Model of the pulmonary ventilation and effects of airway properties on drug delivery to the lungs

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Objectives

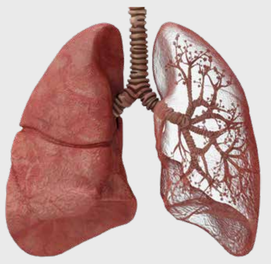
To develop a simple lung network model that outputs key breathing parameters, to inform design and overall drug delivery to the lungs under physiologically relevant conditions.

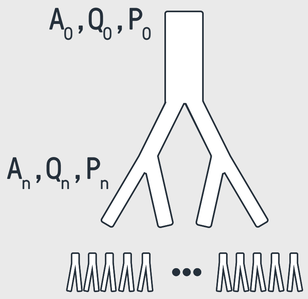
Introduction

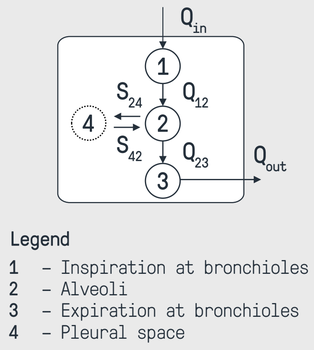
Airway and lung properties change with disease and during normal ageing. These changes could have an effect on the efficacy of inhaled drug delivery. High-dimensional models are computationally expensive and often no more accurate than lower-dimensional ones. This work provides a bifurcating compliant model of the airways, to enable comparative analysis between various states of age and health by adapting mechanical properties and observing the impact to airflow at different generations.

Methods

The airways are modelled as self-similar bifurcating trees, for inhalation and exhalation, such that there are 2^n airways per generation.



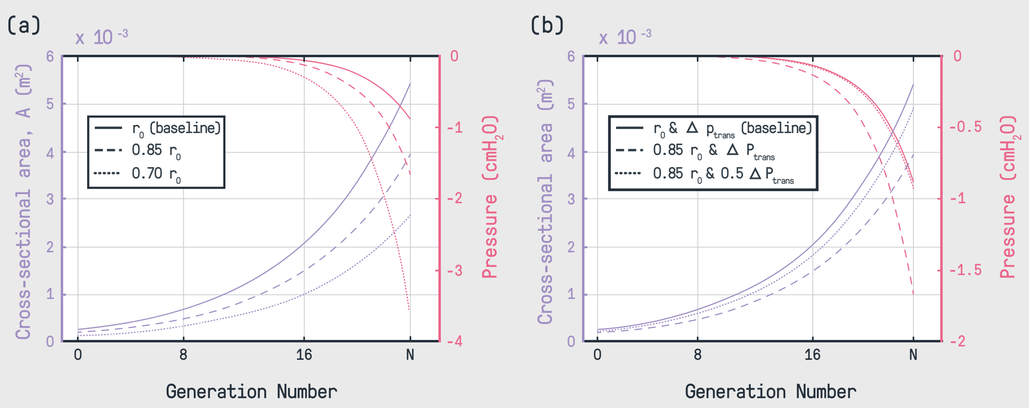




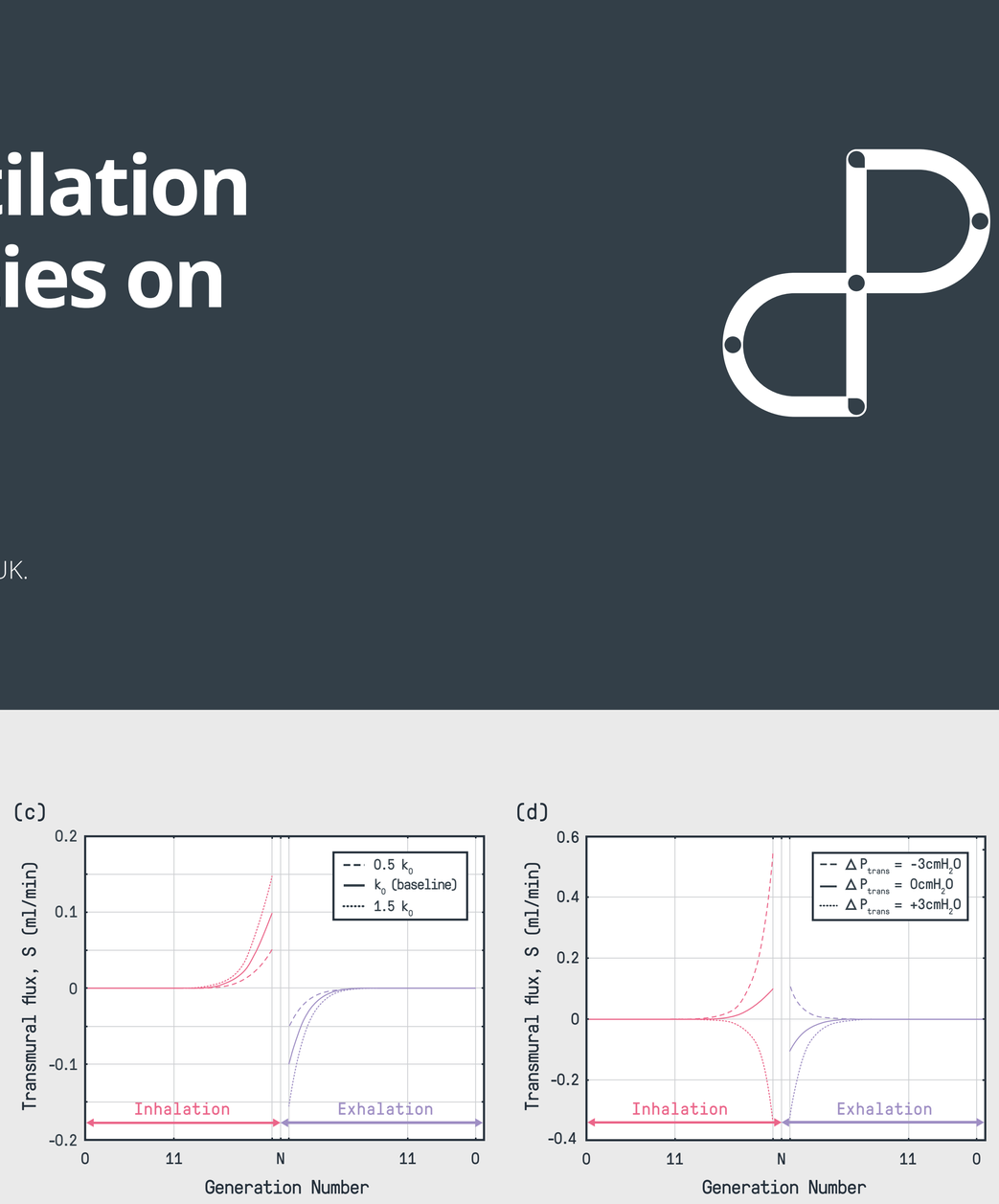
Hagen-Poiseuille flow is assumed for the airways, giving a generational pressure difference as $\Delta p_n = Q\, R_0 \frac{(\xi^n - 1)}{\xi - 1}$, where Q is the volumetric flow rate, R_0 the resistance in generation 0, and ξ^n the resistance scaling factor of generation n. Compliance is introduced by a pressure-area relationship $\Delta p_t = \frac{\beta}{A_0}(\sqrt{A} - \sqrt{A_0})$, where β is a function of the lung's stiffness, and A_0, A the cross-sectional area at generation 0 and n respectively.

Results

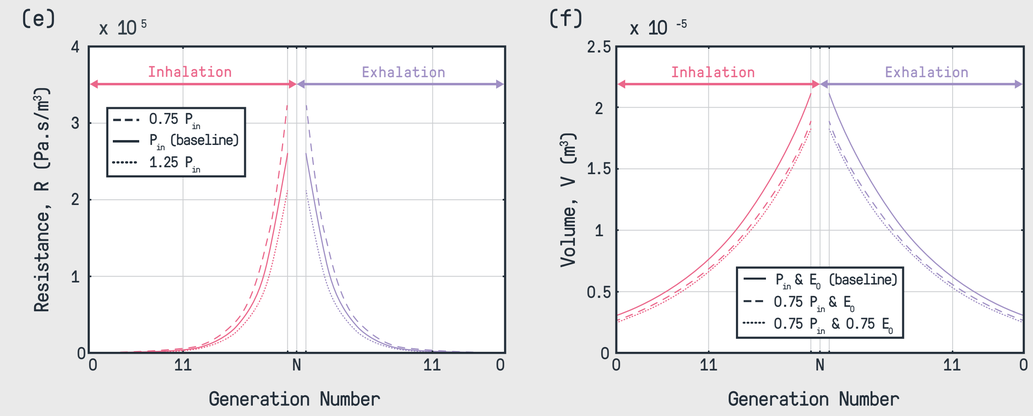
Following verification of the model against experimental anatomical data, inhalation and exhalation behaviour was observed when changes to airway properties were introduced.



Restricting the airway radii in the model to mimic the effect of airway constriction in conditions such as COPD, demonstrates the reduction in cross-sectional area available for gas exchange along with the pressure increase required to inflate the lung in Figure (a). Figure (b) shows that an increase in the transmural pressure of 50% is required while suffering from a 30% reduction in airway diameter to maintain 'normal' inhalation flow.



Concerning gas exchange at the alveoli, Figure (c) shows that changes to permeability only mildly impact transmural flux, but that changes to transmural pressure have a considerable impact, Figure (d). This highlights a potential area of interest for device designers to overcome limitations in radii and lung compliance by attempting to reduce the pressure difference relative to the pleural space to facilitate inflow.



Airway resistance and volume are two parameters of clinical importance in mechanical ventilation and design of inhalers for drug delivery. Results show the airways are resilient to changes in input pressure, Figure (e), including when accompanied by changes in stiffness, Figure (f). This may be due to higher compliance of the lungs relative to the airways, which is an important part of the respiratory system. Device design should therefore prioritise resistance relative to the compliant lung, and changes in compliance over time and disease progression should also be assessed.

Conclusions

The model presented provides a computationally inexpensive tool to assess the pulmonary airways for understanding disease, and an aid for design and development of devices for drug delivery to the lungs such as inhalers. For example, these results indicate how a patient suffering from an airway restriction will have a significantly lower inhalation pressure available to power an inhaler, which leads to a further reduced gas exchange in the alveoli during that breath. Device designers must ensure that this reduction in available drive pressure is accounted for in a Dry Powder Inhaler that is used for COPD treatment or rescue inhalers. The model makes use of compliant airways and scaling factors which will continue to be adapted to provide physiologically realistic parameters to aid study of a variety of scenarios in the respiratory system.

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