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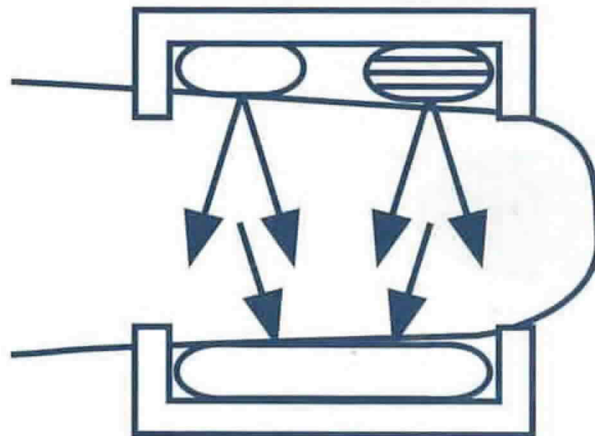

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Design of Pulse Oximeters

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Bristol and Philadelphia

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The Medical Science Series is the official book series of the International Federation for Medical and Biological Engineering (IFMBE) and the International Organization for Medical Physics (IOMP).

IFMBE

The IFMBE was established in 1959 to provide medical and biological engineering with an international presence. The Federation has a long history of encouraging and promoting international cooperation and collaboration in the use of technology for improving the health and life quality of man.

The IFMBE is an organization that is mostly an affiliation of national societies. Transnational organizations can also obtain membership. At present there are 42 national members, and one transnational member with a total membership in excess of 15 000. An observer category is provided to give personal status to groups or organizations considering formal affiliation.

Objectives

- To reflect the interests and initiatives of the affiliated organizations.
- To generate and disseminate information of interest to the medical and biological engineering community and international organizations.
- To provide an international forum for the exchange of ideas and concepts.
- To encourage and foster research and application of medical and biological engineering knowledge and techniques in support of life quality and cost-effective health care.
- To stimulate international cooperation and collaboration on medical and biological engineering matters.
- To encourage educational programmes which develop scientific and technical expertise in medical and biological engineering.

Activities

The IFMBE has published the journal *Medical and Biological Engineering and Computing* for over 34 years. A new journal *Cellular Engineering* was established in 1996 in order to stimulate this emerging field in biomedical engineering. In *IFMBE News* members are kept informed of the developments in the Federation. *Clinical Engineering Update* is a publication of our division of Clinical Engineering. The Federation also has a division for Technology Assessment in Health Care.

Every three years, the IFMBE holds a World Congress on Medical Physics and Biomedical Engineering, organized in cooperation with the IOMP and the IUPESM. In addition, annual, milestone, regional conferences are organized in different regions of the world, such as the Asia Pacific, Baltic, Mediterranean, African and South American regions.

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The administrative council of the IFMBE meets once or twice a year and is the steering body for the IFMBE. The council is subject to the rulings of the General Assembly which meets every three years.

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IOMP

The IOMP was founded in 1963. The membership includes 64 national societies, two international organizations and 12 000 individuals. Membership of IOMP consists of individual members of the Adhering National Organizations. Two other forms of membership are available, namely Affiliated Regional Organization and Corporate Members. The IOMP is administered by a Council, which consists of delegates from each of the Adhering National Organizations; regular meetings of Council are held every three years at the International Conference on Medical Physics (ICMP). The Officers of the Council are the President, the Vice-President and the Secretary-General. IOMP committees include: developing countries, education and training; nominating; and publications.

Objectives

- To organize international cooperation in medical physics in all its aspects, especially in developing countries.
- To encourage and advise on the formation of national organizations of medical physics in those countries which lack such organizations.

Activities

Official publications of the IOMP are *Physiological Measurement, Physics in Medicine and Biology* and the *Medical Science Series*, all published by Institute of Physics Publishing . The IOMP publishes a bulletin *Medical Physics World* twice a year.

Two Council meetings and one General Assembly are held every three years at the ICMP. The most recent ICMPs were held in Kyoto, Japan (1991) and Rio de Janeiro, Brazil (1994). Future conferences are scheduled for Nice, France (1997) and Chicago, USA (2000). These conferences are normally held in collaboration with the IFMBE to form the World Congress on Medical Physics and Biomedical Engineering. The IOMP also sponsors occasional international conferences., workshops and courses.

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PREFACE

Pulse oximetry was introduced in 1983 as a noninvasive method for monitoring the arterial oxygen saturation of a patient's blood. Recognized worldwide as the standard of care in anesthesiology, it is widely used in intensive care, operating rooms, emergency, patient transport, general wards, birth and delivery, neonatal care, sleep laboratories, home care and in veterinary medicine. It provides early information on problems in the delivery of oxygen to the tissue. Those problems may arise because of improper gas mixtures, blocked hoses or airways, inadequate ventilation, diffusion, or circulation, etc. More than 35 companies manufacture and distribute the more than 300 000 pulse oximeters presently in use in the USA.

This book emphasizes the design of pulse oximeters. It details both the hardware and software required to fabricate a pulse oximeter as well as the equations, methods, and software required for effective functioning. Additionally, it details the testing methods and the resulting accuracy. The book should be of interest to biomedical engineers, medical physicists, and health care providers who want to know the technical workings of their measuring instruments.

Chapter 1 reviews the methods of transport of oxygen to the tissue by ventilation, perfusion to the blood, binding to hemoglobin in the red blood cells, and transport through the blood circulation. Chapter 2 describes the problems and diseases that can occur in oxygen transport, which motivate us to measure oxygenation. In chapter 3, we review the many ways oxygenation has been measured in the past, the CO-oximeter used as the gold standard, and provide an introduction to the pulse oximeter.

Chapter 4 begins with Beer's law for the absorption of light by hemoglobin and oxyhemoglobin, and develops the equations required for converting measured light transmission through the tissue to display the hemoglobin oxygen saturation. The light-emitting diodes, which alternately emit red light at 660 nm and infrared light at 940 nm and require precise wavelength control, are described in chapter 5. Chapter 6 covers the variety of light sensors, with emphasis on the single photodiode typically used.

Chapter 7 details the design of reusable and disposable probes and their flexible cables. The probes can transmit light through either the finger or ear, or use reflected light from the scalp or other skin surface. Chapter 8 covers the hardware, with block diagrams showing how red and infrared signals are amplified to yield the ratio of pulse-added red absorbance to the pulse-added infrared absorbance. These signals are used to control light-emitting diode levels and the ratio is used to calculate oxygen saturation. The flow charts and

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algorithms to perform oxygen saturation calculations are given in chapter 9, with worked out examples. Synchronization with the electrocardiogram improves accuracy during patient movement.

Chapter 10 describes ways to test performance of pulse oximeters: the technician's finger, electronic simulators, *in vitro* test systems, and optoelectronic simulators. In chapter 11, we find the resulting accuracies and descriptions of the inaccuracies caused by alternative forms of hemoglobin, optical and electrical interference, colored nail polish, etc. Chapter 12 describes the interface between the pulse oximeter, the operator, and the external world. Chapter 13 covers the many applications for pulse oximetry in intensive care, operating rooms, emergency, patient transport, general wards, birth and delivery, neonatal care, sleep laboratories, home care, and in veterinary medicine.

A glossary provides definitions of terms from both the medical and the engineering world. We also provide instructional objectives as a means of provoking further thought toward learning the information. We gleaned much of the design information from operator's manuals and from patents; periodical literature provided more general information. Rather than giving an exhaustive list of references, we have included review articles and books that can serve as an entry into further study. All contributors are from the Department of Electrical and Computer Engineering at the University of Wisconsin, Madison, WI, USA, and worked as a team to write this book. We would welcome suggestions for improvement of subsequent printings and editions.

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August 1997

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CHAPTER 1

NORMAL OXYGEN TRANSPORT

Susanne A Clark

Oxygen is vital to the functioning of each cell in the human body. In the absence of oxygen for a prolonged amount of time, cells will die. Thus, oxygen delivery to cells is an important indicator of a patient's health.

Several methods have been developed to analyze oxygen delivery. Pulse oximetry is a common, noninvasive method used in clinical environments. This book discusses pulse oximetry, from applications to signal processing. Before continuing, it is essential to understand normal oxygen transport, which is the subject of this chapter.

Oxygen delivery to cells requires the use of the respiratory system as well as the circulatory system. Ventilation is the initial step, moving air into and out of the lungs. Within the lungs, gas exchange occurs. Oxygen is diffused into the blood, while carbon dioxide, a byproduct of cellular respiration, diffuses into the lungs. The oxygenated blood circulates around the body until it reaches oxygen depleted areas, where oxygen is diffused to cells, and carbon dioxide is transferred to the blood returning to the lungs. The ventilatory process is controlled by neurons in the brain stem. The circulatory system also can modulate cardiac output to effect the oxygen delivery.

1.1 VENTILATORY CONTROL

Ventilation is the involuntary, rhythmic process of moving air in and out of the lungs. This process is controlled by respiratory neurons in the brain stem. The respiratory neurons excite motor neurons, which in turn cause the movement of respiratory muscles. The output of the respiratory neurons is modulated by *chemoreceptors* and *mechanoreceptors*.

1.1.1 Neural control

The respiratory neurons in the brain stem are responsible for the pattern generation in normal breathing. The rate and depth of *ventilation* are modulated by these neurons. The respiratory neurons excite motor neurons in the spinal cord. The excitation of the motor neurons causes the contraction of the diaphragm, pectoral muscles, and intercostal muscles. All of these muscles

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combine efforts pulling the ribcage up and out, expanding the lungs, causing inspiration. The activity of respiratory neurons is thought to occur spontaneously, with occasional inhibition allowing the respiratory muscles to relax. This causes the rib cage to contract which yields expiration.

1.1.2 Respiratory feedback

The brain stem receives feedback from many mechanical and chemical receptors. The input from these neurons is analyzed by the respiratory neurons to determine the appropriate rate and depth of ventilation. Mechanoreceptors give feedback related to mechanical aspects of breathing. For example, stretch receptors are mechanoreceptors that provide feedback on the expansion of the lung and chest during both inspiration and expiration. An inflation index is the level of feedback provided that causes inhibition of inspiration, preventing overinflation of the lungs. A deflation index serves a similar purpose in expiration, hindering the collapse of the lungs.

Chemoreceptors provide information on the level of carbon dioxide, oxygen, and hydrogen ions in the blood. Chemoreceptors are located in the carotid arteries, as the oxygenated blood is being sent to the brain, and in the aorta, shortly after the oxygenated blood is being pumped from the heart to the body. Oxygen levels under normal conditions are high in the systemic arteries, and carbon dioxide and hydrogen levels are low.

The brain stem must process all of the information it receives and no single factor controls ventilation. Under normal breathing conditions, the brain stem is most sensitive to the levels of carbon dioxide and hydrogen. The oxygen concentrations are only important when the level is extremely low. Consider an extremely high level of carbon dioxide present in the blood, such as would occur during maximal exercise. However, stretch receptors indicate that the lung and chest are at maximal expansion, meaning the inflation index has been reached. Thus, the rate of breathing increases to compensate without a proportional increase in chest and lung expansion.

An unusual feature of ventilation is that breathing can be brought under voluntary control to some extent. However, it is not possible to commit suicide by refusing to breathe. Once the individual loses consciousness, the input from chemoreceptors will cause ventilation to be restored.

1.2 VENTILATORY MECHANICS

Ventilatory mechanics are based on the principle of air flow from areas of high pressure to areas of lower pressure. The contraction of the intercostal muscles, pectoral muscles, and the diaphragm causes the thoracic cavity to expand, decreasing the pressure in the thoracic cavity. The atmospheric pressure is higher than the pressure inside the lungs, causing air to flow into the lungs, which is termed inspiration. The relaxation of the intercostal muscles and the diaphragm causes the volume of the lungs to decrease, increasing the pressure in the thoracic cavity. As the pressure in the lungs increases reaching levels above the atmospheric pressure, air flows out of the lungs, which is referred to as expiration.

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1.2.1 Inspiration

As discussed previously, the brain stem excites motor neurons in the spinal cord, which, in turn, causes the contraction of the diaphragm, the pectoral muscles, and intercostal muscles, located between the ribs. The contraction of the diaphragm causes the flattening and lengthening of the thoracic cavity. The intercostal muscles and pectoral muscles pull the ribcage up and out. Both of these sets of muscles work to expand the lungs. This means that pressure will be reduced within the lungs, since the air present will have a greater volume to expand in. This will create a pressure differential between the air outside the body and the air inside the body. Thus, air flows into the body (see figure 1.1(*a*)).

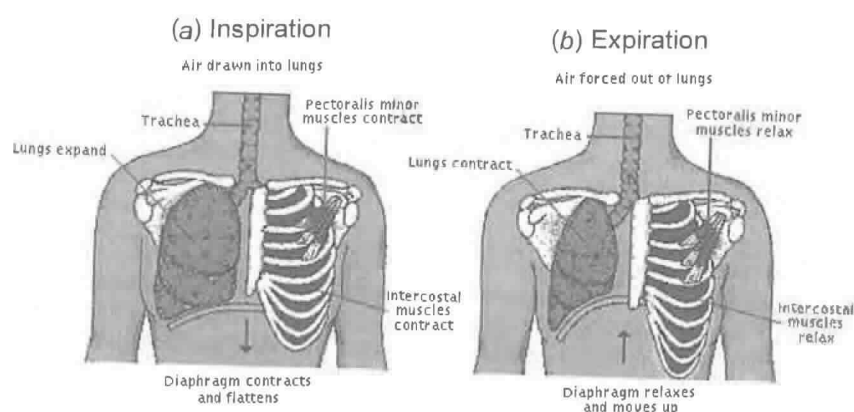

Figure 1.1 During inspiration, (*a*), the diaphragm, intercostal muscles and pectoralis minor muscles contract, causing the lungs to expand and air to enter the lungs. As the diaphragm, intercostal muscles and pectoralis minor relax, the lungs contract, causing air to leave the lungs (*b*), which is referred to as expiration (from Microsoft Encarta).

Air travels through the nasal cavity. Cilia are microscopic hairs within the nasal cavity that act to eliminate pollutants from entering the respiratory tract. Air and food both go through the *pharynx*. When food is swallowed, the epiglottis (part of the *larynx*), pharynx, and mouth cavity work together to shut off the opening to the trachea to avoid the entry of food particles into the lungs.

The larynx is commonly referred to as the voice box. Besides assisting with separation of food particles from air, the larynx contains the cricoid cartilage which reinforces the airway and assists in keeping it open. The larynx also contains the vocal cords. As air vibrates over the vocal cords, a sound is produced. The variation in elasticity and tension of the vocal cords determines the pitch of the sound.

The trachea is composed of ribbed cartilage which extends 10 cm to the bronchi. The trachea also contain cilia which act to filter out further pollutants. Two *bronchi* provide a path to each *lung* (see figure 1.2).

Each bronchus divides into even narrower *bronchioles*. Each bronchiole has five or more *alveolar ducts* at the end, which, in turn, end in *alveolar sacs*. Each alveolar sac contain several *alveoli* (see figure 1.3). Alveoli are the site of gas exchange.

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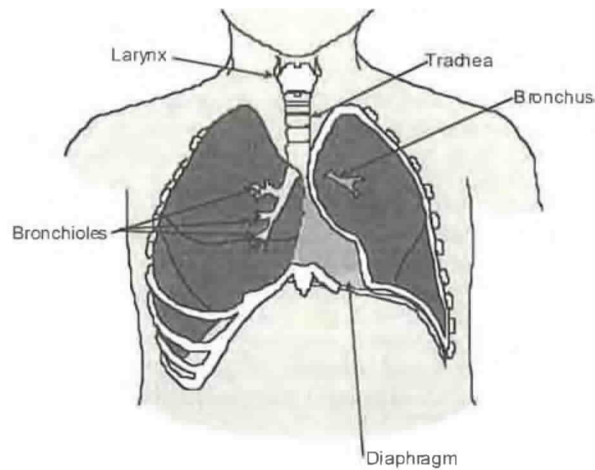

Figure 1.2 Air travels through the nasal cavity, into the pharynx, trachea, bronchi, and finally the lungs. The bronchi, bronchioles, alveolar ducts and alveoli compose the pulmonary tree with its branch like system (adapted from Corel Corporation).

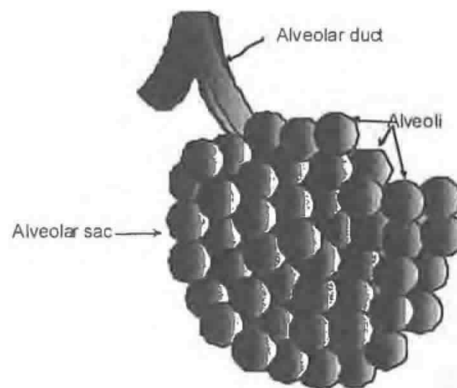

Figure 1.3 Ten or more alveoli are in one alveolar sac (adapted from Corel Corporation).

1.2.2 Expiration

Neurons in the brain stem cyclically inhibit the motor neurons in the spinal cord that cause muscle contraction in the diaphragm, the pectoral muscles, and intercostal muscles. The muscles then relax, causing the rib cage to contract, decreasing the amount of air space. This causes air to flow out of the lungs when the pressure inside the lungs is greater than the pressure outside the lungs (see figure 1.1(*b*)). Usually only 10% of the total lung volume is exchanged in normal breathing. With deeper, more rapid breathing, the turbulence of the air flow increases, causing greater resistance to airflow.

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1.3 DIFFUSION TO BLOOD

The process of ventilation provides a continuous supply of fresh air in the lungs. After oxygenated blood has been circulated through the body, it is brought back to the lungs through arterial capillaries to exchange gases, receiving oxygen and ridding itself of carbon dioxide. Blood is reoxygenated and is then recirculated through the body.

Gas exchange occurs through the process of diffusion. *Diffusion* is the net movement of particles from an area of higher *partial pressure* to a region of lower partial pressure through a process of random motion. The actual gas exchange to the blood takes place through the process of diffusion in the *alveoli*.

1.3.1 The alveoli

The alveoli are surrounded by large *pulmonary* capillary beds. Since diffusion can only occur over a distance of 1 mm, the gas exchange takes between the two cells between the capillary and the alveolus, a distance of only 0.5 μm. The 600 million alveoli each adult has provide 70 m^2 of surface area for gas exchange (Curtis and Barnes 1989).

1.3.2 Gas exchange

Air in the alveoli has a higher partial pressure of oxygen and a lower partial pressure of carbon dioxide than the aortic blood. The pressure gradient causes diffusion to occur. The net movement of carbon dioxide will be towards the alveoli and the net movement of oxygen towards the blood (see figure 1.4). The blood then returns to the heart via a pulmonary venule to be pumped out to the rest of the body. Other gases may diffuse as a result of the partial pressure gradient between the air in the alveoli and the pulmonary arterial blood.

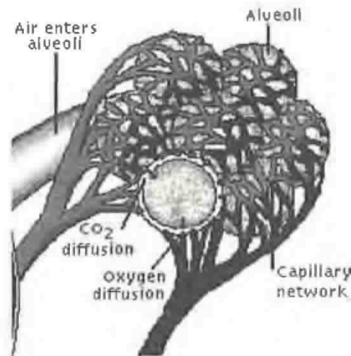

Figure 1.4 The capillaries surround the alveoli, providing the close proximity necessary for diffusion. Carbon dioxide diffuses from the capillary into the alveoli and oxygen diffuses into the blood (from Microsoft Encarta).

The partial pressure gradient of arterial (a) versus alveolar (A) pressure is affected by the concentration of carbon dioxide and water in the alveoli. The alveolar partial pressure of oxygen is

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$$P_AO_2 = (P_{atm} - PH_2O)F_iO_2 - P_aCO_2/0.8 \quad (1.1)$$

where atmospheric pressure P_{atm} is typically 760 mm Hg (101 kPa), the water vapor pressure PH_2O is 47 mmHg (6.3 kPa) at 37 °C, the fraction of inspired O_2, F_iO_2 is 0.21 with room air, P_aCO_2 is the arterial carbon dioxide partial pressure, and 0.8 is the normal *respiratory quotient*. The respiratory quotient is the ratio of volume of CO_2 produced per volume of O_2 consumed.

The rate of gas movement is determined by the pressure gradient, temperature and path length over which the gas exchange occurs. This is defined as

$$\dot{V} = \frac{T\Delta P}{L} \times D \quad (1.2)$$

where $\dot{V}$ is the volume rate of gas exchange, ΔP is the pressure gradient, T is the absolute temperature, L is the path length, and D is a diffusion coefficient for a specific material.

In a living adult, it is not realistic to measure the path length or surface area. Thus, a diffusing capacity of the lung is defined to provide a quantitative measure of the effectiveness of *respiration*. This is defined as

$$D_L = \frac{\dot{V}}{\Delta P} \quad (1.3)$$

where D_L is the diffusing capacity of the lung (Ruch and Patton 1965).

1.4 BIND TO HEMOGLOBIN

Gases are not particularly soluble in blood, which is composed mostly of water. Thus, for effective oxygen transport, a secondary method of transport is required. The compound hemoglobin provides a binding mechanism that allows oxygen to be transported through the blood. *Hemoglobin* plays an essential role in transporting the necessary amount of oxygen to the body. For the same amount of plasma, 65 times more oxygen can be transported with hemoglobin than would be possible without hemoglobin.

1.4.1 Characteristics of hemoglobin

Hemoglobin is a respiratory pigment contained within red blood cells. One red blood cell contains approximately 265 million molecules of hemoglobin (Curtis and Barnes, 1989). Hemoglobin is composed of *heme* units, which are molecules containing iron, and *globin* units, *polypeptide* chains. One hemoglobin molecule contains four heme and four globin units. Each hemo and globin unit can carry one molecule of oxygen. Thus, one hemoglobin molecule can carry four molecules of oxygen (see figure 1.5).

As respiratory pigment, hemoglobin changes color when oxygenated. An oxygenated hemoglobin molecule is bright red, while a deoxygenated hemoglobin molecule, a hemoglobin molecule without oxygen, is dark red. This color change is used in the application of pulse oximetry to measure hemoglobin oxygen saturation.

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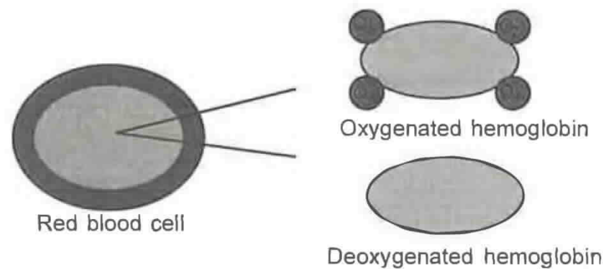

Figure 1.5 Hemoglobin molecules are contained within red blood cells. Each red blood cell contains approximately 265 million molecules of hemoglobin.

After a completely deoxygenated hemoglobin molecule combines with one oxygen molecule, it has a greater affinity for the second oxygen molecule. This is true for each additional oxygen molecule. The reverse process is also true. After the first oxygen molecule is released from the hemoglobin molecule, it is more likely to release the second oxygen molecule. Therefore, the oxyhemoglobin dissociation curve, which relates to the partial pressure of oxygen in the blood, is not a straight line, but a sigmoid.

1.4.2 Oxyhemoglobin dissociation curves

The oxyhemoglobin dissociation curve is the relationship between the partial pressure of oxygen in the blood and the percentage of oxygen bound to hemoglobin compared to the maximum (see figure 1.6). Factors such as decreasing carbon dioxide concentration, increasing pH, and decreasing temperature will shift the curve toward the left. A left-shifted curve implies that the hemoglobin molecules will be more saturated at a lower partial pressure of oxygen.

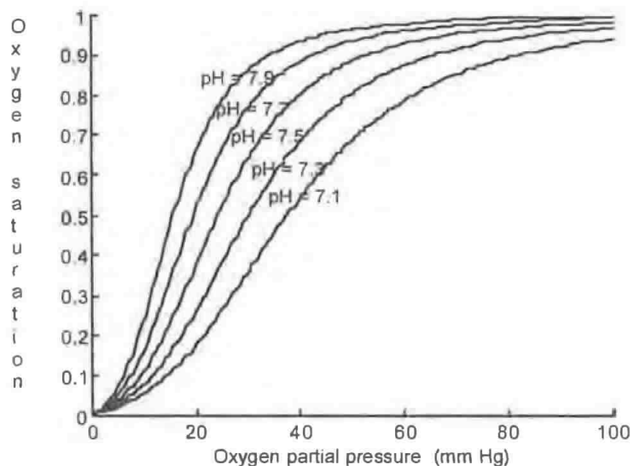

Figure 1.6 Increasing pH causes the oxyhemoglobin dissociation curve to shift to the left at a constant temperature of 37 °C.

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A fetus has a oxyhemoglobin dissociation curve that is to the left of the mother's. This means that the fetus has a greater affinity for oxygen and will take oxygen from the mother's blood to meet its own need.

The volume of oxygen carried by hemoglobin per 100 mL of blood can be defined as follows:

$$C_{HbO_2} = 1.37 \times Hb \times S_aO_2 \tag{1.4}$$

where C_{HbO_2} is the volume of oxygen carried by hemoglobin per unit of 100 mL of blood and is typically around 19 mL O_2/100 mL blood, 1.37 is the number of mL of oxygen bound to 1 g of fully saturated hemoglobin, Hb is the weight of hemoglobin, typically around 14 g Hb/100 mL blood, and S_aO_2 is the percentage of saturation of hemoglobin in arterial blood (Payne and Severinghaus 1986).

1.5 DISSOLVED IN PLASMA

Most of the oxygen transported by the body is bound to hemoglobin, but some oxygen is also dissolved in plasma. The total oxygen content of the blood is the sum of the bound oxygen and the dissolved oxygen.

Hemoglobin increases the amount of oxygen transported to the body by 65 times the amount carried by a specified volume of blood, but some oxygen is still carried dissolved in plasma. The volume of dissolved oxygen per 100 mL of blood is defined as

$$C_DO_2 = 0.003 P_aO_2 \tag{1.5}$$

where C_DO_2 is the volume of dissolved oxygen in blood, 0.003 is the solubility of oxygen in blood as the percent by volume per mmHg, and P_aO_2 is the partial pressure of oxygen in the arteries. C_DO_2 is typically around 0.3 mL O_2/100 mL blood. It is significantly smaller than the bound oxygen content of blood, typically 19 mL O_2/100 mL blood. The oxygen content of the blood is the sum of the oxygen bound to hemoglobin and the oxygen dissolved in the plasma:

$$C_AO_2 = C_{HbO_2} + C_DO_2. \tag{1.6}$$

1.6 CIRCULATION

Once oxygen has been diffused to the blood, it is returned the heart. The *circulatory system* serves to transport oxygenated blood to the cells in the body. The heart is the primary pumping mechanism for transporting blood through the body.

1.6.1 The heart

Blood is pumped through body by the heart. The contraction of the heart is controled by a series of electrical impulses, originating from the sinoatrial node (SA node) and travels to the atrioventricular node (AV node), causing the polarization and depolarization of the muscle fibers of the heart. These electrical impulses can be recorded as the electrocardiogram (see figure 1.7).

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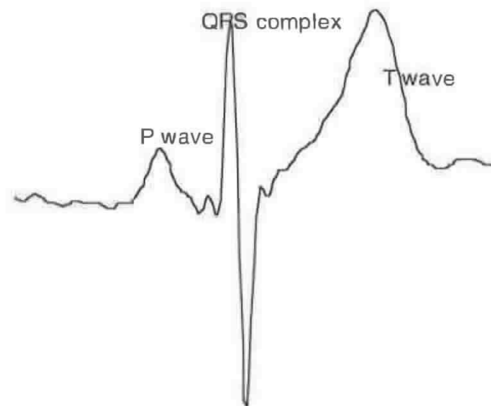

Figure 1.7 The P wave is caused by the depolarization of the atrial fibers just prior to contraction. The QRS complex is caused by the depolarization of the ventricles, causing the contraction of the ventricles. The T wave is caused by the polarization of the ventricles as the muscles relax. The polarization of the atrial fibers occurs simultaneously with the QRS complex and is obscured by the contraction of the larger muscle fibers in the ventricles. The peak of the QRS complex is the R wave. The R–R interval between consecutive heartbeats is used to calculate the heart rate.

1.6.2 Pulmonary circulation

The heart serves as the pumping mechanism for the blood. Blood that is oxygen depleted is pumped from the right *ventricle* of the heart to the lungs. The pulmonary arteries branch into smaller arterioles and eventually into arterial capillaries, which have a thickness of only one cell. This is where gas exchange occurs between the alveoli and the capillaries and blood is reoxygenated. Blood is then returned via pulmonary ventral capillaries to larger venules and eventually pulmonary veins. The pulmonary veins return blood to the left *atrium* of the heart.

1.6.3 Systemic circulation

Reoxygenated blood is returned to the heart in the left atrium. It is then pumped from the left ventricle via the *systemic* arteries to the body. Blood pressure within the arteries varies throughout a single heartbeat, reaching a maximum at systole, caused by the contraction of the ventricles, and a low at diastole, after the ventricles have relaxed. The systemic arteries also branch into smaller arterioles and even smaller capillaries. Oxygen is then exchanged with the tissues of the body. The blood, depleted of oxygen, is then returned via venal capillaries, venules, and veins to the right atrium of the heart where it is again reoxygenated (see figure 1.8).

1.6.4 Cardiac output

Mechanical and chemical stimuli are processed in the brain and provide feedback to the SA node and the AV node which control heart rate and stroke volume. The *cardiac output* (CO) of the heart is the product of the stroke volume (SV) and the

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heart rate (HR). The *cardiac index* (CI) is the cardiac output normalized by *body surface area* (BSA). A typical CI is in the range of 3 to 3.4 L/(min m^2). Normalization of the cardiac output allows comparisons related to circulation of people of varying sizes.

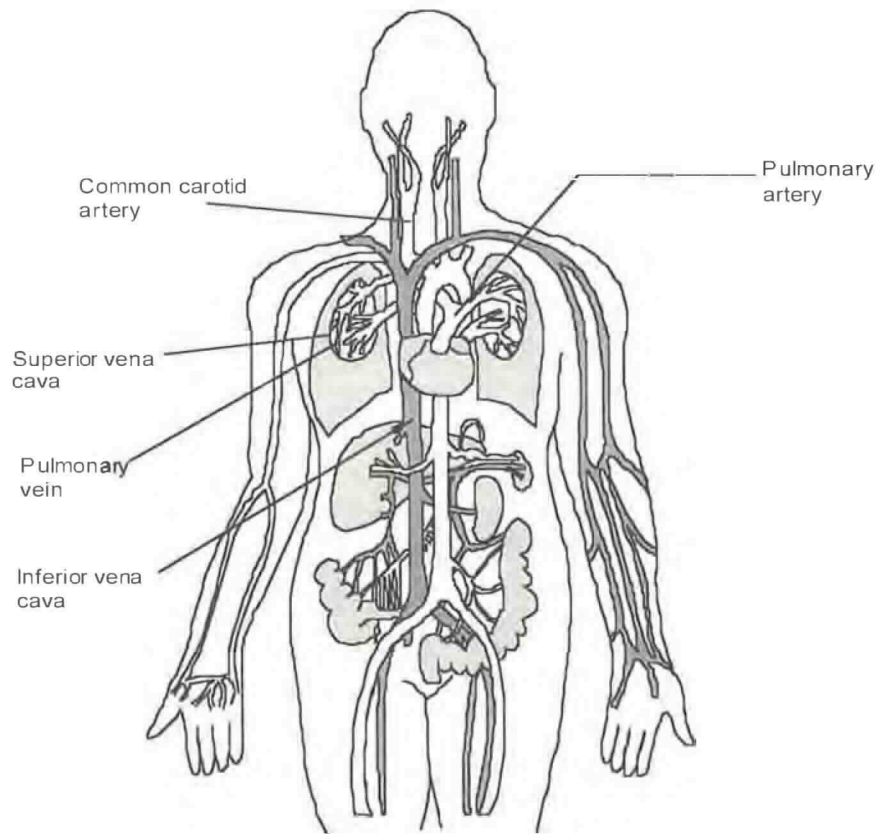

Figure 1.8 The right atrium receives blood from two veins, the superior vena cava and the inferior vena cava. The right ventricle pumps blood through the pulmonary artery, which sends the blood to the lungs to be oxygenated. The oxygenated blood returns to the heart via the pulmonary veins, where it pumped by the left ventricle to be distributed to the rest of the body (adapted from Corel Corporation).

1.7 DIFFUSION TO TISSUE

Diffusion occurs over a distance of about 1 mm. Thus, once blood is oxygenated, although it may pass through oxygen depleted tissue, oxygen does not diffuse until it reaches the capillaries with one cell thickness in the wall. Oxygen diffuses into the *interstitial fluid* and into the cells.

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1.7.1 Diffusion into interstitial fluid and cell

Once blood reaches the systemic capillaries, the surrounding tissue usually has a lower partial pressure of oxygen than that of the blood. Oxygen diffuses into the surrounding tissue. When the tissue has a higher metabolic rate, the difference in partial pressure is greater, and more oxygen is released using the steep part of the oxyhemoglobin dissociation curve. While oxygen diffuses into the interstitial fluid, carbon dioxide diffuses into the blood. Once the oxygen is near the cell, it diffuses through the cell membrane.

1.7.2 Oxygen delivered

The oxygen delivery index (D_IO_2) is defined as

$$D_IO_2 = C_aO_2 \times CI \times 10 \tag{1.7}$$

which is typically 550 to 650 mL/(min m^2). This is a measure of the amount of oxygen available to tissue. The oxygen consumption is a measure of the oxygen diffused into the tissue. It is defined as

$$CI \times (C_aO_2 - C_vO_2) \tag{1.8}$$

where C_vO_2 is the oxygen content of the venous blood. A normal value for oxygen delivery is 115 to 165 mL/(min m^2). This means that not all of the available oxygen diffuses into the tissue (Payne and Severinghaus 1986).

1.7.3 Myoglobin

Myoglobin is a respiratory pigment found in muscles, which is responsible for the reddish brown color of the muscle cells. It has a greater affinity for oxygen than hemoglobin, its oxyhemoglobin dissociation curve is left-shifted, and will not release oxygen under the same conditions as hemoglobin in the blood. Only when the partial pressure of oxygen in the surrounding tissue is below 20 mmHg, such as in exercise, does myoglobin release its stored oxygen. Thus, myoglobin reduces the need for oxygen delivery to muscle tissue beds under extreme conditions, but can only supply a limited amount of oxygen for a short period of time (Hole 1981).

1.8 USE IN CELL

The purpose of respiration is to bring oxygen to cells for cellular respiration. The cells then use oxygen to in turn generate energy. Although a cell may survive for a short time without oxygen, producing energy through anaerobic methods, each individual cell must have oxygen.

Cellular respiration involves the breakdown of molecules, glucose, and releasing energy from them. This process involves oxidation and reduction chemical reactions. *Oxidation* is the loss of an electron, releasing energy, and *reduction* is the gain of an electron. Oxygen atoms serve to attract electrons. Oxygen is needed by the cell to oxidize glucose to release energy. The simplified

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equation for the complex chemical reactions, involving the *Kreb's Cycle*, taking place is

$$\text{glucose} + \text{oxygen} \rightarrow \text{carbon dioxide} + \text{water} + \text{energy} \quad (1.9)$$

where carbon dioxide and water are byproducts of the chemical reaction. Energy is released in the form of *ATP*, a source of cellular energy used in various metabolic processes, and heat, which is lost.

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Ruch T C and Patton H D (eds) 1965 *Physiology and Biophysics* 19th edn (Philadelphia, PA: Saunders)

INSTRUCTIONAL OBJECTIVES

1.1 Describe how the body accommodates for the increased demand for oxygen during exercise.
1.2 Describe how the respiratory system provides for gas exchange.
1.3 Describe the cardiovascular system and its role in transporting oxygen.
1.4 Explain the difference between oxygen content, oxygen saturation, and partial pressure of oxygen.
1.5 Describe the oxyhemoglobin dissociation curve, and factors which can shift the curve.
1.6 Describe the process of diffusion and its role in respiration.
1.7 Describe the neurological control of ventilation.
1.8 Explain why hemoglobin is required for oxygen transport.
1.9 Given alveolar gas concentration, calculate P_aO_2.
1.10 Given P_aO_2, S_aO_2, Hb, calculate C_aO_2.
1.11 Write the chemical equation for the use of oxygen in the cell.
1.12 Describe the muscles used for ventilation.
1.13 Describe the air flow resistance between the alveoli and the mouth.

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CHAPTER 2

MOTIVATION OF PULSE OXIMETRY

Daniel J Sebald

Pulse oximeters have been commercially available for a little more than the last decade and have seen a tremendous growth in popularity becoming a quasi-standard, if not standard, monitoring device in hospital critical care units and surgical theaters. The instrument transcutaneously estimates oxygen saturation of arterial blood and provides vital information about the cardiorespiratory function of the patient. Pulse oximetry provides an empirical measure of arterial saturation. However, with state-of-the-art instrumentation and proper initial calibration, the correlation between the pulse oximeter measurement, S_pO_2, and arterial blood's actual oxygen saturation, S_aO_2, is adequate—generally less than 3% discrepancy provided S_aO_2 is above 70% (Severinghaus and Kelleher 1992)—for medical applications where detecting hypoxemia is essential. Quick acceptance of pulse oximetry as a monitoring device for surgery, recovery, critical care and research has shown that for determining hypoxemia any reasonably small loss in accuracy that may be attributed to measuring arterial oxygen saturation transcutaneously is outweighed by the advantages of noninvasiveness and continuous, immediate availability of data. In applications where accuracy is paramount, such as in detecting hyperoxia, the use of pulse oximetry is not so clear and remains to be decided in the medical community. However, mounting evidence suggests that the pulse oximeter is not very useful in these situations. Nonetheless, the importance of detecting hypoxemia, where pulse oximetry is best suited, is so great that the instrument plays a critical role in medicine despite its limitations.

2.1 PULSE OXIMETER PRINCIPLES

A pulse oximeter shines light of two wavelengths through a tissue bed such as the finger or earlobe and measures the transmitted light signal. The device operates on the following principles:

1. The light absorbance of oxygenated hemoglobin and deoxygenated hemoglobin at the two wavelengths is different. To be more precise, the set of associated extinction coefficients for the absorption of light for these wavelengths is linearly independent with great enough variation for adequate sensitivity but not so large that the blood appears opaque to either of the

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light sources. This model assumes that only oxygenated and deoxygenated hemoglobin are present in the blood.

2. The pulsatile nature of arterial blood results in a waveform in the transmitted signal that allows the absorbance effects of arterial blood to be identified from those of nonpulsatile venous blood and other body tissue. By using a quotient of the two effects at different wavelengths it is possible to obtain a measure requiring no absolute calibration with respect to overall tissue absorbance. This is a clear advantage of pulse oximeters over previous types of oximeters.

3. With adequate light, scattering in blood and tissue will illuminate sufficient arterial blood, allowing reliable detection of the pulsatile signal. The scattering effect necessitates empirical calibration of the pulse oximeter. On the other hand, this effect allows a transmittance path around bone in the finger.

The principles above, associated issues and design and application of pulse oximeters comprise the better part of this text. The remainder of this chapter concentrates on the role and importance of pulse oximetry and limitations of the device.

2.2 S_pO_2 AS MONITOR OF HEMOGLOBIN OXYGENATION

Lack of oxygen can quickly lead to irreversible damage to cell tissue having a high metabolic rate, the heart and central nervous system being two examples. Although the human body is surprisingly robust in many ways, the physiological process of sustaining proper cell function via oxygen transport is a delicate and complex control system; one which if altered too significantly could become unstable and insufficient for meeting oxygen tissue demands. To emphasize the importance of proper tissue oxygenation, Table 2.1 lists survival times for different organ beds after the onset of anoxia, or cardiac arrest. Hence, it is important to safeguard against pathological conditions that might lead to improper tissue oxygenation.

Table 2.1 Organ robustness to anoxia (cardiac arrest), a consequence of metabolic rate and cellular oxygen stores. *Survival* time is the time before cellular damage occurs after total loss of oxygen delivery. *Revival* time is the time before function of the organ can no longer be restored. Revival times are generally four times longer than survival times in most organs except the brain, which has a revival time five times longer than its survival time (adapted from Nunn 1987).

Organ	Survival time after onset of anoxia
Cerebral cortex	less than 1 min
Heart	5 min
Liver and kidney	10 min
Skeletal muscle	2 h

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2.2.1 Comprehensive approach

Arterial saturation, the variable which pulse oximetry is intended to measure, is just one of several variables a physician will consider when assessing the condition of a patient's cardiopulmonary system. In this regard, the clinician will address the fundamental issue of whether or not body tissue is being properly oxygenated (Vender 1992). This requires a comprehensive approach whereby arterial saturation plays a certain role. It is an extremely important one, but physicians typically do not use S_aO_2 as a sole monitor for pathological oxygenation conditions.

2.2.2 Arterial oxygen saturation

Arterial oxygen saturation pertains to blood in the arteries and arterioles throughout the body. This blood is of the same saturation throughout the arterial system. It is at the capillary level that saturation levels change. In a healthy adult, the normal operating range for S_aO_2 is greater than 90%, which corresponds to an arterial partial pressure, P_aO_2, of 60 to 100 mmHg (Ahrens and Rutherford 1993).

Owing to the complexity of the oxygenation process, it is difficult to address the wealth of uses for arterial saturation in critical care settings, operating rooms, and research laboratories. Physicians are interested in knowing S_aO_2 for a variety of reasons. Sometimes it is for quantitative assessment. Sometimes it serves as an important variable for safeguarding against, although it is not a direct indication of the dangerous condition of low cellular oxygenation. Table 2.2 gives several respiratory problems that might cause low S_aO_2, but this is by no means a complete list.

Table 2.2 Respiratory problems that might result in low S_aO_2 (adapted from Des Jardins 1990, Cherniack and Cherniack 1983, and Selecky 1982).

Respiratory problem	Example disease or possible source of problem
Poor lung compliance	Pneumonia, ARDS, fibrosis, emphysema
Increased airway resistance	Asthma, chronic bronchitis, cystic fibrosis
Low pulmonary diffusion capacity	Emphysema, pulmonary alveolar proteinosis
Airway obstruction	Choking, secretions from intubation, obstructive sleep apnea
Ventilatory muscle weakness	Lead poisoning, trauma to phrenic nerve
Increased true venous admixture	Congenital heart disease
Low inspired partial pressure of oxygen	Anesthesia equipment failure, high altitude
Hypoventilation	Acid-base imbalance

2.2.3 Hypoxia and hypoxemia

Hypoxia means lower than normal tissue oxygenation. *Hypoxemia* means lower than normal blood oxygenation. These are two quite different concepts. Hypoxia refers to the critically dangerous condition where cell function is in jeopardy. Table 2.3 shows different categories of hypoxia. The first category, hypoxic hypoxia, is a consequence of low arterial saturation. Hence, hypoxemia is a dangerous condition. However, it is not necessary that hypoxia exist under conditions of hypoxemia. Likewise, as table 2.3 suggests, hypoxia may occur

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when there is no evidence of hypoxemia. Therefore, a clinician carefully interprets results from monitoring blood oxygen content because S_aO_2 and, consequently, S_pO_2 provide *only* a measure of hypoxemia, *not* a measure of hypoxia.

Table 2.3 Different types of hypoxia (adapted from Bredle 1989, and Des Jardins 1990).

Type of hypoxia	Description
Hypoxic hypoxia	Arterial blood is poorly oxygenated due to low F_IO_2 or respiratory disease
Anemic hypoxia	Blood cannot transport adequate oxygen due to hemoglobin abnormalities
Circulatory hypoxia	Cardiac output is low or blood perfusion is inadequate
Histotoxic hypoxia	The tissue is incapable of using otherwise sufficient supplies of oxygen

2.2.4 Role of SpO_2 in avoiding hypoxia

Although monitoring blood oxygen saturation provides only clues to the oxygenation of cells, there is one variable which provides better evidence of hypoxia. That is lactate content of the blood. Energy utilization may take place in an anaerobic environment, and the byproduct of such a process is lactate. However, the anaerobic process is inefficient for generating energy, and cells cannot operate for long in this situation. The presence of lactate is not a problem initially because it may be broken down if oxygen stores are replenished soon enough (Ahrens and Rutherford 1993). Lactic acidosis occurs if this is not the case. This, in turn, affects the pH of blood which influences the cardiac and pulmonary control systems. However, if cardiac output and respiratory rate cannot increase the delivered oxygen, a dangerous situation results.

Although lactic acidosis may be a better indicator of hypoxia than arterial blood saturation, the problem is that lactic acidosis is an after-the-fact occurrence. As pointed out by Vender (1992), cell damage is likely occurring upon noting an increase in lactate. Herein lies the true value of blood saturation measurement. If monitored appropriately, it can help signal dangerous pathological conditions before cell damage occurs. However, as alluded to earlier S_pO_2 (i.e., S_aO_2) alone is not as helpful as when supplemented with measures of cardiac output, functional hemoglobin, blood pressure, heart rate, respiratory rate, urine output, patient comfort and a variety of other variables.

2.2.4.1 Anesthesiology. Tissue oxygenation and, consequently, blood saturation are of extreme importance to the anesthesiologist because the patient's cardiopulmonary system is placed in a state where it can no longer meet oxygen demands on its own. In a sense, the anesthetist becomes the controller for the patient's respiratory system, and S_pO_2 provides one of the better feedback variables. As a monitoring device to assist the anesthetist, pulse oximetry has literally revolutionized the field of anesthesiology because of its noninvasive nature, fast response and affordability (Fairley 1989). Note that the transition to pulse oximetry was not without controversy (Payne and Severinghaus 1985). Cyanosis, heart rate and blood pressure were generally what was available to the anesthesiologist for detecting hypoxia before the advent of pulse oximetry (Fairley 1989). Similar to lactate, all these variables are after-the-fact

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occurrences of hypoxia. Again, S_pO_2 does not give direct indication of hypoxia, which has its drawbacks, but it can be an early warning of its occurrence.

The most frequent use of pulse oximeters is by anesthesiologists during surgery and for about an hour afterwards in the recovery room. Anesthesiologists administer narcotics to the patient to suppress the central nervous system. This stops the patient's desire to breath. In addition, they administer muscle relaxants, which stops the ability to breathe and permits airways to collapse. Thus, it is necessary to restore breathing through intubation and artificial respiration. Anesthesiologists can monitor several variables, but most have limitations of late or unreliable response to an oxygenation problem.

Blood pressure declines long after oxygen declines, and the ECG indicates problems even later than blood pressure. An esophageal stethoscope indicates within one beat when the heart has stopped, but this is also long after oxygen has declined. The anesthesiologist can check for cyanosis. Again, this occurs long after oxygen has declined. Blood gas samples give an accurate measurement of oxygen, carbon dioxide, and pH but take about 5 min to process.

Pulse oximeters solved the problem of delay by continuously and noninvasively monitoring arterial oxygen saturation. Recall that adequate arterial saturation does not imply proper oxygenation. Furthermore, there is a delay between noting a drop in S_pO_2 and its cause. However, of the monitored variables, S_pO_2 is currently the best indication that an oxygenation problem exists or is about to occur, and it does so noninvasively.

The pulse oximeter probe is usually applied to the finger, since the body will decrease blood flow to the finger before more vital organs. It is more difficult to reliably secure probes to the ear, nose, and forehead. An arterial oxygen saturation drop from 98 to 96% alerts the anesthesiologist that something is going on. If the oxygen saturation drops to 90%, the default alarm sounds, which indicates that a serious problem may be at hand.

Continuously monitoring S_pO_2 catches several equipment malfunctions and improper placement of tracheal tubes, but naturally it does not identify the problem (Payne and Severinghaus 1985). The fact that S_pO_2 does not identify the source of the problem should not be viewed as a drawback to the pulse oximeter. Instead, this has implications in how to view pulse oximetry as a monitored variable. Fairley (1989) has figuratively stated the role of pulse oximetry in anesthesiology (Original metaphor attributed to Tremper and Barker (1989)):

> It was not until effective pulse oximetry became commercially available, for the first time, that large numbers of anesthesiologists could continuously monitor their patients' arterial oxygen levels. It is very important to recognize the nature of this monitoring. Since virtually every anesthetized patient breathes an oxygen enriched mixture, desaturation only occurs when there is a substantial increase in the difference between the (perceived) inspired oxygen tension and that in the arterial blood. Metaphorically, as the blindfolded anesthetist walks unknowingly towards the cliff of hypoxia—whether due to problems of inspired gas, equipment failure, underventilation, or abnormal pulmonary shunting—the protective hand of the pulse oximeter sentry stops him from falling over the edge. The oximeter will not tell him why he has been proceeding in that direction, or the direction back! On the other hand, should he start falling, the sentry functions on the vertical part of the dissociation curve and becomes an extremely

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sensitive (if not always accurate) indicator of progress during the drop. Interestingly, it is highly probable that many fewer blood gas samples are being drawn during anesthesia now that pulse oximeters are so universally available. Our detailed insight into our patients' pulmonary oxygen exchange is less than with P_aO_2 measurement but, because of the continuously available sentry, we believe our patients are safer. A prospective study to prove that important point with certainty may never be performed but, already, opinion seems overwhelmingly in favor of that belief.

Pulse oximetry has become a *de facto* standard for the American Society of Anesthesiologists (Eichhorn 1993). This means that, as alluded to in Fairley's description, although definitive statistical proof of the benefit of pulse oximetry may never be shown because of the rarity of complications due to anesthesiology in the operating theater, a large majority of those who use the device feel that it helps to reduce complications.

2.2.4.2 Postoperative and critical care. Pulse oximetry has proven very important to postoperative recovery because the patient's pulmonary control may still be compromised from the effects of anesthesia. For example, a randomized study by Lampe *et al.* (1990) found that of 141 patients having carotid endarterectomy 63% had episodes of S_pO_2 less than 90% and 21% had episodes of S_pO_2 less than 86% during the postoperative period. Similar studies also show large numbers of desaturation episodes, although variation in the data does exist (Severinghaus and Kelleher 1992).

The role of pulse oximetry in intensive and critical care units is similar to that for anesthesiology, although the patient's respiratory system may not be suppressed by narcotics and muscle relaxants. The instrument still acts as the sentry warning of desaturation from a variety of conditions, some of which were listed in table 2.2. In this setting, alarms and temporal records are very useful when constant surveillance of the patient is not possible.

2.2.4.3 Exams and research studies. The pulse oximeter is an excellent device for medical research studies such as sleep apnea and hypoxic ventilatory response (Severinghaus and Kelleher 1992). Medical exams such as stress tests also benefit from the noninvasive, continuous nature of pulse oximetry. In such cases, S_pO_2 may be used to catch hypoxemic events and also correlated with other variables to glean information about the patient's general health.

2.2.5 Photoplethysmography

Most pulse oximeters on the market feature a photoplethysmograph. The signal for the photoplethysmograph is derived from the same waveforms used to calculate S_pO_2. The photoplethysmograph may be used in a clinical setting in the same manner as a plethysmograph. However, the accuracy of the photoplethysmograph suffers from motion artifacts, and the patient must have adequate blood perfusion near placement of the pulse oximeter probe. Just as with the conventional plethysmogram, signal processing can derive heart rate from the photoplethysmogram waveform. Hence, most pulse oximeters also display heart rate. Similar to computing S_pO_2, temporal low-pass filtering abates the effect of motion artifacts on heart rate estimation.

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2.2.6 Hyperoxia

Hyperoxia is the condition where blood in the system contains more than the normal amount of oxygen. Determining excessive levels of oxygen is important in many situations because of the toxic nature of oxygen radicals. Studies suggest that pulse oximetry is not useful for this type of application. For example, the role of S_aO_2 for determining retinopathy of prematurity in neonates is not quite clear, and furthermore the 2 to 3% inaccuracy of S_pO_2 for estimating S_aO_2 adds to this uncertainty (Severinghaus and Kelleher 1992).

2.3 LIMITATIONS

2.3.1 Instrument and operation limitations

Many of the limitations to pulse oximetry will come to light throughout the remainder of this text. However, table 2.4 summarizes some limitations given by Severinghaus and Kelleher (1992). These are described in detail in the original source.

Table 2.4 Limitations to pulse oximetry and its application in a clinical setting. Adapted from Severinghaus and Kelleher (1992).

Pulse oximetry limitations
Instrument incidence of failure
Low signal-to-noise ratio
Light shunting and poorly applied probe
Vasoconstrictors
Low-perfusion limits
Motion artifacts
Abnormal pulses
Ventilator-induced and venous pulse interference
Response times
Ambient light
Electrosurgery
Interference of MRI
Site selection for probe placement
Skin pigments, dyes, and nail polish
Dysfunctional hemoglobins
Burns and other dangers
False alarms and false nonalarms

2.3.2 Limitations in S_aO_2

Often in anesthesiology medical literature, articles regarding a limitation of pulse oximetry appear in which, if read more closely, what is actually meant is a limitation in monitoring arterial oxygen saturation, e.g., Hutton and Clutton-Brock (1993), and Mak (1993). Authors of such articles point out this fact. It is interesting how measuring S_pO_2 has become so associated with measuring S_aO_2.

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Nonetheless, it follows that any limitations associated with S_aO_2 as a monitored variable are also associated with S_pO_2.

There are some caveats to using S_aO_2 to assess the condition of pulmonary function. It is difficult to regard any monitoring technique as foolproof, as there are usually misleading combinations of conditions that will result in the monitored variable appearing fine when, in fact, a potentially dangerous condition could exist for the patient. For example, Hutton and Clutton-Brock (1993) and Mak (1993) point out that pulse oximetry (i.e., S_aO_2) is a poor measure of hypoventilation when inspired oxygen concentration is high. It is in situations like this that a comprehensive approach to oxygenation assessment using other monitored variables is imperative.

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INSTRUCTIONAL OBJECTIVES

2.1 State the fundamental question a clinician should ask when assessing the cardiopulmonary condition of a critically ill patient.
2.2 Give the normal values for S_aO_2 and P_aO_2 in the healthy adult.
2.3 State the difference between hypoxia, hypoxemia and hyperoxia.
2.4 Give several common problems that result in hypoxemia.
2.5 Describe the role of lactate as an indicator of improper oxygen transport.
2.6 Describe the role of S_pO_2 as an indicator of improper oxygen transport.
2.7 List several physiologic variables that may be used in conjunction with S_aO_2 for assessing a patient's cardiopulmonary condition.
2.8 Describe why pulse oximetry data are of importance to anesthesiology.
2.9 State how useful pulse oximetry is in detecting hyperoxia.
2.10 List several limitations to pulse oximetry.

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CHAPTER 3

BLOOD OXYGEN MEASUREMENT

James Farmer

Oximetry is a general term that refers to the optical measurement of oxyhemoglobin saturation in the blood (Peterson 1986). Pulse oximetry is only one of those technologies. There are other methods of measuring oxygen content of the blood as well. Gradwohl (1948) describes two colorimetric methods of estimating the HbO_2 of the blood by direct comparison to a color chart. The Dare method used a thin layer of undiluted blood which was matched against a standard series of colored disks. The Tallqvist method used a drop of undiluted blood placed on absorbent paper. The absorbent paper was compared with a graded scale of colored blocks printed on paper. The Tallqvist method was reported to be inaccurate and not recommended. No information on the reliability of the Dare method was given.

This chapter describes several different chemical and optical methods of determining the oxygen saturation of the blood which are more deterministic than the ones above. The chapter examines the development of oximetry from a historical perspective. The final section of the chapter gives an overview of the design of a pulse oximeter.

Some of the methods described in this chapter find the partial pressure of oxygen (PO_2) and some find the oxygen saturation (SO_2). Chapter 1 describes the relationship between these two. It is interesting to note from a historical perspective that SO_2 was not always an accepted means of reporting blood oxygenation. Gradwohl (1948) stated, 'Hemoglobin estimations are reported in terms of percentage, but this incorrect. They should always be reported in terms of grams per 100 mL.'

3.1 CHEMICAL METHODS

The oxygen content of blood can be determined from a sample by using chemical reactions to remove the oxygen from the blood. These measurements can be done with varying degrees of success. The chemical reactions can be slow also. The Van Slyke method can take up to 20 min.

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3.1.1 Van Slyke method

The Van Slyke apparatus (figure 3.1) is used in a method of measuring the oxygen content of a blood sample. A sample of blood is introduced to the apparatus anaerobically with a sample of potassium ferricyanide. Potassium ferricyanide is a releasing agent that releases the oxygen, carbon dioxide, and other gases from the blood sample. After removing the carbon dioxide from the mixture, the remaining gases are compressed into a fixed volume and the resulting pressure (P_1) is measured from the manometer. The oxygen is then absorbed with a reagent such as sodium hydrosulfite. The remaining gases are then recompressed into the same fixed volume and the final pressure (P_2) is measured (Hill 1966).

The difference of the two pressure measurements is a partial pressure due to the oxygen that was contained in the blood sample. The oxygen content of the blood sample is calculated by

$$\text{mL } O_2/100 \text{ mL blood} = K(P_1 - P_2) \tag{3.1}$$

where K is a constant relating to the reagents, apparatus, and the volume of the blood sample (Adams and Hahn 1982). Alternatively, the oxygen can be extracted from the blood with the Van Slyke apparatus and analyzed with a gas chromatograph (Hill 1966).

The technique is not simple to perform. Technical expertise and experience with chemical reactions are required to obtain accurate, reproducible results. However, the Van Slyke apparatus can provide measurements accurate to ±0.03% (Adams and Hahn 1982). The Van Slyke technique has been in the past a standard by which blood oxygen measurements were made (Miller 1966, Dennis and Valeri 1980).

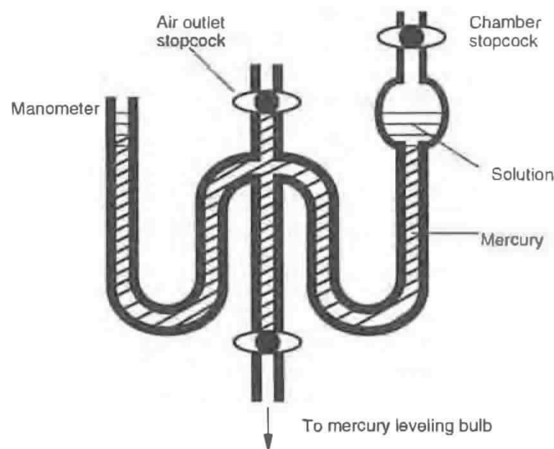

Figure 3.1 The Van Slyke apparatus (adapted from Adams and Hahn 1982).

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3.1.2 Mixing syringe method

The mixing syringe method also measures the amount of oxygen released from a blood sample by a chemical reagent. The apparatus consists of two Luer-lock syringes joined to a manometer tap. One of the syringes is a precision automatic syringe which is able to accept and deliver a fixed volume of reagent. The automatic syringe is filled with the oxygen releasing agent and then emptied. This coats the inside of the syringe with the reagent and keeps the blood from any contact with the air. The oxygen releasing agent has a known oxygen partial pressure (P_r). The automatic syringe then draws a volume of blood (V_b) from the mixing syringe. The volume of blood and a known volume of the reagent (V_r) are mixed back and forth between the syringes. The partial pressure of oxygen of the blood–reagent solution (P_s) is then measured by a blood-gas analyzer. The oxygen content is calculated from the equation

$$\text{mL } O_2/100 \text{ mL blood} = \alpha \frac{V_r + V_b}{V_b}\left[P_s - \left(\frac{V_r}{V_r + V_b} P_r\right)\right] \quad (3.2)$$

where α is the solubility coefficient of oxygen in the blood–reagent solution at the temperature at which the measurement was made. Its value is obtained from either a separate experiment or from reference tables (Adams and Hahn 1982).

3.1.3 The Clark electrode

The Clark electrode uses the basic chemistry principles of oxidation and reduction to measure the PO_2 (partial pressure of oxygen) in a solution. When oxygen is dissolved in an aqueous solution and exposed to a 0.7 V polarizing voltage, the following reaction occurs

$$O_2 + 2H_2O + 4e^- \rightarrow 4OH^-. \quad (3.3)$$

A silver anode immersed in a potassium chloride electrolyte bath will attract anions (Cl^-) to form silver chloride. This oxidation reaction produces a constant flow of electrons. A nearby platinum electrode undergoes a reduction reaction turning oxygen to hydroxyl ions (OH^-) as in equation (3.3). Figure 3.2 shows that the number of electrons used in the platinum cathode reaction is directly proportional to the PO_2 present in the bath. Therefore, by measuring the current between the two electrodes, the PO_2 in the solution is determined.

The entire Clark electrode system (figure 3.3) has a polypropylene sheath which slows the diffusion of oxygen from the blood to the electrode. This prevents the electrode from depleting the PO_2 in a particular place and eliminates the need to stir the blood *in vitro*.

The Clark electrode is the common sensing device used by blood gas analyzers to determine the PO_2 of the blood (Shapiro *et al* 1989). Using a variety of different electrodes, blood gas analyzers also determine the pH and PCO_2 of blood samples as small as 65 μL. The blood gas analyzers are very useful for *in vitro* measurements because they self-calibrate and self-diagnose malfunctions. Thus, interfacing blood gas analyzers with computers allows for automated measurements, patient data storage, and billing.

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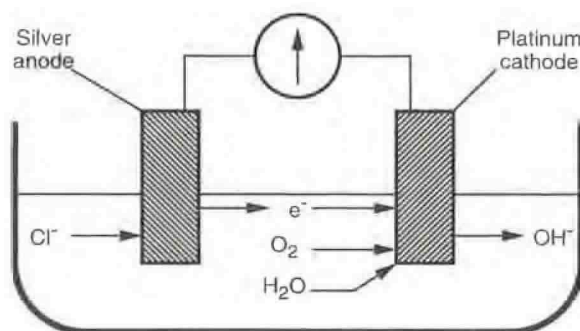

Figure 3.2 Since an aqueous solution has plenty of H_2O and the silver anode is able to supply an abundance of electrons, equation (3.3) is limited by the amount of oxygen present. Thus, the amount of current between the anode and the cathode is determined by the PO_2 present. This reaction shows the chemical reaction that occurs in a Clark electrode.

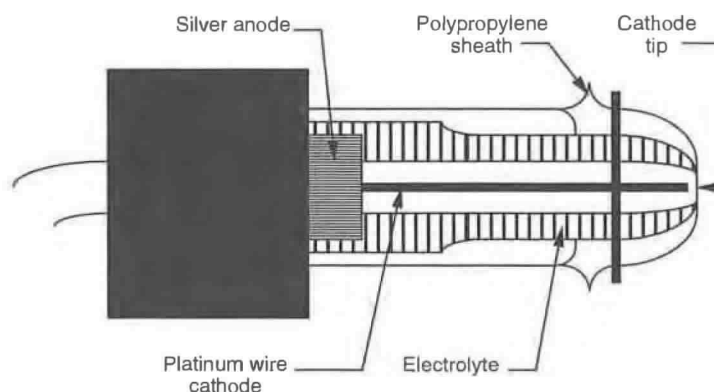

Figure 3.3 A Clark electrode (adapted from Shapiro *et al* 1989).

The Clark electrode can also be used to make *in vivo* measurements when designed to be used as catheter electrodes (Adams and Hahn 1982). Many catheter electrodes are designed specifically to be used with infants and are very small in diameter. Several different versions exist. Some versions have both the anode and cathode within the single electrode, as pictured in figure 3.3. But others have an external anode reference electrode on the skin.

One of the downfalls of the Clark electrode catheter system is calibration. Calibration takes place by drawing a blood sample near the end of the catheter and analyzing the sample with an *in vitro* blood gas analyzer. Another potential problem with the Clark electrode is keeping the tip clean. Though the polypropylene sheath helps to some extent, failure to keep the catheter in the flow of blood can cause errors as blood coagulates on the surface of the electrode.

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3.1.4 The galvanic electrode

The galvanic electrode is similar in operation to the Clark electrode. As oxygen passes across the electrode, a chemical reaction occurs that produces a small electric current. But in this case the cathode is made of gold, the anode of lead, and the electrolyte solution is potassium hydroxide. In the Clark electrode, the silver anode and the platinum cathode participated in the chemical reaction. This made sure that the electrolyte solution was always replenished. But, the galvanic electrode has no means to replenish the electrolyte solution in the electrode and so it has a limited lifetime which depends on the PO_2 and exposure (Shapiro et al 1982).

3.2 TRANSCUTANEOUS PO_2 SENSOR

The Clark electrode can be used noninvasively to determine PO_2 of the blood. Under normal conditions, the PO_2 of the blood near the skin's surface ($P_{tc}O_2$, for the transcutaneous partial pressure of oxygen) is atmospheric. But, hyperemia of the skin can cause the $P_{tc}O_2$ to approach P_aO_2, the arterial partial pressure. Hyperemia of the skin can be induced by drugs, creams, abrasions, or heating the skin. In other words, by placing a Clark electrode on the skin with a heating element, the skin begins to diffuse oxygen so that the $P_{tc}O_2$ is nearly equal to the P_aO_2. The measurements given by the transcutaneous PO_2 electrode are stable with little drift and are widely accepted (Gothgen and Jacobsen 1987).

Heating is the easiest method of inducing hyperemia to control. With a heating element and a thermistor, the skin is heated to between 43 °C and 44 °C. This is the optimal temperature range for the $P_{tc}O_2$ to approach the P_aO_2 with minimal skin damage. The heat causes increased blood flow to the skin at the heating element site. This increased perfusion causes more O_2 to be delivered to this area and the excess O_2 diffuses through the skin more easily (Peura 1998). Figure 3.4 shows a cross sectional view of a transcutaneous PO_2 electrode, showing the heater and the thermistor.

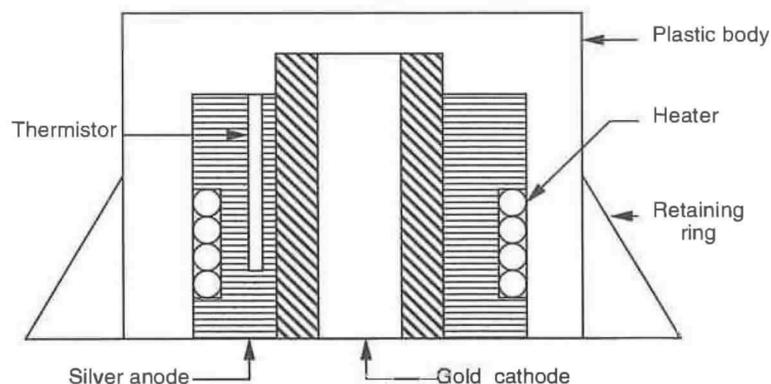

Figure 3.4 A cross section of a transcutaneous PO_2 electrode. The electrolyte below the anode and cathode is held in place by a polypropylene membrane.

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One advantage of the transcutaneous PO_2 electrode is that it measures the *real* $P_{tc}O_2$ and is not an empirical calculation as with the pulse oximeter (Gothgen and Jacobsen 1987). $P_{tc}O_2$ can be thought of as a new PO_2 variable and not an estimation of P_aO_2. This contrasts with the pulse oximeter, which is an estimate of S_aO_2, and whose accuracy is dependent on its ability to predict S_aO_2 (Barker and Tremper 1984). But again, one of the disadvantages of the transcutaneous PO_2 sensor is the calibration. Like the Clark electrodes used with catheters and blood gas analyzers, the transcutaneous PO_2 measurement is based on an electrochemical reaction that needs to be calibrated frequently with some gas mixtures.

The transcutaneous PO_2 electrode has other disadvantages. There is a warm up time of 10 min for the heating element to induce enough blood flow to the measurement site. And even with the thermistor regulating the heating element, there is a risk of burns, especially in infants. It is recommended that the electrode be moved every 4 hours (Burtis and Ashwood 1994).

The $P_{tc}O_2$ does not vary more than 5% from the P_aO_2 in infants but is more dependent on blood flow in adults. The heating is not as effective in adults and so the $P_{tc}O_2$ is usually lower than the P_aO_2 (Barker and Tremper 1984). Also, transcutaneous PO_2 electrodes are unreliable when the blood pressure falls below 100 mmHg or when some anesthetics such as nitrous oxide are administered (Burtis and Ashwood 1994). Even with these problems, the transcutaneous PO_2 electrode has been found useful in clinical situations in the operating room, intensive care units, and emergency rooms (Waxman *et al* 1983).

3.3 *IN VITRO* OXIMETERS

3.3.1 Spectrophotometers

Spectrophotometry is the basis for all oximetry. The atoms of all molecules vibrate in specific patterns for each unique substance. As light passes through a substance, the frequencies of light similar to the vibrational frequencies of the substance are absorbed. A spectrophotometer measures the intensity of light transmitted through a particular substance at particular wavelengths. The fraction of light absorbed at a specific wavelength is determined by the absorptivity, or extinction coefficient, of the substance. The extinction coefficient of a substance can be graphed at various wavelengths as a spectrum. This spectrum is unique for every substance.

A photodetector is a device that converts light intensity into an electric current. A given intensity of light transmitted through a substance produces an electric current proportional to the intensity. By measuring the intensity of incident light on a substance (I_0) and measuring the intensity of light transmitted through the substance (I), the transmittance (T) of the substance can be calculated:

$$T = \frac{I}{I_0}. \tag{3.4}$$

Because each molecule absorbs an equal portion of light, the absorbance of light through a substance is linearly related to the concentration of substance

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present. From the measured transmittance (T), the absorbance (A) can be calculated from

$$A = 2 - \log (\%T). \quad (3.5)$$

Beer's law can now be used to find the amount of substance in a solution. Beer's law can be stated as

$$A = \varepsilon(\lambda)\, c\, d \quad (3.6)$$

where $\varepsilon(\lambda)$ is the extinction coefficient of the substance at a given wavelength λ of light, d is the length of the light path, and c is the concentration of the substance. For all substances, the linear relationship between absorbance and concentration only holds up to a certain concentration. Below this limit we can determine a calibration constant. The calibration constant can then be used as a standard to determine the unknown concentration of a substance with the same extinction coefficient as the standard.

For a solution with two unknown compounds, the absorbances at two wavelengths can be used to calculate the concentrations of both compounds. At the isosbestic point where the two extinction coefficients are equal, Beer's Law for the two samples can be written as

$$d = \frac{A_{ec}}{[c_1 + c_2]\varepsilon(\lambda_{ec})} \quad (3.7)$$

where A_{ec} is the absorbance at the isosbestic point and $\varepsilon(\lambda_{ec})$ is the extinction coefficient of the two substances at the isosbestic point. At the second wavelength Beer's Law gives

$$A_0 = d[c_1\varepsilon_1(\lambda_0) + c_2\varepsilon_2(\lambda_0)] \quad (3.8)$$

where A_0 is the absorbance and $\varepsilon_1(\lambda_0)$ and $\varepsilon_2(\lambda_0)$ are the extinction coefficients for the two compounds at the second wavelength. Because the sum of the concentrations of the two compounds is 1, we can solve equations (3.7) and (3.8) for the two concentrations.

If the solution contains more than just the two compounds as is the case with oximetry, solving equations (3.7) and (3.8) will give the relative concentration of c_1 to c_2 if the assumption can be made that none of the other compounds will absorb light at the two wavelengths used for the measurement. This assumption is sufficient for oximetry where the relative concentrations of Hb and HbO_2 are used to estimate S_aO_2.

Note that measuring the absorbance at the isosbestic point is not necessary to solve for c_1 and c_2. The absorbance at any two wavelengths can be used to solve for the concentrations with equally good results. The motives for the choice of the isosbestic point as one of the wavelengths used in the earliest oximeters are not clear. But the simplified mathematics may have been a reason (Nilsson 1960).

With the concentrations of Hb and HbO_2, an estimation of S_aO_2 is made from

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$$S_pO_2 = \frac{HbO_2}{HbO_2 + Hb} \times 100\% \quad (3.9)$$

This assumes that any other substance present in the solution being measured has no effect on the absorbance of light at the chosen wavelengths. For example, it does not take into account the effect of the other types of hemoglobin present in the blood. These hemoglobin species do absorb light at certain wavelengths, but their relative concentration with respect to Hb and HbO_2 is small enough that for many applications equation (3.9) is an accurate estimate.

3.3.2 The CO-oximeter

CO-oximeters are spectrophotometers specifically designed to analyze the concentrations of several different types of hemoglobin including reduced hemoglobin (Hb), oxyhemoglobin (HbO_2), carboxyhemoglobin (COHb), and methemoglobin (MetHb). Each of these various forms of hemoglobin has its own extinction coefficient curve (figure 4.2). By using as few as four wavelengths of light, the amount of each of these forms of hemoglobin can be determined from a sample.

Instrumentation Laboratories Inc. coined, but did not copyright, the term CO-oximeter and released the first commercial CO-oximeter in 1966 (Moyle 1994). The CO-oximeter was originally introduced to measure COHb using three different wavelengths, 548 nm, 568 nm and 578 nm (Adams and Hahn 1982). The IL-282 CO-oximeter pictured in figure 3.5 uses four wavelengths of light, 535.0 nm, 585.2 nm, 594.5 nm, and 626.6 nm, to measure all four of the relevant forms of hemoglobin. These wavelengths are obtained by four interference filters mounted on a rotating wheel each selecting wavelengths of light from a Tl–Ne hollow cathode lamp (Zwart *et al* 1981). The CO-oximeter is able to operate in this narrow range of light because it only works with diluted plasma samples and like pulse oximeters does not have to deal with skin, muscle, or other tissue (Moyle 1994).

A four wavelength CO-oximeter would obtain absorbance readings on a blank solution at all four different wavelengths (λ_{1-4}). Then a reading is obtained at each wavelength for a diluted, hemolyzed sample. CO-oximeters use hemolyzed samples, blood samples with the red blood cell membranes removed, to reduce the amount of light scattering, which reduces the accuracy of the measurement.

The absorbance readings of the blank solution are subtracted from the readings from the samples at each wavelength to give the absorbance of the blood at each wavelength. From these absorbances of the blood, the concentration of each type of hemoglobin can be calculated from the equations

$$C_{Hb} = K[\varepsilon_{Hb}(\lambda_1)A_1 + \varepsilon_{Hb}(\lambda_2)A_2 + \varepsilon_{Hb}(\lambda_3)A_3 + \varepsilon_{Hb}(\lambda_4)A_4] \quad (3.10)$$

$$C_{HbO_2} = K[\varepsilon_{HbO_2}(\lambda_1)A_1 + \varepsilon_{HbO_2}(\lambda_2)A_2 + \varepsilon_{HbO_2}(\lambda_3)A_3 + \varepsilon_{HbO_2}(\lambda_4)A_4] \quad (3.11)$$

$$C_{MetHb} = K[\varepsilon_{MetHb}(\lambda_1)A_1 + \varepsilon_{MetHb}(\lambda_2)A_2 + \varepsilon_{MetHb}(\lambda_3)A_3 + \varepsilon_{MetHb}(\lambda_4)A_4] \quad (3.12)$$

$$C_{COHb} = K[\varepsilon_{COHb}(\lambda_1)A_1 + \varepsilon_{COHb}(\lambda_2)A_2 + \varepsilon_{COHb}(\lambda_3)A_3 + \varepsilon_{COHb}(\lambda_4)A_4] \quad (3.13)$$

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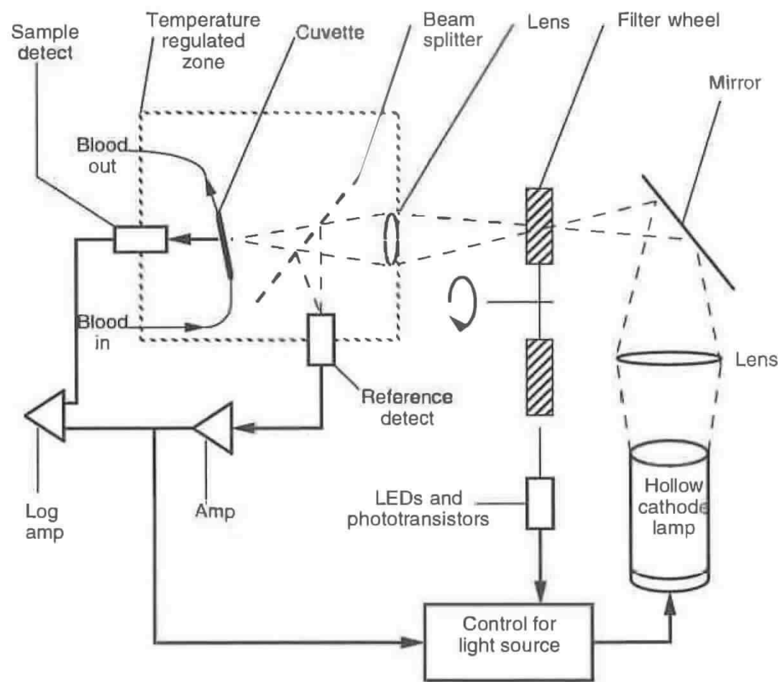

Figure 3.5 A schematic diagram of the IL-282 CO-oximeter (adapted from Zwart *et al* 1981).

where C_x is the concentration of hemoglobin type x, $\varepsilon_x(\lambda_1)$ is the extinction coefficient of hemoglobin type x at the first wavelength, A_1 is the difference between the absorbance value of the blood and the blank solution at the first wavelength, and K is a constant set by the calibration procedure (Shapiro *et al* 1989).

CO-oximeters are subject to many sources of error. Any substances in the sample that scatter light affect the measurements because the amount of light transmitted is no longer solely a function of the light absorbed by hemoglobin species. Samples infected with small portions of lipids or cell fragments are common causes of light scattering. There are also errors associated with fetal hemoglobin samples. Results from CO-oximeters have been known to give falsely high COHb readings in fetal hemoglobin (Zwart *et al* 1981). Some CO-oximeters try to compensate for these errors by using more wavelengths of light. For example the AVL 912 uses 17 wavelengths to try to compensate for other light absorbing fragments that might be present in the solution (Moyle 1994).

Because CO-oximeters make measurements *in vitro* with discrete samples, they provide accurate oxygen saturation readings for only the times at which the samples are drawn. They do have their uses, notably as a standard for calibration of *in vivo* oximeters (Moyle 1994). The CO-oximeter is one of the most accurate methods available for measuring the four clinically relevant hemoglobin species. It is a standard against which other methods of measurement are compared (Shapiro *et al* 1989).

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3.4 *IN VIVO* TWO-WAVELENGTH OXIMETERS

3.4.1 The first in vivo oximeters

In vivo oximetry originated in Germany in the 1930s when the use of the selenium photovoltaic cell became accepted (Peterson 1986). In 1934, Kramer showed that the absorbance of red light depended on oxygen saturation, but his implementation only used one wavelength of light (Payne and Severinghaus 1986). At about the same time, Matthes designed an oximeter which measured the transmission of light through the ear by a lamp with a photocell attached to the earlobe. At the time, regions of optical spectra were broadly defined and depended greatly on the lamp, photocell, and filters used. Matthes used wavelengths of red light, which varied the transmission measurements as the oxygen saturation varied, and compared them to measurements using green light, which did not vary with saturation. He later discovered that infrared light was a better choice than green (Nilsson 1960).

Glen Millikan is credited with coining the term oximeter while, during World War II, attempting to design a hemoglobin saturation meter for the ears of pilots to control the amount of oxygen they received (Severinghaus 1987). Millikan's ear piece was improved by Wood and Geraci in 1949. The biggest improvement was in the infrared filter. They also had the idea of using an inflatable balloon to cut off the circulation to the ear and make it bloodless. This made for a zero setting which tried to account for the other tissue present in the ear. Wood thought he had succeeded in the first absolute reading oximeter but he later showed that inconsistencies in the photocells used for light detection caused the device to be inaccurate (Payne and Severinghaus 1986).

3.4.2 The Cyclops

The Cyclops was a commercially available reflectance oximeter. It was named the Cyclops because of the large sensing device that was placed on the forehead of the patient. It used red and green light to determine SO_2. Limitations in the technology of photocells limited the Cyclops from using infrared light. The theory of the device was based on the fact that any reflection of the green light was due to nonblood reflection. The reflection of the red light was due to both the blood and noncomponents. So, by subtracting the green light reflection from the red light reflection, the reflection due to the blood was found.

The Cyclops was successful in producing trending information about SO_2. And if it was calibrated against two or more arterial blood samples, the Cyclops could produce accurate SO_2 values (Zijlstra 1958).

3.5 FIBER OPTIC OXIMETERS

3.5.1 In vitro reflectance oximeter

Polanyi and Hehir (1962) first described the design of a fiber optic oximeter to use as a catheter measurement device. They also used two wavelengths of light to measure the concentrations of Hb and HbO_2. They chose the specific values for

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their wavelengths of light to be 660 nm and 805 nm; 805 nm is the isosbestic point of HbO_2 and Hb. They used a filter wheel, similar to the one used in the CO-oximeter in figure 3.5, to obtain their wavelengths.

The concentrations of Hb and HbO_2 can be calculated in the same manner as in section 3.3.1. The only difference with this device is that this fiber optic oximeter was a reflectance device and measured an absorbance directly from the backscattered light in the blood. In Section 3.3.1, the measurement was a transmittance of light which was converted to an absorbance.

Polanyi and Hehir presented successful results with their fiber optic oximeter with *in vitro* experiments. But although they intended their device to be used *in vivo*, it did not come to be (Barker 1991).

3.5.2 In vivo reflectance catheter oximeter

In vivo catheter oximeters were not in widespread use until about 1980. These *in vivo* fiber optic catheter oximeters use much the same technology as the pulse oximeter. Many catheter oximeters are two-wavelength devices like the pulse oximeter. Some of them use three wavelengths to try to compensate for changes in pH or other variables. Figure 3.6 shows the basic configuration of a fiber optic reflectance oximeter.

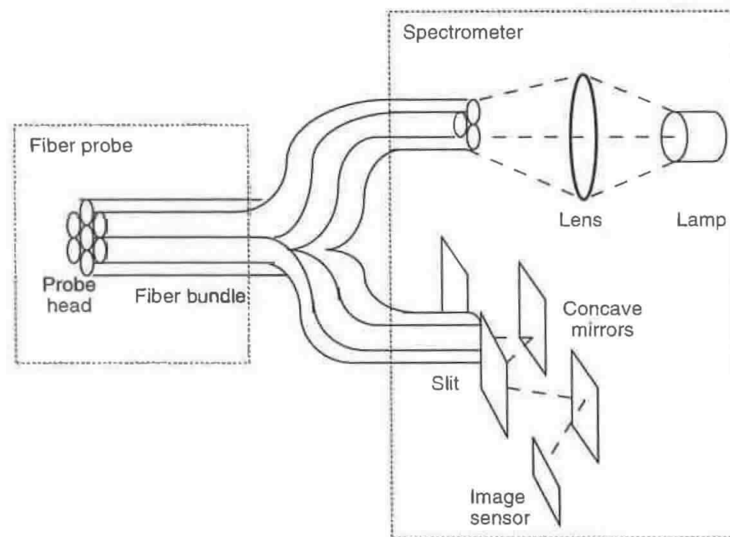

Figure 3.6 A fiber optic reflectance catheter oximeter (adapted from Ono *et al* 1991).

These devices do require user calibration though. The calibration can be done with a CO-oximeter or by the preferred method of *in vivo* calibration. Drift can occur after several hours and the catheter may need to be recalibrated.

Some of the early fiber optic catheters had the problem of wall artifacts, where reflections of light from a vessel wall would cause erroneous values of S_vO_2. New digital filtering techniques have helped to reduce that problem. Early

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catheters had a reputation for being stiff and hard to insert, but the use of plastic fiber optics has helped this issue (Barker 1991).

The early fiber optic oximeters were designed for cardiac catheterization to measure S_vO_2. Features have been added to some fiber optic probes for other uses. For example, some probes have a contact sensor or a pressure sensor to sense contact with tissue. This allows more stable data from *in vivo* tissue because the probe head can avoid excessive pressure which would affect microcirculation. Another application for the fiber optic oximeter is as a dental tool to diagnose SO_2 of gingiva (Ono *et al* 1991).

3.5.3 In vivo chemical oximeter

Peterson and Fitzgerald (1984) describe a chemical fiber optic oximeter suitable for measuring P_aO_2. A fluorescent dye in the tip of the probe reflects light sent by the oximeter back to a sensor. The dye has a unique property that it loses its luminescence in the presence of oxygen. Figure 3.7 shows the chemical fiber optic probe. The difference between this probe and the reflectance fiber optic probe is a small one. The reflectance fiber optic probe measures the change in color of the blood by reflecting light from it. This change in color indicates the degree of saturation. This device measures the change in color of a substance that changes color in the presence of oxygen.

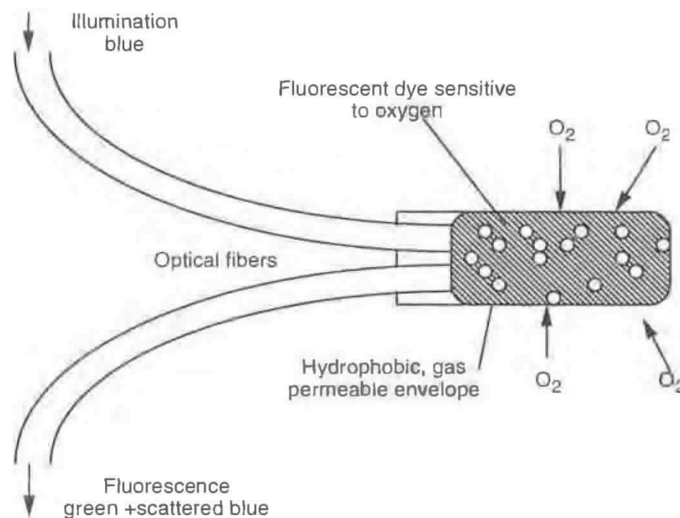

Figure 3.7 This figure shows the probe end of a chemical fiber optic oximeter. The coloration of the probe end changes in response to the amount of oxygen present.

3.6 *IN VIVO* EIGHT-WAVELENGTH OXIMETER

In 1970, Hewlett-Packard marketed an eight-wavelength oximeter, model 47201A. The device was designed to overcome some of the problems of the two-wavelength oximeter. It was designed to be self calibrating, accounted for factors

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like skin pigmentation, and claimed to be unaffected by motion (Merrick and Hayes 1976). The device also claimed to be precalibrated requiring no test samples. The only calibration necessary was an infrequent procedure that gave reference values of light intensity to the device, and did not involve the patient.

Figure 3.8 shows a block diagram of the 47201A. The lamp is a tungsten–iodine lamp which has a high output of light in the wavelengths of interest (650 nm to 1050 nm). The desired wavelengths are obtained with light filters. The filters are mounted on a rotating wheel so they cut the light beam sequentially. The wheel spins at 1300 rpm so about 20 samples at each wavelength are obtained every second.

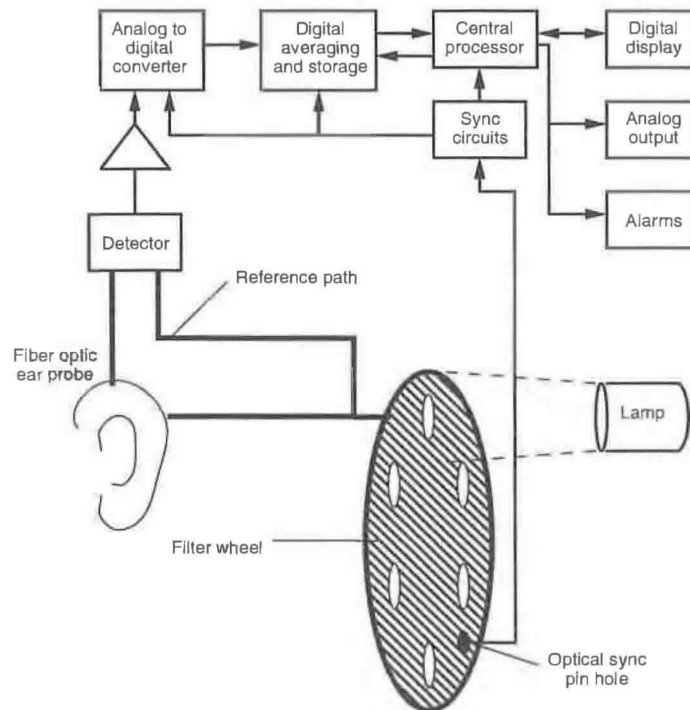

Figure 3.8 Block diagram of the Hewlett-Packard Model 47201A eight-wavelength ear oximeter.

The filtered light travels down two fiber optic paths. The first path leads directly to the photodetector and acts as a reference. This prevents any variations in the measurements due to changes in the light source or slight variations in the filters. The second fiber optic path goes to the ear probe. The filtered light is transmitted through the ear to a fiber optic cable which carries it to the photodetector. The current produced by the photodetector may be on the order of 0.5 nA so the output of the photodetector is amplified by a factor of 10^8. The absorbance is derived from the difference between the reference intensity and the intensity of the light transmitted through the ear.

For a time, the Hewlett-Packard device was the gold standard for oximeters. It worked fairly well and was the first introduction of noninvasive oximetry into

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a clinical environment. But it was found to be inaccurate for saturations less than 70%. And though it was a large improvement over previous devices, the Hewlett-Packard device was not totally immune to motion artifacts or skin pigmentation as it claimed. Also, it still required that the probe heat the skin. Devices that heat the skin put the patient at risk of burns, especially infants who have sensitive skin.

Although giving an improvement in performance, the device was huge, weighing almost 17 kg. The ear probe was also quite large and the fiber optics were fragile. Though it was the *gold standard* of oximeters in its time (Moyle 1994) it was used clinically only in sleep studies, pulmonary medicine, and physiology. The HP eight-wavelength oximeter was never used in anesthesiology or critical care as the pulse oximeter is today. Its use declined even more with improvements in the Clark transcutaneous PO_2 electrode (Severinghaus 1987).

3.7 PULSE OXIMETERS

The idea of exploiting the pulsatile nature of arterial blood in oximetry first belonged to Takuo Aoyagi while working in Japan for Nihon Kohden Corporation (Severinghaus 1987). Nihon Kohden's device used analog circuitry, had bulky fiber optic cables, and still had some of the instability problems of the Hewlett-Packard device. Other companies such as Minolta came up with similar products with similar problems (Santamaria and Williams 1994).

An anesthesiologist named William New saw the pulse oximeter marketed by Minolta and saw how to improve it. New, also an electrical engineer, teamed with Jack Lloyd to found Nellcor, Inc. Nellcor produced a microprocessor-based pulse oximeter, the N100, which was smaller, less expensive, needed no user calibration, and was accurate enough for clinical use. Nellcor is still the market leader in pulse oximetry (Santamaria and Williams, 1994). About the same time, Ohmeda came up with a similar device, the Biox II, which had similar success (Wukitsch *et al* 1988). Today, pulse oximeters exist in every intensive care unit, surgical suite, and in many emergency rooms in the United States (Santamaria and Williams 1994)

This section gives a brief description of the major parts of a pulse oximeter. Further detail of each of these parts can be found in later chapters.

3.7.1 Overview

By taking advantage of the pulsatile flow of blood, the pulse oximeter is able to overcome many of the problems of earlier technologies. The pulse oximeter tracks the change in light absorbance as the blood pulses. By tracking this peak-to-peak ac component, the absorbance due to venous blood or tissue does not have any effect on the measurement.

Light scattering is still a source of inaccuracy in pulse oximeters. Beer's law does not account for the scattering of light. So a direct calculation of S_aO_2 is not possible. The pulse oximeter measures absorbances at the two wavelengths and uses data from CO-oximeters to empirically look up a value for S_pO_2, an estimation of S_aO_2.

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3.7.2 LEDs

One of the large improvements of the pulse oximeter over earlier oximeters is the use of LEDs as the light source. The LEDs can transmit large intensities of light proportional to the amount of drive current. The LED control block in figure 3.9 controls the amount of drive current and the timing of the LEDs. The timing of the pulsations is critical because the photodiode cannot distinguish between different wavelengths of light. The pulse oximeter relies on the microprocessor system to synchronize the pulsations of the LEDs with the samples taken by the ADC so that the absorbances detected by the photodiode can be attributed to the correct LED.

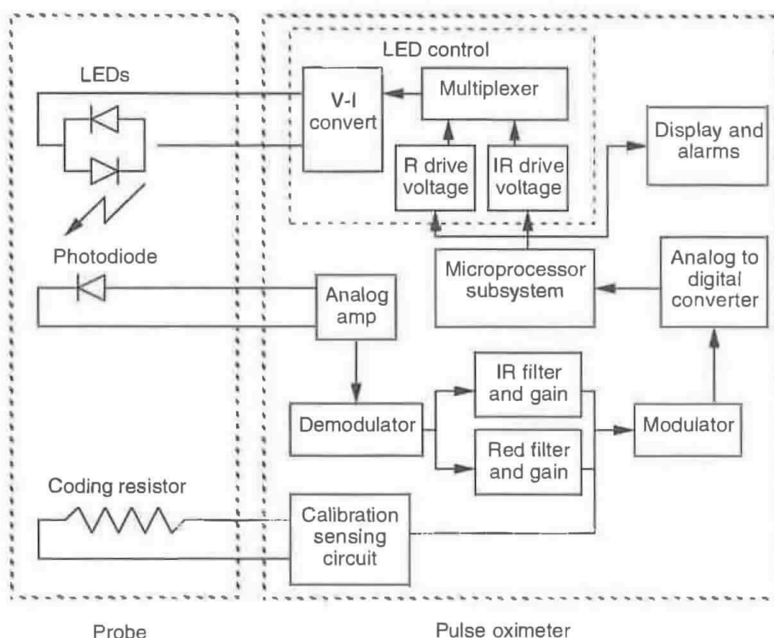

Figure 3.9 Block diagram of a pulse oximeter system. The arrows show the flow of data. The microprocessor also provides control and timing for the demodulator, modulator, and LED control circuits.

The two wavelengths chosen for pulse oximetry are 660 nm and 940 nm. These wavelengths were chosen based on the availability of LEDs at these wavelengths and because the extinction coefficients of Hb and HbO_2 vary as much as possible. HbO_2 has a higher extinction coefficient than Hb at 940 nm and a lower extinction coefficient at 660 nm. In other words, as S_aO_2 increases, the absorbance of light increases at 940 nm and decreases at 660 nm.

One disadvantage of using LEDs as a light source is that the exact wavelength of any single LED can vary by as much as ±15 nm. This would cause significant errors if unaccounted for. To account for this, some manufacturers characterize each LED and code it with a resistor value. By driving the coding resistor (figure 3.9) with a constant current source, the pulse oximeter can

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measure the voltage and take the characterization of the LEDs into account when empirically calculating S_pO_2 (Pologe 1987).

3.7.3 Photodiode

The photodetector is a silicon photodiode that produces current linearly proportional to the intensity of light striking it. Advances in silicon technology allow the photodiode to be small enough to fit in small, finger tip probes. These advances have helped make the pulse oximeter much more accurate and convenient than earlier devices. Early oximeter devices needed frequent calibration because the photoelectric devices used as sensors were often inconsistent (Miller 1966).

A photodiode cannot distinguish between red and infrared light, but to accommodate this, the microprocessor system alternately turns each LED on and off. The pulse oximeter repeatedly samples the photodiode output while the red LED is on, while the infrared LED is on, and while both are off. By sampling with both LEDs off, the pulse oximeter is able to subtract any ambient light that may be present (Pologe 1987).

3.7.4 Probes

Improved technology in photodiodes and LEDs has another benefit. They allow the probe to be small and attach to the pulse oximeter with conventional wires. The Hewlett-Packard eight wavelength oximeter was considered an accurate device, but because bulky fiber optic cables were needed to carry the light source to the patient and the transmitted light back to a light sensor, it was impractical (Rebuck *et al* 1983). Probes for the pulse oximeter are not only smaller, but can be disposable.

Figure 3.10 shows a transmission pulse oximeter and a reflectance pulse oximeter. As the names indicate, a transmission pulse oximeter measures the amount of light that passes through the tissue as in a finger probe. A reflectance pulse oximeter measures the amount of light reflected back to the probe. Both types use the same technology differing only in positioning of the probes and calibration.

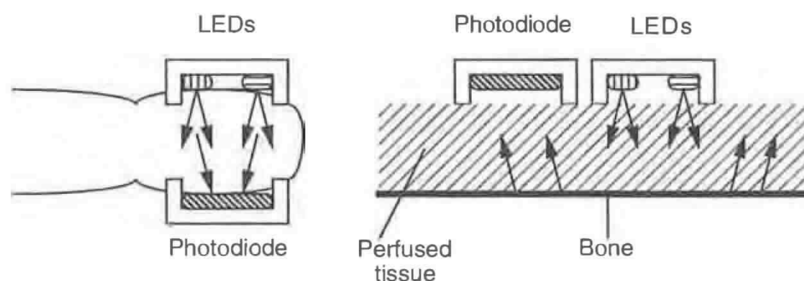

Figure 3.10 On the left is a transmission pulse oximeter measuring the transmission of light by two LEDs through the finger of a patient. On the right is a reflectance pulse oximeter measuring the amount of light reflected back to the probe.

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3.7.5 Analog amplifier and signal processing

The photodiode generates a current proportional to the intensity of light. The analog amplifier converts this current to a voltage. Because the change in voltage due to the pulsations of the arteries is small in comparison to the dc portion of the signal, the dc component of the signal is subtracted from the rest of the signal by the demodulator. The demodulator also uses a sample-and-hold timing circuit to separate samples from the red LED from the samples of the infrared LED. The ac portions of these signals are low-pass filtered to remove electromagnetic interference. Then each signal goes through a programmable gain circuit after which a multiplexer with another sample-and-hold circuit modulates the red and infrared signals back into one to go through an analog-to-digital converter (ADC) for use by the microprocessor.

Using the data gathered from the ADC, the microprocessor calculates what is called a ratio of ratios. From this ratio of ratios and the value of the coding resistor, the microprocessor goes to an empirical look up table for its S_pO_2 value. The empirical look up table is generated by the manufacturer through laboratory tests done with a CO-oximeter. The signal processing algorithms also provide some noise reduction. Some pulse oximeters use an ECG in their signal processing algorithm to minimize errors due to motion artifacts.

3.7.6 A three-wavelength pulse oximeter for COHb determination

Current pulse oximeters estimate the arterial oxygen saturation of the blood by measuring absorbances at two wavelengths of light. Because of this, the pulse oximeter is only able to account for Hb and HbO_2. Increased levels of COHb, for example, will cause an overestimation in S_aO_2 because the pulse oximeter cannot distinguish between HbO_2 and COHb. In cases of carbon-monoxide poisoning, this could have terrible consequences if the clinician is unaware.

Table 3.1 A comparison of pulse oximetry and transcutaneous PO_2 electrodes from New (1985), Barker and Tremper (1984), and Severinghaus (1987).

Pulse oximeters	Transcutaneous $P_{tc}O_2$ electrodes
Require no heating	Have internal heaters which can cause burns and must be moved periodically to avoid skin damage, especially in infants
Have no delay	Require skin and electrode preparation and a warm up period of up to ten minutes
Never require user calibration	Require recalibration
Probes are clipped or taped on	Require operator skill to place monitor
Measure a pure respiratory variable (S_aO_2) and a pure circulatory variable (plethysmograph)	Are a sensitive, but not specific, monitor of blood oxygenation; a drop in $P_{tc}O_2$ may be caused by respiratory deficiency, circulatory deficiency, or both
Give an accurate reading or none at all	Report low PO_2 when electrode may not be placed well
Require pulsating arteries; fails during cardiac arrest, cardiopulmonary bypass, or distal placement to blood pressure cuff.	Detect low cardiac output
Require hemoglobin in the bloodstream and may fail with severe anemia or hemodilution	Are not dependent on hemoglobin
Can be in error with high levels of dyshemoglobin species present in the blood	
Display pulse rate	Do not display pulse rate

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Buinevicius (1987) designed a three wavelength pulse oximeter to solve this problem. An additional LED at 810 nm was used in an attempt to determine the amount of COHb in the blood. Buinevicius also presented a method to calibrate the pulse oximeter for three wavelengths using three-dimensional solutions to Beer's law.

3.7.7 Comparison of pulse oximetry to transcutaneous PO_2 electrodes

Pulse oximeters and transcutaneous PO_2 electrodes are the two main technologies used to provide continuous information about the supply of oxygen to the body. Table 3.1 provides a comparison between the two technologies.

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INSTRUCTIONAL OBJECTIVES

3.1 Explain why transcutaneous PO_2 electrodes require the skin to be heated.
3.2 Explain why a CO-oximeter uses hemolyzed blood samples to determine the hemoglobin components of the blood.
3.3 Explain the difference between absorptivity and absorbance.
3.4 Describe a noninvasive two-wavelength oximeter and its problems.
3.5 Describe a two-wavelength fiber optic oximeter.
3.6 Describe an eight-wavelength oximeter.
3.7 Describe how pulse oximeters overcome some of the problems of earlier oximeters.
3.8 Explain the need for a coding resistor in a pulse oximeter probe.
3.9 Explain why Beer's law cannot be used for direct computation of S_pO_2 and empirical lookup tables are used instead.
3.10 Given the concentrations of oxyhemoglobin and reduced hemoglobin for blood, calculate S_pO_2.
3.11 Explain why a pulse oximeter might not be as accurate for a patient who is a smoker.
3.12 Describe a three-wavelength pulse oximeter to determine COHb concentration and explain it might be more accurate for a patient who is a smoker than a two-wavelength pulse oximeter.

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CHAPTER 4

LIGHT ABSORBANCE IN PULSE OXIMETRY

Oliver Wieben

This chapter describes the theoretical background for the measurement of light absorbance in pulse oximetry as a basis for determining arterial oxygen saturation. Beer's law and the derivation of a theoretical calibration curve for measured light absorbances in pulse oximeters is explained, although this curve is not valid in practice due to the scattering of light. Beer's law is used accurately to determine the oxygen saturation of hemoglobin solutions but does not apply for whole blood because of the scattering effects. Nevertheless, this model helps to develop an understanding of the absorbance of light as it passes through living tissue and why and how pulse oximetry works. The normalization of the measured signals and the calibration curves used in pulse oximeters are explained after an introduction of the theoretical model. The final part of the chapter describes mathematical approaches to incorporate light scattering in the model and describe its effects qualitatively and quantitatively.

4.1 BEER'S LAW

Beer's law (also referred to as Beer–Lambert's or Bouguer's law) describes the attenuation of light traveling through a uniform medium containing an absorbing substance. If monochromatic incident light of an intensity I_0 enters the medium, a part of this light is transmitted through the medium while another part is absorbed. The intensity I of light traveling through the medium decreases exponentially with distance

$$I = I_0 \, e^{-\varepsilon(\lambda) c d} \tag{4.1}$$

where $\varepsilon(\lambda)$ is the *extinction coefficient* or absorptivity of the absorbing substance at a specific wavelength, c the concentration of the absorbing substance which is constant in the medium, and d the optical path length through the medium (see figure 4.1). The concentration c is measured in mmol L^{-1} and the extinction coefficient is expressed in L $mmol^{-1}$ cm^{-1}.

Beer's law is based on the property that the sum of transmitted and absorbed light equals the incident light. It does not account for physical processes which include reflection of the light at the surface of the medium or scattering of light in the medium.

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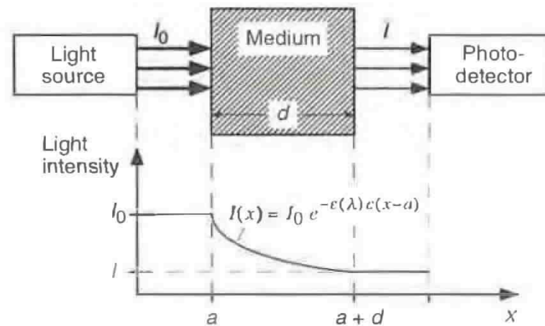

Figure 4.1 Beer's law: Incident light of intensity I_0 travels the distance a from a light source to the medium without being absorbed in the air. The light intensity decreases exponentially with distance in the absorbing medium. The intensity of the transmitted light I is determined by Beer's law. It stays constant after exiting the medium with optical path length d and can be measured by a photodetector.

4.1.1 Transmittance and absorbance of light

The *transmittance* (T) of light traveling through a medium with an absorbing substance is defined as the ratio of transmitted light I to the incident light I_0

$$T = \frac{I}{I_0} = \mathrm{e}^{-\varepsilon(\lambda)cd}. \tag{4.2}$$

The *unscattered absorbance* (A) of this process is defined as the negative natural logarithm of the transmittance of light

$$A = -\ln T = \varepsilon(\lambda)cd. \tag{4.3}$$

The absorbance is sometimes referred to as the optical density of a medium.

4.1.2 Multiple absorbers

The properties of Beer's law are valid even if more than one substance absorbs light in the medium. Each absorber contributes its part to the total absorbance. The mathematical representation of this system of absorbers is a superposition of the individual absorbing processes. The resulting *total absorbance* A_t of light in a medium with n absorbing substances is the sum of their n independent absorbances

$$A_t = \varepsilon_1(\lambda)c_1 d_1 + \varepsilon_2(\lambda)c_2 d_2 + \ldots + \varepsilon_n(\lambda)c_n d_n = \sum_{i=1}^{n} \varepsilon_i(\lambda)c_i d_i \tag{4.4}$$

where $\varepsilon_i(\lambda)$ and c_i represent the extinction coefficient and concentration of the substance i and d_i represents the optical path length through the absorbing substance, which may differ from substance to substance in the medium.

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Therefore, Beer's law allows us to determine the unknown concentrations of n different absorbing substances in a homogeneous medium if the absorbance of light is measured at n different wavelengths and the extinction coefficients of the substances are known.

4.2 HEMOGLOBIN EXTINCTION COEFFICIENTS

Hemoglobin is the main light absorber in human blood at wavelengths used in pulse oximetry. The absorbing characteristics of hemoglobin change with its chemical binding and the wavelength of the incident light. Although oxygenated and reduced hemoglobin absorb most of the light passing through blood, they do not represent the only two hemoglobin species present in human blood. Hemoglobin may combine with other substances such as carbon monoxide or hydrogen sulfide as well, which changes its color.

4.2.1 Functional hemoglobins

Binding oxygen in the pulmonary capillaries and releasing it in the systemic capillaries is the main purpose of hemoglobin. Hemoglobins that are able to bind reversibly with molecular oxygen are called *functional hemoglobins*.

When hemoglobin is fully saturated with oxygen (carrying four oxygen molecules), it is called *oxyhemoglobin* (HbO_2). If it is not fully saturated with oxygen it is called *reduced hemoglobin* (Hb). Therefore oxyhemoglobin and reduced hemoglobin are functional hemoglobins.

Most of the hemoglobins in a healthy individual are functional hemoglobins. The *functional oxygen saturation* (functional SO_2) is measured in percentage and determined by the amount of oxygenated hemoglobin (HbO_2) as compared to the sum of oxygenated and reduced hemoglobin (Hb). Another way to define this ratio is to use the concentrations of oxygenated hemoglobin (c_{HbO_2}) and reduced hemoglobin (c_{Hb})

$$\text{Functional } SO_2 = \frac{HbO_2}{Hb + HbO_2} \times 100\% = \frac{c_{HbO_2}}{c_{HbO_2} + c_{Hb}} \times 100\%. \qquad (4.5)$$

The functional oxygen saturation of explicitly arterial blood is called functional arterial oxygen saturation (functional S_aO_2) and is referred to as functional hemoglobin saturation as well.

4.2.2 Dysfunctional hemoglobins

Dysfunctional hemoglobins (or dyshemoglobins) do not support the transport of oxygen to the tissues. They are either unable to bind reversibly to oxygen or interfere with the ability of oxyhemoglobin to release its oxygen to the tissue.

The four most common dyshemoglobins are methemoglobin (MetHb), carboxyhemoglobin (COHb), sulfhemoglobin, and carboxysulfhemoglobin.

4.2.2.1 Methemoglobin. Methemoglobin is oxidized hemoglobin. It is a result of oxidation of a free heme iron (Fe^{2+}) instead of the reversible binding of oxygen to heme inserted into globin subunits.

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$$HbFe^{2+} \Leftrightarrow HbFe^{3+} + e^{-}. \qquad (4.6)$$

An enzyme system (including cytochrome b_5) is responsible for reducing the methemoglobin in the red cells by maintaining hemoglobin in the reduced state (Fe^{2+}).

Oxidized hemoglobin subunits are not capable of binding oxygen and altering the oxygen binding of the remaining ferrous hemes. Therefore, methemoglobin has a great influence on the functionality of hemoglobin. Under physiological circumstances the amount of methemoglobin remains below 0.6% of the total hemoglobin and this amount varies at a rate of 2 to 3% during the day. The absorbance spectrum of methemoglobin is strongly pH-dependent (Bunn 1986).

4.2.2.2 Carboxyhemoglobin. Carboxyhemoglobin is formed when hemoglobin combines with carbon monoxide (CO). The carbon atom of carbon monoxide is bonded to the iron atom of heme.

The affinity of hemoglobin binding with carbon monoxide is approximately 210 times larger than that of oxygen. Therefore, the presence of a high level of carbon monoxide will reduce the amount of oxygenated hemoglobin significantly. The level of carboxyhemoglobin in the blood varies with the habits and surroundings of the individual. Smoking, working in underground garages, traffic tunnels, mines, etc. increases the amount of CO in the blood. In nonsmokers the level of COHb is usually below 2% but this value varies with the local environment (Wukitsch *et al* 1988).

4.2.2.3 Sulfhemoglobin and carboxysulfhemoglobin. The reaction of oxyhemoglobin and hydrogen sulfide produces sulfhemoglobin. The relevant chemical reactions are complex and not thoroughly understood, although the absorbance spectrum of sulfhemoglobin is known.

The oxygen affinity of the heme iron in sulfhemoglobin is 100-fold lower than the oxygen affinity of unmodified hemoglobin (Bunn 1986). This chemical reaction is irreversible (Nellcor 1993). Carboxysulfhemoglobin results from a reaction of sulfhemoglobin with carbon monoxide. The concentrations of sulfhemoglobin and carboxysulfhemoglobin in human blood are usually not significant.

4.2.2.4 Fractional hemoglobin saturation. The *fractional oxygen saturation* is the fraction of oxygenated hemoglobin to the total hemoglobin. It is usually measured in percentage as well and is determined by the ratio of the concentrations of oxygenated hemoglobin to total hemoglobin

$$\text{Fractional } SO_2 = \frac{c_{HbO_2}}{c_{\text{total hemoglobin}}} \times 100\% \qquad (4.7)$$

where total hemoglobin represents all different species of hemoglobin present in the blood.

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4.2.3 Hemoglobin absorbance spectra

The chemical binding of the different hemoglobin species changes the physical properties of the hemoglobin as well. Figure 4.2 shows the extinction coefficients of oxyhemoglobin, reduced hemoglobin, methemoglobin and carboxyhemoglobin at wavelengths in the range of interest in pulse oximetry.

The absorbance of light in the red region of the spectrum is much higher for reduced hemoglobin than for oxyhemoglobin. The extinction coefficients of both hemoglobin species are equal at the point isosbestic point (805 nm). The reduced hemoglobin is more transparent to light from the infrared region than oxyhemoglobin.

The extinction coefficient of carboxyhemoglobin is about the same as that of oxyhemoglobin at the wavelength of 660 nm while it is almost transparent in the infrared region. Methemoglobin absorbs much light in the red region of the spectrum and its extinction coefficient remains higher than that of oxyhemoglobin in the infrared region.

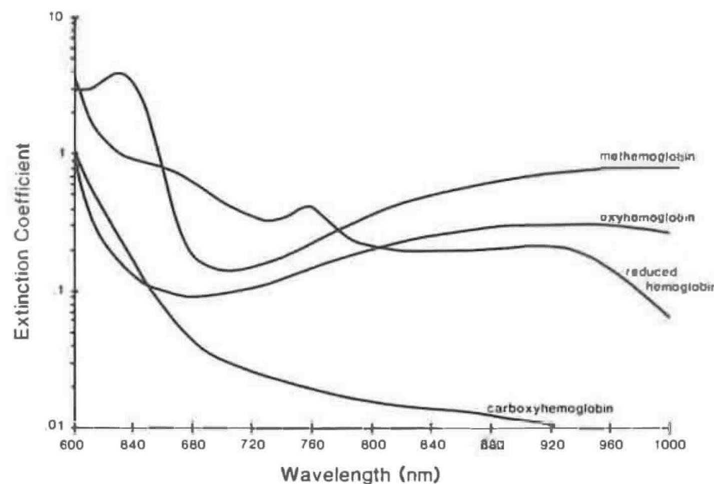

Figure 4.2 Extinction coefficients of the four most common hemoglobin species oxyhemoglobin, reduced hemoglobin, carboxyhemoglobin, and methemoglobin at the wavelengths of interest in pulse oximetry (courtesy of Susan Manson, Biox/Ohmeda, Boulder, CO).

4.3 BEER'S LAW IN PULSE OXIMETRY

Pulse oximeters determine the oxygen saturation of arterial blood by measuring the light absorbance of living tissue at two different wavelengths and using the arterial pulsation to differentiate between absorbance of arterial blood and other absorbers.

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4.3.1 Criteria for the choice of wavelengths

Different reasons lead to the most common choice for wavelengths used in pulse oximetry. The red skin pigmentation absorbs a great amount of light at wavelengths shorter than 600 nm and therefore it is not desirable to measure light absorbance in this range. Large differences in the extinction coefficients of reduced hemoglobin and oxygenated hemoglobin change the absorbance of light significantly, even when the oxygen saturation changes slightly. A good choice for a wavelength in the red region is 660 nm because of a large difference in the extinction coefficients.

Another issue for the wavelength choice is flatness of the absorption spectra shown in figure 4.2 around the chosen wavelength. Otherwise shifts in the peak wavelength of the LEDs (see section 5.3) will result in a larger error. The absorbance spectra of reduced hemoglobin and oxygenated hemoglobin are relatively flat at 660 and 940 nm (Moyle 1994).

Mannheimer *et al* (1997) have shown that sensors fabricated with 735 and 890 nm emitters read more accurately at low saturations under a variety of conditions, while 660 and 990 nm emitters read more accurately at high saturations.

4.3.2 Absorbance in hemoglobin solutions

The different species of hemoglobin are the main light absorbers in arterial and venous blood. Most of the hemoglobin in human blood is either oxygenated or reduced hemoglobin which determine the functional oxygen saturation SO_2 (equation (4.5)). The concentrations of oxygenated hemoglobin (c_{HbO_2}) and reduced hemoglobin (c_{Hb}) can be expressed as a function of SO_2 as a fraction and the sum of the concentrations c_{HbO_2} and c_{Hb}

$$c_{HbO_2} = SO_2(c_{HbO_2} + c_{Hb}) \tag{4.8}$$

$$c_{Hb} = (1 - SO_2)(c_{HbO_2} + c_{Hb}). \tag{4.9}$$

According to Beer's law we derive the total absorbance A_t of a solution containing only reduced and oxygenated hemoglobin as absorbing substances from equation (4.4)

$$A_t = \varepsilon_{HbO_2}(\lambda) c_{HbO_2} d_{HbO_2} + \varepsilon_{Hb}(\lambda) c_{Hb} d_{Hb}. \tag{4.10}$$

Assuming that the optical path length d is the same for the oxygenated hemoglobin (d_{HbO_2}) and reduced hemoglobin (d_{Hb}) and using equations (4.8), (4.9), and (4.10), we derive

$$A_t = \left[\varepsilon_{HbO_2}(\lambda) SO_2 + \varepsilon_{Hb}(\lambda)(1 - SO_2)\right](c_{Hb} + c_{HbO_2})d. \tag{4.11}$$

Thus A_t can be expressed for known concentrations of hemoglobin in terms of functional oxygen saturation as a fraction, the extinction coefficients of hemoglobin, and the length of the optical path. Values for the extinction coefficients of adult reduced hemoglobin (ε_{Hb}) and adult oxygenated hemoglobin

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(ε_{HbO_2}) at the two wavelengths most commonly used in pulse oximetry (660 nm and 940 nm) have been measured by Zijlstra *et al* (1991) (see table 4.1).

Table 4.1 Table of extinction coefficients of reduced and oxygenated hemoglobin in adults at the wavelengths of 660 nm and 940 nm (values from Zijlstra *et al* 1991).

Wavelength, nm	Extinction coefficient, L mmol^{-1} cm^{-1}	
	Hb	HbO_2
660	0.81	0.08
940	0.18	0.29

Figure 4.3 shows the characteristics of light absorbance for a sample with a fixed concentration of total functional hemoglobin ($c_{HbO_2} + c_{Hb}$) of 1 mmol L^{-1}, a fixed path length d of 1 cm and varying functional oxygen saturations. The two lines shown in figure 4.4 represent the properties for the two most commonly used wavelengths in pulse oximetry (660 nm and 940 nm). The absorbance of light at a wavelength of 940 nm increases with an increased oxygen saturation. At 660 nm the absorbance of light decreases rapidly with an increasing functional oxygen saturation (Pologe 1987).

It is possible to determine the concentrations of hemoglobins in hemoglobin solutions or hemolized blood by using a device such as a spectrophotometer (see section 3.3).

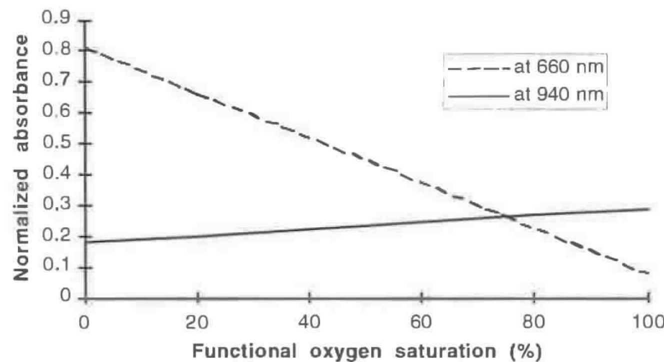

Figure 4.3 Changes in light absorbance in hemoglobin solutions as a function of functional oxygen saturation for the wavelengths used in pulse oximetry. Absorbance decreases rapidly with increasing oxygen saturation at 660 nm (dashed line) but increases slightly with increasing oxygen saturation at 940 nm (solid line).

4.3.3 Pulsation of the blood

Light traveling through biological tissue (e.g. the finger or earlobe) is absorbed by different absorbing substances. Primary absorbers of light in the region of interest are the skin pigmentation, bones, and the arterial and venous blood. Instead of measuring the arterial oxygen saturation of the blood *in vitro* with a sample of arterial blood and a spectrophotometer, or at a wide range of different wavelengths as with the Hewlett-Packard ear oximeter, pulse oximeters take

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advantage of *arterial pulsation*. Figure 4.5 shows the amount of absorbed and transmitted light in living tissue as a function of time.

The arteries contain more blood during systole than during diastole, and therefore, their diameter increases due to increased pressure. This effect occurs only in the arteries and arterioles but not in the veins. The absorbance of light in tissues with arteries increases during systole mainly because of the larger amount of absorbing substances (hemoglobin), due to the fact that the optical path length d in the arteries increases. This alternating part of the total absorbance allows us to differentiate between the absorbance due to venous blood, a constant amount of arterial blood, and other nonpulsatile components such as skin pigmentation (dc component of the total absorbance) and the absorbance due to the pulsatile component of the arterial blood (ac component). The alternating part of the light absorbed by the living tissue usually does not exceed 1% to 2% of the constant absorbance of the dc components. The time varying signal of transmitted light is referred to as the plethysmographic (or photoplethysmographic) signal.

The intensity of the light passing through the tissue during diastole is high (I_H). The absorbers that are present during diastole are the DC components. All DC components except the nonpulsating arterial blood are collectively represented by $\varepsilon_{DC}(\lambda)$, c_{DC}, and d_{DC}. The diameter of the arterial vessels is minimal (d_{min}) and therefore the absorbance due to arterial hemoglobin is minimal and the amount of transmitted light is high (I_H) and has a peak (see figures 4.4 and 4.5)

$$I_H = I_0 \, e^{-\varepsilon_{DC}(\lambda) c_{DC} d_{DC}} e^{-[\varepsilon_{Hb}(\lambda) c_{Hb} + \varepsilon_{HbO_2}(\lambda) c_{HbO_2}] d_{min}} \tag{4.12}$$

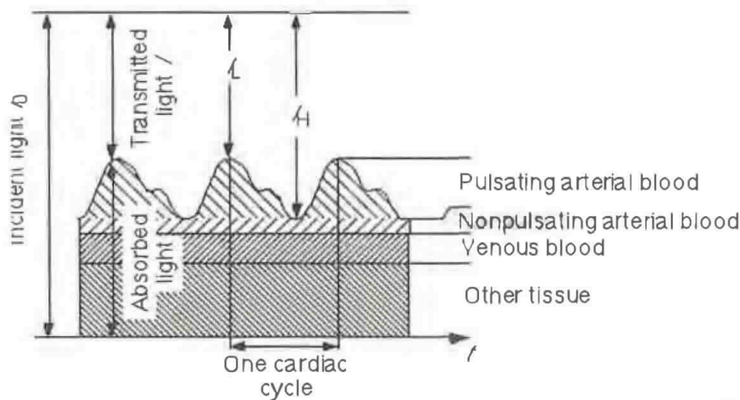

Figure 4.4 Absorbed and transmitted light in living tissue. The amount of absorbed light correlates with the pulsation of arterial blood. A constant amount of light is absorbed by the skin pigmentation, bone, other tissue, venous blood and the nonpulsating part of the arterial blood. More blood is present in the arteries during systole and therefore more light is absorbed. The intensity of the transmitted light varies from I_H (maximum) to I_L (minimum) within one cardiac cycle.

The optical path length in the arteries increases during the systole to d_{max}. The amount of absorbed light reaches a maximum peak and therefore the transmitted light reaches the low peak I_L:

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$$I_L = I_0\, e^{-\varepsilon_{DC}(\lambda) c_{DC} d_{DC}}\, e^{-[\varepsilon_{Hb}(\lambda) c_{Hb} + \varepsilon_{HbO_2}(\lambda) c_{HbO_2}] d_{max}}. \qquad (4.13)$$

The light intensity I of the light arriving at the photodetector is a function of the diameter d of the arteries and arterioles. During one cardiac cycle this diameter changes from d_{min} to d_{max}. By substituting d with $d_{min} + \Delta d$ we derive the following expression from Beer's law, where I is expressed as a function of I_H and Δd, the part of the diameter that changes from 0 to $d_{max} - d_{min}$ with time

$$I = I_H e^{-[\varepsilon_{Hb}(\lambda) c_{Hb} + \varepsilon_{HbO_2}(\lambda) c_{HbO_2}]\Delta d}. \qquad (4.14)$$

Figure 4.5 shows these properties in a simplified model.

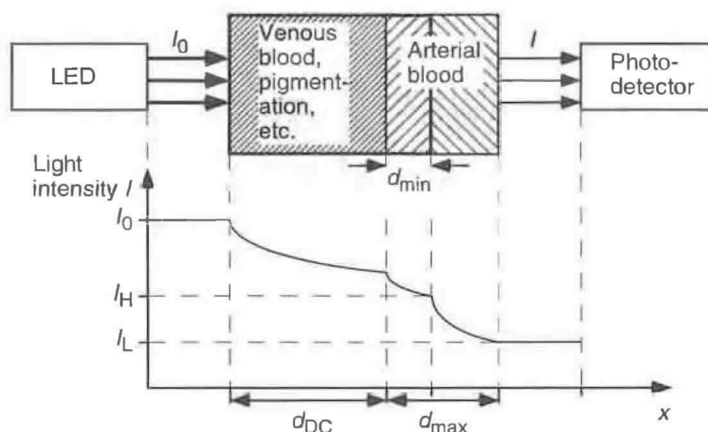

Figure 4.5 Beer's law in pulse oximetry. The DC components of the tissue (e.g. skin pigmentation, bone, venous blood and the nonpulsating part of the arterial blood) absorb a constant amount of the incident light I_0. The effective optical path length in the DC components without the constant level of arterial blood is represented by d_{DC}. During diastole the optical path length through the arteries has a minimum length of d_{min} and the light intensity at the photodetector is maximal (I_H). The optical path length reaches a maximum d_{max} during systole and the hemoglobin in the arteries absorbs a maximum amount, causing I to decrease to a minimum level of I_L.

4.3.4 Measurement of pulse oximeters

The reading of the pulse oximeter S_pO_2 is an estimation of the arterial oxygen saturation S_aO_2. Measuring at two wavelengths allows us to distinguish the concentrations of only two different absorbers (Hb and HbO_2). But in humans more species of hemoglobin, such as carboxyhemoglobin and methemoglobin, are present. These other hemoglobins absorb light as the functional hemoglobins do and therefore influence our measurements. As long as we do not measure at as many wavelengths as absorbers are present in the blood, we can not determine the concentrations of Hb and HbO_2 and therefore the arterial oxygen saturation correctly (Barker and Tremper 1987).

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Due to the fact that Hb and HbO_2 are the main absorbers, the error may be small. Nevertheless, the results of determining either the actual functional or fractional oxygen saturation (see equations (4.5) and (4.7)) of the arterial blood are not exact. This problem is also discussed in sections 10.1.1 and 11.1.1. The oximeter reading becomes less accurate if the concentrations of dyshemoglobins are larger than in normal humans. Section 11.7 deals with the presence of high concentrations of dysfunctional hemoglobins.

4.4 SATURATION VERSUS NORMALIZED RATIO

The arterial oxygen saturation can be derived based on Beer's law as a function of the ratio of absorbances at two wavelengths. Due to nonlinearities in the LEDs, the photodetector, and light absorbance in the tissue, the absorbances have to be normalized in the ratio. This model results in a theoretical calibration curve, but it is not used in practice as will be described in the following sections.

4.4.1 Normalization

The measured light intensities at the different wavelengths have to be *normalized* before they can be compared with each other due to the fact that the light-emitting diodes (LEDs) may emit light with different intensities. The absorbing characteristics of the DC components and the sensitivity of the photodetector differ for the two different wavelengths and the tissue absorption and path length varys widely from patient to patient and with the probe site (de Kock and Tarassenko 1991). The normalized signal I_n is calculated by dividing the transmitted light intensities (the *raw signals*) by their individual maximum peaks ($I_{H,R}$ for the red wavelength and $I_{H,IR}$ for the infrared wavelength). From equation (4.14) we derive

$$I_n = \frac{I}{I_H} = e^{-[\varepsilon_{Hb}(\lambda)c_{Hb} + \varepsilon_{HbO_2}(\lambda)c_{HbO_2}]\Delta d}. \qquad (4.15)$$

This results in normalized signals with the same intensities $I_{H,n}$ during diastole. The normalized signals of the transmitted red and infrared light are independent of the incident light levels and photodetector nonlinearities as shown in figure 4.6. The AC components of the normalized signals represent only changes of transmitted light caused by the pulsation of blood in the arteries and can be compared with each other. They depend on the absorbers present in the arterial blood (ideally Hb and HbO_2) and the actual optical path length d through the volume changing part of the arteries.

4.4.2 Ratio of normalized signals

The absorbance of the light is derived by calculating the natural logarithm of the measured and normalized transmitted light level. Dividing the raw signal by the transmitted light during diastole I_H as in equation (4.15) and calculating the total absorbance then is comparable to calculating the total absorbance only due to the AC components in the pathway. The transmitted light during diastole represents the new nonchanging incident light level and the *ratio R* of these normalized

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absorbances at the red (R) and infrared (IR) wavelengths depends only on the light absorbers present in the arterial blood (see equation (4.3))

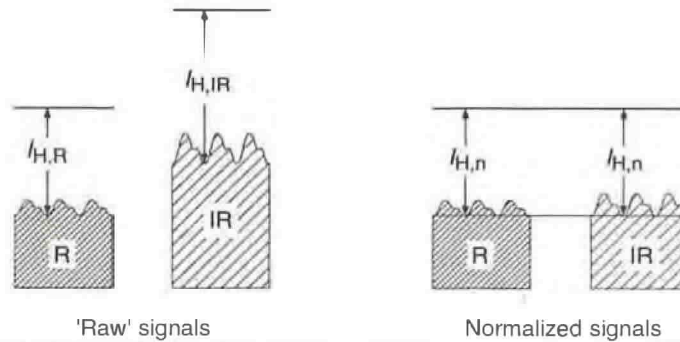

Figure 4.6 The normalization of the signals. The transmitted light from the red LED (R) and from the infrared LED (IR) is divided by its individual DC component. Thus, both normalized light intensities have the same magnitude during diastole. The normalized signals determine the basis for the calculation of the arterial oxygen saturation.

$$R = \frac{A_{t,R}}{A_{t,IR}} = \frac{\ln(I_{L,R} / I_{H,R})}{\ln(I_{L,IR} / I_{H,IR})}. \tag{4.16}$$

By using equation (4.15) the ratio can be derived as

$$R = \frac{[(\varepsilon_{Hb}(\lambda_R)c_{Hb} + (\varepsilon_{HbO_2}(\lambda_R)c_{HbO_2}]\Delta d_R}{[(\varepsilon_{Hb}(\lambda_{IR})c_{Hb} + (\varepsilon_{HbO_2}(\lambda_{IR})c_{HbO_2}]\Delta d_{IR}}. \tag{4.17}$$

Assuming that the optical path lengths d_R for red light and d_{IR} for the infrared light are equal, only the arteries change their diameter, and using equation (4.11)

$$R = \frac{\varepsilon_{Hb}(\lambda_R) + [\varepsilon_{HbO_2}(\lambda_R) - \varepsilon_{Hb}(\lambda_R)]SaO_2}{\varepsilon_{Hb}(\lambda_{IR}) + [\varepsilon_{HbO_2}(\lambda_{IR}) - \varepsilon_{Hb}(\lambda_{IR})]SaO_2}. \tag{4.18}$$

In this form the ratio R is not a function of the optical path length and can be derived from the arterial oxygen saturation instead of the concentration of the hemoglobins in the blood (see de Kock and Tarassenko 1993).

4.4.3 Theoretic calibration curve

Equation (4.18) can be rewritten in a form where S_aO_2 is a function of the measured and calculated ratio R

$$S_aO_2 = \frac{\varepsilon_{Hb}(\lambda_R) - \varepsilon_{Hb}(\lambda_{IR})R}{\varepsilon_{Hb}(\lambda_R) - \varepsilon_{HbO_2}(\lambda_R) + [\varepsilon_{HbO_2}(\lambda_{IR}) - \varepsilon_{Hb}(\lambda_{IR})]R} \times 100\%. \tag{4.19}$$

Therefore, the functional oxygen saturation in arterial blood can be derived theoretically by calculating the ratio R of measured and normalized total light

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absorbances in the red and infrared region and using equation (4.19). Figure 4.7 plots this relationship as the *theoretical calibration curve*.

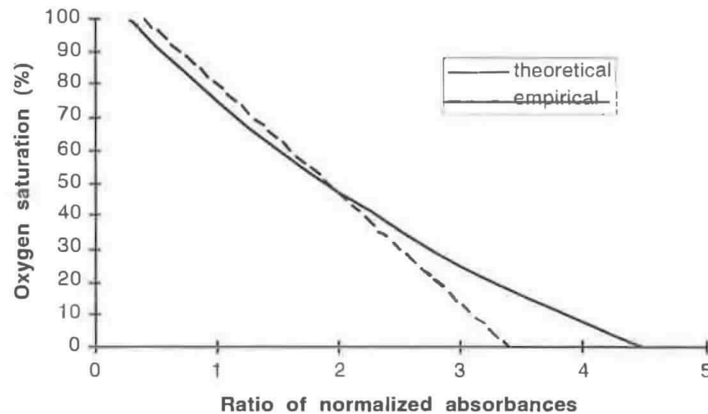

Figure 4.7 Calibration curves for pulse oximeters: the solid line is the theoretical curve by Beer's law and the dashed line is the empirical curve. The difference between these curves is due mainly to light scattering effects. This empirical calibration curve is derived by a second order polynomial.

4.5 VALIDITY OF BEER'S LAW IN PULSE OXIMETRY

Incident light passing through human tissue is not split only into absorbed light and transmitted light as proposed by Beer's law. Some parts of the light are reflected and others are scattered.

Light reflection at the skin surface and light absorbance due to tissue other than the pulsating arterial blood are overcome by using the plethysmographic waveform. However, the skin surface, tissue, muscle, bone and especially blood cause light scattering which increases the absorbance of light (see following section). Blood is a nonhomogeneous liquid, which is capable of nonlinear absorbance of light, e.g. as the concentration of hemoglobins varies (Wukitsch *et al* 1988).

The variation in light absorbance is not entirely due to the increased optical path length during systole. If the change in diameter were the only reason, the variation would be much less. The reason is a change in the axis of the red blood cells, which changes their absorbance as well. Red blood cells have the shape of a biconcave disk. Their major diameter is aligned parallel to the direction of blood flow during diastole and aligns perpendicular to the direction of flow during systole. Therefore, the optical path length is larger during systole and increases light absorbance. Even the light reflectance changes with the axis of the red blood cells, which is important for the use of reflectance probes. As a result of these properties, the absorbance and reflectance of blood in motion varys within the cardiac cycle and with the velocity of blood flow (Moyle 1994).

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4.6 LIGHT SCATTERING

The results of oximetry measurements with whole blood differ from the results of the theory based on Beer's law. A physical phenomenon called *light scattering* highly increases the absorbance of light. Nevertheless, pulse oximeters read the arterial oxygen saturation of the blood accurately enough for clinical use under normal circumstances. This is due to the fact that most of the commercial pulse oximeters use a calibration curve based on empirical data, because modeling the problem of light scattering mathematically for different conditions is very complex. Several approaches have been made to create models which describe the real process within certain limits of accuracy.

4.6.1 Light absorbance in whole blood

Unfortunately Beer's law does not apply for whole blood. The absorbance of light is not simply proportional to the concentration of hemoglobin or to the length of the optical path. Beer's law assumes no light scattering, which is not true in whole blood, besides the fact that the LEDs do not emit monochromatic light.

Shymada and Yoshida (1984) verified that the influence of multiple scattering can not be overcome be subtracting the DC level as had been expected. Kramer *et al* (1951) stated that the absorbance of light due to oxyhemoglobin and reduced hemoglobin is increased in whole blood compared to hemolyzed blood by factors of the order of five.

The reasons for the increased absorbance are mainly *scattering* and *multiple scattering*. Light scattering causes the deviation of a light beam from its initial direction. It occurs when light is refracted by an object of a size similar to the magnitude of the wavelength of the light and a change in the index of refraction at the interface of this object. The wavelengths of red and infrared light do have the same order of magnitude as the geometric dimensions of red blood cells (approximately 7 μm in diameter). The discontinuity in the index of refraction at the interface between plasma and red blood cells and the great proportion of red blood cells in blood yield a highly light scattering medium. Light that is scattered once will likely be scattered again by cells and therefore multiple scattering occurs (Steinke and Shepherd 1986). Multiple scattering increases the optical path length and therefore increases the absorbance.

The intensity of the light scattered by the tissue depends on such factors as the red blood cell concentration in the blood; on the size, shape, orientation, and index of refraction of the scattering particles; on the tissue thickness; and on the aperture cone of the detector (Fine and Weinreb 1995). The thickness of the tissue, the distance between the LED and the photodiode, and the concentration of hemoglobin will vary from patient to patient and the shape and orientation of the red blood cells is irregular. Thus it is difficult to develop a physical model which can be used under different circumstances.

4.6.2 Models for light absorbance including scattering

It would be very useful to find a relationship between S_aO_2 and the ratio R of normalized absorbances for whole blood instead of only for hemoglobin solutions. An accurate scattering theory for whole blood could replace the

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empirical calibration curves used for the S_pO_2 readings. A few attempts are described below.

4.6.2.1 Twersky's multiple scattering theory. Twersky (1962, 1970a,b) has developed an analytical theory to describe the scattering of light by large, low-refracting, and absorbing particles. It is based on electromagnetic field theory and uses statistical averages to expand the theory for scattering and absorbing valid for a single particle, to find a formulation valid for multiple scattering (de Kock and Tarassenko 1993).

The total absorbance of whole blood can be expressed as the sum of absorbance as described by Beer's law and a second term representing the attenuation of light due to scattering. These two processes can be treated as independent processes. The intensity of scattering depends on variables such as those mentioned in section 4.6.1. The theory can be adapted for a special setting and will provide accurate results, but once the physiological conditions change, recalibration is required (Fine and Weinreb 1995). Hitachi, Ltd uses Twersky's approach in one of their US patents (Ito *et al* 1993).

4.6.2.2 Comparison of different models. Steinke and Sheperd (1986) compared Twersky's theory of radiation scattering and photon diffusion equations. They found Twersky's original equation to give the best fit for the measured data.

Marble *et al* (1994) found the three dimensional photon diffusion theory to be useful for modeling tissue optics although the pulse oximeter system violates many of the requirements of the model. However, they came to the conclusion that this theory can not replace clinical calibration studies.

De Kock and Tarassenko (1993) also found Twersky's theory to give the best fit to the experimental data. They compared results of this model with the photon diffusion theory and the Kubelka–Munk theory.

4.6.3 Influence of scattering on pulse oximeter readings

Although the assumptions of Beer's law are violated in pulse oximetry, the actual readings of the devices show a good correlation between the measurement and the actual arterial oxygen saturation.

Steinke and Sheperd (1986) found that the scattering effects of the light passing through whole blood depend on the wavelength of the light and the oxygen saturation. The relationship between oxygen saturation and total scattering effects (absorbance due to hemoglobin plus multiple scattering) is approximately linear and so scattering does not influence the linearity of the pulse oximeter in a negative way. In contrast, the total absorbance has a larger slope than that due only to the absorbance of hemoglobin following Beer's law. Therefore, light scattering increases the sensitivity of the whole blood oximeter.

Fine and Weinreb (1993, 1995) demonstrate that the ratio of total absorbances is a function of the effective blood layer thickness and the concentration of hemoglobin. Therefore physiological factors such as temperature or peripheral vasoconstriction reduce the accuracy of saturation readings. The error increases as the level of arterial oxygen saturation decreases. This is dangerous because the clinician has to question the readings of the oxygen saturation when it is most critical for the patient.

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4.6.4 Calibration curves used for pulse oximeters

Commercial pulse oximeters are calibrated from *in vitro* data (see section 10.1). A large set of data obtained in clinical studies is collected containing information about the ratio R of the absorbances calculated by the pulse oximeter and the actual arterial oxygen saturation S_aO_2 measured by a very accurate method such as the CO-oximeter (see section 3.3). Lookup tables or equations are used to find the relationship of these two variables for a pulse oximeter reading.

To relate the measured values of the ratio R to the reading of the pulse oximeter, the equation of the theoretical calibration curve based on Beer's law can be modified as Mendelson and Kent (1989) described

$$S_pO_2 = \frac{k_1 - k_2 R}{k_3 - k_4 R}. \qquad (4.20)$$

In this equation the extinction coefficients from equation (4.19) are replaced by constants k_i. These constants are determined by clinical studies to give the curve a best fit to the *in vitro* measured data. Another approach for a mathematical representation is the use of a polynomial such as found for example in the Ohmeda 3700 and Radiometer OX100 pulse oximeters (Fine and Weinreb 1995)

$$S_pO_2 = k_1 + k_2 R + k_3 R^2. \qquad (4.21)$$

Figure 4.7 provides an example of a calibration curve used in pulse oximeters in comparison to the theoretical calibration curve.

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INSTRUCTIONAL OBJECTIVES

4.1 Describe the properties and limitations of Beer's law.
4.2 Describe different species of hemoglobin and their effect on the oxygenation of blood.
4.3 Describe the functional and the fractional hemoglobin saturation and their difference.
4.4 Describe the properties and assumptions of the spectrophotometric method to determine oxygen saturation in hemoglobin solutions.
4.5 Describe the principles of pulse oximetry and what a pulse oximeter measures.
4.6 Describe why and how a pulse oximeter measures the absorbance in the arterial blood only.
4.7 Describe the normalization of the signals and the reasons for this normalization.
4.8 Explain how and why the ratio of the normalized signals is calculated.
4.9 Explain errors in the spectrophotometric method when used for whole blood samples.
4.10 Describe the different physical phenomena occurring when light travels through tissue and blood.
4.11 Describe what light scattering is and where it occurs in pulse oximetry.
4.12 Describe the influence of light scattering on the accuracy of a pulse oximeter.

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CHAPTER 5

LIGHT-EMITTING DIODES AND THEIR CONTROL

Brad W J Bourgeois

In order to make pulse oximetry practical in the modern medical environment, a light source is required that is powerful enough to penetrate more than a centimeter of tissue yet diminutive enough to fit in a small probe. Chapter 4 shows that it also is desirable for the light source at each desired wavelength to have a very narrow *emission spectrum*, which minimizes error in the measurement of arterial oxygen saturation (S_aO_2). Fortuitously, light-emitting diodes (LEDs) fulfill all the requirements for the light source in a pulse oximeter.

However, LEDs are not without drawbacks. The primary problem faced by pulse oximeter designers is how to deal with variations and shifts in the *peak wavelength* of each LED. Because the main function of a pulse oximeter, measuring arterial oxygen saturation, is so heavily dependent upon accurate values for the two wavelengths of light, a design which does all it can to compensate for LED wavelength changes will outperform its competition.

This chapter discusses important characteristics of LEDs, a LED driver circuit in a pulse oximeter, and various problems with the use of LEDs in pulse oximetry.

5.1 AN INTRODUCTION TO LIGHT-EMITTING DIODES

Light-emitting diodes are the light source of choice for all pulse oximeters on the market today. Their small size, excellent drive characteristics, and large light output over a very narrow bandwidth make them the ideal choice for the source of light at both the red and infrared wavelengths used in pulse oximetry.

The fact that LEDs are available for use in pulse oximetry is due to a combination of science and luck. LEDs are only available over an approximately 700 nm range of wavelengths, from blue in the visible spectrum into the near infrared. By contrast, the electromagnetic spectrum extends over a range of 10^{14}. Another fortuitous fact is that the window of low absorption on the hemoglobin extinction curves occurs within the range of LED availability. The common LED wavelengths of 660 and 940 nm work very well in pulse oximetry, which allows for lower cost due to the off-the-shelf availability of these LEDs.

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