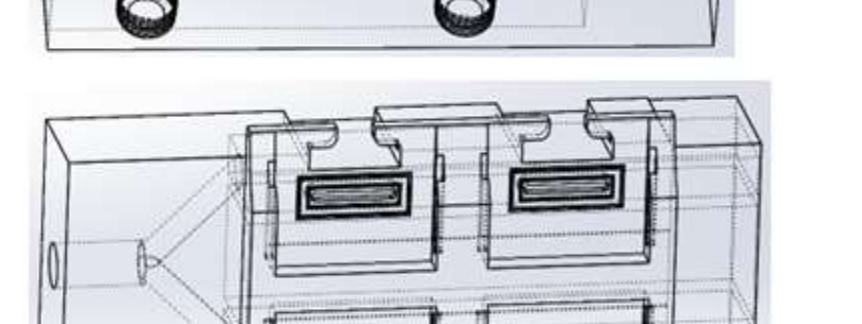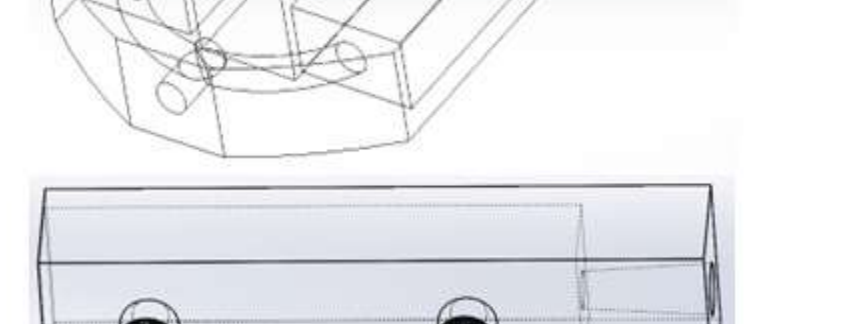## Aerosol Generating Systems and 3D-Printed Adaptors

Nose-Cone Aerosol System

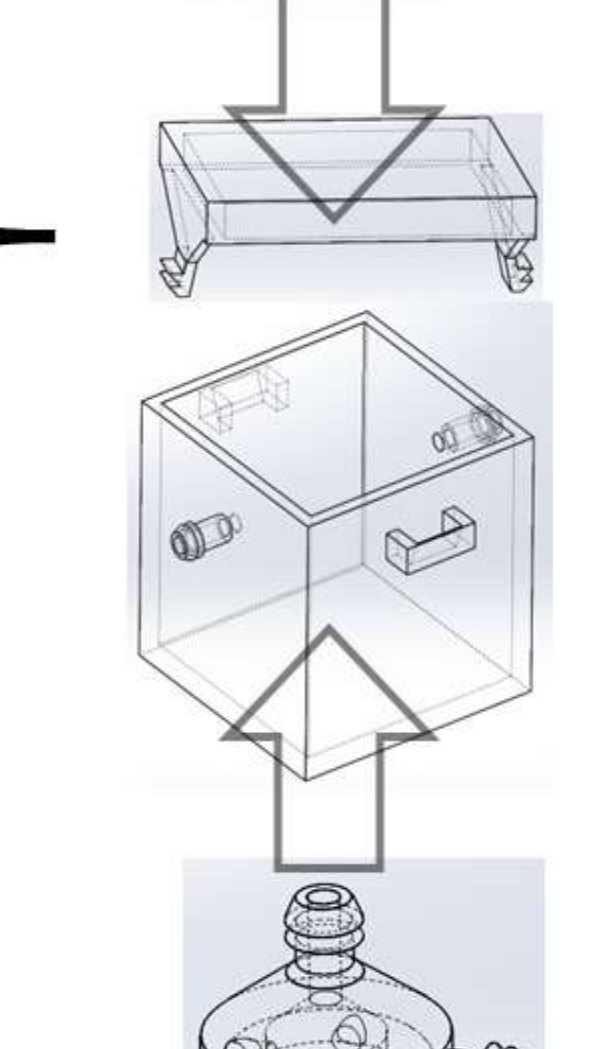**Nose-Cone Settling Chamber**

Nose-Cone Direct-Impact Chamber

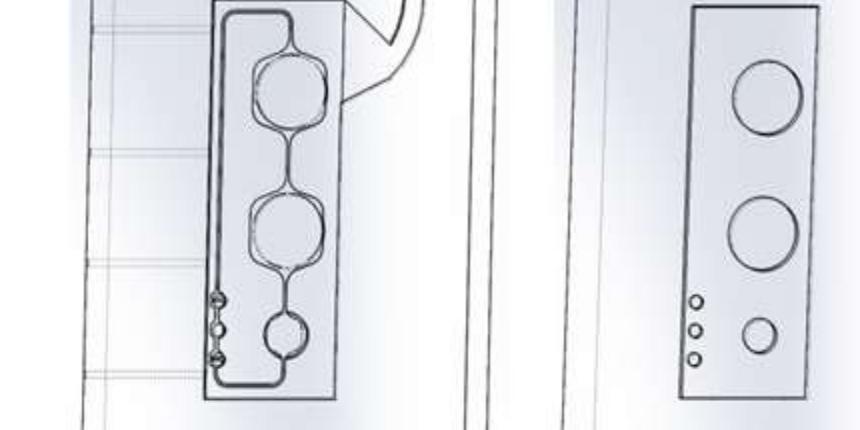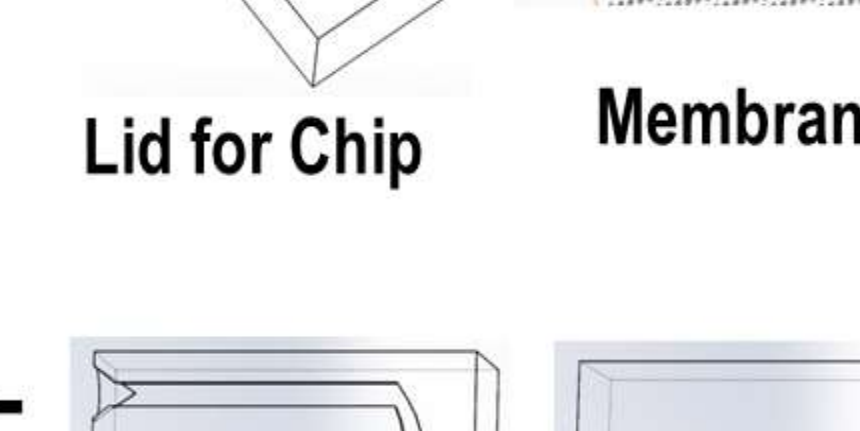**Aerosol Settling System**

Aerosol Settling Chambers
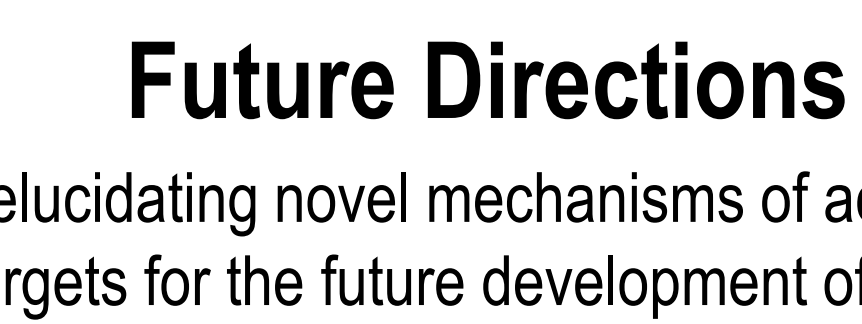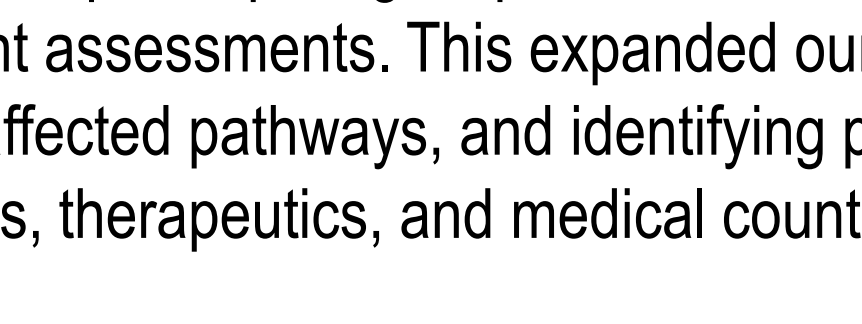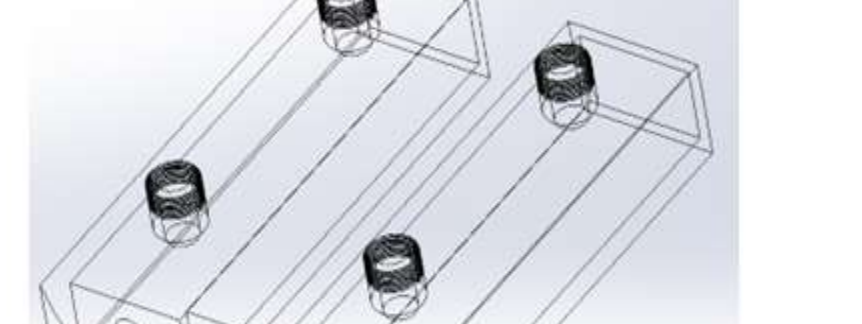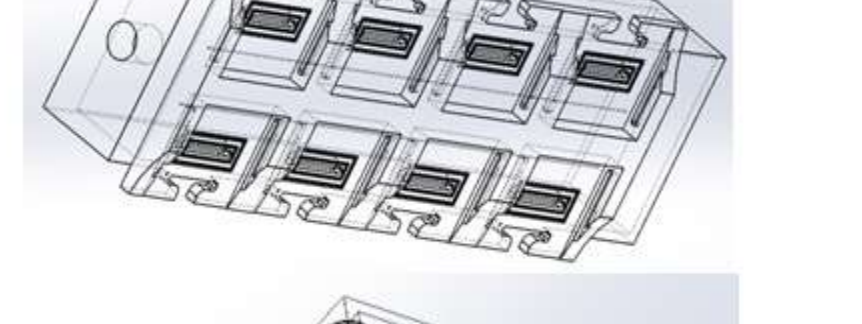
Vapor Systems

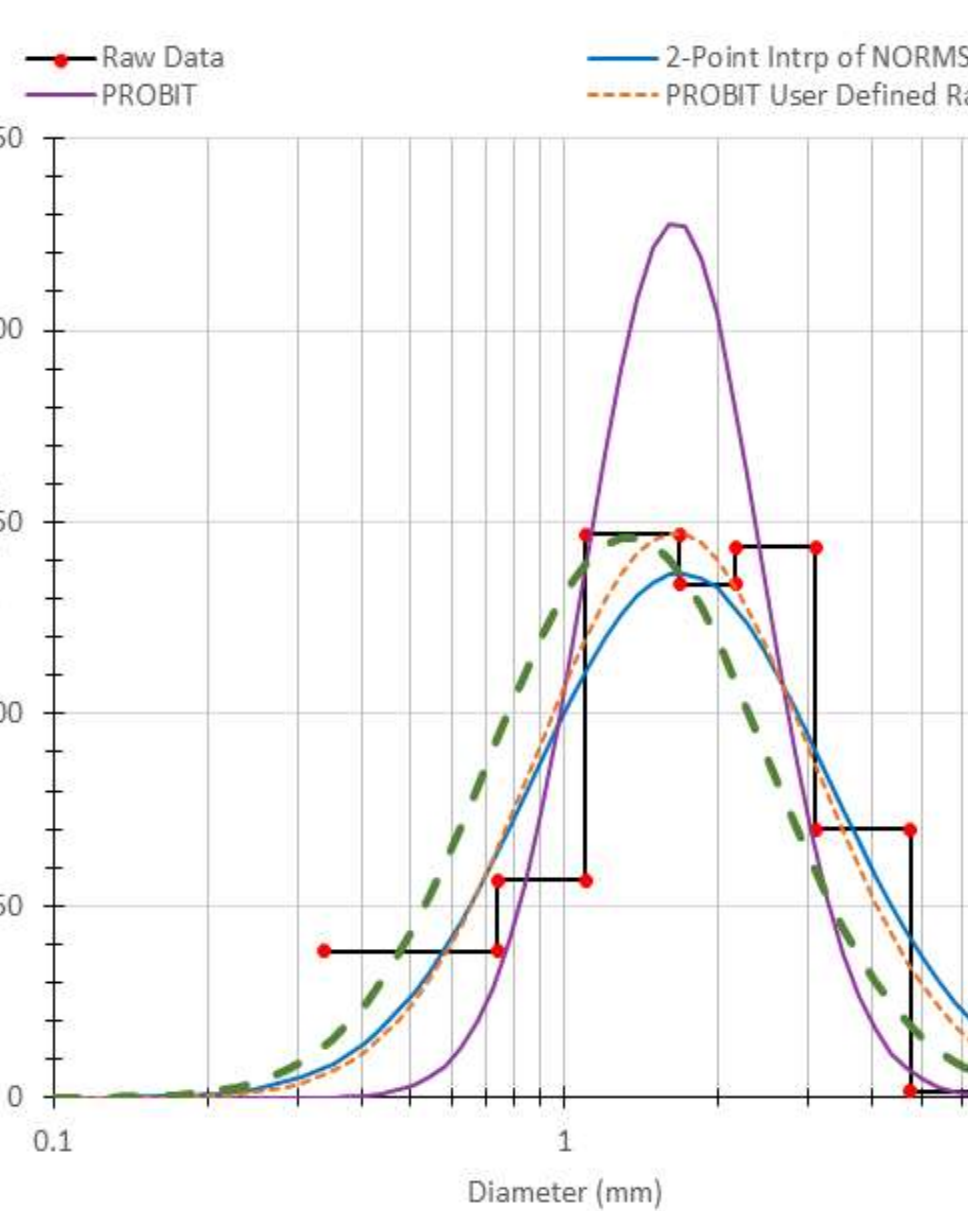## Open-Top Lung Chips

Top of Chip — **Bottom of Chip**

Lid for Chip — **Membrane**

Injection Mold
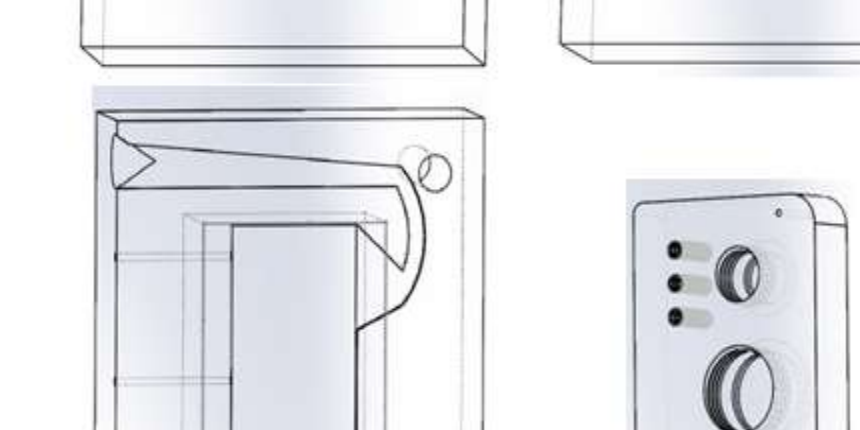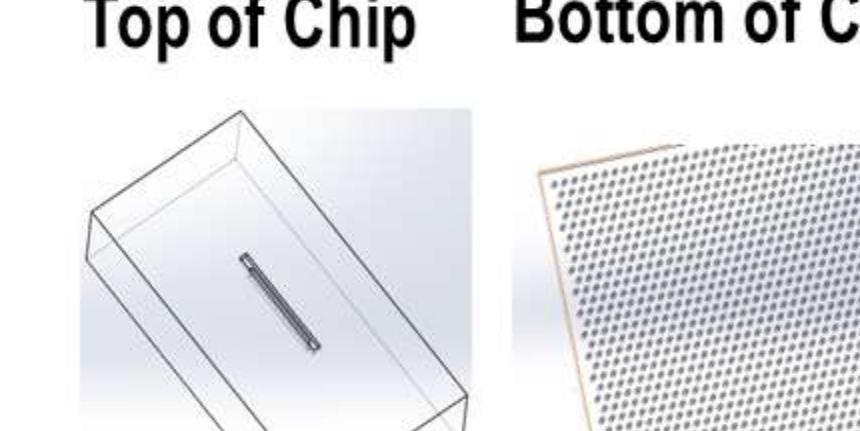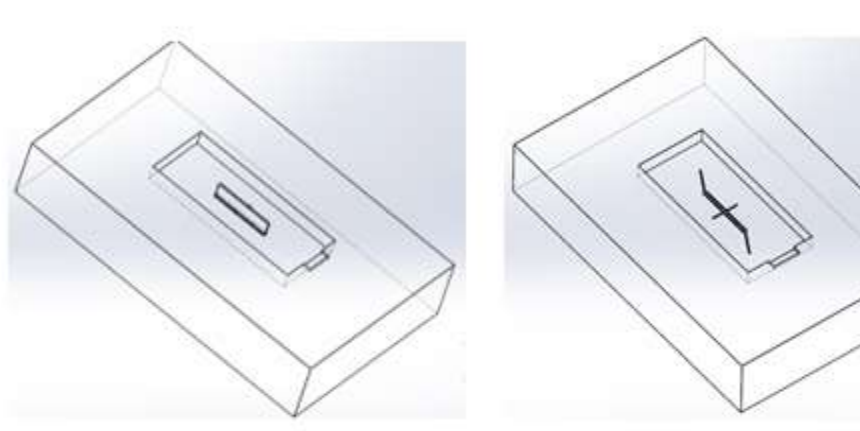
Aerosol Amendable Open-Top Lung-Chips
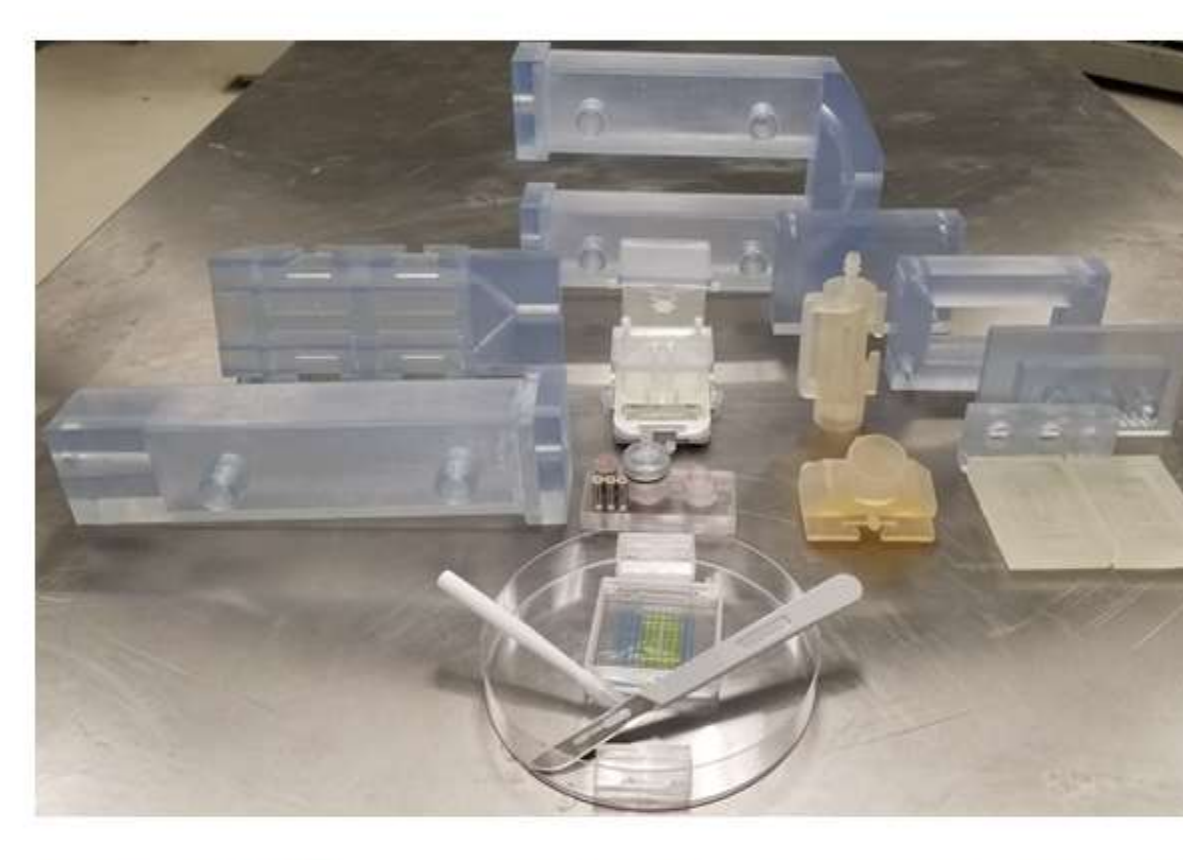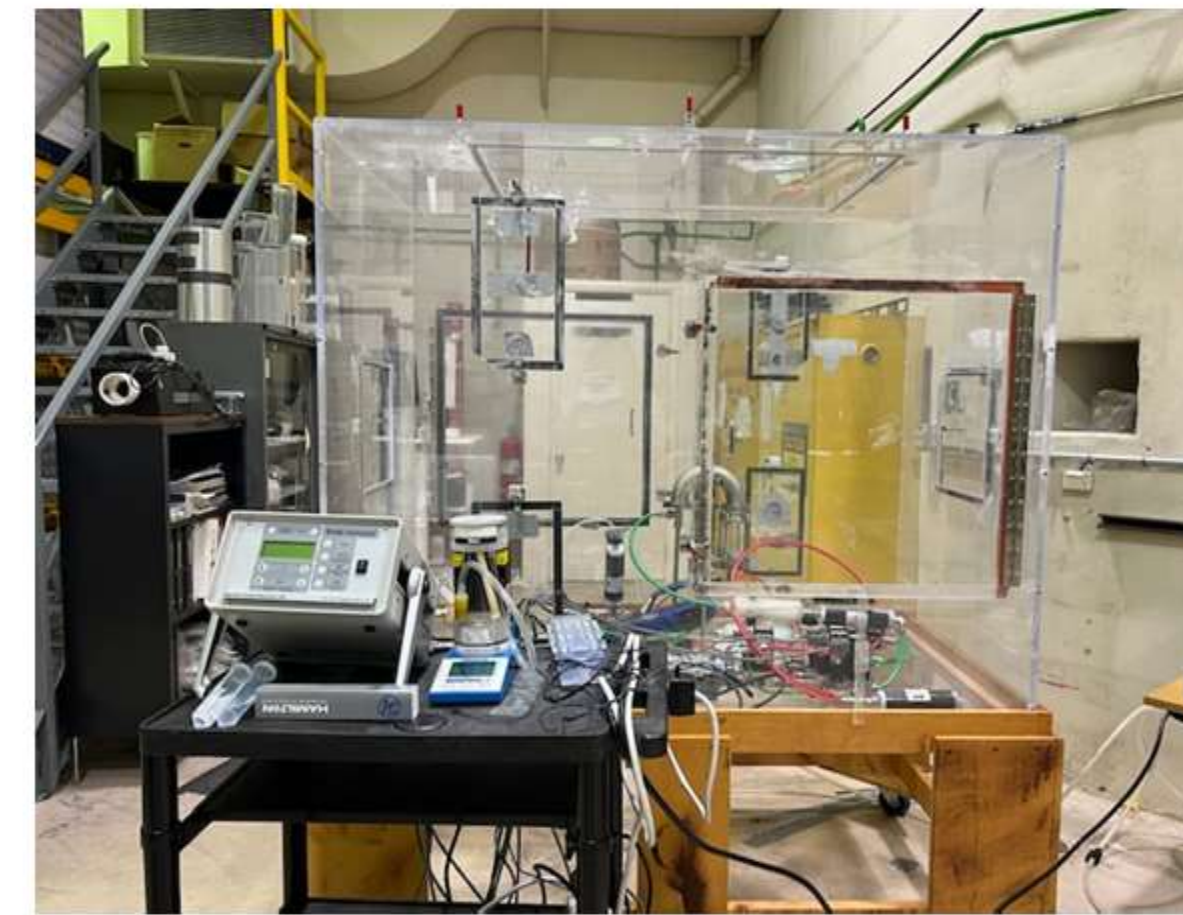
Characterization of Aerosol Profiles

Log Probability Graph of Cascade Impactor

MMAD: 1.68 µm
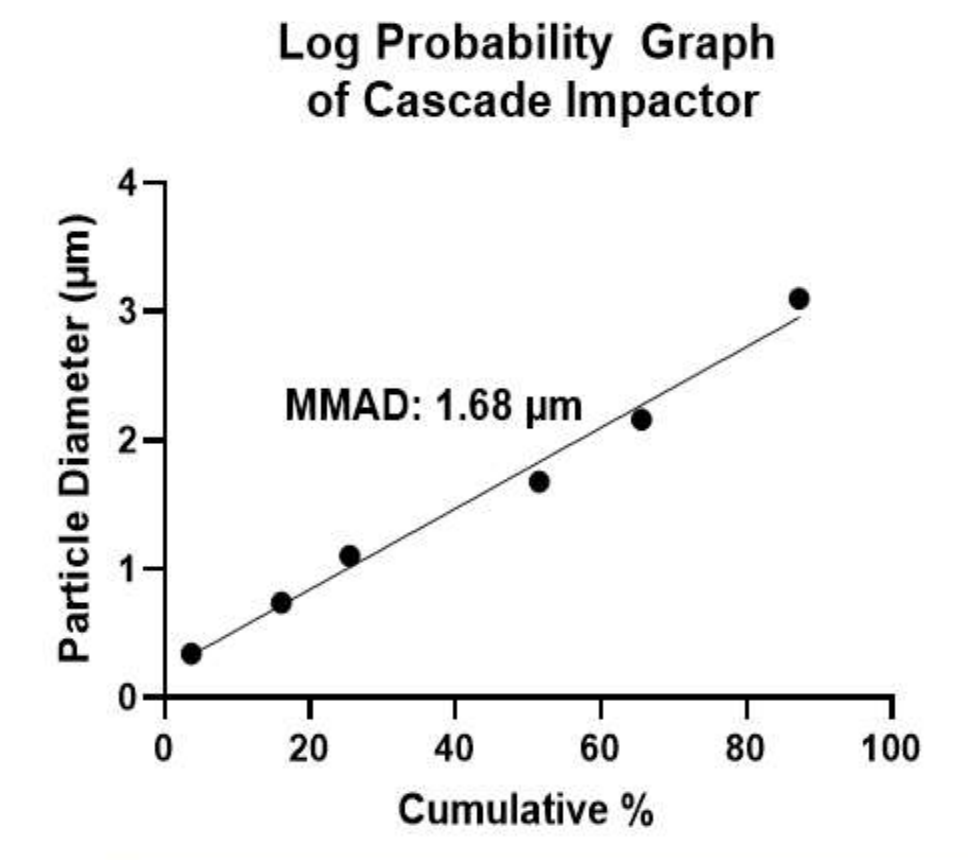
| PARAMETER	2 POINT INTERPOLATION of NORMSINV DATA
MMAD (µm)	1.690
GSD	1.958

Conclusion

We designed, generated, and evaluated novel open-top lung-chips that will be used downstream to facilitate the unique needs of the U.S. Army's aerosol toxicological agent assessments. This expanded our capabilities for elucidating novel mechanisms of action, furthering our understanding of affected pathways, and identifying potential targets for the future development of diagnostics, therapeutics, and medical countermeasures.

Future Directions

This expanded our aerosol capabilities for elucidating novel mechanisms of action, furthering our understanding of affected pathways, and identifying potential targets for the future development of diagnostics, therapeutics, and medical countermeasures. In the future we plan to determine differences between aerosol exposures and direct liquid dosing of chemical and biological agents on a lung chip.
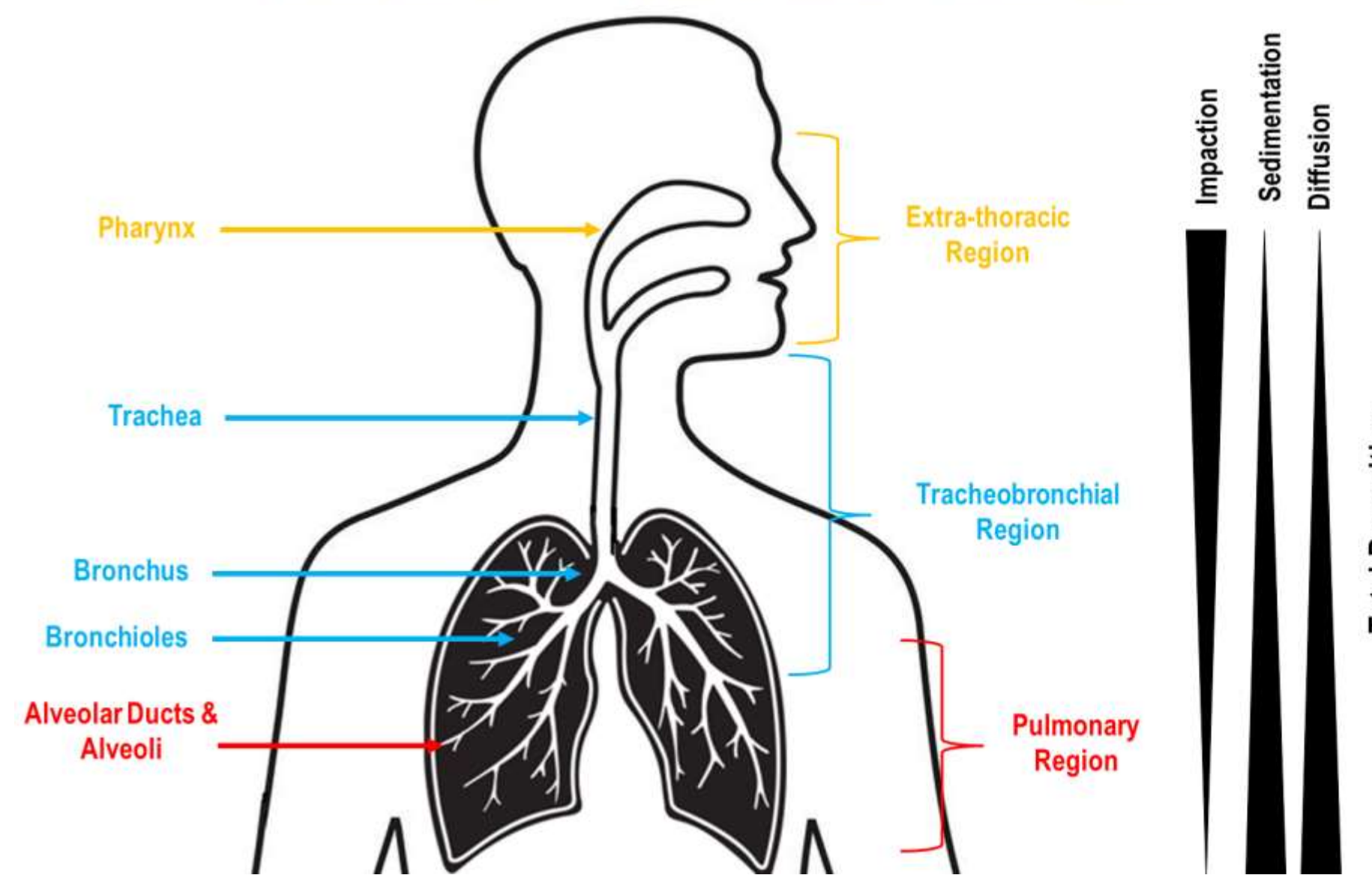
Respirable Aerosol Deposition
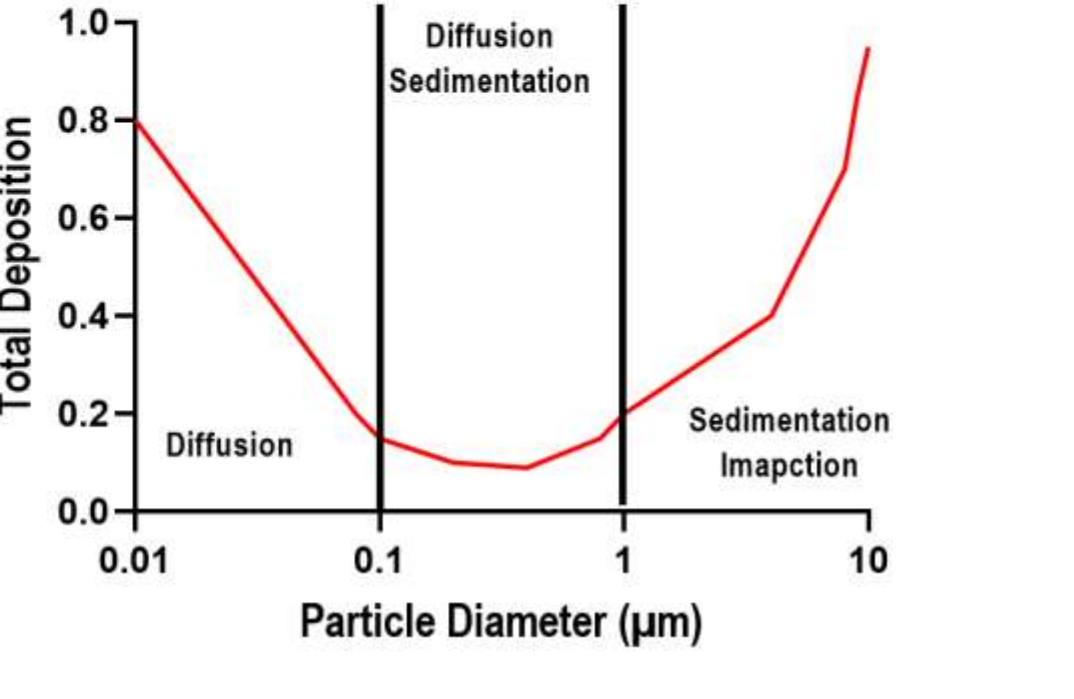
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