Modeling of mucus draining from the lungs.

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The questions.

Chest physiotherapy is a common treatment,
used to treat infant bronchiolitis, cystic fibrosis, COPD, etc.

But :

1- CP technics are **numerous**: what are the best ones?
2- CP technics are **empirical**: do they work?
3- CP efficiency has been subjected to a **controversy**: how to answer?

To deal with these questions,
the phenomena induced by CP in the lungs need **to be studied scientifically.**

One way is to **model** the biophysical phenomena occuring in the lungs during CP.

Modelling!

The **modelling process** decomposes into

Physiology

What are the biological, morphological, medical properties of the organ(s) involved in CP?

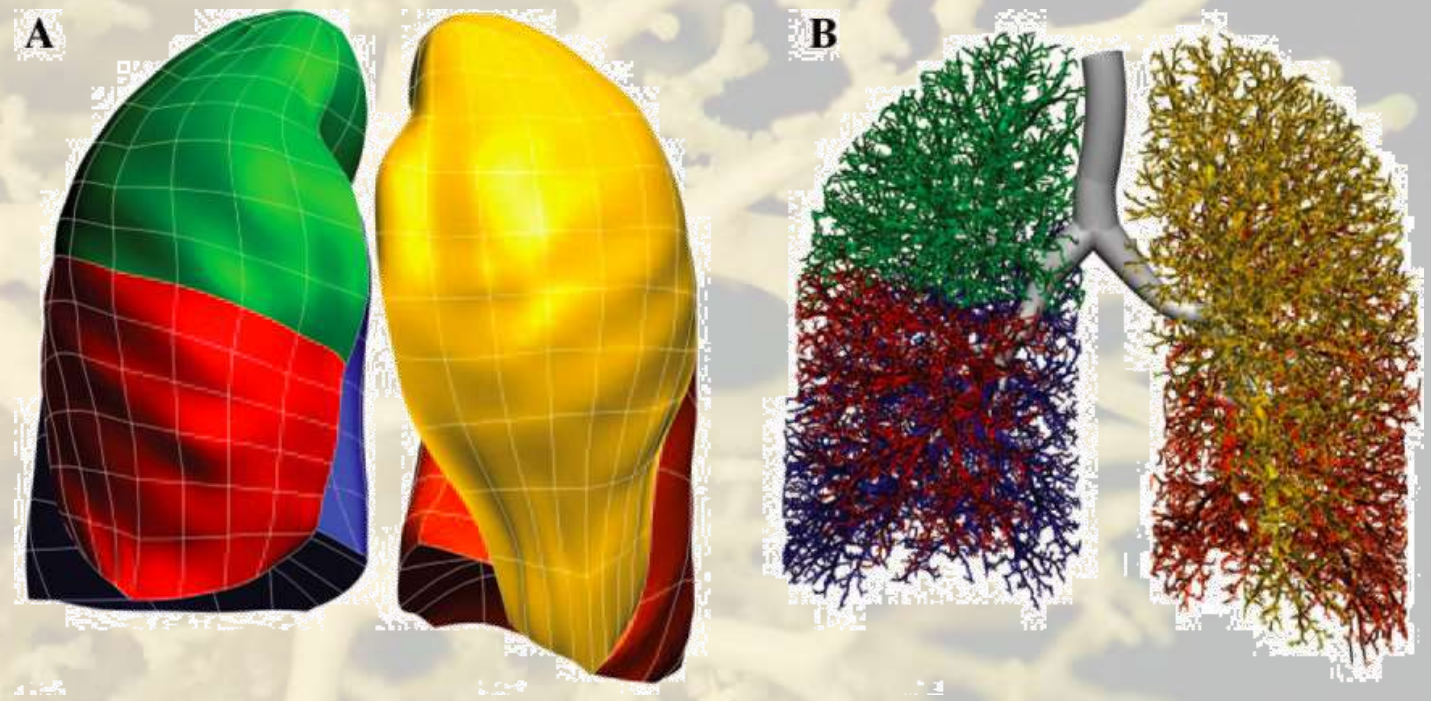
Physics

What physical processes are relevant and are driving the problem we want to study?

Mathematics

How do the interactions between physiology and physics can be translated into mathematical language, and studied?

Physiology - geometry.



From Merryn H. Tawhai et al, J. App. Physiol, 2004

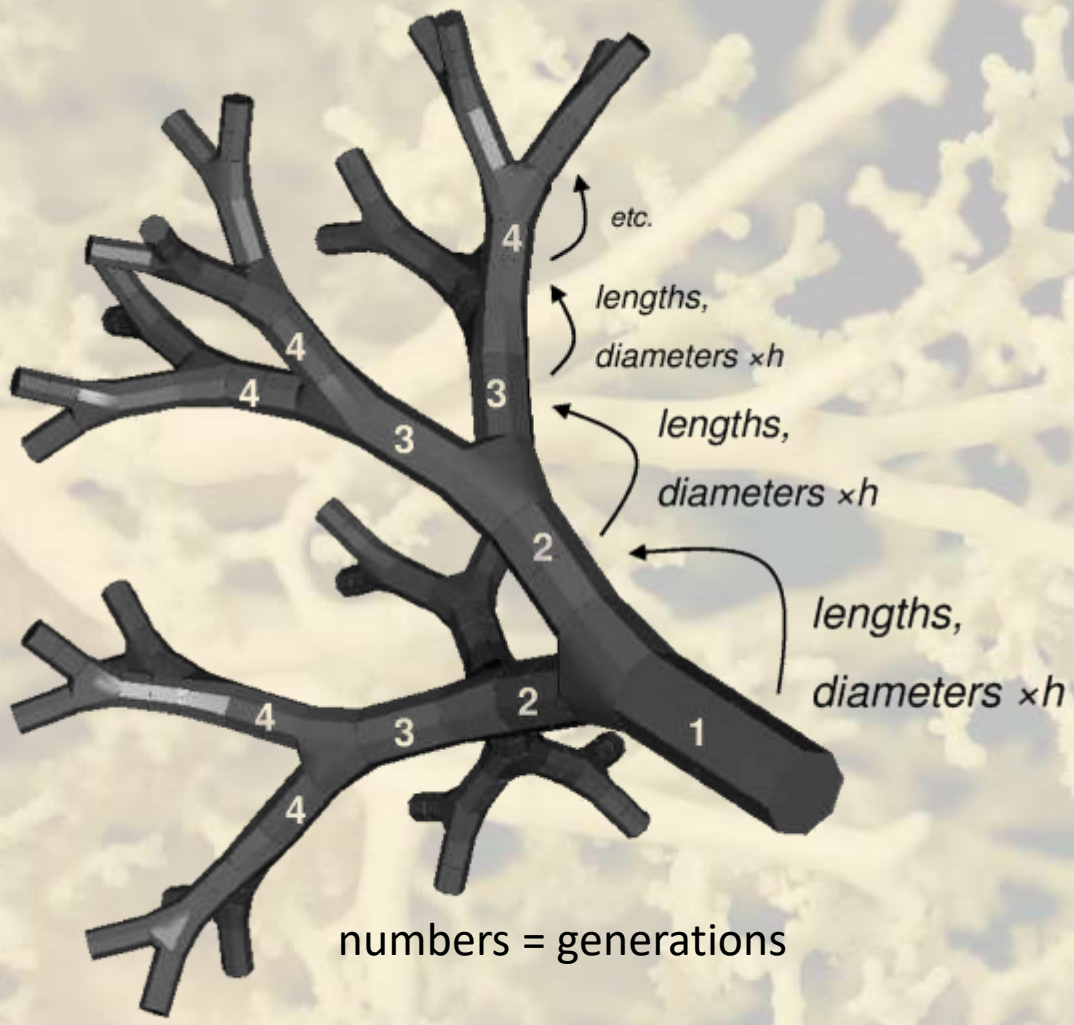
Physiology - geometry.

Hypotheses:

Each bronchus is a cylinder.

The lung is modeled as a symmetric, bifurcating fractal tree.

Physiology - geometry.



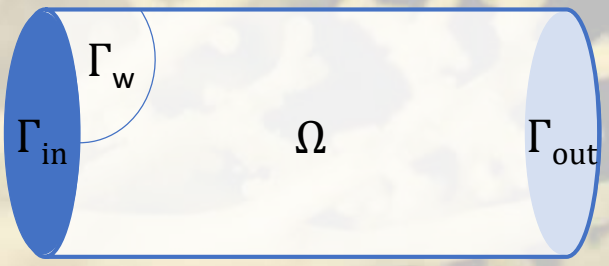
numbers = generations

$$r_n = h^{n-1} r_1$$

$$l_n = h^{n-1} l_1$$

Physics - Airflow

Air is flowing inside the bronchi and checks the incompressible Navier-Stokes equations.



$$\rho \frac{\partial u}{\partial t} + \rho\,(u.\nabla)u - div(\Sigma) = 0$$

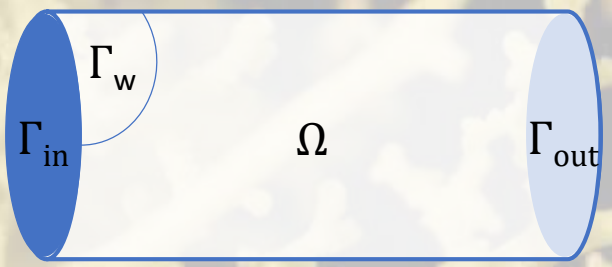
$$\Sigma = -pI + \frac{\mu_a}{2}(\nabla u + {}^t\nabla u)$$

$$div(u) = 0$$

$$u|_{\Gamma w} = 0$$

$$\Sigma.n|_{\Gamma_{in} \cup \Gamma_{out}} = f(x,t)$$

Simplification of Navier-Stokes equations.



Global existence and smoothness of solutions
for 3D Navier-Stokes equations is still an open problem.

As of today, partial results only have been proven.

$$\rho \frac{\partial u}{\partial t} + \rho\,(u.\nabla)u - div(\Sigma) = 0$$

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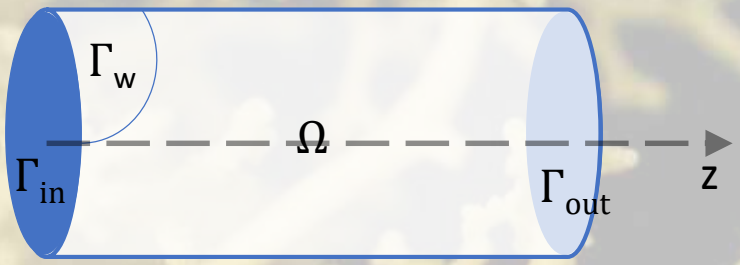
Properties of Navier-Stokes equations.



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axi-symmetry
stationary
developed

$$-\frac{1}{r}\frac{\partial}{\partial r}(r\,\sigma_{zr}) + \frac{dp}{dz} = 0$$

$$\sigma_{zr} = \mu_a \frac{du_z}{dr}$$

$$u_z|_{\Gamma w} = 0$$

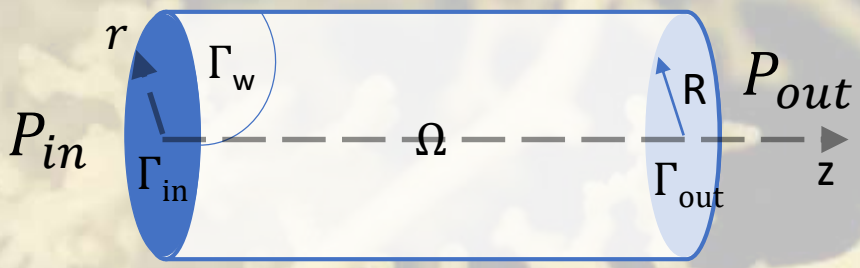
$$p|_{\Gamma_{in}} = P_{in}$$

$$p|_{\Gamma_{out}} = P_{out}$$

Developed -> air velocity is independent on z

Galdi showed that the velocity profile on a section of a semi infinite tube converges exponentially toward the Poiseuille profile along the tube axis

Properties of Navier-Stokes equations: Poiseuille's law



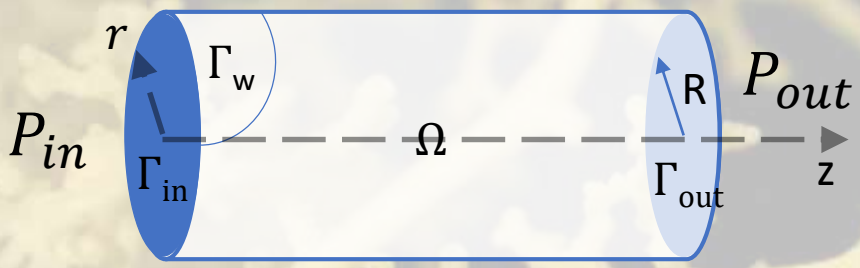
Poiseuille profile

$$u_z(r) = u_0(1 - r^2/R^2)$$

$$p(z) = Pout + z\,(Pin - Pout)/L$$

$$P_{in} - P_{out} = R\,\phi$$

Properties of Navier-Stokes equations: Poiseuille's law



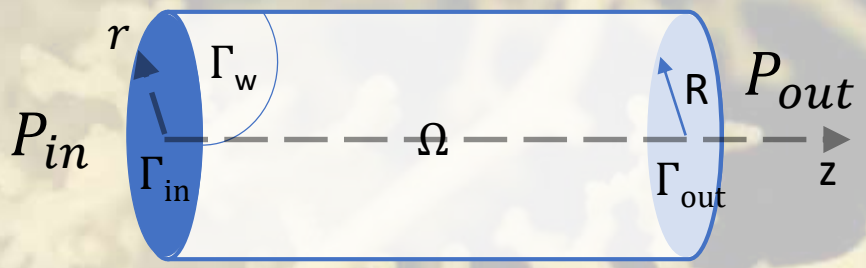
Poiseuille profile

$$u_z(r) = u_0(1 - r^2/R^2)$$

$$p(z) = Pout + z\,(Pin - Pout)/L$$

$$\approx \text{Force}\ \boxed{P_{in} - P_{out}} = R\,\boxed{\phi}\ \approx \text{Amount of matter motioned}$$

Properties of Navier-Stokes equations: Poiseuille's law



Poiseuille profile

$$u_z(r) = u_0(1 - r^2/R^2)$$

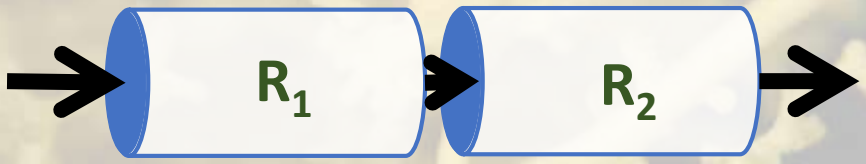
$$p(z) = Pout + z\,(Pin - Pout)/L$$

$$R = \frac{8\mu_a l}{\pi r^4}$$

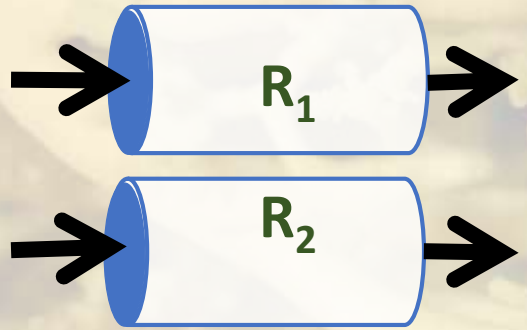
Hydrodynamic resistance

≈ Force $\boxed{P_{in} - P_{out}} = \boxed{R}\,\boxed{\phi}$ ≈ Amount of matter motioned

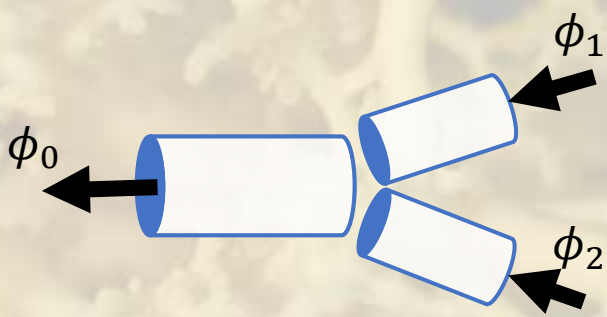
Properties of Navier-Stokes equations.



$$R = R_1 + R_2$$

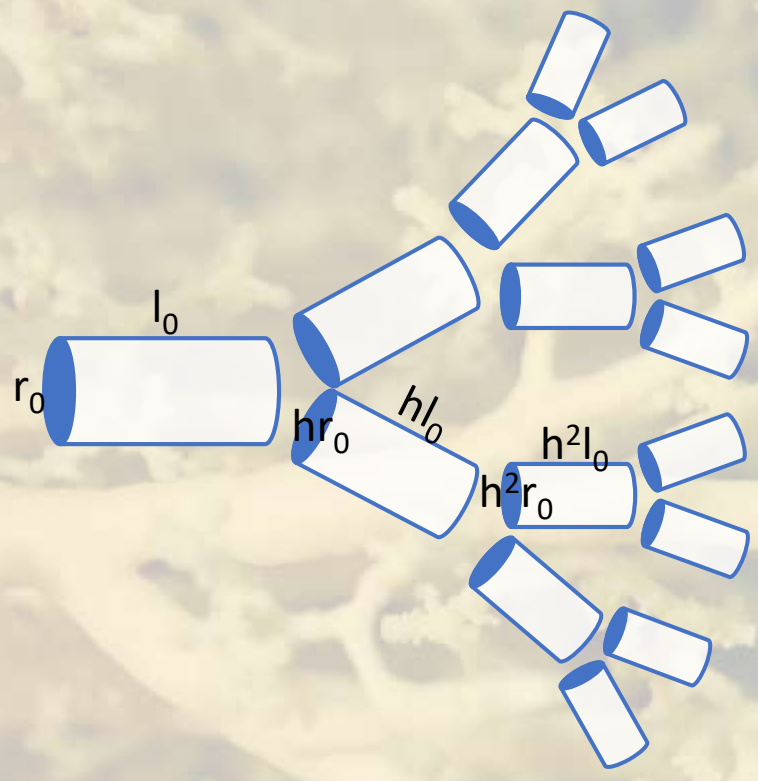


$$1/R = 1/R_1 + 1/R_2$$



$$\phi_0 = \phi_1 + \phi_2$$

Properties of Navier-Stokes equations.



Hydrodynamic resistance of the first generation

$$R = \sum_{i=0}^{N} \frac{1}{2^i} \frac{8\mu_a h^i l_0}{\pi h^{4i} {r_0}^4} = \boxed{\frac{8\mu_a l_0}{\pi {r_0}^4}} . \frac{1 - \left(\frac{1}{2h^3}\right)^{N+1}}{1 - \frac{1}{2h^3}}$$

We have here a **simple model** for studying the **airflow in the lungs**:

$$P_{muscles} = R|\phi|$$

More **complex** models exist, for example if the bronchi are not **bifurcating symetrically**, this involves a large symmetric positive definite matrix called the **resistance matrix** with remarkable properties (introduced by Grandmont, Maury, Meunier).

Physiology - mucus.

messy picture here,
to illustrate mucus
physiology
(you really do not want to
see that)

Mucus is localized **on the bronchi walls** where it forms a layer.

It is regularly replaced and motioned up the bronchial tree thanks to cilia located on the bronchi walls and to cough.

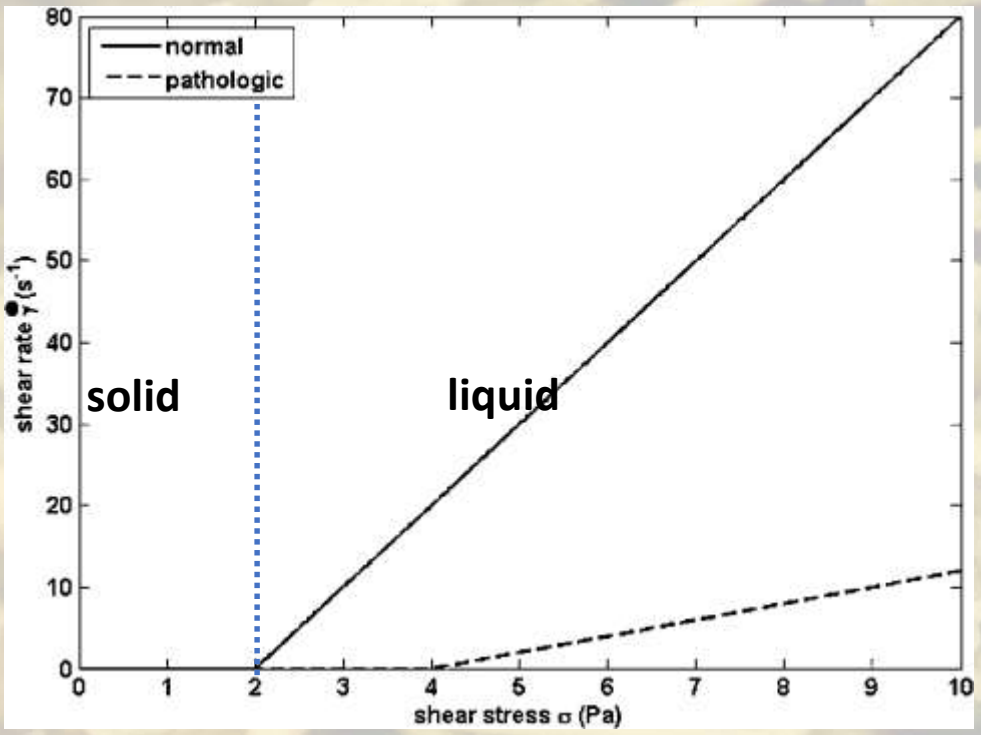
Mucus is present down to the seventeenth generation
and **mainly near the seventh generation**.

Mucus is a **viscoelastic rheofluidifying** fluid.

Physics - mucus.

We will assume **mucus to behave as a Bingham fluid**:

shear rate $\approx \frac{dv_z}{dr}$



if **inner shear forces are strong** enough, then mucus behaves as a **Newtonian fluid**;

otherwise mucus is solid.

The physical law reads (developed flow case):

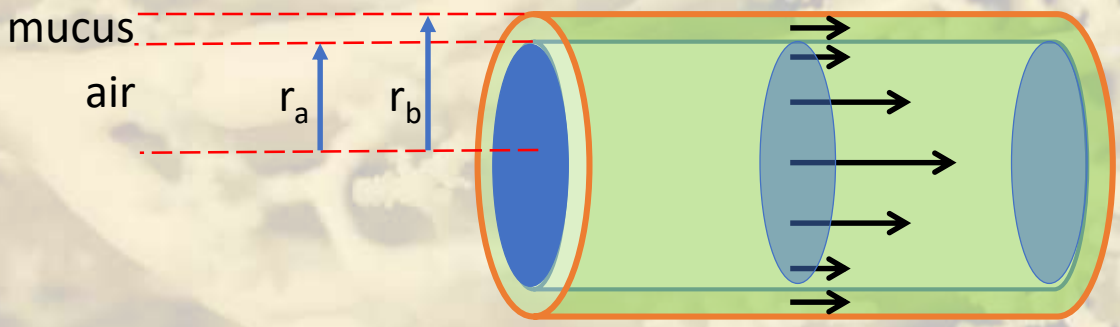
$$\sigma_{zr} = \sigma_0 + \mu_m \frac{dv_z}{dr} \qquad \text{if } \sigma_{zr} \geq \sigma_0$$

$$\frac{dv_z}{dr} = 0 \quad \text{otherwise}$$

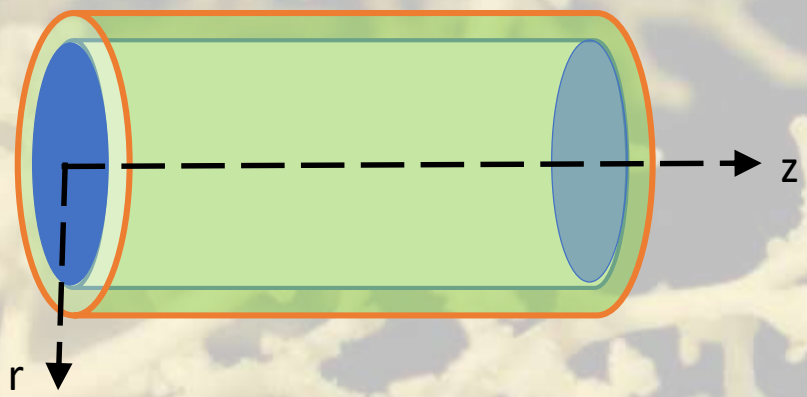
Model for mucus distribution.

We assume mucus to be distributed **homogeneously** on the bronchus wall, in a **layer whose thickness is constant**.

The problem is still assumed **axi-symmetric.**



$$R = \sum_{i=0}^{N} \frac{1}{2^i} \frac{8\mu_a l_i}{\pi {r_{a,i}}^4}$$



In air and “liquid” mucus

$$\rho \frac{\partial u}{\partial t} + \rho\,(u.\nabla)u - div(\Sigma) = 0$$

stationary, developed,
axi-symmetric

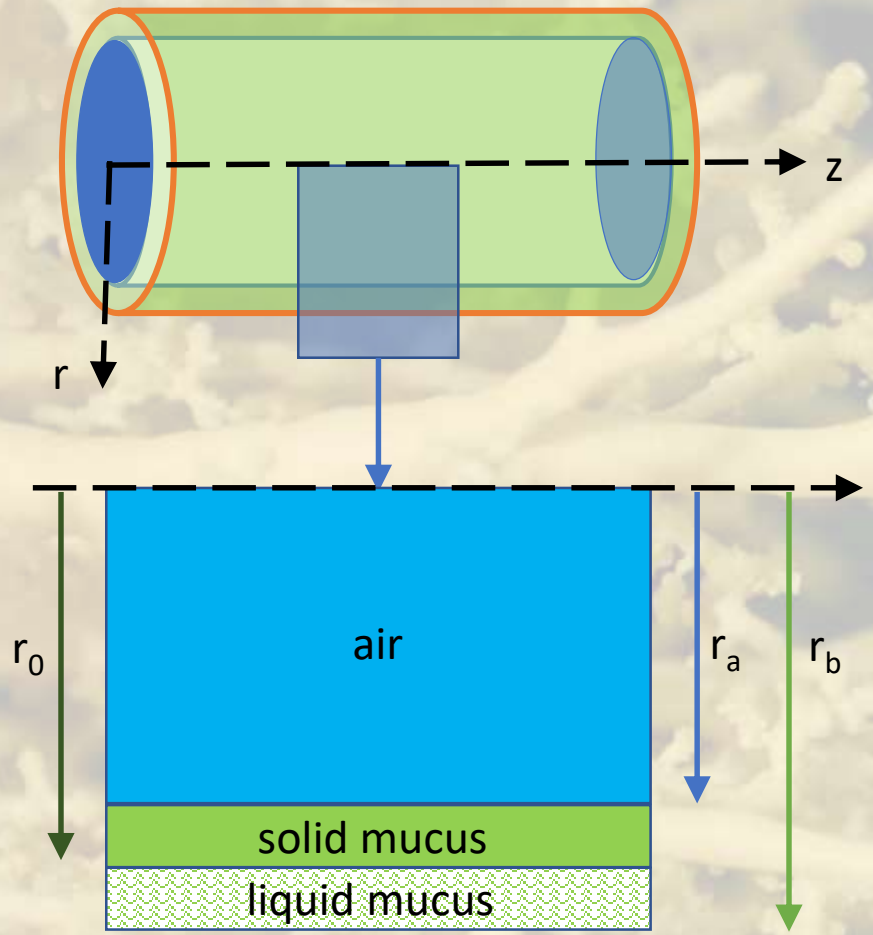
$$-\frac{1}{r}\frac{\partial}{\partial r}(r\,\sigma_{zr}) + \frac{dp}{dz} = 0$$

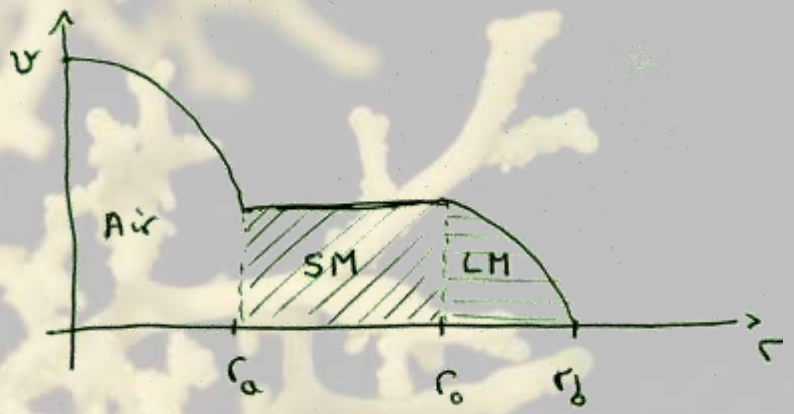
$$\sigma_{zr} = \mu_a \frac{du_z}{dr}$$ in air

$$\sigma_{zr} = \sigma_0 + \mu_m \frac{du_z}{dr}$$ in liquid mucus

$$\left(and\ \frac{dv_z}{dr} = 0\ in\ solid\ mucus \right)$$

Mucus properties.



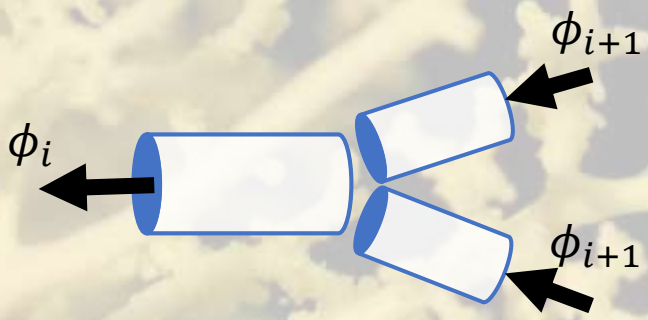


$$\phi_A = 2\pi \int_0^{r_a} u_z(s) s \, ds$$

$$\phi_M = 2\pi \int_{r_a}^{r_b} u_z(s) s \, ds$$

If mucus is both solid and liquid then the liquid mucus is closer to the wall.

Extending the model to the whole tree (quasi-static).



$$\phi_{A,i} = 2\phi_{A,i+1} \quad \rightarrow \quad \phi_{A,i} = \phi_{A,0}/2^i$$

$$\mathcal{V}_{mucus,i} = \pi\left(r_{b,i}^2 - r_{a,i}^2\right) l_i$$

$$\rightarrow \begin{cases} \dfrac{dr_{a,i}}{dt} = \dfrac{\phi_{M,i}(r_{a,i}, r_{b,i}, \phi_{A,i}) - 2\phi_{M,i+1}(r_{a,i+1}, r_{b,i+1}, \phi_{A,i+1})}{2\pi l_i r_{a,i}} \\ r_{a,i}(0) = r_{a,i,0} \\ \phi_{M,18} = 0 \end{cases}$$

Full quasi-static model.

∀ i=0, …, 17

$$\frac{dr_{a,i}}{dt} = \frac{\phi_{M,i}(r_{a,i}, r_{b,i}, \phi_{A,i}) - 2\phi_{M,i+1}(r_{a,i+1}, r_{b,i+1}, \phi_{A,i+1})}{2\pi l_i r_{a,i}}$$

$$r_{a,i}(0) = r_{a,i,0}$$

$$-\frac{1}{r}\frac{\partial}{\partial r}\left(r\,\sigma_{zr,i}\right) + \frac{dp_i}{dz} = 0$$

$$\sigma_{zr,i} = \mu_a \frac{du_{z,i}}{dr}$$ in air

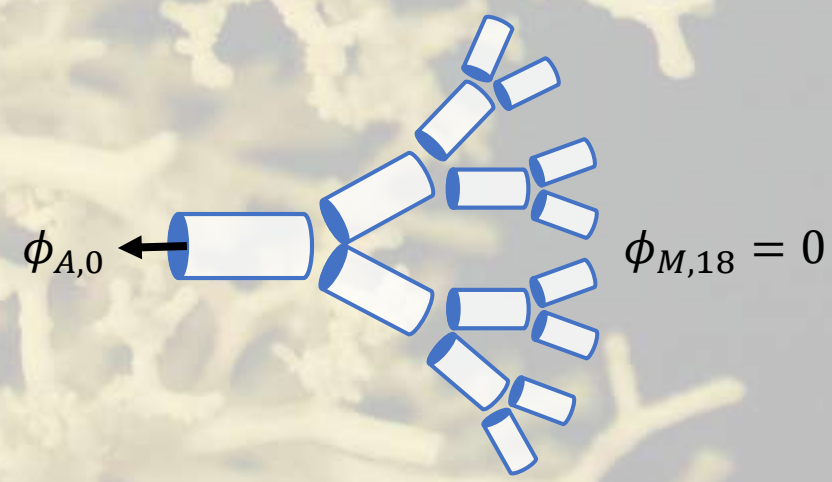
$$\sigma_{zr,i} = \sigma_0 + \mu_m \frac{du_{z,i}}{dr}$$ if $\sigma_{zr} \geq \sigma_0$ (in liquid mucus)

$\frac{du_{z,i}}{dr} = 0$ (in solid mucus)

$$\phi_{A,i} = \phi_{A,0}/2^i$$

$$\phi_{A,i} = 2\pi \int_0^{r_a} u_{z,i}(s)\, s\, ds$$

$$\phi_{M,i} = 2\pi \int_{r_a}^{r_b} u_{z,i}(s)\, s\, ds$$



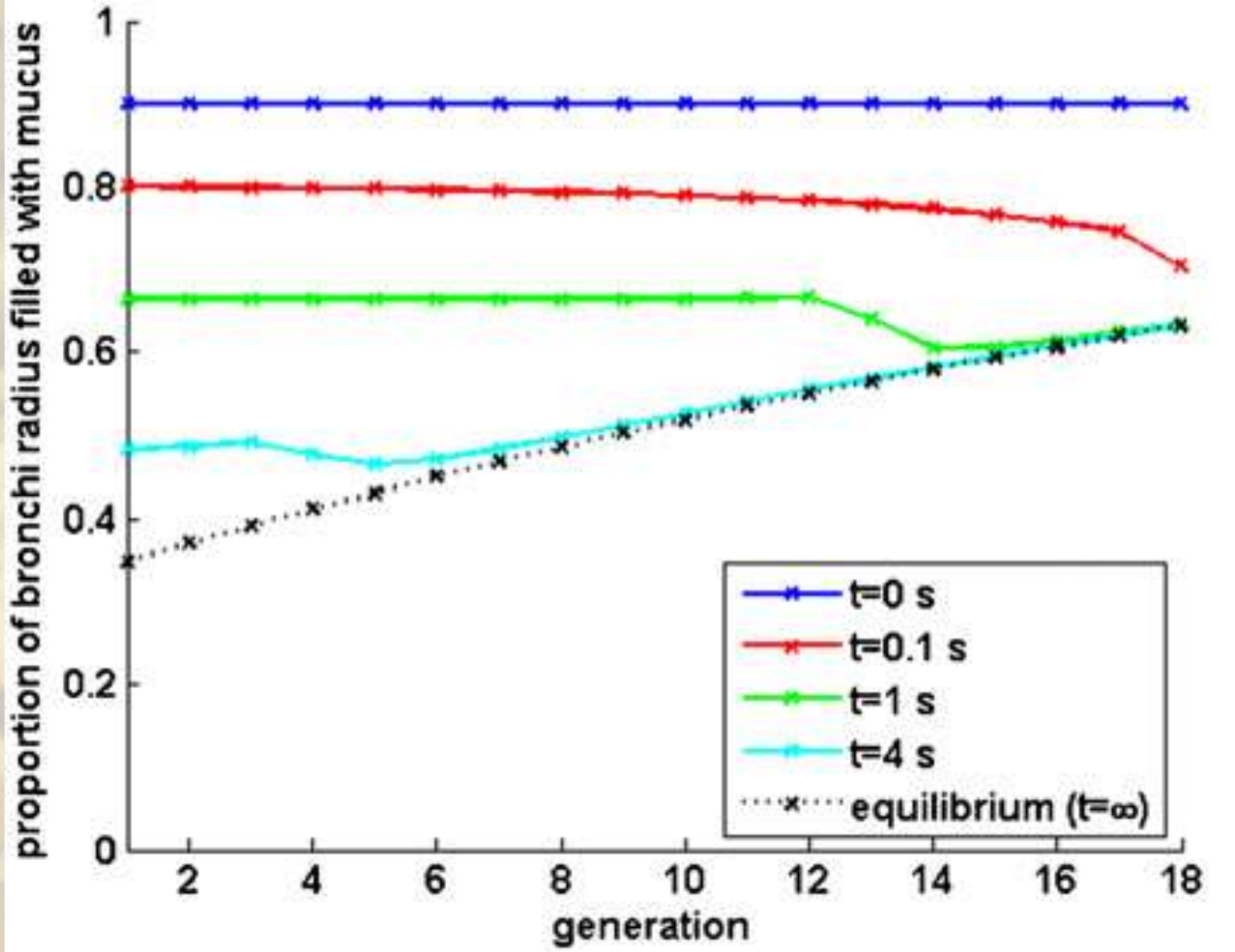
We can show that, **in the limit of our model**,

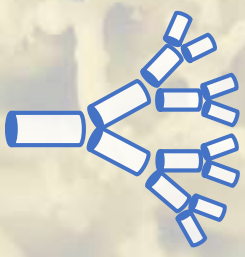
- If mucus is both solid and liquid then the **liquid mucus layer is the layer closer to the wall**

- There **exists a time asymptotic "maximal" distribution of mucus** that is at equilibrium with a given airflow in the tree

- The **time asymptotic "maximal" distribution of mucus has a fractal distribution** correlated to that of the tree, its diameter reduction factor is $h_m = (h/2)^{\frac{1}{4}}$

- Under some specific (physiologic) hypotheses, any mucus motion **has for effect to decrease the hydrodynamic resistance** of the lung


proportion of bronchi radius filled with mucus
1
0.8
0.6
0.4
0.2
0
2
4
6
8
10
12
14
16
18
generation
t=0 s
t=0.1 s
t=1 s
t=4 s
equilibrium (t=∞)



Asymptotic distribution of mucus, equations.

$\forall$ i=0, …, 17

$$\mathbf{0} = \phi_{M,i}(r_{a,i}, r_{b,i}, \phi_{A,i}) - 2\phi_{M,i+1}(r_{a,i+1}, r_{b,i+1}, \phi_{A,i+1})$$

$$-\frac{1}{r}\frac{\partial}{\partial r}(r\,\sigma_{zr,i}) + \frac{dp_i}{dz} = 0$$

$$\sigma_{zr,i} = \mu_a \frac{du_{z,i}}{dr}$$ in air

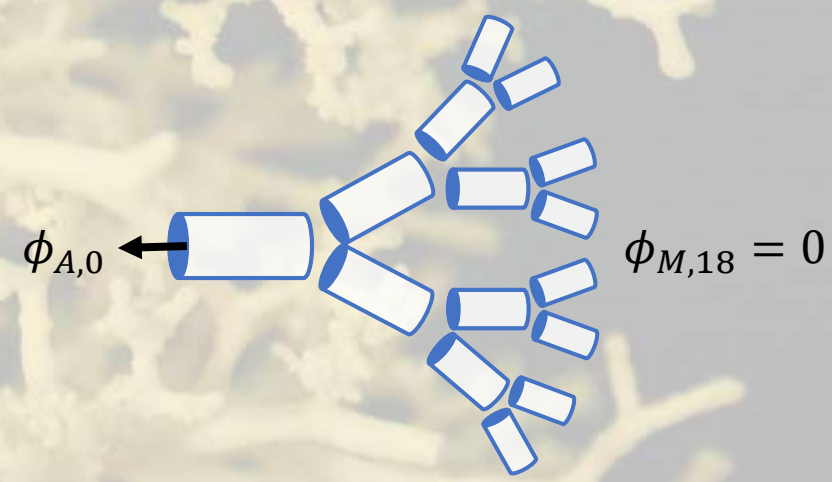
$$\sigma_{zr,i} = \sigma_0 + \mu_m \frac{du_{z,i}}{dr}$$ if $\sigma_{zr,i} \geq \sigma_0$ (in liquid mucus)

$$\frac{du_{z,i}}{dr} = 0$$ (in solid mucus)

$$\phi_{A,i} = \phi_{A,0}/2^i$$

$$\phi_{A,i} = 2\pi \int_0^{r_{a,i}} u_{z,i}(s)s\,ds$$

$$\phi_{M,i} = 2\pi \int_{r_{a,i}}^{r_{b,i}} u_{z,i}(s)s\,ds$$



Asymptotic distribution of mucus, equations.

$$\phi_{M,i}\left(r_{a,i}, r_{b,i}, \phi_{A,i}\right) = 0 \qquad \forall\ i=0, \ldots, 17$$

no mucus

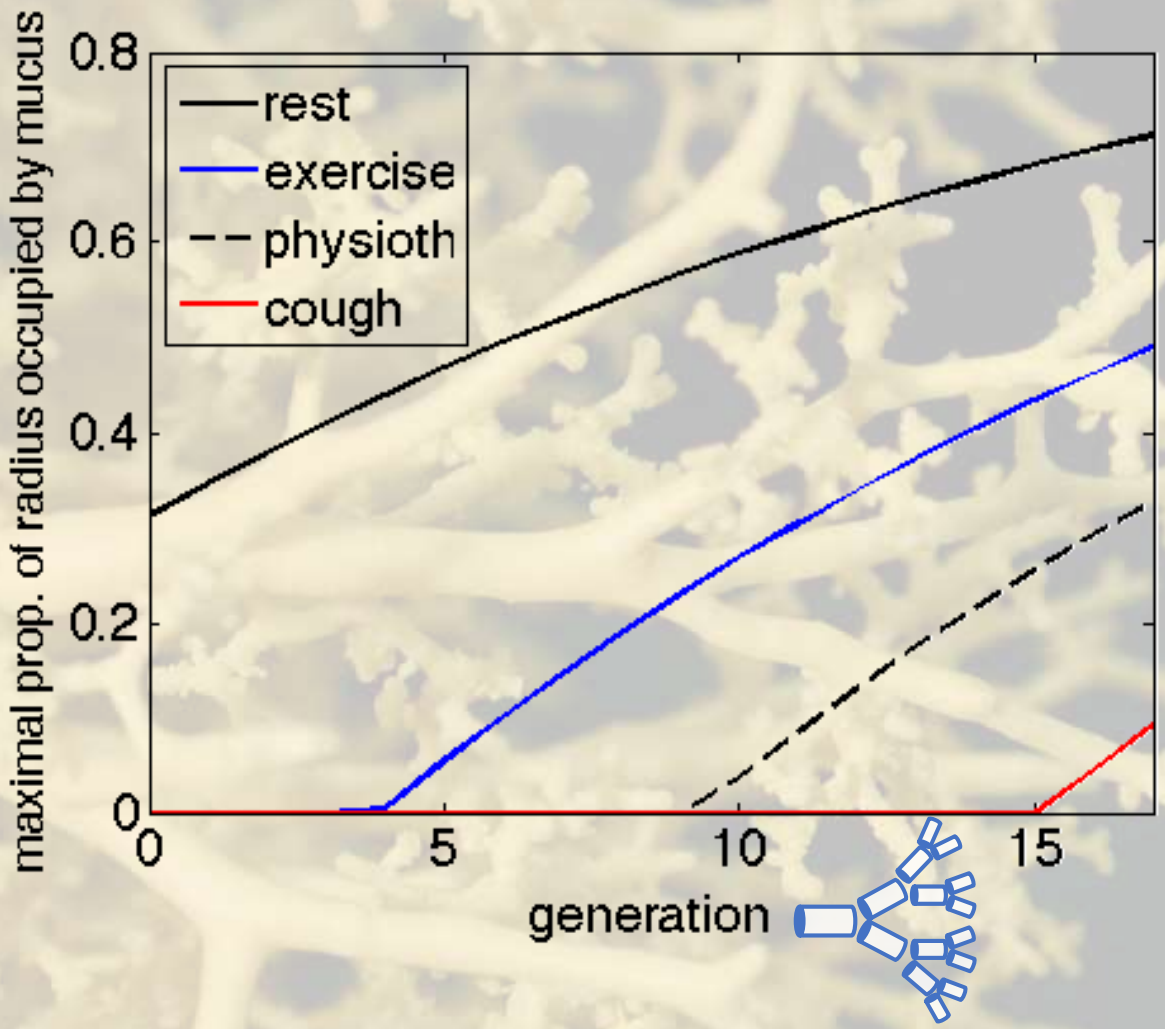
$$r_{a,i} = r_{b,i}$$

mucus is solid in the whole bronchus

$$r_{0,i} \geq r_{b,i}$$

There is **not a unique solution** to the stationary problem,
but
we can define and characterize **a unique "maximal" solution**.

$$r_{a,i} = \left(\frac{h}{2}\right)^{\frac{i}{4}} r_{a,0} \qquad r_{a,0} = \left|\frac{4\mu_A \phi_{A,0} r_{b,0}}{\pi \sigma_0}\right|^{\frac{1}{4}}$$



Maximal mucus distribution in the lung's model at different ventilation's regimes.

Ref: Towards the modeling of mucus draining from human lung: role of the geometry of the airway tree. B. Mauroy, C. Fausser, D. Pelca, J. Merckx and P. Flaud. Phys Biol. 8(5):056006, 2011.

But let us go back to the approximations made
and think how they **affect the meaning of these results**?

- Is the hypothesis of developed flow regime valid?

- What about the effect of the bifurcations on the flow?

- Is the lung really fractal?

- Are the bronchi really rigid, cylindrical, etc?

- What about the role of inspiratory flow?

- …

The results presented before are **true in the limit of the model**,

and **blind extrapolation is dangerous**!

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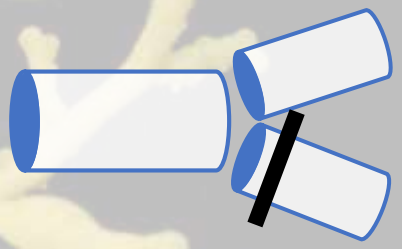

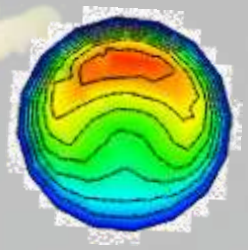

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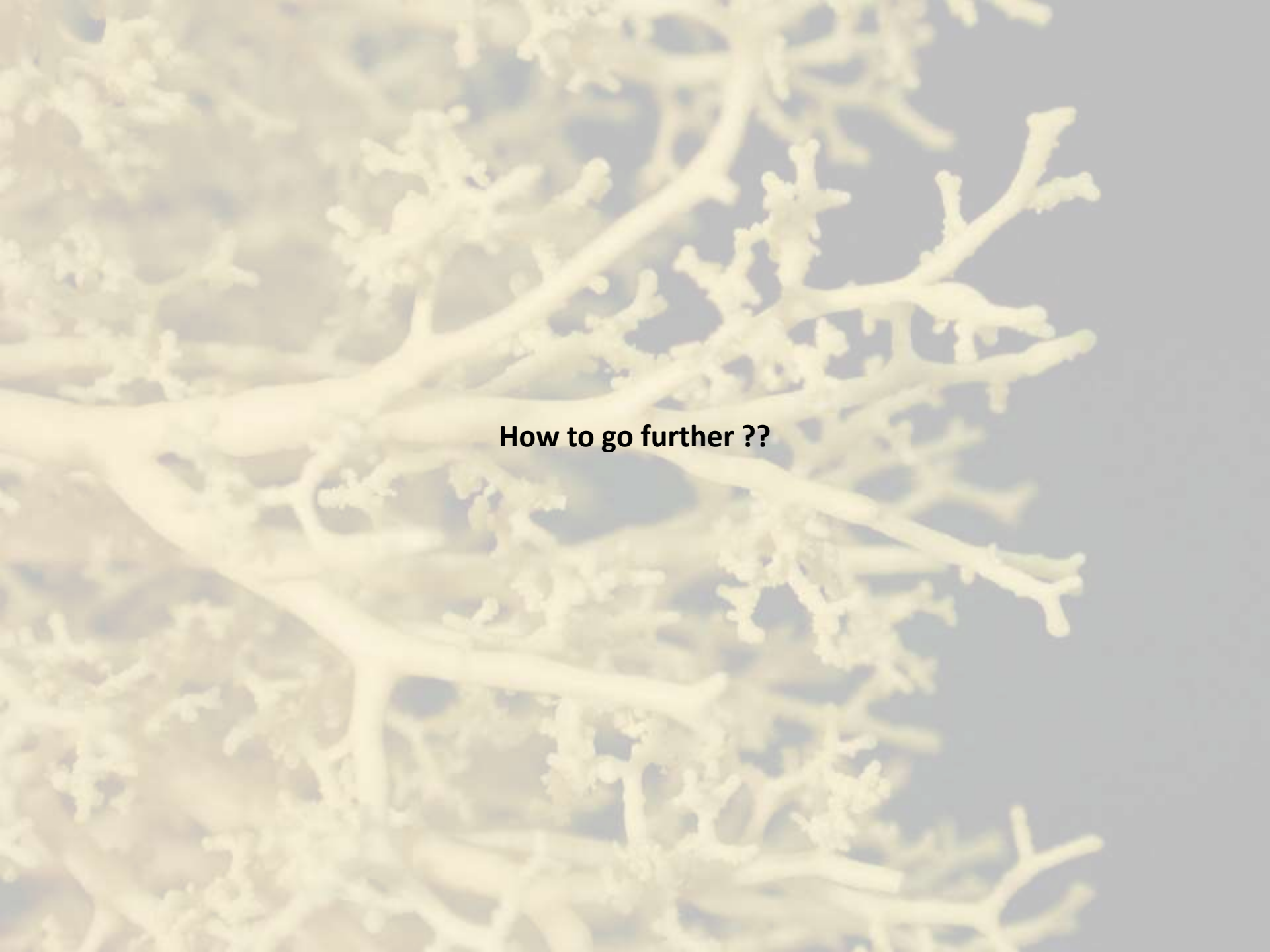
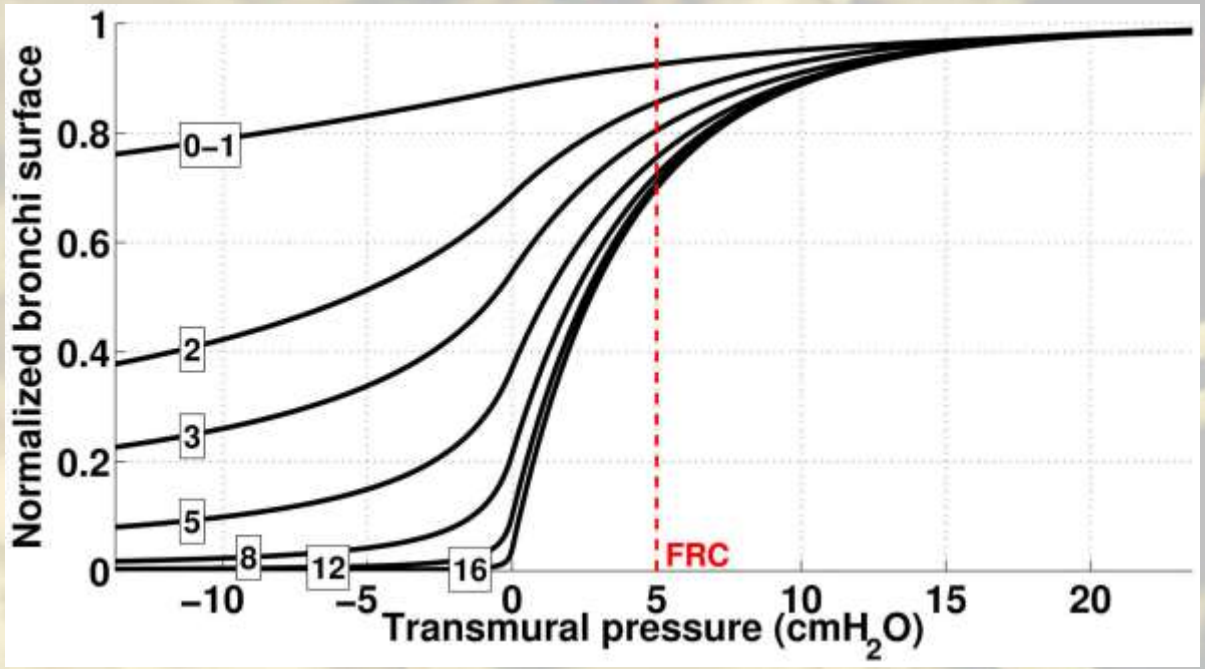


How to go further ??

Adding bronchi deformations and the ventilation cycle.

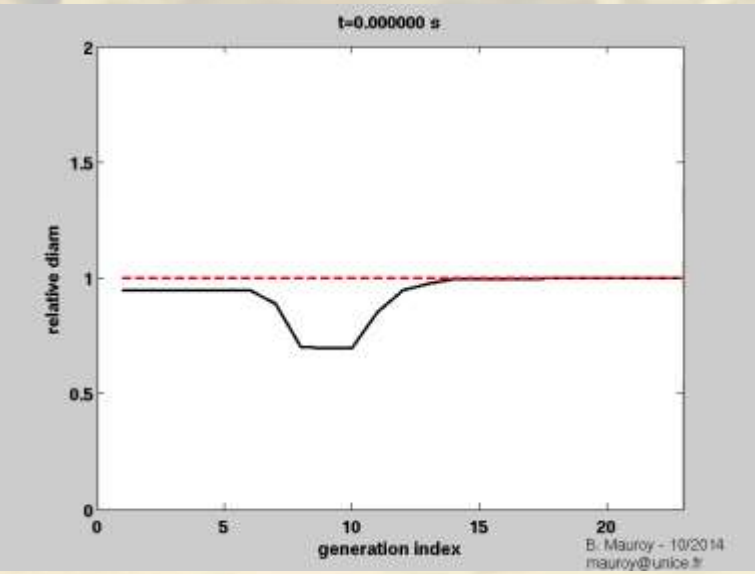


Lambert et al, 1982: bronchi static behavioral laws.

The **diameter of a bronchus** depends **on the fluid mechanics** in the bronchus, which in turns depends **on the diameter of the bronchus**. This “loop” is also dependent **on the whole tree structure**, through the fluid mechanics.

We have an **implicit** definition of the mucus distribution and motion.

This new model is well posed (with M. Lin, Institute of Technology of Cambodia) and is numerically easily tractable.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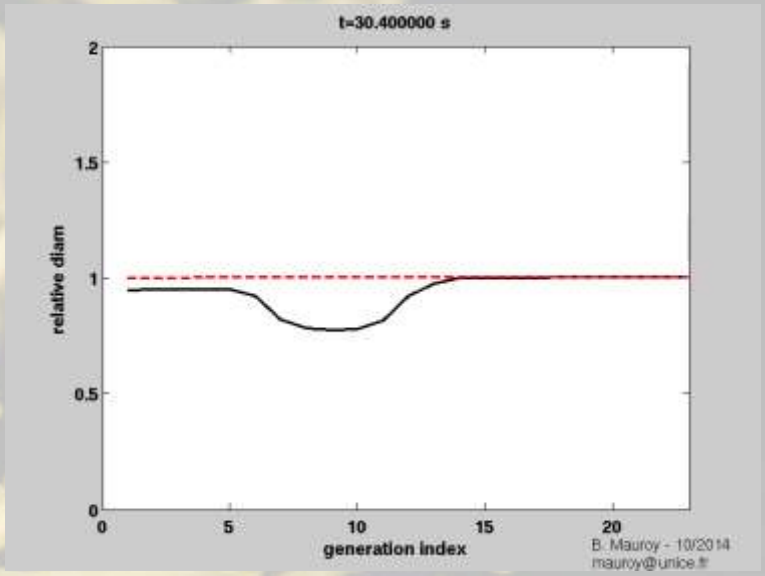
B. Mauroy - 10/2014
mauroy@unice.fr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B. Mauroy - 10/2014
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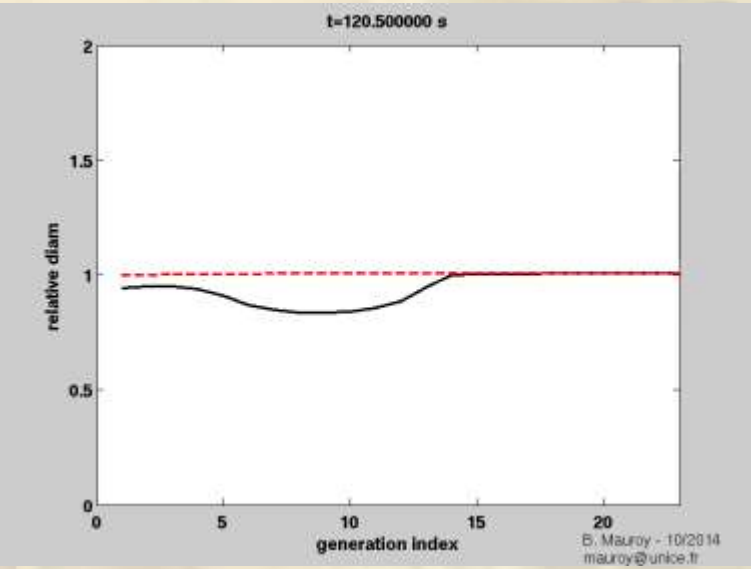
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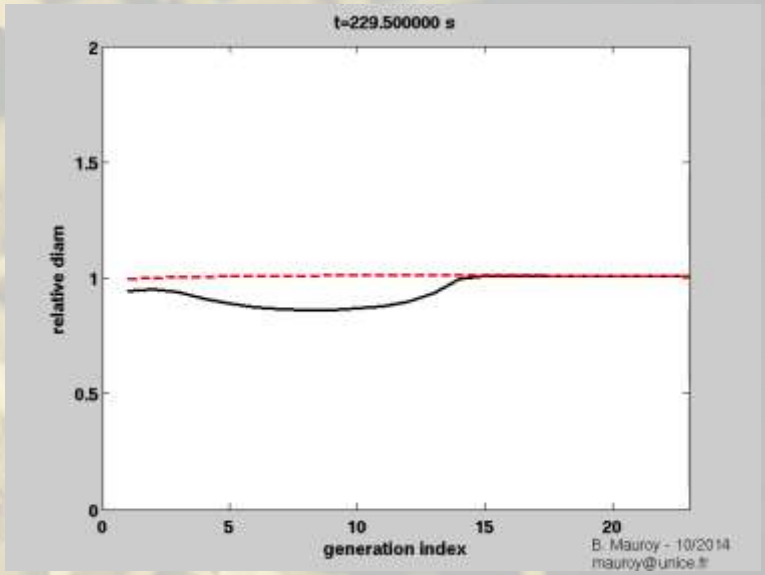
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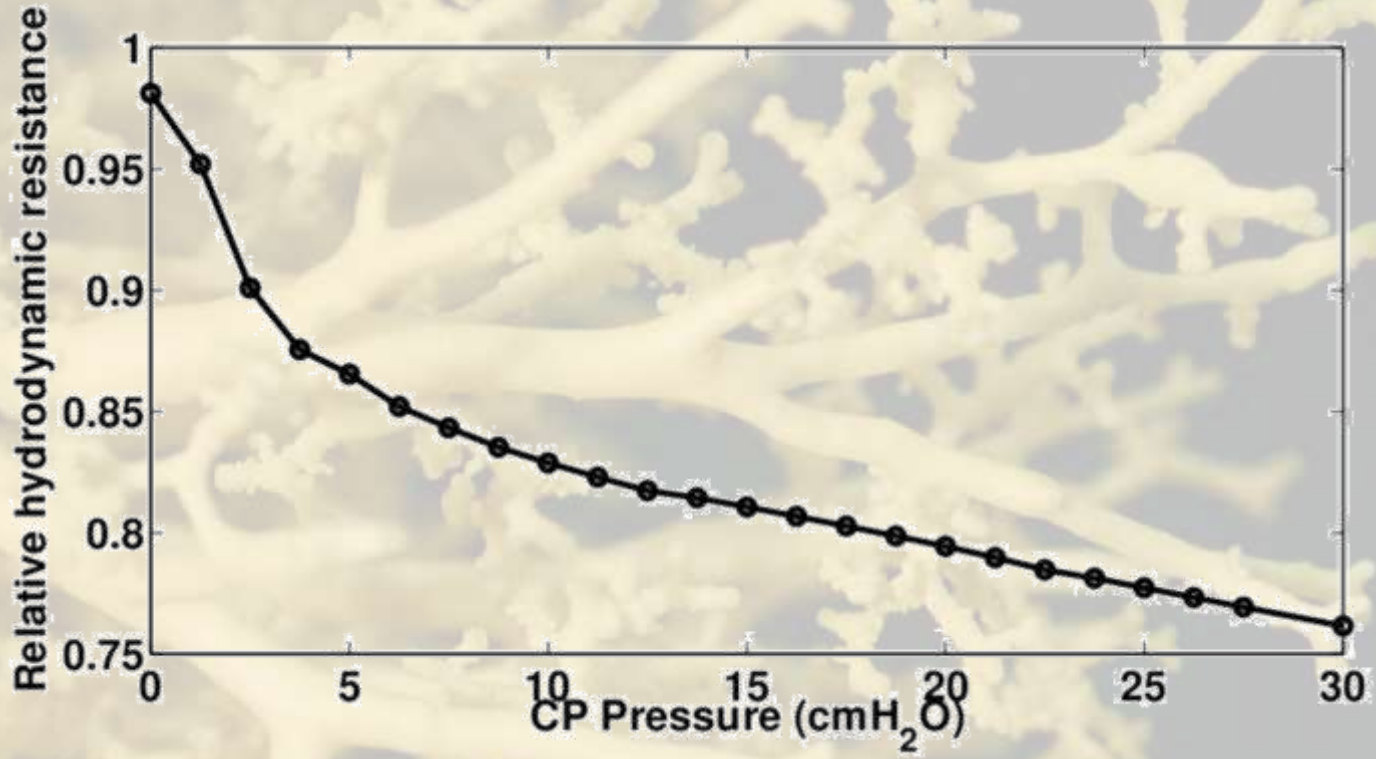
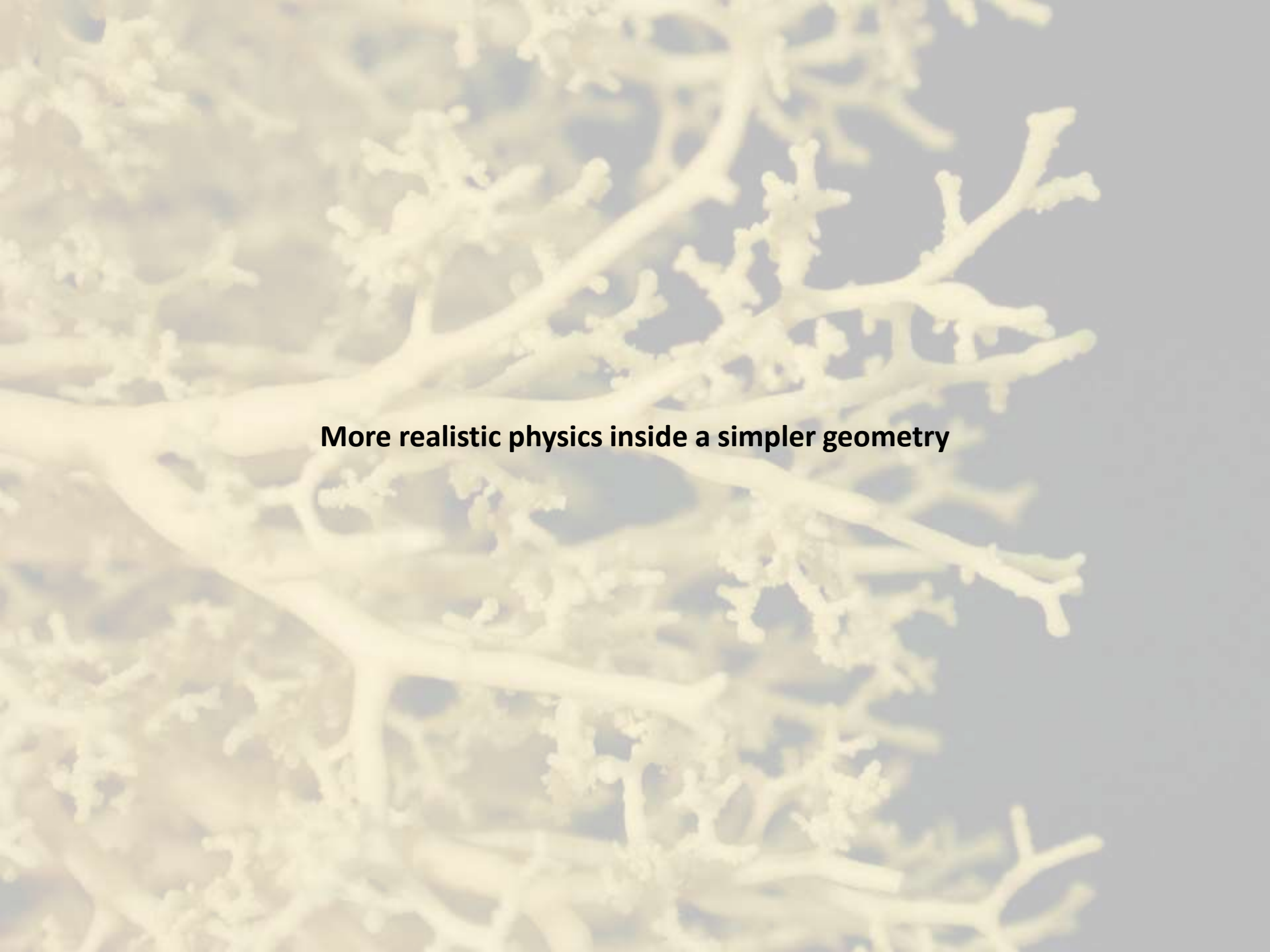
mauroy@unice.fr



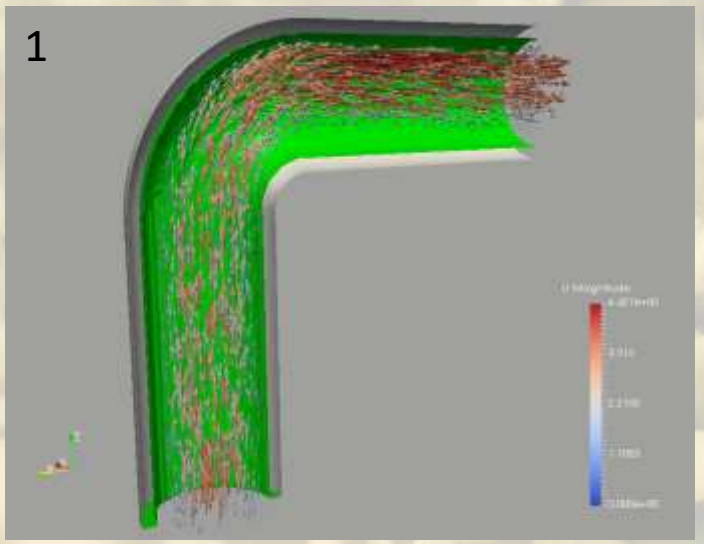
In this model, airflow is controlled by physiotherapy pressure on the chest.

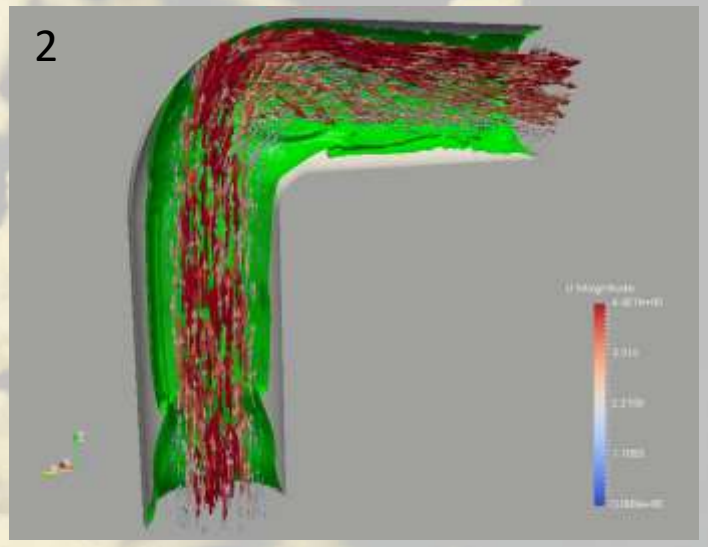
Ref: Towards the modeling of mucus draining from human lung : role of airways deformation on air-mucus interaction. B. Mauroy, P. Flaud, D. Pelca, C. Fausser, J. Merckx, B. R. Mitchell. Frontiers in Physiology, 6:214, 2015.

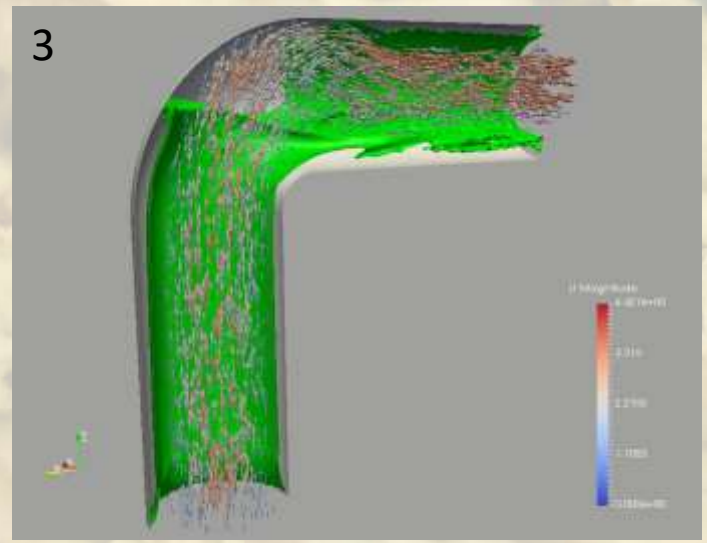


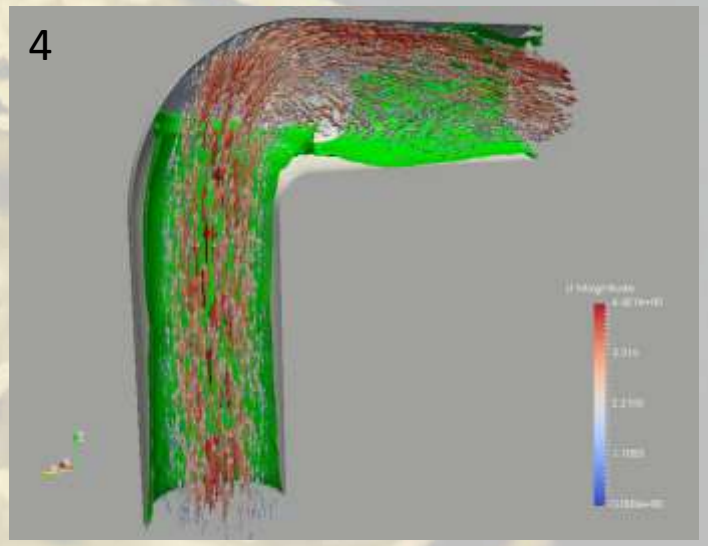
More realistic physics inside a simpler geometry

Bi-fluid modelling using VOF method (OpenFoam, from Ubbink 1997) with H. Kumar, ABI, Auckland University.









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