NUMERICAL STUDY ON RED BLOOD CELLS AND DRUG-LOADED CAPSULES UNDER STOKES FLOW CONDITION

By

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Outline

- **Introduction**
  - IBM, IIM
- **Model formulation**
  - Governing equations, Boundary conditions
- **Numerical method**
  - Projection method coupled with IIM, Jump conditions
- **Code validation**
  - Simple shear flow, capsule-substrate adhesion
- **RBC & IRBC (impermeable)**
- **Drug-loaded capsule (permeable)**
  - Effect of permeability, initial concentration, flow velocity, initial position, and adhesion
Introduction

-Applications

- Biological processes such as inflammatory response
- Malaria-infected Red Blood Cell adhesion onto capillary walls
- Drug delivery using drug loaded capsules (e.g. for bladder cancer treatments)
Introduction

- The Immersed interface method (IIM) is a second order numerical scheme. It has proven to be robust for deformable and impermeable boundary problems.

- There is a lack of research work on IIM for permeable and deformable boundary problems.

  - Layton (2006), Jayathilake et al. (2010 a, b), Jayathilake et al. (2011)

- It is needed to extend the IIM for a permeable capsule moving along a capillary.
Introduction

- **Peskin’s Immersed Boundary Method (IBM)**
  - Fluid dynamics of blood flow in human heart
  - Biological flows: platelet aggregation, bacterial organisms
  - Rigid boundaries

- **Immersed Interface Method (IIM by LeVeque and Li)**
  - Elliptic equations, PDEs
  - Stokes flows with elastic boundaries
  - Navier-Stokes equations with flexible boundaries
  - Streamfunction-vorticity equations on irregular domains
Peskin’s IBM

- Use a discrete delta function to spread the force density to nearby Cartesian grid points.

\[
F(x, t) = \sum_{k=1}^{N} f_k(t) D_h(x - X_k(t)) \Delta s
\]

\[
D_h(x) = \delta_h(x) \delta_h(y)
\]

\[
\delta_h(r) = \begin{cases} 
\frac{1}{4h} \left( 1 + \cos \left( \frac{\pi r}{2h} \right) \right), & |r| \leq 2h \\
0, & \text{otherwise}
\end{cases}
\]

- Smearing out sharp interface of $O(h)$.
- First-order accurate for problems with non-smooth solutions.
Immersed Interface Method

- Incorporate the jumps in the solutions and their derivatives into the finite difference scheme near the interface

$$v_x(x_i) = \frac{v_{i+1} - v_{i-1}}{2h} + C\{v_x\}_i$$

$$C\{v_x\}_i = C([v],[v_x],[v_{xx}],\alpha)$$

- Avoid smearing out sharp interface
- Maintain second-order accuracy
Model formulation

Assumptions

- Fluid density and viscosity, and mass diffusivity are constant throughout the computational domain.

- Thickness of the membrane is negligible, Neo-Hookean rheology is assumed for the membrane.

- A minimum gap between the capsule and the walls are assumed to maintain the numerical stability of the code.

- Uniform inlet flow is assumed for the capillary flows.
Model formulation

Governing equations

\[ \rho(\ddot{u} + \bar{u}\nabla \dot{u}) = -\nabla p + \mu \nabla^2 \bar{u} + \bar{F} \]

\[ \nabla \bar{u} = 0 \]

\[ c_t + u \nabla c = D \nabla^2 c \]

Motion equations

(N-S and mass conservation equations)

Transport equation

\[ F(x,t) = \int_{\Gamma} f(s,t) \delta_d(x - \bar{X}(s,t)) ds \]

Interfacial force

\[ \bar{f}(s,t) = \frac{\partial}{\partial s} \left( T_e(s,t)\bar{\tau}(s,t) + T_b(s,t)\bar{n}(s,t) \right) - \frac{\partial W}{\partial y} \bar{n} \]

Force strength

\[ \text{Elastic tension} \]
\[ \text{Bending tension} \]
\[ \text{Adhesive force} \]
Model formulation

**Membrane tension & mass flux**

- Membrane tension
  \[ T_e = E_e (\varepsilon^{1.5} - \varepsilon^{-1.5}) \]
  \[ T_b = \frac{\partial}{\partial S} [E_b (\kappa - \kappa_R)] \]

- Bending modulus

- Elastic modulus

- Adhesion potential
  \[ W = W_{ad} \left[ \left( \frac{d_m}{y} \right)^4 - 2 \left( \frac{d_m}{y} \right)^2 \right] \]

- Adhesion strength

- Solvent flux across the membrane
  \[ J_v = -L_p ([p] - \sigma R T_{abs} [c]) \]
  \[ J_s = J_v (1 - \sigma) c_{av} - \omega R T_{abs} [c] \]

- Reflection coefficient

- Hydraulic conductivity

- Solute diffusivity

- Solute flux across the membrane

References:
- Zhang et al., 2008
- Seifert, 1991
- Kedem and Katchalsky, 1958
Model formulation

Boundary conditions

- Along boundary - $\partial \Omega$
  
  Periodic boundary condition in the $x$ direction and the no-slip boundary condition in the $y$ direction are imposed.
  
  $c = 0$ at $y = b_1, b_2$

- Along Membrane - $\Gamma$

  $U(\vec{X}(s,t),t) = u(\vec{X}(s,t),t) - J_v(s,t) \cdot \cos(\theta)$

  $V(\vec{X}(s,t),t) = v(\vec{X}(s,t),t) - J_v(s,t) \cdot \sin(\theta)$

  $J_v = -L_p \left[ [p] - \sigma RT_{abs} \left[ c \right] \right]$

  $(J_v c - D c_n)_{\Gamma^+} = J_s$
Model formulation

- **Non-dimensionalization**

\[
\nabla . \vec{u}^* = 0
\]
\[
\frac{\partial \vec{u}^*}{\partial t^*} + \vec{u}^* \cdot \nabla \vec{u}^* = -\nabla p^* + \frac{1}{\text{Re}} \nabla^2 \vec{u}^* + \vec{F}^*
\]
\[
\vec{F}^* (x^*, t^*) = \int f^* (s^*, t^*) \delta_D (x^* - X^* (s^*, t^*)) ds^*
\]
\[
\frac{\partial f^* (s^*, t^*)}{\partial s^*} = \frac{\partial}{\partial s^*} \left( T_e^* (s^*, t^*) \tau (s^*, t^*) + T_b^* (s^*, t^*) n (s^*, t^*) \right) - \frac{\partial W^*}{\partial y^*} \nabla \vec{n}^*
\]
\[
\frac{\partial c^*}{\partial t^*} + \vec{u}^* \cdot \nabla c^* = \frac{1}{\text{Pe}} \nabla^2 c^*
\]
\[
J_v^* = -\left( f_n^* C_1 - \sigma C_2 [c^*] \right), \quad J_s^* = (1 - \sigma) J_v^* c_{av}^* - C_3 [c^*]
\]

- **Re** = \( \frac{\rho U_r}{\mu} \),  **Pe** = \( \frac{U_r}{D} \),  **C_1** = \( \frac{E_e L}{U_d} \),  **C_2** = \( \frac{RT_{abs} \bar{c} L}{U} \),  **C_3** = \( \frac{\omega RT_{abs}}{U} \)
Numerical method

A pressure-increment projection algorithm is employed on a MAC staggered grid to solve N-S equations. The transport equations are solved as reported in Jayathilake et al. (2010 a, b).
Numerical method

Solving equations of motion

First the membrane configuration is updated explicitly, and then the Projection method combined with IIM is employed to solve N-S equations.

\[ \dot{X}^{*,m+1} = X^{*,m} + \Delta t^{*} \cdot \dot{Y}^{*,m}, \quad \dot{Y}^{*,m+1} = Y^{*,m} + \Delta t^{*} \cdot \dot{V}^{*,m} \]

\[ \frac{\ddot{u}^{*,m+1} - \ddot{u}^{*,m}}{\Delta t^{*}} + (\dddot{u}^{*,\nabla u^{*}})^{m+1/2} = -\nabla p^{*,m+1/2} + \frac{1}{2 \text{Re}} \left( \nabla^{2} \ddot{u}^{*,m+1} + \nabla^{2} \ddot{u}^{*,m} \right) - Q\{\ddot{u}^{*}\} \]

\[ \nabla . \ddot{u}^{*,m+1} = 0 \]

\[ \frac{\dddot{u}^{*,m} - \dddot{u}^{*,m}}{\Delta t^{*}} = -\left( \dddot{u}^{*,\nabla u^{*}} \right)^{m+1/2} - \nabla p^{*,m+1/2} + \frac{1}{\text{Re}} \nabla^{2} \ddot{u}^{*,m+1/2} - Q\{\dot{u}^{*}\} \]

\[ \nabla^{2} \phi^{*,m+1} = \frac{\nabla . \ddot{u}^{*,m}}{\Delta t^{*}} + \frac{C\{\nabla . \ddot{u}^{*,m}\}}{\Delta t^{*}} - C\{\nabla^{2} p^{*,m+1/2}\} + C\{\nabla^{2} p^{*,m-1/2}\} + \xi \left[ \nabla p^{*} \right]_{t} ; \quad \nabla \nabla \phi^{*,m+1} = 0 \]

\[ \dddot{u}^{*,m+1} = \dddot{u}^{*,m} - \Delta t^{*} \cdot \nabla \phi^{*,m+1} - \Delta t^{*} \left( C\{\nabla p^{*,m+1/2}\} - C\{\nabla p^{*,m-1/2}\} \right) \]

\[ p^{*,m+1/2} = p^{*,m-1/2} + \phi^{*,m+1} - \frac{1}{2 \text{Re}} \left( \nabla . \ddot{u}^{*,m} \right) - \frac{1}{2 \text{Re}} C\{\nabla . \ddot{u}^{*,m}\} \]
Numerical method

Some spatial correction terms for motion equations

Spatial correction terms are calculated by Taylor series expansions at intersection points $l_1$ and $l_2$ as below:

\[
C_{i,j} \{ p_x \} = -\frac{1}{2h} \left\{ (p_x^{*})_{l_1}^{m+1} + h_1 [p_x^{*}]_{l_1}^{m+1} + (h_1^2 / 2)[p_{xx}]_{l_1}^{m+1} \right\}
\]

\[
C_{i,j} \{ p_y \} = -\frac{1}{2h} \left\{ (p_y^{*})_{l_2}^{m+1} + h_2 [p_y^{*}]_{l_2}^{m+1} + (h_2^2 / 2)[p_{yy}]_{l_2}^{m+1} \right\}
\]

\[
C_{i,j} \{ \nabla^2 p \} = -\frac{1}{h^2} \left\{ (p^{*})_{l_1}^{m+1} + (p^{*})_{l_2}^{m+1} + h_1 [p_x^{*}]_{l_1}^{m+1} + h_2 [p_y^{*}]_{l_2}^{m+1} + (h_1^2 / 2)[p_{xx}]_{l_1}^{m+1} + (h_2^2 / 2)[p_{yy}]_{l_2}^{m+1} \right\}
\]

\[
h_1 = x_{i+1} - x_{l_1}, \quad h_2 = y_{j+1} - y_{l_2}
\]
Numerical method

Pressure and velocity jump conditions needed for correction terms are given below:

\[
\begin{align*}
[p^*] &= \beta' f^*_N \\
[p'_n] &= \beta' \frac{\partial}{\partial S} f^*_T \\
[u^*_n] &= [v^*_n] = 0 \\
[u^*_n] &= \beta f^*_T \sin \theta \\
[v^*_n] &= -\beta f^*_T \cos \theta
\end{align*}
\]

These jump conditions are derived using the equations of motion as reported in *LeVeque and Li (1997)*.

\[
\beta = \frac{E_e}{\mu \bar{V}} \quad \beta' = \frac{E_e}{\rho \bar{V}^2 \bar{r}}
\]
Numerical method

- Solving transport equation

Transport equation is solved as reported in *Jayathilake et al.* (2010a).

\[
c_i^* + u^* \frac{c_i^*}{x} + v^* \frac{c_i^*}{y} = \frac{1}{Pe} \left( \frac{c_{x_i}^*}{x} + \frac{c_{y_i}^*}{y} \right)
\]

\[
\frac{c_{i,j}^{*,m+1} - c_{i,j}^{*,m}}{\Delta t^*} + Q_{i,j} - \frac{1}{Pe} \left\{ \nabla^2 c_{i,j}^{*,m+1} + C_{i,j} (\nabla^2 c^*) \right\} = -u_{i,j}^{*,m} \left\{ c_{x,i,j}^{*,m} + C_{i,j} (c_x^*) \right\} - v_{i,j}^{*,m} \left\{ c_{y,i,j}^{*,m} + C_{i,j} (c_y^*) \right\}
\]

\[
Q_{i,j} = \begin{cases} 
\pm \frac{1}{\Delta t^*} \left\{ c_{i_1}^{*,1} + (t_{m}^{*,1} - t_{1}^{*,m})[c_{t_i}^{*,1}] \right\}, & t_{m}^{*,m} < t_{1}^{*,m} < t_{m}^{*,m+1} \\
\pm \frac{1}{\Delta t^*} \left\{ c_{i_1}^{*,1} + (t_{m}^{*,m+1} - t_{1}^{*,m})[c_{t_i}^{*,1}] \right\}, & t_{m}^{*,m+1} < t_{1}^{*,m+1} < t_{m}^{*,m+2}
\end{cases}
\]
Numerical method

Concentration jump conditions

Approximate jump conditions are computed using the boundary condition at the membrane and Kedem-Katchalsky relations.

\[
\begin{align*}
c_k^{*,-,m+1} &= \frac{(4c_k^{*,m+1} - c_k^{*,m+1}) - 2h^* PeJ_{s,k}^{*,m}}{3 - 2h^* PeJ_{v,k}^{*,m}} \\
k^{*,+,m+1} &= (4c_k^{*,m+1} - c_k^{*,m+1}) + 2h^* PeJ_{s,k}^{m} \\
\left[ c_k^{*,m+1} \right] &= c_k^{*,+,m+1} - c_k^{*,-,m+1} \\
\left[ c_n^{*,m+1} \right] &= J_v^{*,m+1} Pe \left( c_k^{*,+,m+1} - c_k^{*,-,m+1} \right)
\end{align*}
\]
Code Validation: Simple shear flow

Steady state velocity field at shear rate, $G = 0.0125$

Comparison with *Breyiannis* and *Pozrikidis* (2000)
Capsule-substrate adhesion
Code Validation: Adhesion

The theoretical solution is derived considering the energy balance for the membrane.

\( r_1 = \frac{S_T}{2\pi} \)

\[ r_2 = \sqrt{\frac{A_{eq}}{\pi}} \]

\[ L_{ad} \sim r_1 (1 - \frac{r_2}{r_1})^{1/3} \]

\[ \log\left( \frac{L_{ad}}{r_1} \right) \sim \left( \frac{1}{3} \right) \log\left( 1 - \frac{r_2}{r_1} \right) \]

Comparison with Cantat and Misbah (1999)

(Cantat and Misbah, 1999)

(Jayathilake et al., 2010 b)
The detachment force for IRBC is 5 to 10 $\times 10^{-11}$ N (Nash et al., 1992).

The adhesive coefficient for IRBC is estimated as $1 \times 10^{-5}$ N/m (approximately).
## Parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>RBC: impermeable</th>
<th>IRBC: impermeable</th>
<th>Drug-loaded capsule (fairly similar to IRBC): permeable</th>
</tr>
</thead>
<tbody>
<tr>
<td>( r = 4 \mu m )</td>
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<td>( r = 4 \mu m )</td>
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<td>( E_e = 6 \times 10^{-6} N / m )</td>
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<td>( E_b = 1.8 \times 10^{-19} Nm )</td>
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<td>( \mu = 4 \times 10^{-3} N.s / m^2 )</td>
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<tr>
<td>( \rho = 1000 kg / m^3 )</td>
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</tr>
<tr>
<td>( W_{ad} = 0 )</td>
<td>( W_{ad} = 10^{-5} N / m )</td>
<td>( W_{ad} = 10^{-5} N / m )</td>
<td>( W_{ad} = 10^{-5} N / m )</td>
</tr>
<tr>
<td><strong>No adhesion</strong></td>
<td><strong>Impermeable membrane</strong></td>
<td><strong>Impermeable membrane</strong></td>
<td><strong>Impermeable membrane</strong></td>
</tr>
</tbody>
</table>

\( L_p = \omega RT_{abs} = 0 \)

\( \omega RT_{abs} = 10^{-3} m / s \)

\( \sigma = 0 \)

\( D = 1.5 \times 10^{-9} m^2 / s \)

The uniform inlet velocity \( U_{in} = 100-500 \mu m/s \)
Results: RBC & IRBC

RBC deformation in plasma flow, $U_{in} = 100$ μm/s (uniform inlet velocity)

IRBC deformation in plasma flow, $U_{in} = 100$ μm/s (uniform inlet velocity)
Results: Flow resistance

- Flow resistance in the presence of RBC and IRBC

- Resistance by IRBC > Resistance by RBC
- Therefore, IRBC may cause microvascular blockage
Results: Drug loaded capsule

Concentration distribution

\[ \omega R T_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{\text{in}} = 0, W_{\text{ad}} = 0 \]

capsule is stationary \((U_{\text{in}} = 0)\)
Results: Drug loaded capsule

**Effect of membrane permeability**

\[ \omega RT_{abs} = 1 \times 10^{-5} - 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{in} = 0, W_{ad} = 0 \]

(a) solute mass of the capsule

(b) solute mass of the surrounding field
Results: Drug loaded capsule

Effect of membrane permeability

\[ \omega RT_{\text{abs}} = 1 \times 10^{-5} - 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{\text{in}} = 0, W_{\text{ad}} = 0 \]

(c) solute mass absorbed by the walls
Results: Drug loaded capsule

- Effect of initial solute concentration of capsule

\[ \omega RT_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}, \quad \gamma = 50-500, \quad U_{\text{in}} = 0, \quad W_{\text{ad}} = 0 \]

(a) solute mass of the capsule

(b) solute mass of the surrounding field
Results: Drug loaded capsule

Effect of initial solute concentration of capsule

\[ \omega R T_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}, \gamma = 50-500, U_{\text{in}} = 0, W_{\text{ad}} = 0 \]

(c) solute mass absorbed by the walls
Results: Drug loaded capsule

- Effect of imposed velocity

\[ \omega R T_{abs} = 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{in} = 100-1000 \mu \text{m/s}, W_{ad} = 0 \]
Results: Drug loaded capsule

Effect of imposed velocity

\[ \omega R T_{\text{abs}} = 1 \times 10^{-3} \text{ m/s, } \gamma = 150, \ U_{\text{in}} = 100-1000 \, \mu \text{m/s, } W_{\text{ad}} = 0 \]
Results: Drug loaded capsule

- **Effect of adhesion & initial position**
  - $\omega R T_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}$, $\gamma = 150$, $U_{in} = 500 \mu\text{m/s}$

(a) initial non-adhesive capsule is away from the walls

(b) initial non-adhesive capsule is near a wall

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Results: Drug loaded capsule

Effect of adhesion & initial position

$\omega RT_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{\text{in}} = 500 \mu\text{m/s}$

(c) initial adhesive capsule is near a wall, $W_{\text{ad}} = 20\mu\text{J/m}^2$
Results: Drug loaded capsule

- Effect of adhesion & initial position
  \[ \omega R T_{\text{abs}} = 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{\text{in}} = 500 \mu \text{m/s} \]

(a) solute mass of the capsule

(b) solute mass of the surrounding field
Results: Drug loaded capsule

- Effect of adhesion & initial position
  \[ \omega RT_{abs} = 1 \times 10^{-3} \text{ m/s}, \gamma = 150, U_{in} = 500 \mu\text{m/s} \]

(c) solute mass absorption by walls
Conclusions

- The numerical approach is deemed reasonable for simulating capsule-substrate adhesion in the presence of a flow field.

- The numerical results in the absence of a flow field show that the solute transfer between the capsule and the vessel walls can be modulated by changing the membrane permeability and the initial solute concentration of the capsule.

- The capsule moving near to one wall would increase the solute absorption by walls as opposed to the case of the capsule moving along the centre line of the vessel. The adhesion between the capsule and walls would further increase marginally the total solute transfer between the capsule and vessel walls.
Related Publications

**Journals**


**Conferences**


References

THREE-DIMENSIONAL NUMERICAL SIMULATION OF HUMAN NASAL CILIA IN THE PERICILIARY LIQUID LAYER
Outline

Introduction
- Human lungs
- Airways surface liquid
- Structure of cillum
- Cilia beating
- Fluid dynamics models of cilia motion

Numerical Modeling
- Governing equations & Boundary conditions
- Some of 2D modeling work
- 3D modeling

Results
- Standard problem
- Effect of cilia beat frequency
- Extension for a 2 layers problem

Conclusions
Introduction

Human lungs

- During normal breathing, the airways transport air into the lungs. However, this air is often polluted with a variety of particles, fungi and bacteria that become deposited on the airway surface liquid (ASL).
Introduction

Airway surface liquid

One of the main protections of the upper airway and the lungs is a fluid layer covering the interior epithelial surface of the bronchi and bronchioles. This is known as the airway surface liquid.

The airway surface liquid exhibits a two-layer structure. There are two types of fluids: the watery PCL and the mucus layer. An array of cilia is immersed in the PCL.
Introduction

- **Structure of a cilium**
  - Cilia are microscopic, hair-like organelles projecting from a cell’s surface.
  - The cilium is moved when outer microtubules slide past each other.
Cilia beating

- Each cilium performs a repetitive beat cycle consisting of recovery and effective stroke.
- During the effective stroke the cilium moves forward.
- During the recovery stroke the cilium moves backwards.
- The work done during the effective stroke is several times the amount of work done during the recovery stroke.
Introduction

- Fluid dynamic models of cilia motion

No. of layers-L
1L 2L 3L
PCL + Mucus + Air

No. of dimensions-D
2D 3D
PCL + Mucus

Cilia beating
Volume force
Prescribed beating
Discrete cilia
Couple-internal mechanics/fluid-structure interaction
Numerical Modeling

- PCL & mucus motion is governed by NS equations

\[ \rho \left( \frac{\partial \vec{u}}{\partial t} + \vec{u} \cdot \nabla \vec{u} \right) = -\nabla p + \mu \nabla^2 \vec{u} + \vec{F}; \quad \nabla \vec{u} = 0 \]

- In this numerical study, the time-dependent incompressible fluid-flow problem is solved by the projection method.
- The interaction between cilia and PCL is imposed using the Immersed Boundary Method (IBM).
- MAC scheme is used for discretization.
Numerical Modeling

MAC Scheme in 2D

\[ u_{i,j}^{k+1} = u_{i,j}^k + \Delta t \left( \nabla \cdot \mathbf{v}_{i,j} + \frac{\mathbf{v}_{i,j} \cdot \mathbf{n}}{\Delta x} \right) \]

\[ v_{i,j}^{k+1} = v_{i,j}^k + \Delta t \left( \nabla \cdot \mathbf{u}_{i,j} + \frac{\mathbf{u}_{i,j} \cdot \mathbf{n}}{\Delta y} \right) \]

\[ p_{i,j}^{k+1} = p_{i,j}^k + \Delta t \frac{\nabla^2 p_{i,j}}{\Delta x} \]

\[ \mathbf{v}_{i,j} = \nabla \mathbf{u}_{i,j} \]

\[ \mathbf{u}_{i,j} = \mathbf{v}_{i,j} + \mathbf{p}_{i,j} \]

- \( \mathbf{u} \)-mesh points
- \( \mathbf{v} \)-mesh points
- \( \mathbf{p} \)-mesh points
- Control points
Numerical Modeling

Interaction force

\[ \vec{F}_{i,j,k}^{n+1} = \rho \left( \frac{\vec{U}'_{i,j,k}^{n+1} - \vec{u}_{i,j,k}^{n}}{\Delta t} - (\vec{u} \cdot \nabla \vec{u})_{i,j,k}^{n} \right) + \left( \nabla p \right)_{i,j,k}^{n} - \left( \mu \nabla^2 \vec{u} \right)_{i,j,k}^{n} \]

Distributed cilium velocity at a Cartesian grid point

\[ \vec{U}'_{i,j,k}^{n+1} = f(i, j, k, \vec{X}) \vec{U}(\vec{X}) \]

Cilium velocity

\[ f(i, j, k, \vec{X}) = \frac{1 - \tanh((r - 1)/0.5)}{2} \]

Sanderson & Sleigh (1981)

Or

Gheber & Priel (1997)
Numerical Modeling: 2D-2L

- Cilia motion

- Mucus velocity = 4.4.10^{-3} \text{ cm/s}
- Mucus velocity in Smith et al. (2007) = 3.8.10^{-3} \text{ cm/s}
Numerical Modeling: 2D-2L

Some results

- Mucus velocity depends linearly on Cilia beat frequency.
- Mucus velocity decreases with mucus viscosity.
Numerical Modeling: 3D-1L

Prescribed cilia beating

Side view

Top view
Numerical Modeling: 3D-1L

Prescribed cilia beating.

Side view

Top view
Results: 3D-1L

**STANDARD** Problem

- Computational domain = \([-24, 24] \times [-6, 6] \times [0, 8] \, \mu m^3\)
- The length of the cilium = 6.0 \, \mu m
- PCL density = 1 \, g/cm^3
- PCL viscosity = 0.01 \, P
- Cilia beating frequency = 10 Hz
- No. of cilia = 24 (in two rows, i.e. 12x2)
- Mesh = 120x30x20
- No. of control points on each cilium = 20
Results: 3D-1L

- Computational domain
Results: 3D-1L

- Cilia & Velocity field

**Side view**

**Top view**
Results: 3D-1L

- Cilia & Pressure field

![Side view](image1)
![Top view](image2)
Results: 3D-1L

The total PCL flow $Q$

$$Q(x) = \iiint u(x, y, z) dydzdt$$

- Average PCL velocity $= 2.3 \times 10^{-5} \text{ cm/s}$
- Average PCL velocity in Smith et al. (2007) $= 3.1 \times 10^{-5} \text{ cm/s}$
Results: 3D-1L

- Effect of Cilia Beat Frequency (CBF)

- CBF = 5, 10, 15, 20, 25 Hz

- The average PCL velocity is linearly dependent on CBF.

- It has been shown experimentally that ciliary forces depend linearly on CBF (Teff et al., 2008).
Results: 3D-2L

- A more accurate model
Conclusions

- In the present work, multiple human nasal cilia immersed in the PCL are simulated by using 2D and 3D Projection Method combined with the Immersed Boundary Method.

- The present results are found to be in reasonable agreement with previously reported results for the mucus and PCL velocities of human respiratory system.

- The present model is a basic one. A more realistic model including non-Newtonian mucus layer is being developed.
THANK YOU