Morphometry and Advective Mixing Results in a Mouse Lung Acinar Model

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MOTIVATION

Understanding of transport to and within the acinar region has practical applications in targeting deposition to specific locations and hence reducing systemic absorption, and improving estimates for retention of inhaled pollutants. A recent study by Kumar et al. (2011) demonstrated the importance of alveolar geometry in estimating mixing and dispersion. Efforts at three-dimensional (3D) characterization of alveolar spaces and acini in the mammalian lung are sparse and more recent. In particular, the use of realistic 3D models of acinus for airflow and transport simulations is rare.

METHODS

A realistic 3D representation of the acinus is first obtained in a murine lung fixed using vascular perfusion at an inflation pressure of 20cmH2O. For this purpose, segmentation and isolation of a single (entire) acinus that branches out of a terminal bronchiole is carried out. S/V is computed for the acinus and its sub-structures. The model represents a single volume of the acinus. A volumetric mesh is generated and alveolar wall motion is prescribed assuming normal breathing conditions with a simple sinusoidal breathing curve. Air flow and advective mixing (of aerosol-like particles) calculations are performed.

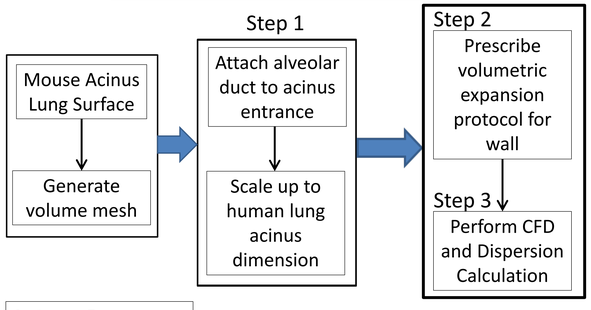
RESULTS

The final acinar structure has a S/V value of 47.5 mm^{-1}. The acinus and its sub-structure taken anywhere within its volume is observed to have almost similar Surface-to-Volume S/V ratio irrespective of the number of branches (or number of acinar generations) within the structure indicative of an inherent geometric similarity. Advective mixing analysis is performed using tracking of diffusionless particles. The particle transport calculations indicate the following. Previous calculations on simple idealized honey-comb acinar models showed that a dye released in the flow develops a fold-like characteristic at the end of one-oscillatory flow cycle. This model lacked branching and the resulting dispersion was due to (in a low-Re flow) presence of alveoli attached to a duct. In the presence of a multi-generational branching, qualitatively similar folding structures are observed. This phenomenon is related to streaming. The realistic acinar geometry obtained above is a complex 3D structure and hence the net effect of dispersion of a dye in this model is the result of both alveolation and branching.

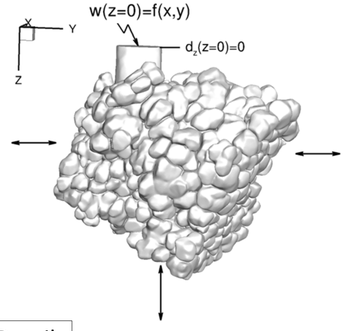
Micro-CT Image Acquisition

- C57Bl/6 mouse lung fixed by vascular perfusion at 20cm$H_2$0 (ex-vivo)
- A multi resolution scanner (MicroXCT 400, Xradia) is used. The 10x magnification provides a necessary field of view of 2×2×2mm
- Resolution of 2µm/voxel was used to allow visualization of the septal walls

Building a CFD model



Acinar Geometry

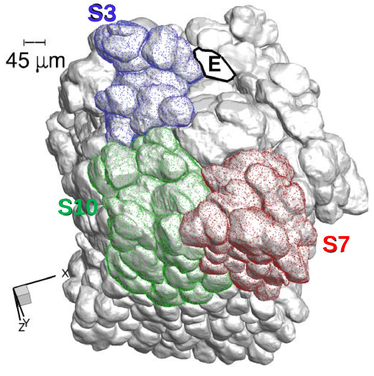


CFD Model Details

- Only radial expansion of acinar duct entrance is allowed [$d_z(z=0)=0$].
- The acinus expands uniformly in all three directions
- Expansion ratio: $(V_{max} - V_{min})/V_{min} = 0.3$
- CFD volume mesh:
  13.5 million tetrahedral elements
  2.59 million nodes
- Peak inspiratory flow : $Re_D=0.54$

Results

Morphometry Results



E → Entrance to acinus branching out of an airway

S3, S7 and S10 are sub-structures.

S3 has 7 branches and spans over last 3 acinar generations.

S7 and S10 span last 5 acinar generations.

Table of Surface-Volume Ratio (S/V):

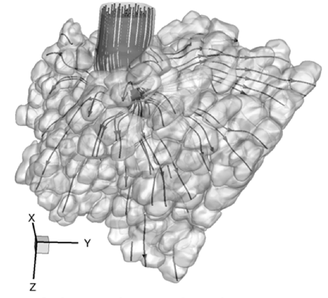
Structure Name	Number of branch points	S, surface area (mm^2)	V, volume (mm^3)	S/V (mm^{-1})
S3	3	0.2979	0.00624	47.74
S7	7	0.5608	0.01201	46.69
S10	10	0.7780	0.01654	47.04
Acinus	81	6.9154	0.14553	47.52

Summary

- S is Surface area. V is air volume. Note that
  $S_{S10} \approx 2.6$times S_{S3}
  but still $(S/V)_{S10} \approx (S/V)_{S3}$
- A geometric similarity exists in the acinus. S/V is approximately preserved independent of the number of branches

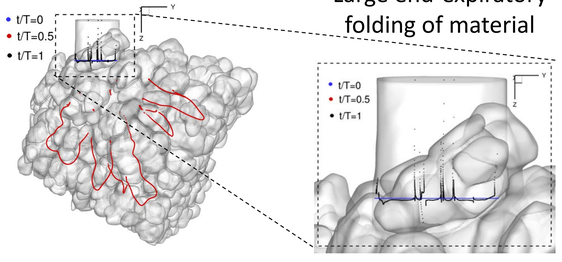
CFD and Advective Mixing Results

Snapshot of streamlines at Peak Inspiration t=T/4



Advective mixing of dye released at beginning of inspiration

Large end-expiratory folding of material



Summary

- Significant advective mixing in the form of folded dye pattern is observed at the end of one complete cycle.
- Evidence of streaming-related mixing is observed in the presence of multi-generational branching of acinus.

Acknowledgement

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