Many-Scale Modeling of Lung Poromechanics

Context & Objectives

The lungs are the primary organs of the respiratory system in humans and many animals, responsible for molecular exchanges between external air and internal blood through mechanical ventilation. It has an extraordinary complex architecture, with the inherent fractal structure of the bronchial and blood vessel trees, as well as the hierarchical structure of the parenchyma. Lung biomechanics has been extensively studied by physiologists, experimentally as well as theoretically, from the air flow, blood flow and tissue stress points of view, laying the ground for our current fundamental understanding of the relationship between function and mechanical behavior. However, many questions remain, notably in the intricate coupling between the multiple constituents, between the many phenomena taking place at different spatial and temporal scales in health and disease. For example, even for healthy lungs, there is no quantitative model allowing to link tissue-level and organ-level experimental material responses.

These fundamental questions represent real clinical challenges, as pulmonary diseases are an important health burden. Interstitial lung diseases, for instance, affect several million people globally. Idiopathic Pulmonary Fibrosis (IPF), notably, a progressive form of interstitial lung diseases where some alveolar septa get thicker and stiffer while others get completely damaged, remains poorly understood, poorly diagnosed, and poorly treated, with a current median survival rate inferior to 5 years. It has, however, been hypothesized that a mechanical vicious cycle is in place within the parenchyma of IPF patients, where fibrosis and damage induce large stresses, which in turn favor fibrosis.

The general goal of this project is twofold: (i) scientifically, to better understand pulmonary (solid) mechanics, from the alveolar scale to the organ in health and (IPF) disease; (ii) clinically, to improve diagnosis and prognosis of (IPF) patients through personalized computational modeling. More precisely, the student will develop a many-scale model of the parenchymal biomechanics, at all relevant spatial scales from the alveolus to the organ, and at the temporal scales of the breathing cycle and fibrosis process. Different representations at successive spatial scales will be linked by a computational nonlinear homogenization strategy with a priori model reduction based on a neural network. The model will integrate the rather unique experimental data produced by Drs. Bel-Brunon and Trunfio-Sfarghiu from LaMCoS

(INSA-Lyon), *i.e.*, microtomography images at alveolar scale and inflation tests of lobules: microstructures will be extracted from the images and systematically analyzed, and model parameters will be estimated from the mechanical tests. The model will also integrate clinical-radiological data provided by Profs. Nunes and Brillet from Avicenne APHP Hospital, *i.e.*, standard pulmonary function tests and thoracic computed tomography imaging on IPF patients as well as normal lung controls: a pipeline to estimate observable model parameters from clinical data will be set up, and generic values will be defined for the remaining parameters. The model and estimation procedure will represent augmented diagnosis and prognosis tools for the clinicians.

Keywords

Pulmonary Biomechanics; Image-based Modeling; Finite Element Method; Computational Homogenization; Neural Networks; Data assimilation

Candidate profile

The candidate will have to master continuum mechanics, with if possible knowledge of finite strains, biomechanics, and numerical methods. He/She will also have an interest in the application in pneumology, especially for interacting with clinical collaborators.

Work environment

The thesis will take place within the M3DISIM team (joint between École Polytechnique & Inria and within the Solid Mechanics Laboratory), on the École Polytechnique campus. It will be in tight collaboration with the LaMCoS at INSA-Lyon. It will be co-directed by Martin Genet, Aline Bel-Brunon & Dominique Chapelle. It should start in 2020.

Bibliography

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