6.2 Problem Set
Gas Transport and pH Disturbances

1. A. An elderly woman has a hemoglobin concentration of $10\ \mathrm{g\ dL^{-1}}$. Her O_2 dissociation curve is normal (when expressed as S_{O_2}). Assume that her resting O_2 consumption (Q_{O_2}) is within normal limits, $225\ \mathrm{mL\ min^{-1}}$, and that Q_a, the cardiac output, is $4.5\ \mathrm{L\ min^{-1}}$; $P_{a_{O_2}} = 95$ mmHg is normal.
   A.1 What is the total oxygen content (in $\mathrm{mL\ dL^{-1}}$) of her arterial blood?
   A.2 What is the total oxygen content of her mixed venous blood?
   A.3 What is the S_{O_2} of venous blood?
   B. Assume that the S_{O_2} of venous blood in this woman is the normal 75%.
   B.1 What would be the $P_{v_{O_2}}$?
   B.2 What would the oxygen content of her mixed venous blood be?
   C. If arterial blood has $P_{a_{O_2}} = 95$ mmHg as in part A and mixed venous blood has $S_{O_2} = 75\%$ (part B), how much O_2 would be extracted by the tissues per L of blood?
   D. Given the $[O_2]_a - [O_2]_v$ from part C, what must Q_a be for tissue extraction to match her Q_{O_2} of $225\ \mathrm{mL\ min^{-1}}$?
   E. According to your calculations, the response to anemia in principle could be to keep cardiac output, Q_a, constant and let $P_{v_{O_2}}$ fall, or to raise Q_a to keep $P_{v_{O_2}}$ constant. With your new knowledge of respiratory and circulatory physiology, which do you think happens?
2. The circulating blood volume typically is 7% of body weight. Assume that a person weighs 80 kg and that the hemoglobin concentration is $14.5\ \mathrm{g\ dL^{-1}}$.
   A. What is the total amount of hemoglobin in the circulation?
   B. What is the maximum amount of O_2 that could be in the blood if *all* the blood has a $P_{O_2} = 100$ mmHg?
   C. If $Q_{O_2} = 275\ \mathrm{mL\ min^{-1}}$, how long would this O_2 last if the person stopped breathing? (Assume that Q_{O_2} is constant. In reality, it would decrease as $P_{a_{O_2}}$ falls.)
   D. If all the blood had a $P_{CO_2} = 46$ mmHg, estimate how much total CO_2 it would contain. (Include dissolved, carbamino Hb, and HCO_3^-) *Hint*: Use the numbers in Table 6.PS2.1.
   E. If $R = 0.8$, how much would the total CO_2 change during the time calculated in Part C?
3. Table 6.PS2.2 gives the $[Hb \cdot O_2]$ in blood containing $15\ \mathrm{g\ Hb\ dL^{-1}}$. Perform a Hill plot on these data to obtain h and the P_{O_2} at 50% saturation. This is called the P_{50}, the oxygen partial pressure at one-half maximal saturation. The theoretical basis for the Hill plot is described below. To do this, define a saturation fraction, v, given as

$$v = \frac{[Hb \cdot O_2]}{[Hb \cdot O_2]_{max}} \qquad [6.PS2.1]$$

From Eqn (6.4.2), this equation is

$$v = \frac{[O_2]^h}{K + [O_2]^h} \qquad [6.PS2.2]$$

We can write from this equation that

$$1 - v = 1 - \frac{[O_2]^h}{K + [O_2]^h}$$

$$= \frac{K + [O_2]^h}{K + [O_2]^h} - \frac{[O_2]^h}{K + [O_2]^h} \qquad [6.PS2.3]$$

$$= \frac{K}{K + [O_2]^h}$$

Taking the ratio of Eqn (6.PS2.2) to Eqn (6.PS2.3), we get

$$\frac{v}{1 - v} = \frac{[O_2]^h}{K} \qquad [6.PS2.4]$$

Taking the logarithm on both sides, we get

$$\log \frac{v}{1 - v} = -\log K + h \log [O_2] \qquad [6.PS2.5]$$

This last equation forms the basis of the Hill plot with K as a dissociation constant rather than as an association constant. Plotting log $(v/1 - v)$ against log $[O_2]$ allows calculation of h as the slope. Since $[O_2] = \alpha P_{O_2}$, we can plot $\log P_{O_2}$ and get the same h. When $v = ½$, log $(v/1 - v) = 0$ and at this point $P_{O_2} = P_{50}$.

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TABLE 6.PS2.1 Transport of O_2 and CO_2 to and from the Tissues

Variable	Arterial Blood	Mixed Venous Blood	A − V Difference	Transport = $Q_a \times (A - V)$
S_{O_2} (%)	98	74	24	
P_{O_2} (mmHg)	95	40	55	
Plasma $[O_2]$[a]	0.16 mL dL^{-1}	0.07 mL dL^{-1}	0.09 mL dL^{-1}	5 mL min^{-1}
RBC $[O_2]$[a]				
Dissolved	0.13 mL dL^{-1}	0.05 mL dL^{-1}	0.08 mL dL^{-1}	4 mL min^{-1}
Bound	19.8 mL dL^{-1}	15.0 mL dL^{-1}	4.8 mL dL^{-1}	240 mL min^{-1}
Total $[O_2]$	20.1 mL dL^{-1}	15.1 mL dL^{-1}	5.0 mL dL^{-1}	250 mL min^{-1}
pH	7.4	7.37		
P_{CO_2} (mmHg)	40	46		
Plasma $[CO_2]$[a]				
Dissolved	1.53 mL dL^{-1}	1.76 mL dL^{-1}	−0.23 mL dL^{-1}	−11 mL min^{-1}
HCO_3^-	30.28 mL dL^{-1}	32.50 mL dL^{-1}	−2.22 mL dL^{-1}	−111 mL min^{-1}
RBC $[CO_2]$[a]				
Dissolved	0.97 mL dL^{-1}	1.11 mL dL^{-1}	−0.14 mL dL^{-1}	−7 mL min^{-1}
HCO_3^-	12.6 mL dL^{-1}	13.8 mL dL^{-1}	−1.20 mL dL^{-1}	−60 mL min^{-1}
Carbamino Hb	1.68 mL dL^{-1}	1.89 mL dL^{-1}	−0.21 mL dL^{-1}	−11 mL min^{-1}
Total $[CO_2]$	47.1 mL dL^{-1}	51.1 mL dL^{-1}	−4.0 mL dL^{-1}	200 mL min^{-1}

The various forms of dissolved and bound O_2 and CO_2 are partitioned into the parts contributed by plasma and the red blood cells for each form of gas. Normal values assumed were as follows: 15 g Hb dL^{-1}; cardiac output (Q_a) of 5 L min^{-1}; temperature of 37°C; hematocrit of 0.45; respiratory quotient, $R = 0.8$; resting O_2 consumption of 250 mL min^{-1}.

[a]Values are given in terms of dL of blood, not the fluid indicated. For example, the plasma $[O_2]$ is *not* the concentration per dL of plasma; it is the contribution that plasma makes to the total $[O_2]$ per dL of *blood*. The RBC $[O_2]$ is not the concentration of O_2 per dL of RBCs; it is the contribution that the RBCs make to the total $[O_2]$ per dL of blood.

Adapted from R. Klocke, Carbon dioxide transport, in A.P. Fishman, ed., Handbook of Physiology, *Section 3, Volume IV, American Physiological Society, Washington, DC, 1986; C. Geers and G. Gros, Carbon dioxide transport and carbonic anhydrase in blood and muscle,* Physiological Review ***80****:681–715, 2000.*

TABLE 6.PS2.2 Oxygen Saturation of Hemoglobin

P_{O_2} (mmHg)	$[Hb \cdot O_2]$ (mL dL^{-1})	Fractional Saturation, v	Log $[v/(1-v)]$	Log P_{O_2}
10	1.93			
20	6.51			
30	11.51			
40	15.01			
50	17.10			
60	18.27			
70	18.91			
80	19.28			
90	19.40			
100	19.58			
110	19.66			
120	19.74			

4. In the table, calculate the missing values using the Henderson–Hasselbalch equation and identify the acid–base condition.

Part	pH	$P_{a_{CO_2}}$ (mmHg)	$[HCO_3^-]$ (mM)	Condition
A	7.40	40		
B		35	24.13	
C	7.14		33.0	
D	7.60	40		
E	7.31		20.0	

5. Consider the 80-kg person in Problem no. 2. Assume the person has a hematocrit of 0.40. If we infuse this person with 100 mL of 150 mM $NaHCO_3^-$, assuming instant equilibration with the plasma, exchange across the red blood cells is slow, and before respiratory or renal compensation can occur, what would happen to blood pH? If we could somehow wave a magic wand and remove the equivalent amount of HCO_3^-, what would happen to plasma pH?
6. Five samples of whole blood were equilibrated at 37°C with gas mixtures containing various percentages of carbon dioxide. The P_{CO_2} in blood was calculated by assuming that it was equal to the P_{CO_2} in the gas mixture. Plasma was removed from the erythrocytes anaerobically (why?) And the plasma was analyzed for the total carbon dioxide. Given the [total CO_2] and P_{CO_2} in the table below, calculate $[CO_2]$ and $[HCO_3^-]$. *Hint*: [Total CO_2] is the sum of all forms of CO_2 in the sample; for free $[CO_2]$ use the solubility and pH. Graph the results on the pH – HCO_3^- diagram as the **normal buffer line**.

Sample	P_{CO_2} (mmHg)	[Total CO_2] (mM)	$[CO_2]$ (mM)	$[HCO_3^-]$ (mM)	pH
1	85.1	32.3			
2	46.5	26.4			
3	40.0	25.2			
4	33.3	24.0			
5	23.3	21.5			

7. During exercise, both Q_{O_2} and Q_{CO_2} increase as well as cardiac output, Q_a. Suppose that during exercise Q_{O_2} increases to 2000 mL min^{-1}, and the respiratory quotient remains at 0.8, and that Q_a increases to 18 L min^{-1}. Assume that $P_{a_{O_2}}$ remains at 95 mmHg and $P_{a_{CO_2}}$ is 40 mmHg and that blood [Hb] = 15 g%.
   A. What is the total arterial content of O_2?
   B. What is the venous content of O_2?
   C. What is the $P_{v_{O_2}}$?
   D. What is the Q_{CO_2}?
   E. Assuming an arterial pH of 7.4, what is the total CO_2 content of arterial blood? (*Hint*: See the table in Problem no. 4.)
   F. Can you determine the total CO_2 content of venous blood?
   G. Can you determine the $P_{v_{CO_2}}$?
   H. Determine the new alveolar ventilation from the alveolar ventilation equation.
   I. Calculate the predicted $P_{a_{O_2}}$ from the alveolar gas equation.
8. In the Hill equation, $K = 4550\ \text{mmHg}^{2.62}$ and $h = 2.62$ (the exponent of mmHg is 2.62 because it adds with P_{O_2} in the Hill equation. If P_{O_2} is in units of mmHg, $P_{O_2}^{2.62}$ is in units of mmHg$^{2.62}$). Note that $K = 4550$ is $24.9^{2.62}$. Calculate the P_{O_2} for the following saturation fractions. *Hint*: See the equations in Problem no. 3. $S_x = [Hb \cdot O_2]x/[Hb \cdot O_2]_{max}$
   A. S_{25}
   B. S_{50}
   C. S_{75}
   D. S_{98}
   E. Repeat the calculations for A–D if h were equal to 1. In this case, $K = 24.9$ mmHg (why?)
9. For the phosphate buffer system, calculate the concentrations of $[H_2PO_4^{-1}]$ and $[HPO_4^{-2}]$ at pH 7.4 if the total phosphate concentration is 1 mM. *Hint*: Use the Henderson–Hasselbalch equation and the K_D given in Eqn (6.5.14).
10. Using the Henderson–Hasselbalch equation, plot the normal isobar on the pH – HCO_3^- diagram for $P_{a_{CO_2}} = 40$ mmHg.
11. Venous blood has a higher P_{CO_2} than arterial blood. As a consequence, it is slightly more acidic.
   A. If **arterial** plasma has a $P_{CO_2} = 40$ mmHg and a pH = 7.4, what is the $[HCO_3^-]$? Convert this to mL of CO_2 per dL of plasma (STPD).
   B. If **venous** plasma has a $P_{CO_2} = 46$ mmHg and a pH = 7.37, what is its $[HCO_3^-]$? Convert this to mL of CO_2 per dL of plasma (STPD).
   C. From the results in A and B, calculate the separate contributions of venous and arterial plasma HCO_3^- to the total blood CO_2 (sum of dissolved CO_2, HCO_3^-, and carbamino Hb), **in mL CO_2 per dL of blood**, using a hematocrit of 0.45.
   D. The intracellular pH of the red blood cell in the **arteries** is 7.25. Calculate the $[HCO_3^-]$ in the red blood cell cytoplasm assuming equilibration of 40 mmHg P_{CO_2} across the RBC membrane. Convert this to mL of CO_2 per dL of RBC ICF (STPD).
   E. The intracellular pH of the red blood cell in the veins is 7.23. Calculate the $[HCO_3^-]$ in the red blood cell cytoplasm assuming equilibration of 46 mmHg P_{CO_2} across the RBC membrane. Convert this to mL of CO_2 per dL of RBC ICF (STPD).
   F. From the results of D and E, calculate the separate contributions of venous and arterial blood RBC HCO_3^- to the total blood CO_2 (sum of dissolved CO_2, HCO_3^-, and carbamino Hb), **in mL CO_2 per dL of blood**, using a hematocrit of 0.45 and RBC water content of 72% of its volume.

G. From the results of C and F, calculate the total CO_2 as HCO_3^- in arterial and venous blood, in $mL\ dL^{-1}$. Assuming a cardiac output, $Q_a = 5\ L\ min^{-1}$, calculate the delivery of CO_2 from tissues to lungs in the form of HCO_3^-.

12. The solubility of CO_2 in water at 37°C is $0.0747\ mL\ dL^{-1}\ mmHg^{-1}$ (see Table 6.3.3). Given a hematocrit of 0.45, a RBC water content of 72% of its volume, and a water content of 93% of the plasma volume:
  A. What is the dissolved CO_2 content of arterial and venous blood? ($P_{a_{CO_2}} = 40$ mmHg and $P_{v_{CO_2}} = 46$ mmHg). This should be in units of mL CO_2 per dL.
  B. If $Q_a = 5\ L\ min^{-1}$, calculate the delivery of CO_2 from tissues to lungs in the form of dissolved CO_2.

13. Assume that the [carbamino Hb] is 0.00123 [Hb][P_{CO_2}] where [carbamino Hb] is in units of mM, [Hb] is in $g\ dL^{-1}$ **of red blood cell volume**, and P_{CO_2} is in mmHg. The Hct = 0.45.
  A. Calculate the concentration of carbamino Hb in arterial and venous blood given $P_{a_{CO_2}} = 40$ mmHg and $P_{v_{CO_2}} = 46$ mmHg, and [Hb] = 15 $g\ dL^{-1}$ **of whole blood**; give this in $mL\ dL^{-1}$.
  B. If $Q_a = 5\ L\ min^{-1}$, calculate the delivery of CO_2 from tissues to lungs in the form of carbamino Hb.

14. Add up the delivery of CO_2 from tissues to lungs in Problems 11−13. Is this reasonable compared to Q_{CO_2}?

15. You are approaching your final exam in Quantitative Physiology and you are nervous and find yourself hyperventilating. Your tidal volume is now 0.6 L and your breathing frequency is 20 min^{-1}. Assume your dead space volume is 150 mL. Normally your tidal volume is 0.5 L, breathing frequency is 12 min^{-1}, and $P_{a_{CO_2}}$ is 40 mmHg.
  A. What is your pulmonary ventilation?
  B. What is your alveolar ventilation?
  C. If your Q_{CO_2} has not changed from 200 mL min^{-1}, what is your new $P_{a_{CO_2}}$?
  D. Based on the normal buffer line in Figure 6.5.3, estimate your plasma pH.
  E. Name your acid−base status.