Modelling the Mucociliary Clearance (MCC) in the airways

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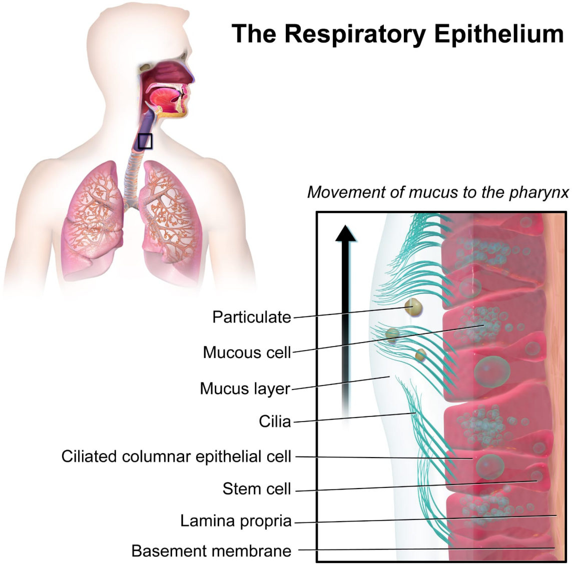
Introduction

- The lung is constantly exposed to pathogens that are removed primarily by the MCC system.
- MCC is the primary innate defense mechanism that keeps our airways clean.
- MCC utilizes a protective layer of mucus that lines the airways and traps inhaled particles.
- Failure leads to mucus accumulation causing stagnation and plug formation.

MCC Physiology/ Mechanism

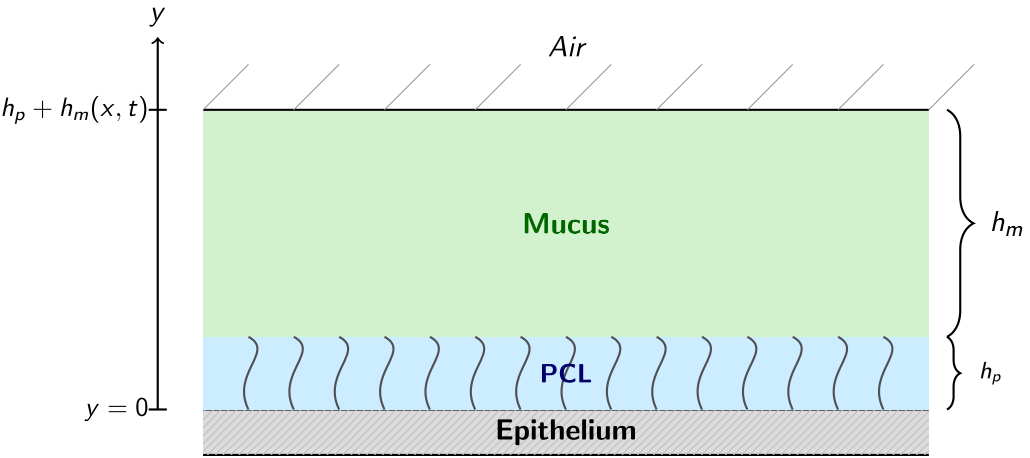


- Mucus: Thicker, viscoelastic fluid layer above the PCL, traps inhaled particles and pathogens.
- Cilia are numerous hair-like structures that beat coordinately to drive directional fluid flow, supported by the thin periciliary liquid (PCL) layer, which prevents cilia from being trapped in mucus.
- Epithelial layer: Acts as a solid wall.

Aims

- The main aim of this study is to build a framework modelling the evolution of the mucus over time: Both the mucus and the PCL fluids are Newtonian, and then only the mucus is a non-Newtonian fluid.

Model Structure



Con...

- The mucus and PCL fluids are assumed to be incompressible.
- Both layers are considered to be Newtonian.
- Both layers are viscous, with mucus slightly more viscous than the PCL.
- The cilia beat at a specific frequency, enabling the mucus to move upward.
- The force is applied only in the PCL layer due to cilia beating.

Model Build Up

We consider the Navier-Stokes equations

$$\rho \left[\frac{\partial \underline{v}}{\partial t} + (\underline{v} \cdot \underline{\nabla})\underline{v} \right] = -\underline{\nabla} p + \rho \underline{F} + \mu \nabla^2 \underline{v} \tag{1}$$

$$\underline{\nabla} \cdot \underline{v} = 0 \tag{2}$$

The fluid exhibits highly viscous flow behaviour. Consequently, the inertial term can be neglected. This approximation is justified in these scenarios:

1. $Re \ll 1$, $Re = \frac{uL}{\gamma}$,
2. Thin Film fluid theory, $\frac{H}{L} \ll 1$.

The Governing Equations - Newtonian

$2D$ flow of Mucociliary Clearance

$$\rho\left(\frac{\partial u}{\partial t}+u\frac{\partial u}{\partial x}+v\frac{\partial u}{\partial y}\right)=-\frac{\partial p}{\partial x}+\rho F_x+\mu\left[\frac{\partial^2 u}{\partial x^2}+\frac{\partial^2 u}{\partial y^2}\right]. \tag{3}$$

$$\rho\left(\frac{\partial v}{\partial t}+u\frac{\partial v}{\partial x}+v\frac{\partial v}{\partial y}\right)=-\frac{\partial p}{\partial y}+\rho F_y+\mu\left[\frac{\partial^2 v}{\partial x^2}+\frac{\partial^2 v}{\partial y^2}\right]. \tag{4}$$

Dimensionless variables

$$\bar{t}=\frac{t}{\frac{L}{u}}=\frac{u}{L}t,\quad \bar{x}=\frac{x}{L},\quad \bar{y}=\frac{y}{H},\quad \bar{u}=\frac{u}{U_0}, \tag{5}$$
$$\bar{v}=\frac{v}{V_0},\quad \bar{p}=\frac{p}{P_0},\quad \bar{F}=\frac{F}{F_0}.$$

Con...

$$\left(\frac{H}{L}\right)^2 \frac{\rho U_0 L}{\mu}\left(\frac{\partial \bar{u}}{\partial \bar{t}} + \bar{u}\frac{\partial \bar{u}}{\partial \bar{x}} + \bar{v}\frac{\partial \bar{u}}{\partial \bar{y}}\right) = \left(\frac{H}{L}\right)^2 \frac{\partial^2 \bar{u}}{\partial \bar{x}^2} + \frac{\partial^2 \bar{u}}{\partial \bar{y}^2} + \frac{\rho F_0 H^2}{\mu U_0^2}\bar{F} - \frac{P_0 H^2}{L U_0 \mu}\frac{\partial \bar{p}}{\partial \bar{x}} \quad (6)$$

The general form of the model,

$$\begin{aligned}
\frac{\partial p_i}{\partial x} &= \mu_i \frac{\partial^2 u_i}{\partial y^2} + \rho_i F_x \\
\frac{\partial p_i}{\partial y} &= \rho_i F_y \\
\frac{\partial u_i}{\partial x} + \frac{\partial v_i}{\partial y} &= 0
\end{aligned} \quad (7)$$

Con...

Periciliary Layer (PCL)

$$
\begin{aligned}
\frac{\partial p_p}{\partial x} &= \mu_p \frac{\partial^2 u_p}{\partial y^2} + \rho_p F_x \\
\frac{\partial p_p}{\partial y} &= 0 \\
\frac{\partial u_p}{\partial x} + \frac{\partial v_p}{\partial y} &= 0
\end{aligned}
\tag{8}
$$

Mucus Layer

$$
\begin{aligned}
\frac{\partial p_m}{\partial x} &= \mu_m \frac{\partial^2 u_m}{\partial y^2} \\
\frac{\partial p_m}{\partial y} &= 0 \\
\frac{\partial u_m}{\partial x} + \frac{\partial v_m}{\partial y} &= 0
\end{aligned}
\tag{9}
$$

Boundary Condition

- **At** $y = 0$:

$$u_p(0,t) = 0, \qquad v_p(0,t) = 0, \tag{10}$$

- **Between PCL and Mucus** $y = h_p$:
  Continuity of tangential velocity:

$$u_p(h_p,t) = u_m(h_p,t). \tag{11}$$

  No interpenetration (normal stress continuity).

$$v_p(h_p,t) = v_m(h_p,t). \tag{12}$$

  Pressure continuity.

$$p_p(x,t) = p_m(x,t) \quad \text{at } y = h_p. \tag{13}$$

Con...

Continuity of tangential shear stress.

$$\mu_p \frac{\partial u_p}{\partial y}(h_p, t) = \mu_m \frac{\partial u_m}{\partial y}(h_p, t). \tag{14}$$

- **At** $y = h_p + h_m(x, t)$:
  Tangential stress balance

$$\mu_m \frac{\partial u_m}{\partial y}\bigg|_{y=h_p+h_m(x,t)} = 0. \tag{15}$$

Kinematic free-surface condition.

$$\frac{\partial}{\partial t}\Big(h_p + h_m(x, t)\Big) + u_m \frac{\partial}{\partial x}\Big(h_p + h_m(x, t)\Big) = v_m \tag{16}$$

Simulation Results

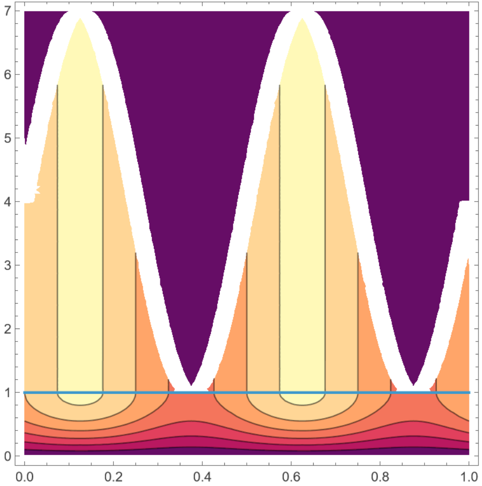


Figure: Evolution of mucus and pcl for $0 \leq t \leq 1$

Navier-Stokes equation - Power-law

for the x-direction,

$$\rho \left[v_x \frac{\partial v_x}{\partial x} + v_y \frac{\partial v_x}{\partial y} \right] = -\frac{\partial P}{\partial x} + \frac{\partial S_{xx}}{\partial x} + \frac{\partial S_{yx}}{\partial y}, \tag{17}$$

and for the y-direction,

$$\rho \left[v_x \frac{\partial v_y}{\partial x} + v_y \frac{\partial v_y}{\partial y} \right] = -\frac{\partial P}{\partial y} + \frac{\partial S_{xy}}{\partial x} + \frac{\partial S_{yy}}{\partial y}, \tag{18}$$

and the conservation of mass equation

$$\frac{\partial v_x}{\partial x} + \frac{\partial v_y}{\partial y} = 0, \tag{19}$$

Con...

$$S_{ik} = \mu_e A_{ik}, \tag{20}$$

where A_{ik} is the rate of strain tensor and μ_e is the effective viscosity.

$$A_{ik} = \frac{\partial v_i}{\partial x_k} + \frac{\partial v_k}{\partial x_i}, \tag{21}$$

and the effective viscosity is given by

$$\mu_e = b \left| \sqrt{\frac{1}{2} tr(A^2)} \right|^{n-1} \tag{22}$$

where b is constant.

Con...

Periciliary Layer (PCL)

$$
\begin{aligned}
\frac{\partial p_p}{\partial x} &= \mu_p \frac{\partial^2 u_p}{\partial y^2} + \rho_p F_x \\
\frac{\partial p_p}{\partial y} &= 0 \\
\frac{\partial u_p}{\partial x} + \frac{\partial v_p}{\partial y} &= 0
\end{aligned}
\tag{23}
$$

Mucus Layer

$$
\begin{aligned}
\frac{\partial p_m}{\partial x} &= \mu_m \frac{\partial}{\partial y}\left[\left|\frac{\partial u_m}{\partial y}\right|^{n-1} \frac{\partial u_m}{\partial y}\right] \\
\frac{\partial p_m}{\partial y} &= 0 \\
\frac{\partial u_m}{\partial x} + \frac{\partial v_m}{\partial y} &= 0
\end{aligned}
\tag{24}
$$

Conclusion and Future Work

Conclusion

- We developed a two-layer model of MCC consisting of the PCL and mucus layers.
- The model captures the essential coupling between ciliary-driven PCL flow and mucus transport.
- Our model successfully captures the essential dynamics of mucociliary clearance under healthy physiological conditions.

Future Work

- Model the mucus layer using a Carreau-Yasuda non-Newtonian formulation.
- Extend the governing equations to incorporate disease states.
- Develop a viscoelastic model to better represent MCC dynamics.

Thank you