Chapter 10. Chemical Biosensors
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Blood or Fluid Analysis

- Usually carried out in central labs with problems of time delay costs and potential mislabelling
- Drive toward more bedside or treatment room analysis (OR, ICU, etc)
- Need for continuous or very periodic analysis
- Non-invasive blood analysis (e.g. SaO_2 or So_2)
- Future non-invasive or invasive sensors using electronic or photonic means (glucose for insulin injection control?)

Table 10.1 Critical-Care Analytes and Their Normal Ranges in Blood

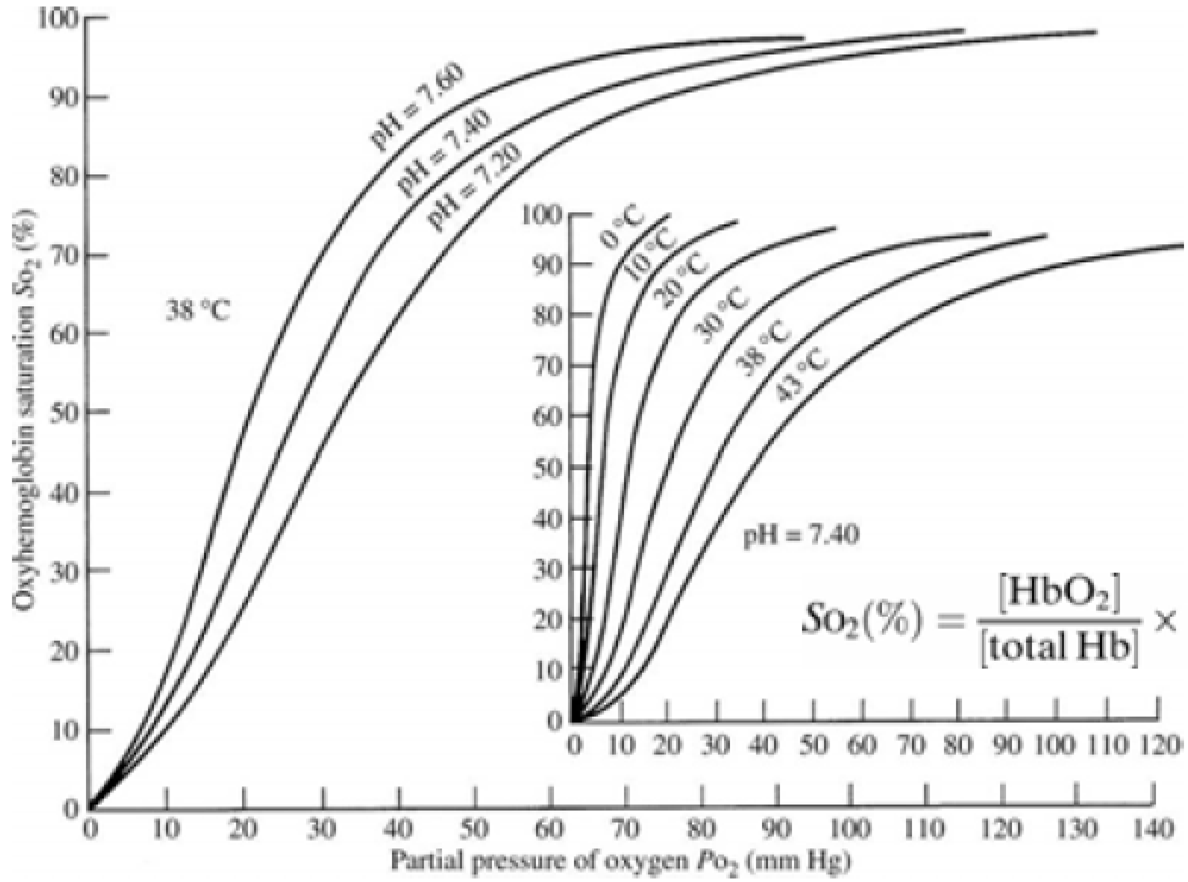
Blood Gases and Related Parameters		Electrolytes		Metabolites	
P_{O_2}	80–104 mm Hg	Na^+	135–155 mmol/l	Glucose	70–110 mg/ 100 ml
P_{CO_2}	33–48 mm Hg	K^+	3.6–5.5 mmol/l	Lactate	3–7 mg/ 100 ml
pH	7.31–7.45	Ca^{2+}	1.14–1.31 mmol/l	Creatinine	0.9–1.4 mg/ 100 ml
Hematocrit	40–54%	Cl^-	98–109 mmol/l	Urea	8–26 mg/ 100 ml
Total hemoglobin	13–18 g/100 ml				
O_2-saturation	95–100%				

SOURCE: M. E. Collison and M. E. Meyerhoff, "Chemical sensors for bedside monitoring of critically ill patients," *Anal. Chem.*, 1990, 62, 425A–437A.

Table 10.1

Measurement of O_2 in Blood

- 98% of O_2 in blood is combined with hemoglobin in red blood cells with 2% directly dissolve in plasma (partial pressure PO_2)
- For young adults normal range of Po_2 in arterial blood is from 90 to 100 mm Hg
- Normal Pco_2 in arterial blood is 35 to 40 mm Hg
- Normal pH (acid-base status) is 7.38 to 7.44
- Decreases in pH associated with decreased rate of CO_2 excretion or production of fixed acid



$$So_2(\%) = \frac{[HbO_2]}{[\text{total Hb}]} \times 100$$

Figure 10.1 The oxyhemoglobin dissociation curve, showing the effect of pH and temperature on the relationship between *S*O2 and *P*O2.

Clinical Blood Gas Levels

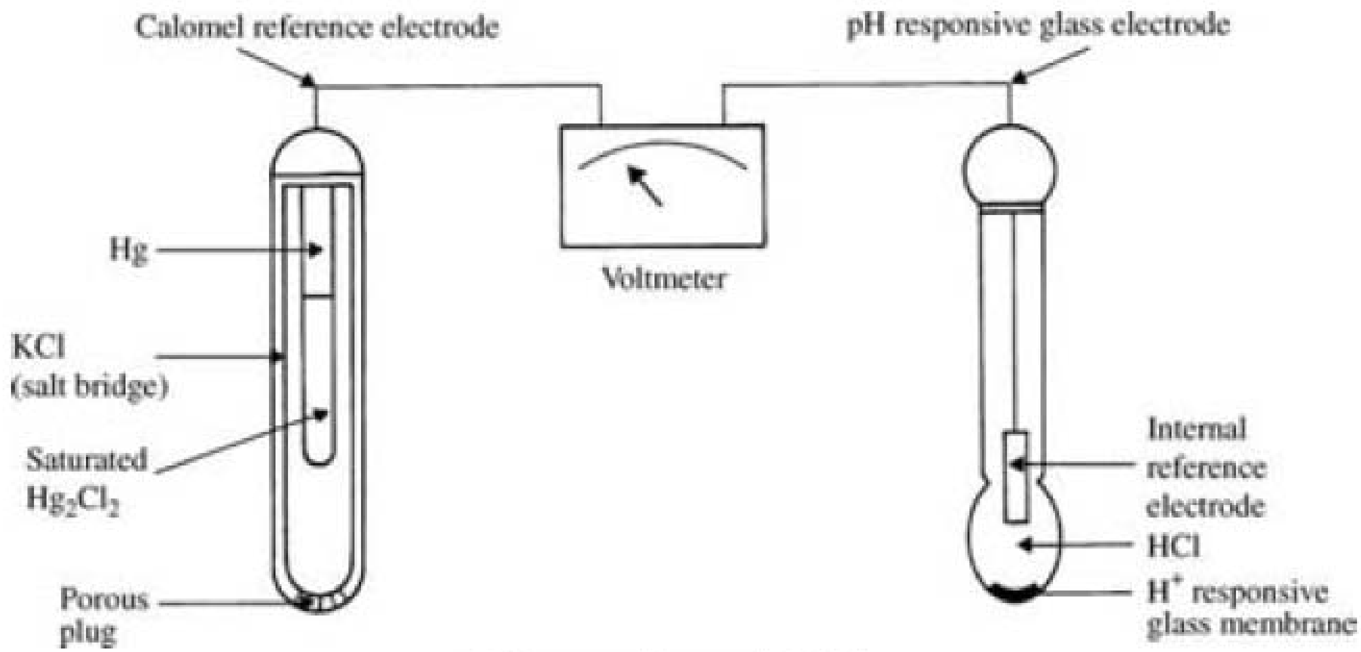
Table 10.2 Examples of Arterial Blood Gases in Different Clinical Situations

Example	PCO_2, mm Hg	pH	PO_2, mm Hg	Interpretation	Likely Causes	Therapy
1	40 ± 3	7.40 ± 0.03	90 ± 5	Normal blood gas		None
2	44 ± 3	7.37 ± 0.03	88 ± 5	Normal blood gas while asleep		
3	22	7.57	106	Hyperventilation	Anxiety	None
4	68	7.10	58	Hypoventilation	Central nervous system depression; blockage of upper airway	Mechanical ventilation; relieve the cause
5	58	7.21	39	Hypoventilation and hypoxemia	Pneumonia; small-airway obstruction; severe asthma	Oxygen; bronchodilators; mechanical ventilation
6	61	6.99	29	Combined respiratory and metabolic acidosis and hypoxemia	Birth asphyxia; near-drowning	Oxygen; mechanical ventilation; buffers?
7	60	7.37	106	Chronic respiratory acidosis with metabolic compensation; patient is receiving supplemental oxygen	Patient has chronic lung disease and is on oxygen	Treat chronic disease; no additional therapy may be necessary
8	29	7.31	106	Metabolic acidosis with respiratory compensation	Diabetic; ketoacidosis; dehydration	Treat the cause; buffers?

SOURCE: B. G. Nickerson and F. Monaco, "Carbon dioxide electrodes, arterial and transcutaneous," in J. G. Webster (ed.), Encyclopedia of Medical Devices and Instrumentation. New York: Wiley, 1988, pp. 564–569.

Electrochemical Sensors (pH)

- In following slide both glass tubes are immersed in fluid (blood)
- Sensor tube has glass membrane that reacts specifically to hydrogen ion [H^+] with each ion injecting a +ve charge into solution of known pH (HCl)
- Action similar to semipermeable membrane of cells and Nernst equation gives the membrane potential 60 mV/pH unit.
- Range of physiological pH is only .06 pH units so meter must measure 0.1 mV accurately
- Reference electrode is Ag-AgCl or calomel electrode (shown). Salt bridge stops saturated Hg_2Cl_2 from mixing with measured solution

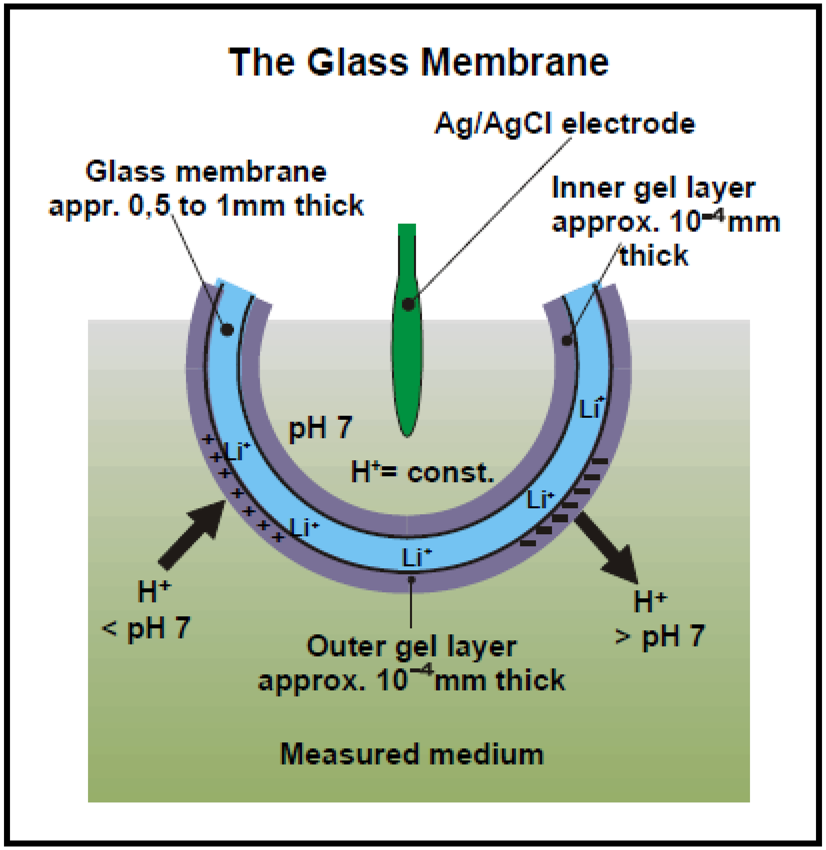


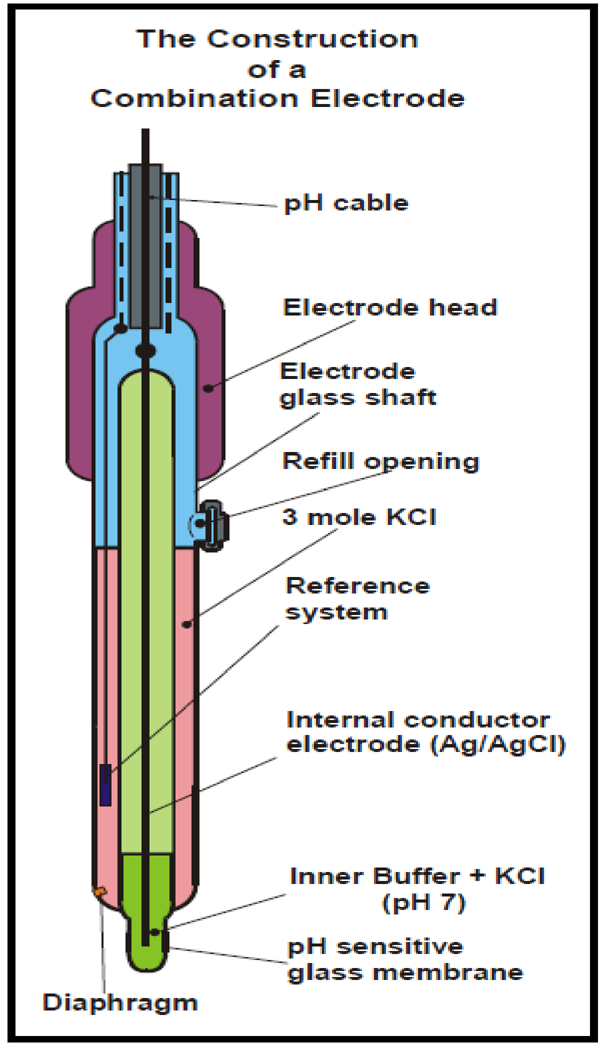
$$pH = -\log_{10}[H^+]$$

Figure 10.2 pH electrode (From R. Hicks, J. R. Schenken, and M. A. Steinrauf, Laboratory Instrumentation. Hagerstown, MD: Harper & Row, 1974. Used with permission of C. A. McWhorter.)

Glass Membrane

- A gel layer forms on both sides of membrane (Li is alkaline ions in glass)





Connecting Electronics

- Electrodes have very high impedance bcause of special glass interface (10 to 100 MΩ)
- Need to compensate for ambient temperature since Nernst equation has a temperature term
- Amplifier needs high input impedance, low bias current, low voltage offset drift

AD549

FEATURES

Ultralow input bias current
- 60 fA maximum (AD549L)
- 250 fA maximum (AD549J)

Input bias current guaranteed over the common-mode voltage range

Low offset voltage
- 0.25 mV maximum (AD549K)
- 1.00 mV maximum (AD549J)

Low offset drift
- 5 μV/°C maximum (AD549K)
- 20 μV/°C maximum (AD549J)

Low power
- 700 μA maximum supply current
- Low input voltage noise

4 μV p-p over 0.1 Hz to 10 Hz

MIL-STD-883B parts available

APPLICATIONS

Electrometer amplifier
Photodiode preamp
pH electrode buffer
Vacuum ion gauge measurement

CONNECTION DIAGRAM

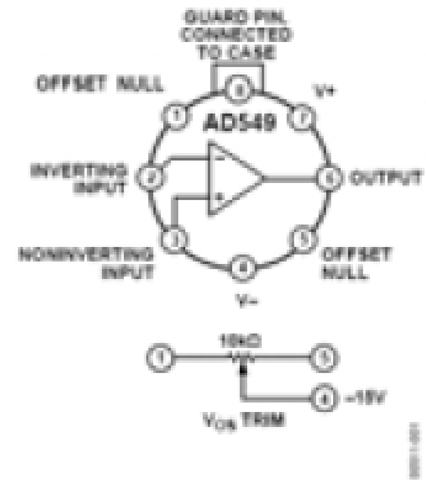


Figure 1.

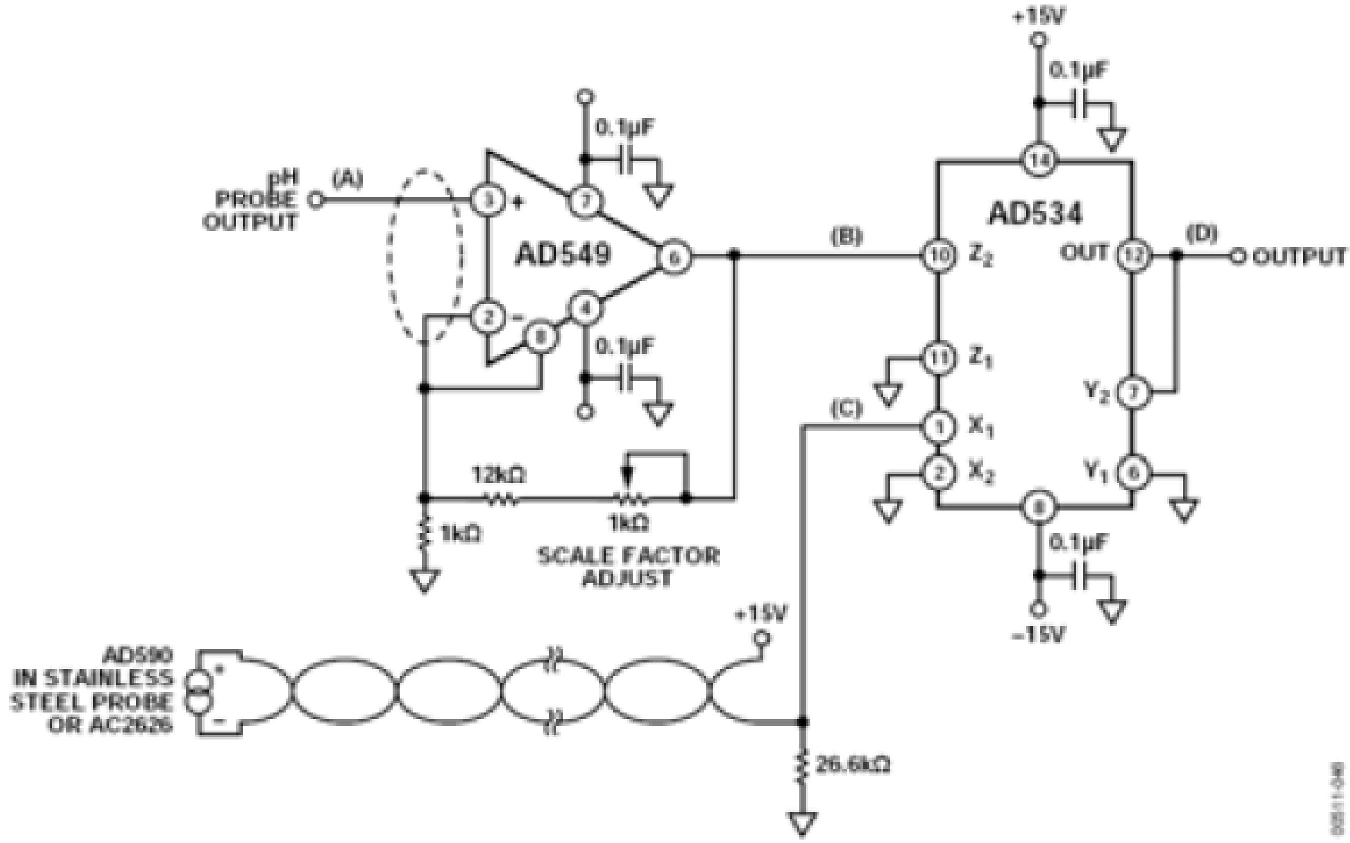
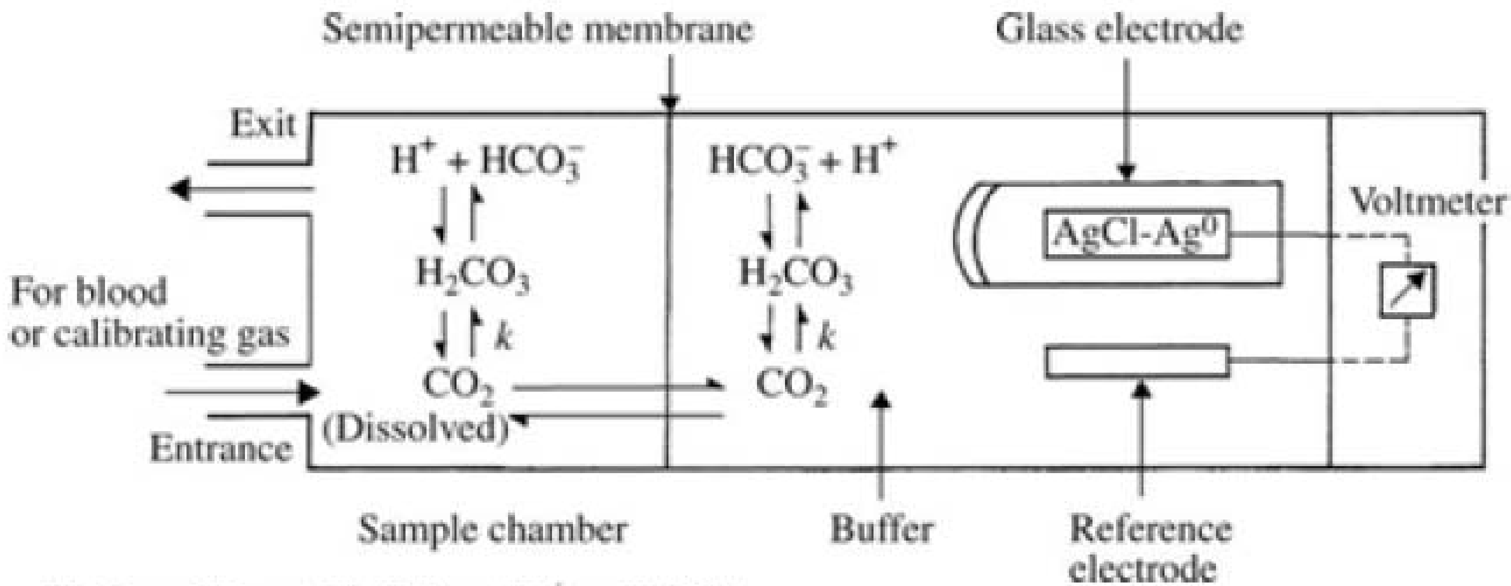


Figure 46. Temperature Compensated pH Amplifier

Electrochemical Sensors (Pco_2)

- Relationship between log Pco_2 and pH is linear over range of 10 to 90 mm Hg
- In following figure first chamber contains fluid (blood) while second chamber has buffer solution of bicarbonate and NaCl
- A pH electrode is placed in second chamber along with the reference electrode
- Chambers separated by a semipermeable membrane (Teflon or silicon rubber) that allows passage of dissolved CO_2 but not H^+ or HCO_3^-



$$H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$[CO_2] = a(P_{CO_2})$$

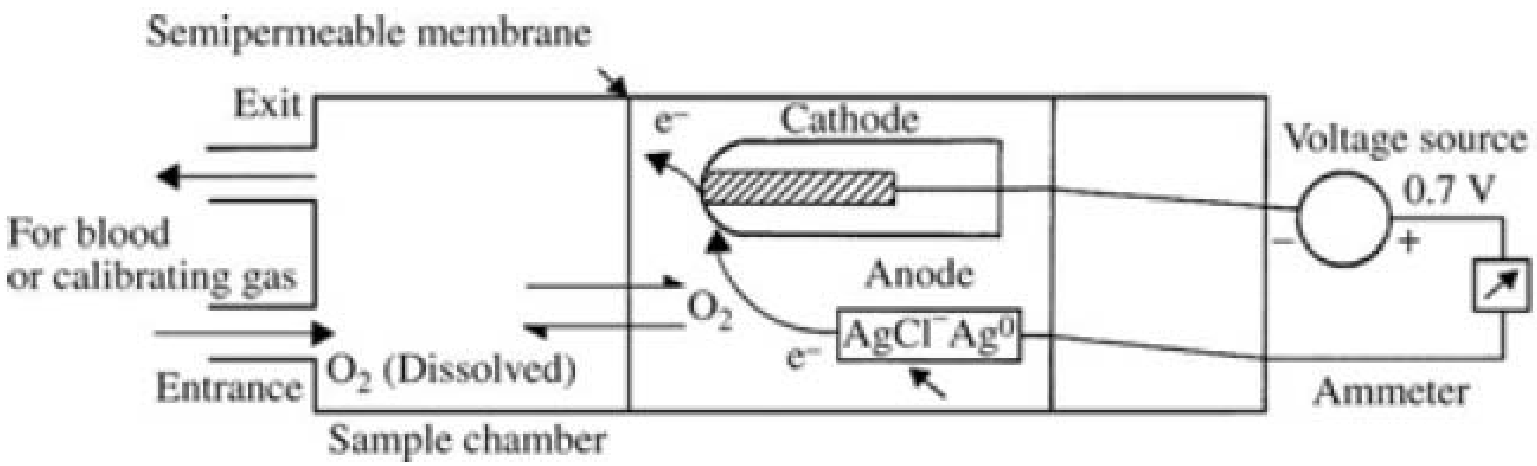
$$\log[H^+] + \log[HCO_3^-] - \log k - \log a - \log P_{CO_2} = 0$$

$$pH = \log[HCO_3^-] - \log k - \log a - \log P_{CO_2}$$

Figure 10.3 *P*CO2 electrode (From R. Hicks, J. R. Schenken, and M. A. Steinrauf, Laboratory Instrumentation. Hangerstown, MD: Harper & Row, 1974. Used with permission of C. A. McWhorter.)

Electrochemical Sensors (Po_2)
(Clark Electrode)

- Oxygen is reduced at the glass coated Pt cathode (4 electrons required)
- Anode is reference electrode where AgCl gives up 4 electrons
- Require polarizing voltage of about 0.7 V to control the reaction
- Membrane is permeable to O_2 and other gases and separates electrodes from measured blood
- Second chamber includes buffering solution



$$O_2 + 2H_2O + 4e^- \rightarrow 2H_2O_2 + 4e^- \rightarrow 4OH^-$$

$$4OH^- + 4KCl \rightarrow 4KOH + 4Cl^-$$

$$4Ag + 4Cl^- \rightarrow 4AgCl + 4e^-$$

Figure 10.4 *P*O2 electrode (From R. Hicks, J. R. Schenken, and M. A. Steinrauf, Laboratory Instrumentation. Hangerstown, MD: Harper & Row, 1974. Used with permission of C. A. McWhorter.)

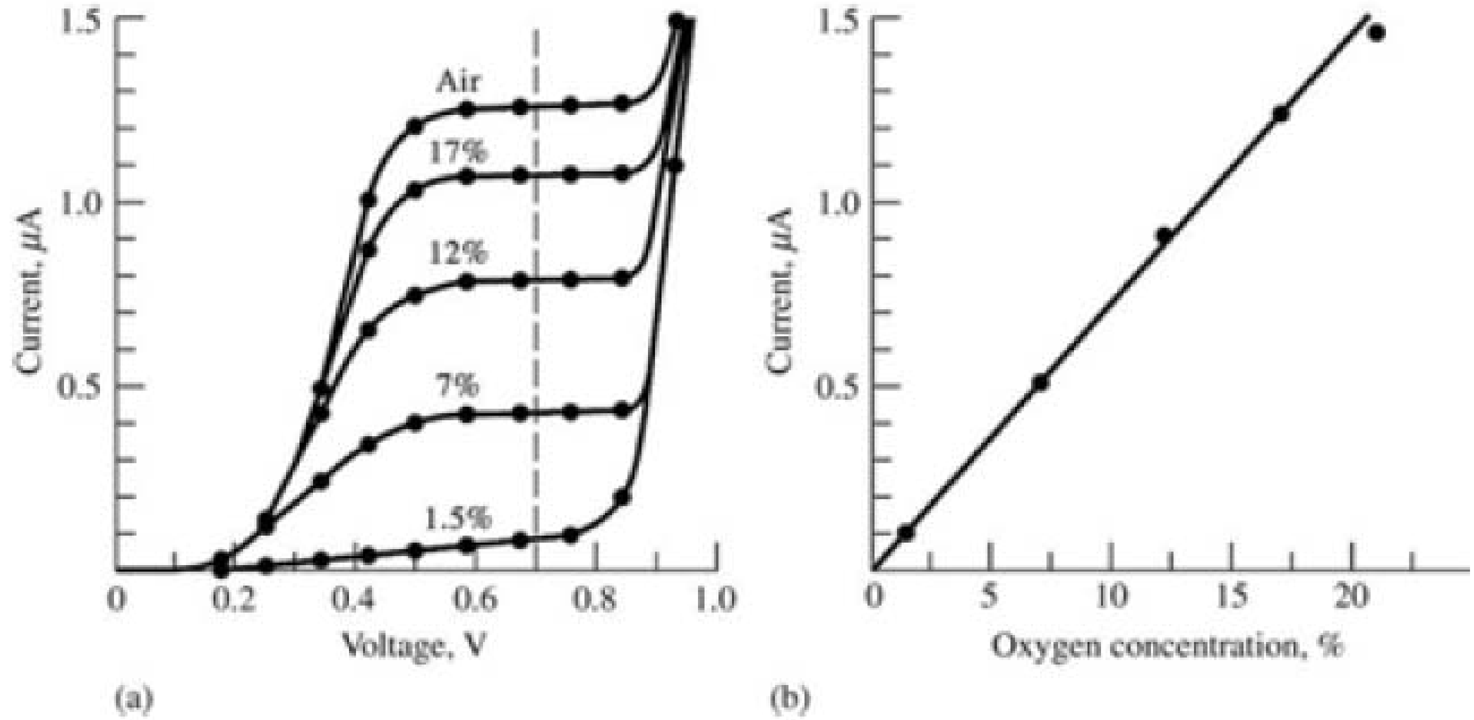


Figure 10.5 **(a) Current plotted against polarizing voltage for a typical *P*O2 electrode for the percents O2 shown. (b) Electrode operation with a polarizing voltage of 0.68 V gives a linear relationship between current output and percent O2.**