**Biological buffering of blood**

There are three major contributors to regulating the pH of blood. Bicarbonate, phosphate and proteins.

**Blood pH Must be Kept Close to 7.4**

- Hydrogen ion is extremely reactive and effects many molecules which regulate physiological processes.
- Blood pH is set at a slightly alkaline level of 7.4 (pH 7.0 is neutral).
- A change of pH of 0.2 units in either direction is considered serious.
- Blood pHs below 6.9 or above 7.9 are usually fatal if they last for more than a short time.

- The bicarbonate system is the most important and is controlled by the rate of respiration.
  - Carbon dioxide in water reacts to form carbonic acid:
    \[
    \text{CO}_2(\text{g}) \leftrightarrow \text{CO}_2(\text{aq}) + \text{H}_2\text{O} \rightarrow \text{H}_2\text{CO}_3
    \]
    Carbonic acid
  - The pKa of carbonic acid is 6.35. The pH of blood is 7.4 so the acid is greater than 1 pH away from the pKa and it is primarily dissociated:
    \[
    \text{H}_2\text{CO}_3 \rightarrow \text{H}^+ + \text{HCO}_3^-
    \]
    Bicarbonate
  - Under physiological conditions the equilibrium for the first reaction is far to the left, and the combined pKa for the two reactions is 6.4:

- At first glance this does not look like a good buffer for blood. The buffering capacity is poor. To maintain a pH of 7.4 there would have to be a ratio of 11 to 1 of bicarbonate to carbon dioxide.

  \[
  \text{pH} = 6.4 + \log \left[ \frac{\text{HCO}_3^-}{\text{CO}_2} \right]
  \]

  Because this is an open system, the CO₂ dissolved and the bicarbonate can rapidly change. Changes resulting in loss of carbonic acid are replaced by CO₂ dissolving - This is an open system.

  Normal concentration of carbon dioxide is 1.2 mM and bicarbonate is 15 mM.
**Acidosis and Alkalosis**

A decrease in arterial carbon dioxide partial pressure causes the bicarbonate/carbon dioxide ratio to exceed 20 and the pH to rise above 7.45 - Alkalosis

Increases in partial pressure of CO\(_2\) have the opposite affect and decrease the pH below 7.2 - Acidosis

**There can be metabolic reasons for either condition**
- Metabolic acidosis results from an increase in loss of bicarbonate (such as diarrhea) or overproduction of acids (ketosis, anaerobic metabolism)
- Metabolic alkalosis results from Conditions that lead to a reduced amount of fluid in the body, like vomiting or excessive urination due to use of diuretic drugs, or excess bicarbonate ingestion.

**There can also respiratory reasons for either condition:**
- Respiratory acidosis results from hypoventilation which is manifested by the accumulation of CO\(_2\) in the blood and a drop in blood pH.
  - Central Nervous System Depression (Sedatives, CNS disease, Obesity Hypoventilation syndrome)
  - Lung Disease (emphysema, pneumonia)
  - Musculoskeletal disorders (Myasthenia Gravis, Polio)

- Respiratory alkalosis results from hyperventilation which is manifested by excess elimination of CO\(_2\) from the blood and a rise in the blood pH
  - Catastrophic CNS event (CNS hemorrhage)
  - Drugs (salicylates, progesterone)
  - Pregnancy (especially the 3rd trimester)
  - Decreased lung compliance (interstitial lung disease)
  - Liver cirrhosis
  - Anxiety

**Adjusting Levels - Compensation**

- In reality the kidneys regulate the bicarbonate concentration. If there is too little bicarbonate, the kidneys filter and excrete H\(+\), causing a shift in the equilibrium to increase bicarbonate.
- If there is too much bicarbonate, Kidneys will excrete it.

The carbon dioxide is replaced by metabolism (Food -> H\(_2\)O and CO\(_2\))

Changes in breathing can increase or decrease the CO\(_2\)

- Breathe too fast and what happens. Decrease the breathing rate and alter the pH as well. (think of the last time you got sick and threw up)
**Titration of a buffer**
The easiest way to visualize the buffer action is to draw the titration curve.
- Note where the pH resists change (within 1 pH unit of the midpoint)
- The midpoint is the pK of a dissociable group
- At the midpoint pH = pK and HA = A-

**Summary of pH**
1 pK is defined as the – log of K where K is an equilibrium constant
2 pK is the pH of the solution where the [HA] = [A-]
3 pK is the pH at the midpoint of a titration curve
4 pK is the pH where half of the acid is ionized
5 pK measures the concentration of protons in the solution that suppresses ionization
6 An acidic group with a pK of 4 is 100 times weaker than one with a pK of 2
   A group with a pK of 6 is 90% ionized at pH 7, 50% at pH 6, and 10% at pH 5