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Mucus and ciliated cells of human lung : splitting strategies for particle methods and 3D stokes flows

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ABSTRACT

Lung walls are covered by a film of mucus, whose motility is fundamental for a healthy behavior. Indeed, mucus traps inhaled aerosols (bacteria, dust, ...), and moves from smallest to largest airways, until it reaches esophagus where it is swallowed or expectorated. A lot of biological parameters are responsible for mucus motion [6], such as the vibrations of ciliated cells covering lung walls (cilia height, frequency, ...), mucus/air interaction, water saturation in mucin network, mucus thickness, ...

A change in these biological parameters can lead to dramatic dysfunction of mucus, usually leading to insufficient motility. One of our focuses is cystic fibrosis, which results in an increased mucus viscosity, leading to bacteria proliferation and severe pathologies [1]. Another example is ciliotoxic inhalation, such as nicotine, leading to stop the beating of ciliated epithelium. The numerical simulation allows to split apart different phenomena and to investigate which one is dominant, depending on the biological configuration considered.

The present work focuses on numerical strategies to compute mucus flow around a ciliated epithelium cell (see figure 1). We consider a variable viscosity flow around a complex moving geometry. The Reynolds number $Re \simeq 10^{-8}$ is very small and governing equations of momentum are reduced to the quasi-static Stokes problem. Viscosity and density are spatially variable and satisfy the same transport equation depending on mucus velocity, itself satisfying the 3D Stokes equation depending of viscosity.

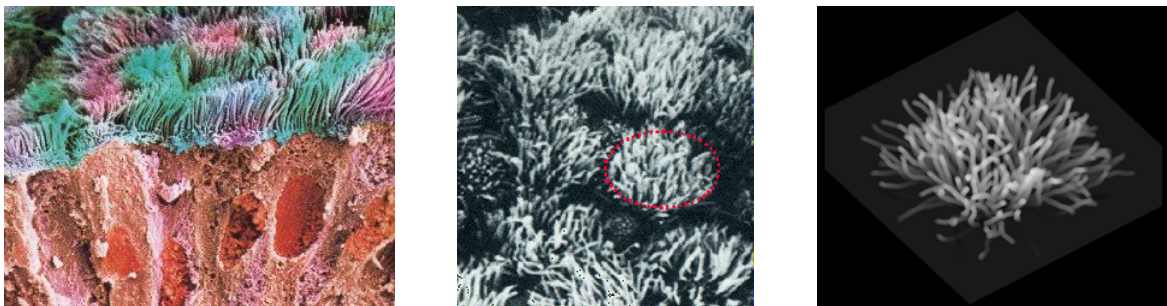


Figure 1: Views of respiratory epithelial cells (to the left and to the middle, red dots show a cell delimitation) and ciliated cells used in numerical simulation (to the right).

Here we consider a computational box Q split into a body denoted $B(t)$ containing the epithelial cell, and a fluid domain denoted $\Omega(t) = Q \setminus \overline{B(t)}$. In body $B(t)$, velocity is imposed $u = \bar{u}$ by a penalization method. The cilia velocity \bar{u} follows a first order hyperbolic equation taking into account the actin polymerization process of beating (model of elastic beams of variable modulus). This sets up a one-way coupling between cells and fluid.

Given these assumptions the fluid equations in complex and moving geometry are

$$\partial_t \mu + u \cdot \nabla \mu = 0 \quad \text{in } Q \quad (1)$$

$$-\operatorname{div}(\tau) + \nabla p + \frac{\chi(t)}{\varepsilon}(u - \bar{u}) = f \quad \text{and} \quad \operatorname{div} u = 0 \quad \text{in } Q \quad (2)$$

$$u(x, t) = 0 \quad \text{or} \quad \partial_n u(x, t) = 0 \quad \text{on } \partial Q \quad (3)$$

where $\chi(t)$ is the characteristic function of body $B(t)$, and $\tau = \mu(\nabla u + \nabla u^T)$ the strain rate tensor. At a Mathematical level, this is a non-linear coupling between second-order elliptic and first order hyperbolic partial differential equations.

As transport phenomena are dominant, a particle method is used to solve equation (1) using grid-particle formulation. Velocity follows the 3D Stokes equation (2) and is computed on staggered grids, on which geometry is penalized (such as in [2]). Interpolated between grid and particles by means of Monaghan's M_4' kernel. To the opposite of moderate or high Reynolds number flows, effect of boundary conditions (3) are not localized in the wall neighborhood [4] and panel methods are not efficient: a fixed point based on a divergence free projection is then used [3] to satisfy boundary conditions.

One can rewrite the diffusion term as $\mu^{-1} \operatorname{div} \tau = -\Delta u + \tau \nabla \ln \mu$ which allows to solve equation (2) by means of an iterative process involving only Poisson equations, and thus allowing the use of fast second and fourth-order elliptic solvers. These standard PDEs are fast to solve and also avoid to store matrix coefficients, in the same philosophy as most modern particle or vortex methods.

Future work will use heavily this computational method in order to identify biological behavior by means of neural networks, with a machine learning performed in the same spirit as [5].

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