Chapter 1 – Dissolved Oxygen in the Blood

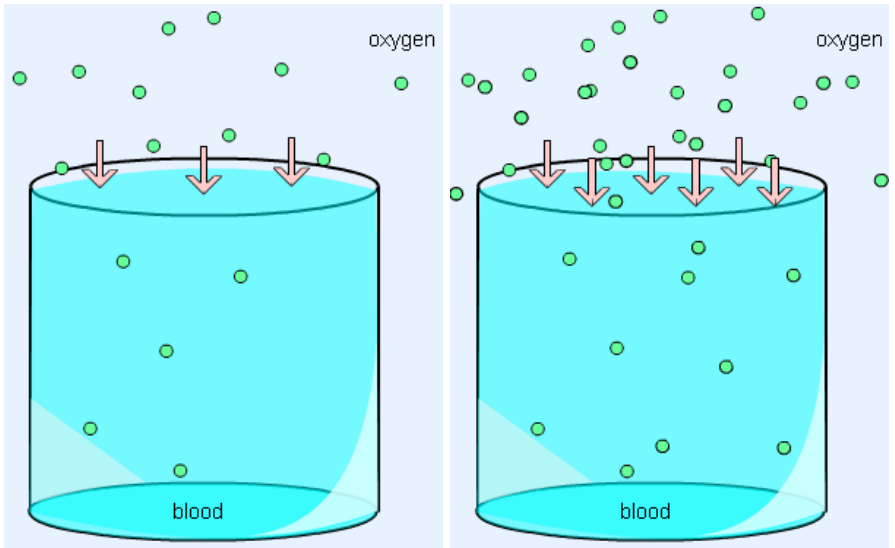
Say we have a volume of blood, which we'll represent as a beaker of fluid. Now let's include oxygen in the gas above the blood (represented by the green circles).

The oxygen exerts a certain amount of partial pressure, which is a measure of the concentration of oxygen in the gas (represented by the pink arrows).

This pressure causes some of the oxygen to become dissolved in the blood.

If we raise the concentration of oxygen in the gas, it will have a higher partial pressure, and consequently more oxygen will become dissolved in the blood.

Keep in mind that what we are describing is a dynamic process, with oxygen coming in and out of the blood all the time, in order to maintain a certain concentration of dissolved oxygen. This is known as *dynamic equilibrium*.



a) low partial pressure of oxygen b) high partial pressure of oxygen

As you might expect, lowering the oxygen concentration in the gas would lower its partial pressure and a new equilibrium would be established with a lower dissolved oxygen concentration.

In fact, the concentration of DISSOLVED oxygen in the blood (the C_{dO2}) is directly proportional to the partial pressure of oxygen (the P_{O2}) in the gas.

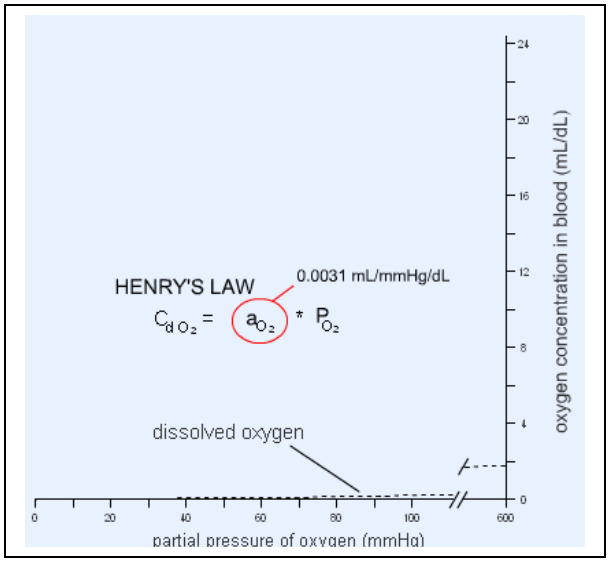
This is known as Henry's Law. In this equation, the constant of proportionality is called the solubility coefficient of oxygen in blood (a_{O2}). It is equal to 0.0031 mL / mmHg of oxygen / dL of blood. With these units, the dissolved oxygen concentration must be measured in mL / dL of blood, and the partial pressure of oxygen must be measured in mmHg.

Henry's Law

$$C_{dO2} = a_{O2} \times P_{O2}$$

(a_{O2} = 0.0031 mL O_2/ mmHg O_2 / dL blood)

In its entirety then, Henry's Law states that a gas dissolves in a liquid in direct proportion to its partial pressure and solubility.



Notice that this describes a linear graph. So, if we plot partial pressure of oxygen on the x-axis, ranging from 0 to 600 mmHg; and we plot oxygen concentration in the blood on the y-axis in mL of oxygen per deciliter of blood, we will have a straight line graph with a slope equal to the solubility coefficient of oxygen in blood.

Recall that this coefficient is 0.0031 mL / mmHg of oxygen / dL of blood - a rather small number.

Let's do an example.

What would the concentration of dissolved oxygen be when the partial pressure of oxygen in the gas is 100 mmHg, which is a normal alveolar value?

Our equation ($C_{dO2} = a_{O2} \times P_{O2}$) tells us that the dissolved concentration, C_{dO2}, equals:

0.0031 mL/mmHg/dL x 100 mmHg or about 0.3 mL of oxygen per dL of blood.

Given that a normal individual has about 5 L of blood, we can quickly calculate that a normal individual would have only about 15 mL of oxygen DISSOLVED in their blood at any given time.

0.3 mL O_2 / dL blood	x	5 L blood	x	10 dL blood / L blood	=	15 mL O_2
(oxygen conc. dissolved)		(total blood)		(conversion from dL^{-1} to L^{-1})		

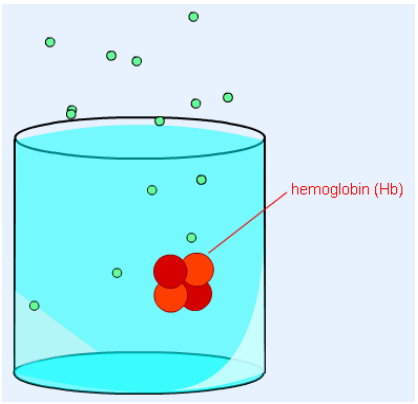
Since humans consume around 250 mL of oxygen per minute, we find that survival based on dissolved oxygen alone would not be possible.[1] So we need some way to increase the oxygen levels in our blood.

Hemoglobin is important because it does exactly this, and that's what we'll explore next.

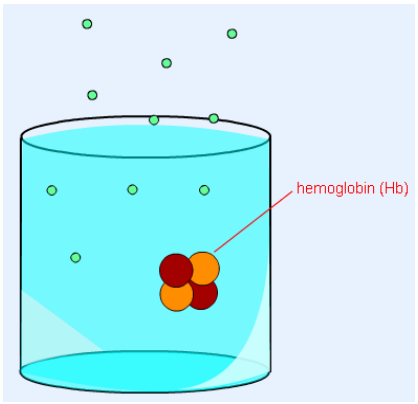
[1] Note that our calculation did not actually tell us this directly, as it does not say anything about actual oxygen delivery which is also dependent on total blood flow in addition to the concentration. That calculation, however, is beyond the scope of this module. Even without it though, it is fairly intuitive given a human's demand for oxygen that this concentration of oxygen would not be sufficient to sustain a human.

Chapter 2 – Bound Oxygen in the Blood

Without oxygen, hemoglobin is found in the tense state. It's called "tense," because subtle changes in its conformation give it slightly less affinity for oxygen. Its tense structure does not allow it to bind oxygen as well as it could if it were relaxed.



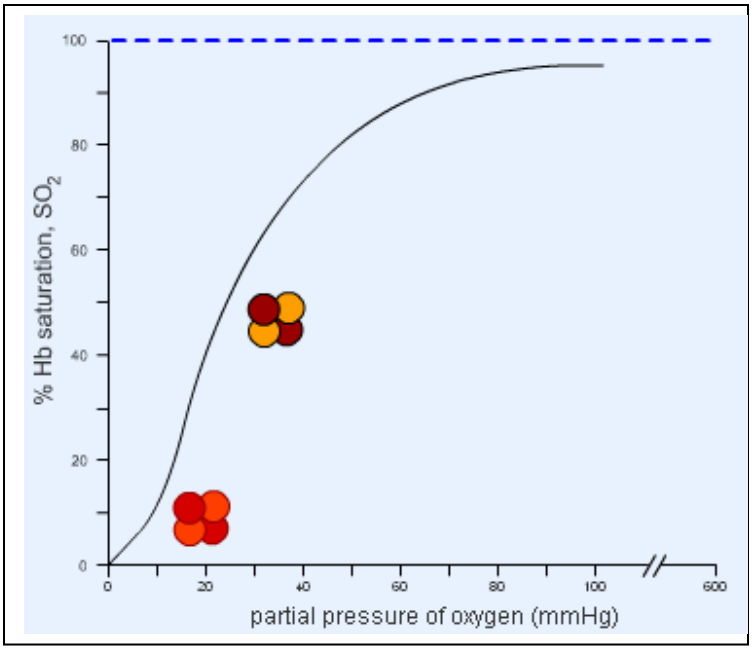
a) Tense hemoglobin doesn't bind oxygen avidly.



b) Hemoglobin becomes relaxed after binding some oxygen. Relaxed hemoglobin can better bind more oxygen.

With enough oxygen present, however, a little will bind to it, and a conformational change will ensue that increases hemoglobin's affinity to bind to more oxygen – hemoglobin begins to assume its relaxed state. In other words, binding to some oxygen makes it easier for hemoglobin to bind to more oxygen.

Let's take a look at what's happening graphically. On the x-axis we have the partial pressure of oxygen again, in mmHg.



On the y-axis now we have the percent saturation of Hb, the S_{O2}, which is defined as the amount of oxygen bound to hemoglobin divided by the oxygen carrying capacity of hemoglobin. More simply, you can think of this as hemoglobin with oxygen over total hemoglobin.

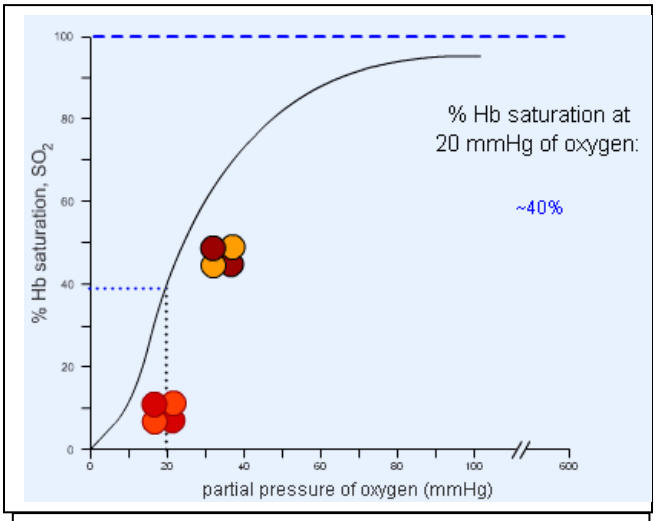
$$S_{O2} = \frac{O_2 \text{ bound to Hb}}{\text{Hb's } O_2 \text{ carrying capacity}}$$

More simply…

$$S_{O2} = \frac{\text{Hb w/ } O_2}{\text{total Hb}}$$

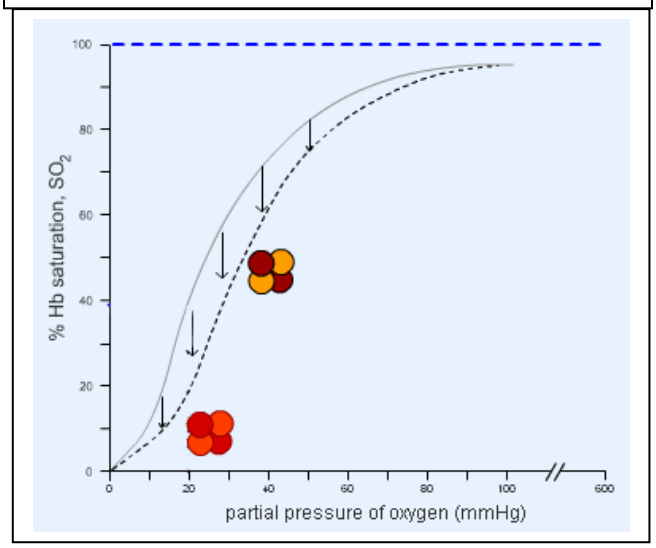
As we were saying, at low oxygen levels, hemoglobin is mostly in the tense state, and binding is limited, which explains the small slope of our curve at low oxygen levels. As oxygen levels increase, more oxygen is bound to hemoglobin, which allows it to assume the relaxed state, which will bind oxygen much more readily. This phenomenon, known as *cooperativity*, is the reason for the increased slope of the curve here. Eventually, the curve levels out as hemoglobin reaches saturation where 100% of the available sites are bound to oxygen.

We can now use this graph to find the hemoglobin saturation at different P_{O2} levels. For instance, when the partial pressure of oxygen is 20 mmHg, we find that the hemoglobin saturation for the individual represented by this curve is about 40 percent.



A few moments ago, we generated the hemoglobin saturation curve intuitively through our understanding of how hemoglobin goes from the tense state to the relaxed state which allows it to more readily bind oxygen.

Consider the case where we stabilize the tense state. With the tense state stabilized, it will take a higher oxygen level for hemoglobin to transition to the relaxed state, so the transition from tense to relaxed states will be right-shifted on this graph.

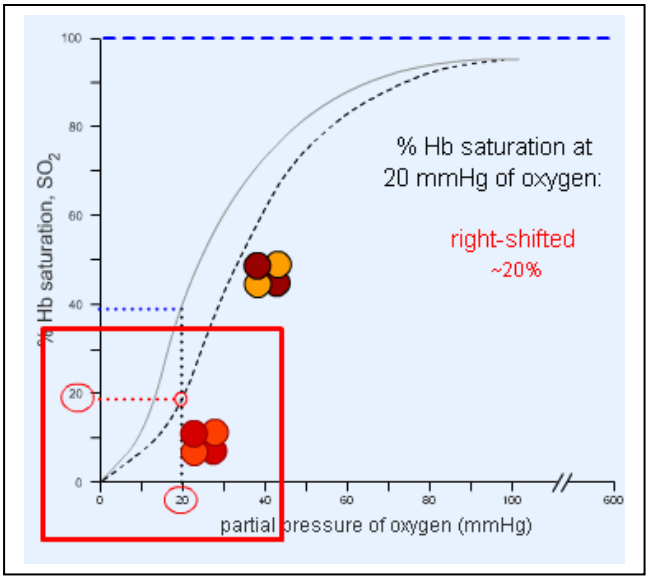


Recall that the tense state is less willing to bind to oxygen, so at any partial pressure along our curve, we will have a lower percent saturation.

Eventually though, it will level off like our first curve, as hemoglobin approaches 100% saturation.

So anything that stabilizes the tense state will right-shift the hemoglobin saturation curve.

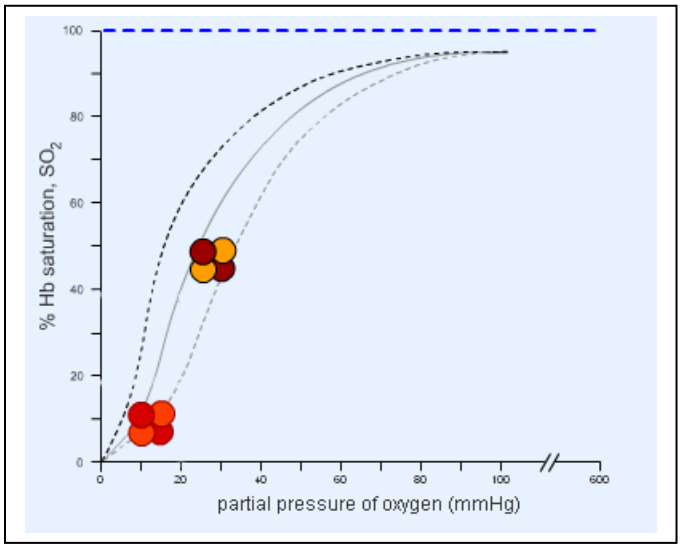
Let's use this new curve to determine what the hemoglobin saturation at 20 mmHg is.



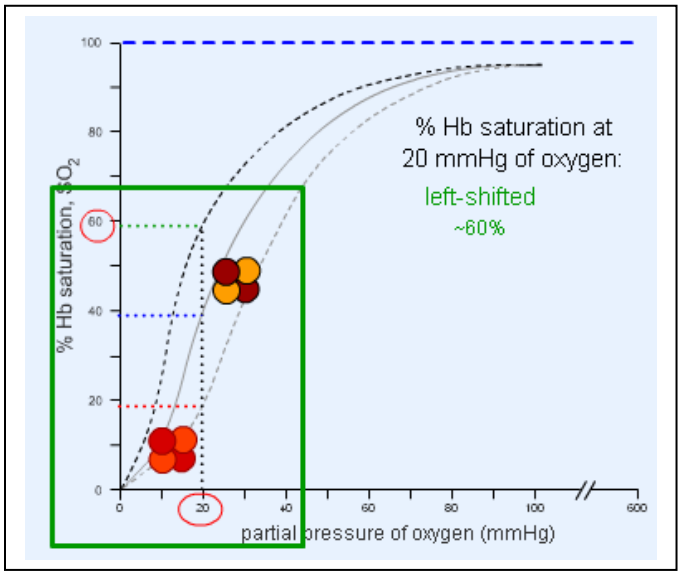
We find that it is about 20%. This double checks our intuition that stabilizing the tense state allows for less oxygen binding at any given partial pressure of oxygen.

If we destabilize the tense state, it will transition to the relaxed state more readily - at lower P_{O2} values.

Recall that the relaxed state is better able to bind oxygen, so for this "left-shifted" graph that hemoglobin will be more saturated at any given P_{O2} level.



Using this curve to determine the hemoglobin saturation at 20 mmHg, we find that it is about 60%, which follows from how we set up this graph. Hemoglobin is easier to saturate when the tense state is destabilized, as it more readily adopts the oxygen-loving relaxed state.



Where would a left-shifted Hb saturation curve provide a functional advantage: in the tissues or in the lungs?[2] Where would a right-shifted Hb saturation curve provide a functional advantage: in the tissues or in the lungs?[3]

[2] In the lungs – Recall that left-shifting allows hemoglobin to become more saturated, allowing it to carry more oxygen with it from the lungs.

[3] In the tissues – Recall that right-shifting decreases hemoglobin saturation. This means more oxygen is released than with an unshifted curve – which is preferable in the tissues, not in the lungs.

As you saw in the questions, a right-shifted curve is more desirable in the tissues. We have also seen that right-shifting is accomplished by stabilizing the tense state. It is no surprise then that the tense state has evolved to become stable in response to an environment more like that in the tissues.

Decreased pH, increased CO_2 levels and increased temperature all stabilize the tense state, causing the release of more oxygen than would otherwise occur.

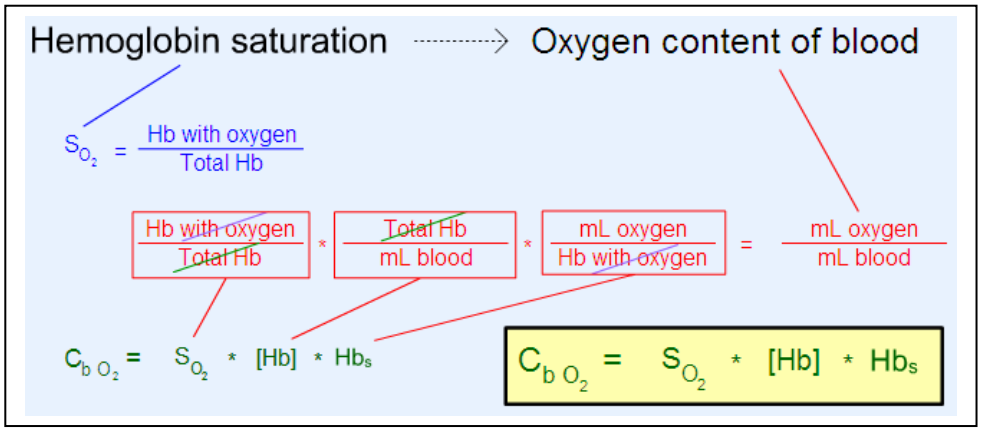
Think of an exercising muscle that needs oxygen to remember this. It has a more acidic environment, it is releasing lots of CO_2 due to its high metabolism and its temperature is increased.

The questions also revealed that a left-shifted curve is more desirable in the lungs. The factors that destabilize the tense state to accomplish this are just the opposite as those which stabilized the tense state - increased pH, decreased CO_2 levels, and a decrease in temperature. All of these are more present in the environment we have in the lungs.

Until now, we have discussed how the partial pressure of oxygen relates to the hemoglobin saturation. But what we really care about is how much oxygen we're getting to the tissues, not how saturated hemoglobin is. We want to know about the oxygen content – the concentration – of the blood due to hemoglobin binding. So how do we go from hemoglobin saturation to oxygen content?

One way to approach this question is to break saturation down to its components.

As we noted earlier hemoglobin saturation is essentially hemoglobin with oxygen over total hemoglobin. So let's take this and multiply by total hemoglobin over the total volume of blood and then by the volume of oxygen over oxygen-carrying hemoglobin ("oxyhemoglobin"). Our result is a term that expresses the volume of oxygen per unit volume of blood, which is exactly what we wanted to find. This is the concentration of oxygen in the blood.



Now let's write this as an equation. The concentration of oxygen bound to hemoglobin in the blood (the C_{bO2}) equals the hemoglobin saturation multiplied by the total hemoglobin over the total volume of blood (which is by definition the hemoglobin concentration in the blood) ... multiplied by the amount of oxygen per oxyyhemoglobin, Hb_s, which is called the saturated oxyhemoglobin content - this is simply how much oxygen a gram of saturated oxyhemoglobin will carry.

This completes our equation and we can now calculate the bound oxygen content of blood given these terms.

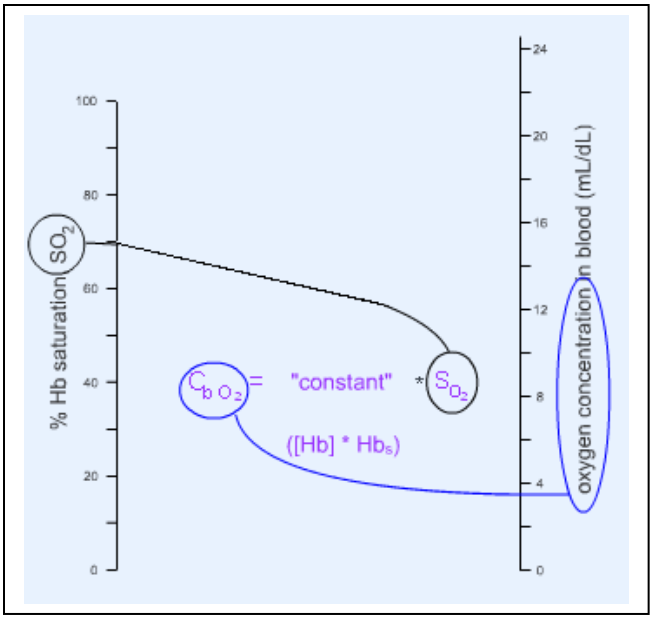
The saturated oxyhemoglobin content is a constant, 1.36 mL of oxygen per gram of hemoglobin.

The hemoglobin concentration varies from person to person, but within an individual generally has negligible fluctuations, so we can consider it to be constant as well.

So for any individual we now see that the concentration of bound oxygen is directly related to the hemoglobin saturation, with only a scalar factor (the hemoglobin concentration times the saturated oxyhemoglobin content) between them.

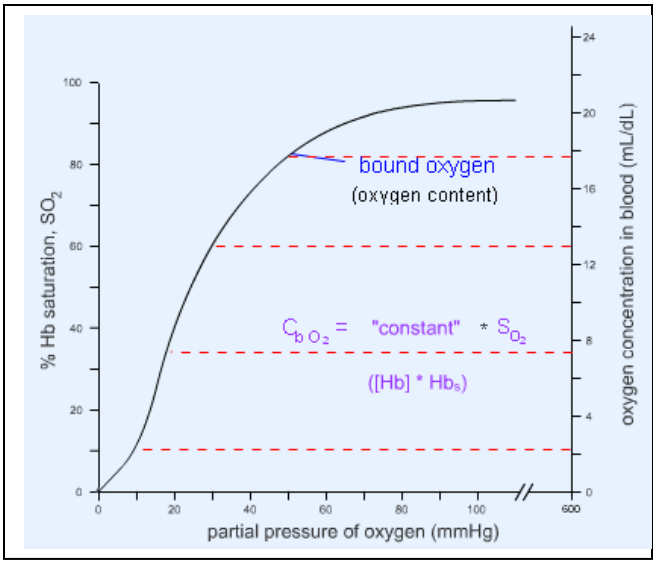
Graphically, they can be lined up as shown, with hemoglobin saturation on the left and oxygen concentration in the blood on the right.

Notice that the two scale linearly.

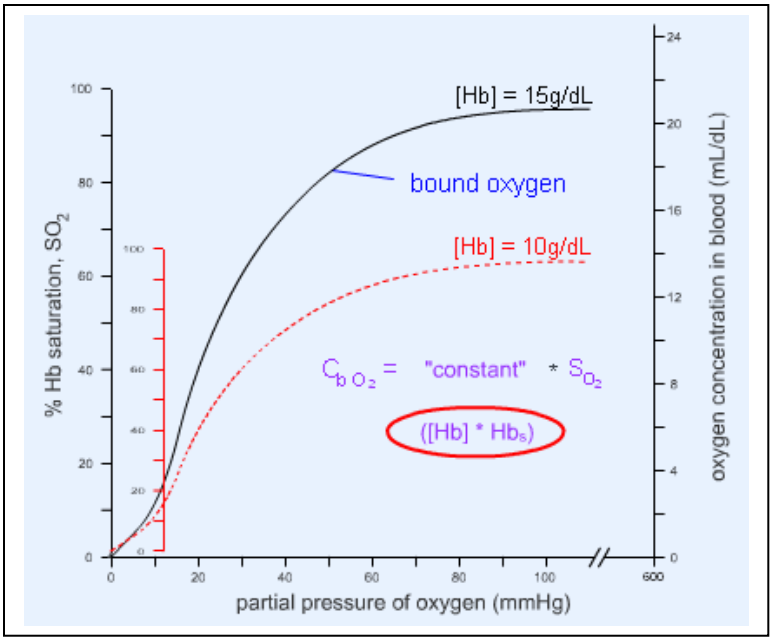


We can superimpose the hemoglobin saturation curve we derived earlier.

By tracing over to the right axis we can now find the oxygen content without any need for calculation. (The calculation has already been accounted for in the scaling of the axes.)



Recall that this scalar factor is the hemoglobin concentration times the saturated oxyhemoglobin content.



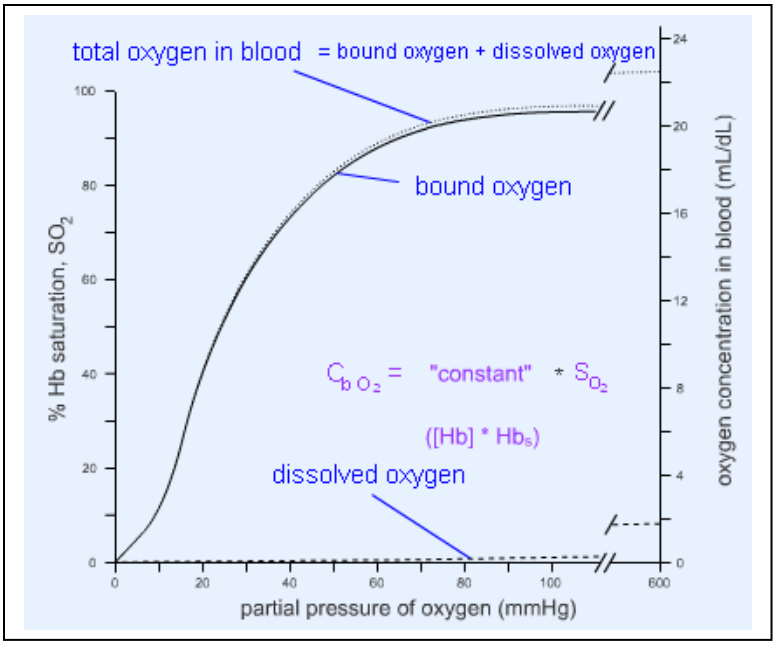
The saturated oxyhemoglobin content was given earlier and is constant at 1.36 mL O2 / g Hb. But differences can exist between DIFFERENT individuals' hemoglobin concentrations.

Normally, the hemoglobin concentration is about 15 g / dL.

In an anemic individual, this value can be as low as 10 g / dL, which changes our scalar factor. This can be accounted for graphically by the appropriate scaling of our axes, as illustrated here.[4]

Let us consider again the first hemoglobin saturation curve we drew.

We have found that from this we can derive the concentration of oxygen BOUND in the blood.



At the beginning of this lesson we learned about Henry's law and the amount of oxygen that is found dissolved in the blood, which we can add to our graph.

It is evident from this picture, that the majority of oxygen in the blood is bound to hemoglobin, not dissolved.

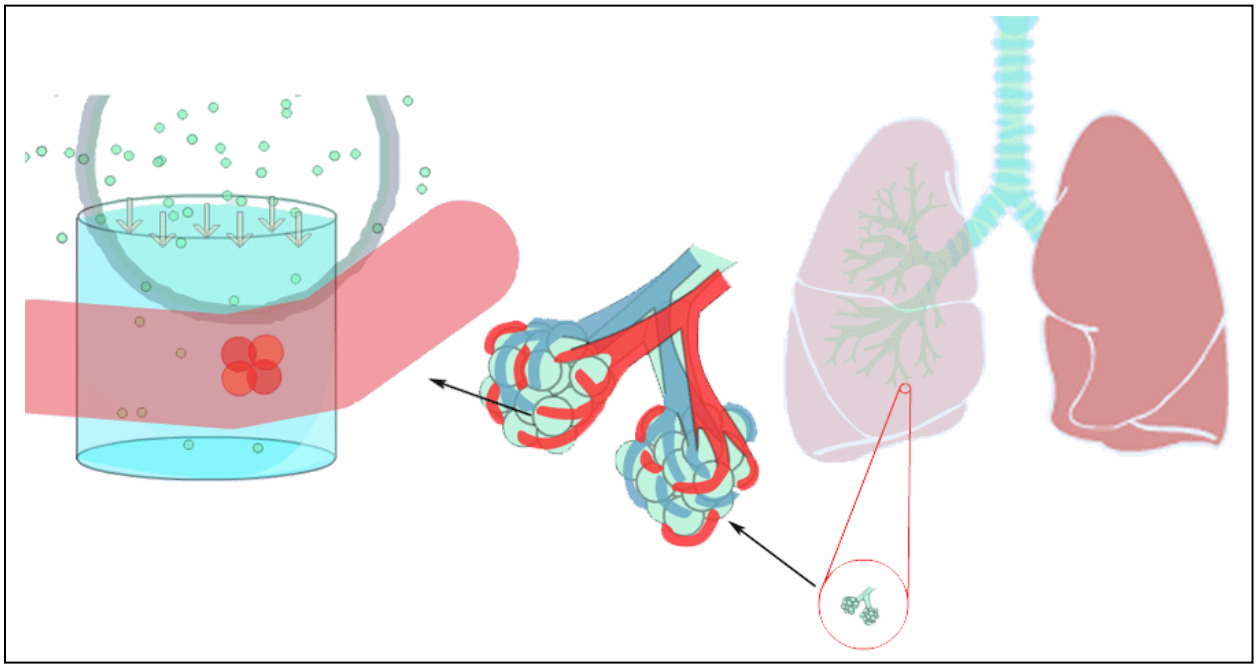
We can get the total oxygen concentration in the blood by summing the bound and dissolved oxygen concentrations, as shown here graphically..

[4] The implications of this are that an anemic individual will lower oxygen concentrations in the blood, even if their Hb is 100% saturated! This is why you cannot simply rely on Hb saturation as a measure of adequate oxygen concentrations!

Up until this point, we have spoken generally about hemoglobin and blood in order to develop our understanding of the situation.

We now turn to the body to see more specifically how this all plays out.

First let's look in the lungs. As we zoom in on the alveoli, we gain an appreciation for the fact that there is an oxygen-blood interface present, exactly like the one we've been representing schematically.



To start with, let's consider that we're already at dynamic equilibrium between the gas and dissolved oxygen and that hemoglobin is in the tense state.

Since oxygen is at high concentration in the lungs, hemoglobin will become more saturated. Recall that the hemoglobin saturation curve is *left-shifted in the lungs*, which makes hemoglobin saturation occur more readily.

Hemoglobin saturates by taking oxygen out of the blood, which transiently decreases the dissolved concentration, thus transiently disrupting the equilibrium we had before.

Since the dissolved oxygen concentration depends on the partial pressure in the gas, which is unchanged, Henry's Law dictates that more oxygen from the gas will become dissolved.

This is the dynamic process that allows many hemoglobin molecules to become saturated with oxygen while in the lungs.

As the blood is rushed back to the heart and then to the body tissues, there is not much opportunity for the dissolved oxygen to escape, so when the blood finally reaches the tissue capillary beds, hemoglobin is still mostly saturated and our dissolved oxygen concentration is still high.

But, the partial pressure of oxygen here is much lower here.[5] Now our dynamic equilibrium works to satisfy Henry's Law and move oxygen out of the blood and into the tissue.

As this happens, the DISSOLVED oxygen concentration transiently decreases and hemoglobin finds itself on the lower end of its saturation curve, so it releases oxygen. Recall also that the hemoglobin saturation curve is *right-shifted in the tissues*, which makes hemoglobin release oxygen more readily.

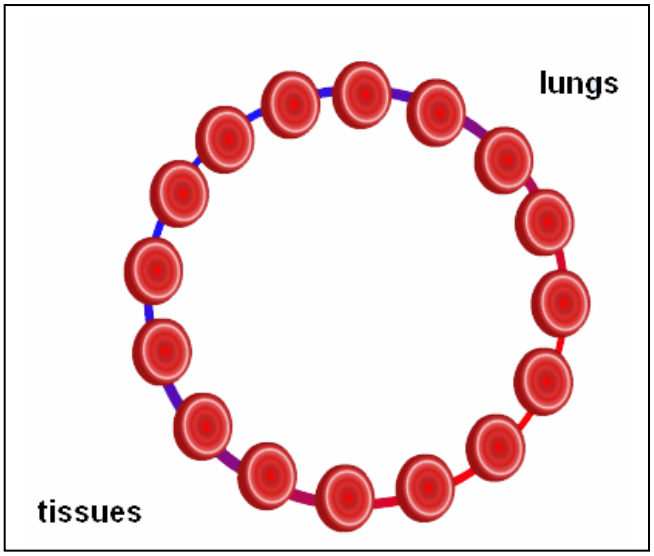
This whole process is dynamic, so as hemoglobin releases more of its oxygen to become dissolved in plasma, oxygen from the plasma is being released to the tissues, in accordance with Henry's Law.

This is the process that allows the tissues to receive oxygen as the hemoglobin returns to the tense state.

Keep in mind that this is a cycle, with hemoglobin traveling around and around in the circulation.

Lastly, it's not just hemoglobin flying freely in the blood. Hemoglobin molecules are actually found inside of red blood cells, which circulate.

Since there are many red blood cells found throughout the circulation, we realize that the dynamic process of oxygen transport we've just explored is actually occurring continuously in the lungs and tissues.



This module is available at http://www.umich.edu/~projbnb/cvr/o2.html

It was developed by Daniel Saddawi-Konefka and Ben Bryner.

Special thanks to Dr. Lou D'Alecy and Dr. Rob Paine.

[5] Note that we refer to the partial pressure of oxygen in the tissues, even though the tissues are not a gas. This is commonly done everywhere in the body. When we refer to a concentration of oxygen as a certain partial pressure in the tissues, what we really are referring to is the partial pressure of gaseous oxygen that would be in dynamic equilibrium with the concentration of oxygen in the tissue. Thus, it is an indirect but appropriate measure of oxygen concentration in the tissue.