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PARTICLE METHODS FOR THE DYNAMICS OF POROUS BIOFILMS WITH HETEROGENEOUS RHEOLOGY AND ITS INTERACTION WITH LUNG EPITHELIUM

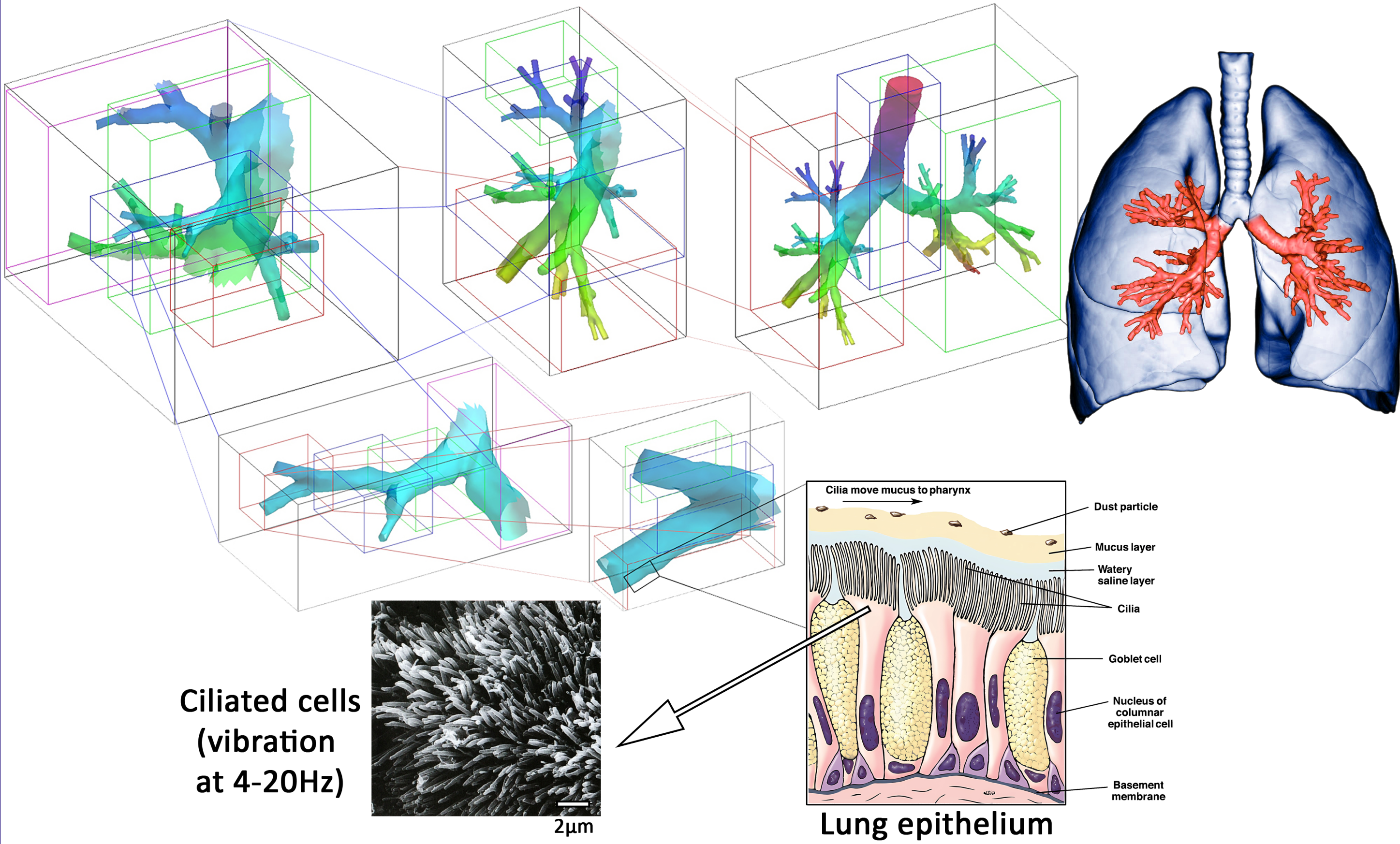
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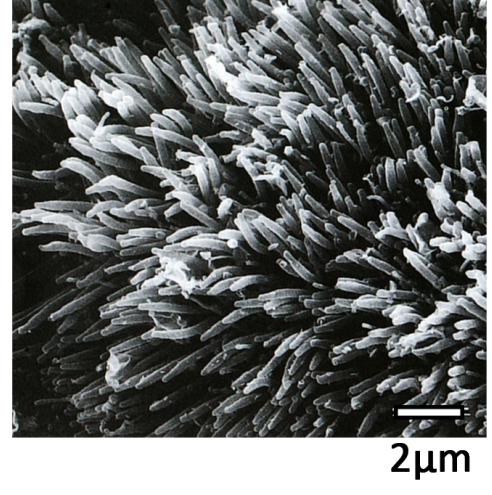
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CONTEXT: UPSCALING FLOW AROUND LUNG CELLS



Ciliated cells
(vibration
at 4-20Hz)



Lung epithelium

Multiscale description of human lung from trachea ($\sim 2\text{cm}$) to its epithelium at the 6-7th generations ($\sim 10\mu\text{m}$ 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 ε , which defines a pure liquid phase where $\varepsilon = 1$ and a solid matrix where ε is small :

$$\varepsilon^{-1} \frac{\partial(\rho u)}{\partial t} + \varepsilon^{-1} \text{div} (\varepsilon^{-1} \rho u \otimes u) - \varepsilon^{-1} \text{div} (2\mu D(u)) + \mu^* K^{-1} u = f - \nabla p \quad (1)$$

along with $\text{div } u = 0$, 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

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

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

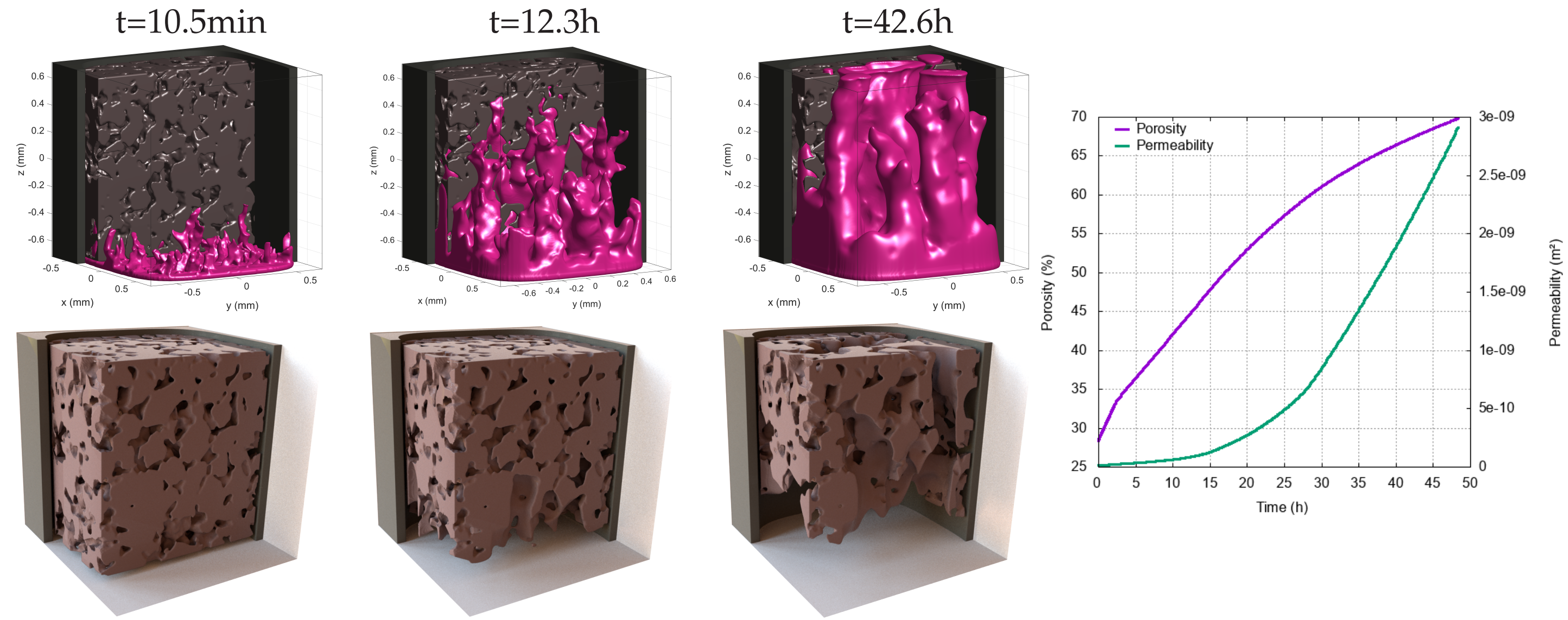
$$\frac{\partial C}{\partial t} + \text{div} (\varepsilon^{-1} u C) - \text{div} (d_m \varepsilon^{1+\beta} \nabla \varepsilon^{-1} C) = -r(C, \varepsilon) \quad \text{and} \quad \frac{\partial \varepsilon}{\partial t} = -m r(C, \varepsilon) \quad (3)$$

where d_m is molecular diffusion of the acid and β 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 ξ_p . Then, one gets the *particle formulation* of (3) :

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

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

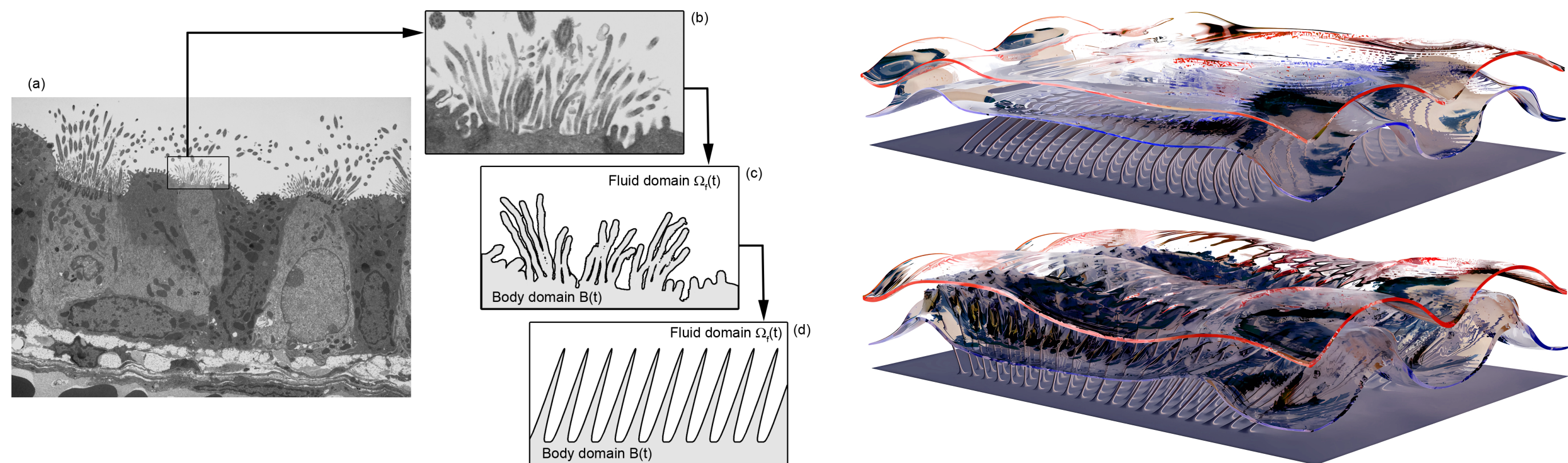
The lung epithelium (the ciliated cells $B(t)$) is surrounded by a Newtonian pericelial liquid (PCL) of viscosity μ_∞ and a miscible shear-thinning mucus composed of mucin proteins at concentration C .

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) :

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

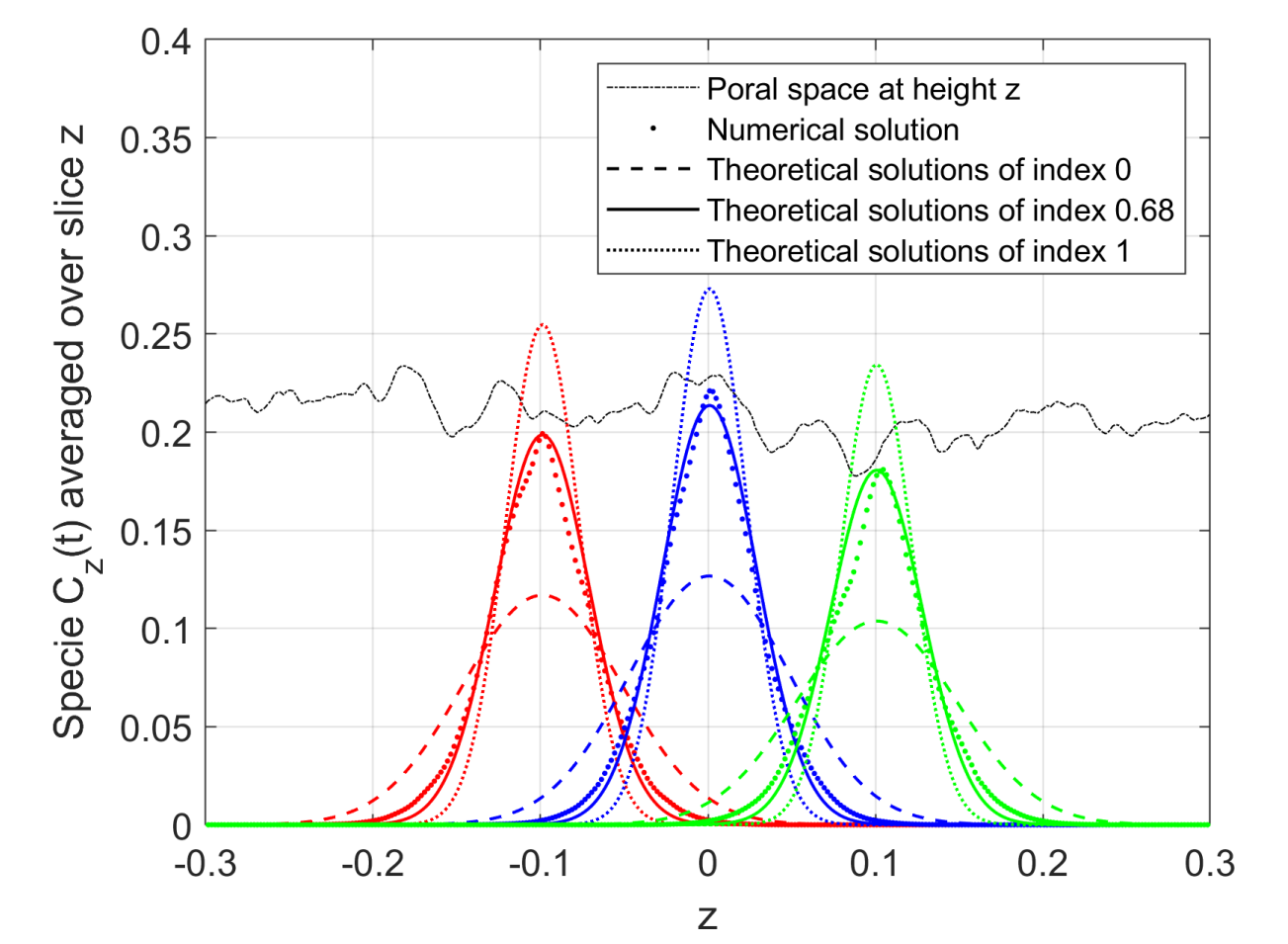
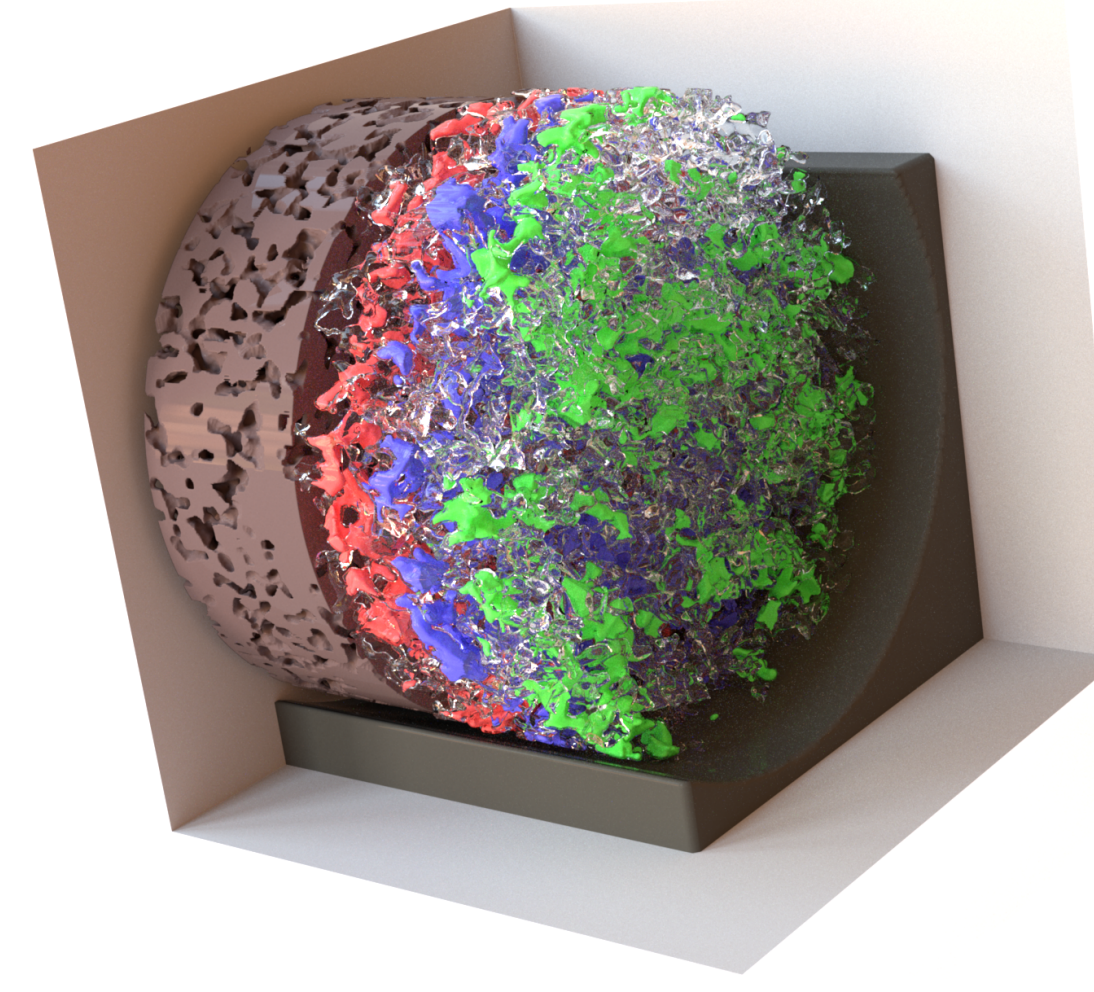
where D is the shear-rate and $\alpha = C/C_0$ the renormalized concentration of mucin (d_0 is the cut-off frequency and C_0 the maximum admissible concentration of mucins).

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).

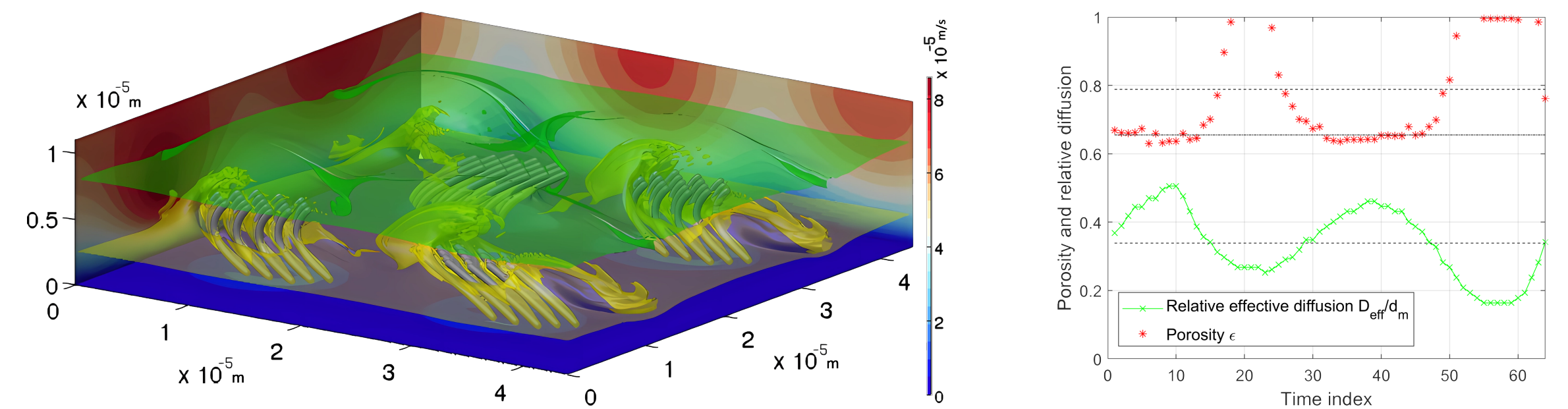
FROM THE UPSCALING OF THE PORE SCALE DIFFUSION



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 ε^β 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.

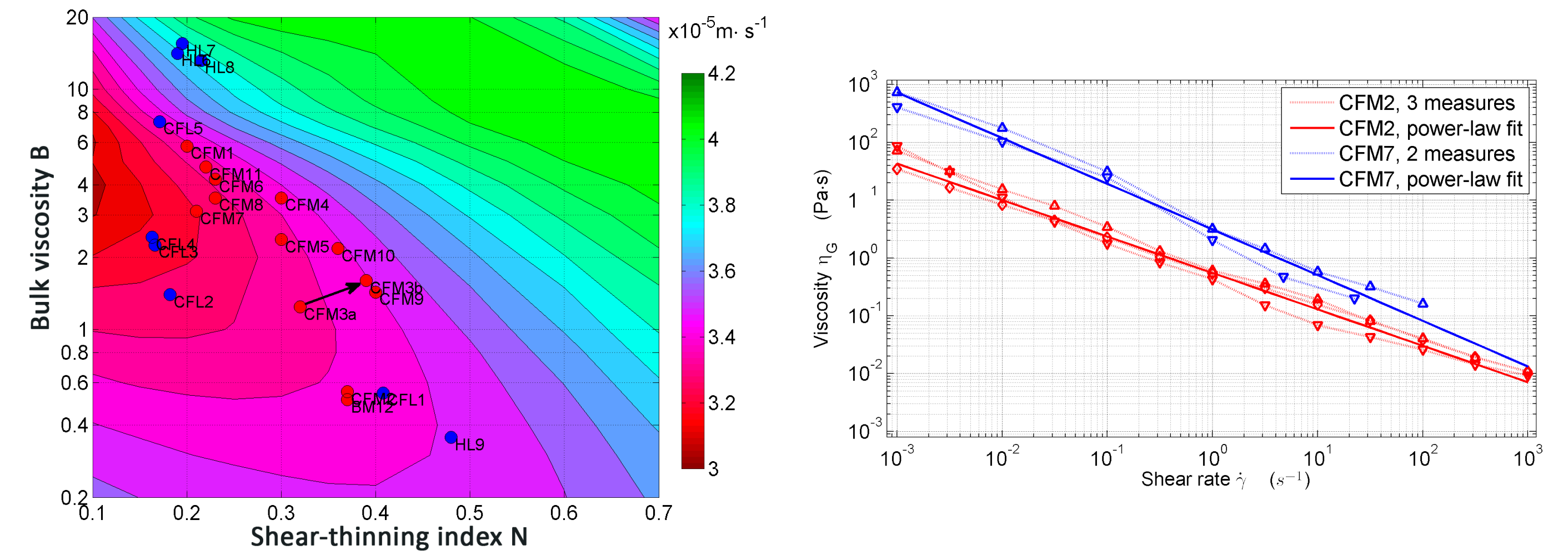


Cilia carpet with time-dependent geometry (left picture, from [7]) and resulting time-dependant effective diffusion and porosity (right picture). This leads to a **tortuosity index at $\beta \simeq 0.4$** when not in flat shape configuration.

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° , 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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AUTHORS AND ACKNOWLEDGMENTS



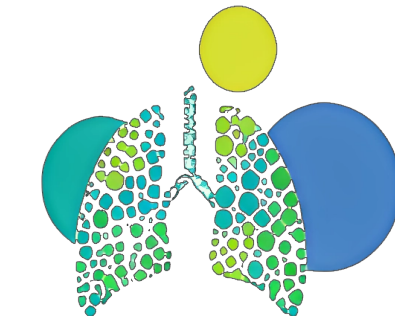
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— In the memory of Stephen Whitaker —