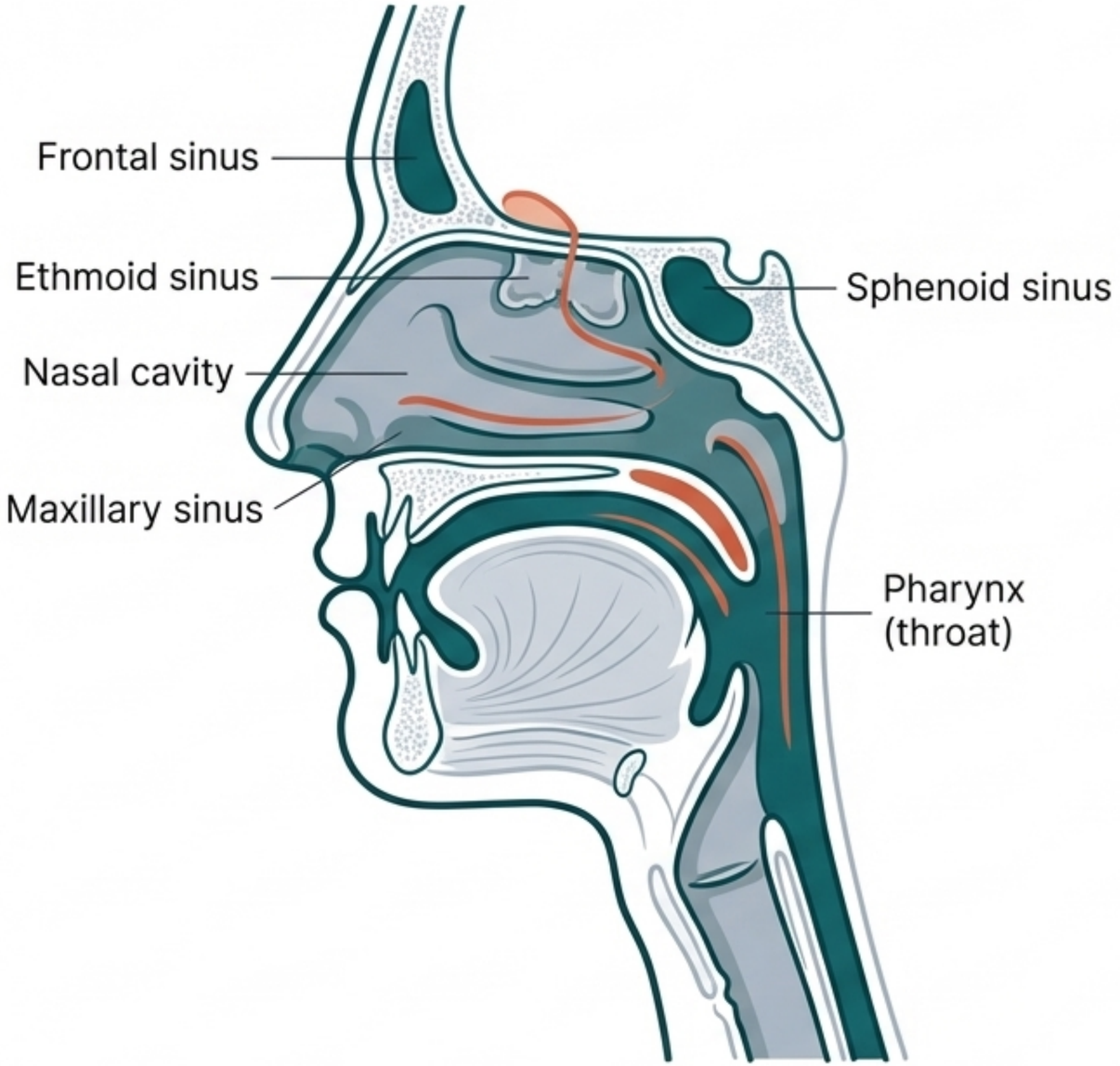
The Unseen Guardian

Modelling the Mechanics of Airway Defense: A Multiscale Challenge in Muco-ciliary Clearance

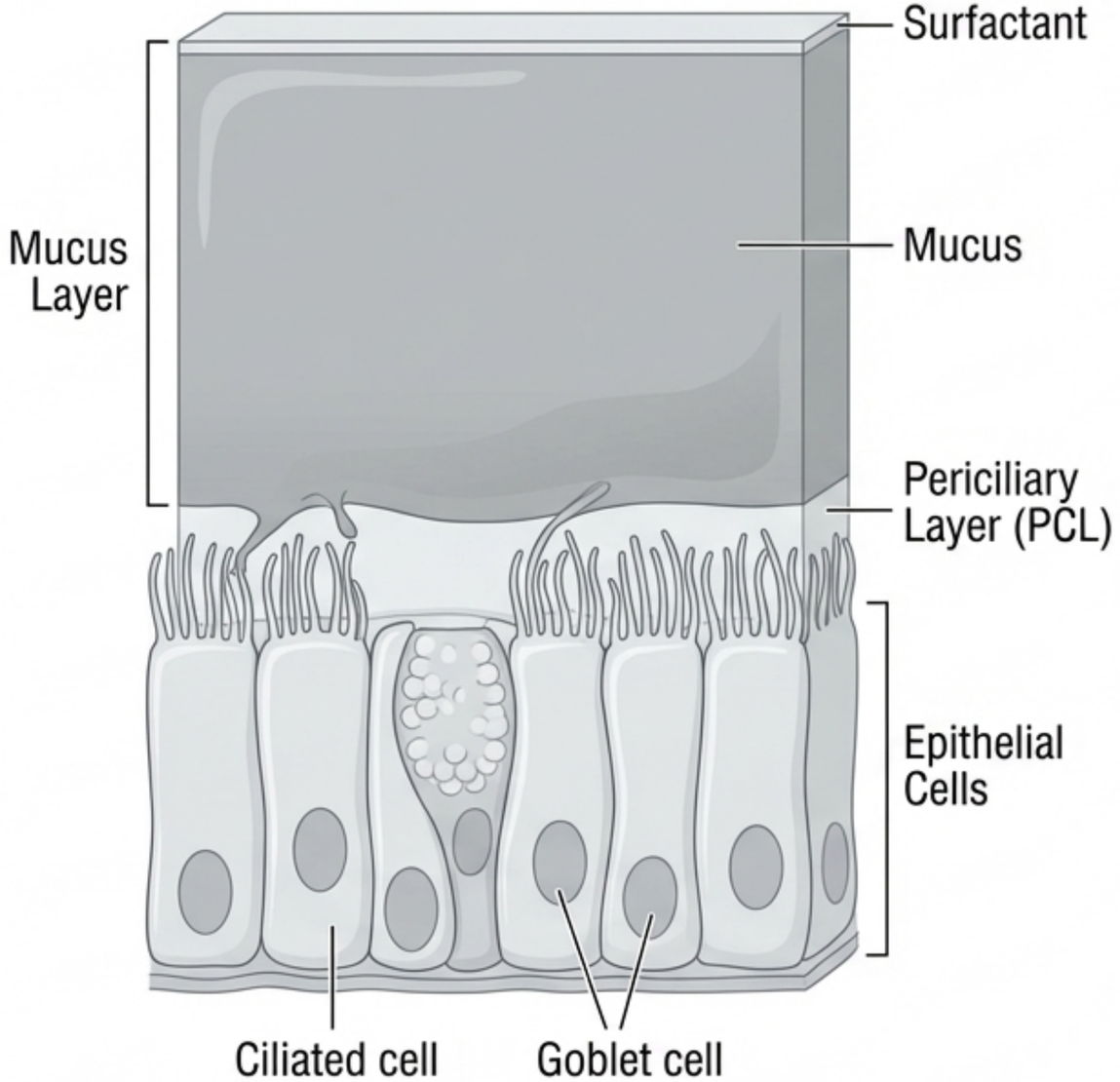
A Workshop for Students & Lecturers in Applied Mathematics and Bioengineering



The First Line of Defense

Our respiratory tract is constantly exposed to pathogens, pollutants, and particulates with every breath. Mucociliary clearance (MCC) is the primary innate defense mechanism that keeps our airways clean.

- **Continuous Removal:** MCC is a transport system that continuously traps and removes inhaled foreign material.
- **Failure = Disease:** When this transport fails, mucus accumulates, leading to infection, chronic inflammation, and obstruction.
- **Clinical Relevance:** This mechanical failure is a key factor in diseases like:
  - **Cystic Fibrosis** (abnormally high mucus viscosity)
  - **Chronic Bronchitis** (excess mucus production)
  - **RSV Bronchiolitis** (airway obstruction and epithelial damage)



A Finely Tuned Two-Layer System

The airway surface is coated by the Airway Surface Liquid (ASL), which is not a single fluid but a two-layer composite with distinct mechanical roles.

1. **Mucus Layer (Top):** A thick, sticky, and rheologically complex gel. Its primary function is to trap particles.
2. **Periciliary Layer (PCL)** (Bottom): A thin, watery, low-viscosity fluid. It acts as a lubricant, allowing the cilia to beat freely without getting stuck in the mucus.

A crucial insight: Cilia beat within the PCL and only interact with the mucus at the tips of their strokes. Regular Source Serif Pro (400, #2D3748)

Bridging Microscopic Action to Macroscopic Flow

A fundamental challenge in modeling MCC is the enormous separation of scales.

How to connect these scales?

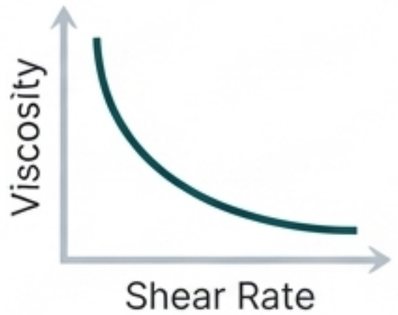
Length: 5–7 micrometres (µm)
Time: 10–20 Hz (milliseconds)

Length: Millimetres to centimetres (cm)
Time: Seconds to minutes

The Problem: A fully resolved simulation of millions of individual cilia is computationally impossible and conceptually unnecessary. We must systematically link these scales.

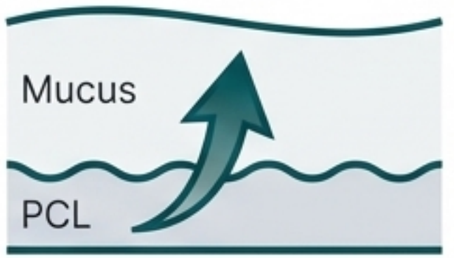
Key Ingredients for a Predictive Model

A successful model cannot oversimplify the physics. It must incorporate four critical mechanical components:



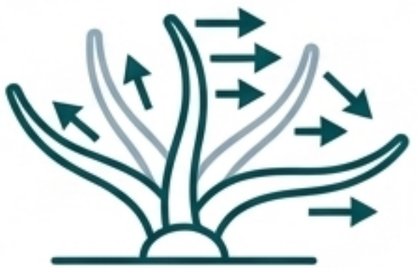
1. Mucus Rheology

Mucus is a non-Newtonian fluid. Its viscosity changes with shear rate (shear-thinning), and it has elastic properties (viscoelasticity).



2. PCL Mechanics

The PCL is not a passive spacer. Its thickness and viscosity determine how efficiently ciliary force is transmitted to the mucus.



3. Explicit Ciliary Forcing

The model must be driven by the action of cilia. Simply prescribing a mucus velocity tells us nothing about *why* the system might fail.

4. Airflow Coupling

Breathing generates shear stress at the mucus-air interface. This can either assist or hinder clearance and must be included.

A Powerful Reduction of Complexity

The Navier-Stokes equations are too complex to solve directly. Fortunately, the physics of the system allows for a major simplification using **thin-film theory** (or lubrication theory).

Justification 1: Small Aspect Ratio

The thickness of the mucus layer (~10 μm) is vastly smaller than its length (cm).

Implication: We can simplify the governing equations by assuming flow is primarily primarily parallel to the surface.

Justification 2: Low Reynolds Number

The flow is extremely slow and viscous. Inertial forces are negligible compared to viscous forces.

Implication: The messy nonlinear terms in Navier-Stokes can be dropped, leaving a balance between pressure and viscous stress.

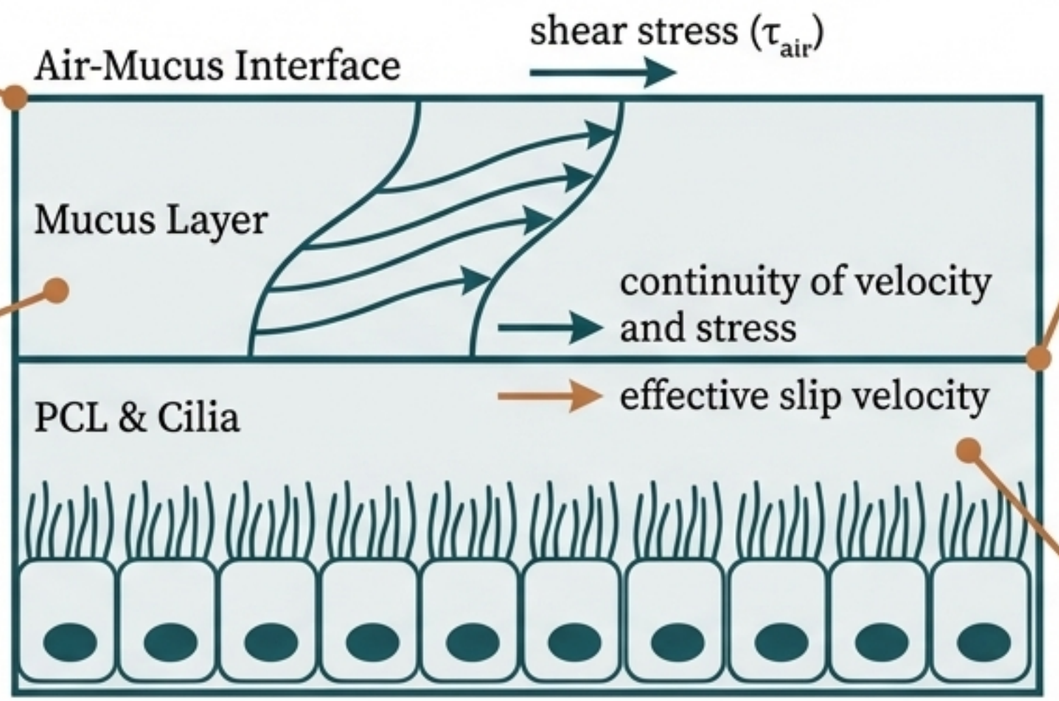
This is a mathematically controlled limit, not a crude approximation.

Building the Mathematical Framework

We apply thin-film theory to our two-layer system:

Air-Mucus Interface:
Airflow from breathing imposes a **shear stress** (τ_{air}). Surface tension effects are also present.

Mucus Layer:
Governed by thin-film equations with non-Newtonian viscosity.



Mucus-PCL Interface:
We enforce **continuity of velocity** and stress. Ciliary action is modeled as an **effective slip velocity** or body force that drives the system.

PCL & Cilia: Modeled as a low-viscosity Newtonian fluid or a porous medium (Brinkman equation) to account for the cilia.

From Individual Cilia to Continuum Forcing

"Multiscale" means we systematically translate microscale physics into macroscale parameters. This is a physics-based upscaling, not empirical curve-fitting.

1. Microscale Model

Describes the beat pattern, geometry, and phase of individual cilia.
(These details are NOT resolved in the final model.)

Averaging & Homogenization

2. Effective Forcing Term

The net effect of thousands of cilia is averaged over space and time. This produces an **effective slip velocity** or **body force** at the PCL-mucus interface.

Input into...

3. Macroscale Model (Thin-Film PDE)

This averaged forcing term drives the evolution of the mucus layer thickness (h) over long time and length scales.

One Equation, Multiple Physical Mechanisms

The final result of our derivation is a single Partial Differential Equation (PDE) for the mucus layer thickness, $h(x,t)$. Each term has a direct physical meaning:

Rate of Change of Mucus Thickness = Transport by Cilia + Transport by Airflow + Flow due to Pressure/Curvature

∂h/∂t (Accumulation Term):

Represents local thickening or thinning of the mucus layer.

Advective Terms:

Represent transport driven by the two main forces: the internal **ciliary action** and the external **airflow shear**.

Diffusive-like Terms:

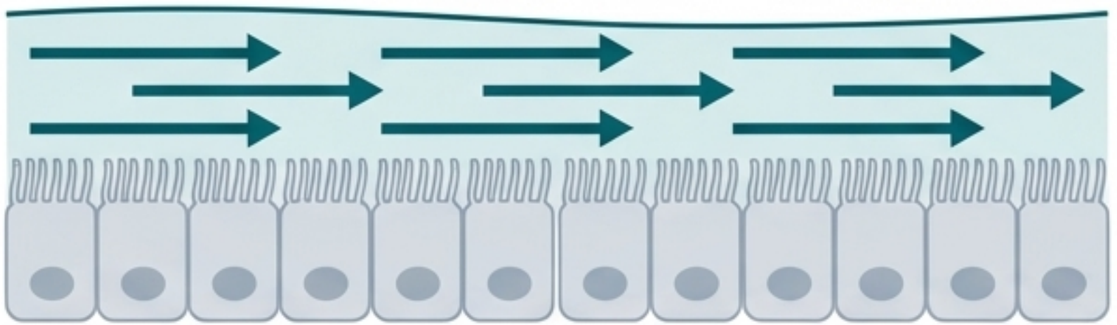
Represent **pressure-driven flow** due to surface tension and gradients in the layer's thickness.

Note: Non-Newtonian rheology is captured in how these terms depend on shear rates.

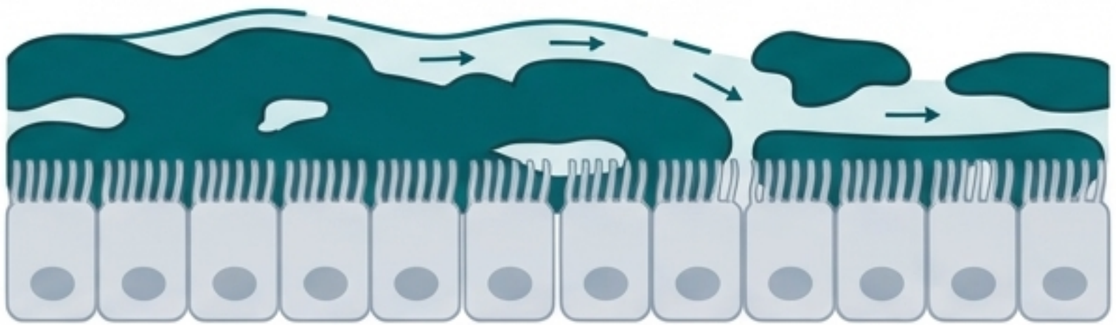
What Does “Failure” Look Like?

The model allows us to define and predict the transition from healthy transport to pathological failure. We can identify two distinct failure modes:

Healthy Clearance



Pathological Failure



1. Mucus Stagnation

- **Physically:** The net transport velocity of the mucus blanket approaches zero.
- **Cause:** Often due to increased mucus viscosity or reduced ciliary forcing. The system is too ‘sticky’ or the ‘motor’ is too weak.

2. Plug Formation

- **Physically:** The uniform mucus film becomes unstable, leading to local thickening, loss of connectivity, and eventual airway occlusion.
- **Mathematically:** Corresponds to an instability where small perturbations in film thickness grow over time.

Your Challenge: Explore the Mechanics of Failure

Using this modeling framework, you can now investigate fundamental questions about airway health. Your task is to use the model to answer:

- **Sensitivity:** How sensitive is clearance to small changes in mucus viscosity or PCL thickness? Are there sharp, critical thresholds where transport collapses?
- **Airflow's Role:** Does increased airflow from rapid breathing always improve clearance, or can it destabilize the mucus film and trigger plug formation?
- **Dominant Mechanisms:** Which physical parameters are most critical for maintaining healthy clearance? In different disease states, which mechanisms dominate the failure?
- **Regime Mapping:** Can you create a 'phase diagram' that maps out parameter combinations (e.g., viscosity vs. ciliary force) corresponding to healthy, stagnant, and unstable regimes?

An Ideal Blend of Theory and Application

This problem provides a perfect opportunity to apply fundamental principles to a complex, real-world system.

Builds on Core Concepts

It starts with classical fluid mechanics (Navier-Stokes) and applies standard mathematical techniques (scaling, approximation).

Incrementally Complex

Biological realism is added step-by-step through boundary conditions and non-Newtonian constitutive laws.

Scalable Challenge

The problem can be tackled at multiple levels—from analytical calculations to numerical simulations—making it suitable for both MSc and PhD-level work.

Direct Impact

The results connect directly to pressing physiological questions in respiratory medicine.

What You Will Accomplish

By the end of this workshop, you will have:

- **Derived** a reduced-order PDE model that governs mucus transport from first principles.
- **Implemented** the model (analytically or numerically) to simulate clearance dynamics.
- **Identified** the key parameter regimes that separate healthy clearance from pathological failure modes like stagnation and plug formation.
  pathological failure modes like stagnation and plug formation in venniabies.
- **Developed** a framework that provides a solid foundation for future research, extensions, and potential publication.

Simple Models, Deep Insight

Relatively simple mathematical models, when carefully constructed from physical principles, can yield profound insights into the complex physiological processes that govern our health.

Multiscale modeling is not an optional extra in biological fluid mechanics—it is essential.