MUCUS FLOW IN HUMAN LUNG AIRWAYS BY USING MATHEMATICAL METHODS

Abstract

Mucus flow in human lung airways can be modelled using mathematical equations that describe the transport and properties of the mucus. There are various approaches to modelling mucus flow, but a common one is to use the Navier-Stokes equations, which describe the motion of fluids. The Navier-Stokes equations can be applied to the mucus layer in the airways, considering it as a non-Newtonian fluid. Non-Newtonian fluids have complex rheological properties that are dependent on the applied stress and strain rate. The mucus layer in the airways is a viscoelastic fluid, which means it has both viscous and elastic properties.

Keywords: Mucus flow, human lung airways, mathematical modelling, Navier stokes equation.

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I. INTRODUCTION

Mucus flow in the human lung airways has been studied by several researchers and investigators [Lucas, Douglas (1934),Wilkision (1960), Weibel (1963), Barton, Raynor (1967), Schroter, Sudlow (1969), Pedley et al.(1970), Blake(1971a, 1971b, 1973, 1974, 1975), Clarke et al. (1970), Clarke (1973), Ross. Corrsin (1974), Sleigh (1977,1990), Scherer and Burtz (1978), Blake and Winet (1980), Winet and Blake (1980), Yeats et al.(1980,1981), Wanner (1981), Blake and Fulford (1984), Puchelle et al.(1980), Sleigh et al. (1988), Zahm et al. (1989,1991), Agarwal et al. (1989), King et al. (1982,1985,1989,1993,1995), Bennet et al. (1990), Mogami et al. (1992), Tomkiwicz et al. (1994), Agarwal and Verma (1997,1998), Kim (1997), Rubin (2002), Verma (2007,2009,2010,2011,2012), Satpathi (2007), Smith et al.(2008), Polak (2008), Benjamin (2011), Shivesh Mani Tripathee (2017), V. S Verma, S.M. Triapthee(2011), V.S. Verma, S.M. Tripathee (2013), V.S. Verma, S.M. Tripathee (2013), HarendraVerma, Vishnu Narayan Mishra, Pankaj Mathur (2022)https://doi.org/10.1016/j.isatra.2021.01.033. , HarendraVerma, Nidhi Pandya, Vishnu Narayan Mishra, and Pankaj Mathur(2020)https://doi.org/10.1142/S2661335220500082, HarendraVerma, Vishnu Narayan Mishra, Pankaj Mathur (2021), D. Bhardwaj, A. Singh, R. Singh (2019), S. Munjal, A. Singh, Facile and Green (2019), . S. Bhatt, A. Singh, S. Munjal and P. Kumar Poonia (2018), S. Munjal, P. Srivastava, A. Singh, P. Jyani, P. S. Gour (2020), R. Singh, S. A.Ganaie, A. Singh (2019), R. Singh, A. Singh andD. Bhardwaj (2019)].

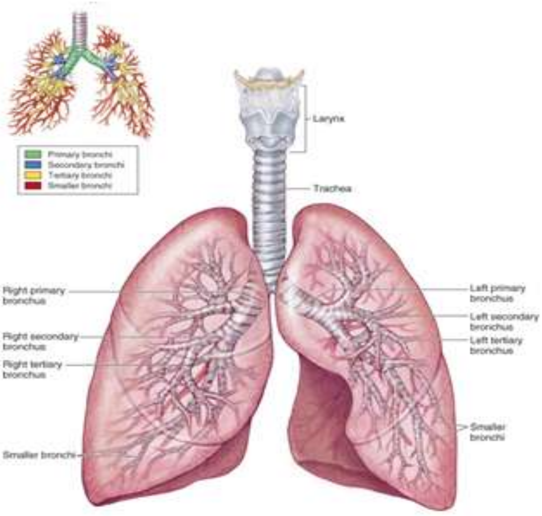

Figure 1: A general structure of Human Lung

In 1967 Barton and Raynor presented a mathematical model for the flow of mucus by taking cilium as an vibrating cylinder with a larger height during the effective stroke (forced) and smaller height during the recovery stroke. In 1975 Blake assumed a two-layer Newtonian fluid (which follow the Newton's Law of viscosity) model, one serous layer fluid (watery fluid) and the other mucus layer fluid (periciliary layer) and pointed out the importance of gravitational force and effect of air-velocity flow on mucus flow. In 1980, Blake and Winet gave two layer mathematical models. They studied that if cilia just enter the upper, much more viscous layer , then the mucus flow rates would be substantially enhanced.

In 1969 Schroter and Sudlowstudied the air flow resistance in the bronchial airways of human lung and in 1970 Pedaly and his team studied the same. In their experimental studies Clarke (1973), Clarke et al. (1970) and many others, including Puchelle et al. (1983), Zahm et al. (1989), King et al. (1982,1985,1989) found the role of mucus interaction with mucus in bronchial clearance. In 1978 Scherer and Burtz performed an experiments relevant to coughing and showed that how viscosity of the fluid is important. In 1982 King et al. also showed the interaction of airflow with the mucus in a simulated cough machine under study state (Time independent state)and oscillatory airflow conditions and pointed out the importance of mucus gel viscosity on flow of the mucus. In 1989 Agarwal et al. found thatmucus flow increases as the viscosity of the serous layer fluid decreases or as the mucus filance (spinnability) decreases.

II. MATHEMATICAL MODELLING

It may be noted here that very few attention has been paid to describe these experimental observations using mathematical or analytical models. In 2007 Prof V. S. Verma presented a two layer laminar steady state (Time Independet) mathematical model to study mucus flow in the respiratory tracts (human lungs) due to airflow and forming cilia as porous bed in serous sub- layer in contact with epithelia. The effect of airflow was taken by prescribing air velocity at the interface of mucus and air. It had been seen that mucus flow increases as the pressure drop or gravitational force due to air velocity and porosity parameter increase. It was also found that mucus flow increases as the mucus or serous layer fluid viscosity decreases.

In recent past decades, the mucus flow in human lung airways has been studied by several researchers and investigators. Agarwal and Verma (1997) and Verma (2007, 2010) have studied the mucus flow by considering the effect of porosity parameter which occurs due to formation of porous matrix bed by dead cilia.

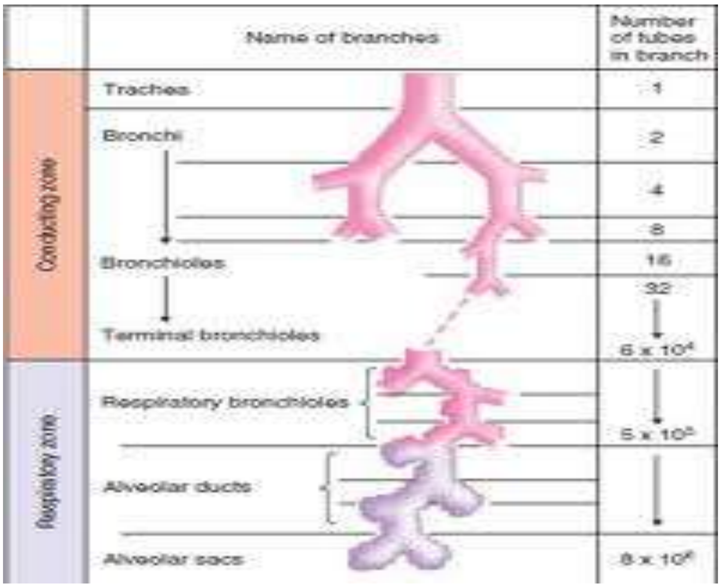

Figure 2: A schematic diagram of human lung

The flow of mucus is controlledby cilia beating and airflow as a effective stroke, which are encountered by frictional and inertial forces of the mucus as recovery stroke and also by thebronchial secretion. The cilia lie in the serous layer while the mucus layer lies at the top of the cilia. It is assumed that the serous layer fluid and mucus layer fluid may be separated by a layer of surfactant. It is seen that only the mucus layer fluid is flowed, but serous layer is essential for mucus flow because it provides the necessary conditions for the cilia to beat effectively in effective stroke.

To investigate the flow of serous layer fluid and mucus layer fluid in the human respiratory tracts due to beating activity of cilia of length L, we suppose that one of the tubes in the lung under consideration is cylindrical having its radius R. The total depth of fluids (serous fluid and mucus) at the top of the cilia is assumed to be H as shown in Fig 3: In healthy conditions of the lung, the ratio H/R is very smallwhich is equal to the order of magnitude of L/R. But in unhealthy conditions this ratio may becomes larger but in airways of the lung, the ratio L/R is always very small equal to the order of 10^{-2}, therefore, we can approximate the cilia sub-layer and mucus layer as shown in Fig.4.

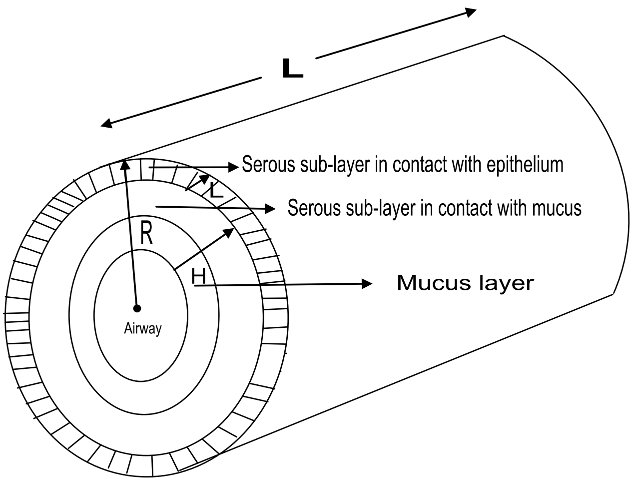

Figure 3: Circular model mucus flow in respiratory tracts.

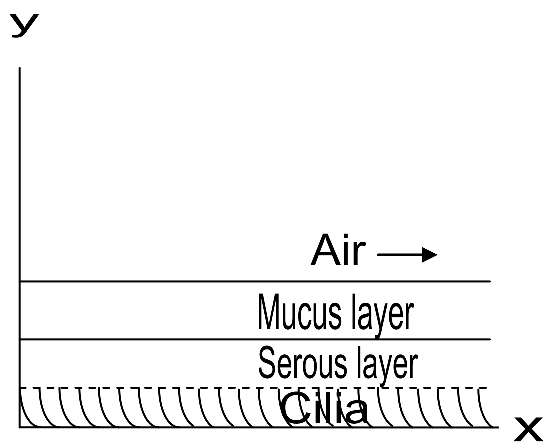

Figure 4: Laminar flow model of mucus in the human lung airways

Cilia beating consist of an effective stroke (power stroke), in which the extended cilia sweep through a large volume of fluid and a recovery stroke (return stroke), in which the cilia bent and perform an unrolling movement across the cell surface. The Fig.5 shows the ciliary beat activity:

In the effective stroke, the cilium moves in a plane nearly perpendicular to the cell surface, but in most cases it moves one side in the recovery stroke, keeping near the cell surface, increasing the difference in height between the two strokes and maximizing the net flow of fluid by reducing the back-flow produced by the recovery (return) stroke.

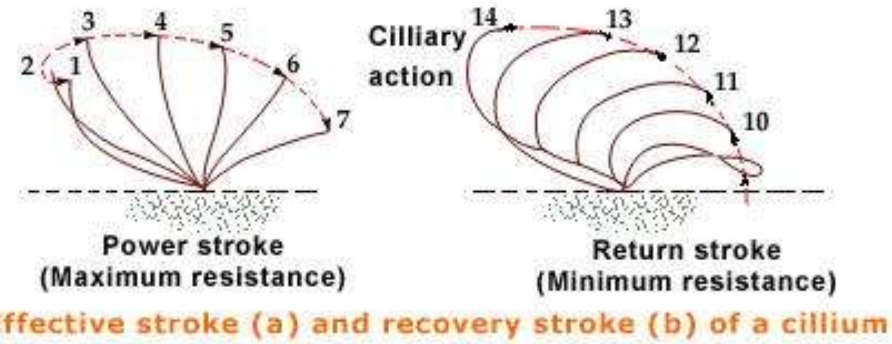

Figure 5 Ciliary beat activity
(http://www.tutorvista.com/content/biology/biology-iii/cell-organization/nonmembranous-cell-organelles.php)

Most serous layer fluid propelling cilia perform three-dimensional cycle, usually cilia move counter clockwise in the recovery stroke.

Serous layer fluid propelling cilia seldom stop moving the effective and recovery strokes merging together where the transitions occur between them, so that instantaneous pressure show all cilia in some phase of active movement. By contrast, mucus propelling cilia normally rest between beats and this rest takes place after the effective stroke has been completed, so that the tip of the resting cilium points in the direction of the mucus flow from this rest position, the curve of cilia movement moves through a clockwise recovery stroke, which leads directly into the effective stroke.

Cilia that propel serous layer fluid and those that propel mucus commonly beat at frequencies of between 10 to 20 Hz, although frequencies above 50 Hz have been recorded in some water propelling examples. The main propulsive thrust of the effective stroke is imparted to serous layer fluid or mucus by the distal part of the cilium. At the same frequency, the tip velocity of a serous layer fluid propelling cilium is higher than that of a mucus propelling cilium because the former is longer, although the proportion of the cycle time occupied by the effective stroke tends to be smaller for a mucus propelling cilium because of the rest phase. Because of its visco-elastic nature, the transport rate of mucus by cilia beating is similar to the tip velocity of cilia concerned, where as serous fluid is less viscous and is transported at only about one fourth of the tip velocity of the cilia. The flow rate of mucus to be relatively independent of the load but under some conditions the effective strokes of the cilia may be slowed and transport rates fall.

The closely packed cilia on a mucus-flowing epithelium rest in each cycle and each beat begins with a recovery stroke. Before any movement occur the cilia of an area lie still with the cilia bent over in the direction of mucus flow [Sleigh et al. (1972)].

The equations of motion for the flow of fluid under assumption depend the Reynolds number which gives the relation between inertial and viscous forces and determine the type of flow weather it is laminar, turbulent or transitional. While investigating cilia induced flow, the Reynolds number of basic importance is the Cilium Reynolds number $R_e|_{cilium}$ which is defined as follows:

$$R_e|_{cilium} = \frac{\sigma L R_0}{\nu} \qquad (1)$$

whereσ is the angular frequency, L is the length, R_0 is the radius of cilia, while ν is the kinematic viscosity. In the human lung, the Cilium Reynolds number is always very small i.e. of the order of 10^{-4} indicating that the viscous effect is more important. The equations of motion which is called the Navier Stokes equations at low Reynolds number may be written as:

$$\mu\nabla^2\boldsymbol{q} = \nabla p \text{ and } \boldsymbol{\nabla}.\boldsymbol{q} = 0 \qquad \textbf{(2)}$$

where$p$ is the pressure of the fluid , $\boldsymbol{q}$ is the velocity vector and $\mu$is the viscosity which gives relation with kinematic viscosity ν as follows :

$$\nu = \frac{\mu}{\rho} \text{ , where} \rho \text{ is the density.} \qquad (3)$$

In our case when cilia become immotile and form a porous matrix bed (or porous medium), the fluid flows between two regions. Region-I, where fluid flows freely due to no porous medium, which is also called free flow region. Region-II, is called as porous region, where fluid flows between the pores of the porous medium. Flows through these two regions are matched by suitable conditions at the interfaces called as matching conditions. The mathematical theory of the flow of a viscous fluid through a porous medium was established by Darcy and is known as by his name as Darcy's law. Since then, Darcy's law has been verified experimentally by several workers. In our case, we use the boundary conditions given by Beavers and Joseph in 1967 at the interface under consideration. We are interested to study mucus flow in the respiratory tracts of the lung which will give us a better understanding of hydro-dynamical point of view and some physiological aspects of mucus flow in the human lung airways. We shall use the principles and theories of Fluid Mechanics while discussing the flow of mucus problems. It is well aware that the flow problems concerning the motion of incompressible viscous fluids or Newtonian fluids are given by the Navier-Stokes equations which may be written as:

$$\frac{\partial q}{\partial t} + \boldsymbol{q}.\boldsymbol{gradq} = \frac{\nabla p}{\rho} + \nu\nabla^2\boldsymbol{q} + \frac{F}{\rho} \qquad (4)$$

Along with the continuity equation

$$div\boldsymbol{q} = 0 \qquad (5)$$

Where$\boldsymbol{q}$ is the velocity vector, $\boldsymbol{p}$ the pressure, F the external force, ν isthe kinematic coefficient of viscosity in the second term in the L.H.S.. We shall consider some flow motion problems by writing equation (2) in non-dimensional form as given below:

$$R_e q.gradq = -qgradq + \nabla^2 q \qquad (6)$$

Where $R_e = \frac{LU_0}{\nu}$ is Reynolds Number, L is the Characteristic length and U_0 is the characteristic velocity. Thus if Reynolds number approaches to zero we get the following equation

$$0 = -q grad q + \nabla^2 q \qquad (7)$$

We find the solution of above equations by assuming some boundary and matching conditions and by applying simple methods of solving PDEs (Partial differential equations) or by any other method like integral transform such as Laplace Transform, method separation of variables etc. . After finding the solution, we interpret the results which will be very helpful in pathological point of view in case of the respiratory diseases.Thus we may gain tools for diagnosis, prognosis and for evaluation of therapy for some respiratory tracts diseases and hence have much intrinsic scientific interest.

III. METHODOLOGY

The flow of viscoelastic fluids over and between porous media has been the subject of increasing studies during past decades because of its importance in several problems. In our case when cilia become immotile and form a porous matrix bed (or porous medium), the fluid flows between two regions. Region-I, fluid flows freely due to no porous medium which is called free flow region and Region-II which is called as porous region, where fluid flows between the pores of the porous medium. Flows through these two regions are matched by suitable boundary conditions at the interface called as matching conditions [Fig .4].

The mathematical theory of the flow of a viscous fluid through a porous medium was established by Darcy and is known as by his name as Darcy's law. Since then, Darcy's law has been verified experimentally by several researchers. In our case, we will use the boundary conditions given by Beavers and Joseph in 1967 at the interface under consideration.

1. **Steady State Planar Model:**Let an incompressible viscous fluid be in steady motion bounded by planes $y = 0$ and $y = h$. Let the plane $y = 0$.i.e x- axis be at rest while plate $y = h$ has a velocity U along x- axis. If $\boldsymbol{q}$ be the fluid velocity at point **P** (x, y, z), then,

   $\boldsymbol{q} = \boldsymbol{q}(u, 0,0)$**(12)**

   Therefore, from continuity equation (1) , we can write

   $\frac{\partial u}{\partial x} = 0$**(13)**

   so that u is independent of x. Also, by symmetry u is independent of z.
   Consequent $u = u(y)$**(14)**

   Again, from Navier- Stokes equations of motion (4), in absence of body forces, we have

   $\frac{\partial \boldsymbol{q}}{\partial t} + \boldsymbol{q}. grad\, \boldsymbol{q} = -\frac{\nabla p}{\rho} + \nu \nabla^2 \boldsymbol{q}$**(15)**

   Since motion is steady state, therefore, we have $\frac{\partial \boldsymbol{q}}{\partial t} = 0$
   Thus we have $\boldsymbol{q}. grad\, \boldsymbol{q} = u\frac{\partial \boldsymbol{q}}{\partial x} = u\frac{\partial \boldsymbol{i}u}{\partial x} = \boldsymbol{i}u\frac{\partial u}{\partial x} = 0$ [by (13) and (14)]

Now, equation (15) becomes
$-\frac{\nabla p}{\rho}+\ \nu\nabla^2 \boldsymbol{q}=0or-\nabla p+\mu\boldsymbol{i}\nabla^2 u=0$**(15)**

This is equivalent to the following equations:
$\frac{\partial p}{\partial x}=\mu\nabla^2 u$**(16)**
$\frac{\partial p}{\partial y}=0$**(17)**
$\frac{\partial p}{\partial z}=0$**(18)**

From (1.16) and (1.17), it is clear that p is a function of x only i.e. $p=p(x)$
Therefore, from equations (1.12) and (1.15) we can write:

$\frac{dp}{dx}=\mu\frac{d^2u}{dy^2}$**(19)**

From equation (15), it is seen that left hand side is a function of x only while right hand side is a function of y only. Hence, each side is a constant. As the fluid is flowing in a positive direction of x, the pressure $p(x)$ decreases as y increases so that

$$\frac{dp}{dx}<0\ \forall\ x>0$$

Thus , we may take
$\frac{dp}{dx}=\mu\frac{d^2u}{dy^2}=-\phi\ where\ \phi>0$**(20)**

This implies that $\frac{d^2u}{dy^2}=-\frac{\phi}{\mu}\Longrightarrow\frac{du}{dx}=-\frac{\phi y}{\mu}+A\Longrightarrow u=-\frac{\phi y^2}{2\mu}+Ay+B$ (21)
Using conditions (i) $u=0,\ y=0$ and (ii) $u=U,\ y=h$,equation (21) may be written as :
$u=-\frac{y^2}{2\mu}\phi+\left(\frac{U}{h}+\frac{\phi h}{2\mu}\right)y$ **(22)**
This shows that the velocity profile between the two plates is parabolic.
The volumetric transport rate Q is given by
$Q=\int_0^h u\,dy=\int_0^h\left[-\frac{y^2}{2\mu}\phi+\left(\frac{U}{h}+\frac{\phi h}{2\mu}\right)y\right]dy$ (23)

or$Q=\frac{h^3\phi}{12\mu}+\frac{1}{2}hU$ (24)

2. **Steady State Circular Model:**Let an incompressible viscous fluid be in steady motion in a cylindrical pipe. We take axis of z along the axis of cylinder. Also suppose that the direction of flow is parallel to z axis so that$\boldsymbol{q}=\boldsymbol{q}(0,0,u)$. In this case, equation of continuity is given by
$\frac{\partial u}{\partial z}=0$ (25)
Navier Stokes equations of motion in absence of body forces become:
$\frac{\partial \boldsymbol{q}}{\partial t}+\ \boldsymbol{q}.grad\ \boldsymbol{q}=-\frac{\nabla p}{\rho}+\ \nu\nabla^2 q$ (26)
Since motion is steady state, therefore, we have $\frac{\partial \boldsymbol{q}}{\partial t}=0$ (27)

Thus, we have $\boldsymbol{q}.grad\,\boldsymbol{q} = u\frac{\partial \boldsymbol{q}}{\partial z} = u\frac{\partial \boldsymbol{k}u}{\partial z} = \boldsymbol{k}u\frac{\partial u}{\partial z} = 0$

Now, equation (26) becomes

$$-\frac{\nabla p}{\rho} + \nu\nabla^2 \boldsymbol{q} = 0 \text{or} -\nabla p + \mu\boldsymbol{k}\nabla^2 u = 0 \quad (28)$$

This is equivalent to the following equations:

$$\frac{\partial p}{\partial x} = 0, \quad \frac{\partial p}{\partial y} = 0, \frac{\partial p}{\partial z} = \mu\nabla^2 u \quad (29)$$

From equations (26), (28) and (29), we can write:

$$\frac{dp}{dz} = \mu\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right) \quad (30)$$

Inspection of (30) shows that left hand side is a function of z only while right hand part of the equation is is a function of and y . Hence, each side is a constant. Further, since fluid is moving along positive direction of z axis, the pressure $p(z)$ should decrease as z increases. Thus, we have

$$\frac{dp}{dz} < 0 \;\forall\; z > 0$$

Thus, we may take $\frac{dp}{dz} = \mu\left(\frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right) = -\phi$ (31)

Changing the above equation into cylindrical co-ordinates(r, θ, z) using the transformations $x = r\cos\theta, y = r\sin\theta, z = z$, we obtain

$$\mu\left(\frac{\partial^2 u}{\partial r^2} + \frac{1}{r}\frac{\partial u}{\partial r}\right) = -\phi \quad (32)$$

From (32), we can also write $\frac{1}{r}\frac{d}{dr}\left(r\frac{du}{dr}\right) = -\frac{\phi}{\mu}$ or $\frac{d}{dr}\left(r\frac{du}{dr}\right) = -\frac{\phi r}{\mu}$ (33)

Integrating (33), we have

$$u = -\frac{\phi r^2}{4\mu} + A\log r + B \quad (34)$$

IV. CONCLUSION

The study of mathematical models on mucus flow in respiratory tracts i.e in human lung airways involves many mathematical ideas. One of the primary mathematical tools used in this field is fluid mechanics, which deals with the behavior of fluids in motion. Specifically, researchers use the principles of fluid dynamics to understand the movement of mucus through the airways.

There are several mathematical models used to describe mucus flow in the airways. One of the most common is the two-phase model, which considers mucus as a non-Newtonian fluid that is transported by a layer of air flowing through the airways. This model takes into account the complex rheological properties of mucus, which makes it difficult to move through the narrow airways.

Other mathematical models include the continuum model, which assumes that the air and mucus are continuous fluids, and the discrete particle model, which treats mucus as a collection of discrete particles. Researchers use these models to study different aspects of mucus transport, such as the effects of cilia movement and mucus composition on transport rates.

In addition to fluid mechanics, mathematical tools such as computational fluid dynamics (CFD) and finite element analysis (FEA) are used to simulate the transport of mucus in the airways. These tools allow researchers to visualize and analyze mucus transport under different conditions and to test different hypotheses about the underlying mechanisms. Overall, the mathematical study of mucus transport in human lung airways is a complex and interdisciplinary field that requires the integration of multiple disciplines, including mathematics, physics, biology, and engineering. However, advances in mathematical modeling and simulation techniques are helping researchers gain a better understanding of this crucial biological process and develop new treatments for respiratory diseases.

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