

INTRODUCTION

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The purpose of the LungSim program is to investigate the human bronchial tree for geometry and function. The bronchial tree has a complex multifractal property with 23 branching generations (see Schmidt A, Zidowitz S, Kriete A, Denhard T, Krass S, Peitgen HO. (2004): A digital reference model of the human bronchial tree. *Comput Med Imaging Graph.* Jun;28(4):203-11.). The program allows to import tree data sets of a simple format, in which the branching topology is represented as a directed graph. Such trees are typically generated by image analysis of thoracic CT image sequences. These trees can be edited or extended by additional branching orders and respiratory units (acini) to improve realism in simulations. A typical complete tree contains 3000-5000 branches (bronchioles) and 30,000 respiratory units.

LungSim simulates respiratory dynamics by solving mass transport equations iteratively that include convection, diffusion and uptake. A sinusoidal pattern of inhalation and expiration is assumed. The implementation follows a method previously described (Mercer, R. R., Anjilvel, S., Miller, F. J. & Crapo, J. D. (1991): Inhomogeneity of ventilatory unit volume and its effects on reactive gas uptake. *J Appl Physiol* 70: 2193-205.). The default values are set for 10,000 time steps for a 4 second breathing cycle. The calculation time, depending on the tree complexity, can take anywhere from 10 minutes to several hours. To get acquainted with the software, the user is encouraged to reduce the number of time steps in initial trials (see under `Getting started`). The concentration values at the end of each time step are stored and can be visualized and user defined branches and paths can be investigated. The software allows to run the simulation in different simulation modes, the mode `PRESSURE` uses a predefined pressure difference between the trachea and respiratory units, where the path of the gradient is defined by the Hagen-Poiseuille law and the topology of the branching network.

LungSim can perform simulations with rudimentary graphs generated by MD-CT imaging, by adding drain volumes, also denoted as `leaves` in the software description. These drain volumes define the supplied volumes for each terminating branch. For more realistic simulations, the software allows to construct additional branches according to known branching properties. This requires to upload two additional files, a file that contains the outer surface of both lung lobes or lung segments (STL-file) and a file that contains a regular pattern of reference points (Point-files) within the volume. With these additional anatomical boundaries and landmarks, the tree can be extended up to approximately the 16th order with 7 generations spared for the respiratory units. Respiratory units consist of geometric segments with defined size and uptake properties (see Kriete A. (1998): Form and function of mammalian lung: analysis by scientific computing. *Adv Anat Embryol Cell Biol.*;145:III-IX, 1-105.). These acinar segments vary in size with breathing cycle. Properties like surface-to-volume ratios can be modified to represent changes as they occur in emphysema.