

# AN OVERVIEW OF RESPIRATION AND AN INTRODUCTION TO DIFFUSION AND SOLUBILITY OF GASES<sup>1</sup>

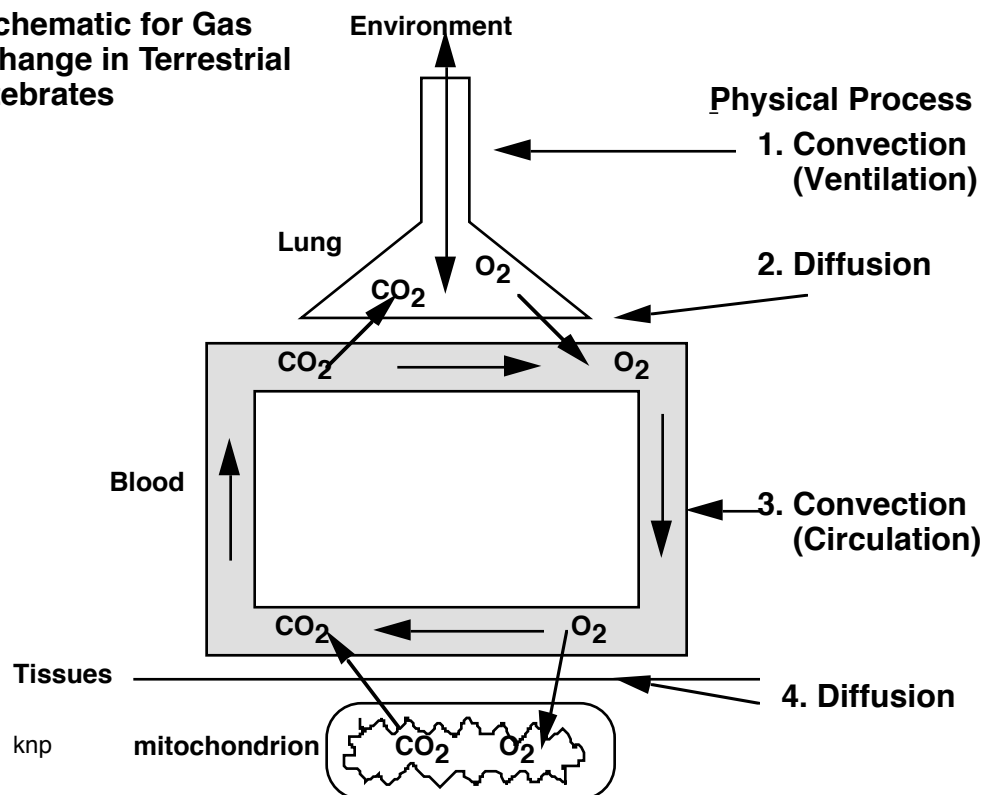
**Summary:** This set of notes gives an overview of respiration and then follows the overview with a detailed discussion of the physical constraints that act on respiration. It is foundational to everything else we will cover on respiration. The central part of this foundation is a series of equations for respiratory gas exchanged. These include partial pressures, volume conversions to correct for temperature, pressure, and vapor pressure, solubilities, and a revised version of Fick's Law of diffusion that used Krogh's Diffusion Coefficient, K. We will also overview the movement of gases during diffusion.

## I. OVERVIEW -- THE RESPIRATORY SYSTEM OF ANIMALS THAT USE A CIRCULATORY SYSTEM TO MOVE GASES ABOUT. VERTEBRATES AS AN EXAMPLE.

A. Earlier, you gained a solid understanding of cellular energetics. In this unit, we will consider how large animals (meaning anything more than a few cell layers thick) manage to move respiratory gases about.

B. Here is a model system that applies to vertebrates in general. We will later see other systems used by other taxa. In vertebrates we should view the respiration process above the cell level as a 4-step process:

### A Schematic for Gas Exchange in Terrestrial Vertebrates



The four stages are:

- (i) between the ENVIRONMENT and the LUNG via VENTILATION;
- (ii) between the ALVEOLAR AIR and the BLOOD via DIFFUSION
- (iii) between the LUNG and the TISSUES via CIRCULATION, and

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(iv) Between the BLOOD and the MITOCHONDRIA via DIFFUSION and MICRO-CONVECTIVE PROCESSES.

2. A series of equations to **approximate** what happen for each step have been written. In the series of equations given below, note that they are written for O<sub>2</sub> since for mammals this is usually the limiting gas. However, they could be written for any other gas including CO<sub>2</sub> and N<sub>2</sub>:

3. The equations are spoken of as **CONDUCTANCE EQUATIONS** since they quantify the movement of the gas from one of the compartments (shown in the diagram above) to another, that is, these equations quantify conduction of gas.

Don't panic over these equations. They are actually quite easy. Note that most of this set of notes will be concerned with diffusion and so the equations for alveolar/blood and tissue/blood exchange given below will be amplified on later in these notes.

a. **STEP 1 - VENTILATION**: From the outside air to the alveolar space of the lungs, essentially a **CONVECTIVE PROCESS**

$$1. \dot{V}_{O_2 \text{ vent}} = \dot{V}_I * C_{IO_2} - \dot{V}_E * C_{EO_2}$$

where  $\dot{V}_{O_2 \text{ vent}}$  is the total oxygen that is exchanged in ventilation,  $\dot{V}_I$  and  $\dot{V}_E$  are the inspired and expired minute volumes, respectively, and  $C_{IO_2}$  and  $C_{EO_2}$  are the oxygen concentrations of inspired and expired air, respectively.

b. **STEP 2 - ALVEOLAR EXCHANGE**: refers to the total amount of gas that is exchanged between the alveoli and the blood, this is a diffusive process and it is determined by:

$$2. \dot{V}_{O_2 \text{ alv}} = D_{L_{O_2}} (\bar{P}_{AO_2} - \bar{P}_{vO_2})$$

where  $\bar{P}_{vO_2}$  is the **mean partial pressure of oxygen in the venous blood as it flows through the capillaries of the alveoli**;  $\bar{P}_{AO_2}$  is the mean partial pressure of O<sub>2</sub> in the alveolar air; and  $D_{L_{O_2}}$  is the diffusive conductance of the lung for oxygen (i.e., the capacity of the lung to diffuse O<sub>2</sub>). Since alveolar exchange is a **diffusive process**,  $D_{L_{O_2}}$  is largely determined by factors from something Fick's Law (which will be covered in detail shortly):

$$3. D_{L_{O_2}} \propto \frac{KA}{L}$$

where **K** is the **Krogh diffusion coefficient for lung tissue**, **A** is the alveolar surface area, and **L** is the length of the diffusion distance (i.e., the thickness of the alveoli). Other

important factors include the amount of O<sub>2</sub> carrier (hemoglobin) in the blood (see the notes for the next class -- be sure you understand why, how and under what circumstances hemoglobin concentration can affect DL<sub>O<sub>2</sub></sub>).

**c. STEP 3 - CIRCULATION:** the second convective process is described by an equation that we have seen before when we considered circulation:

$$4. \dot{V}_{O_2 \text{ circ}} = \dot{Q}(C_{aO_2} - \bar{C}_{vO_2})$$

where C<sub>aO<sub>2</sub></sub> refers to the arterial blood oxygen content (the arterial blood, of course, is going to the tissues) and C<sub>vO<sub>2</sub></sub> refers to the **mean venous O<sub>2</sub> content (the blood leaving the tissues** -- sometimes referred to as mixed venous blood), and  $\dot{Q}$  is the **cardiac output**, that is, the blood being circulated per unit time by the heart.

**d. STEP 4 - BLOOD-TISSUE EXCHANGE:** the second diffusive process, this is the exchange of O<sub>2</sub> between the arterial blood and the tissue mitochondria, leaving venous blood as the result:

$$5. \dot{V}_{O_2 \text{ tissue}} = D_{tO_2} (\bar{P}_{\text{capillary}O_2} - \bar{P}_{\text{tissue}O_2})$$

where  $D_{tO_2}$  is the Krogh diffusion coefficient (see eq. #3) for oxygen between the plasma and the mitochondria,  $\bar{P}_{\text{tissue}O_2}$  is the average P<sub>O<sub>2</sub></sub> of the tissues surrounding the capillaries and  $\bar{P}_{\text{capillary}O_2}$  is the average P<sub>O<sub>2</sub></sub> of the blood entering the capillaries (we will see that this is normally the same as value for arterial blood)

**4. Note that the  $\dot{V}_{O_2}$  for all steps must, over the long run, be equal.**

a. At any times when all of these  $\dot{V}_{O_2}$  s are equal we are in a **RESPIRATORY STEADY-STATE**. If one or more are not equal, we are in **NON-STEADY STATE**. Obviously, this situation cannot continue for long.

b. **Non-steady state conditions are characterized by the loading or depletion of stores of O<sub>2</sub> that are found mostly in the blood and to a lesser extent in the alveolar air and tissues** (in descending order of importance).

5. Also note that **partial pressure appears in some of the exchange equations, and concentration in others.**

6. Finally, you should be able to write and understand a similar series of conductance equations for any other gas especially CO<sub>2</sub> and to a lesser degree N<sub>2</sub>. Remember that all we have said about non-steady states also applies to these gases.

**Notice that** concentration is used in some equations and partial pressure in others. We will shortly see why this is the case.  
Write similar equations for CO<sub>2</sub> and N<sub>2</sub>.

We will return to these notes (with a vengeance) after we have finished our discussion of O<sub>2</sub> and CO<sub>2</sub> exchange.

**II. INTRODUCTION AND BASIC EQUATIONS:**

A. A review of equations and relationships important to the description of movements of gases:

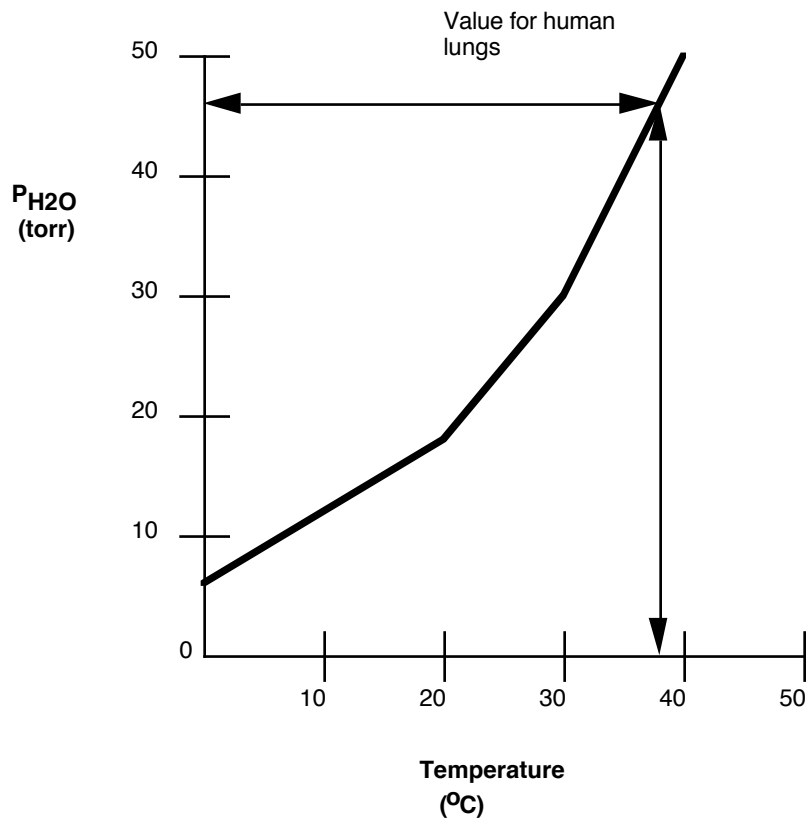
1. **Partial Pressure:** the proportion of the total pressure exerted by a gas mixture that is due to a single gas. Thus, the total pressure, **P<sub>t</sub>** (or **P<sub>b</sub>**) equals the sum of the partial pressures:

6.  $P_t = P_{O_2} + P_{CO_2} + P_{N_2}$  (includes argon, etc.)  $+ P_{H_2O}$

2. The partial pressure of water vapor,  $P_{H_2O}$ , is proportional to the temperature **when the gas sample is saturated**. Below is a table of saturated  $P_{H_2O}$  values for relevant temperatures:

**Vapor Pressure and Temperature under Saturated Conditions**

Temp (°C)	P <sub>H2O</sub> (torr)
20	17.5
21	18.6
22	19.8
23	21.1
24	22.4
25	23.8
26	25.2
27	26.7
28	28.4
29	30.0
30	31.8
31	33.7
32	35.7
33	37.7
34	39.9
35	42.2
36	44.6
37	47.1
38	49.7
39	52.4
40	55.3



knp

**FOR OUR PURPOSES, WE WILL ALWAYS ASSUME THAT GASES ARE EITHER SATURATED WITH H<sub>2</sub>O OR THAT THEY ARE ABSOLUTELY DRY.**

3. Corrections for temperature, pressure, and water vapor:

a. Gas volumes are usually compared under a standard set of conditions. The reason for this is obvious: we know that animals commonly exist at a variety of different temperatures. We also know that for a constant number of gas particles, the volume of a gas is directly proportional to the temperature and inversely proportional to the pressure acting on the gas.

1. We may be interested in either the number of gas particles used or produced by an organism under different sets of conditions (such as when we are interested in metabolism since these numbers of course are directly relatable to oxidative phosphorylations) or in the actual volumes occupied by a certain number of gas molecules under varying conditions of temperature and pressure.

? When would a physiologist be more interested in gas volumes *per se* than in numbers of molecules of, say, O<sub>2</sub> and CO<sub>2</sub>?

2. The general relationship between pressure, volume, temperature, and number of particles is, of course:

7. 
$$V = \frac{n * R * T}{P} \quad \text{or} \quad PV = nRT$$

where  $n$  is the number of mols of an ideal gas that are present,  $R$  is the gas constant,  $T$  is the absolute temperature in °K, and  $P$  is pressure in one of several sets of units (which must agree with the gas constant). More on the units of  $P$  later. We will not usually use this equation except to derive more specialized equations that are suitable to specific purposes.

b. In order to make conversions of gas volumes at one temperature to another, we use a general conversion equation that is derived from the gas law (eq. 2) for the condition where  $n$  and  $R$  remains constant for different values of  $P$  and  $T$ :

8. 
$$V_2 = V_1 * \frac{P_1}{P_2} * \frac{T_2}{T_1}$$

where the subscripts 2 and 1 simply refer to two different sets of conditions. Notice that this is simply a restatement of the what is given in equation #2: volume is directly proportional to temperature (thus  $V_2$  is directly proportional to the ratio of  $\frac{T_2}{T_1}$ ) and  $V$  is inversely proportional to the pressure (thus  $V_2$  is proportional to the ratio of  $\frac{P_1}{P_2}$ ).

c. Since most commonly we are interested in a standard set conditions as compared to an ambient set of conditions, we will now make a more specific expression of equation #3.

1. The standard conditions are referred to as: STANDARD TEMPERATURE AND PRESSURE, DRY GAS or **STPD**. The standard temperature and pressure values we use are, of course, 0°C (i.e., 273°K) and 1 atmosphere (760 mmHg).

2. The set of measurement conditions are referred to as AMBIENT TEMPERATURE AND PRESSURE FOR A SATURATED GAS SAMPLE or **ATPS**. Notice that we assume that for ATP

conditions (not the compound ATP!) we assume that we are interested in a saturated gas. That will not always be the case in real practice. However, this is school and as we all know it is not the real world. We will assume that ambient gas samples are always saturated

3. One specialized set of ATPS conditions is for the gas that is **WITHIN A SPECIFIC ORGANISM** as verses in some gas-collecting device. We refer to these sets of conditions as **BODY TEMPERATURE AND PRESSURE, SATURATED, or BTPS**. For our purposes, these will refer to conditions found within human lungs -- the temperature will be taken as the actual body temperature (usually, but not always 37°C) with the corresponding vapor pressure, and the barometric pressure as being the pressure of the gas that is being inspired by the person.

? When might body pressure be very different from 760 mmHg? Try to think of at least two meaningful examples related to different human enterprises.

4. We can now restate eq. #8:

$$9. \quad V_{STPD} = V_{ATPS} * \frac{273}{(273 + T_a)} * \frac{(P_b - P_{H_2O})}{760}$$

where  $T_a$  refers to the ambient temperature in °C, and  $P_b$  refers to the barometric pressure or pressure of the gas in the subject's lungs in units of mmHg or torr (see below) and  $P_{H_2O}$  refers to the partial pressure of water vapor pressure (we assume the sample is saturated).

? Re-write the above equation to convert from STPD to ATPS or BTPS. Explain why each ratio is set-up as written. It is to your advantage to understand rather than to memorize this equation.  
 Why is  $P_{H_2O}$  subtracted from  $P_b$  instead of standard pressure, 760 torr?  
 What is the effect of immersing a sample of gas in water on its volume? Assume that the gas is in a container such as an inverted test tube such that water is in contact with the gas.  
 For the same example, what happens to the partial pressure of each gas in the submerged inverted test tube? Explain this mathematically.

5. **Units of Pressure:** Pressures in physiology are expressed most commonly in units of mmHg. In respiratory physiology, we most commonly refer to the mmHg by another name, the **TORR**. Thus, 1 mmHg = 1 torr . A less used set of measurements are **ATMOSPHERES (ATM)** where 1 ATM = 760 torr. Finally, the least commonly used measure of pressure is **NEWTONS**  $\frac{M^2}{M^2}$  or **pascals (Pa)**. Standard pressure is about **101.3 kPa** .

**Note: it is very important to know what units of pressure are used in different values; this is especially true of constants that are often (unfortunately) given in ATM instead of torr or kPa.**

4. **GAS FRACTIONS.** A concept related to partial pressure is the gas fraction. **A gas fraction is the proportion of a total gas sample that is due to a certain type of gas.** More succinctly:

$$10. \quad F_{gas} = \frac{P_{gas}}{P_{total}}$$

Generally, gas fractions are considered on the basis of dry gas, i.e. they are calculated as:

$$11. \quad F_{gas} = \frac{P_{gas}}{(P_t - P_{H_2O})}$$

**4. SOLUTIONS CONTAINING GASES.** In biological systems we will always consider gases in solutions. There are many types of solutions that we must consider. Air for example is one. Other examples are the various aqueous solutions that are found in the body, each with different specific properties in terms of the types of solutes and their amounts and finally, solutions in various non-polar substances such as membranes. It is vital to realize that all gases must be dissolved in various solutions before a cell can use them. Most importantly, these solutions are aqueous and so we will spend most of our time considering aqueous solutions of gases.

a. In order to determine the amount of gas that is dissolved in volume of solvent (**vol. of gas/total vol. -- often as given as vol. of gas per 100 vols. of solvent, i.e., vol. %**), we need to know two things:

1. **The Partial Pressure of the gas in the solution.** Normally, we assume that the dissolved gas has come into equilibrium with the gas in contact with ("above") the solution. However, realize that this may often not be the case. Nevertheless, if nothing else is mentioned, assume that the dissolved gas is in equilibrium with the atmosphere.

2. **The solubility coefficient of the gas**, called  $\alpha$ . This is a constant for a given set of circumstances that describes how much gas will dissolve in a particular solvent per unit of pressure.

a. **Notice that the units of pressure and volume given with solubility coefficients vary greatly.** They may be given as torr or ATM, ml or liters. Thus, be careful to notice if the  $\alpha_{gas}$  is given as, for example, ml gas/(ATM \* liter) or ml gas/(torr \* ml solvent), etc.

b. The value of the solubility coefficient is strongly dependent on:

1. **The interaction between the gas and solvent molecules. Oxygen and nitrogen, which are non-polar molecules, are relatively insoluble in water while CO<sub>2</sub> is very soluble (since it is polar). On the other hand, the opposite is true of fat.**

2. **The temperature. Generally, solubility is inversely related to temperature.** Thus, cold water holds more O<sub>2</sub> than warm water.

3. **The total amount of other solutes and their nature.** This is usually the least important consideration in biological systems.

c. Mathematically, solubility is given as:

$$12. \quad \alpha = \frac{(V_{dissolved\ gas})}{V_{solvent} * P_{gas}}$$

-- or --

$$13. \frac{V_{(\text{dissolved gas})}}{V_{\text{solution}}} = \alpha_{\text{gas}} * P_{\text{gas}}$$

d. A solution is said to be **SATURATED** when it is in equilibrium with the gas **above it** -- that is the partial pressure of the gas in the solution is the same as in the gas.

e. Note that **the partial pressure of a dissolved gas does not increase with depth unless there is some place where the gas is being produced. However, a bubble taken from the surface will show an increase in P gas as depth increases since this gas will be compressed** (see previous example).

Solubilities at 20°C in  $\frac{\text{ml gas}}{(\text{ml solvent} * \text{torr})}$ :

gas or ratio	air	water	<u>air</u> water
O <sub>2</sub>	1.23	0.0408	30.14
CO <sub>2</sub>	1.23	1.162	1.05
O <sub>2</sub> / CO <sub>2</sub>	1	0.035	

Interpretation:

i) Each gas is equally soluble in air.

ii) CO<sub>2</sub> is much more soluble in water. CO<sub>2</sub> is 28X more soluble. (This also does not include that the fact that even more CO<sub>2</sub> is carried in acid and bicarbonate form -- see packet 20). This same point is summarized in the data that the air to water ratio for O<sub>2</sub> is 30X greater than that of CO<sub>2</sub> (right-hand column).

5. Volumes of gas and numbers of particles. Just to remind everyone, we sometimes will be interested in numbers of gas particles and not volumes. We will assume that all respiratory gases are ideal gases (not really true of CO<sub>2</sub>); therefore:

$$14. \text{ mols of gas} = \frac{\text{liters of gas}}{(22.4 \text{ liters/mol})}$$

**B. Next, let's consider Fick's Law of diffusion:**

$$15. \frac{\Delta Q}{\Delta t} = D * A * \frac{\Delta U}{\Delta X}$$



where  $\frac{\Delta Q}{\Delta t}$  is the diffusion flux in  $\frac{\text{mols}}{\text{time}}$ , (usually given as  $\frac{\text{ml}}{\text{s}}$  @ STPD); **A** is the area through which diffusion is occurring (usually  $\text{cm}^2$ );  $\frac{\Delta U}{\Delta X}$  is the concentration gradient in mols of  $\frac{\text{gas}}{\text{cm}^4}$  (i.e.,  $\frac{\text{mols}}{(\text{cm}^3 * \text{cm})}$ ) and **D** the diffusion coefficient is given as  $\frac{\text{cm}^3 * \text{cm}}{\text{sec.} * \text{cm}^2}$  or  $\frac{\text{cm}^2}{\text{s}}$ .

**Remember:** D is a measure of the velocity at which a gas diffuses.

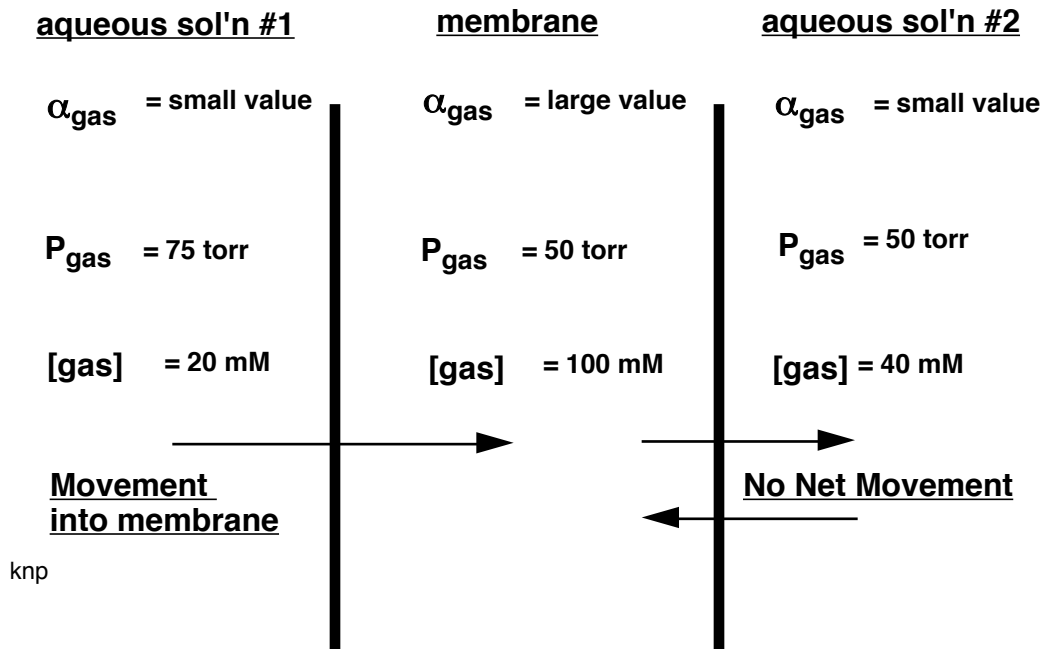
C. Fick's Law as given in eq. 10 is only valid when the gas is moving through a uniform medium such as air or a simple water solution.

1. In biological systems, the tissues that we deal with often have strikingly different properties in terms of how a gas will diffuse. The basis for these different properties is the fact that solubilities in different places in a cell differ. This is due to the many different types of solutions that are encountered in the body. For example between the air in the alveoli of the lungs and the blood, oxygen is dissolved in air, at least two membranes, and several different solutions.

a. We quickly find that **dissolved gases do not always move down concentration gradients as predicted by eq. 10.**

b. For example, a gas may be less concentrated in a the plasma surrounding a cell than in the membrane of the cell. Nevertheless, gas continues to move to the membrane:

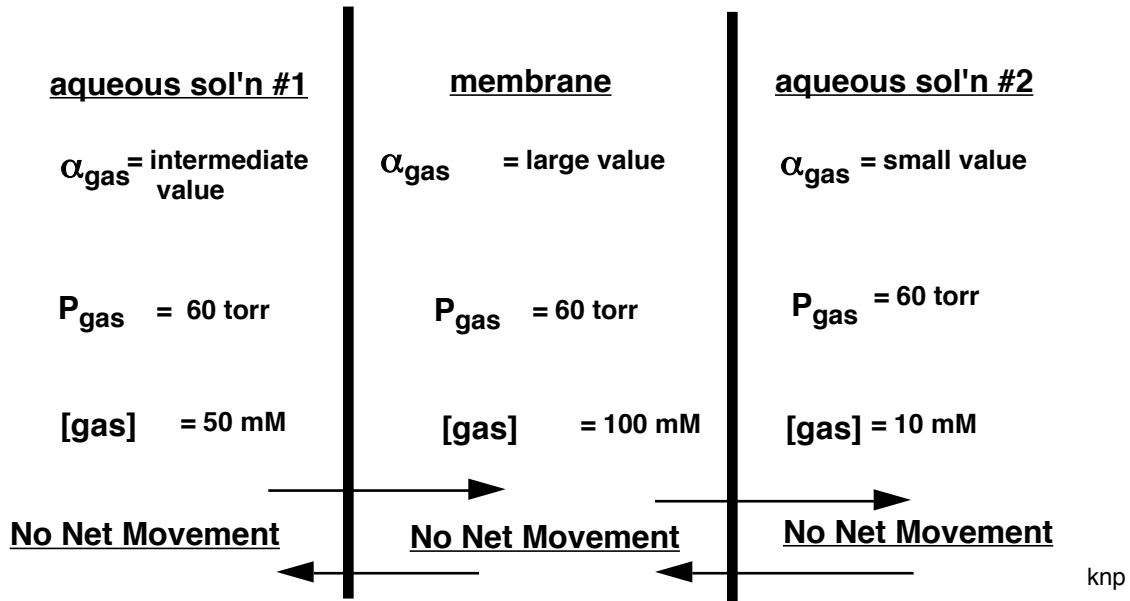
### The Movement of Gas Through a Membrane, 1



c. We already know the explanation for this: the concentration of gases is due to two factors, partial pressure and the solubility coefficient. Based on eqs. 7 and 8 (solubility), we can easily see that different solutions with different solubilities can all be in equilibrium with each other yet they can all have different concentrations of gases dissolved in them. Nevertheless there will

be no net movement since the partial pressure is the same in all of them; they are in partial pressure equilibrium:

### The Movement of Gas Through a Membrane, 2



Thus, we see that partial pressure, not concentration, is the crucial factor in determining the movement of gases. Concentration is a valid measure only when a homogeneous solution (such as diffusion only in air or only in water) is considered.

2. We now need to restate Fick's Law so it will be useful in the complex situations we find in biological systems: **WE MUST TAKE INTO ACCOUNT PARTIAL PRESSURE GRADIENTS AND SOLUBILITY.**

$$16. \frac{\Delta Q}{\Delta t} = K * A * \frac{\Delta P}{\Delta X}$$

where  $\frac{\Delta P}{\Delta X}$  is the PARTIAL PRESSURE GRADIENT and  $K$  is known as KROUGH'S DIFFUSION COEFFICIENT.

a. Thus, if we define a new diffusion coefficient  $K$  that takes solubility into account; it has the units of  $\frac{\text{cm}^3 * \text{cm}}{\text{cm}^2 * \text{torr} * \text{sec}}$  or  $\frac{\text{cm}^2}{\text{torr} * \text{sec}}$ .

b. Notice that this simply is the product of the old value of  $D$  and the solubility coefficient  $\alpha$  for a particular complex system:

$$17. K = D * \alpha$$

-- dimensionally --

$$18. \frac{\text{cm}^2}{\text{torr} * \text{sec}} = \frac{\text{cm}^2/\text{s} * \text{cm}^3}{\text{cm}^3 * \text{torr}}$$

### III. The Movement of Gases and Respiration:

A. General features of the exchange of respiratory gases:

1. All aerobic respiration is ultimately a matter of diffusion of respiratory gases; there is no active transport of either O<sub>2</sub> or CO<sub>2</sub>.

2. Thus, on at least some level, respiration must be described as a diffusive process.

B. Given the ultimate importance of diffusion and the fact that organisms have changing and often large demands for respiratory gas exchange, then we need to look in detail at the rate of diffusion and the factors that influence diffusion rate.

1. Obviously all of the factors of Fick's Law are involved in determining the rate of diffusion. Go over each factor and see how an animal could maximize diffusion rate.

2. At present let's look at the diffusion coefficient -- *K* or *D*.

a. The rate of diffusion of a gas is proportional to the square of the distance over which diffusion occurs:

$$19. \quad \text{time} \propto d^2$$

thus to travel twice as far by simple diffusion, the required time will go up 4 fold.

Here is a table of some values of *D* and a short explanation as to their meaning:

**(i) Using the Diffusion Coefficient, *D***

	air	distilled water	<u>air</u> water
$D_{O_2}$	$1.78 \times 10^{-1}$	$2.5 \times 10^{-5}$	7120
$D_{CO_2}$	$1.39 \times 10^{-1}$	$1.8 \times 10^{-5}$	7722
$D_{O_2} / D_{CO_2}$	1.28	1.4	

**Interpretation:** The diffusion coefficient is a measure of the rate that something diffuses over a unit distance  $\frac{\text{ml}}{\text{s} * \text{length}}$ . Note that for both O<sub>2</sub> and CO<sub>2</sub>, diffusion is more rapid in air than

water (about 7000 - 8000X greater). However, remember that this refers only to a rate of movement (velocity) of gas molecules, not to the actual amount that are moving. Furthermore,

note that O<sub>2</sub> always moves more rapidly (has a greater velocity per particle) than CO<sub>2</sub> (see  $\frac{O_2}{CO_2}$  ratio). This is due to its smaller size and is predicted by Grahams' Law. Also, O<sub>2</sub>, unlike CO<sub>2</sub>, is an ideal gas.

To get a measure that takes into account the total movement of gases, we must take into account the solubility of a gas in a solution. To do this we use Krogh's diffusion coefficient, *K*.

Using *K* values for O<sub>2</sub> and CO<sub>2</sub> (units:  $\frac{\text{ml}}{\text{sec} * \text{torr} * \text{cm}}$  )

air	water	<u>air</u> water
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O <sub>2</sub>	2.19 X 10 <sup>-1</sup>	1.02 X 10 <sup>-6</sup>	215,000
CO <sub>2</sub>	1.71 X 10 <sup>-1</sup>	2.09 X 10 <sup>-5</sup>	8,174
O <sub>2</sub> / CO <sub>2</sub>	1.28	0.049	

**INTERPRETATION:** (1) The difference in this table as compared to that for D (above) is due to the vastly different values of the solubility coefficient for CO<sub>2</sub> and O<sub>2</sub>.

2) Since CO<sub>2</sub> is 28X more soluble in water than is O<sub>2</sub>, the value for *K* will be corresponding larger (i.e., this simply means that since more CO<sub>2</sub> is carried per liter of water, for a given partial pressure gradient, more will diffuse).

3) Likewise, due to the remarkable difference in solubility of O<sub>2</sub> in air vs. water, for a given difference in partial pressure, 200,000 to 300,000X (DEPENDING ON THE TEMPERATURE -- REMEMBER THAT SOLUBILITY IN WATER IS VERY TEMP. DEPENDENT) more O<sub>2</sub> will diffuse per unit time in air. Since the disparity between CO<sub>2</sub> solubility in air and water is not as great, the ratio is smaller.

? What does the above tell you about the ability of an organism to get O<sub>2</sub> via diffusion in air vs. water? To remove CO<sub>2</sub>?