BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 29, 1967

# ANALYTICAL INVESTIGATION OF CILIA INDUCED MUCOUS FLOW

CHARLES BARTON AND SEVERIN RAYNOR
Department of Mechanical Engineering and Astronautical Sciences,
Northwestern University,
Evanston, Illinois

This is an analytic study of mucous flow caused by ciliary motion. The computed flow data may be compared with that already found experimentally. The effects of mucous density, viscosity and layer depth on flow phenomena are investigated. The effects of cilia diameter, length, spacing and oscillation frequency are determined from the equations governing the flow of the mucous blanket. A pertinent finding of the analysis is that the mucous flow in the airway tubes can satisfy physical constraints only through the assumption of a variable viscosity in the covering mucous blanket. The mucous viscosity must increase considerably from the low value at the cilium layer to a much higher value at the air-mucus interface.

*Introduction.* Cilia are small, hairlike cell structures which project from the free surfaces of cells lining the bronchial system. The length of a bronchial cilium is on the order of a few microns. Its diameter is a fraction of a micron and the distance between cilia is approximately three and one-half diameters (Rivera, 1966, p. 12).

The inner lining of the bronchial system is covered by a mucous blanket. The motion of the cilia causes the mucous layer covering the bronchial tubes to move upward. Ciliary propulsion is unique because it moves fluid in completely open airway tubes.

The system can be described as consisting of tiny oscillating hairlike elements attached to the tubular wall. They propel a relatively thick layer of mucus at low velocity against the forces of gravitation.

*Mathematical analysis outline.* The first problem considered in this analysis is to find the velocity distribution in the fluid surrounding one cilium as well as the force exerted by one cilium on the fluid.

The computations are then extended to describe the fluid motion and force exerted on the fluid by an array of cilia. The average of the velocity and of the force are computed.

The problem is then reduced to steady state flow of a fluid layer up the wall

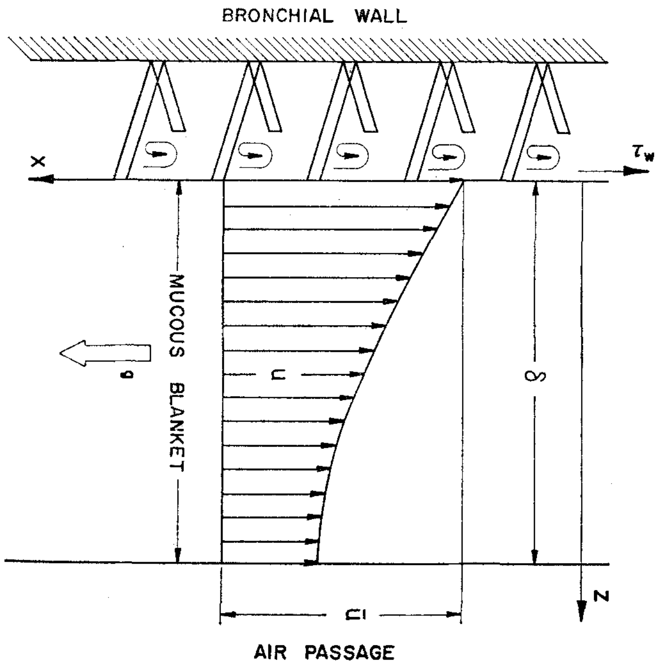


Figure 1. Schematization of idealized cilia motion and overlying mucous blanket

under the influence of gravity and ciliary action. Ciliary propulsion is replaced by the action of a thin layer moving with a constant velocity upwards and propelling the overlying mucous blanket with a known shear stress as shown in Figure 1.

The viscosity of the mucus in the cilium layer is assumed to have a low value as the mucus issues from the membrane underlying the cilia. As the mucus moves extremely slowly along the length of the cilia and toward the air-mucus interface its viscosity increases, reaching a maximum at the interface. These assumptions were made on the basis of observation and by the requirement that the mucous velocity at the air-mucus interface should be upward. An upward interface velocity is necessary to remove dust particles that enter with the inspired air from the airway tubes. Flow without velocity reversal in the mucous blanket was found to be impossible if a constant viscosity, corresponding to that at the cilia bases, was used in the computation. On the other hand, to assume low viscosity of aged, air exposed mucus in the immediate vicinity of the membrane underlying the cilia seems unreasonable.

The motion of a cilium may be separated into two distinct strokes during the complete cycle. There is the effective stroke during which the cilium is extended straight and moves in the direction of flow of the covering mucous blanket. During the recovery stroke the cilium tip is bent down toward the

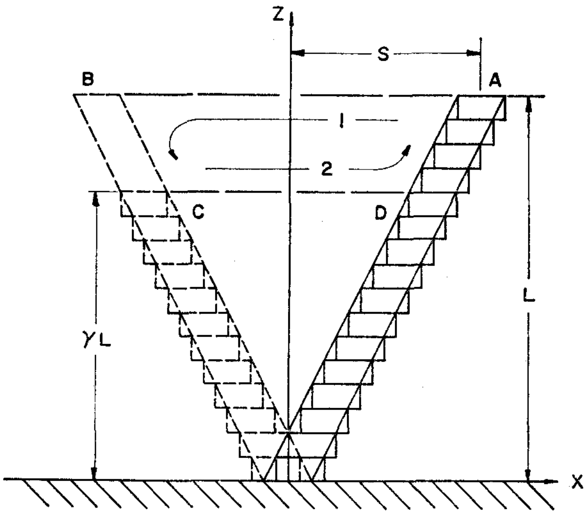


Figure 2. A model of the cilium motion. The pendulous motion of the cilium is replaced by translatory motion of elementary circular cylinders

cell membrane as the cilium goes in the opposite direction to the net mucous flow. During the effective stroke the projected area of the cilium in the direction of net flow is greater than during the recovery stroke. Hence there is a net propelling force on the fluid in the flow direction.

For the purpose of the mathematical analysis, the cilium will be replaced by a straight cylinder of variable length, as shown in Figure 2. The net effect of the bending of the cilium during the recovery stroke is replaced in the mathematical analysis by a sudden shortening of the cilium.

The cilium model will consist of a cylinder of variable length hinged to a stationary point on an infinite plane. The cilium will be considered as a series of infinitesimally short sections of circular cylinders in oscillating translatory motion. The axis of each cylinder element is perpendicular to the membrane and each has its own velocity parallel to the membrane. End effects near the cilium tip will be neglected.

In summary, the mathematical model of the cilium used in this study is defined as follows:

(*a*) The cilium is a cylinder hinged to a large flat plate. It performs simple harmonic translatory oscillations. The translatory amplitude of each cylinder element is assumed to be proportional to the distance from the hinge point.

(*b*) Throughout a particular stroke, the cilium tip will remain at a constant distance from the cell membrane. This distance is less during the recovery stroke than during the effective stroke.

(*c*) Any cross section of the cilium taken parallel to the cell membrane will remain circular throughout the motion.

(*d*) The effective and recovery strokes are of equal duration.

(*e*) The mucus has Newtonian properties.

With the cilium model defined in terms of oscillating cylinder segments for both effective and recovery strokes, let us investigate the two-dimensional flow of an infinite viscous fluid around an oscillating cylinder.

The solution will give fluid velocity in the neighborhood of the oscillating cylinder as well as the drag force on the cylinder.

*Equations describing the flow around a slowly oscillating cylinder.* The flow caused by the oscillation of a rigid body in a viscous fluid is characterized by a penetration depth $\delta$ which is the distance from the body where the velocity has decreased by a factor *e*. $\delta$ is of the order of $(\nu/\omega)^{\frac{1}{2}}$ where $\nu$ is the kinematic viscosity of the fluid and $\omega$ is the angular oscillation frequency of the body.

In the case of ciliary motion the frequency $\omega$ is of the order of 100 radians per second: the cilium radius $a$ is approximately 0.15 microns; the mucous viscosity $\nu$ is of the order of 0.1 stokes; the cilium velocity is of the order of $\omega S$, where $S$ is the amplitude of the cilium during the effective stroke. These values result in a penetration depth $10^3$ times greater than the cilium diameter. This is the case of slow oscillation, which implies that the time derivative of velocity can be neglected in the general equation of motion (Landau and Lifshitz, 1959, p. 91).

The Reynolds number $2\omega Sa/\nu$ is of the order of $10^{-5}$ indicating creeping flow.

The drag coefficient for uniform flow around a stationary cylinder at small Reynolds numbers was found (Tomotika and Aoi, 1951) to be

$$C_D = (8\pi/RK)\{1 - (1/32)(5/16\,K - \tfrac{1}{2} + K) + 0[(R^2 \ln R)^2]\}, \qquad (1)$$

where $R$ is the Reynolds number, and

$$K = \tfrac{1}{2} - \gamma + \ln(8/R),$$

$\gamma$ is the Euler's constant $\gamma = 0.5772157\ldots$. Oseen's linearized equations of motion were used to obtain this expression for $C_D$ and for the stream function

$$\psi = Ua \sin\theta((\tfrac{1}{2}K)\{(r/a)[2\ln(r/a) - 1] + a/r\} + R\cos\theta[(\tfrac{1}{8}K)(r/a)^2 \ln(r/a) - (\tfrac{1}{8})\ln(r/a)^2 - (1/16\,K - \tfrac{1}{4}) + (a/r)^2(1/16\,K - \tfrac{1}{8})]), \tag{2}$$

where $r$ and $\theta$ are polar coordinates measured from the center of the cylinder; $U$ is the uniform velocity far from the cylinder.

In terms of $\psi$ the velocity in the $x$ direction (direction of the principal flow) is

$$u = \sin\theta \frac{\partial\psi}{\partial r} + \frac{\cos\theta}{r}\frac{\partial\psi}{\partial\theta}. \tag{3}$$

Due to the smallness of the Reynolds number for the flow near the cilia the expressions for $C_D$ and $\psi$ can be truncated to

$$C_D = 8\pi[R\ln(4\nu/|U|a)]^{-1}, \tag{4}$$

$$\psi = Ua\sin\theta[(r/a)(2\ln(r/a) - 1) + a/r][2\ln(4\nu/|U|a)]^{-1}. \tag{5}$$

*Force exerted on the fluid by one cilium.* From equation (4) it follows that the drag force per unit length on a uniformly translating cylinder is given by

$$F_x = 4\pi\mu U/\ln(4\nu/Ua), \tag{6}$$

where $\mu$ is the absolute viscosity of the fluid.

Consider the temporal average of the force on the fluid due to the oscillatory motion of a cylinder having a projected length $L$ during the effective stroke, and a projected length $\gamma L$ during the recovery stroke; $0 < \gamma < 1$. The motion of the cylinder is shown in Figure 2. The tip of the cilium moves on the path $ABCD$ in a complete cycle.

If the amplitude of the oscillation of the cilium tip is $S$, then the amplitude of a cylinder element located at a distance $Z$ from the wall is

$$S_0(Z) = SZ/L. \tag{7}$$

The instantaneous velocity at this point is

$$u = -S\omega(Z/L)\sin\omega t. \tag{8}$$

The instantaneous value of the force is obtained by integrating the force per unit length over the length of the cilium. The temporal average is obtained by integration over a full period

$$\bar{F}_x = (1/T) \int_0^{T/2} dt \int_{\gamma L}^{L} F_x(Z, t)\, dZ. \tag{9}$$

The symmetric oscillation between the rigid wall and the layer thickness $\gamma L$ does not contribute to the net force.

Integration of equation (9) yields approximately

$$\bar{F}_x = \frac{2S\omega(1 - \gamma^2)L\mu}{\ln [\omega a S(1 + \gamma)/4\pi\nu]}. \tag{10}$$

*Velocity field due to oscillating cilium.* The fluid velocity $u$ in the $x$ direction can be obtained from equations (3) and (5) as

$$u = Ua \sin^2 \theta[a^{-1}(2 \ln r/a - 1) + 2/a - a/r^2][2 \ln (4\nu/|U|a)]^{-1}$$
$$+ Ua \cos^2 \theta\{a^{-1}[2 \ln (r/a) - 1] + a/r^2\}[2 \ln (4\nu/|U|a)]^{-1} - U. \tag{11}$$

*Interface velocity.* Define the region $\gamma L < Z < L$ as the mucous sublayer. The dynamic variable of interest is the average mucous velocity $\bar{u}$ at the interface between the mucous blanket and the mucous sublayer.

The value of $\bar{u}$ during the effective strokes $\bar{u}_1$ may be computed from equation (11) by averaging $u$ over the "effective area" of one cilium, and the duration of the stroke. In performing the space average it is assumed that the fluid velocity in the vicinity of a particular cilium is not influenced by neighboring cilia. Thus, the region of influence of a single cilium is $a < r < na$, where $n \simeq 3.5$, corresponding to the observed average spacing between cilia.

The average velocity $\bar{u}_1$ is then

$$\bar{u}_1 = \frac{\omega}{\pi} \int_0^{\pi/\omega} dt \int_0^{2\pi} d\theta \int_{\gamma L}^{L} dZ \int_a^{na} \frac{u}{\pi(n^2 - 1)a^2(1 - \gamma)L}\, r dr, \tag{12}$$

where the "effective area" per cilium is

$$A_c = \pi a^2(n^2 - 1). \tag{13}$$

Integration of (12) yields approximately

$$\bar{u}_1 = \frac{1 + \gamma}{\pi}\, \omega S \left(\{\ln [4\pi\nu/(1 + \gamma)\omega S a]\}^{-1} \left(\frac{n^2}{n^2 - 1} \ln n - \tfrac{1}{2}\right) - 1\right). \tag{14}$$

The average interface velocity during the recovery stroke $\bar{u}_2$ lies between two extremes. If the mucous sublayer were inviscid, the interface velocity would remain $\bar{u}_1$. For a very high sublayer viscosity the interface would move opposite to the net flow at the velocity $\bar{u}_2^*$. $\bar{u}_2^*$ corresponds to $\bar{u}_1$, but is evaluated at the height of the cilium during the recovery stroke. The velocity during the recovery stroke is therefore estimated to be

$$\bar{u}_2 = (\bar{u}_1 + \bar{u}_2^*)/2, \tag{15}$$

where

$$\bar{u}_2^* = -\frac{2\gamma}{\pi}\omega S\left\{[\ln 4\pi\nu/(1+\gamma)\omega Sa]^{-1}\left(\frac{n^2}{n^2-1}\ln n - \tfrac{1}{2}\right) - 1\right\}. \tag{16}$$

Since the effective and recovery strokes are assumed to be of equal duration, the net interface flow velocity is

$$\bar{u} = (\bar{u}_1 + \bar{u}_2)/2. \tag{17}$$

*Interface shear stress.* In order to compute the flow of the mucous blanket it is necessary to know the interface velocity $\bar{u}$ and the interface shear stress $\tau_w$. The shear stress may be obtained by considering a sublayer element in equilibrium. The element is subjected to shear stress on both interfaces, ciliary forces and gravitational force. Since the sublayer is an order of magnitude thinner than the mucous blanket, the gravitational forces in the sublayer will be neglected $[\tau_w \gg g\rho L(1-\gamma)]$; thus,

$$\tau_w = \frac{F_x}{A_c} - \mu_o\frac{\bar{u}}{L}, \tag{18}$$

where $\mu_o$ is the viscosity of the sublayer.

*Numerical results.* The average flow velocity of the sublayer was computed for a cilium diameter of $2a = 0.3$ microns, cilium length of $L = 7$ microns, a cilium spacing $n = 3.5$, a ratio of recovery to effective stroke $\gamma = 0.75$, and a circular frequency $\omega = 100$ Rad/sec.

It was found that the value of $\bar{u}$ depends very weakly on the viscosity of the sublayer; $\mu = 0.01$ poise results in $\bar{u} = 6.63$ mm/min; $\mu = 0.5$ poise results in $\bar{u} = 6.75$ mm/min. This value compares favorably with the reported value of 4.2 mm/min (Ewert, 1965).

*Flow of the mucous blanket.* The mucous blanket can be idealized as a layer of fluid pumped vertically up against the force of gravity $g$ by a shear stress $\tau_w$ applied at the outer boundary which is moving with the velocity $\bar{u}$. Since the mucous blanket layer is of an order of magnitude thicker than the height of the cilia, the fluid transport in the cilia region will be neglected.

The viscosity of the mucous blanket changes appreciably with depth. Air flowing past the blanket to the lungs tends to dry the mucus. The cells under the blanket continually add moisture to it making the outer blanket region more viscid than the inner region. There is also a temperature gradient across the mucous blanket which accentuates the viscosity increase towards the air-mucus interface.

Two approaches to the flow of the mucous blanket may be taken: one following the statement contained in (Ewert, 1965) and implied in (Lucas and Douglas, 1934); "the mucous sheet produced by glands and goblet cells and covering the epithelium is composed of two layers, an outer viscous stratum resting on the tip of the moving cilia and an inner stratum of lower viscosity which forms a suitable medium for the vibrating cilia."

This approach implies that the outer layer is basically solid and moves with the average sublayer flow velocity $\bar{u}$, as computed in the preceding section.

In the second approach it is assumed that the viscosity changes linearly with depth according to

$$\mu = \mu_0\left(1 + \frac{\alpha\xi}{\delta}\right). \tag{19}$$

Correspondingly, the kinematic viscosity is then

$$\nu = \nu_0\left(1 + \frac{\alpha\xi}{\delta}\right). \tag{20}$$

In the expressions for $\nu$ and $\mu$, $\delta$ is the blanket thickness, and $\xi$ is the position in the blanket measured from the blanket-sublayer interface.

Mucous viscosities reported in the literature are of the order of 100 poise while the viscosity of water is 0.007 poise at 37°C. The value of $\alpha$ can be of the order of magnitude of $10^3$.

The Newtonian approximation of mucous properties is rather crude and can be justified only because of the simplifications it makes in the already complex analysis.

The equilibrium of a blanket element requires that

$$\frac{d}{d\xi}\left[\mu(\xi)\frac{du}{d\xi}\right] = -g\rho, \tag{21}$$

or

$$\frac{d}{d\xi}\left[\nu(\xi)\frac{du}{d\xi}\right] = -g. \tag{22}$$

The boundary conditions to be satisfied by the velocity $u(\xi)$ in the blanket are

$$\frac{du}{d\xi} = 0 \text{ at the air-mucus interface } \xi = \delta, \tag{23}$$

$$u = \bar{u} \text{ at the sublayer-blanket interface } \xi = 0, \tag{24}$$

$$\frac{du}{d\xi} = -\frac{\tau_w}{\mu_o} \text{ at the sublayer-blanket interface } \xi = 0. \tag{25}$$

Integration of (22) and introduction of the boundary conditions yields

$$u = \bar{u} - \frac{g\delta^2(1 + \alpha)}{\nu_o\alpha^2} \ln\left(1 + \alpha\frac{\xi}{\delta}\right) + \frac{g\delta\xi}{\nu_o\alpha}. \tag{26}$$

The volumetric flow may be computed by integration of the velocity profile over the blanket thickness, as

$$Q = \pi D\delta\left\{\bar{u} - \frac{g\delta^2}{2\nu_o\alpha^2}\left[\frac{(1 + \alpha)^2}{\alpha} \ln(1 + \alpha)^2 - 2 - 3\alpha\right]\right\}; \tag{27}$$

where $D$ is the diameter of the member containing the mucous blanket.

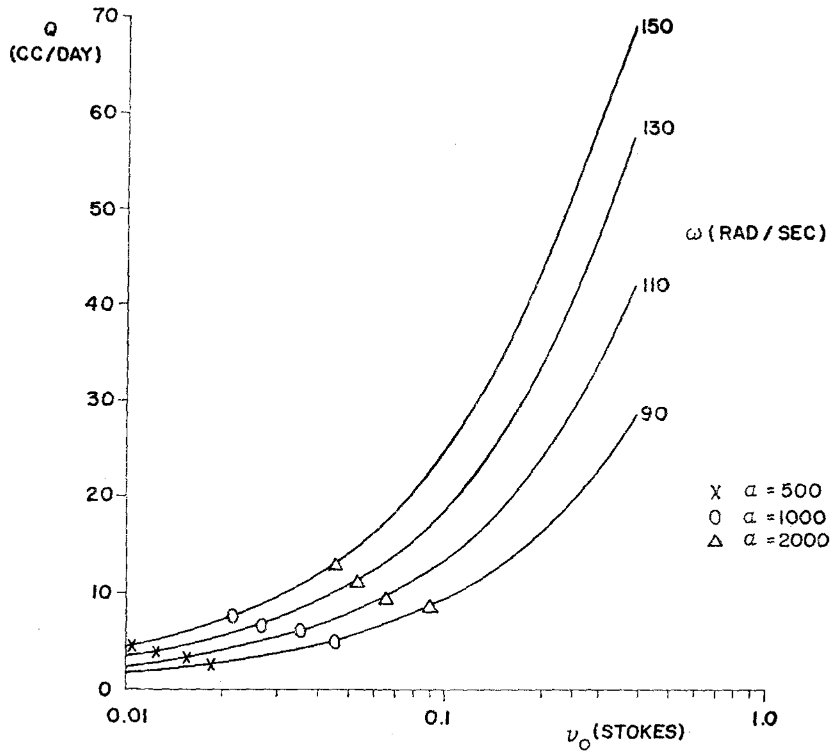


Figure 3. Minimum flow rates

Under normal circumstances the flow must be positive in order to keep the mucus moving away from the lungs, and the mucous velocity at the mucus-air interface should be positive to prevent foreign particles from entering the lungs. The minimum flow occurs when the velocity at the air-mucus interface is zero. This minimum flow rate was computed and is presented as a function of $\nu_0$ and $\omega$ in Figure 3.

*Conclusions.* (*a*) There is good agreement between the computed average mucous velocity and observed values. (*b*) The computed minimum rate of flow is of the right order of magnitude. (*c*) For $\alpha$ large the flow rate is proportional to the square of the maximum cilium tip velocity $\omega s$ times $(3 - \gamma)(1 - \gamma^2)$. The dependence on viscosity is nearly linear while the dependence of $Q$ on the viscosity variation $\alpha$ is

$$Q \text{ proportional to } \frac{\ln \alpha}{\alpha} \text{ for large } \alpha.$$

(*d*) The dependence of $Q$ on the cilia geometry is $Q$ proportional to $L/[a^2(n^2 - 1)]$.

Thanks are due to the Bio-medical Engineering Center at Northwestern University for awarding one of the authors, Charles Barton, a training stipend under N. I. H. Training Grant 5T1 GM 874-04 which permitted the completion of this paper.

## LITERATURE

Ewert, G. 1965. "On the Mucus Flow in the Human Nose." *Acta Otolaryngol.*, Suppl. 200.

Landau, L. D. and E. M. Lifshitz. 1959. *Fluid Mechanics.* Boston: Addison-Wesley Press, p. 91

Lucus, A. M. and L. C. Douglas. 1934. "Principles Underlying Ciliary Activity in the Respiratory Tract, II. A Comparison of Nasal Clearance in Man, Monkey, and other Mammals." *Arch. Otolaryngol.*, **20**, 518–541.

Rivera, J. A. 1962. *Cilia, Ciliated Epithelium, and Ciliary Activity.* New York: Pergamon Press, p. 12.

Tomotika, S. and T. Aoi. 1951. "An Expansion Formula for the Drag on a Circular Cylinder Moving Through a Viscous Fluid at Small Reynolds Numbers." *Q. J. Mech.*, **4**, 401–406.

RECEIVED 11-28-66