HUMAN RESPIRATORY MECHANICS, part 1:
THE BIOMECHANICS OF THE LUNG[1]

Summary: We begin a detailed study of ventilation in mammals -- this will be pursued over the next three classes. We start in this packet with a review of physical processes that will affect elasticity and then examine the static forces that exist in lungs at different volumes and the causes of these forces.
We then move on to the nature of air-fluid interactions within the alveoli with special reference to alveolar surfactants. Related to this is a discussion of the Law of Laplace and the pre-mature neonatal condition called respiratory distress syndrome. Two parts: examination of the V/P relationships of the lung itself -- what determines its elastic properties. Then we will look at external forces that act on the lung at rest and during ventilation and how these forces stretch or compress the elastic elements of the lung. Finally, in Packet R-5 we will add flow and consider how the muscles, elastic elements and airways interact during ventilation.

I. Introduction

A. The next two classes will examine the elastic properties in the respiratory system. Although you have probably never thought that elasticity had much to do with breathing, it is very important in understanding breathing .

B. In these first two packets we will look at static conditions -- i.e., those without flowing air. Do not be confused by the fact that we will examine the respiratory system at many different volumes -- volume (inflation) has nothing to do with we are dealing with a static condition -- it is simply a condition when there is no air flow. Once we have mastered static conditions, it will be possible to move on to a sophisticated understanding of what happens when air flows -- that is, dynamic conditions.

C. About this and the next packet: In this packet we will examine the factors that cause elasticity within a lung. In the next, we will look at how external forces work on these elastic elements and on others in the body to affect respiration.

☞ Much of the material in the next section should be review and so we will race over it rapidly. The material on elasticity, however, is much more detailed than what we covered before and makes good background.

II. Physical forces important to understanding the operation of the lung

A. **PASSIVE INTERACTIONS BETWEEN MATERIALS THAT RESULT IN ELASTIC FORCES IN TISSUES**

1. **INTRAMOLECULAR ELASTIC PROPERTIES**: when external forces act on any molecule they can cause it to be compressed or expanded. Some of the applied mechanical energy is stored in the chemical and hydrogen bonds of the molecules and will be released if the applied force is removed. This is the molecular basis of elasticity, a property of all molecules.

a. As a result of their structures, molecules differ in how much they will stretch without failing in response to a certain amount of mechanical force.

b. Two common proteins that are important in connective tissue and are relatively elastic but that differ significantly in how "stretchy" they are:

(i) **collagen** -- a relatively stiff compound

(ii) **elastin** -- comparatively speaking, "stretchier"

c. Both of these are common in the inter-cellular spaces of connective tissues; they have very different primary and secondary structures.

2. <u>INTERACTIONS BETWEEN DIFFERENT MOLECULES</u>:

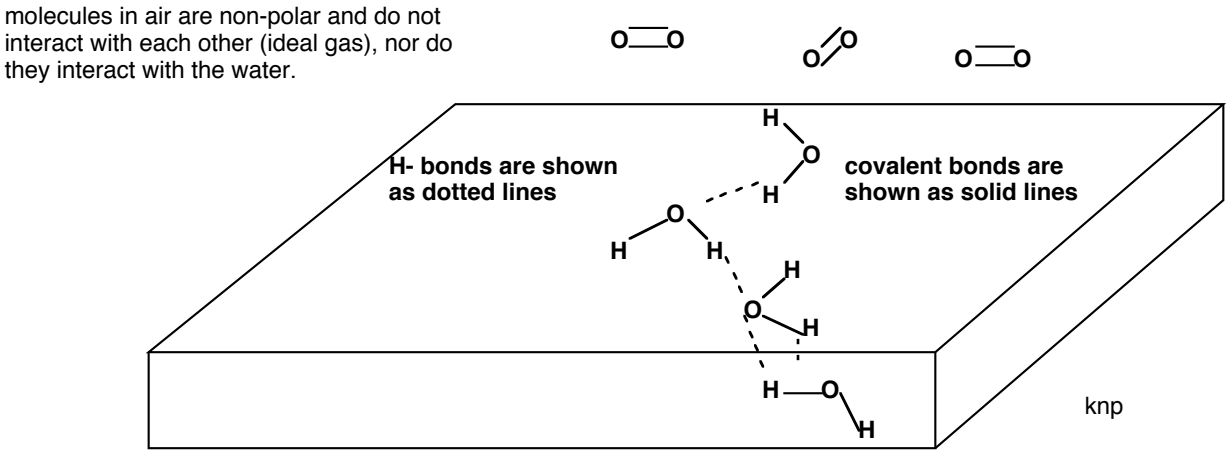
a. **<u>COHESION</u>** -- binding interactions between molecules of the same type, principally as a result of hydrogen bonding. An important consequence of cohesion is surface tension, which is reviewed below.

b. **<u>ADHESION</u>** -- interactions between molecules of different types, again primarily by H-bonding.

c. Both of these forces may be quite large. For example, adhesion between polar constituents of plasma membranes and water result in the lungs being held, by adhesion, to the inner side of the chest wall and the diaphragm. There are no direct tissue connections (in fact, such connections are quite adverse when they form)

3. **<u>SURFACE TENSION</u>**: this is an **<u>interface phenomenon</u>** due to <u>cohesion of liquids</u> (e.g., water solutions -- since we are dealing with organisms) <u>being greater than the adhesion of the liquid to air</u>. As a result there are <u>uneven forces at the air water interface</u> and the water molecules pull more towards each other than to the air. This results in a rather rigid liquid surface due to the fact that surface water molecules are pulled down and sideways (by other liquid molecules) but not upward. Surface tension has units of force/length.

Surface Tension



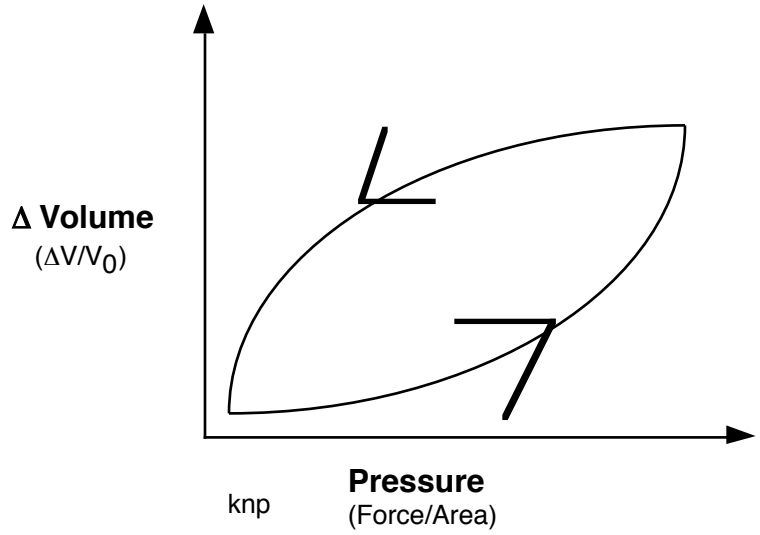
Molecules of water under the surface interact with each other and with the molecules on the surface. Since this interaction is not balanced by an opposite pull from the air above the water's surface, there is a tendency to pull the surface molecules downward . Since they also interact with other molecules on the surface plane, there exists a certain tensile strength at the boundary, the **SURFACE TENSION.**

Note that surface tension for pure water is independent of the surface area. In other words, spreading a given volume of water thinner will not increase the surface tension since it is given as a normalized force. We will consider this in more detail later in this set of notes when we see that the addition of certain substances to water can cause surface tension to vary with area!

4. **COMPLIANCE AND ELASTANCE**: All of the factors just considered (intra- and inter-molecular) work together to determine the elastic properties of tissues and organs. We have already considered these two opposite sides of the same coin when we discussed muscles. However, please go to the **Appendix** at the end of this packet to see a **review of compliance and elastance** and be sure that you understand each. For the moment, the main new conventions that you need to be aware of are:

(a) when working with the respiratory system, we will be dealing primarily with compliance curves

(b) we will be using volumes instead of length and so data will normally be plotted as in the figure below:



Note how this differs from the plots for muscle (see examples in the next section of these packets and in the muscle packets).

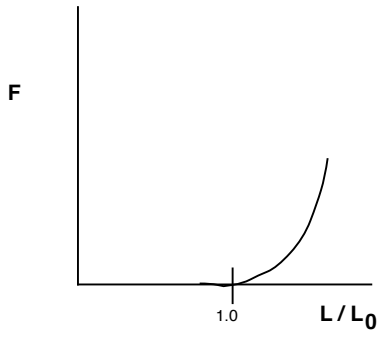
(c) Also note from the graph above that we will usually see a considerable difference between the volume-pressure curve of a tissue that is being expanded (i.e., during inspiration) as compared to one that is decreasing in size after having been expanded (i.e., expiration). This difference is called **hysteresis** and represents an energy loss within the material caused when molecules re-arrange themselves to some degree. We will see that in the respiratory system, this loss normally takes place primarily as a result of what happens at the air water interface.

B**. ACTIVE MUSCULAR FORCES: HOW DO MATERIALS IMPORTANT IN RESPIRATION ACT WHEN MUSCULAR FORCES ARE INVOLVED**?

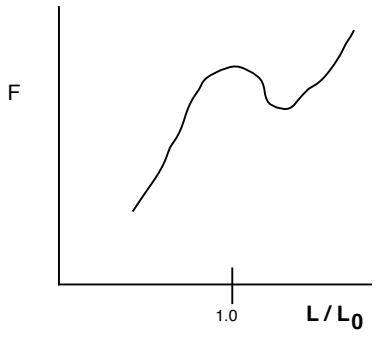
1. Respiration will obviously involve the action of both the passive elements mentioned above and also active element -- that is muscles.

a. When they are not contracting, muscles act as passive elements. As we have seen earlier, their force vs. length diagrams are similar to most other elastic substances in the thorax including the LUNGS and BONE.

b. However, when they are contracting (actually when they are developing internal tension instead of passively responding to external tension), their force is related to the length at which they are working. Recall that:



Relaxed Muscle Length Determines Tension



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Active muscle -- length helps to determine tension along with the degree of the active state.

☞ In the next section we will consider the **entire thoracic region** (including **both** the **active (contracting muscular) and passive elements (including elastic, adhesive, cohesive, and surface phenomenon elements**) in order eventually to understand how we breathe.

III. BASIC FUNCTIONAL ANATOMY:

A. **PASSIVE ELEMENTS**:

1. Primary Materials that determine the elastic nature of the passive elements:

a. **ELASTIN** can be stretched to about 2X its resting length; i.e., it has high compliance.

b. **COLLAGEN** resists any stretching, however, it is normally built into the lungs such that it is only straightened out at maximal lengths. Collagen has high elastance.

Both of these materials are found to some extent in both soft tissues and bones.

2. **PASSIVE ELEMENTS IN THE LUNGS:** The lungs can be considered anatomically to consist of the following components, each with a certain elastic nature:

a. **WITHIN THE EXCHANGE AREAS**: These are the **alveoli and terminal bronchi**. Together they are often referred to as the **ALVEOLAR SPACE** -- essentially all blood-gas exchange occurs in these. There are large amounts of connective tissue in the alveolar walls, the blood vessels and the matrix of material that connect the outer surfaces of the alveoli within the lungs. The tissues in these areas tend to be very thin and therefore highly compliant. However, their compliance will be greatly modified by surface tension, as we will see.

b. **CONDUCTING SYSTEM**, also referred to as the **DEAD SPACE**, this is the part of the lungs that is concerned with the conduction of respiratory gas from the lung to the outside. These include the many generations of different sized **BRONCHIOLES**. No appreciable gas exchange occurs here. These have a proportionally much greater amount of collagen than does the alveolar space and they are therefore much stiffer. In addition, the larger elements of the conducing system (such as the primary bronchi) have cartilage (made up of very stiff materials such as collagen) that add further stiffness).

3. **PASSIVE ELEMENTS OF THE THORAX**: Includes **bones** (mainly ribs), **connective tissue** and **relaxed muscles**. Think about the relative compliances in each of these.

B. **ACTIVE ELEMENTS IN THE RESPIRATORY SYSTEM**

1. **Materials**

a. **Smooth muscle:** used to control the size of airways and blood vessels (**autonomically controlled**)

b. **Striated muscle**: makes up the **diaphragm**, when it is present, the abdominal wall muscles used in forced expiration and also the two groups of muscles in the thoracic cage.

2. **Lungs**: *in amphibians and reptiles, the lungs have muscle* invested in them, in mammals the only substantial muscle is smooth muscle that controls airway diameter.

3. **Thorax:**

a. **External Intercostals**: elevate the rib cage and thus increase the chest volume

b. **Internal Intercostals**: depress the ribs and thereby decrease the size of the thorax.

c. **Diaphragm** it is the major inspiratory muscle in mammals.

d. **Abdominal Wall Muscles**: we're getting ahead of ourselves, but let it suffice that when these contract vigorously, they push against the viscera, propel it upward against the diaphragm and thereby help in forced expirations.

IV. RESPIRATORY STATICS:

A. Main Questions: We want to learn about

1. the physical properties of the lung and

2. **how these properties define the equilibrium states of chest expansion** that we see. That is:

(a) how do the elastic properties determine the exact volume to which the chest is filled when no muscular work is being done? This amount of air is called the **functional reserve capacity** (FRC) and it is what may seem to you to be a surprisingly large amount of air (3 or so liters)

(b) how do these elastic forces influence the process and work of breathing. Is breathing energetically expensive? Why or why not?

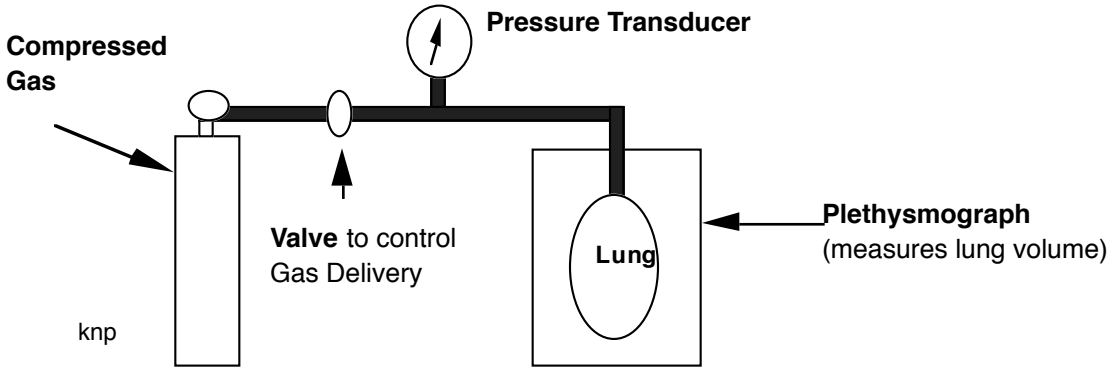
(c) Finally, we will look at some applied aspects and see how some of these factors change as a result of disease or injuries.

B. **DEFINITION OF RESPIRATORY STATICS**: the study of the respiratory system in situations where there is no convective flow of gas.

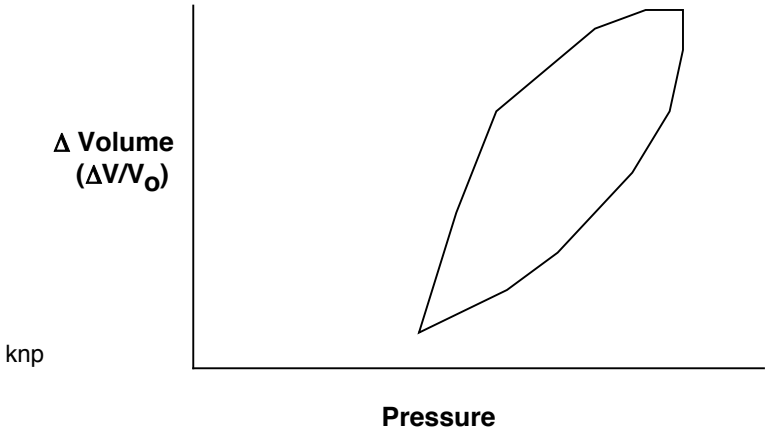
C. **PROPERTIES OF THE ISOLATED LUNG**: We'll start with the gross, but very illuminating study of isolated lungs, that have been freshly "donated" by some animal.

These experiments all involve the addition of enough air to expand the lungs to some new volume. When the expansion has stopped, the pressure of the air inside of the lung is measured (next page):

A Device to Measure Compliance (Pressure-Volume) Curves



1. THE COMPLIANCE OF THE ISOLATED LUNG: If we use a device containing the elements found in the diagram above, we can generate a volume pressure curve for an isolated lung:



(**Note that compliance is not a constant for the lung.**)

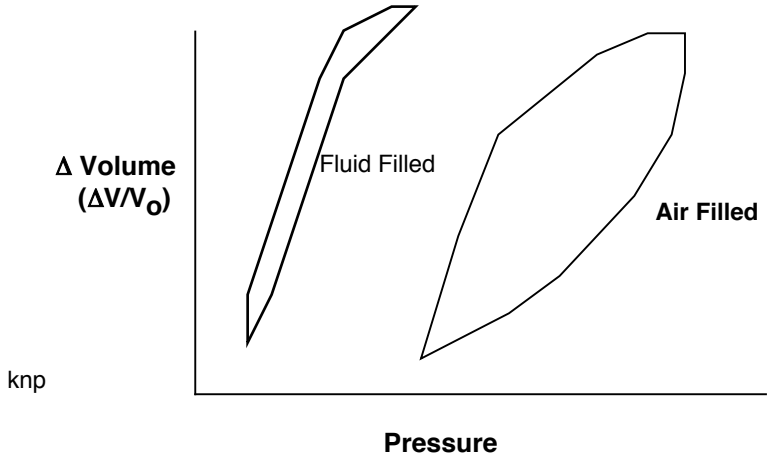
2. There are a **large number of air-water interfaces in the lung**. In every single alveolus there is such an interface.

a. Therefore we would expect a lot of surface tension in the lung.

b. In order **to learn about the elastic properties of the lung tissue itself, it is necessary to remove the influences caused by surface tension at the air-fluid interface in the alveoli**.

c. We can remove surface tension by filling the lung with saline and then measuring the compliance. In this case, the experiment consists of filling the lung with enough saline to achieve a certain volume and then measure the pressure on the water in the lung. The resulting plot shows the compliance due to tissue elastance only; it is on the left:

COMPLIANCE IN AIR AND SALINE-FILLED LUNGS:



3. Explanation and observations of the saline curve vs. the intact lung:

a. The **presence of air - water interfaces reduce compliance (increases elastance)** -- more pressure is required to expand the lung a given amount when air is present. Put another way, **the tissue in the lungs is normally not the major component of the lung stiffness.**

b. **Hysteresis is reduced in saline-filled lungs**. This implies that **the main thing that is undergoing volume dependent re-arrangements has been removed**.

Be sure you understand this experiment and what it says about the determinant of lung compliance.

4. **A description of the causes of the elastic properties of the lung tissue**:

a. Before we start looking at the surface tension component, we need to understand what causes the elasticity of the lung tissue, even though we have seen that in a normal lung this is a minor effect.

b. Since it is mostly connective tissue, the elastic nature of the lung tissue is determined by the presence of

(i) elastin (very distensible, can double in length) and
(ii) collagen (stiff, resists distension).

(see graph of relative stiffness of these two in the appendix to these notes)

5. At **low lung volumes**, **both of these fibers are somewhat unfolded and not near their maximal stretch,** this explains why the lungs are so compliant at low lung volumes. However, as the lungs are expanded, more and more of the fibers are stretched beyond their resting lengths and they contribute more and more to making the lung more elastant:

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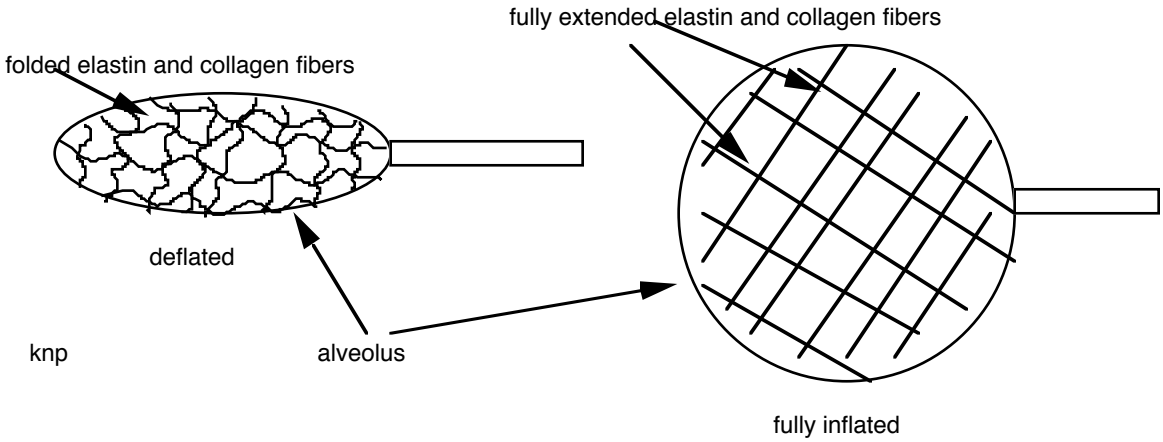
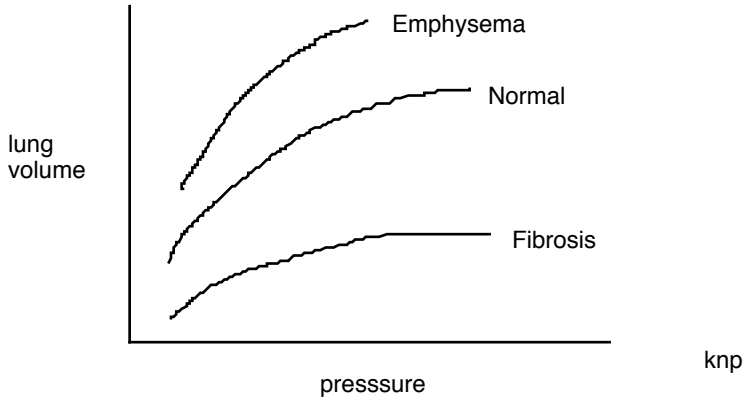


6. Changes in the amount of collagen and elastin occur in disease states, these change the elastic properties of the lungs:

Pressure-Volume Relations for Lungswith Different Compliances



? Does compliance increase or decrease with emphysema? Fibrosis?
? What are common causes of these two general types of lung disease?
? What sorts of changes (on a tissue level) could account for these changes?

D. SURFACE TENSION AND THE LUNG

1. We have just seen that the compliance of a saline-filled lung is greater than an air-filled lung.

a. The volume-pressure (compliance) curve of the isolated saline-filled lung was both steeper and shifted to the left of that of an isolated lung that was expanded with air at different pressures.

b. Since filling the lung with saline removed the air-water interfaces, i.e., any surface tension effects, the saline-filled lung prep gives us the compliance of the lung tissue only.

c. We will now explore the surface tension-related phenomena of the lung. Obviously, these are relatively large important since the saline curve is very different than the air-filled lung curve.

2. SURFACE PHENOMENA

a. The differences between the saline and air-filled lungs are due to the presence of an air-water interface on the surface of the alveoli. At this interface, a surface tension exists.

b. If we wash out a fresh lung and save these lung washings, we can investigate the surface tension properties of this solution.

c. To look at surface tension, we place the "lung washings" in a square-shaped trough with a dam that can be moved laterally to increase or decrease the surface area of the lung washings.

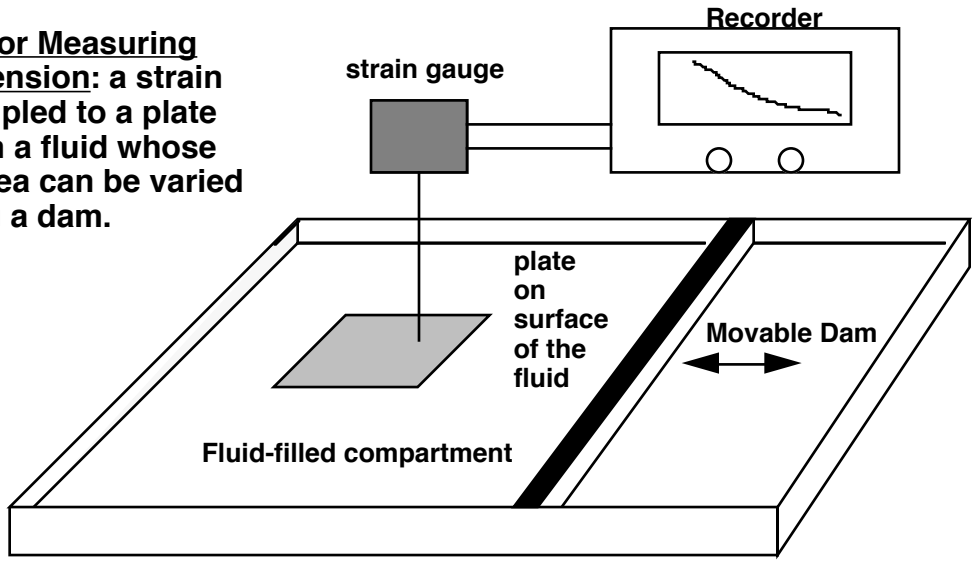
i. Thus, the apparatus holds a constant volume of lung washings.

ii. As the surface area is increased, the depth of the solution decreases. (Recall that the depth is irrelevant to surface tension; depth matters here only in that volume is the source for more liquid as the liquid is spread over larger areas.)

iii. A plate that is attached to a strain gauge is placed on the surface of the washings and is used to record the surface tension.

Here is what the apparatus looks like:

A Device for Measuring Surface Tension: a strain gauge coupled to a plate floating on a fluid whose surface area can be varied by moving a dam.



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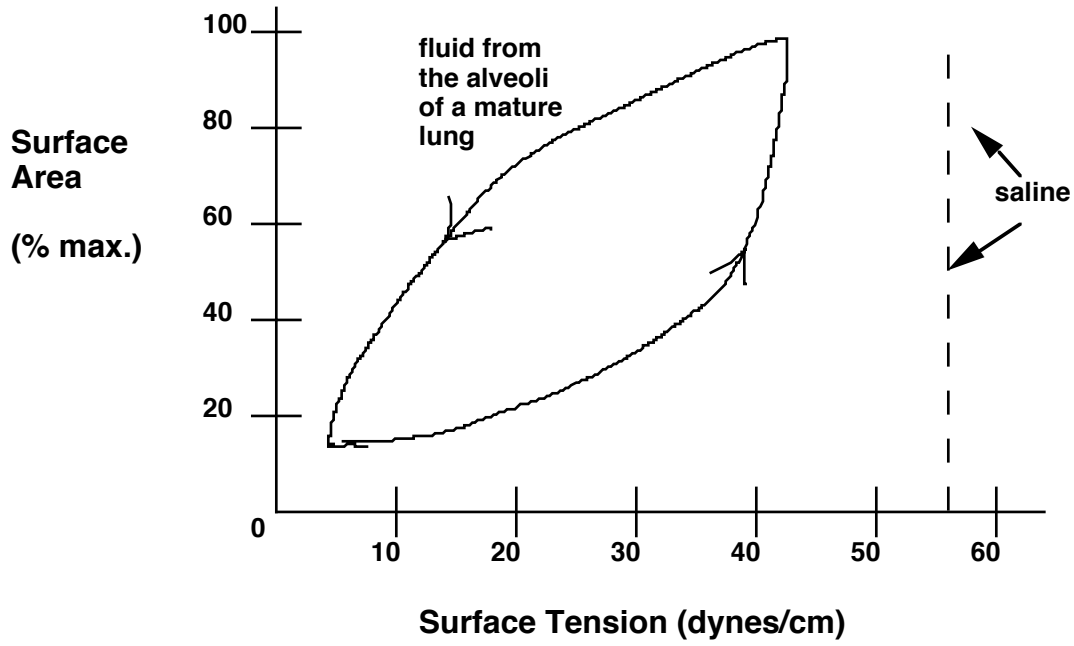
d. Experimental Results:



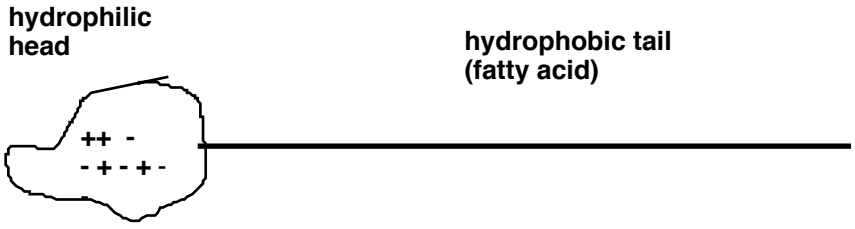
c. **Summary of the most significant results when lung washing surface tension is compared to that of isotonic saline**:

i. The **washed-out lung fluid has a surface tension that is always lower than that of saline**.

ii. The **surface tension of the lung washings are area-dependent**; by contrast for **saline where they are area-independent**.

iii These phenomena are due to the presence of **LECITHIN-RELATED SURFACTANT** molecules

(a) These **surfactants have hydrophobic and hydrophilic regions:**



(b) They **lower ST by decreasing the number of water-water interactions:**

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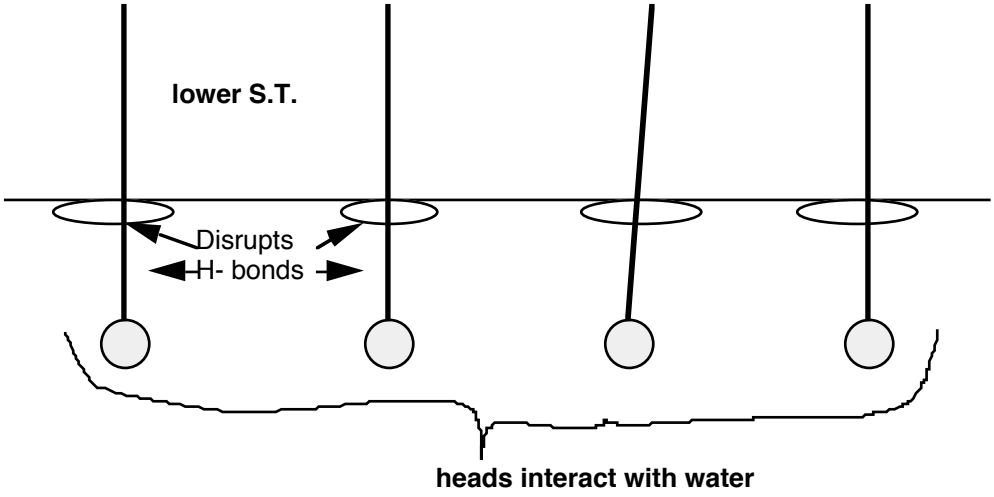

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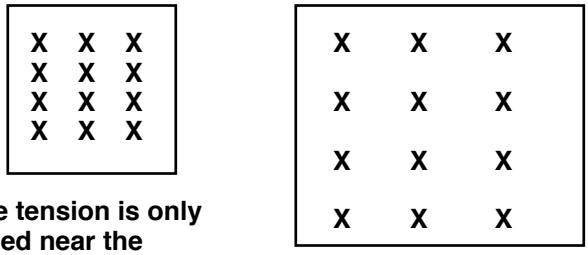
(c) **Since there are only a limited number of them, their effect will be greatest at low SA (low lung volume) and will diminish as SA increases**.

Low Lung S.A. **High Lung S.A**.



Surface tension is only disrupted near the surfactant moleculeS.

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(d)The hysteresis is due to the fact that at low SAs some of the surfactant is pushed below the surface of the water and does not contribute to decreasing the surface tension when the lung is being expanded. Thus, for a given lung volume (and therefore a given alveolar surface area), a greater amount of pressure (surface tension) exists during inspiration than expiration. During expiration (alveolar surface area and lung volume both decreasing), all of the surfactant is on the surface and the total surface tension is lower than during inspiration.

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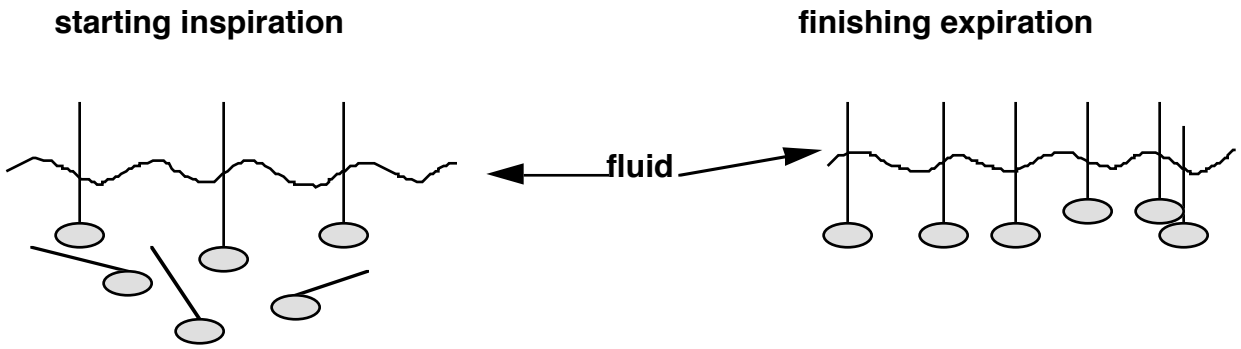

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e. **EFFECTS OF SURFACTANT ON BREATHING**:

(i) **Surfactants reduce the work associated with breathing**. The work of expanding a volume can such as the lung or an alveolus can be calculated with the following integral:

1. $$W = \int_{v_1}^{v_2} P dV$$

For any lung volume the pressure is lower in a lung with surfactant than in a lung without surfactant (i.e., a lung with saline lined air interface). Thus, the work required, for example, to increase lung volume will be less when surfactant is present.

(ii) **The work required to open any nearly collapsed alveoli is decreased when surfactant is present**. Without surfactant, the work is large since the surface tension is high and according to the Law of Laplace (see next item below) the pressure needed to open a small radius alveolus with a given (high) surface tension is large. However, **with surfactant, the surface tension in small alveoli is reduced to a minimum and therefore the work needed to open small radius alveoli is much less than in would be in their absence**.

(iii) **Surfactants stabilize the alveolar size**:

(a) This is a consequence of the **LAW OF LAPLACE**. The Law of Laplace deals with "bubbles" such as alveoli. In such a bubble, there is a single air/water interface (on the inside of the alveolus). The Law of Laplace states that where there is a single interface between a lumen and wall:

2. $$P = \frac{2T}{r}$$

where ***P*** represents the pressure within that "bubble" (i.e., alveolus), ***T*** the tension, and ***r*** the radius of the bubble (alveolus).

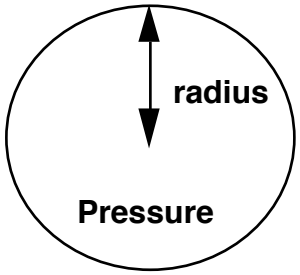
Notice that this is a different formulation of the Law of Laplace then the one we saw with capillaries. The reason has to do with the fact that we treat an alveolus like it has two surfaces (like a soap bubble) and therefore the surface phenomena are twice as great.

For our purposes:

(i) ***T*** refers to the **tension in the alveolus** and we will **assume for these calculations that it is entirely due to the surface tension of whatever fluid lines the alveolus**

(ii) ***r*** is the **radius of the alveolus** and

(iii) ***P*** is the **pressure of the air inside the alveolus**.



tension (at interface)

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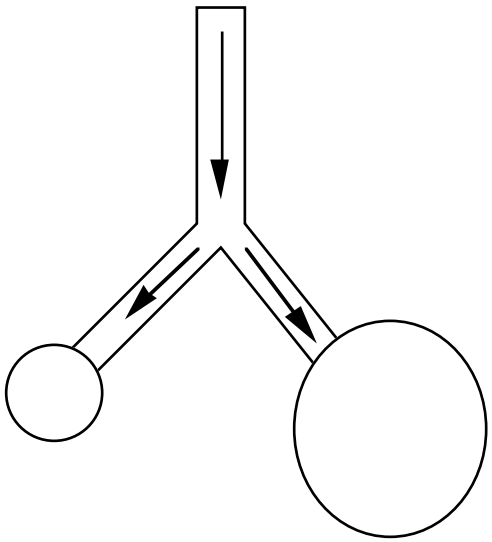
(b) **Condition #1 -- NO SURFACTANT**: Assume we have **two alveoli connected to a common bronchus**.

(i) **When the fill with air, they fill to different radii**. (this is quite likely).

(ii) Since **they are lined with a saline solution they have equal tensions in their walls** (since the surface tension of a saline solution is independent of area).

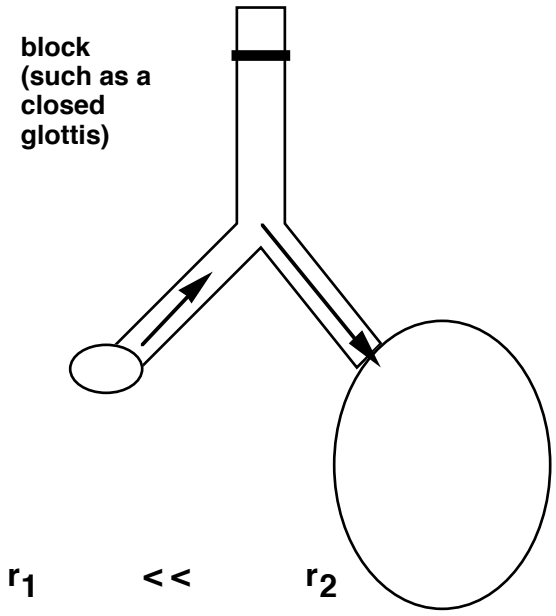
(iii) Then, according to the Law of Laplace, **the small alveolus will empty into the larger on due to its larger internal pressure:**



$r_1 < r_2$

$P_1 = P_2$

A non-steady state exists here due to the action of the respiratory muscles.



$r_1 << r_2$

$P_1 > P_2$

No airflow to the outside; as a result the small alveoli empty into the large according to the law of Laplace.

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(iv) The result of this is a **decrease** of **TOTAL LUNG SA** (the area of the individual large alveoli increases but there are few of these big alveoli) and an **INCREASE OF AVERAGE DIFFUSION DISTANCE**. **According to Fick's law, less diffusion will occur.**

c. **Condition #2: SURFACTANT IS PRESENT**

(i) **Surface tension is now dependent on surface area**.

(ii) **The larger the surface area, the higher the surface tension and vice versa.** (See graph of the effects of surfactant on surface tension).

(iii) The result is the **pressure is roughly the same in large and small alveoli**. **The small alveoli no longer empty into the large ones.**

(iv) With surfactant, **THE ALVEOLI ARE SAID TO BE STABILIZED WITH RESPECT TO SIZE** (however, remember this is not an absolutely perfect system -- some flow does go on between different sized alveoli).

IMPORTANT NOTE: While I have said that alveolar compliances are due mainly to the surface tension of the saline-air interface, remember that there is also a component due to the elastic forces of the material that makeup the alveoli.

Questions:

? What experimental basis can you cite for the supposition that the total alveolar tension is mostly determined by the surface tension?

? If the alveolar wall tension was the main determining factor of alveolar tension, then, is it likely that two alveoli with different sized radii would have the same tensions? Explain using the compliance curve for lung tissue

? What is the consequence of different connective tissue diseases (discussed last class) on alveolar stability?

f. **PATHOLOGICAL STATES ASSOCIATED WITH LOW-LEVELS OF SURFACTANT: RESPIRATORY DISTRESS SYNDROME (RDS)**

1. When a child is born prematurely but with a chance to survive (such as between the 28th and 32nd week of pregnancy) the lungs do not yet contain surfactants. The host of problems mentioned above will be visited on the child.

2. The disease can be detected during birth and its likely severity assessed by determining the **SPHINGOMYELIN TO LECITHIN RATIO OF THE AMNIOTIC FLUID: if greater than 2 to 1, RDS is likely.** Notice that sphingomyelin is always present in the amniotic fluid in certain amounts since it is a common constituent of plasma membranes; the high concentrations of lecithin compounds, on the other hand, are associated with the secretion of surfactants.

SUMMARY OF THE COMPLIANT PROPERTIES OF THE LUNGS:

The compliance of the lungs is due to both surface phenomena (surface tension) and also the elastic properties of the lung itself. In normal lungs, most of the stiffness is due to surface tension at the alveolar lining with air, although this surface tension is greatly reduced and becomes surface area dependent due to the action of alveolar surfactants. Some diseases result in change in tissue compliance that may affect the stiffness of lungs.