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# MODELLING OF DRUG TRANSPORT IN LUNG AIRWAYS BY POPULATION BALANCE EQUATION

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The mathematical and computational modelling of drug transport and deposition in lung airways has potential to accurately quantify effectiveness of drug delivery for respiratory diseases such as asthma and cystic fibrosis. Most of these studies have applied the Eulerian-Lagrangian (EL) approach to simulate drug transport in 3D patient-specific lung airways [1]. In the EL approach, the carrier phase (air) is resolved by the Navier-Stokes equations on an Eulerian grid and the Lagrangian tracking of individual drug particles is modelled by Newton's equation of motion. Even though the EL approach provides highly resolved fluid field with drug deposition maps, the number of simulated drug particles is limited up to a few tens of millions due to the computational cost. The number of drug particles in a single inhaled dose is much higher, therefore it is still an open question how to model inhalation of a realistic dosage with an accurate and effective model and how realistic dosages alter transport and deposition. To address these research questions, we propose to use an Eulerian-Eulerian (EE) approach, where a univariate population balance equation (PBE) coupled with the fluid solver is used to model the particle phase dynamics. The univariate PBE equation with evolving particle size distribution is given as

$$\frac{\partial n(\xi,\boldsymbol{x},t)}{\partial t} + \nabla_x \cdot [n(\xi,\boldsymbol{x},t)\widetilde{\boldsymbol{u}}] - \nabla_x \cdot [\Gamma \nabla_x n(\xi,\boldsymbol{x},t)] = \bar{B}^a(\xi,\boldsymbol{x},t) - \bar{D}^a(\xi,\boldsymbol{x},t) + \bar{B}^b(\xi,\boldsymbol{x},t) - \bar{D}^b(\xi,\boldsymbol{x},t) \quad (1)$$

where $n(\xi,\boldsymbol{x},t)$ is the number density function, $\xi$ is the particle phase size, $\widetilde{\boldsymbol{u}}$ is the "resolved" fluid velocity, $\Gamma$ is the effective diffusivity coefficient of particle phase. On the right-hand-side of Eq. (1), $\bar{B}^n(\xi,\boldsymbol{x},t)$ and $\bar{D}^n(\xi,\boldsymbol{x},t)$ denote birth and death rates, respectively. The superscript "$n$" denotes whether the birth or death rate is due to aggregation "$a$" or breakage "$b$" [2]. These terms account for the evolution of particle size distribution due to particle-particle collisions and interactions such as van der Walls or electrostatic forces. The PBE is solved by the direct quadrature method of moments implemented in the open-source OpenQBMM [2] (developed in the framework of OpenFOAM).

We performed EE simulations in *in vitro* lung airways studied by Banko et al. [3] (Fig. 1-a). We first compared the single phase flow field results with of Banko et al. measurement (Fig. 1-b) and obtained very good agreement. We then assessed the PBE model predictions of drug deposition maps through those of highly-resolved EL simulations (Fig. 1-c). EE predictions provided more uniform deposition than EL results. The source of discrepancy will be studied in a future study where we will include the particle phase velocity as an additional internal coordinate in Eq. (1).

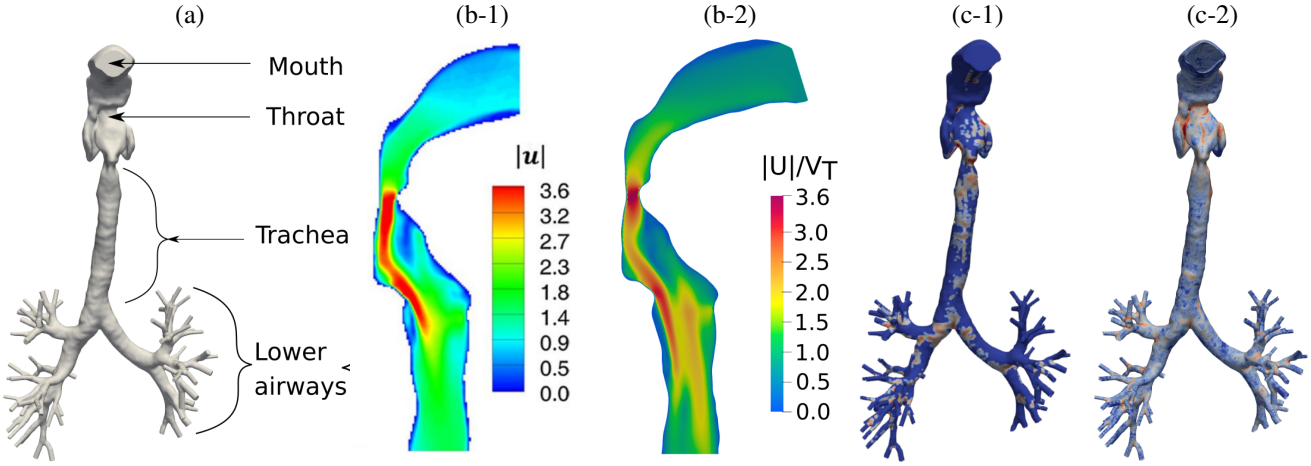


Figure 1: a) Computational domain. b) Time-averaged fluid velocity flow field in the upper airway: (b-1) *in vitro* experimental data [3], (b-2) EE predictions. c) Comparison of regional deposition with 4 $\mu$m particles simulated by c-1) EL [4] and c-2) EE predictions. Blue and red colours refer to zero and high deposition, respectively.

## References

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