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# Particle methods for the dynamics of porous biofilms with heterogeneous rheology and its interaction with lung epithelium

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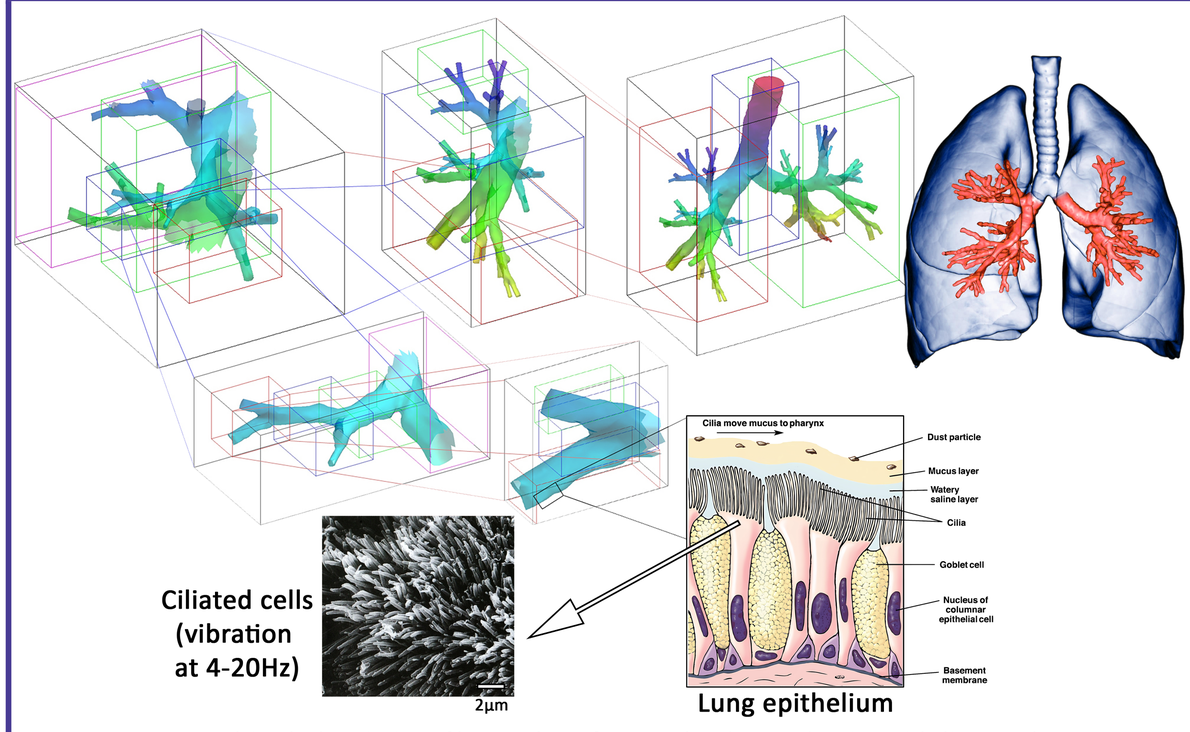
## Context: upscaling flow around lung cells




*Multiscale description of human lung from trachea ($\sim 2cm$) to its epithelium at the 6-7th generations ($\sim 10\mu m$ high), one cilia being 100nm wide (sketch inspired from [8]).*

## From DNS of the pore scale reactive flows

The superficial velocity $u$ follows the Darcy-Brinkman-Stokes equation in a porosity field $\varepsilon$, which defines a pure liquid phase where $\varepsilon = 1$ and a solid matrix where $\varepsilon$ is small :

$$\varepsilon^{-1}\frac{\partial(\rho u)}{\partial t} + \varepsilon^{-1}\mathrm{div}\,\left(\varepsilon^{-1}\rho u \otimes u\right) - \varepsilon^{-1}\mathrm{div}\,\left(2\mu D(u)\right) + \mu^* K^{-1} u = f - \nabla p \qquad (1)$$

along with $\mathrm{div}\, u = 0$, using the usual notations. The permeability $K$ of the lower scale is driven by the Kozeny-Carman relation $K(\varepsilon) = K_0\varepsilon^3(1-\varepsilon)^{-2}$. Given the scales, it reduces to

$$-\mathrm{div}\,(2\mu D(u)) + \mu^* K_0^{-1}\frac{(1-\varepsilon)^2}{\varepsilon^2}u = \varepsilon(f - \nabla p) \qquad (2)$$

An acid of concentration $C$ dissolves a solid of molar volume $m$ at rate $r$ following

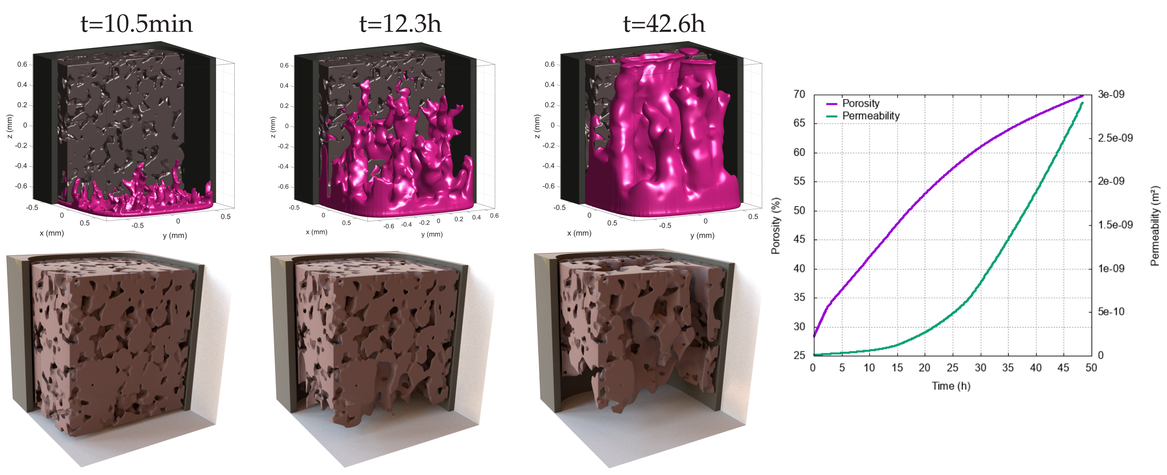
$$\frac{\partial C}{\partial t} + \mathrm{div}\,(\varepsilon^{-1}u\,C) - \mathrm{div}\,(d_m\varepsilon^{1+\beta}\nabla\varepsilon^{-1}C) = -r(C,\varepsilon) \quad \text{and} \quad \frac{\partial \varepsilon}{\partial t} = -m\,r(C,\varepsilon) \qquad (3)$$

where $d_m$ is molecular diffusion of the acid and $\beta$ is the index of tortuosity within the solid.

Using a particle method for (3) means that we describe the fluid by a set of volumes $v_p$, concentrations $c_p$, and locations $\xi_p$. Then, one gets the *particle formulation* of (3) :

$$\frac{dC_p}{dt} = \left[\mathrm{div}\,(d_m\varepsilon^{1+\beta}\nabla\varepsilon^{-1}C) - Cu\cdot\nabla\varepsilon^{-1}\right]_{\xi_p},\ \frac{d\xi_p}{dt} = \varepsilon^{-1}u(\xi_p),\ \frac{dv_p}{dt} = \left[\mathrm{div}\,(\varepsilon^{-1}u)\right]_{\xi_p} v_p \qquad (4)$$

with back and forth high order interpolations from the grid used to solve (2).




*Dissolution of a 5% porous calcite body (1.43mm wide) at pH=2, following model (2, 3). See [2] for more details and the validation of the numerical method (4) in [3]. The resulting porosity/permeability is displayed to the right.*

## To the DNS of lung cells with PCL/mucus biofilm

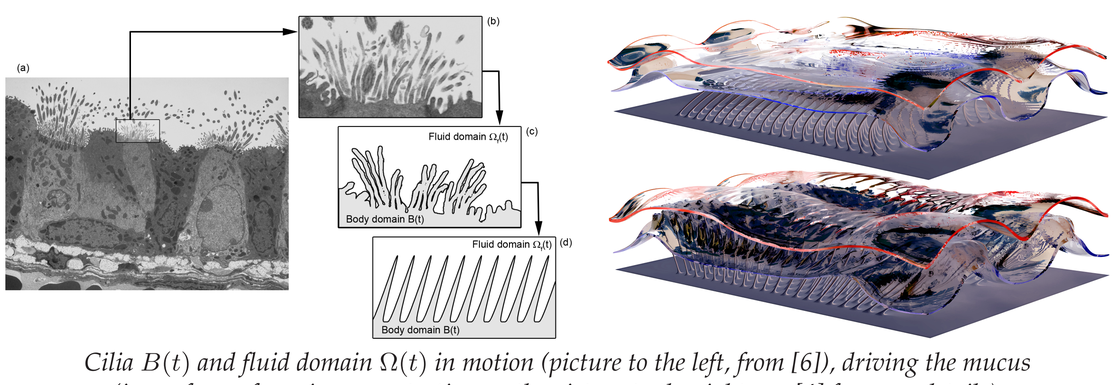
The lung epithelium (the ciliated cells $B(t)$) is surrounded by a Newtonian pericelial liquid (PCL) of viscosity $\mu_\infty$ and a miscible shear-thinning mucus composed of mucin proteins at concentration $C$.

Model (2, 3) is still valid but in this case, the fluid is not reacting ($r = 0$) and $K(\varepsilon) = \mathbf{1}_{B(t)}/\varepsilon$. Here (2) and (3) are coupled by means of the Carreau relationship defining the viscosity of the heterogeneous non-Newtonian fluid (see [5] for instance) :

$$\mu(\alpha, D) = \mu_\infty + \mu_\infty\left[\left(\frac{B}{\mu_\infty}\right)^\alpha d_0^{1-N} - 1\right]\left[1 + 2\frac{D:D}{d_0^2}\right]^{\alpha(N-1)/2} \qquad (5)$$

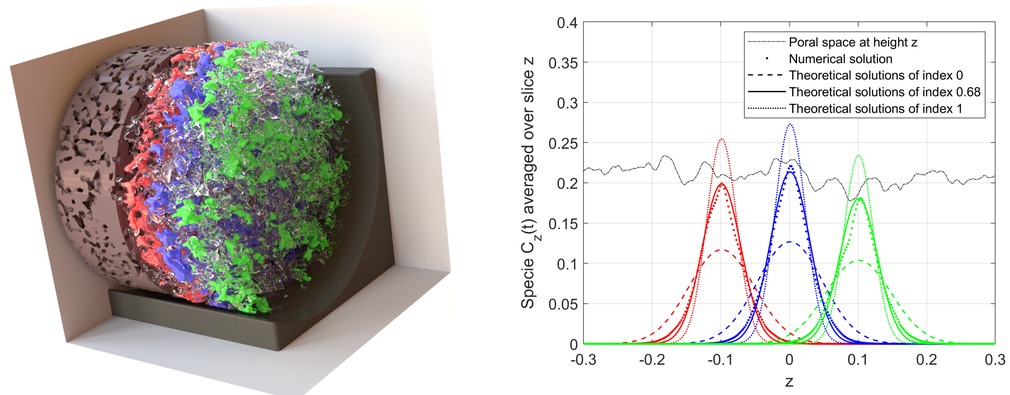
where $D$ is the shear-rate and $\alpha = C/C_0$ the renormalized concentration of mucin ($d_0$ is the cut-off frequency and $C_0$ the maximum admissible concentration of mucins).

In this model, only two "patient specific" parameters remain: the bulk viscosity $B$ and the shear-thinning index $N$ (see the clinical context thereafter).




*Cilia $B(t)$ and fluid domain $\Omega(t)$ in motion (picture to the left, from [6]), driving the mucus (isosurfaces of mucin concentration on the picture to the right, see [4] for more details).*

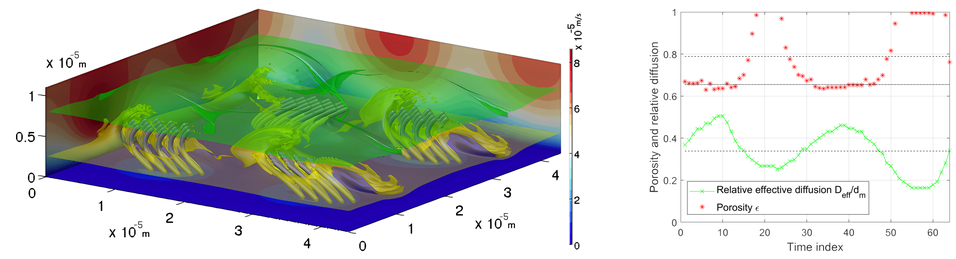
## From the upscaling of the pore scale diffusion




*Diffusion in this sandstone, which is 21% porous, leads to a **tortuosity index of $\beta = 0.68$**. This means that the upscaled diffusion coefficient in an homogeneous medium is $\varepsilon^\beta$ times the molecular diffusion (taken from [1]).*

## To the upscaling of the diffusion within lung cell

Diffusion within ciliated cell with time-dependent geometry is upscaled and computed using the same technique as above. It is required in order to estimate the mucin slip-through dynamics. The resulting tortuosity index $\beta(t)$ is shown to be relatively time independent.

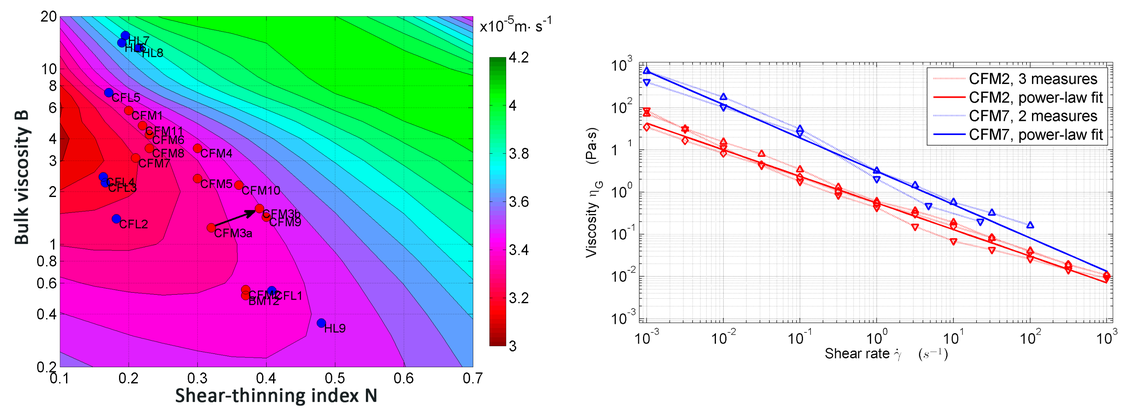



*Cilia carpet with time-dependent geometry (left picture, from [7]) and resulting time-dependant effective diffusion and porosity (right picture). This leads to a **tortuosity index at $\beta \simeq 0.4$** when not in flat shape configuration.*

## Clinical context: monitoring of therapies for cystic-fibrosis

Rheology coefficients $B$ and $N$ have been measured from expectoration samples of cystic fibrosis patients. Experiments were carried out on a Mars III rheometer equipped with a cone and plate geometry (angle $1^o$, diameter 35mm) which required a small volume of fluid (0.2ml).

It has been shown in [5] that numerical simulation of mucus dynamics are coherent with clinical data: slow mucus motion coincides with CF patients, while the highest mucus motions correspond to healthy people.




*$(B, N)$ phase diagram with clinical data from [5] (figure to the left). Examples of robust estimation of coefficients $B$ and $N$ by rheometry, using aliquoting of mucus samples (figure to the right) .*

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*— In the memory of Stephen Whitaker —*