Harvard-MIT Division of Health Sciences and Technology
HST.542J: Quantitative Physiology: Organ Transport Systems
Instructors: Roger Mark and Jose Venegas

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Departments of Electrical Engineering, Mechanical Engineering, and the Harvard-MIT Division of Health Sciences and Technology

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PROBLEM SET 7

SOLUTIONS

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Problem 1

In this problem, consider the different factors which, in combination, give rise to the pressure differences encountered in the lung during breathing. For this purpose, use a simple model comprised of five generations with the geometry described below.

Generation	Number of Airways	Total Cross-sectional Area (cm^2)	Length (cm)
1	1	2	10
2	4	3	2
3	16	5	1.5
4	128	10	1.0
5	2000	50	0.5

In the following questions, consider inspiration at a normal breathing rate of 0.5 L/sec. Assume the flow to be steady and the fluid to be $\nu = 0.15$ cm^2/sec and $\rho = 2 \times 10^{-3}$ gm/cm^3. (Remember $\nu = \mu/\rho$, the kinematic viscosity.)

A. Compute the mean flow velocity in each generation assuming a uniform distribution of ventilation.

   See Table 1.

B. Assume the flow to be *inviscid* and calculate the total pressure difference between the first and fifth generations. This represents the pressure difference necessary to decelerate a fluid particle as it passes through the network.

   If flow is inviscid and steady, use Bernoulli:

$$
\begin{aligned}
P_1 + \frac{1}{2}\rho v_1^2 &= P_2 + \frac{1}{2}\rho v_2^2 \\
\rho &= 2 \times 10^{-3} \\
P_1 &= 0 \\
P_2 &= \left(\frac{1}{2}\right)\left(2 \times 10^{-3}\right)(250)^2 - \frac{1}{2}\left(2 \times 10^{-3}\right)10^2 \\
&= 10^{-3} \times 62,500 - 10^{-1} \\
&= 62.5 \textit{ dynes/cm}^2
\end{aligned}
$$

C. Assume, as a first approximation, that the flow in each airway is laminar (check your Reynolds numbers to see if this is reasonable) and fully developed. Calculate the pressure difference acting across the network (first to fifth generation) due to viscous forces alone. This represents the pressure drop necessary to overcome the tendency of wall friction to impede the flow. (Note that the actual pressure drops in the upper airways will tend to be greater than those estimates due to secondary flow and the boundary layer developing after each branch.)

Table 1: Pressure drop for tracheal flow of 500 cc/sec

Generation	*Branches*	*Length*	*Total A (cm2)*	*Indiv. Diam (cm)*	D^4	*Velocity*	*Re*	*Flow (cc/sec)*	*R*	*Press. drop*
1	1	10.0	2	1.60	6.491	250.00	2660.29	500.00	0.003	1.39
2	4	2.0	3	0.98	0.913	166.67	1086.06	125.00	0.004	0.49
3	16	1.5	5	0.63	0.158	100.00	420.63	31.25	0.017	0.53
4	128	1.0	10	0.32	0.010	50.00	105.16	3.91	0.182	0.71
5	2000	0.5	50	0.18	0.001	10.00	11.90	0.25	0.887	0.22
Total pressure drop from viscosity										3.34

Reynolds numbers are in Table 1 and range from 2660 in the trachea to 11.9 in the generation 5 airways. Flow may be laminar, especially in the smallest airways, but is most likely transitional because of time-varying flows and branching.

If we make the assumption of fully developed laminar flow and use Poiseuille formula for resistance:

$$
\begin{aligned}
R &= \frac{8}{\pi} \cdot \mu \frac{l}{r^4} = \frac{8}{\pi} \cdot \nu \rho l \left(\frac{16}{D^4} \right) = \frac{8(0.15)}{3.14} \left(3 \times 10^{-4} \right) (16) \frac{l}{D^4} \\
&= \left(1.8 \times 10^{-3} \right) \frac{l}{D^4}
\end{aligned}
$$

See Table 1 for individual values. Total viscous pressure drop is 3.34 dynes/cm^2.

D. Recognizing that, in the real case, these two factors act in concert to produce the observed pressure difference, compare your answers in (B) and (C) to see which effect dominates.

   In this problem the viscous forces are a small effect, only about 5% of the total pressure drop from kinetic energy changes.

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Problem 2

If a dog is breathing ordinary air, and the left main bronchus is suddenly occluded, the left lung will completely collapse in about 1/2 hour. If the dog had been breathing 100% 0_2 for some tine previously, collapse occurs in about 5 minutes. Discuss the process of collapse and explain the more rapid collapse after breathing pure oxygen. Include as part of your discussion a qualitative description of the total pressure in the left lung as a function of time. You may find the following typical values of arterial and venous partial pressure useful.

	Breathing Air	**Breathing 100% O_2**
Arterial	$P_{O_2} = 100$, $P_{CO_2} = 40$	$P_{O_2} = 660$, $P_{CO_2} = 40$
Venous	$P_{O_2} = 40$, $P_{CO_2} = 46$	$P_{O_2} = 90$, $P_{CO_2} = 46$

You may assume that as the total volume of gas in the left lung changes, the total gas pressure remains close to atmospheric.

Air trapped in an occluded segment of the lung will tend to equilibrate with mixed venous gas. If equilibration were to proceed to completion, the gas composition would be:

$$\begin{aligned} P_{O_2} &= 40 \text{ torr} \\ P_{CO_2} &= 45 \text{ torr} \\ P_{H_2O} &= 47 \text{ torr} \\ P_{N_2} &= 573 \text{ torr} \\ \hline P_{total} &= 705 \text{ torr} \end{aligned}$$

This, being substantially below normal atmospheric pressure, would cause either a local collapse of the lung, or an accumulation of liquid (alveolar edema) effectively filling the lung.

If the gas within the lung initially is primarily O_2, the absorption of alveolar gas takes place rapidly, primarily due to the high solubility of O_2 in blood. If the gas is largely composed of nitrogen which has a much lower solubility, the rate of gas transfer will be slower, delaying total collapse.

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Problem 3

On a hot summer day, a dog pants to eliminate heat. During panting, breathing rates of 300 breaths per minute are common and tidal volumes fall to roughly equal to the dog's dead space volume.

A. Using the conventional model of pulmonary gas exchange (based an the division of the lung into a single dead space and single alveolar space) compare the following two ventilation states in terms of relative values for P_{a,O_2} and P_{a,CO_2}:

Normal Breathing	**Panting**
$f = 20/\text{min}$	$f = 300/\text{min}$
$V_T = 400\text{ml}$	$V_T = 167\text{ml}$
$V_D = 150\text{ml}$	
$V_A = 2000\text{ml}$	

assuming that cardiac output, metabolic rate, and inspired gas composition all remain constant.

Normal Breathing: $\dot{V}_A = 20(400 - 150) = 5$ *l/min*

Panting $\dot{V}_A = 300(167 - 150) = 5$ *l/min*

Since $\dot{V}_A$s are identical, all gas tensions will be the same!

B. What objections might be raised to the use of such a simplistic model for high frequency, low tidal volume breathing?

The actual lung is highly asymmetrical and the distribution of ventilation is non-uniform. consequently, when $V_T \rightarrow V_D$, $\dot{V}_A$ will be strongly influenced by these inhomogeneities and cannot be predicted with such a simple model.

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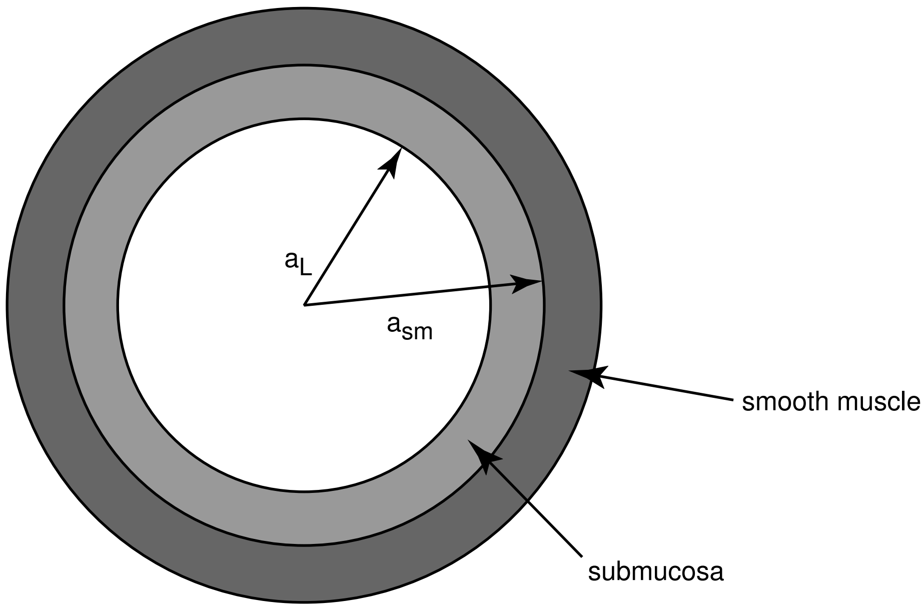
Problem 4

It is thought that airway smooth muscle can shorten by as much as about 30% when exposed to a broncho-constrictive agent such as histamine. In asthmatics, the effect of smooth muscle constriction has been shown to be accentuated by a pathologic thickening of the airway wall. In order to analyze the consequence of these two effects in concert, consider the following simple model of a small airway, shown here in cross-section. In this model, the smooth muscle is assumed to be confined to a band surrounding the inner tissues of the wall (submucosa, mucosa).



A. Obtain an expression for the ratio of lumenal radii before and after a 30% reduction in smooth muscle length $a_L/a_{L,o}$ (the subscript "o" indicates a pre-constriction value). Assume that the wall area inside of the smooth muscle A_W remains constant and that both the smooth muscle and the internal lumen remain circular in cross-section.

   In both cases, the smooth muscle and luminal radii are related throught the expression:

$$A_W = \pi a_{sm}^2 - \pi a_L^2$$

   or

$$a_L = \left(a_{sm}^2 - \frac{A_W}{\pi} \right)^{1/2}$$

   A 30% reduction in smooth muscle length translates into a 30% reduction in a_{sm}. Therefore, if the initial value of a_L is $a_{L,o}$, the constricted value is

$$a_{L,c} = \left[\left(0.7 a_{sm,o}\right]^2 - \frac{A_W}{\pi} \right)^{1/2}$$

The ratio of constricted to initial radii is

$$\frac{a_{L,c}}{a_{L,o}} = \left[\frac{\left(0.7a_{sm,o}\right)^2 - \frac{A_W}{\pi}}{a_{sm,o}^2 - \frac{A_W}{\pi}} \right]^{1/2}$$

B. A typical value for $a_{sm,o}/a_{L,o}$ might be 1.05; for an asthmatic airway, the same ratio might be 1.1 (or higher). Calculate the ratio of $a_L/a_{L,o}$ in both cases. Assuming that these airways are located sufficiently peripheral so that the Reynolds number is < 50, by what percentage does the flow resistance of the normal airway change? What happens to the resistance of the asthmatic airway? Consider the implications of inhomogeneity in the degree of smooth muscle constriction or the degree of wall thickening on the distribution of ventilation.

For $\frac{a_{sm,o}}{a_{L,o}} - 1.05$, A_W *can be expressed as*

$$\begin{aligned} A_W &= \pi a_{sm,o}^2 \left[1 - \left(\frac{1}{1.05} \right)^2 \right] \\ &= 0.29 a_{sm,o}^2 \end{aligned}$$

For a thickened airway:

$$A_W = 0.54 a_{sm,o}^2$$

To calculate the ratio of constricted to pre-constricted radii for the normal airway:

$$\begin{aligned} \frac{a_{L,c}}{a_{L,o}} &= \left[\frac{(0.7)^2 - \frac{0.29}{\pi}}{1 - \frac{0.29}{\pi}} \right]^{1/2} \\ &= 0.66 \end{aligned}$$

For a thickened airway:

$$\frac{a_{L,c}}{a_{L,o}} = \left[\frac{(0.7)^2 - \frac{0.54}{\pi}}{1 - \frac{0.54}{\pi}} \right]^{1/2} = .61$$

Since $\mathrm{Re} < 50$, *the resistance,* R, *varies as* a^{-4},

$$\frac{R_c}{R_0} = \left(\frac{a_0}{a_c} \right)^4 = 12.7$$

Inhomegeneity can produce huge changes in ventilation distribution!

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