Immersed boundary-lattice Boltzmann method for simulation of muco-ciliary transport: effect of mucus depth at various amounts of cilia beat frequency

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Abstract. Numerical simulation based on immersed boundary-lattice Boltzmann method has been employed to study 2D muco-ciliary transport problem. The periciliary liquid (PCL) and mucus layers in this study are considered as the Newtonian and viscoelastic fluid respectively. An Oldroyd-B model is used as the constitutive equations of mucus layer. To simulate accurate effects of the cilia and PCL-mucus interface on the fluid, immersed boundary method is used. Numerical simulations have been performed to investigate the effects of mucus depth on the muco-ciliary clearance at various values of cilia beat frequencies. Our results show that, by increasing mucus depth, which results from air pollution and smoking, mean mucus velocity decreases. But it can be completely modified by increasing cilia beat frequency and the cilia beat frequency has great effect on the muco-ciliary clearance.

1. Introduction
The mechanics of muco-ciliary transport is one of the fundamental problems in respiratory mechanics and the study of this problem have attracted a great deal of research efforts. The airways surface liquid layer (ASL) of the human respiratory system is normally from 5 to 10 µm deep [1]. This liquid consists of two sub layers: the innermost watery periciliary liquid layer (PCL) and the outermost viscoelastic mucus layer [2]. The main function of the mucus layer is in cleaning the inspired air of unwanted particles, cellular debris and secretions from the airways of the lung [3]. The airways of the lung are lined with a dense mat of cilia which beat back and forth in a co-ordinated wave and hence the mucus layer together with entrapped particles is propelled out of the lungs [4]. These Cilia have two quite distinct stages of their beating cycle in which the effective stroke when the cilium is extended out of the cell surface and the recovery stroke when it moves back slowly to the start of its effective stroke. The effective stroke occupies a shorter period of the beat than the recovery stroke so the work done during the effective stroke is several times the amount of work done performed during the recovery stroke [5].

Structural and functional disorders of cilia may be caused by genetic disorders such as Primary Ciliary Dyskinesia (PCD) and some acquired insults such as exposing to toxins and pollutants leading to inefficiency in muco-ciliary transport [6]. The PCD is a cilia-related disease in which cilia beat in abnormal patterns or beat slowly or become completely stationary, results from some defects in the components of the axonemes [7]. Due to disorder in cilia motion, the velocity of mucus layer reduces and mucus would accumulate with airways which leads to airway blockage, lung damage and infections [8]. PCD lead to the abnormalities in the cilia beat frequency (CBF), cilia beat pattern
(CBP), and Nitric Oxide (NO) diseases which have been reported in the literature. Rossman et al. [9] reported two patterns of abnormal ciliary beat (CBP); an oscillating and a rotating type of motion. Their results show that this abnormal motion was present in up to 40 percent of cells and the remainder were totally immotile. Another abnormal CBP is reported in Rutland et al. [10] which is called “windscreen wiper” motion. Chilvers et al. [11] stated that abnormalities in the cilia beat frequency (CBF) is the result of nasal rhinorrhoea or blockage and moist-sounding cough which is results from PCD. Their study [11] show that determining ciliary beat pattern related to specific ultrastructural ciliary defects might help in the diagnosis of PCD. In addition, some investigation [12-14] stated that nasal NO is found in very small quantities in PCD patients. Variation in CBF play vital role on muco-ciliary transport process [15, 16]. Although smoking has no effect [17] or has a less effect [10] on CBF, CBF is increased by ethanol [17]. The characteristics of the PCL layer such as temperature, pH, tonicity, viscosity, relative humidity, and pressure influence CBF [6].

1.1. Problem Statement
In this study, two-layer model consisting of an upper viscoelastic mucus layer and a lower Newtonian periciliary layer (PCL) is developed to simulate the effects of mucus depth on the muco-ciliary transport process at three different cilia beat frequency. A schematic of the problem is shown in figure 1.

![Figure 1. A schematic geometry for the muco-ciliary transport.](image)

1.2. Significance of the Study
As metioned before CBF has a great effect on the muco-ciliary clearance. On the other hand many air pollutants, especially tobacco smoke, have a detrimental effect on the mucus transport [18]. One reason is increasing the depth of mucus layer. In this study the effect of mucus depth at various amounts of CBF has been studied. The main contribution of the present study is considering mucus as an Oldroyd-B fluid for the first time. This model is discussed in term of the convected components of the stress tensor and the metric coefficients of the convected coordinate system. Material constants appears in this constitutive equation and also temperature history may be included if it is desired to account for nonisothermal effects [19].

2. Mathematical formulation
In this part the governing equations and the numerical method for solving the muco-ciliary problem process is defined. As Figure 1 shows, in this problem, ASL is considered as two separate layers, the lower periciliary liquid layer consists of watery and nearly Newtonian liquid and the upper mucus layer is a viscoelastic fluid. Immersed boundary method [20] is used to simulate precise effects of the cilia and PCL-mucus interface on the fluid. At the beginning of this section, the standard parameter set which we use for reference is defined as follows [15, 16]:

Length of cilia is \( L=6\mu m \), the spacing between any two neighboring cilia along the epithelium wall is chosen as \( 3 \mu m \), the standard depth of PCL as \( LPCL=6\mu m \), and the depth of the mucus layer as \( LM=4\mu m \), the density of the fluid is. The stiffness constant of the virtual membrane is \( T0=32\times10^{-3} \).
N/m, the cilia beat frequency is set at $\sigma = 60$ rad/s, the viscosity of PCL is $\eta_{\text{PCL}} = 0.001$ Pa.s, and the viscosity of mucus layer is $\eta_{\text{M}} = 0.0482$ Pa.s. As mentioned before, $\eta_{\text{M}}$ is decomposed into viscous and elastic parts. Since a full viscoelastic characterization for mucus is not yet available, we assume that the standard viscosity of Newtonian part of mucus is as the same as the viscosity of PCL i.e. $\eta_{\text{M},\text{N}} = 0.001$ Pa.s. For the reference parameters the viscosity ratio is $\beta = 0.98$. The standard value of relaxation time of mucus is about $\lambda = 0.034$ s.

2.1. Governing Equations

The governing equations of incompressible fluid flow in a model which is shown in figure 1 can be written as follows [15]:

$$\nabla \cdot \vec{u} = 0 \quad (1)$$

$$\frac{\partial \vec{u}}{\partial t} + \vec{u} \cdot \nabla \vec{u} + \frac{1}{\rho} \nabla p = -\nabla \sigma + \mathbf{f} \quad (2)$$

$$\vec{f}(\vec{x}, t) = \int_{\Gamma} \vec{f}(s, t) \delta(\vec{x} - \vec{X}(s, t)) ds \quad (3)$$

$$\frac{\partial \vec{X}(s, t)}{\partial t} = \vec{U}(\vec{X}(s, t), t) = \int_{\Gamma} \vec{u}(\vec{x}, t) \delta(\vec{x} - \vec{X}(s, t)) d\vec{x}. \quad (4)$$

Where $\vec{x}$ is the Eulerian coordinates, $\vec{u}$ is the velocity vector, $\rho$ is density, $p$ is static pressure, $t$ is time, $\sigma$ is the stress tensor and $\mathbf{f}$ is the boundary force acting on the fluid field. Also $\vec{X}$ is the Lagrangian coordinates, $\vec{U}$ is the velocity vector of Lagrangian nodes, $s$ is the arc length of Lagrangian nodes and $\Gamma$ is the boundary force density which contains cilia and membrane forces. In addition $\delta(\vec{x} - \vec{X}(s, t))$ is a Dirac delta function. Equation (1) and (2) describe the interaction between the immersed boundary and the fluid by distributing the boundary force at the Lagrangian points to Eulerian points and interpolating the velocity at the Eulerian points to Lagrangian points.

The cilia have a cyclic motion in PCL. There is no interface material between the PCL and mucus layers so the cilia can penetrate the mucus-PCL interface. In addition effect of the surface tension is added by the force generated due to an imaginary elastic membrane. In this study the flow is assumed to be periodic in the horizontal direction. The bottom boundary is assumed to be no-slip wall and the top boundary is assumed to be free-slip boundary [15].

2.1. Constitutive Equations

Previous experimental studies have concluded that viscoelasticity play a vital role on effective transport of mucus [1,16]. In this study an Oldroyd-B model is used as a constitutive equation for mucus. In this model, the stress tensor $\sigma$ can be decomposed into two parts [19]:

$$\sigma_{\text{M}} = \sigma_{\text{M,N}} + \sigma_{\text{M,E}} \quad (5)$$

$\sigma_{\text{M,N}}$ is related to Newtonian part of stress tensor and the second term ($\sigma_{\text{M,E}}$) is related to the elastic contribution of it which can be calculated as:

$$\sigma_{\text{M,N}} = 2\eta_{\text{M,N}} D \quad (6)$$

$$\sigma_{\text{M,E}} + \lambda \sqrt{\sigma_{\text{M,E}}} = 2\eta_{\text{M,E}} D \quad (7)$$

In equation (7), $\lambda$ is the relaxation time, which gives an indication of the magnitude of the elastic nature of the fluid. The viscosity of mucus also decomposed into Newtonian ($\eta_{\text{M,N}}$) and elastic ($\eta_{\text{M,E}}$) viscosities as follows:
\[ \eta_M = \eta_{M,N} + \eta_{M,E}, \quad \beta = \frac{\eta_{M,E}}{\eta_M} \] (8)

and the upper convected derivative of \( \sigma_{M,E} \) is defined as:

\[ \sigma_{M,E}^v = \frac{\partial \sigma_{M,E}}{\partial t} + \bar{u} \nabla \sigma_{M,E} - \sigma_{M,E} \nabla \bar{u} - \nabla \bar{u}^T \sigma_{M,E} \] (9)

In equation (3) and (4) \( D \) is the rate of deformation which is defined as:

\[ D = \frac{1}{2} (\nabla \mathbf{V} + \nabla \mathbf{V}^T) \] (10)

The Oldroyd-B constitutive equation can be derived from a molecular model in which the polymer molecule is idealized as an infinitely extensible Hookean spring connecting two Brownian beads [19].

2.2. Numerical Method

In this part 2D numerical model based on immersed boundary-lattice Boltzmann method has been used to simulate mucociliary clearance problem (Figure 1). This method uses a fixed Cartesian mesh to represent fluid phase, which is composed of Eulerian points. For the boundary immersed in the fluid, a set of Lagrangian points are used to represent it [20].

At the beginning of this part to simulate real rheology properties of the mucus layer and also the real dimension of the geometry, transformation coefficients form the physical domain to the lattice Boltzmann domain are introduced as:

\[ C_{h_x} = \frac{\Delta x^{ph}}{\Delta x^b}, \quad C_{h_y} = \frac{\Delta y^{ph}}{\Delta y^b}, \quad C_t = \frac{\Delta t^{ph}}{\Delta t^b}, \quad C_p = \frac{\rho^{ph}}{\rho_0^{lb}} \] (11)

In equation (11) \( \Delta x^{ph} \) and \( \Delta y^{ph} \) are grid spacing in \( x \) and \( y \) direction, \( \Delta t^{ph} \) is time spacing and \( \rho^{ph} \) is density for physical domain. In addition \( \Delta x^b \) and \( \Delta y^b \) are grid spacing, \( \Delta t^b \) is time spacing and \( \rho_0^{lb} \) is referenced density in LBM domain. In addition \( C_{h_x}, C_{h_y}, C_t \) and \( C_p \) are related to space in \( x \) and \( y \) direction, time and density transformation coefficients respectively. In this study “\( lb \)” superscript is related to LBM variables and for simplicity, physical variables are shown without any superscript.

In equation (11) by considering \( \Delta x = \Delta y \) and \( \Delta x^b = \Delta y^b \) we can write \( C_{h_x} = C_{h_y} = C_h \). The other transformation coefficients can be obtained as follows:

\[ C_u = \frac{\bar{u}}{\bar{u}^{lb}} = \frac{1}{C_h}, \quad C_v = \frac{\nu_N}{\nu_N^{lb}} = \frac{C_h^2}{C_t}, \quad C_p = \frac{P}{P^{lb}} = C_p \left( \frac{C_h}{C_t} \right)^2 \] (12)

where \( \nu_N \) is the kinematic viscosity of Newtonian part of the fluid. \( C_u, C_v \) and \( C_p \) are velocity, Newtonian kinematic viscosity and pressure transformation coefficients respectively.

The lattice Boltzmann equations in fluid points can be shown as follows [26]:

\[ f_\alpha \left( \tilde{x}^{lb} + \tilde{c}_\alpha \Delta t^b, t^{lb} + \Delta t^b \right) - f_\alpha \left( \tilde{x}^{lb}, t^{lb} \right) = -\frac{1}{\tau} \left( f_\alpha \left( \tilde{x}^{lb}, t^{lb} \right) - f_\alpha \left( \tilde{x}^{lb}, t^{lb} \right) \right) + \tilde{F}_\alpha \Delta t^b \] (13)

\[ F_\alpha = \omega_\alpha \left( 1 - \frac{1}{2\tau} \right) \left( \tilde{c}_\alpha^2 - \tilde{u}^{lb} \frac{\tilde{c}_\alpha}{c_s^2} + \tilde{c}_\alpha \tilde{u}^{lb} \frac{\tilde{c}_\alpha}{c_s^2} \right) \tilde{F}^{lb} \] (14)

\[ \rho^{lb} = \sum_\alpha \tilde{c}_\alpha f_\alpha \] (15)
\[
\rho^b \vec{u}^b = \sum_a \vec{e}_a \cdot f_a \frac{\rho^b}{2} \vec{J}^b \Delta t^b 
\]

where \( f_a \) is the distribution function, \( f_a^{eq} \) is its corresponding equilibrium distribution function for the discrete velocity \( \vec{e}_a \), \( F_a \) is the discrete force term, \( \vec{J}^b \) is the force density action on the fluid field, \( \omega_a \) is weighting coefficient which depends on the selected lattice velocity model, \( \tau \) is the single relaxation time, \( \rho^b \) is the density of fluid in LB domain, \( c_s = c/\sqrt{3} \) is the sound speed and \( c = \Delta x^b / \Delta t^b \) is the lattice speed where \( \Delta x^b \) and \( \Delta t^b \) are the lattice constant and the time step size, respectively. \( f_a^{eq} \) is the equilibrium distribution function (EDF) defined as:

\[
f_a^{eq} = \rho^b \omega_a \left[ 1 + \frac{3(\vec{e}_a \cdot \vec{u}^b)}{c^2} + \frac{9(\vec{e}_a \cdot \vec{u}^b)^2}{c^2} - \frac{3|\vec{u}^b|^2}{2c^2} \right] 
\]

Here, the two-dimensional nine velocities (D2Q9) model is used. The particle velocity \( \vec{e}_a \) and weighting coefficients \( \omega_i \) may be written as:

\[
\vec{e}_a = \begin{cases} 
[0,0] \\
\epsilon \cos(\frac{(\alpha-1)\pi}{2}), \sin(\frac{(\alpha-1)\pi}{2}) \\
\sqrt{2c}[\cos(\frac{(\alpha-5)\pi}{2} + \frac{\pi}{4}), \sin(\frac{(\alpha-1)\pi}{2} + \frac{\pi}{4})]
\end{cases}, \quad \omega_a = \begin{cases} 
\frac{4}{9} \\
\frac{1}{9} \\
\frac{1}{36}
\end{cases}, \quad \alpha = 0-8
\]

The single relaxation time in LB equations (\( \tau \)) is calculated as:

\[
\tau = \frac{V_{lb}}{c_s^2 \Delta t^b} + 0.5 
\]

where \( V_{lb} \) is the kinematic viscosity in LBM domain.

In equation (14), \( \vec{J}^b \) consists of three different forces as follows:

\[
\vec{J}^b = \vec{J}^b_E + \vec{J}^b_{Cilia} + \vec{J}^b_{Mem} 
\]

\( \vec{J}^b_E \) is related to the elastic part of the stress tensor in mucus layer, \( \vec{J}^b_{Cilia} \) is related to the force that each cilium impose to the fluid and \( \vec{J}^b_{Mem} \) is related to the elastic force on the interface between the mucus and PCL. The first force which should be added to LB equations due to elastic part of the stress tensor of mucus. For calculating this force using the physical velocity field at the time level \( t = t_n \) and using finite difference method, the elastic part of the stress tensor (equation (7)) is solved and the value of \( \sigma_E \) in each time step is calculated. So the elastic force of stress tensor can be calculated as:

\[
\vec{F}_E = \frac{1}{\rho} \nabla \sigma_{M,E} 
\]

Since \( \vec{F}_E \) is defined as the physical variables, so it should be multiplied by force transformation coefficient to transform into LB force as follows:

\[
\vec{J}^b_{E} = \frac{\vec{J}^b_{E}}{C_h^2} 
\]
Immersed boundary method has been employed to simulate cilia forces. In this method, the interpolated velocity of fluid at the cilia points is enforced to be equal to the velocity of the cilia at the same position at every evolution time step by a set of velocity correction $\delta U_l^{ib}$. For calculating this velocity correction the following system of equations should be solved [20]:

$$AX = B$$

$$X = \{\delta U_1^{ib}, \delta U_2^{ib}, \ldots, \delta U_m^{ib}\}^T$$

$$A = \begin{bmatrix}
\delta_{11} & \delta_{12} & \cdots & \delta_{1n} \\
\delta_{21} & \delta_{22} & \cdots & \delta_{2n} \\
\vdots & \vdots & \ddots & \vdots \\
\delta_{ml} & \delta_{m2} & \cdots & \delta_{mn}
\end{bmatrix} \begin{bmatrix}
\delta_{11} & \delta_{12} & \cdots & \delta_{1n} \\
\delta_{21} & \delta_{22} & \cdots & \delta_{2n} \\
\vdots & \vdots & \ddots & \vdots \\
\delta_{ml} & \delta_{m2} & \cdots & \delta_{mn}
\end{bmatrix} = \begin{bmatrix}
\delta U_1^{ib} \\
\delta U_2^{ib} \\
\vdots \\
\delta U_m^{ib}
\end{bmatrix}$$

$$B = \begin{bmatrix}
\delta_{11} & \delta_{12} & \cdots & \delta_{1n} \\
\delta_{21} & \delta_{22} & \cdots & \delta_{2n} \\
\vdots & \vdots & \ddots & \vdots \\
\delta_{ml} & \delta_{m2} & \cdots & \delta_{mn}
\end{bmatrix} \begin{bmatrix}
|U_1^{ib} - U_2^{ib}| \\
|U_1^{ib} - U_2^{ib}| \\
\vdots \\
|U_1^{ib} - U_2^{ib}|
\end{bmatrix}$$

Here, $m$ is the number of Lagrangian points on the cilia, and $n$ is the number of Eulerian points. $\vec{U}_l^{ib}$ ($l=1,2,\ldots,m$) is the velocity vector of Lagrangian (cilia) points and $\delta U_l^{ib}$ ($l=1,2,\ldots,m$) is the unknown velocity correction vector at the Lagrangian points. In equation (25), $\delta y_l = D_y(x_l^{ib} - X_l^{ib})\Delta s^b$ and $\delta y_l = D_y(x_l^{ib} - X_l^{ib})\Delta s^b$ where $\Delta s_l^{ib}$ is the arc length of cilia elements and $D_y(x_l^{ib} - X_l^{ib})$ is Delta function which defined as [7]:

$$\delta(r) = \begin{cases} 
1-|r|, & |r| \leq 2 \\
0, & |r| > 2
\end{cases}$$

In this method cilia forces at Lagrangian points ($\vec{F}_{Cilia}^{ib}$) can be calculated as [25]:

$$\vec{F}_{Cilia}^{ib} = \frac{2\delta U_l^{ib}}{\delta t}$$

By interpolating the value of cilia forces from Lagrangian (cilia) nodes to Eulerian (fluid) points the cilia force on each node of fluid can be calculated as:

$$\vec{F}_{Cilia}^{ib} = \sum_i \vec{F}_{Cilia}^{ib} D_{ij}(x_{ij}^{ib} - X_l^{ib})\Delta s_l^{ib}$$

$F_{Mem}$ is the elastic force exerted by the membrane interface of PCL and mucus to the fluid is calculated as [15]:

$$F_{Mem} = \frac{1}{\rho} \frac{\partial}{\partial s} \left[T(s)\tau(s)\right]$$

Where $T(s)$ and $\tau(s)$ are defined as:

$$T(s) = T_0 \left(\frac{\partial X_{Mem}}{\partial s_0} - 1\right)$$
In equation (32) $\tau(s)$ is the unit tangential vector to the PCL–mucus membrane interface. The arc-lengths $s$ and $s_0$ are measured along the current and initial configuration of the membrane interface, respectively. The scalar $T_0$ is the stiffness constant which describes the elastic property of the flexible boundary.

Using force transformation coefficients, $F_{Mem}$ can be transformed into LB force as follows:

$$F_{Mem}^{lb} = F_{Mem} \frac{C_t^2}{C_b}$$

(33)

By interpolating the value of membrane force ($F_{Mem}^{lb}$) from Lagrangian (membrane) nodes to Eulerian (fluid) points the membrane force on each node of fluid can be calculated as:

$$F_{Mem}^{lb} = \sum_l F_{Mem}^{lb} D_{ij} (X_{ij}^{lb} - X_{Mem,l}^{lb} \Delta X_{Mem,l})$$

(34)

Lastly the membrane velocity $U_{Mem}(X_{Mem})$ interpolated from the neighboring grid points. Subsequently, the location of the membrane interface is updated as:

$$\frac{\partial X_{Mem}}{\partial t} = U_{Mem}$$

(35)

3. Results and discussion

In this section using the numerical scheme introduced in mathematical formulation, 2D numerical simulation has been employed to study the effects mucus depth at various values of cilia beat frequency on the muco-ciliary clearance problem. The main feather of the present study is using an Oldroyd-B model for simulating mucus, in which the effect of mucus theology can be considered more accurate. In addition, for simulating cilia forces and also mucus-PCL interface an immerse boundary method is used.

The cilium beat pattern in our study is the cilium beat cycle reported in Folfurd and Blake [4] which is shown in figure 2(a). In our numerical model, there are 13 cilium and each cilium has a cyclic motion. The cilia arrangements for $t=8T/13$ is plotted in figure 2(b) Where T is the consecutive beat cycle.

Figure 2. (a)The beat cycle derived by Fulford and Blake [4] and (b) Arrangement of the cilia for $t=8T/13$
The time average mucus velocity at the outlet boundary of the domain calculated as:

$$u_0 = \frac{1}{T(H_2 - H_1)} \int_0^T \int_0^{H_2} u_m dy dt$$  \hspace{1cm} (36)$$

In equation (36) $H_2 - H_1$ is the depth of mucus layer and $T$ is the consecutive beat cycle. The experimental investigation of Matsui et al. [21] showed a mean mucus transport of $39.2 \, \mu m/s$ . ICRP [22] reported a wide range of values depending upon disease, ambient conditions and other factors. For healthy subjects, values of 70 and $92 \, \mu m/s$ for tracheal transport, and $40 \, \mu m/s$ for bronchial transport were reported. Smith et al. [16] showed a mean mucus velocity of $38.3 \, \mu m/s$. Also numerical simulation of Lee et al. [15] and Jayathilake et al. [2] predicts a mean mucus velocity of $44.38 \, \mu m/s$ using the standard parameter set. Our simulation using the standard parameter set predicts a time average mucus velocity of $u_0=44.07 \, \mu m/s$ which is in a reasonable agreement with the previous reported results. The velocity field and the beating cilia at $t=4T/13$ for the standard parameter set have been plotted in figure 3. This Figure shows a high forward velocity around the cilium at its effective stroke and the largest mucus velocity occurs close to the mucus-PCL interface.

Table 1 shows the variation of mean mucus velocity as a function of mucus depth at three different values of cilia beat frequency. In this table the other numerical settings are equal to the standard setting. This table indicates that CBF has great influence on mucus flow and increasing in CBF as indicated in the literature leads to increase in mean mucus velocity. This table also shows that increasing mucus depth does not have a great effect on the mucus flow.

**Figure 3.** The velocity field and the beating cilia at (a) $t=4T/13$ and (b) $t=T$ for the standard parameter set.
Table 1. Variation of mean mucus velocity (µm/s) with respect to the mucus layer depth for various amounts of CBF.

| \( L_M (\mu m) \) | 3   | 3.5 | 4   | 4.5 | 5   | 5.5 | 6   |
|-------------------|-----|-----|-----|-----|-----|-----|-----|
| \( \sigma (rad/s) \) | 40  | 38.41| 33.46| 33.28| 33.48| 33.78| 32.55| 31.65 |
| 60                | 50.6| 44.64| 44.07| 44.49| 44.27| 43.06| 41.91|       |
| 80                | 63.7| 56.67| 55.52| 56.36| 55.66| 54.6 | 52.64|       |

For better understanding these variations, non-dimensional mean mucus velocity as a function of mucus depth and CBF has been plotted in figure 4. As this figure indicates that, at lower values of mucus depth because of lower volume of mucus above the PCL, mucus velocity increases significantly. Changing the depth of mucus from 3.5µm to 5µm does not have a great effect on mucus velocity, but by increasing the depth of mucus from 5µm since the cilia are propelling a considerably larger volume of mucus, leads to slightly slower mucus transport and this variation is same for various amounts of CBF. This figure also illustrates that, the effect of CBF is more than mucus depth and decreasing mean mucus velocity because of increasing in mucus depth (which is results from air pollution or smoking) can be simply modified by increasing in CBF. For example, for \( \sigma=80 rad/s \) at the worst condition for mucus depth when \( L_M=6\mu m \), mean mucus velocity is almost 1.2 times the standard value. On the other hand by reducing the value of CBF, e.g. when \( \sigma=40 rad/s \) for the lowest value of mucus depth, i.e. \( L_M=3\mu m \), \( M/u_0 \) is about 0.9 and it reduces to 0.7 by increasing mucus depth.

Figure 4. Mean mucus velocity for various amounts of depth of mucus layer at different values of CBF.

4. Conclusions
In this study a 2D numerical code based on the immersed boundary-lattice Boltzmann method has been developed to study the effect of mucus depth on muco-ciliary transport for various amounts of CBF. The main feature of the present investigation is considering mucus layer as a viscoelastic fluid and an Oldroyd-B model is used as the constitutive equation of it. So mucus could be modeled more realistically compared with the previous investigations reported in the literature. Interacting forces are modelled using the Immersed Boundary Method. Our results show that at lower values of mucus layer depth, mean mucus velocity increases and by increasing mucus depth of 3.5µm to 5µm, mean mucus velocity remains almost constant and by increasing this value from 5µm mucus flow reduces. The results also indicate that although increasing in mucus depth leads to decrease in mucus flow, increasing CBF can completely modify it and CBF has more effect on mucus flow. In future studies,
we will include the nonlinear differential models as the constitutive relation of mucus to predict more important characteristics of real fluid material functions and flow behaviour.

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