Alveolar Gas Exchange and Gas Balances on the Lung

What we want to do is to develop a quantitative model of gas exchange in the lung which we can use to examine how the lung works. Further, because the cardiovascular system is also deeply involved in gas exchange, we would like to relate the lung model of gas exchange to a cardiovascular model of gas exchange, so that we can examine how the "system" works and how the respiratory "sub"-system and cardiovascular "sub"-system might interact.

Our approach to model building will be to pick the variables which we think are the most important and to do a balance on the variables over some part of the "system".

We can do a balance in the following ways (remember the first lecture): For materials which are produced such as $CO_2$

$$Quantity\,Produced = Quantity\,In - Quantity\,Out\quad (1)$$

and for materials which are consumed such as $O_2$

$$Quantity\,Consumed = Quantity\,Out - Quantity\,In\quad (2)$$

Notice that there is a sign reversal here. Negative sign is usually given to flows out of the system and positive sign to flows into the system. Recall also that the governing equation for the "balance" equation is:

$$Change\,of\,Concentration = Quantity\,In - Quantity\,Out + Consumption - Production.\quad (3)$$

If we assume that there is no change of concentration in the system (i.e. a steady state) then

$$Change\,of\,concentration = 0\quad (4)$$

and

$$0 = Quantity\,In - Quantity\,Out + Consumption - Production.\quad (5)$$

This condition is known as the "steady-state" condition and it means literally that there is no net change in the quantity in the system. The steady-state equation (eqn. 5) can be manipulated (algebraically) to solve for whatever of the remaining variables we wish. Presumably, we try to isolate those variables that we can measure on the right of the =, those that we can’t and wish to solve for on the left of the =.

We then have to deal with two issues:

1. We have to pick the system to do the balance on or some part of the system.
2. We have to build quantitative definitions for our variables.

Any of our major variables can be and generally will be composed of several other variables (and this can be confusing) but the units of the group of variables comprising the major variable (in eqs. 1-5) must reduce to the same as the major variable (e.g. quantity or concentration). Further, the units or dimensions on the left and right hand sides of the = must be equal. This last constraint is called dimensional homogeneity.

The tool that we are going to use is the balance- we must do a balance on the lung or on some part of it. A balance for what? Well, because we are talking about gas exchange and the major gases exchanged by the lung are oxygen, carbon dioxide nitrogen and water vapor, we can think of doing balances for \( O_2, CO_2, N_2 \) and \( H_2O \). We will concentrate on the first two for what I hope are obvious reasons. Next we need to define the quantity of \( O_2 \) and \( CO_2 \). Well, concentration (C) comes immediately to mind

\[
C = \frac{n}{V} \tag{6}
\]

where \( n \) is the number of molecules and \( V \) is the volume of gas in which the molecules are found. Gas concentration is difficult to deal with however. The gas law

\[
P \cdot V = n \cdot R \cdot T \tag{7}
\]

where \( P \) is partial pressure in mmHg or kPa (remember that 760 mmHg is about equivalent to 101 kPa), \( R \) is the gas constant and \( T \) is the temperature, gives us a convenient way out. Rearranging, we get

\[
P = \frac{n}{V} \cdot R \cdot T \tag{8}
\]

and then

\[
\frac{P}{R \cdot T} = C \tag{9}
\]

That is, the concentration of a gas is given by the partial pressure divided by the \( R \) and \( T \). So where ever we use \( C \), we can substitute \( \frac{P}{RT} \). Partial pressure, \( P \) is easily measured using various kinds of electrodes. You should also recall that the total pressure in a multi-gas mixture (like the atmosphere or the gas in your lung) is the sum of the partial pressures of the individual gases:

\[
P_t = P_{O_2} + P_{CO_2} + P_{N_2} + P_{H_2O} + P_{\text{trace gases}} \tag{10}
\]

and we can neglect (i.e. disregard as too small) \( P_{\text{trace gases}} \). This equation is another way of saying that the total concentration of gas in the volume is equal to the sum of all the individual gas concentrations. Can you explain why?
Total pressure is generally measured (and described) as barometric pressure: \( P_t = P_b \). We can also parameterize concentration in another way. We can say that the fraction \((F)\) of a gas in the total volume of gas is:

\[
F_{\text{gas}} = \frac{P_{\text{gas}}}{P_b}
\]  
(11)

We usually standardize this to dry conditions in the following way:

\[
F_{\text{gas}} = \frac{P_{\text{gas}}}{P_b - P_{\text{H}_2\text{O}}}
\]  
(12)

This is because water vapor in the air can be quite variable and is usually different than in the lung (where it is saturated at body temperature \((T_B)\)), indeed we usually standardize our partial pressure to standard temperature and pressure, dry (STPD). You should know how to do that. Now, we are going to use both partial pressure and fraction as measures of quantity but as you can see they are inter-convertible.

Back to our system? Well, let's do our initial balance on the entire lung. We know that \(O_2\) is consumed by the lung (i.e. it disappears from the lung–to where?) and that \(CO_2\) is produced by the lung (i.e. it appears in the lung–from where?). Let us do a balance on \(O_2\):

\[
\text{Change of } O_2 \text{ concentration} = O_2 \text{ in} - O_2 \text{ out} - O_2 \text{ consumed}
\]  
(13)

You should understand by now where this came from!!! If we pick a suitable interval of time (a time encompassing many breathes rather than one or less), then the lhs is 0 and:

\[
O_2 \text{ consumed} = O_2 \text{ in} - O_2 \text{ out}
\]  
(14)

Now we convert these quantities to symbols (parameterize): quantity of \(O_2\) in must equal the fraction of \(O_2\) in the air going in times the quantity \((\dot{V}_I)\) of air actually going in or \(F_{I O_2} \cdot \dot{V}_I\) and similarly for the quantity out, \(F_{E O_2} \cdot \dot{V}_E\). The \(\dot{V}\) is defined as the rate of change of volume. \(I\) means inspired and \(E\) means expired. \(O_2\) consumed is represented as \(\dot{V}_{O_2}\) or sometimes as \(\dot{M}_{O_2}\). What are the units (dimensions) of the lhs and rhs? Our equation now looks like this:

\[
\dot{V}_{O_2} = F_{I O_2} \cdot \dot{V}_I - F_{E O_2} \cdot \dot{V}_E
\]  
(15)

We can simplify this by letting \(\dot{V}_I\) equal \(\dot{V}_E\) and calling them both \(\dot{V}_E\). This sounds like a good thing to do but, in fact, \(\dot{V}_I \geq \dot{V}_E\) but we will deal with this later. Our eqn. then simplifies to:

\[
\dot{V}_{O_2} = \dot{V}_E \cdot (F_{I O_2} - F_{E O_2})
\]  
(16)

and we can solve for the \(O_2\) coming out of the lung by rearranging:

\[
F_{E O_2} = F_{I O_2} - \frac{\dot{V}_{O_2}}{\dot{V}_E}
\]  
(17)
Figure 1: $P_{AO_2}$ as a function of $V_A$. $\dot{V}_{O_2}$ is set to 200 and 400 ml · min$^{-1}$.

If we now multiple the equation through by $P_b - P_{H_2O}$ from eqn. 12, we have converted to partial pressures (where $K$ is the conversion factor):

$$P_{EO_2} = P_{Io_2} - K \cdot \frac{\dot{V}_{O_2}}{\dot{V}_E}$$

(18)

Now think about what this says. Indeed, look at the relationship between inspired and expired $O_2$ by plotting $P_{EO_2}$ vs $\dot{V}_E$ on a graph or graphing calculator (a TI-82 or TI-85 would work fine). Let $K = 0.863$, this actually corrects the partial pressures to STPD. Let $P_{Io_2}$ equal 155 mmHg, the partial pressure of $O_2$ in air at sea level. Let $\dot{V}_{O_2}$ equal 200 $ml \cdot min^{-1}$ and $\dot{V}_E$ equal 5 $L \cdot min^{-1}$. First vary $\dot{V}_E$, then double $\dot{V}_{O_2}$ and vary $\dot{V}_E$ again. You should get a figure that looks much like Fig. 1. Do you?

Now do a balance on lung $CO_2$ just as you did for $O_2$. Remember, or note if you don’t know, that there is essentially no $CO_2$ in inspired air!!!! You should get something that looks like this:

$$F_{ECO_2} = \frac{\dot{V}_{CO_2}}{\dot{V}_E}$$

(19)

$$P_{ECO_2} = K \cdot \frac{\dot{V}_{CO_2}}{\dot{V}_E}$$

(20)

Use the same values as you used to generate fig. 1 and plot the appropriate graph. In words, what happens to $CO_2$ and $O_2$ when ventilation changes at a constant ventilation?
This is moderately interesting but in fact the point of this process from your perspective is that you should know how to do a respiratory gas balance on the lung. Let’s do it now on part of the lung!! If we look at total lung volume, that volume can be sub-divided into two smaller volumes, the volume of non-gas exchanging air way ($V_D$, the dead space) and the alveolar volume ($V_A$) where gas exchange actually occurs:

$$V_{total} = V_A + V_D$$  \hspace{1cm} (21)

Similarly, we could say that expired volume of gas coming from the lung must be composed of gas coming from the dead space and gas coming from the alveolar space:

$$\dot{V}_E = \dot{V}_A + \dot{V}_D$$  \hspace{1cm} (22)

Now we (you) can do a balance for $CO_2$ and $O_2$ on the alveolar space—just on the alveolar space. You do it just the way that you did it for the lung but now using only the alveolar volume. Substitute $\dot{V}_A$ for $\dot{V}_E$ and proceed in the same way! You need the quantity in, the quantity out and the production or consumption. You should get equations that look like this:

$$F_{ACO_2} = \frac{\dot{V}_{CO_2}}{V_A}$$  \hspace{1cm} (23)

$$P_{ACO_2} = K \cdot \frac{\dot{V}_{CO_2}}{V_A}$$  \hspace{1cm} (24)

$$F_{AO_2} = F_{I0_2} - \frac{\dot{V}_{O_2}}{V_A}$$  \hspace{1cm} (25)

$$P_{AO_2} = P_{I0_2} - K \cdot \frac{\dot{V}_{O_2}}{V_A}$$  \hspace{1cm} (26)
Why are eqns. 17 – 20 and 23 – 26 useful? Well, they tell us the the \(O_2\) and \(CO_2\) coming out of the lung and out of the alveolar space are related to ventilation and to metabolism, further they tell us how they are related. Indeed, it is the ratio of metabolism to ventilation which determines the level of \(O_2\) and \(CO_2\) in the expired gas and in the alveolar gas. It is this ratio which has to change if there is to be a change in the expired or alveolar gases. We can go further with these equations. Notice that we can solve eqn. 20 and eqn. 24 for \(\dot{V}_{CO_2}\); that is, move \(\dot{V}_{CO_2}\) to the rhs and everything else to the lhs. Now we can equate the two lhs’s and get:

\[
\dot{V}_A = \dot{V}_E \cdot \frac{P_{ECO_2}}{P_{ACO_2}}
\]  

(27)

What does eqn. 27 say? Well, if \(P_{ECO_2}\) equals \(P_{ACO_2}\) then \(\dot{V}_A\) equals \(\dot{V}_E\). But of course, we know that there is a dead space so \(\dot{V}_A\) can not equal \(\dot{V}_E\) and therefore \(P_{ECO_2}\) cannot equal \(P_{ACO_2}\). How much do they differ and in what direction. Because of the dead space and eqn. 22, \(\dot{V}_A\) must be less than \(\dot{V}_E\) (after all the alveolar space and dead space sum to the total volume). Then \(P_{ECO_2}\) must be less than \(P_{ACO_2}\). Why? Indeed, the ratio of the two quantities is a measure of the dead space volume. How?

\(P_{ECO_2}\) is easy to measure but \(P_{ACO_2}\) is not. but we can approximate it. \(P_{ECO_2}\) is the \(P_{CO_2}\) in the blood coming out of the lung (after gas exchange) and it is very close to \(P_{ACO_2}\) because \(CO_2\) equilibrates between the alveolar space and the blood during gas exchange (such is not true for \(O_2\)). The blood coming out of the lung, enters the left heart and is pumped into the systemic circulation. By sampling arterial blood as close to the heart as we can get (for example, arterial blood from the arm), we can get a very good measure of \(P_{ECO_2}\). Reasonable values for \(P_{ECO_2}\) and \(P_{AECO_2}\) are 27 mmHg and 38 mmHg respectively.

We can now substitute the lhs of eqn. 27 into the lhs of eqn. 22 and solve for \(\dot{V}_D\):

\[
\dot{V}_D = \dot{V}_E \cdot (1 - \frac{P_{ECO_2}}{P_{ACO_2}})
\]  

(28)

Eqn. 28 tells us that \(\dot{V}_D\) is 0.29 of \(\dot{V}_E\). Make sure you get the same number when you solve eqn. 28. \(\dot{V}_E\) is typically around 500 ml, \(\dot{V}_A\) is around 350 ml and \(\dot{V}_D\) is around 150 ml. This dead space, measured using the alveolar gas exchange equations, is called the physiological deadspace and can be measured easily in a physician’s clinic. It is a measure of how well the lung is functioning physiologically.

We haven’t finished yet, however. We can define another variable, the respiratory quotient \((RQ = R_Q)\) as the ratio of the \(CO_2\) production to the \(O_2\) consumption:

\[
R_Q = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}
\]  

(29)
Figure 3: The $P_{O_2}$-$P_{CO_2}$ diagram. The two families of curves are for $P_{I O_2}$’s of 155 and 100 respectively. What might differences in $P_{I O_2}$ represent?

When the body burns a fuel such as glucose, down to $H_2O$ and $CO_2$ a quantity of $O_2$ equal to the quantity of $CO_2$ produced is required. The $R_Q$ is 1. Different fuels produce different $R_Q$’s. Proteins have $R_Q$’s around 0.84 and lipids have $R_Q$’s around 0.7. If the $R_Q$ is less than 1, this means that more $O_2$ is taken out of the lung than $CO_2$ is put into the lung and $\dot{V}_E$ is less than $\dot{V}_I$. Remember, we made the assumption that they are equal, when they are not, the gas exchange equations must be corrected for the difference. Eqn. 29 is useful in another way however. We can solve the respective expired gas equations (eqns. 17-20) and alveolar gas exchange equations (eqns. 23-26) for $\dot{V}_{CO_2}$ and for $\dot{V}_{O_2}$ (i.e. isolate each on the lhs of the equation) and substitute the rhs’s into eqn. 29. That is, we can relate $P_{E CO_2}$ to $P_{E O_2}$ and $P_{A CO_2}$ to $P_{A O_2}$. For the alveolar gases:

$$P_{A CO_2} = \frac{R_Q \cdot P_{I O_2}}{(1 - F_{I O_2}) \cdot (1 - R_Q)} - \frac{R_Q}{(1 - F_{I O_2}) \cdot (1 - R_Q)} \cdot (P_{A O_2})$$  \hspace{1cm} (30)$$

The term $R_Q/(1 - F_{I O_2}) \cdot (1 - R_Q)$ is the correction for difference in $\dot{V}_E$ and $\dot{V}_I$ when $R_Q$ is not equal to 1. Note that the term becomes 1 when $R_Q = 1$. We can write the same expression for expired gas:

$$P_{E CO_2} = \frac{R_Q \cdot P_{I O_2}}{(1 - F_{I O_2}) \cdot (1 - R_Q)} - \frac{R_Q}{(1 - F_{I O_2}) \cdot (1 - R_Q)} \cdot (P_{E O_2})$$  \hspace{1cm} (31)$$

Now as I have written eqns. 30 and 31, they are equations for straight line, $y = a - b \cdot x$ where $a = \frac{R_Q \cdot P_{I O_2}}{(1 - F_{I O_2}) \cdot (1 - R_Q)}$ and $b = \frac{R_Q}{(1 - F_{I O_2}) \cdot (1 - R_Q)}$. The families of lines generated by these equations (figure 3) have been discussed in lecture. You should know how to interpret them!!
Blood Gas Transport

Oxygen \((O_2)\) and carbon dioxide \((CO_2)\) are transported to and from the lung by blood (pumped by the heart). We can also do a mass balance for each gas on the blood entering and exiting the lung. For \(O_2\):

\[
\dot{V}_{O_2} = \dot{Q} \cdot (C_{aO_2} - C_{\bar{v}O_2}) \tag{32}
\]

Here the blood flow is \(\dot{Q}\), the concentration of \(O_2\) in the arterialized blood (leaving the lung) is \(C_{aO_2}\) and the concentration of \(O_2\) in venous blood (entering the lung) is \(C_{\bar{v}O_2}\). The form is the same as earlier, the quantity in minus the quantity out is equal to the oxygen consumption. The mass balance for \(CO_2\) is:

\[
\dot{V}_{CO_2} = \dot{Q} \cdot (C_{\bar{v}O_2} - C_{aO_2}) \tag{33}
\]

where the concentration of \(CO_2\) coming into the lung is \(C_{\bar{v}O_2}\) and the concentration of \(CO_2\) coming out of the lung is \(C_{aO_2}\). The problem that we have is that the concentration of \(O_2\) and \(CO_2\) is not a linear function of the partial pressure (as is the concentration of gas in the lung). This problem was discussed in some detail in lecture. We can proceed anyway (keeping this in mind). Note that we have expressions each for \(\dot{V}_{O_2}\) and \(\dot{V}_{CO_2}\), one for the lung (i.e ventilation) and one for blood (i.e. perfusion). These can be equated:

\[
0.863 \cdot \dot{V}_A \cdot P_{ACO_2} = \dot{Q} \cdot (C_{\bar{v}O_2} - C_{aO_2}) \tag{34}
\]

and

\[
0.863 \cdot \dot{V}_A \cdot (P_{IO_2} - P_{AO_2}) = \dot{Q} \cdot (C_{aO_2} - C_{\bar{v}O_2}) \tag{35}
\]

Rearrange and solve for \(\dot{V}_A\) and \(\dot{Q}\):

\[
\frac{\dot{V}_A}{\dot{Q}} = \frac{(C_{\bar{v}O_2} - C_{aO_2})}{P_{ACO_2}} \tag{36}
\]

and

\[
\frac{\dot{V}_A}{\dot{Q}} = \frac{(C_{aO_2} - C_{\bar{v}O_2})}{(P_{IO_2} - P_{AO_2})} \tag{37}
\]

The ratio \(\frac{\dot{V}_A}{\dot{Q}}\) is called the VAQ ratio, or the ventilation-perfusion ratio. The ratio for each gas varies as a function of the distribution of ventilation in the lung and the distribution of perfusion in the lung. Remember that the top of the lung is overventilated relative to the bottom of the lung and the top of the lung is underperfused relative to the bottom of the lung. That is, in the normal upright lung, there is a "mismatch" of ventilation to perfusion.