

Blood, Sweat, and Buffers: pH Regulation During Exercise

Acid-Base Equilibria Experiment



Authors: Rachel Casiday and Regina Frey
Revised by: C. Markham, A. Manglik, K. Castillo,
K. Mao, and R. Frey
Department of Chemistry, Washington University
St. Louis, MO 63130



For information or comments on this tutorial, please contact Kit Mao at mao@wustl.edu.

Key Concepts:

- Exercise and how it affects the body
- Acid-base equilibria and equilibrium constants
- How buffering works
 - Equilibrium Constants
 - Henderson-Hasselbalch Equation
 - Direction of Equilibrium Shifts
 - Application to Blood pH

Related Tutorials:

- [Hemoglobin and the Heme Group: Metal Complexes in the Blood for Oxygen Transport](#)
- [Iron Use and Storage in the Body: Ferritin and Molecular Representations](#)
- [Maintaining the Body's Chemistry: Dialysis in the Kidneys](#)

How Does Exercise Affect the Body?

Many people today are interested in exercise as a way of improving their health and physical abilities. When we exercise, our heart rate, systolic blood pressure, and cardiac output (the amount of blood pumped per heart beat) all increase. Blood flow to the heart, the muscles, and the skin increase. The body's metabolism becomes more active, producing CO_2 and H^+ in the muscles. We breathe faster and deeper to supply the oxygen required by this increased metabolism. With strenuous exercise, our body's metabolism exceeds the oxygen supply and begins to use alternate biochemical processes that do not require oxygen. These processes generate lactic acid, which enters the blood stream. As we develop a long-term habit of exercise, our cardiac output and lung capacity increase, even when we are at rest, so that we can exercise longer and harder than before. Over time, the amount of muscle in the body increases, and fat is burned as its energy is needed to help fuel the body's increased metabolism.

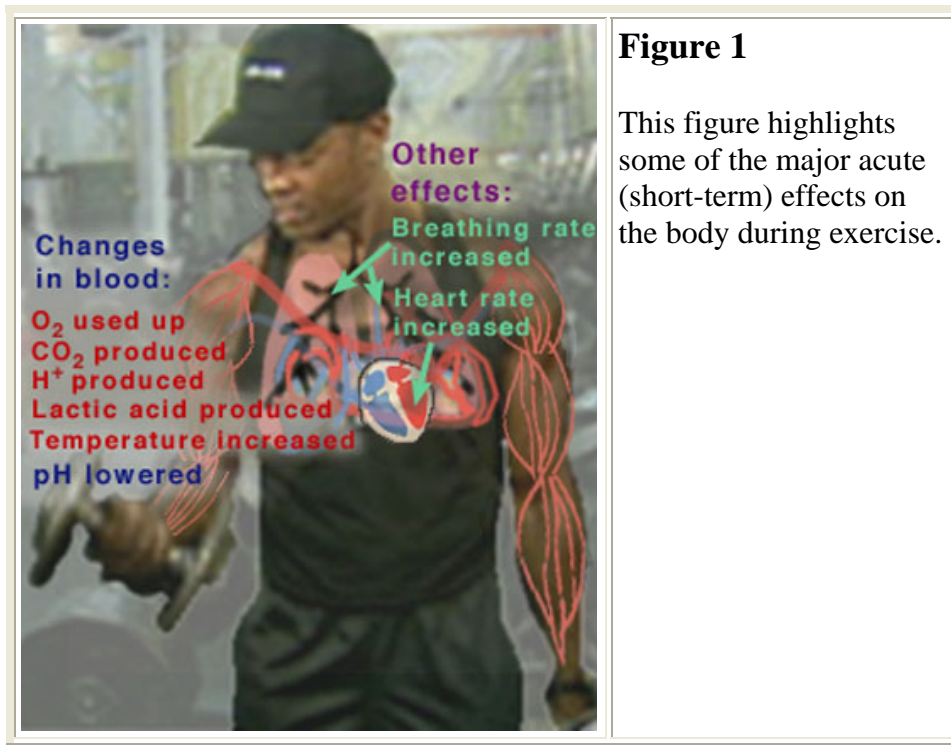


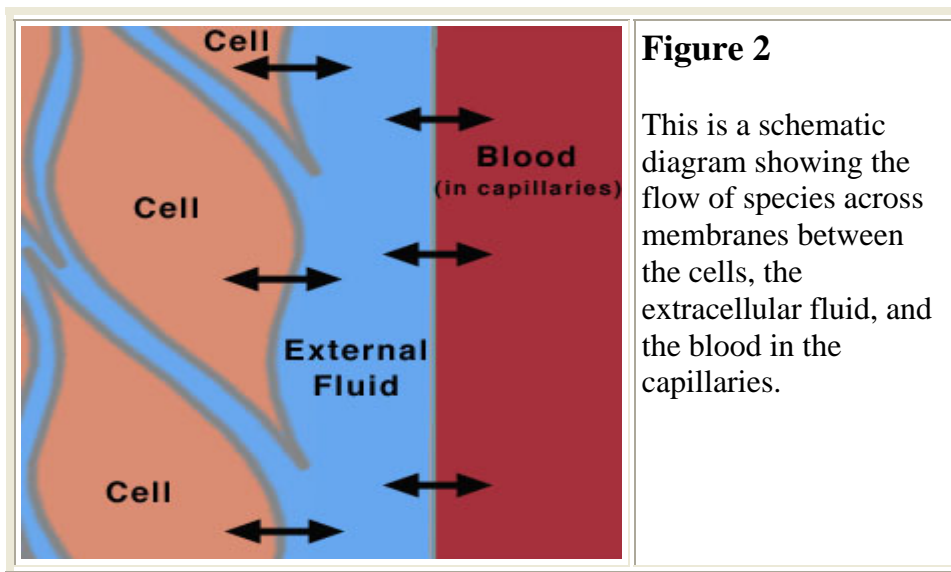
Figure 1

This figure highlights some of the major acute (short-term) effects on the body during exercise.

During exercise, the muscles use up oxygen as they convert the chemical energy in glucose to mechanical energy. This O_2 comes from hemoglobin in the blood. CO_2 and H^+ are produced during the breakdown of glucose, and they are removed from the muscles via the blood. The production and removal of CO_2 and H^+ , together with the use and transport of O_2 , cause chemical changes in the blood. These chemical changes, unless offset by other physiological functions, cause the pH of the blood to drop. If the pH of the body gets too low (below pH 7.4), a condition known as **acidosis** results. This can be very serious because many of the chemical reactions that occur in the body, especially those involving proteins, are pH-dependent. Ideally, the pH of the blood should be maintained at 7.4. If the pH drops below 6.8 or rises above 7.8, death may occur. Fortunately, we have buffers in the blood to protect against large changes in pH.

How Chemicals Are Exchanged in the Body

All cells in the body continually exchange chemicals (*e.g.*, nutrients, waste products, and ions) with the external fluid surrounding them (Figure 2). This external fluid, in turn, exchanges chemicals with the blood being pumped throughout the body. Diffusion through membrane channels is a dominant mode of exchange between these fluids (cellular fluid, external fluid, and blood). The diffusion is due to a **concentration gradient** associated with the contents of the fluids. Hence, the chemical composition of the blood (and therefore of the external fluid) is extremely important for the cell. If, for instance, the pH of the blood and external fluid is too low (too many H^+ ions), then an excess of H^+ ions will enter the cell and disrupt normal chemical processes. In order to maintain the proper chemical composition *inside* the cells, the chemical composition of the fluids *outside* the cells must be kept relatively constant. This constancy is known in biology as **homeostasis**.



The body has a wide array of mechanisms to maintain homeostasis in the blood and extracellular fluid. *The most important way that the pH of the blood is kept relatively constant is by buffers dissolved in the blood.* Other organs help enhance the homeostatic function of the buffers. For example, the kidneys remove H^+ ions and other components of the pH buffers that build up in excess. Acidosis that results from failure of the kidneys to perform this excretory function is known as **metabolic acidosis**. On the other hand, **acute acidosis** is a condition that results from a sudden decrease in pH (*e.g.*, during exercise). This occurs because excretion by the kidneys is a process that takes too long to prevent acute acidosis. The lungs provide a faster way to help control the pH of the blood. In response to exercise, the body increases its breathing rate which helps to counteract the pH-lowering effects of exercise by removing CO_2 , a component of the principal pH buffer in the blood. Acidosis that results from failure of the lungs to eliminate CO_2 as fast as it is produced is known as **respiratory acidosis**.

How Buffers Work: A Quantitative View

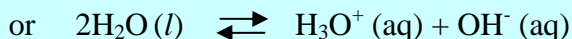
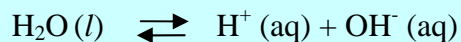
The kidneys and the lungs work together to help maintain a blood pH of 7.4 by affecting the components of the buffers in the blood. To understand how these organs help control the pH of the blood, we must first discuss how buffers work in solution.

Acid-base buffers confer resistance to a change in the pH of a solution when hydrogen ions (protons) or hydroxide ions are added or removed. An acid-base buffer consists of a **weak acid** and its **conjugate base** (from a salt) or a **weak base** and its **conjugate acid** (from a salt). A buffer works because it contains a substantial amount of a weak acid and a weak base (the conjugate acid-base pair) at equilibrium with each other. When protons (from an external source) are added to the buffer, some of the base component of the buffer will react with the protons and turn into the conjugate acid (which is the weak-acid component of the buffer) and thus neutralizing most of the protons added. When hydroxide ions are added (or, equivalently, when protons are removed from the buffer), some of the weak-acid component of the buffer will dissociate and turn into the conjugate base (which is the weak-base component of the buffer) thus replenishing most of the protons removed. Hence, adding a small amount of acid or base to a buffer solution merely changes the ratio of the conjugate acid and conjugate base in an acid-base equilibrium. Thus, the effect on the pH of the solution is small, within certain limitations of the amount of H^+ or OH^- added or removed. Some fundamental acid-base concepts are summarized in the blue box below.

Recap of Fundamental Acid-Base Concepts

Dissociation of Water and the p-Scale

Water molecules dissociate to form H^+ and OH^- ions:



H^+ ions in water are surrounded by many water molecules, symbolically, we use H_3O^+ to represent a solvated proton, where $[\text{H}^+] = [\text{H}_3\text{O}^+]$. Using the Law of Mass Action, the equilibrium constant for the dissociation reaction of water can be written as:

$$K_w = [\text{H}^+][\text{OH}^-] \quad (1)$$

H_2O is not included in the equilibrium-constant expression because it is a pure liquid. Like all the equilibrium constants, K_w is a function of temperature only, not affected by the concentrations of H^+ and OH^- ions. In a neutral solution, the concentrations of H^+ and OH^- equal each other. If $[\text{H}^+]$ increases (in the situation of an acidic solution), $[\text{OH}^-]$ will decrease such that their product equals to the constant K_w .

A p-Scale is defined to express small values:

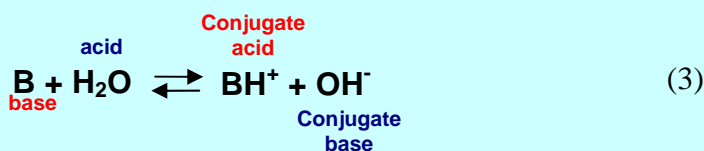
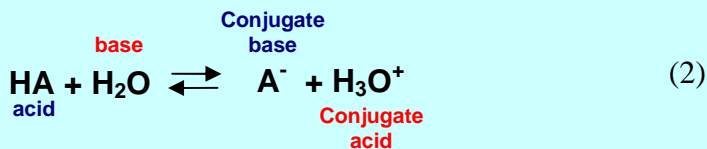
$$p^x \equiv -\log [x]$$

Therefore, $\text{pH} \equiv -\log [\text{H}^+] = -\log [\text{H}_3\text{O}^+]$, and $\text{pOH} = -\log [\text{OH}^-]$

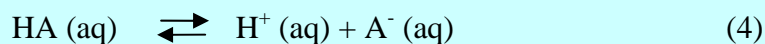
From Eq. (1) $\text{p}K_w = \text{pH} + \text{pOH}$

Acid-Base Equilibrium

According to the common Bronstead-Lowry definition, an **acid** (HA) is a chemical species that can donate a proton (H^+), and a **base** is a species that can accept (gain) a proton. The conjugate base of an acid is the species formed after the acid loses a proton (A^-); the conjugate base can then gain a proton to return to the acid. In solution, these two species (the acid and its conjugate base) exist in equilibrium as illustrated by Eq. (2). Similarly, a base (B) can gain a proton from water and exists in equilibrium with its conjugate acid (BH^+) as illustrated by Eq. (3).



For simplicity, the dissociation of a weak acid can also be expressed by Eq.(4).



Using the Law of Mass Action, the equilibrium constants for the dissociation of a weak acid and a weak base in equations (2) and (3), known as K_a and K_b , are defined as:

$$K_a = \frac{[\text{H}_3\text{O}^+][\text{A}^-]}{[\text{HA}]} \quad (5)$$

$$K_b = \frac{[\text{OH}^-][\text{BH}^+]}{[\text{B}]} \quad (6)$$

pH of Buffer Solutions

In a weak-acid solution, the concentration of the dissociated species, (that is, the conjugate base A^-), is typically small compared to the un-dissociated HA molecules; similarly, $[\text{BH}^+]$ is small compared to $[\text{B}]$ in a weak base solution. A buffer solution contains a weak acid and a substantial amount of its conjugate base from a soluble salt (that is, the concentrations of HA and A^- are comparable), or a weak base and a substantial amount of its conjugate acid from a soluble salt (in which, $[\text{B}]$ and $[\text{BH}^+]$ are comparable.).

We can derive a convenient equation for calculating the pH of a buffer solution. Taking the logarithm of each side of Equation (5) gives:

$$\log K_a = \log[\text{H}_3\text{O}^+] + \log \frac{[\text{A}^-]}{[\text{HA}]} \quad (7)$$

Rearrange to obtain: $-\log[\text{H}_3\text{O}^+] = -\log K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$

Which becomes $pH = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$ (8)

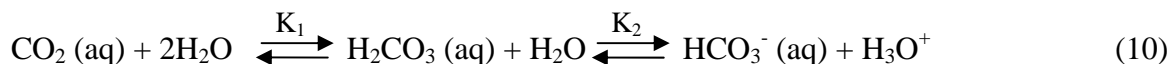
Note that $[\text{HA}]$ and $[\text{A}^-]$ are the concentrations of the weak acid and its conjugate base at equilibrium. Since the dissociation of a weak acid is typically very small, we can assume that $[\text{HA}]$ and $[\text{A}^-]$ are similar to the initial concentrations, $[\text{HA}]_i$ and $[\text{A}^-]_i$. Equation 8 is known as the **Henderson-Hasselbalch Equation**. This equation shows that the pH of a buffer solution is very close to the pK_a value of the weak acid making the buffer. This is because the logarithm term will be small unless the concentrations of A^- and HA differ by several orders of magnitude.

For a basic buffer consisting of a weak base and its conjugate acid, one can begin with Eq.(6) and follow similar derivation steps to obtain:

$$pOH = pK_b + \log \frac{[\text{BH}^+]}{[\text{B}]} \quad (9)$$

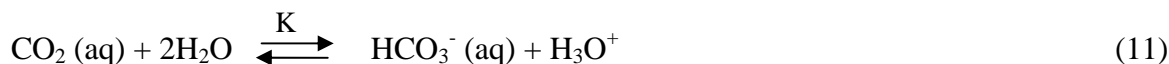
The Carbonic-Acid-Bicarbonate Buffer in the Blood

By far the most important buffer for maintaining acid-base balance in the blood is the carbonic acid-bicarbonate buffer. The dissolved carbon dioxide and bicarbonate ion are at equilibrium (Eq. 10). We are interested in the change in the pH of the blood; therefore, we want an expression for the concentration of H^+ in terms of an equilibrium constant and the concentrations of the other species in the reaction (HCO_3^- , H_2CO_3 , and CO_2).



Where $K_1 = \frac{[H_2CO_3]}{[CO_2]}$ and $K_2 = \frac{[HCO_3^-][H_3O^+]}{[H_2CO_3]}$

The equilibrium on the right is an acid-base reaction where carbonic acid is the acid and water is the base. The conjugate base for H_2CO_3 is HCO_3^- (bicarbonate ion). The equilibrium on the left is the association of the dissolved carbon dioxide with a water molecule to form carbonic acid. This equilibrium favors the CO_2 side; hence, the concentration of H_2CO_3 in solution is very small. Since both reactions are at equilibrium, we can simplify Eq. (10) by removing the middle step.



Where $K = \frac{[HCO_3^-][H_3O^+]}{[CO_2]}$ (12)

One can see that $K_1 K_2 = \frac{[H_2CO_3][HCO_3^-][H_3O^+]}{[CO_2][H_2CO_3]} = \frac{[HCO_3^-][H_3O^+]}{[CO_2]} = K$

Remember, we are doing all these simplifications to obtain an equation that tells us how the concentrations of carbon dioxide and bicarbonate affect the pH of our blood. Starting from Equation (12), and following the steps of how Henderson-Hasselbalch Equation is derived from Eq. (5) in the blue box, we can obtain an equation that relates the concentrations of CO_2 and HCO_3^- to the pH in the blood (try the algebra on your own to make sure you are comfortable with it):

$$pH = pK + \log\left(\frac{[HCO_3^-]}{[CO_2]}\right) \quad (13)$$

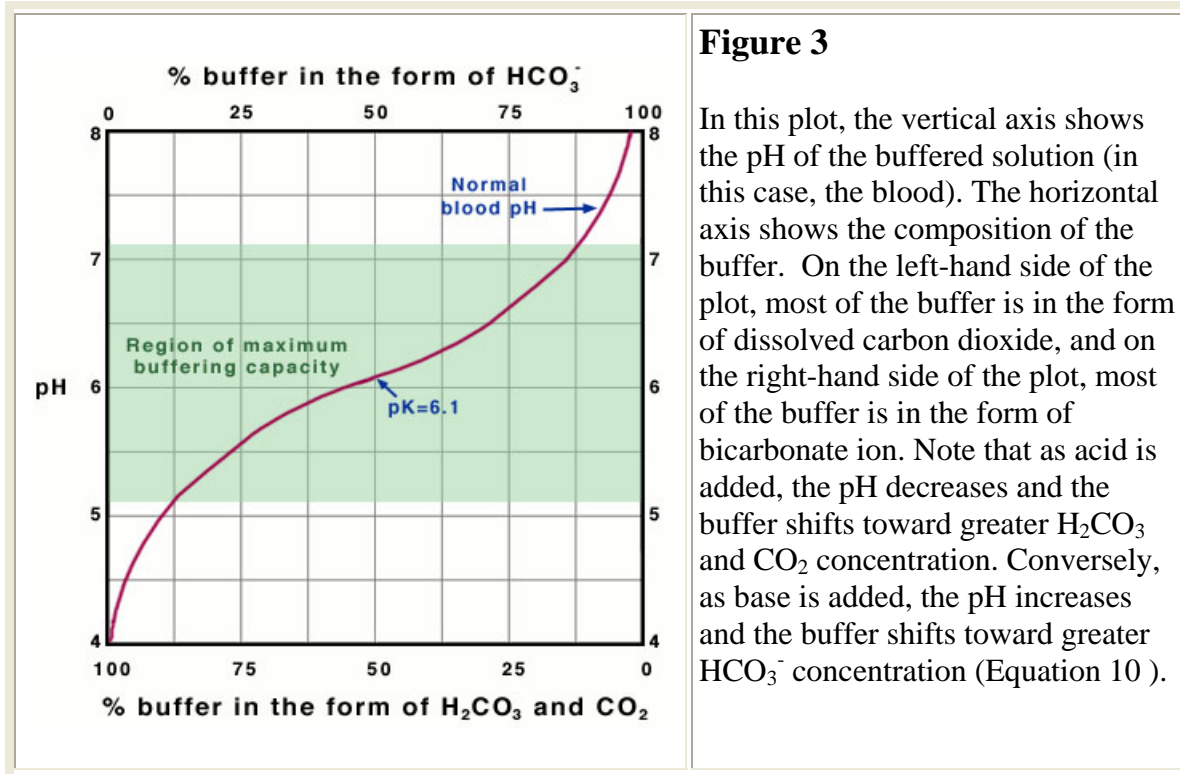
At normal body temperature, the value of pK is 6.1. Notice that Equation (13) is in a similar form to the Henderson-Hasselbalch Equation. However, Equation (13) does not meet the strict definition of a Henderson-Hasselbalch equation because this equation takes into account a non-acid-base reaction (*i.e.*, the association of dissolved carbon dioxide and water). Nonetheless, the relationship shown in Equation 11 is frequently referred to as the **Henderson-Hasselbalch Equation** for the buffer in physiological applications.

Equation (13) shows that the pH of the buffered solution (the blood) is dependent only on the ratio of the amount of CO_2 to the amount of HCO_3^- (at a given temperature, so that pK remains constant). This ratio remains relatively constant because the concentrations of both buffer components (HCO_3^- and CO_2) are very large compared to the amount of H^+ added to the blood during normal activities

and moderate exercise. When H^+ is added to the blood as a result of metabolic processes, the amount of HCO_3^- (relative to the amount of CO_2) decreases; however, the change is tiny compared to the amount of HCO_3^- present in the blood.

The Optimal Buffering Capacity is at $pH = pK$

The buffering capacity of a buffer is highest when the pK_a value of the buffer is closest to the desired pH value. This can be explained by the Henderson-Hasselbach equation. According to Eq. (8), the buffer solution will have greatest capacity when the concentration of the acid and the conjugate base equal each other. When this is the case, their concentration ratio equals 1 making the logarithm term zero and $pH = pK_a$. In the case of the carbonic acid-bicarbonate buffer, $pK=6.1$ at normal body temperature; Figure 3 (below) shows a plot of the pH and the composition of a carbonic acid-bicarbonate buffer at this temperature. The slope of the curve is flattest (thus the change in pH is smallest) where the pH is equal to the pK value of 6.1 for the buffer. Here, the buffering capacity is greatest because a shift in the relative concentrations of bicarbonate and carbon dioxide produces only a small change in the pH of the solution. However, at pH values higher than 7.1 or lower than 5.1, the slope of the curve is much higher. In this case, a shift in the relative concentrations of bicarbonate and carbon dioxide produces a large change in the pH of the solution.



Hence, the physiological blood pH of 7.4 is outside the optimal buffering range of the carbonic acid-bicarbonate buffer. The addition of protons to the blood due to strenuous exercise may be too great for the buffer alone to effectively control the blood's pH . When this happens, other organs must help control the amounts of CO_2 and HCO_3^- in the blood. The lungs remove excess CO_2 from the blood (helping to raise the pH as equilibria in Eq. 10 shift to the left as predicted by the Le Chatelier's Principle). When the pH of the body is excessively high (a condition known as **alkalosis**), the kidneys remove bicarbonate ion (HCO_3^-) from the blood (helping to lower the pH as equilibria in Eq. 10 shift to the right).

Other pH-Buffer Systems in the Blood

Other buffers perform minor roles than the carbonic-acid-bicarbonate buffer in regulating the pH of the blood. The phosphate buffer consists of H_2PO_4^- in equilibrium with HPO_4^{2-} and H^+ . The pK for the phosphate buffer is 6.8, which allows this buffer to function within its optimal buffering range at physiological pH. The phosphate buffer only plays a minor role in the blood, however, because H_2PO_4^- and HPO_4^{2-} are found in very low concentration in the blood. Hemoglobin also acts as a pH buffer in the blood. Recall from the “[Hemoglobin and the Heme Group: Metal Complexes in the Blood for Oxygen Transport](#)” tutorial from Chem 151 that the hemoglobin protein can reversibly bind either H^+ (to the protein) or O_2 (to the Fe of the heme group), and that when one of these substances is bound, the other is released (as explained by the Bohr effect). During exercise, hemoglobin helps to control the pH of the blood by binding some of the excess protons that are generated in the muscles. At the same time, molecular oxygen is released for use by the muscles.

Summary: What Happens to the Blood During Exercise?

When you exercise, many of the processes that we have discussed in this and in previous tutorials work together to determine how the pH of the blood will change (Figure 4).

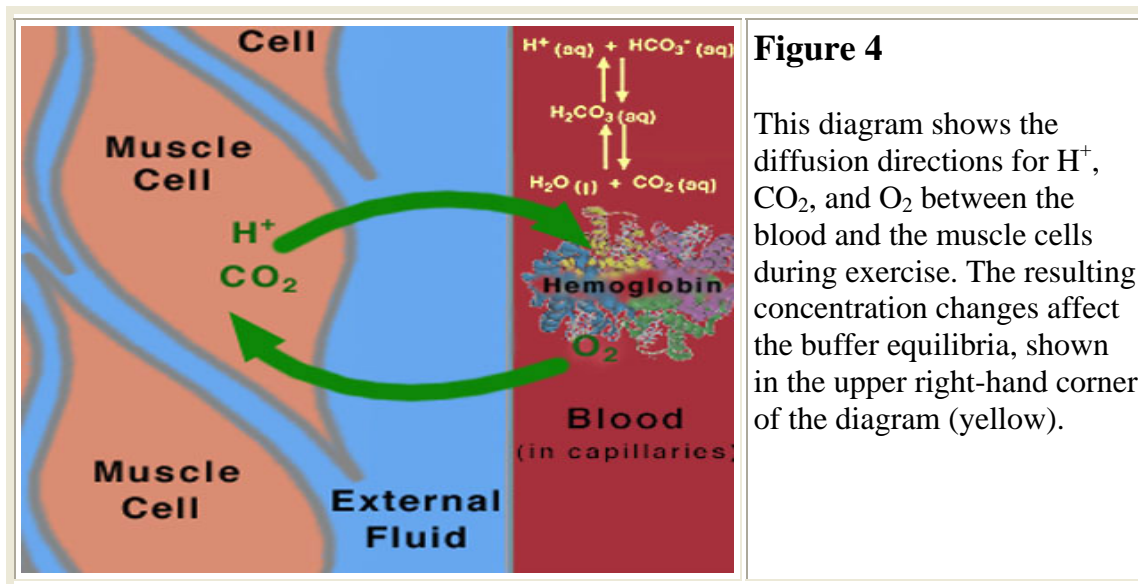


Figure 4

This diagram shows the diffusion directions for H^+ , CO_2 , and O_2 between the blood and the muscle cells during exercise. The resulting concentration changes affect the buffer equilibria, shown in the upper right-hand corner of the diagram (yellow).

The following steps outline the processes that affect the buffers in the blood during exercise.

- [Hemoglobin](#) carries O_2 from the lungs to the muscles through the blood.
- The muscles need more O_2 than normal because their metabolic activity is increased during exercise. The amount of oxygen in the muscle is therefore depleted, setting up a concentration gradient between the muscle cells and the blood in the capillaries. Oxygen diffuses from the blood to the muscles, via this concentration gradient.
- The muscles produce CO_2 and H^+ as a result of increased metabolism, setting up concentration gradients in the opposite direction from the O_2 gradient.
- The CO_2 and H^+ flow from the muscles to the blood via these concentration gradients.
- The buffering action of hemoglobin picks up the extra H^+ and CO_2 .
- If the amounts of H^+ and CO_2 exceed the capacity of hemoglobin, they affect the carbonic acid equilibrium (Equation 10). This lowers the pH of the blood, causing acidosis.
- The lungs and [kidneys](#) respond to pH changes by removing CO_2 , HCO_3^- , and H^+ from the blood.

The body has developed finely tuned chemical processes based on buffering and acid-base equilibria that work in combination to handle the changes that exercise produces.

Additional Links:

- This Wikipedia entry gives a great overview of [metabolic acidosis](#).
 - This Wikipedia entry gives a great overview of [carbonic acid](#) and the effect of CO₂ (g) on carbonic acid solutions.
 - This link from the [Ask A Scientists chemistry archive](#) explains why there is a negligible amount of carbonic acid when water is present.
-

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Acknowledgements:

The authors thank Dewey Holten, Michelle Gilbertson, Jody Proctor and Carolyn Herman for many helpful suggestions in the writing of this tutorial.

The development of this tutorial was supported by a grant from the Howard Hughes Medical Institute, through the Undergraduate Biological Sciences Education program, Grant HHMI# 71195-502005 to Washington University.

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Revised July 2007.

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