CHAPTER

10

Biomedical Sensors

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OUTLINE

AT THE CONCLUSION OF THIS CHAPTER, STUDENTS WILL BE ABLE TO:

- Describe the different classifications of biomedical sensors.
- Describe the characteristics that are important for packaging materials associated with biomedical sensors.
- Calculate the half-cell potentials generated by different electrodes immersed in an electrolyte solution.
- Describe the electrodes that are used to record the ECG, EEG, and EMG and those that are used for intracellular recordings.
- Describe how displacement transducers, airflow transducers, and thermistors are used to make physical measurements.
- Describe how blood gases are measured.
- Describe how enzyme-based and microbial biosensors work and some of their uses.
- Explain how optical biosensors work and describe some of their uses.

10.1 INTRODUCTION

Diagnostic bioinstrumentation is used routinely in clinical medicine and biological research for measuring a wide range of physiological variables. Generally, the measurement is derived from sensors or transducers and further processed by the instrument to provide valuable diagnostic information. Biomedical sensors or transducers are the main building blocks of diagnostic medical instrumentation found in many physician offices, clinical laboratories, and hospitals. They are routinely used in vivo to perform continuous invasive and noninvasive monitoring of critical physiological variables, as well as in vitro to help clinicians in various diagnostic procedures. Similar devices are also used in nonmedical applications such as in environmental monitoring, agriculture, bioprocessing, food processing, and the petrochemical and pharmacological industries.

Increasing pressures to lower health care costs, optimize efficiency, and provide better care in less expensive settings without compromising patient care are shaping the future of clinical medicine. As part of this ongoing trend, clinical testing is rapidly being transformed by the introduction of new tests that will revolutionize the way physicians will diagnose and treat diseases in the future. Among these changes, patient self-testing and physician office screening are the two most rapidly expanding areas. This trend is driven by the desire of patients and physicians alike to have the ability to perform some types of instantaneous diagnosis right next to the patient and to move the testing apparatus from an outside central clinical laboratory closer to the point of care.

Generally, medical diagnostic instruments derive their information from sensors, electrodes, or transducers. Medical instrumentation relies on analog electrical signals for an input. These signals can be acquired directly by biopotential electrodes—for example, in monitoring the electrical signals generated by the heart, muscles or brain, or indirectly by transducers that convert a nonelectrical physical variable such as pressure, flow, or temperature, or biochemical variables, such as partial pressures of gases or ionic concentrations, to an electrical signal. Since the process of measuring a biological variable is commonly referred to as sensing, electrodes and transducers are often grouped together and are termed *sensors*.

Biomedical sensors play an important role in a wide range of diagnostic medical applications. Depending on the specific needs, some sensors are used primarily in clinical laboratories to measure in vitro physiological quantities such as electrolytes, enzymes, and other biochemical metabolites in blood. Other biomedical sensors for measuring pressure, flow, and the concentrations of gases, such as oxygen and carbon dioxide, are used in vivo to follow continuously (monitor) the condition of a patient. For real-time continuous in vivo sensing to be worthwhile, the target analytes must vary rapidly and, most often, unpredictably.

10.1.1 Sensor Classifications

Biomedical sensors are usually classified according to the quantity to be measured and are typically categorized as physical, electrical, or chemical, depending on their specific applications. Biosensors, which can be considered a special subclassification of biomedical sensors, are a group of sensors that have two distinct components: a biological recognition element, such as a purified enzyme, antibody, or receptor, that functions as a mediator and provides the selectivity that is needed to sense the chemical component (usually referred to as the

analyte) of interest, and a supporting structure that also acts as a transducer and is in intimate contact with the biological sensing sensed by the biological recognition element into a quantifiable measurement, typically in the element. The purpose of the transducer is to convert the biochemical reaction into the form of an optical, electrical, or physical signal that is proportional to the concentration of a specific chemical. Thus, a blood pH sensor is not considered a biosensor according to this classification, although it measures a biologically important variable. It is simply a chemical sensor that can be used to measure a biological quantity.

10.1.2 Sensor Packaging

Packaging of certain biomedical sensors, primarily sensors for in vivo applications, is an important consideration during the design, fabrication, and use of the device. Obviously, the sensor must be safe and remain functionally reliable. In the development of implantable biosensors, an additional key issue is the long operational lifetime and biocompatibility of the sensor. Whenever a sensor comes into contact with body fluids, the host itself may affect the function of the sensor, or the sensor may affect the site in which it is implanted. For example, protein absorption and cellular deposits can alter the permeability of the sensor packaging that is designed to both protect the sensor and allow free chemical diffusion of certain analytes between the body fluids and the biosensor. Improper packaging of implantable biomedical sensors could lead to drift and a gradual loss of sensor sensitivity and stability over time. Furthermore, inflammation of tissue, infection, or clotting in a vascular site may produce harmful adverse effects. Hence, the materials used in the construction of the sensor's outer body must be biocompatible, since they play a critical role in determining the overall performance and longevity of an implantable sensor. One convenient strategy is to utilize various polymeric covering materials and barrier layers to minimize leaching of potentially toxic sensor components into the body. It is also important to keep in mind that once the sensor is manufactured, common sterilization practices by steam, ethylene oxide, or gamma radiation must not alter the chemical diffusion properties of the sensor packaging material.

10.1.3 Sensor Specifications

The need for accurate medical diagnostic procedures places stringent requirements on the design and use of biomedical sensors. Depending on the intended application, the performance specifications of a biomedical sensor may be evaluated in vitro and in vivo to ensure that the measurement meets the design specifications.

To understand sensor performance characteristics, it is important first to understand some of the common terminology associated with sensor specifications. The following definitions are commonly used to describe sensor characteristics and selecting sensors for particular applications.

Sensitivity

Sensitivity is typically defined as the ratio of output change for a given change in input. Another way to define sensitivity is by finding the slope of the calibration line relating the input to the output (i.e., $\Delta\text{Output}/\Delta\text{Input}$), as illustrated in Figure 10.1. A high sensitivity implies that a small change in input quantity causes a large change in its output.

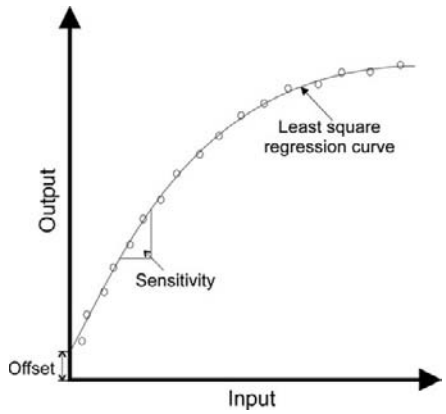

FIGURE 10.1 Input versus output calibration curve of a typical sensor.

For example, a temperature sensor may have a sensitivity of 20 μV/°C; that is, the output of this sensor will change by 20 μV for 1°C change in input temperature. Note that if the calibration line is linear, the sensitivity is constant, whereas the sensitivity will vary with the input when the calibration is nonlinear, as illustrated in Figure 10.1. Alternatively, sensitivity can also be defined as the smallest change in the input quantity that will result in a detectable change in sensor output.

Range

The *range* of a sensor corresponds to the minimum and maximum operating limits that the sensor is expected to measure accurately. For example, a temperature sensor may have a nominal performance over an operating range of −200 to +500°C.

Accuracy

Accuracy refers to the difference between the true value and the actual value measured by the sensor. Typically, accuracy is expressed as a ratio between the preceding difference and the true value and is specified as a percent of full-scale reading. Note that the true value should be traceable to a primary reference standard.[1]

Precision

Precision refers to the degree of measurement reproducibility. Very reproducible readings indicate a high precision. Precision should not be confused with accuracy. For example, measurements may be highly precise but not necessary accurate.

Resolution

When the input quantity is increased from some arbitrary nonzero value, the output of a sensor may not change until a certain input increment is exceeded. Accordingly, *resolution* is defined as the smallest distinguishable input change that can be detected with certainty.

[1]An independently calibrated reference obtained by an absolute measurement of the highest quality that is subsequently used in the calibration of similar measured quantities.

Reproducibility

Reproducibility describes how close the measurements are when the same input is measured repeatedly over time. When the range of measurements is small, the reproducibility is high. For example, a temperature sensor may have a reproducibility of $\pm 0.1^{\circ}$C for a measurement range of 20°C to 80°C. Note that reproducibility can vary depending on the measurement range. In other words, readings may be highly reproducible over one range and less reproducible over a different operating range.

Offset

Offset refers to the output value when the input is zero, as illustrated in Figure 10.1.

Linearity

Linearity is a measure of the maximum deviation of any reading from a straight calibration line. The calibration line is typically defined by the least-square regression fit of the input versus output relationship. Typically, sensor linearity is expressed as either a percent of the actual reading or a percent of the full-scale reading.

The conversion of an unknown quantity to a scaled output reading by a sensor is most convenient if the input-output calibration equation follows a linear relationship. This simplifies the measurement, since we can multiply the measurement of any input value by a constant factor rather than using a "lookup table" to find a different multiplication factor that depends on the input quantity when the calibration equation follows a nonlinear relation. Note that although a linear response is sometimes desired, accurate measurements are possible even if the response is nonlinear as long as the input-output relation is fully characterized.

Response Time

The response time indicates the time it takes a sensor to reach a certain percent (e.g., 95 percent) of its final steady-state value when the input is changed. For example, it may take 20 seconds for a temperature sensor to reach 95 percent of its maximum value when a change in temperature of 1°C is measured. Ideally, a short response time indicates the ability of a sensor to respond quickly to changes in input quantities.

Drift

Drift refers to the change in sensor reading when the input remains constant. Drift can be quantified by running multiple calibration tests over time and determining the corresponding changes in the intercept and slope of the calibration line. Sometimes, the input-output relation may vary over time or may depend on another independent variable that can also change the output reading. This can lead to a *zero* (or *offset*) *drift* or a *sensitivity drift*, as illustrated in Figure 10.2. To determine zero drift, the input is held at zero while the output reading is recorded. For example, the output of a pressure transducer may depend not only on pressure but also on temperature. Therefore, variations in temperature can produce changes in output readings even if the input pressure remains zero. Sensitivity drift may be found by measuring changes in output readings for different nonzero constant inputs. For example, for a pressure transducer, repeating the measurements over a range of temperatures will reveal how much the slope of the input-output calibration line varies with temperature. In practice, both zero

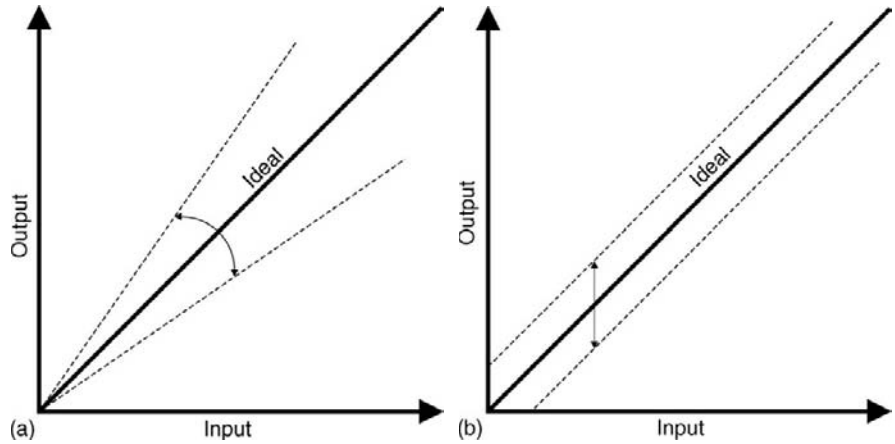

FIGURE 10.2 Changes in input versus output response caused by (a) sensitivity errors and (b) offset errors.

and sensitivity drifts specify the total error due to drift. Knowing the values of these drifts can help to compensate and correct sensor readings.

Hysteresis

In some sensors, the input-output characteristic follows a different nonlinear trend, depending on whether the input quantity increases or decreases, as illustrated in Figure 10.3. For example, a certain pressure gauge may produce a different output voltage when the input pressure varies from zero to full scale and then back to zero. When the measurement is not perfectly reversible, the sensor is said to exhibit *hysteresis*. If a sensor exhibits hysteresis, the input-output relation is not unique but depends on the direction change in the input quantity.

The following sections will examine the operation principles of different types of biomedical sensors, including examples of invasive and noninvasive sensors for measuring biopotentials and other physical and biochemical variables encountered in different clinical and research applications.

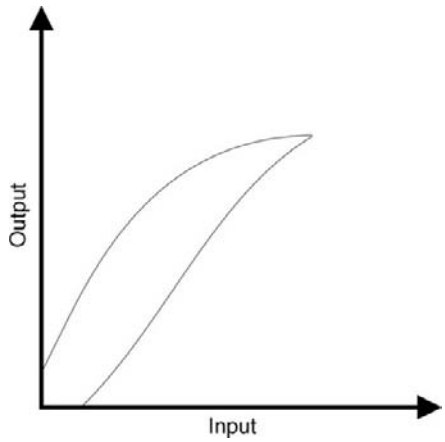

FIGURE 10.3 Input versus output response of a sensor with hysteresis.

EXAMPLE PROBLEM 10.1

A new temperature sensor produced the readings in Table 10.1.

TABLE 10.1 Sample Calibration Data for a Temperature Sensor

Temperature (°C)	Reading (mV)
0	12.3
10	18.2
20	25.4
30	37.0
40	43.6
50	55.8
60	62.0
70	67.8
80	70.4
90	72.1
100	73.0

1. Plot the input-output calibration for this sensor.
2. Find the offset and sensitivity for readings between 0 to 70°C.
3. Estimate the average sensitivity for readings ranging between 70°C to 100°C.

Solution

1.

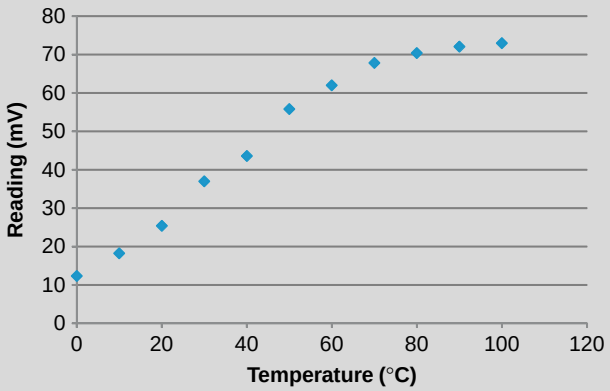

FIGURE 10.4 Input-Output Calibration for a Temperature Sensor.

Continued

2. The equation of the linear regression line describing the input-output calibration data can be written as

$$\text{Reading} = a \cdot (\text{Reference temperature}) + b$$

where, $a =$ is the slope and b is the y-intercept of the regression line. Accordingly, the offset (b) and sensitivity (a) are equal to 10.87 mV and 0.84 mV/°C, respectively.
3. From the equation of the linear regression line, the average sensitivity for readings between 70°C to 100°C is 0.17 mV/°C.

10.2 BIOPOTENTIAL MEASUREMENTS

Biopotential measurements are made using different kinds of specialized electrodes. The function of these recording electrodes is to couple the ionic potentials generated inside the body to an electronic instrument. Biopotential electrodes are classified either as noninvasive (skin surface) or invasive (e.g., microelectrodes or wire electrodes).

Biopotential measurements must be carried out using high-quality electrodes to minimize motion artifacts and ensure that the measured signal is accurate, stable, and undistorted. Body fluids are very corrosive to metals, so not all metals are acceptable for biopotential sensing. Furthermore, some materials are toxic to living tissues. For implantable applications, we typically use relatively strong metal electrodes made, for example, from stainless steel or noble materials such as gold, or from various alloys such as platinum-tungsten, platinum-iridium, titanium-nitride, or iridium-oxide. These electrodes do not react chemically with tissue electrolytes and therefore minimize tissue toxicity. Unfortunately, they give rise to large interface impedances and unstable potentials. External monitoring electrodes can use nonnoble materials such as silver with lesser concerns of biocompatibility, but they must address the large skin interface impedance and the unstable biopotential. Other considerations in the design and selection of biopotential electrodes are cost, shelf life, and mechanical characteristics.

10.2.1 The Electrolyte/Metal Electrode Interface

When a metal is placed in an electrolyte (i.e., an ionizable) solution, a charge distribution is created next to the metal/electrolyte interface, as illustrated in Figure 10.5. This localized charge distribution causes an electric potential, called a half-cell potential, to be developed across the interface between the metal and the electrolyte solution.

The half-cell potentials of several important metals are listed in Table 10.2. Note that the hydrogen electrode is considered to be the standard electrode against which the half-cell potentials of other metal electrodes are measured.

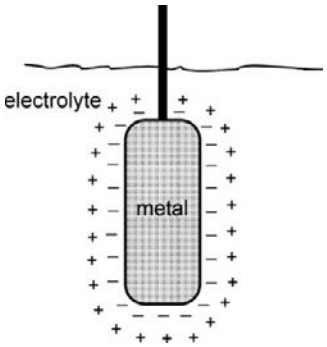

FIGURE 10.5 Distribution of charges at a metal/electrolyte interface.

TABLE 10.2 Half-Cell Potentials of Important Metals

Primary metal and chemical reaction	Half-cell potential (V)
$Al \rightarrow Al^{3+} + 3e^{-}$	−1.706
$Cr \rightarrow Cr^{3+} + 3e^{-}$	−0.744
$Cd \rightarrow Cd^{2+} + 2e^{-}$	−0.401
$Zn \rightarrow Zn^{2+} + 2e^{-}$	−0.763
$Fe \rightarrow Fe^{2+} + 2e^{-}$	−0.409
$Ni \rightarrow Ni^{2+} + 2e^{-}$	−0.230
$Pb \rightarrow Pb^{2+} + 2e^{-}$	−0.126
$H_2 \rightarrow 2H^{+} + 2e^{-}$	0.000 (standard by definition)
$Ag \rightarrow Ag^{+} + e^{-}$	+0.799
$Au \rightarrow Au^{3+} + 3e^{-}$	+1.420
$Cu \rightarrow Cu^{2+} + 2e^{-}$	+0.340
$Ag + Cl^{-} \rightarrow AgCl + 2e^{-}$	+0.223

EXAMPLE PROBLEM 10.2

Silver and zinc electrodes are immersed in an electrolyte solution. Calculate the potential drop between these two electrodes.

Solution

From Table 10.2, the half-cell potentials for the silver and zinc electrodes are 0.799 V and −0.763 V, respectively. Therefore, the potential drop between these two metal electrodes is equal to

$$0.799\text{V} - (-0.763\text{V}) = 1.562\text{V}$$

Typically, biopotential measurements are made by utilizing two similar electrodes composed of the same metal. Therefore, the two half-cell potentials for these electrodes would be equal in magnitude. For example, two similar biopotential electrodes can be taped to the chest near the heart to measure the electrical potentials generated by the heart (electrocardiogram, or ECG). Ideally, assuming that the skin-to-electrode interfaces are electrically identical, the differential amplifier attached to these two electrodes would amplify the biopotential (ECG) signal, but the half-cell potentials would be cancelled out. In practice, however, disparity in electrode material or skin contact resistance could cause a significant DC offset voltage that would cause a current to flow through the two electrodes. This current will produce a voltage drop across the body. The offset voltage will appear superimposed at the output of the amplifier and may cause instability or base line drift in the recorded biopotential.

EXAMPLE PROBLEM 10.3

Silver and aluminum electrodes are placed in an electrolyte solution. Calculate the current that will flow through the electrodes if the equivalent resistance of the solution is equal to 2kΩ.

Solution

$$0.799\ \text{V} - (-1.706\ \text{V}) = 2.505\ \text{V}$$
$$2.505\ \text{V}/2\ \text{k}\Omega = 1.252\ \text{mA}$$

10.2.2 ECG Electrodes

Examples of different types of noninvasive biopotential electrodes used primarily for ECG recording are shown in Figure 10.6. A typical flexible biopotential electrode for ECG recording is composed of certain types of polymers or elastomers that are made electrically conductive by the addition of a fine carbon or metal powder. These electrodes (Figure 10.6a) are available with prepasted AgCl gel for quick and easy application to the skin using a double-sided peel-off adhesive tape.

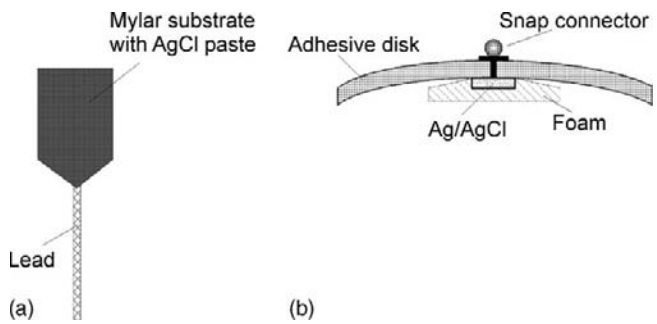

FIGURE 10.6 Biopotential skin surface ECG electrodes: (a) flexible Mylar electrode and (b) disposable snap-type Ag/AgCl electrode.

The most common type of biopotential electrode is the silver/silver chloride electrode (Ag/AgCl), which is formed by electrochemically depositing a very thin layer of silver chloride onto a silver electrode (Figure 10.6b). These electrodes are recessed from the surface of the skin and imbedded in foam that has been soaked with an electrolyte paste to provide good electrical contact with the skin. The electrolyte-saturated foam is also known to reduce motion artifacts that could be produced, for example, during stress testing when the layer of the skin moves relative to the surface of the Ag/AgCl electrode. This motion artifact could cause large interference in the recorded biopotential and, in extreme cases, could severely degrade the measurement.

10.2.3 EMG Electrodes

A number of different types of biopotential electrodes are used in recording electromyographic (EMG) signals from different muscles in the body. The shape and size of the recorded EMG signals depend on the electrical property of these electrodes and the recording location. For noninvasive recordings, proper skin preparation, which normally involves cleansing the skin with alcohol or the application of a small amount of an electrolyte paste, helps to minimize the impedance of the skin-electrode interface and improve the quality of the recorded signal considerably. The most common electrodes used for surface EMG recording and nerve conduction studies are circular discs, about 1 cm in diameter, that are made of silver or platinum.

For direct recording of electrical signals from nerves and muscle fibers, a variety of percutaneous needle electrodes are available, as illustrated in Figure 10.7. The most common type of needle electrode is the concentric bipolar electrode shown in Figure 10.7a. This electrode is made from thin metallic wires encased inside a larger canula or hypodermic needle. The two wires serve as the recording and reference electrodes. Another type of percutaneous EMG electrode is the unipolar needle electrode (Figure 10.7b). This electrode is made of a thin wire that is mostly insulated by a thin layer of Teflon, except about 300 μm near the distal tip. Unlike a bipolar electrode, this electrode requires a second unipolar reference electrode to form a closed electrical circuit. The second recording electrode is normally placed either adjacent to the recording electrode or attached to the surface of the skin.

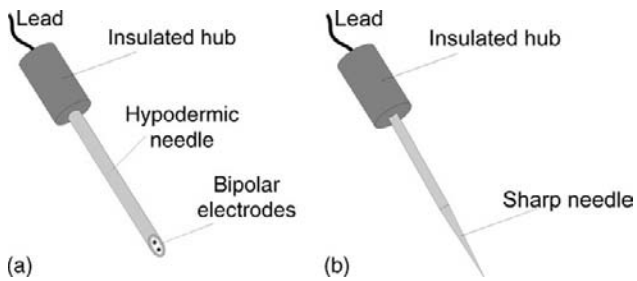

FIGURE 10.7 Intramascular biopotential electrodes: (a) bipolar and (b) unipolar configuration.

10.2.4 EEG Electrodes

The most commonly used electrodes for recording electroencephalographic signals from the brain (EEG) are cup electrodes and subdermal needle electrodes. Cup electrodes are made of platinum or tin approximately 5–10 mm in diameter. These cup electrodes are filled with a conducting electrolyte gel and can be attached to the scalp with an adhesive tape.

Recording of electrical potentials from the scalp is difficult because hair and oily skin impede good electrical contact. Therefore, clinicians sometimes prefer to use subdermal EEG electrodes instead of metal surface electrodes for EEG recording. These are basically fine platinum or stainless-steel needle electrodes about 10 mm long by 0.5 mm wide, which are inserted under the skin to provide a better electrical contact.

10.2.5 Microelectrodes

Microelectrodes are biopotential electrodes with an ultrafine tapered tip that can be inserted into individual biological cells. These electrodes serve an important role in recording action potentials from single cells and are commonly used in neurophysiological studies. The tip of these electrodes must be small with respect to the dimensions of the biological cell to avoid cell damage and at the same time sufficiently strong to penetrate the cell wall. Figure 10.8 illustrates the construction of three typical types of microelectrodes: glass micropipettes, metal microelectrodes, and solid-state microprobes.

In Figure 10.8a, a hollow glass capillary tube, typically 1 mm in diameter, is heated and softened in the middle inside a small furnace and then quickly pulled apart from both ends. This process creates two similar microelectrodes with an open tip that has a diameter on the

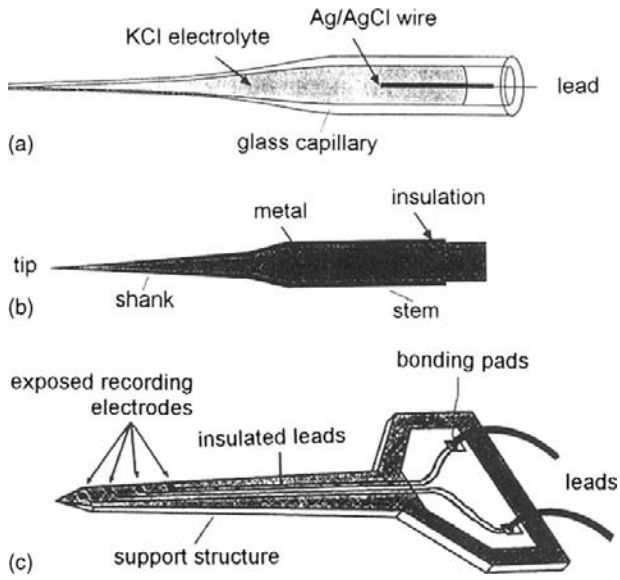

FIGURE 10.8 Biopotential microelectrodes: (a) a capillary glass microelectrode, (b) an insulated metal microelectrode, and (c) a solid-state multisite recording microelectrode.

order of 0.1 to 10 μm. The larger end of the glass tube (the stem) is then filled typically with a 3M KCl electrolyte solution. A short piece of Ag/AgCl wire is inserted through the stem to provide an electrical contact with the electrolyte solution. When the tip of the microelectrode is inserted into an electrolyte solution, such as the intracellular cytoplasm of a biological cell, ionic current can flow through the fluid junction at the tip of the microelectrode. This establishes a closed electrical circuit between the Ag/AgCl wire inside the microelectrode and the biological cell.

A different kind of microelectrode made from a small-diameter strong metal wire (e.g., tungsten or stainless steel) is illustrated in Figure 10.8b. The tip of this microelectrode is usually sharpened down to a diameter of a few micrometers by an electrochemical etching process. The wire is then insulated up to its tip.

Solid-state microfabrication techniques commonly used in the production of integrated circuits can be used to produce microprobes for multichannel recordings of biopotentials or for electrical stimulation of neurons in the brain or spinal cord. An example of such a microsensor is shown in Figure 10.8c. The probe consists of a precisely micromachined silicon substrate with four exposed recording sites. One of the major advantages of this fabrication technique is the ability to mass-produce very small and highly sophisticated microsensors with highly reproducible electrical and physical properties.

10.3 PHYSICAL MEASUREMENTS

10.3.1 Displacement Transducers

Displacement transducers are typically used to measure physical changes in the position of an object or medium. They are commonly employed in detecting changes in length, pressure, or force. Variations in these parameters can be used to quantify and diagnose abnormal physiological functions. In this section, we will describe inductive types of displacement transducers that can be used to measure blood pressure, electromagnetic transducers to measure blood flow, potentiometer transducers to measure linear or angular changes in position, and other types of elastic, strain gauge, capacitive, and piezoelectric type transducers.

Inductive Displacement Transducers

Inductive displacement transducers are based on the inductance L of a coil given by

$$L = \mu \times n^2 \times l \times A \tag{10.1}$$

where μ is the permeability of the magnetically susceptible medium inside the coil (in henry per meter), n is the number of coil turns (in turns per meter), l is the coil length (in meters), and A is the cross-sectional area of the coil (in square meters). These types of transducers measure displacement by changing either the self-inductance of a single coil or the mutual inductance coupling between two or more stationary coils, typically by the displacement of a ferrite or iron core in the bore of the coil assembly. A widely used inductive displacement transducer is the linear variable differential transformer (LVDT) shown in Figure 10.9.

This device is essentially a three-coil mutual inductance transducer that is composed of a primary coil (P) and two secondary coils (S_1 and S_2) connected in series but opposite in

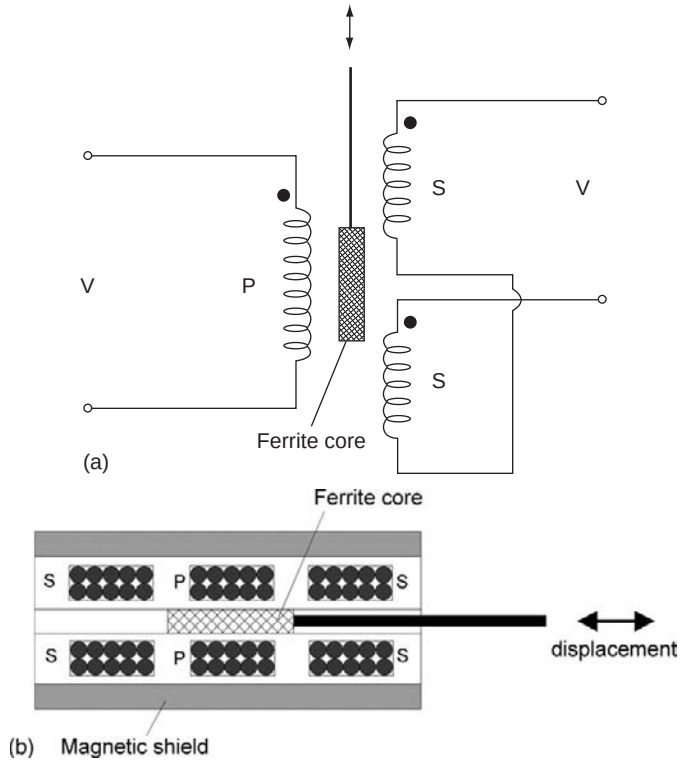

FIGURE 10.9 LVDT transducer: (a) an electric diagram and (b) a cross-section view.

polarity in order to achieve a wider linear output range. The mutual inductance coupled between the coils is changed by the motion of a high-permeability slug. The primary coil is usually excited by passing an AC current. When the slug is centered symmetrically with respect to the two secondary coils, the primary coil induces an alternating magnetic field in the secondary coils. This produces equal voltages (but of opposite polarities) across the two secondary coils. Therefore, the positive voltage excursions from one secondary coil will cancel out the negative voltage excursions from the other secondary coil, resulting in a zero net output voltage. When the core moves toward one coil, the voltage induced in that coil is increased proportionally to the displacement of the core, while the voltage induced in the other coil is decreased proportionally, leading to a typical voltage-displacement diagram, as illustrated in Figure 10.10. Since the voltages induced in the two secondary coils are out of phase, special phase-sensitive electronic circuits must be used to detect both the position and the direction of the core's displacement.

Electromagnetic Flow Transducer

Blood flow through an exposed vessel can be measured by means of an electromagnetic flow transducer. It can be used in research studies to measure blood flow in major blood vessels near the heart, including the aorta at the point where it exits from the heart.

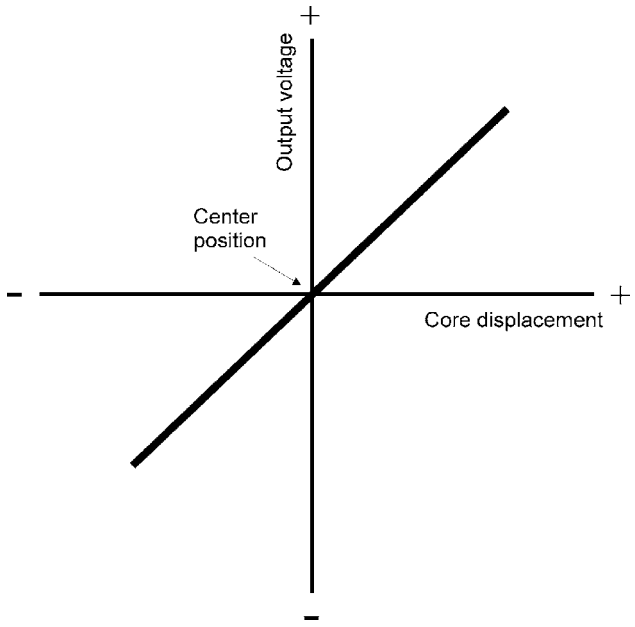

FIGURE 10.10 Output voltage versus core displacement of a typical LVDT transducer.

Consider a blood vessel of diameter, l, filled with blood flowing with a uniform velocity, $\vec{u}$. If the blood vessel is placed in a uniform magnetic flux, $\vec{B}$ (in weber), that is perpendicular to the direction of blood flow, the negatively charged anion and positively charged cation particles in the blood will experience a force, $\vec{F}$ (in newton), which is normal to both the magnetic field and blood flow directions and is given by

$$\vec{F} = q(\vec{u} \times \vec{B}) \tag{10.2}$$

where q is the elementary charge (1.6×10^{-19} C). As a result, these charged particles will be deflected in opposite directions and will move along the diameter of the blood vessels according to the direction of the force vector, $\vec{F}$. This movement will produce an opposing force, $\vec{F}o$, which is equal to

$$\vec{F}o = q \times \vec{E} = q \times \frac{V}{l} \tag{10.3}$$

where $\vec{E}$ is the net electrical field produced by the displacement of the charged particles and V is the potential produced across the blood vessel. At equilibrium, these two forces will be equal. Therefore, the potential difference, V, is given by

$$V = B \times l \times u \tag{10.4}$$

and is proportional to the velocity of blood through the vessel.

EXAMPLE PROBLEM 10.4

Calculate the voltage induced in a magnetic flow probe if the probe is applied across a blood vessel with a diameter of 5×10^{-3} m and the velocity of blood is 5×10^{-2} m/s. Assume that the magnitude of the magnetic field, B, is equal to 1.5×10^{-5} Wb/m^2.

Solution

From Eq. (10.4),

$$V = B \times l \times u = (1.5 \times 10^{-5}\ \text{Wb/m}^2) \times (5 \times 10^{-3}\ \text{m}) \times (5 \times 10^{-2}\ \text{m/s}) = 37.5 \times 10^{-10}\ \text{V}$$

(*Note*: [Wb] = [V × S])

Practically, this device consists of a clip-on probe that fits snugly around the blood vessel, as illustrated in Figure 10.11. The probe contains electrical coils to produce an electromagnetic field that is transverse to the direction of blood flow. The coil is usually excited by an AC current. A pair of very small biopotential electrodes are attached to the housing and rest against the wall of the blood vessel to pick up the induced potential. The flow-induced voltage is an AC voltage at the same frequency as the excitation voltage. Using an AC method instead of DC excitation helps to remove any offset potential error due to the contact between the vessel wall and the biopotential electrodes.

Potentiometer Transducers

A potentiometer is a resistive-type transducer that converts either linear or angular displacement into an output voltage by moving a sliding contact along the surface of a resistive element. Figure 10.12 illustrates linear and angular-type potentiometric transducers. A voltage, V_i, is applied across the resistor, R. The output voltage, Vo, between the sliding contact and one terminal of the resistor is linearly proportional to the displacement. Typically, a constant current source is passed through the variable resistor, and the small change in output voltage is measured by a sensitive voltmeter using Ohm's law (i.e., $I = V/R$).

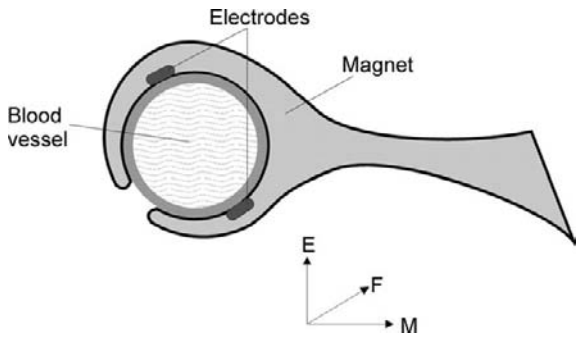

FIGURE 10.11 Electromagnetic blood flow transducer.

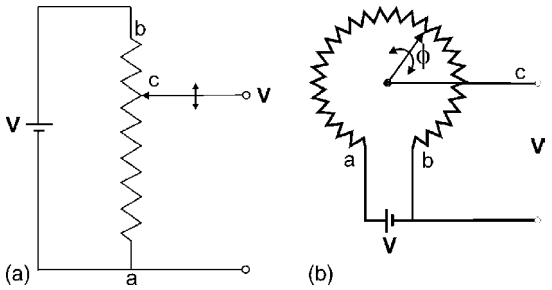

FIGURE 10.12 Linear translational (a) and angular (b) displacement transducers.

EXAMPLE PROBLEM 10.5

Calculate the change in output voltage of a linear potentiometer transducer that undergoes a 20 percent change in displacement.

Solution

Assuming that the current flowing through the transducer is constant, from Ohm's law,

$$\Delta V = I \times \Delta R$$

Hence, since the resistance between the sliding contact and one terminal of the resistor is linearly proportional to the displacement, a 20 percent change in displacement will produce a 20 percent change in the output voltage of the transducer.

Elastic Resistive Transducers

In certain clinical situations, it is desirable to measure changes in the peripheral volume of a leg when the venous outflow of blood from the leg is temporarily occluded by a blood pressure cuff. This volume-measuring method is called plethysmography and can indicate the presence of large venous clots in the legs. The measurement can be performed by wrapping an elastic resistive transducer around the leg and measuring the rate of change in resistance of the transducer as a function of time. This change corresponds to relative changes in the blood volume of the leg. If a clot is present, it will take more time for the blood stored in the leg to flow out through the veins after the temporary occlusion is removed. A similar transducer can be used to follow a patient's breathing pattern by wrapping the elastic band around the chest.

An elastic resistive transducer consists of a thin elastic tube filled with an electrically conductive material, as illustrated in Figure 10.13. The resistance of the conductor inside the flexible tubing is given by

$$R = \rho \frac{I}{A} \tag{10.5}$$

where ρ is the resistivity of the electrically conductive material (in $\Omega \times$ m), l is the length, and A is the cross-sectional area of the conductor.

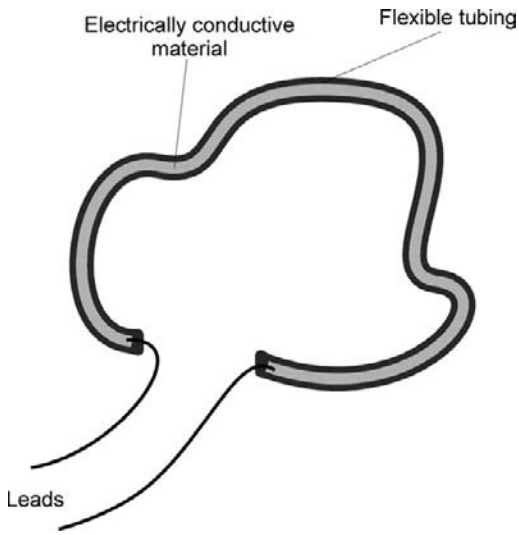

FIGURE 10.13 Elastic resistive transducer.

EXAMPLE PROBLEM 10.6

A 0.1 m long by 0.005 m diameter elastic resistive transducer has a resistance of 1 kΩ. (1) Calculate the resistivity of the electrically conductive material inside the transducer, and (2) calculate the resistance of the transducer after it has been wrapped around a patient's chest having a circumference of 1.2 m. Assume that the cross-sectional area of the transducer remains unchanged.

Solution

1. The cross-sectional area of the transducer (A) is equal to $\pi\ (0.0025)^2\ \text{m}^2 = 1.96 \cdot 10^{-5}\ \text{m}^2$. From Eq. (10.5), $\rho = \dfrac{RA}{l} = \dfrac{1 \cdot 10^3\ \Omega \cdot 1.96 \cdot 10^{-5}\ \text{m}^2}{0.1\ \text{m}} = 0.196\ \Omega \cdot \text{m}$

2.

$$R_{\text{stretched}} = 0.196\ \Omega \cdot \text{m} \cdot \left(\frac{1.2\ \text{m}}{1.96 \cdot 10^{-5}\ \text{m}^2}\right) = 12\ \text{k}\Omega$$

EXAMPLE PROBLEM 10.7

Calculate the change in voltage that is induced across the elastic transducer in Example Problem 10.6 assuming that normal breathing produces a 10 percent change in chest circumference and a constant current of 0.5 mA is passed through the transducer.

Solution

From Ohm's law ($V = I \times R$), $V = 0.5\ \text{mA} \times 12\ \text{k}\Omega = 6\ \text{V}$. If R changes by 10 percent, $\Delta V = 0.6\ \text{V}$.

Strain Gauge Transducers

Strain gauges are displacement-type transducers that measure changes in the length of an object as a result of an applied force. These transducers produce a resistance change that is proportional to the fractional change in the length of the object, also called strain, S, which is defined as

$$\mathrm{S} = \frac{\Delta l}{l} \tag{10.6}$$

where Δl is the fractional change in length, and l is the initial length of the object. Examples include resistive wire elements and certain semiconductor materials.

To understand how a strain gauge works, consider a fine wire conductor of length, l, cross-sectional area, A, and resistivity, ρ. The resistance of the unstretched wire is given by Eq. (10.5). Now suppose that the wire is stretched within its elastic limit by a small amount, Δl, such that its new length becomes $(l + \Delta l)$. Because the volume of the stretched wire must remain constant, the increase in the wire length results in a smaller cross-sectional area, $A_{\text{stretched}}$. Thus,

$$lA = (l + \Delta l) \times A_{\text{stretched}} \tag{10.7}$$

The resistance of the stretched wire is given by

$$R_{\text{stretched}} = \rho \times \frac{l + \Delta l}{A_{\text{stretched}}} \tag{10.8}$$

The increase in the resistance of the stretched wire ΔR is

$$\Delta R = R_{\text{stretched}} - \rho \times \frac{l}{A} \tag{10.9}$$

Substituting Eq. (10.8) and the value for $A_{\text{stretched}}$ from Eq. (10.7) into Eq. (10.9) gives

$$\Delta R = \rho \times \frac{(l + \Delta l)^2}{l \times A} - \rho \times \frac{l}{A} = \frac{\rho \times (l^2 + 2l\Delta l + \Delta l^2 - l^2)}{l \times A} \tag{10.10}$$

Assume that for small changes in length, $\Delta l << l$, this relationship simplifies to

$$\Delta \mathrm{R} = \rho \times \frac{2 \times \Delta l}{A} = \frac{2 \times \Delta l}{l} \times R \tag{10.11}$$

The fractional change in resistance, (ΔR/R), divided by the fractional change in length, ($\Delta l/l$), is called the gauge factor, G. Note that G is a unitless number. Accordingly, the gauge factor provides sensitivity information on the expected change in resistance for a given change in the length of a strain gauge. The gauge factor varies with temperature and the type of material. Therefore, it is important to select a material with a high gauge factor and small temperature coefficient. For a common metal wire strain gauge made of constantan, G is approximately equal to 2. Semiconductor strain gauges made of silicon have a gauge factor about 70 to 100 times higher and are therefore much more sensitive than metallic wire strain gauges.

EXAMPLE PROBLEM 10.8

Calculate the strain in a metal wire gauge for a fractional change in resistance of 10 percent.

Solution

Combine Eqs. (10.6) and (10.11) to obtain

$$\frac{\Delta R}{R} = \frac{2 \times \Delta l}{l} = 2 \times S$$

$$\frac{0.1}{R} = 2 \times S$$

$$S = \frac{0.05}{R}$$

Strain gauges typically fall into two categories: bonded or unbonded. A bonded strain gauge has a folded thin wire cemented to a semiflexible backing material, as illustrated in Figure 10.14.

An unbonded strain gauge consists of multiple resistive wires (typically four) stretched between a fixed and a movable rigid frame. In this configuration, when a deforming force is applied to the structure, two of the wires are stretched, and the other two are shortened proportionally. This configuration is used in blood pressure transducers, as illustrated in Figure 10.15. In this arrangement, a diaphragm is coupled directly by an armature to a movable frame that is inside the transducer. Blood in a peripheral vessel is coupled through a thin fluid-filled (saline) catheter to a disposable dome that is sealed by the flexible diaphragm. Changes in blood pressure during the pumping action of the heart apply a force on the diaphragm that causes the movable frame to move from its resting position. This movement causes the strain gauge wires to stretch or compress and results in a cyclical change in resistance that is proportional to the pulsatile blood pressure measured by the transducer.

In general, the change in resistance of a strain gauge is typically quite small. In addition, changes in temperature can also cause thermal expansion of the wire and thus lead to large changes in the resistance of a strain gauge. Therefore, very sensitive electronic amplifiers

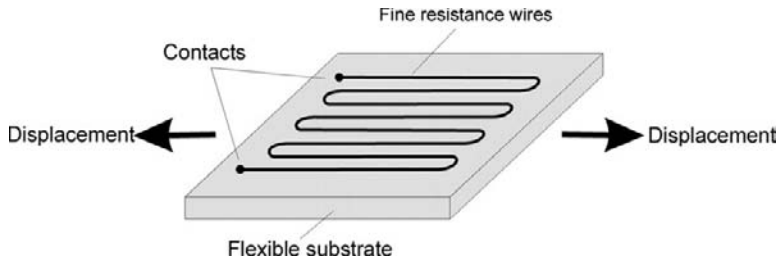

FIGURE 10.14 A bonded-type strain gauge transducer.

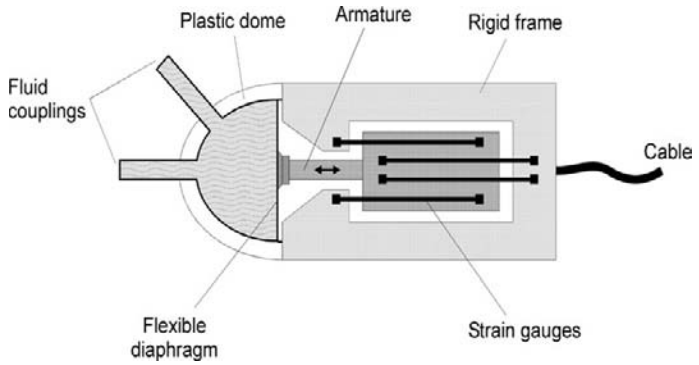

FIGURE 10.15 A resistive strain gauge (unbounded-type) blood pressure transducer.

with special temperature compensation circuits are typically used in applications involving strain gauge transducers.

Capacitive Transducers

The capacitance, C (in farad), between two equal-size parallel plates of cross-sectional area, A, separated by a distance, d, is given by

$$C = \varepsilon_o \times \varepsilon_r \times \frac{A}{d} \tag{10.12}$$

where ε_o is the dielectric constant of free space (8.85×10^{-12} F/m), and ε_r is the relative dielectric constant of the insulating material placed between the two plates. The method that is most commonly employed to measure displacement is to change the separation distance, d, between a fixed and a movable plate, as illustrated in Figure 10.16a. This arrangement can be used to measure force, pressure, or acceleration. Alternatively, it is possible to add a third plate and form a differential-type capacitance transducer (Figure 10.16b). In this configuration, two of the plates are stationary, whereas the middle plate can be moved freely relative to the position of the other plates, thus creating two variable-size capacitors.

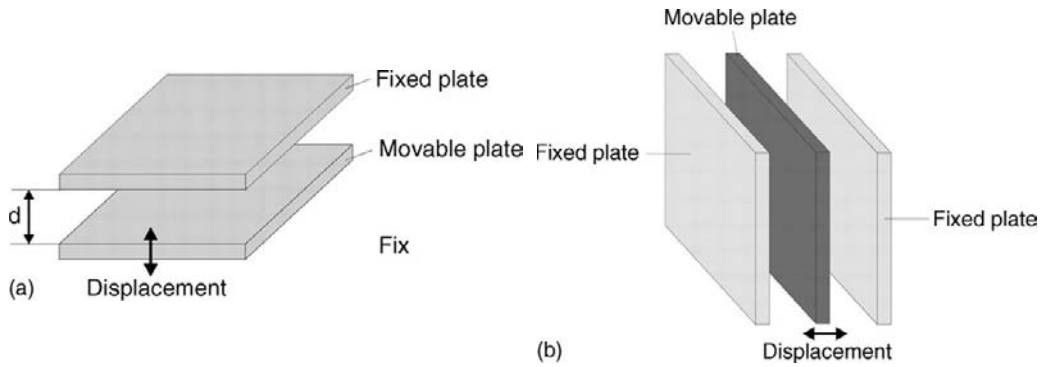

FIGURE 10.16 Capacitive displacement transducer: (a) single capacitance and (b) differential capacitance.

Accordingly, movement of the middle plate, which will change the initial distance, d, by $\pm\Delta d$, will change the distance between two adjacent plates such that one capacitor will increase while the other will decrease in value. This double-capacitor arrangement provides improved sensitivity and can be incorporated into a Wheatstone bridge configuration. Capacitance sensors can be mass-produced using solid-state microfabrication techniques that are commonly employed in making integrated circuits.

EXAMPLE PROBLEM 10.9

Two metal plates with an area of 0.4×10^{-3} m^2 and separation distance of 1×10^{-4} m are used to form a capacitance transducer. If the material between the two plates has a dielectric constant $\varepsilon_r = 2.5$, calculate the capacitance of the transducer.

Solution

$$C = \varepsilon_o \times \varepsilon_r \frac{A}{d} = 8.85 \times 10^{-12}\ \text{F/m} \times 2.5 \times 4 \times 10^{-4}\ \text{m}^2/(1 \times 10^{-4}\ \text{m}) = 0.885\ \text{F}$$

Capacitive displacement transducers can be used to measure respiration or movement by attaching multiple transducers to a mat that is placed on a bed. A capacitive displacement transducer can also be used as a pressure transducer by attaching the movable plate to a thin diaphragm that is in contact with a fluid or air. By applying a voltage across the capacitor and amplifying the small AC signal generated by the movement of the diaphragm, it is possible to obtain a signal that is proportional to the applied external pressure source.

Piezoelectric Transducers

Piezoelectric transducers are used in cardiology to listen to heart sounds (phonocardiography), in automated blood pressure measurements, and for measurement of physiological forces and accelerations. They are also commonly employed in generating ultrasonic waves (high-frequency sound waves typically above 20 kHz) that are used for measuring blood flow or imaging internal soft structures in the body.

A piezoelectric transducer consists of a small crystal (e.g., quartz) that contracts if an electric field (usually in the form of a short voltage impulse) is applied across its plates, as illustrated in Figure 10.17. Conversely, if the crystal is mechanically strained, it will generate a small electric potential. Besides quartz, several other ceramic materials, such as barium titanate and lead zirconate titanate, are also known to produce a piezoelectric effect.

The piezoelectric principle is based on the phenomenon that when an asymmetrical crystal lattice is distorted by an applied force, F, the internal negative and positive charges are reoriented. This causes an induced surface charge, Q, on the opposite sides of the crystal. The induced charge is directly proportional to the applied force and is given by

$$Q = k \times F \tag{10.13}$$

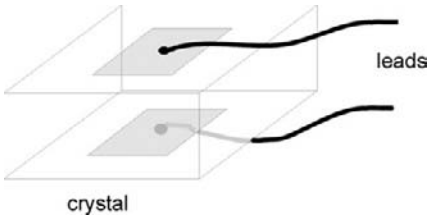

FIGURE 10.17 Ultrasonic transducer.

where k is a proportionality constant for the specific piezoelectric material. By assuming that the piezoelectric crystal acts like a parallel plate capacitor, the voltage across the crystal, V, is given by

$$\Delta V = \frac{\Delta Q}{C} \tag{10.14}$$

where C is the equivalent capacitance of the crystal.

EXAMPLE PROBLEM 10.10

Derive a relationship for calculating the output voltage across a piezoelectric transducer that has a thickness, d, and area, A, in terms of an applied force, F.

Solution

The capacitance of a piezoelectric transducer can be approximated by Eq. (10.12). Equation (10.14) is combined with the relationship given by Eq. (10.13) to give

$$\Delta V = \frac{\Delta Q}{C} = \frac{k \times F}{C} = \frac{k \times F \times d}{\varepsilon_0 \times \varepsilon_r \times A}$$

Since the crystal has an internal leakage resistance, any steady charge produced across its surfaces will eventually be dissipated. Consequently, these piezoelectric transducers are not suitable for measuring a steady or low-frequency DC force. Instead, they are used either as variable force transducers or as mechanically resonating devices to generate high frequencies (typically from 1 to 10 MHz) either in crystal-controlled oscillators or as ultrasonic pulse transducers.

Piezoelectric transducers are commonly used in biomedical applications to measure the thickness of an object or in noninvasive blood pressure monitors. For instance, if two similar crystals are placed across an object (e.g., a blood vessel), one crystal can be excited to produce a short burst of ultrasound. The time it takes for this sound to reach the other transducer can be measured. Assuming that the velocity of sound propagation in soft tissue, c_t, is known (typically 1500 m/s), the time, t, it takes the ultrasonic pulse to propagate across the object can be measured and used to calculate the separation distance, d, of the two transducers from the following relationship:

$$d = c_t \times t \tag{10.15}$$

Microelectromechanical System Transducers

Microelectromechanical system (MEMS) transducers are fabricated using solid-state micromachining techniques commonly used by the semiconductor industry in the production of integrated circuits. A pressure sensor based on MEMS technology is based on the deflection of a micromachined silicon diaphragm mounted on a piezoresistive transducer that changes its output voltage with corresponding variations in the applied pressure. Common commercial applications of MEMS sensors include automobile airbag restraints and fuel injection systems.

To date, the biggest success in medical MEMS technology is the development as a disposable transducer for use in invasive blood pressure monitoring (Figure 10.18). The MEMS transducer measures blood pressure through a silicon-based dielectric gel applied between the sensor element and the saline solution filling the intravascular catheter. The function of the gel is to protect the sensitive electrical circuitry by providing electrical isolation between the MEMS sensor and the saline solution.

MEMS-based medical sensors are used, for example, in intrauterine pressure measurement to monitor contractions during delivery, automatic noninvasive blood pressure cuffs, respiratory monitors, infusion pumps, and kidney dialysis machines. MEMS transducers are also used as accelerometers in implantable pacemakers to monitor body motion to determine patient exertion level and suitably adjust the pacing rate to match changes in metabolic demand.

10.3.2 Airflow Transducers

One of the most common airflow transducers is the Fleish pneumotachometer, shown in Figure 10.19. The device consists of a straight short-tube section with a fixed screen

FIGURE 10.18 An MEMS pressure transducer. *Courtesy of Measurement Specialties, Inc.*

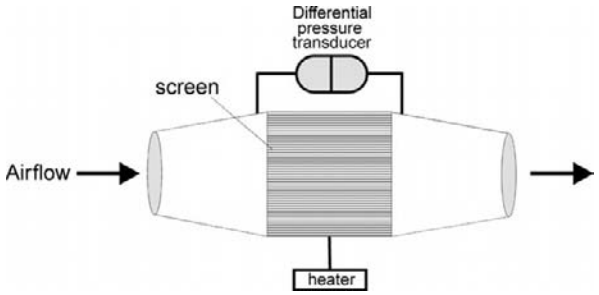

FIGURE 10.19 Fleish airflow transducer.

obstruction in the middle that produces a slight pressure drop as the air is passed through the tube. The pressure drop created across the screen is measured by a differential pressure transducer. The signal produced by the pressure transducer is proportional to the air velocity. The tube is normally shaped in a cone to generate a laminar airflow pattern. A small heater heats the screen so water vapor does not condense on it over time and produce an artificially high pressure drop. Fleish-type pneumotachometers are used to monitor volume, flow, and breathing rates of patients on mechanical ventilators.

10.3.3 Temperature Measurement

Body temperature is one of the most tightly controlled physiological variables and one of the four basic vital signs used in the daily assessment of a patient's health. The interior (core) temperature in the body is remarkably constant—about 37°C for a healthy person—and is normally maintained within ±0.5°C. Therefore, elevated body temperature is a sign of disease or infection, whereas a significant drop in skin temperature may be a clinical indication of shock.

There are two distinct areas in the body where temperature is measured routinely: the surface of the skin under the armpit or inside a body cavity such as the mouth or the rectum. Several sensors exist to measure body temperature.

Thermistors

Thermistors are temperature-sensitive transducers made of compressed sintered metal oxides (such as nickel, manganese, or cobalt) that change their resistance with temperature. Commercially available thermistors range in shape from small beads to large disks, as shown in Figure 10.20.

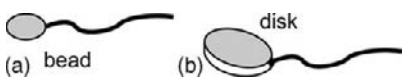

FIGURE 10.20 Common forms of thermistors.

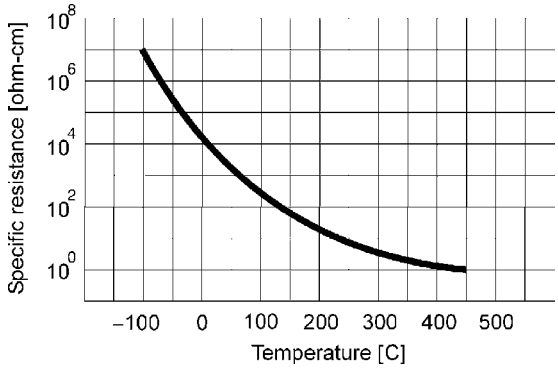

FIGURE 10.21 Resistivity versus temperature characteristics of a typical thermistor.

Mathematically, the resistance-temperature characteristic of a thermistor can be approximated by

$$R_T = R_0 \times \exp\left[\beta \times \left(\frac{1}{T} - \frac{1}{T_0}\right)\right] \tag{10.16}$$

where R_0 is the resistance at a reference temperature, T_0 (in degrees K), R_T is the resistance at temperature, T (in degrees K), and β is a material constant, typically between 2,500 and 5,500 K. A typical resistance-temperature characteristic of a thermistor is shown in Figure 10.21. Note that unlike metals and conventional resistors that have a positive temperature coefficient (as the temperature increases, the resistance increases), thermistors have a nonlinear relationship between temperature and resistance and a negative temperature coefficient. Increasing the temperature decreases the resistance of the thermistor.

EXAMPLE PROBLEM 10.11

A thermistor with a material constant β of 4,500 K is used as a thermometer. Calculate the resistance of this thermistor at 25°C. Assume that the resistance of this thermistor at body temperature (37°C) is equal to 85 Ω.

Solution

Using the resistance-temperature characteristic of a thermistor (Eq. (10.16)) gives

$$R_T = 85 \times \exp\left[4500 \times \left(\frac{1}{298} - \frac{1}{310}\right)\right] = 152.5\ \Omega$$

The size and mass of a thermistor probe in a medical thermometer must be small in order to produce a rapid response time to temperature variations. The probe is normally covered with a very thin sterile plastic sheet that is also disposable to prevent cross-contamination between patients.

A thermistor sensor can be employed in a Swan-Ganz thermodilution technique for measuring cardiac output (the volume of blood ejected by the heart each minute) and assessing ventricular function. The procedure is normally performed in the operating room or the intensive care unit. It involves a rapid bolus injection of a cold indicator solution, usually 3–5 ml of a sterile saline or dextrose solution kept at 0°C, into the right atrium via a flexible pulmonary artery catheter (Figure 10.22).

The 5 or 7 French-size thermodilution catheter contains a small balloon and is normally inserted into either the femoral or internal jugular veins. The catheter is constructed of a radiopaque material to enable easy visualization by an x-ray machine. It contains three ports: a balloon inflation port to guide the flexible tip to the right location, a proximal central venous port, and a distal pulmonary artery port. After the balloon is inflated, the tip of the flexible catheter is passed across the tricuspid valve through the right ventricle, across the pulmonary valve, and into the pulmonary artery. The proximal and distal ports can

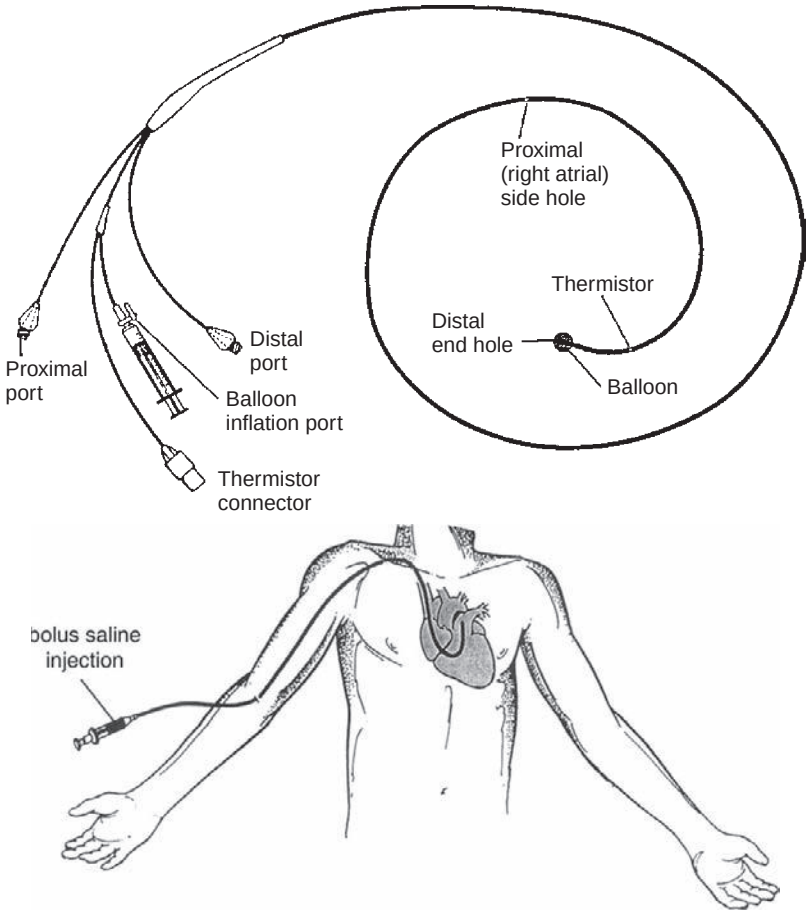

FIGURE 10.22 A Swan-Ganz thermodilution catheter.

be connected to pressure transducers that measure blood pressure inside the right side of the heart while the catheter is advanced into the right atrium.

After the catheter is inserted, a cold bolus is injected into the right atrium through the proximal lumen of the catheter. The bolus solution mixes with the venous blood in the right atrium and causes the blood to cool slightly. The cooled blood is ejected by the right ventricle into the pulmonary artery, where it contacts a thermistor that is located in the wall of the catheter near its distal tip. The thermistor measures the change in blood temperature as the blood passes on to the lungs. An instrument computes the cardiac output by integrating the change in blood temperature immediately following the bolus injection, which is inversely proportional to cardiac output.

Thermocouples

Thermocouples are temperature transducers formed by joining together two dissimilar metals, based on the discovery by Seebeck in 1821. When the two junctions of these dissimilar materials are maintained at different temperatures, an electromotive force (EMF) is generated. The magnitude of the EMF is dependent on the temperature at the junctions and the properties of the materials. This means that the thermocouple is only capable of recognizing a temperature difference between two points and it cannot measure absolute temperature directly. To determine the absolute temperature of the measured environment, the temperature of the reference junction must be determined independently and factored into the absolute temperature calculation. In principle, one junction can be maintained at a constant reference temperature (for example, 0°C if the reference junction is placed in an insulated ice water bath) while the other junction is used to measure the unknown temperature of the environment. However, the use of an ice water bath is not very practical and complicates the measurement considerably. To simplify this process, special integrated circuits have been developed and are available commercially to perform "cold junction compensation." If a closed circuit is formed, as shown in Figure 10.23, the current flowing in the

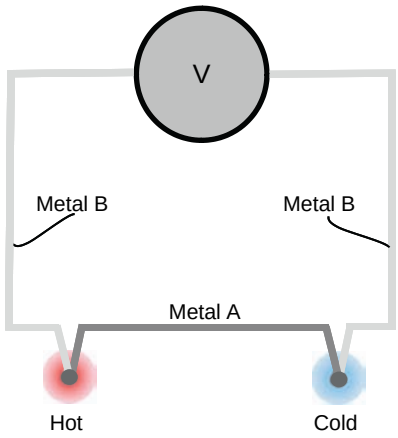

FIGURE 10.23 Principle of a thermocouple-type temperature transducer.

circuit is proportional to the temperature difference between the two junctions over a reasonable wide range of temperatures.

The relationship between the EMF across a junction of two dissimilar metals, E, and the temperature of the measurement junction, T, assuming the cold reference junction is maintained at 0°C, can be approximated using the following truncated power series expansion:

$$E = c_o + c_1 T + c_2 T^2 + \cdots \tag{10.17}$$

where c_i are empirically derived calibration coefficients, T is given in degrees Centigrade, and E is in mV. The Seebeck coefficient α, which describes the temperature sensitivity of the thermocouple, can be derived by differentiating Eq. (10.17) with respect to T:

$$\alpha = \frac{dE}{dT} = c_1 + 2c_2 T + \cdots \tag{10.18}$$

Note that α is a function of temperature. The properties of commonly used thermocouple materials are given in Table 10.3.

The small size, fast response, and rugged design of thermocouple probes make them very attractive for in vivo applications. They can be inserted into the body through a hypodermic needle or a catheter. Examples of medical applications of thermocouples include medical equipment, deep-tissue hyperthermia, and cryogenic therapy.

EXAMPLE PROBLEM 10.12

A Chromel/Alumel thermocouple has the following empirical coefficients:

$$C_0 = -1.76004 \times 10^{-2}$$
$$C_1 = 3.89212 \times 10^{-2}$$
$$C_2 = 1.85587 \times 10^{-5}$$

Find the EMF generated by this thermocouple at a temperature of 500°C.

Solution

Substituting the calibration coefficients just given into Eq. (10.17) yields E ≅ 24.1 mV.

TABLE 10.3 Properties of Selected Thermocouple Materials

Thermocouple	Sensitivity μV/°C (@25°C)	Operating Range (°C)
Chromel/Alumel	40.6	−270 to 1,300
Copper/Constantan	40.9	−270 to 600
Iron/Constantan	51.7	−270 to 1,000
Chromel/Constantan	60.9	−200 to 1,000

EXAMPLE PROBLEM 10.13

Find the Seebeck coefficient for the Chromel/Alumel thermocouple at a temperature of 500°C.

Solution

Using Eq. (10.18) with the coefficients given in Example Problem 10.12 yields $\alpha \cong 57\ \mu V/°C$.

Tympanic Thermometer

Noncontact thermometers measure the temperature of the ear canal near the tympanic membrane, which is known to track the core temperature by about 0.5–1.0°C. Basically, as shown in Figure 10.24, infrared radiation from the tympanic membrane is channeled to a heat-sensitive detector through a metal waveguide that has a gold-plated inner surface for better reflectivity. The detector, which is either a thermopile or a pyroelectric sensor that converts heat flow into an electric current, is normally maintained at a constant temperature environment to minimize inaccuracies due to fluctuation in ambient temperature. A disposable speculum is used on the probe to protect patients from cross-contamination.

Temporal Artery Thermometer

A noninvasive scanning thermometer was developed by Exergen Corporation as an alternative to the tympanic thermometer for measuring core body temperature, essentially eliminating the discomfort caused by a mouth, ear, or rectal thermometer (Figure 10.25). The measurement is based on scanning the area above the temporal artery using an IR detector similar to the sensor used in the tympanic thermometer. The superficial temporal artery extends directly from the external carotid artery and travels in front of the ear. Anatomically, it is lying approximately 1 mm below the skin, readily accessible, and maintains good blood perfusion. Assuming zero thermal loss to the environment, the skin surface over the temporal artery area would be at the same temperature as the arterial blood in the aorta, which is essentially equal to core body temperature. Since ambient temperature

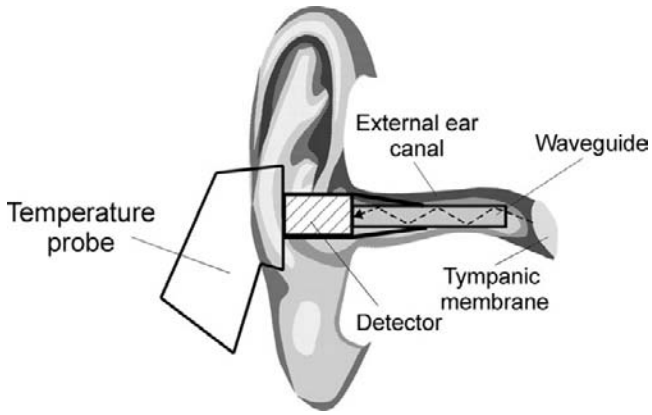

FIGURE 10.24 Noncontact-type infrared ear thermometer.

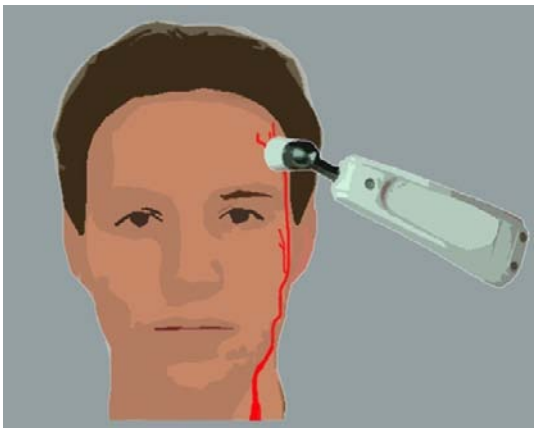

FIGURE 10.25 Temporal artery thermometry.

is normally lower than core body temperature, there is a cooling effect at the skin surface due to the radiative heat loss to the surrounding air. To account for errors due to the natural heat loss, the hand-held scanning thermometer measures ambient temperature at the same time it measures the absolute temperature of the skin surface over the temporal artery and computes arterial temperature using a heat balance equation.

Ingestible Temperature Pill

Heat exhaustion (also known as hyperthermia or heatstroke) occurs when the body cannot adequately dissipate an internal rise in core body temperature. It can be caused by an excessive exposure to heat or dehydration—particularly in football players during sporting activities, astronauts during space flights, or soldiers, and can ultimately lead to life-threatening brain damage or even death. To minimize the potential of heatstroke, an ingestible thermometer pill was developed in the mid-1980s in collaboration with NASA (Figure 10.26) to monitor core body temperature in real-time with an accuracy of 0.1°C. Once ingested into the body, the $^3/_4$-inch-long battery-operated pill transmits wirelessly core body temperature as it travels harmlessly through the gastrointestinal tract. A small quartz crystal oscillator inside the pill vibrates at a frequency that is proportional to core body temperature. The pill converts this change in crystal frequency to a magnetic field with a radius of about 1 meter that can be picked up wirelessly by an external data recorder. The silicone-coated pill remains in the body for about 24–36 hours before it is excreted.

10.4 BLOOD GAS SENSORS

Measurements of arterial blood gases (pO_2, pCO_2 and pH) are frequently performed on critically ill patients in both the operating room and the intensive care unit. They are used by the physician to adjust mechanical ventilation or to administer pharmacological agents. These measurements provide information about the respiratory and metabolic imbalances in the body and reflect the adequacy of blood oxygenation and CO_2 elimination.

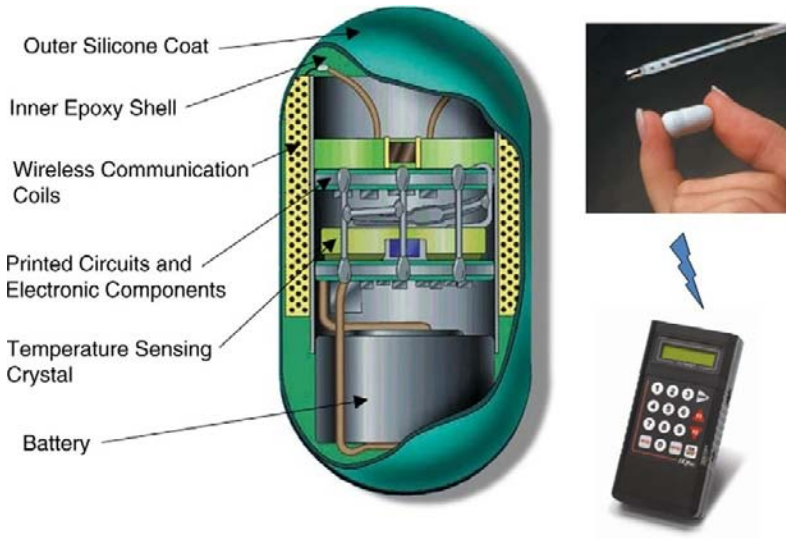

FIGURE 10.26 Ingestible temperature pill. *Courtesy of HQ, Inc., Palmetto, FL.*

Traditionally, arterial blood gas analysis has been performed by withdrawing blood from a peripheral artery. The blood sample is then transported to a clinical laboratory for analysis. The need for rapid test results in the management of unstable, critically ill patients has led to the development of newer methods for continuous noninvasive blood gas monitoring. This allows the physician to follow trends in the patient's condition as well as receive immediate feedback on the adequacy of certain therapeutic interventions.

Noninvasive sensors for measuring O_2 and CO_2 in arterial blood are based on the discovery that gases, such as O_2 and CO_2, can easily diffuse through the skin. Diffusion occurs due to a partial pressure difference between the blood in the superficial layers of the skin and the outermost surface of the skin. This concept has been used to develop two types of noninvasive electrochemical sensors for transcutaneous monitoring of pO_2 and pCO_2. Furthermore, the discovery that blood changes its color depending on the amount of oxygen chemically bound to the hemoglobin in the erythrocytes has led to the development of several optical methods to measure the oxygen saturation in blood.

10.4.1 Oxygen Measurement

A quantitative method for measuring blood oxygenation is of great importance in assessing the circulatory and respiratory condition of a patient. Oxygen is transported by the blood from the lungs to the tissues in two distinct states. Under normal physiological conditions, approximately 2 percent of the total amount of oxygen carried by the blood is dissolved in the plasma. This amount is linearly proportional to the blood pO_2. The remaining 98 percent is carried inside the erythrocytes in a loose, reversible chemical combination with hemoglobin (Hb) as oxyhemoglobin (HbO_2). Thus, there are two options for measuring blood oxygenation: either using a polarographic pO_2 sensor or measuring oxygen saturation (the relative amount of HbO_2 in the blood) by means of an optical oximeter.

A pO_2 sensor, also widely known as a Clark electrode, is used to measure the partial pressure of O_2 gas in a sample of air or blood. This sensor is categorized as an amperometric (i.e., the measurement is based on the production of a current when a voltage is applied between two electrodes) sensor and requires an external polarizing bias voltage source. The measurement is based on the principle of polarography, as shown in Figure 10.27. The electrode utilizes the ability of O_2 molecules to react chemically with H_2O in the presence of electrons to produce hydroxyl (OH^-) ions. This electrochemical reaction, called an oxidation/reduction or redox reaction, generates a small current and requires an externally applied constant polarizing voltage source of about 0.6V.

Oxygen is reduced (consumed) at the surface of a noble metal (e.g., platinum or gold) cathode (the electrode connected to the negative side of the voltage source) according to the following chemical reaction:

$$O_2 + 2H_2O + 4e^- \leftrightarrow 4OH^-$$

In this reduction reaction, an O_2 molecule takes four electrons and reacts with two water molecules, generating four hydroxyl ions. The resulting OH^- ions migrate and react with a reference Ag/AgCl anode (the electrode connected to the positive side of the voltage source), causing a two-step oxidation reaction to occur as follows:

$$Ag \leftrightarrow Ag^+ + e^-$$
$$Ag^+ + Cl^- \leftrightarrow AgCl\downarrow$$

In this oxidation reaction, silver from the electrode is first oxidized to silver ions, and electrons are liberated to the anode. These silver ions are immediately combined with

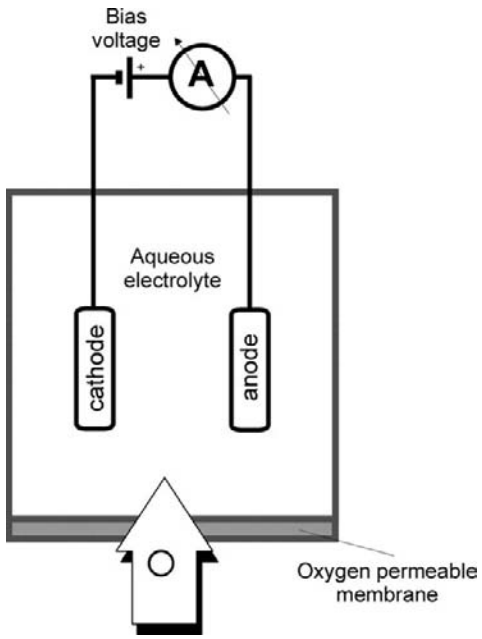

FIGURE 10.27 Principle of a polarographic Clark-type pO_2 sensor.

chloride ions to form silver chloride that precipitates on the surface of the anode. The current flowing between the anode and the cathode in the external circuit produced by this reaction is directly (i.e., linearly) proportional to the number of O_2 molecules constantly reduced at the surface of the cathode. The electrodes in the polarographic cell are immersed in an electrolyte solution of potassium chloride and surrounded by an O_2-permeable Teflon or polypropylene membrane that permits gases to diffuse slowly into the electrode. Thus, by measuring the change in current between the cathode and the anode, the amount of oxygen that is dissolved in the solution can be determined.

With a rather minor change in the configuration of a polarographic pO_2 sensor, it is also possible to measure the pO_2 transcutaneously. Figure 10.28 illustrates a cross section of a Clark-type transcutaneous pO_2 sensor. This sensor is essentially a standard polarographic pO_2 electrode that is attached to the surface of the skin by double-sided adhesive tape. It measures the partial pressure of oxygen that diffuses from the blood through the skin into the Clark electrode, similar to the way it measures the pO_2 in a sample of blood. However, since the diffusion of O_2 through the skin is normally very low, a miniature heating coil is incorporated into the housing of this electrode to cause gentle vasodilatation (increased local blood flow) of the capillaries in the skin. By raising the local skin temperature to about 43°C, the pO_2 measured by the transcutaneous sensor approximates that of the underlying arterial blood. This electrode has been used extensively in monitoring newborn babies in the intensive care unit. However, as the skin becomes thicker and matures in adult patients, the gas diffusion properties of the skin change significantly and cause large errors that result in inconsistent readings.

Various methods for measuring the oxygen saturation, SO_2 (the relative amount of oxygen carried by the hemoglobin in the erythrocytes), of blood in vitro or in vivo in arterial blood (S_aO_2) or mixed venous blood (S_vO_2), have been developed. This method, referred to as oximetry, is based on the light absorption properties of blood and, in particular, the

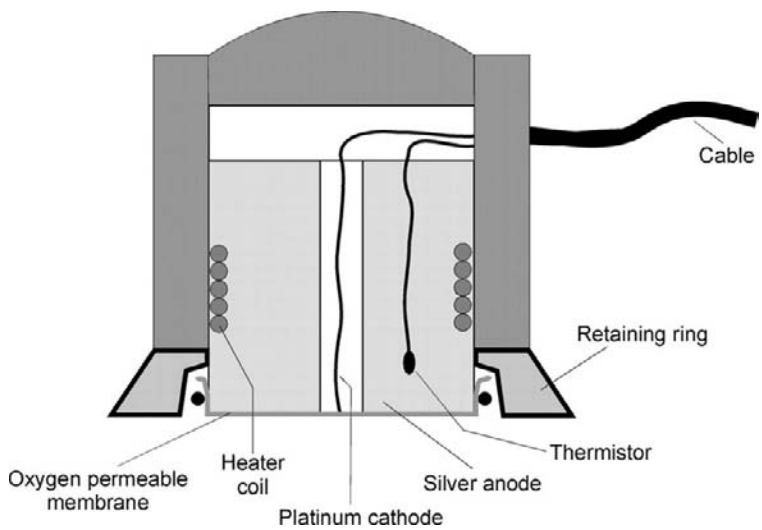

FIGURE 10.28 Transcutaneous pO_2 sensor.

relative concentration of Hb and HbO_2, since the characteristic color of deoxygenated blood is blue, whereas fully oxygenated blood has a distinct bright red color.

The measurement is performed at two specific wavelengths: a red wavelength, λ_1, where there is a large difference in light absorbance between Hb and HbO_2 (e.g., 660 nm), and a second wavelength, λ_2, in the near-infrared region of the spectrum. The second wavelength can be either isobestic (a region of the spectrum around 805 nm, where the absorbencies of Hb and HbO_2 are equal) or around 940–960 nm, where the absorbance of Hb is slightly smaller than that of HbO_2. Figure 10.29 shows the optical absorption spectra of blood in the visible and near-infrared region.

The measurement is based on Beer-Lambert's law that relates the transmitted light power, P_t, to the incident light power, P_0, according to the following relationship:

$$P_t = P_0 \times 10^{-abc} \tag{10.19}$$

where a is a wavelength-dependent constant called the extinction coefficient (or molar absorptivity) of the sample, b is the light path length through the sample, and c is the concentration of the sample.

Assuming for simplicity that (i) $\lambda_1 = 660$ nm and $\lambda_2 = 805$ nm (i.e., isobestic), (1) the hemolyzed blood sample (blood in which the erythrocytes have been ruptured—i.e., the hemoglobin has been released and uniformly mixed with the plasma) consists of a two-component mixture of Hb and HbO_2, and (2) the total light absorbance by the mixture of these two components is additive, a simple mathematical relationship can be derived for computing the oxygen saturation of blood:

$$SO_2 = A - B \times \left[\frac{OD(\lambda_1)}{OD(\lambda_2)}\right] \tag{10.20}$$

where A and B are two coefficients that are functions of the specific absorptivity of Hb and HbO_2, OD (or absorbance) is defined as the optical density—that is, $\log_{10}(1/T)$—where

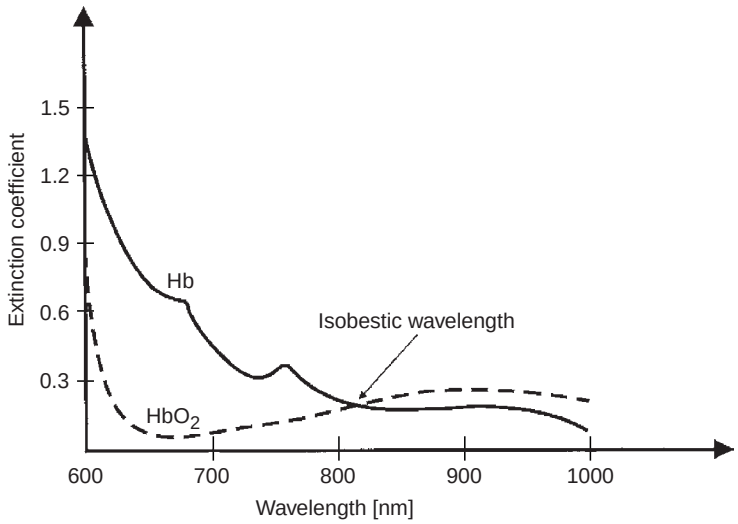

FIGURE 10.29 Optical extinction coefficients of Hb and HbO_2.

T represents the light transmission through the sample and is given by P_t/P_0, and SO_2 is defined as $c_{HB}/(c_{HB} + c_{HBO_2})$.

The measurement of SO_2 in blood can be performed either in vitro or in vivo. In vitro measurement using a bench top oximeter requires a sample of blood, usually withdrawn from a peripheral artery. The sample is transferred into an optical cuvette (a parallel-wall glass container that holds the sample), where it is first hemolyzed and then illuminated sequentially by light from an intense white source after proper wavelength selection using narrow-band optical filters.

SO_2 can also be measured in vivo using a noninvasive pulse oximeter. Noninvasive optical sensors for measuring S_aO_2 by a pulse oximeter consist of a pair of small and inexpensive light-emitting diodes (LEDs)—typically a red (R) LED around 660 nm and an infrared (IR) LED around 940–960 nm—and a single, highly sensitive silicon photodetector. These components are typically mounted inside a reusable spring-loaded clip or a disposable adhesive wrap (Figure 10.30). Electronic circuits inside the pulse oximeter generate digital switching signals to turn on and off the two LEDs in a sequential manner and synchronously

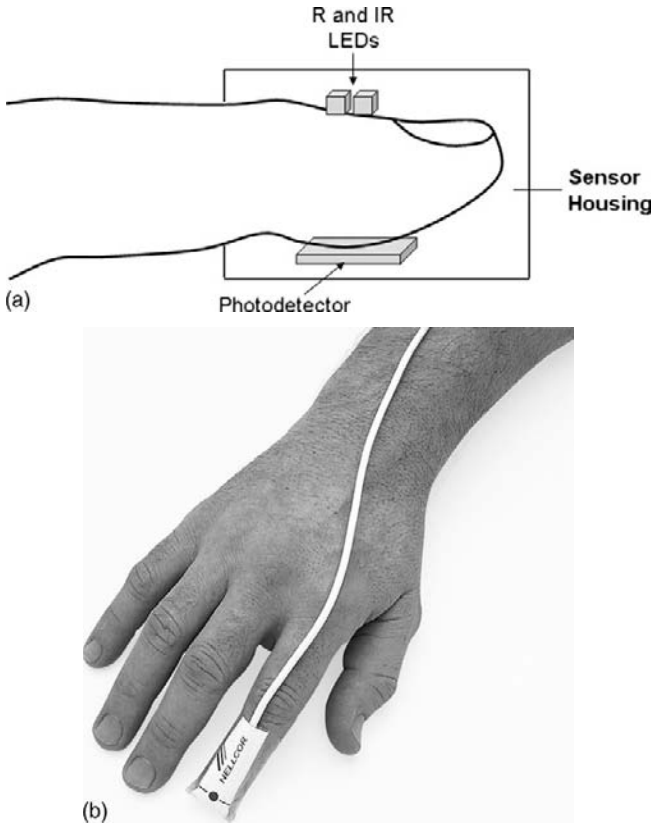

FIGURE 10.30 (a) Transmission-type pulse oximeter finger probe, and (b) disposable finger sensor. *Courtesy of Nellcor Puritan Bennett, Inc., Pleasanton, CA.*

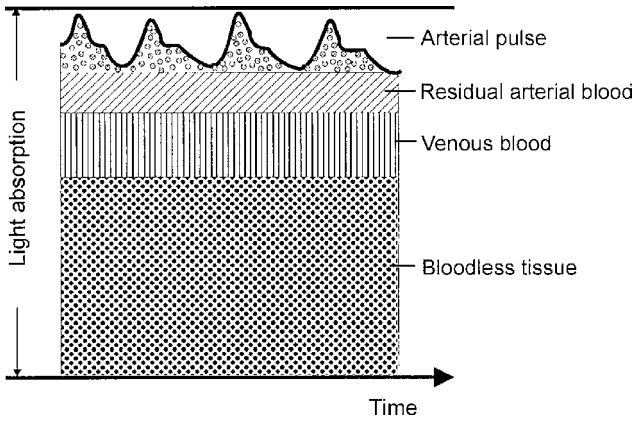

FIGURE 10.31 Time dependence of light absorption by a peripheral vascular tissue bed showing the effect of arterial pulsation.

measure the photodetector output when the corresponding LEDs are turned on. The sensor is usually attached either to the fingertip or earlobe so the tissue is sandwiched between the light source and the photodetector.

Pulse oximetry relies on the detection of a photoplethysmographic signal, as shown in Figure 10.31. This signal is caused by changes in the arterial blood volume associated with periodic contraction of the heart during systole. The magnitude of this signal depends on the amount of blood ejected from the heart into the peripheral vascular bed with each cardiac cycle, the optical absorption of the blood, the composition and color of the skin and underlying tissues, and the wavelengths used to illuminate the blood. S_aO_2 is derived by analyzing the magnitude of the red and infrared photoplethysmograms measured by the photodetector. Electronic circuits separate the red and infrared photoplethysmograms into their pulsatile (AC) and nonpulsatile (DC) signal components. An algorithm inside the pulse oximeter performs a mathematical normalization by which the AC signal at each wavelength is divided by the corresponding DC component that is mainly due to the light absorbed by the bloodless tissue, residual arterial blood when the heart is in diastole, venous blood, and skin pigmentation. Since it is assumed that the AC portion in the photoplethysmogram results only from the pulsatile arterial blood component, this scaling process provides a normalized red/infrared ratio, R, which is highly dependent on the color of the arterial blood and is therefore related to S_aO_2 but is largely independent of the volume of arterial blood entering the tissue during systole, skin pigmentation, and thickness. Hence, the instrument does not need to be recalibrated for measurements on different patients. The mathematical relationship between S_aO_2 and R is programmed by the manufacturer into the pulse oximeter.

10.4.2 pH Electrodes

pH describes the balance between acid and base in a solution. Acid solutions have an excess of hydrogen ions (H^+), whereas basic solutions have an excess of hydroxyl ions (OH^-). In a dilute solution, the product of these ion concentrations is a constant (1.0×10^{-14}).

Therefore, the concentration of either ion can be used to express the acidity or alkalinity of a solution. All neutral solutions have a pH of 7.0.

The measurement of blood pH is fundamental to many diagnostic procedures. In normal blood, pH is maintained under tight control and is typically around 7.40 (slightly basic). By measuring blood pH, it is possible to determine whether the lungs are removing sufficient CO_2 gas from the body or how well the kidneys regulate the acid-base balance.

pH electrodes belong to group of potentiometric sensors (i.e., electrochemical sensors producing a voltage). These sensors generate a small potential difference without the need to polarize the electrochemical cell. A pH electrode essentially consists of two separate electrodes: a reference electrode and an active (indicator) electrode, as shown in Figure 10.32. The two electrodes are typically made of an Ag/AgCl wire dipped in a KCl solution and encased in a glass container. A salt bridge, which is essentially a glass tube containing an electrolyte enclosed in a membrane that is permeable to all ions, maintains the potential of the reference electrode at a constant value regardless of the solution under test. Unlike the reference electrode, the active electrode is sealed with hydrogen-impermeable glass except at the tip. The reference electrode may also be combined with the indicator electrode in a single glass housing.

The boundary separating two solutions has a potential proportional to the hydrogen ion concentration of one solution and, at a constant temperature of 25°C, is given by

$$V = -59\ \text{mV} \times \log_{10}[H^+] + C \tag{10.21}$$

where C is a constant. Since pH is defined as

$$\text{pH} = -\log_{10}[H^+] \tag{10.22}$$

the potential of the active pH electrode, V, is proportional to the pH of the solution under test and is equal to

$$V = 59\ \text{mV} \times \text{pH} + C \tag{10.23}$$

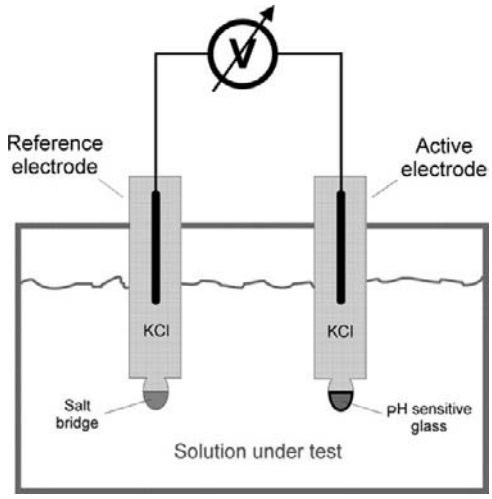

FIGURE 10.32 Principle of a pH electrode.

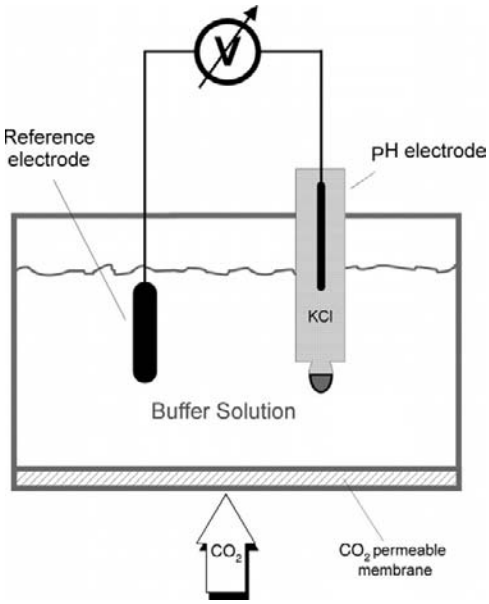

FIGURE 10.33 Principle of a pCO_2 electrode.

The value of C is usually compensated for electronically when the pH electrode is calibrated by placing the electrode inside different buffer solutions with known pH values.

10.4.3 Carbon Dioxide Sensors

Electrodes for measurement of partial pressure of CO_2 in blood or other liquids are based on measuring the pH, as illustrated in Figure 10.33. The measurement is based on the observation that when CO_2 is dissolved in water, it forms a weakly dissociated carbonic acid (H_2CO_3) that subsequently forms free hydrogen and bicarbonate ions according to the following chemical reaction:

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

As a result of this chemical reaction, the pH of the solution is changed. This change generates a potential between the glass pH and a reference (e.g., Ag/AgCl) electrode that is proportional to the negative logarithm of the pCO_2.

10.5 BIOANALYTICAL SENSORS

Biomolecules such as enzymes, antibodies, and microorganisms, as well as animal and plant cells, have been used as biological sensing elements. Among these, microorganisms offer unique advantages by their ability to detect a wide range of chemical substances, amenability to genetic modification, and broad operating pH and temperature range, making them ideal as biological sensing materials.

The number of analytes that can be measured with biosensors can be increased significantly by adding biologically specific mediators (reagents that either undergo reactions or act as catalysts) to the semipermeable membrane structure. Several biosensors that have been constructed and used mainly for research applications have different enzymes and bacteria as the primary sensing elements. Although these biosensors have been used successfully in vitro to demonstrate unique medical and industrial applications, further technical improvements are necessary to make these sensors robust and reliable enough to fulfill the demanding requirements of routine analytical and clinical applications. Examples of some interesting sensor designs are given in the following sections.

10.5.1 Enzyme-Based Biosensors

Enzymes are the most widely used biological sensing element in the fabrication of various biosensors. Enzymes constitute a group of more than 2,000 proteins having so-called biocatalytic properties. These properties give the enzymes the unique and powerful ability to accelerate chemical reactions inside biological cells. Most enzymes react only with specific substrates even though they may be contained in a complicated mixture with other substances. It is important to keep in mind, however, that soluble enzymes are very sensitive both to temperature and pH variations, and they can be inactivated by many chemical inhibitors. For practical biosensor applications, these enzymes are normally immobilized by insolubilizing the free enzymes via entrapment into an inert and stable matrix such as starch gel, silicon rubber, or polyacrylamide. This process is important to ensure that the enzyme retains its catalytic properties and can be reusable.

The action of specific enzymes can be utilized to construct a range of different biosensors. A typical example of an enzyme-based sensor is a glucose sensor that uses the enzyme glucose oxidase. Glucose plays an important role in metabolic processes. In patients suffering from diabetes mellitus, the pancreas does not produce sufficient amounts of insulin to control adequately the level of glucose in their blood. Therefore, to manage the disease, these patients must monitor and regulate their blood glucose level on a regular basis by medication and insulin injections. Currently available glucose sensors are based on an immobilized enzyme, such as glucose oxidase, that acts as a catalyst. Glucose is detected by measuring electrochemically either the amount of gluconic acid or hydrogen peroxide (H_2O_2) produced or by measuring the amount of oxygen consumed, according to the following chemical reaction:

$$\text{Glucose} + O_2 + H_2O \xleftarrow{\text{glucose oxidase}} \text{gluconic acid} + H_2O_2$$

A glucose sensor is similar to a pO_2 sensor and is shown in Figure 10.34. Glucose and oxygen enter through the outside membrane to allow glucose to interact with the glucose oxidase enzyme. The remaining oxygen penetrates through the second oxygen-permeable membrane and is measured by the oxygen electrode.

Biocatalytic enzyme-based sensors generally consist of an electrochemical gas-sensitive transducer or an ion-selective electrode with an enzyme immobilized in or on a membrane that serves as the biological mediator. The analyte diffuses from the bulk sample solution into the biocatalytic layer, where an enzymatic reaction takes place. The electroactive

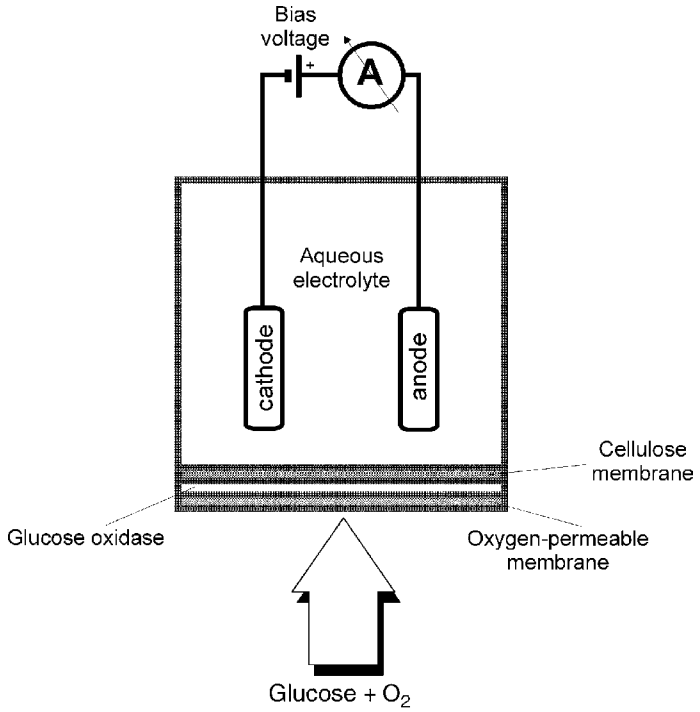

FIGURE 10.34 Principle of a glucose sensor.

product that is formed (or consumed) is usually detected by an ion-selective electrode. A membrane separates the basic sensor from the enzyme if a gas is consumed (such as O_2) or is produced (such as CO_2 or NH_3). Although the concentration of the bulk substrate drops continuously, the rate of consumption is usually negligible. The decrease is detected only when the test volume is very small or when the area of the enzyme membrane is large enough. Thus, this electrochemical analysis is nondestructive, and the sample can be reused. Measurements are usually performed at a constant pH and temperature either in a stirred medium solution or in a flow-through solution.

10.5.2 Microbial Biosensors

The fundamental basis of a microbial biosensor is the close proximity between an immobilized microorganism that serves as a specific recognition element and an electrochemical or optical sensing transducer that is used to convert the biochemical signal into an electronic signal that can be processed.

The fabrication of a microbial biosensor requires the immobilization of the microorganisms on a transducer by chemical or physical methods. Since the response, operational stability, and long-term use of a microbial biosensor is a function of the immobilization strategy used, immobilization technology plays a very important role in the successful design of microbial biosensors, and the choice of immobilization technique is critical.

Chemical methods of microbe immobilization include covalent binding and cross-linking. Covalent binding methods rely on the formation of a stable covalent bond between functional groups of the cell wall components of the microorganism and the transducer. To successfully achieve this goal, whole cells are exposed to harsh chemical reactions that can damage the microbial cell membrane and decrease the biological viability of the cells. Determining how to overcome this drawback remains a practical challenge. Cross-linking, on the other hand, involves bridging between functional groups on the outer cell membrane by multifunctional reagents (e.g., glutaraldehyde) to form a network. Because of the speed and simplicity, the method has found wide acceptance for the immobilization of microorganisms. The cells may be cross-linked directly onto the transducer surface or on a removable support membrane that can then be placed on the transducer. While cross-linking has advantages over covalent binding, the cell viability can be affected by the cross-linking agents. Therefore, cross-linking is suitable in constructing microbial biosensors where cell viability is not important and only the intracellular enzymes are involved in the detection.

Physical methods of microbe immobilization include adsorption and entrapment. Because these methods do not involve covalent bond formation with microbes and provide relatively small perturbation of microorganism native structure and function, these methods are preferred when viable cells are required. Physical adsorption is the simplest method for microbe immobilization. Typically, a microbial suspension is incubated with the electrode or an immobilization matrix, such as glass bead. The microbes are immobilized due to adsorptive interactions (i.e., ionic or polar bonding) and hydrophobic interaction. However, immobilization using adsorption alone generally leads to poor long-term stability because of desorption of microbes. The immobilization of microorganisms by entrapment can be achieved, for example, by the retention of the cells in close proximity of the transducer surface using a dialysis membrane. However, a major disadvantage of entrapment immobilization is the additional diffusion resistance offered by the entrapment material, which will result in a lower sensitivity and detection limit.

A number of microbial sensors have been developed mainly for online control of biochemical processes in various environmental, agricultural, food, and pharmaceutical applications. Microbial biosensors typically involve the assimilation of organic compounds by the microorganisms, followed by a change in respiration activity (metabolism) or the production of specific electrochemically active metabolites, such as H_2, CO_2, or NH_3, that are secreted by the microorganism.

Examples of microbial biosensors include ammonia (NH_3) and nitrogen dioxide (NO_2) sensors that utilize nitrifying bacteria as the biological sensing component. An ammonia biosensor can be constructed based on nitrifying bacteria, such as *Nitrosomonas sp.*, that use ammonia as a source of energy and oxidize ammonia as follows:

$$NH_3 + 1.5O_2 \xrightarrow{\textit{Nitrosomonas sp.}} NO_2 + H_2O + H^+$$

This oxidation process proceeds at a high rate, and the amount of oxygen consumed by the immobilized bacteria can be measured directly by a polarographic oxygen electrode placed behind the bacteria.

Nitric oxide (NO) and NO_2 are the two principal pollution gases of nitrogen in the atmosphere. The principle of a NO_2 biosensor is shown in Figure 10.35. When a sample of

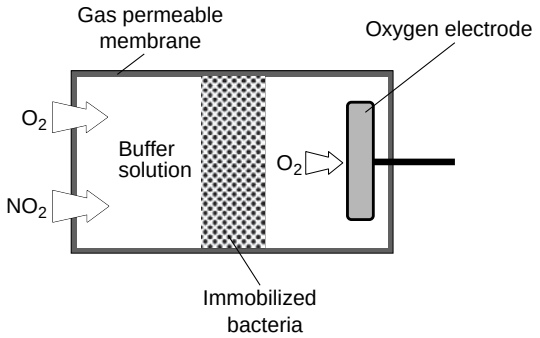

FIGURE 10.35 Principle of an NO_2 microbial-type biosensor.

NO_2 gas diffuses through the gas-permeable membrane, it is oxidized by the *Nitrobacter sp.* bacteria as follows:

$$2NO_2 + O_2 \xrightarrow{\textit{Nitrosomonas sp.}} 2NO_3$$

Similar to an ammonia biosensor, the consumption of O_2 around the membrane is determined by an electrochemical oxygen electrode.

The use of microbial cells in electrochemical sensors offers several advantages over enzyme-based electrodes, the principal one being the increased electrode lifetime to several weeks. On the other hand, microbial sensors may be less favorable compared with enzyme electrodes with respect to specificity and response time.

10.6 OPTICAL SENSORS

Optical sensors play an important role in the development of highly sensitive and selective methods for biochemical analysis. The fundamental principle that is employed is based on the change in optical properties of a biological or physical medium. The change produced can be the result of physical perturbations or intrinsic changes in absorbance, reflectance, scattering, fluorescence, polarization, or refractive index of the biological medium.

10.6.1 Optical Fibers

Optical fibers can be used to transmit light from one location to another with minimal attenuation and without any transport of heat from the light source. Therefore, they are used in a whole range of miniature sensors for biomedical applications. Optical fibers are small, flexible, and intrinsically immune to electromagnetic and radio frequency interferences. They can produce an instantaneous response to subtle changes in the microenvironments that surround their optical surface. Therefore, optical fibers permit in vivo measurements in small blood vessels or in delicate tissues such as the brain.

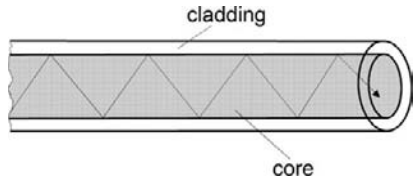

FIGURE 10.36 Principle of optical fibers.

Optical fibers are typically made from two concentric and transparent glass or plastic materials, as shown in Figure 10.36. The center piece is known as the core, and the outer layer, which serves as a coating material, is called the cladding.

The core and cladding of an optical fiber have a different index of refraction, n. The index of refraction is a number that expresses the ratio of the light velocity in free space to its velocity in a specific material. For instance, the refractive index for air is equal to 1.0, whereas the refractive index for water is equal to 1.33. Assuming that the refractive index of the core material is n_1 and the refractive index of the cladding is n_2 (where $n_1 > n_2$), according to Snell's law,

$$n_1 \times \sin \phi_1 = n_2 \times \sin \phi_2 \tag{10.24}$$

where ϕ is the angle of incidence, as shown in Figure 10.37.

Accordingly, any light passing from a lower refractive index to a higher refractive index is bent toward the line perpendicular to the interface of the two materials. For small incident angles, ϕ_1, the light ray enters the fiber core and bends inward at the first core/cladding interface. For larger incident angles, ϕ_2, the ray exceeds a minimum angle required to bend it back into the core when it reaches the core/cladding boundary. Consequently, the light escapes into the cladding. By setting $\sin\phi_2 = 1.0$, the critical angle, ϕ_{cr}, is given by

$$\sin \phi_{cr} = \frac{n_2}{n_1} \tag{10.25}$$

Any light rays entering the optical fiber with incidence angles greater than ϕ_{cr} are internally reflected inside the core of the fiber by the surrounding cladding. Conversely, any entering light rays with incidence angles smaller than ϕ_{cr} escape through the cladding and are therefore not transmitted by the core.

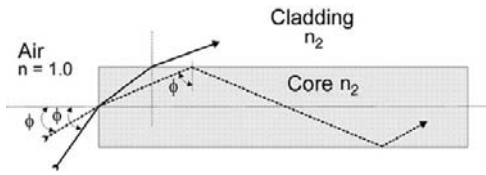

FIGURE 10.37 Optical fiber illustrating the incident and refracted light rays. The solid line shows the light ray escaping from the core into the cladding. The dashed line shows the ray undergoing total internal reflection inside the core.

EXAMPLE PROBLEM 10.14

Assume that a beam of light passes from a layer of glass with a refractive index $n_1 = 1.47$ into a second layer of glass with a refractive index of $n_2 = 1.44$. Using Snell's law, calculate the critical angle for the boundary between these two glass layers.

Solution

$$\phi_{cr} = \arcsin \times \left(\frac{n_2}{n_1}\right) = \arcsin(0.9796)$$

$$\phi_{cr} = 78.4^\circ$$

Therefore, light that strikes the boundary between these two glasses at an angle greater than 78.4° will be reflected back into the first layer.

The propagation of light along an optical fiber is not confined to the core region. Instead, the light penetrates a characteristic short distance (on the order of one wavelength) beyond the core surface into the less optically dense cladding medium. This effect causes the excitation of an electromagnetic field, called the "evanescent-wave," that depends on the angle of incidence and the incident wavelength. The intensity of the evanescent-wave decays exponentially with distance, according to Beer-Lambert's law. It starts at the interface and extends into the cladding medium.

10.6.2 Sensing Mechanisms

Optical sensors are typically interfaced with an optical module, as shown in Figure 10.38. The module supplies the excitation light, which may be from a monochromatic source such as a diode laser or from a broadband source (e.g., quartz-halogen) that is filtered to provide a narrow bandwidth of excitation. Typically, two wavelengths of light are used: one that is sensitive to changes in the species to be measured and one that is unaffected by changes in the analyte concentration. This wavelength serves as a reference and is used to compensate for fluctuations in source output and detector stability. The light output from the optic module is coupled into a fiber optic cable through appropriate lenses and an optical connector.

Several optical techniques are commonly used to sense the optical change across a biosensor interface. These are usually based on evanescent wave spectroscopy, which plays a major role in fiber optic sensors, and a surface plasmon resonance principle.

In fluorescence-based sensors, the incident light excites fluorescence emission, which changes in intensity as a function of the concentration of the analyte to be measured. The emitted light travels back down the fiber to the monitor, where the light intensity is measured by a photodetector. In other types of fiber optic sensors, the light-absorbing properties of the sensor chemistry change as a function of analyte chemistry. In the absorption-based design, a reflective surface near the tip or some scattering material within the sensing chemistry itself is usually used to return the light back through the same optical

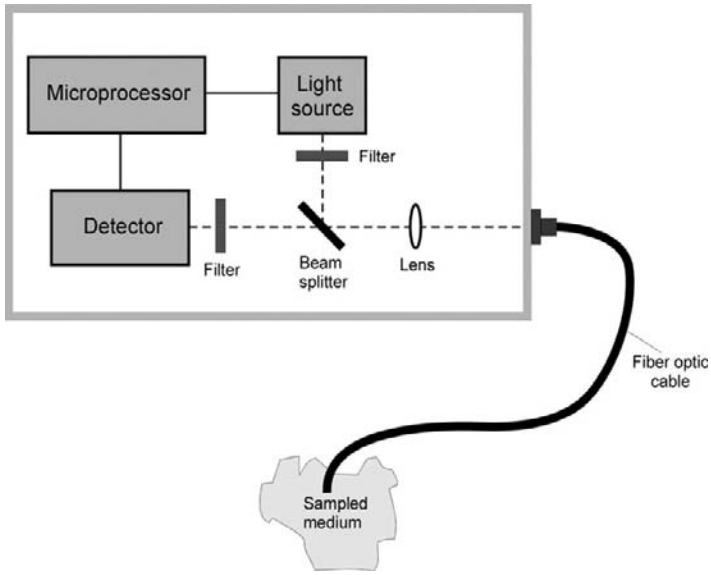

FIGURE 10.38 General principle of a fiber optic–based sensor.

fiber. Other sensing mechanisms exploit the evanescent-wave interaction with molecules that are present within the penetration depth distance and lead to attenuation in reflectance related to the concentration of the molecules. Because of the short penetration depth and the exponentially decaying intensity, the evanescent-wave is absorbed by compounds that must be present very close to the surface. The principle has been used to characterize interactions between receptors that are attached to the surface and ligands that are present in solution above the surface.

The key component in the successful implementation of evanescent-wave spectroscopy is the interface between the sensor surface and the biological medium. Receptors must retain their native conformation and binding activity, and sufficient binding sites must be present for multiple interactions with the analyte. In the case of particularly weak absorbing analytes, sensitivity can be enhanced by combining the evanescent-wave principle with multiple internal reflections along the sides of an unclad portion of a fiber optic tip. Alternatively, instead of an absorbing species, a fluorophore[2] can also be used. Light that is absorbed by the fluorophore emits detectable fluorescent light at a higher wavelength, thus providing improved sensitivity.

10.6.3 Intravascular Fiber Optic Blood Gas Sensors

Considerable effort has been devoted over the last three decades to develop disposable extracorporeal sensors (for ex vivo applications) or intra-arterial fiber optic sensors that

[2]A compound that produces a fluorescent signal in response to light.

can be placed in the arterial line (for in vivo applications) to enable continuous trending of arterial blood gases. With the advent of continuous arterial blood gas monitoring, treatment modalities can be proactive rather than reactive, which is vital for therapeutic interventions in ICU patients who may experience spontaneous and often unexpected changes in acid-base status.

Intra-arterial blood gas sensors typically employ a single- or a double-fiber configuration. Typically, the matrix containing the indicator is attached to the end of the optical fiber. Since the solubility of O_2 and CO_2 gases, as well as the optical properties of the sensing chemistry itself, is affected by temperature variations, fiber optic intravascular sensors include a thermocouple or thermistor wire running alongside the fiber optic cable to monitor and correct for temperature fluctuations near the sensor tip. A nonlinear response is characteristic of most chemical indicator sensors. Therefore, the operating range of these sensors is typically optimized to match the range of concentrations according to the intended application.

Intra-arterial fiber optic blood gas sensors are normally placed inside a standard 20-gauge arterial cannula that is sufficiently small, thus allowing adequate spacing between the sensor and the catheter wall. The resulting lumen is large enough to permit the withdrawal of blood samples, introduction of a continuous or intermittent anticoagulant (e.g., heparin) flush, and the recording of a blood pressure waveform. In addition, the optical fibers are encased in a protective tubing to contain any fiber fragments in case they break off. The material in contact with the blood is typically treated with a covalently bonded layer of heparin, resulting in low susceptibility to fibrin deposition. Despite excellent accuracy of indwelling intra-arterial catheters in vitro compared to blood gas analyzers, when these multiparameter probes were first introduced into the vascular system, it quickly became evident that the readings (primarily pO_2) vary frequently and unpredictably, mainly due to the sensor tip intermittently coming in contact with the wall of the arterial blood vessel and intermittent reductions in blood flow due to arterial vasospasm.

A more advanced multiparameter disposable probe (Figure 10.39) consisting of pO_2, pCO_2, and pH sensors was developed by Diametrics Medical, Inc. The sensor has a diameter of 0.5 mm and can be inserted intravascularly through a 20-gauge indwelling cannula. Clinical studies confirmed that the system is adequate for trend monitoring, eliminating invasive blood sampling, potential errors in analysis, and significant delays in obtaining results, which may affect treatment. The device has been evaluated in neurosurgical patients for continuous monitoring in the brain and in critically ill pediatric patients.

Fiber Optic pO_2 Sensors

Various fiber optic sensors were developed to measure pO_2 in blood based on the principle of fluorescence quenching. Quenching reduces the intensity of the emitted fluorescence light and is related to the concentration of the quenching molecules. For example, quenching can result from collisions encountered between the fluorophore (a fluorescent substance) and the quencher. For quenching to occur, the fluorophore and quencher must be in contact. When light is absorbed by a molecule, the absorbed energy is held as an excited electronic state of the molecule. It is then lost by coupling to the mechanical movement of the molecule (heat), reradiated from the molecule in a mean time of about 10 ns (fluorescence), or converted to another excited state with a much longer mean lifetime

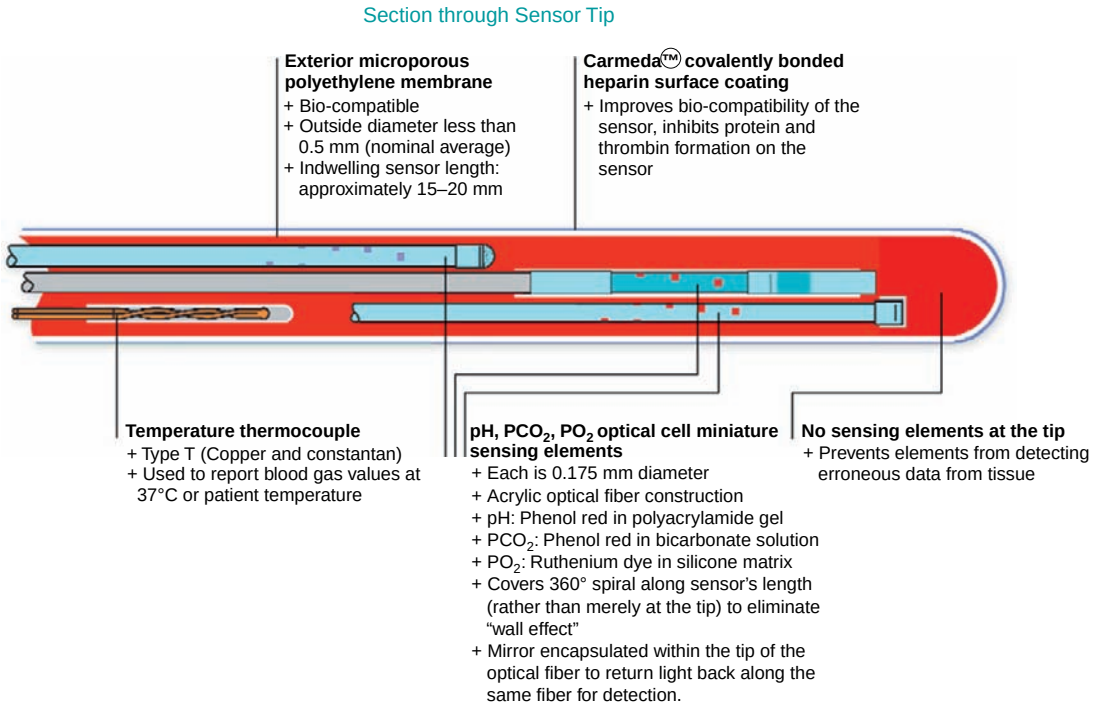

FIGURE 10.39 Principle of an indwelling arterial optical blood gas catheter. A heparin-coated porous polyethylene membrane encapsulates the optical fibers and a thermistor. *Courtesy of Diametrics, Inc., St. Paul, MN.*

(phosphorescence). A wide variety of substances act as fluorescence quenchers. One of the best-known quenchers is molecular oxygen.

A typical fiber optic sensor for measuring pO_2 using the principle of fluorescence quenching consists of a dye that is excited at 470 nm (blue) and fluoresces at 515 nm (green) with an emitted intensity that depends on the pO_2. If the excited dye encounters an oxygen molecule, the excess energy will be transferred to the oxygen molecule, decreasing the fluorescence signal. The degree of quenching depends on the concentration of oxygen. The optical information is derived from the ratio of light intensities measured from the green fluorescence and the blue excitation light, which serves as an internal reference signal. The ratio of green to blue intensity is described by the Stern-Volmer equation

$$I_o/I = 1 + KpO_2 \tag{10.26}$$

where I_o and I are the fluorescence emission intensities in the absence (i.e., $pO_2 = 0$) and presence of the oxygen quencher, respectively. K is the Stern-Volmer quenching coefficient, which is dependent on temperature. The method provides a nearly linear readout of pO_2 over the range of 0–150 mmHg (0–20 kPa), with a precision of about 1 mmHg (0.13 kPa). The slope of the plot described by Eq. (10.26) is a measure of the oxygen sensitivity of the sensor. Note that the sensor will be most sensitive to low levels of oxygen.

Fiber Optic pH Sensors

A fiber optic pH sensor can be designed by placing a reversible color-changing dye as an indicator at the end of a pair of optical fibers. For example, the popular indicator phenol red can be used because this dye changes its absorption properties from the green to the blue part of the spectrum as the acidity is increased. The dye can be covalently bound to a hydrophilic polymer in the form of water-permeable microbeads to stabilize the indicator concentration. The indicator beads are contained in a sealed hydrogen ion-permeable envelope made out of hollow cellulose tubing, forming a miniature spectrophotometric cell at the end of the optical fibers.

The phenol red dye indicator is a weak organic acid, and its unionized acid and base forms are present in a concentration ratio that is determined by the ionization constant of the acid and the pH of the medium according to the familiar Henderson-Hasselbach equation.[3] The two forms of the dye have different optical absorption spectra. Hence, the relative concentration of one form, which varies as a function of pH, can be measured optically and related to variations in pH. In the pH sensor, green and red lights that emerge from the distal end of one fiber pass through the dye, where it is backscattered into the other fiber by the light-scattering beads. The base form of the indicator absorbs the green light. The red light is not absorbed by the indicator and is used as an optical reference. The ratio of green to red light is related to the pH of the medium.

A similar principle can also be used with a reversible fluorescent indicator where the concentration of one indicator form is measured by its fluorescence rather than by the absorbance intensity. Light, typically in the blue or UV wavelength region, excites the fluorescent dye to emit longer-wavelength light. The concept is based on the fluorescence of weak acid dyes that have different excitation wavelengths for the basic and acidic forms but the same emitted fluorescent wavelength. The dye is encapsulated in a sample chamber that is permeable to hydrogen ions. When the dye is illuminated with the two different excitation wavelengths, the ratio of the emitted fluorescent intensities can be used to calculate the pH of the solution that is in contact with the encapsulated dye.

Fiber Optic pCO_2 Sensors

The pCO_2 of a sample is typically determined by measuring changes in the pH of a bicarbonate solution that is isolated from the sample by a CO_2-permeable membrane but remains in equilibrium with the CO_2 gas. The bicarbonate and CO_2, as carbonic acid, form a pH buffer system. By the Henderson-Hasselbach equation, the hydrogen ion concentration is proportional to the pCO_2 of the sample. This measurement can be done with either a pH electrode or a dye indicator.

Mixed Venous Oxygen Saturation Sensors

Fiber optic catheters can be used in vivo to measure mixed venous oxygen saturation (SvO_2) inside the pulmonary artery, which represents the blood outflow from all tissue

[3] $pH = 6.1 + \log \frac{HCO_3^-}{CO_2}$

beds. Under normal conditions, oxygen saturation in the pulmonary artery is normally around 75 percent, and oxygen consumption is less than or equal to the amount of oxygen delivered. However, in critically ill patients, oxygen delivery is often insufficient for the increased tissue demands because many such patients have compromised compensatory mechanisms. If tissue oxygen demands increase and the body's compensatory mechanisms are overwhelmed, the venous oxygen reserve will be tapped, and that change will be reflected as a decrease in SvO_2. For this reason, SvO_2 is regarded as a reliable indicator of tissue oxygenation and, therefore, can be used to indicate the effectiveness of the cardiopulmonary system during cardiac surgery and in the ICU.

The fiber optic SvO_2 catheter consists of two separate optical fibers; one fiber is used for transmitting incident light to the flowing blood, and the other directs the backscattered light to a photodetector. The catheter is introduced into the vena cava and further advanced through the heart into the pulmonary artery by inflating a small balloon located at the distal end. The flow-directed catheter also contains a small thermistor for measuring cardiac output by thermodilution.

The principle is based on the relationship between SvO_2 and the ratio of the infrared-to-red (IR/R) light backscattered from the red blood cell in blood

$$SvO_2 = A - B(\mathrm{IR/R}) \tag{10.27}$$

where, A and B are empirically derived calibration coefficients.

Several problems limit the wide clinical application of intravascular fiber optic oximeters. These include the dependence of the optical readings on motion artifacts due to catheter tip "whipping" against the blood vessel wall. Additionally, the introduction of the catheter into the heart requires an invasive procedure and can sometimes cause arrhythmias.

10.6.4 Intravascular Fiber Optic Pressure Sensors

Pressure measurements provide important diagnostic information. For example, pressure measurements inside the heart, cranium, kidneys, and bladder can be used to diagnose abnormal physiological conditions that are otherwise not feasible to ascertain from imaging or other diagnostic modalities. In addition, intracranial hypertension resulting from injury or other causes can be monitored to assess the need for therapy and its efficacy. Likewise, dynamic changes of pressure measured inside the heart, cranial cavities, uterus, and bladder can help to assess the efficiency of these organs during contractions.

Several approaches can be used to measure pressure using minimally invasive sensors. The most common technique involves the use of a fiber optic catheter. Fiber optic pressure sensors have been known and widely investigated since the early 1960s. The major challenge is to develop a small enough sensor with high sensitivity, high fidelity, and adequate dynamic response that can be inserted either through a hypodermic needle or in the form of a catheter. Additionally, for routine clinical use, the device must be cost-effective and disposable.

A variety of ideas have been exploited for varying a light signal in a fiber optic probe with pressure. Most designs utilize either an interferometer principle or measure changes in light intensity. Interferometric-based pressure sensors are known to have a high sensitivity, but they involve complex calibration and require complicated fabrication. On the other

FIGURE 10.40 Fiber optic in vivo pressure sensor. *Courtesy of Fiso Technologies, Quebec, Canada.*

hand, fiber optic pressure sensors based on light intensity modulation have a lower sensitivity but involve simpler construction.

The basic operating principle of a fiber optic pressure sensor is based on light intensity modulation. Typically, white light or light produced by a light emitting diode (LED) is carried by an optical fiber to a flexible mirrored surface located inside a pressure-sensing element. The mirror is part of a movable membrane partition that separates the fiber end from the fluid chamber. Changes in the hydrostatic fluid pressure cause a proportional displacement of the membrane relative to the distal end of the optical fiber. This in turn modulates the amount of light coupled back into the optical fiber. The reflected light is measured by a sensitive photodetector and converted to a pressure reading.

A fiber optic pressure transducer for in vivo application based on optical interferometry using white light was developed by Fiso Technologies (Figure 10.40). The sensing element is based on a Fabry-Pérot principle. A miniaturized Fabry-Pérot cavity is defined on one end by a micromachined silicon diaphragm membrane that acts as the pressure sensing element and is bonded on a cup-shaped glass base attached to the opposite side of the optical fiber. When external pressure is applied to the transducer, the deflection of the diaphragm causes variation of the cavity length that in turn is converted to a pressure reading. Due to its extremely small size (dia: 550 μm), the sensor can be inserted through a hypodermic needle.

10.6.5 Intravascular Fiber Optic Temperature Sensors

Miniature fiber optic temperature sensors, also commercialized by Fiso Technologies, are based on a similar Fabry-Pérot principle utilized in the construction of a miniaturized fiber optic pressure transducer. The Fabry-Pérot cavity in these designs is formed by two optical fibers assembled into a glass capillary tube or a transparent semiconductor material. The cavity length changes with temperature variations due to differences in the thermal expansion coefficient between the glass capillary and optical fibers. Due to their miniature construction (dia: 210–800 μm), the thermal inertia is close to zero, allowing ultrafast temperature response. The miniature size of the sensor allows the integration into minimally invasive medical devices for direct in situ measurement in space-restricted cavities.

10.6.6 Indicator-Mediated Fiber Optic Sensors

Since only a limited number of biochemical substances have an intrinsic optical absorption or fluorescence property that can be measured directly with sufficient selectivity by standard spectroscopic methods, indicator-mediated sensors have been developed to use specific reagents that are immobilized either on the surface or near the tip of an optical

fiber. In these sensors, light travels from a light source to the end of the optical fiber, where it interacts with a specific chemical or biological recognition element. These transducers may include indicators and ion-binding compounds (ionophores), as well as a wide variety of selective polymeric materials. After the light interacts with the biological sample, it returns either through the same optical fiber (in a single-fiber configuration) or a separate optical fiber (in a dual-fiber configuration) to a detector, which correlates the degree of light attenuation with the concentration of the analyte.

Typical indicator-mediated sensor configurations are shown schematically in Figure 10.41. The transducing element is a thin layer of chemical material that is placed near the sensor tip and is separated from the blood medium by a selective membrane. The chemical-sensing material transforms the incident light into a return light signal with a magnitude that is proportional to the concentration of the species to be measured. The stability of the sensor is determined by the stability of the photosensitive material that is used and also by how effective the sensing material is protected from leaching out of the probe. In Figure 10.41a, the indicator is immobilized directly on a membrane that is positioned at the end of the fiber. An indicator in the form of a powder can also be physically retained in position at the end of the fiber by a special permeable membrane, as shown in Figure 10.41b, or a hollow capillary tube, as shown in Figure 10.41c.

10.6.7 Immunoassay Sensors

The development of immunosensors is based on the observation of ligand-binding reaction products between a target analyte and a highly specific binding reagent. The key

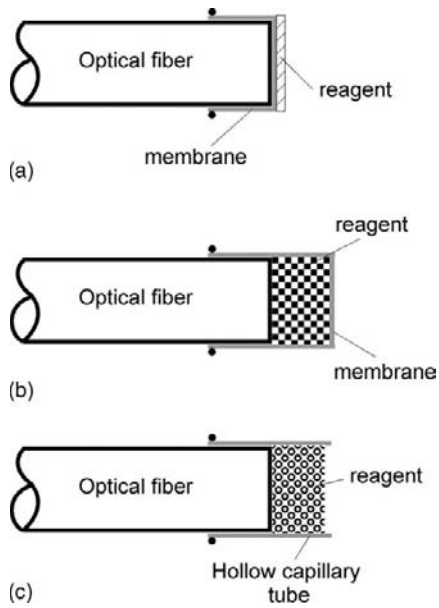

FIGURE 10.41 Different indicator-mediated fiber optic sensor configurations.

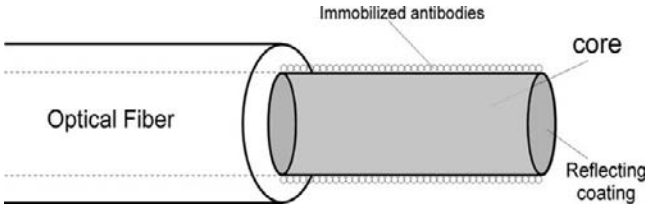

FIGURE 10.42 Principle of a fiber optic immunoassay biosensor.

component of an immunosensor is the biological recognition element, which typically consists of antibodies or antibody fragments. Immunological techniques offer outstanding selectivity[4] and sensitivity through the process of antibody-antigen interaction. This is the primary recognition mechanism by which the immune system detects and fights foreign matter and has therefore allowed the measurement of many important compounds at micromolar and even picomolar concentrations in complex biological samples.

Evanescent-type biosensors can be used in immunological diagnostics to detect antibody-antigen binding. Figure 10.42 shows a conceptual diagram of an immunoassay biosensor. The immobilized antibody on the surface of the unclad portion of the fiber captures the antigen from the sample solution, which is normally introduced into a small flow through a chamber where the fiber tip is located. The sample solution is then removed and a labeled antibody is added into the flow chamber. A fluorescent signal is excited and measured when the labeled antibody binds to the antigen that is already immobilized by the antibody.

10.6.8 Surface Plasmon Resonance Sensors

When monochromatic polarized light (e.g., from a laser source) impinges on a transparent medium having a conducting metallized surface (e.g., Ag or Au), there is a charge density oscillation at the interface. When light at an appropriate wavelength interacts with the dielectric-metal interface at a defined angle, called the resonance angle, there is a match of resonance between the energy of the photons and the electrons at the metal interface. As a result, the photon energy is transferred to the surface of the metal as packets of electrons, called plasmons, and the light reflection from the metal layer will be attenuated. This results in a phenomenon known as surface plasmon resonance (SPR) and is shown schematically in Figure 10.43. The resonance is observed as a sharp dip in the reflected light intensity when the incident angle is varied. The resonance angle depends on the incident wavelength, the type of metal, the polarization state of the incident light, and the nature of the medium in contact with the surface. Any change in the refractive index of the medium will produce a shift in the resonance angle and thus provide a highly sensitive means of monitoring surface interactions.

[4]The sensor's ability to detect a specific substance in a mixture containing other substances.

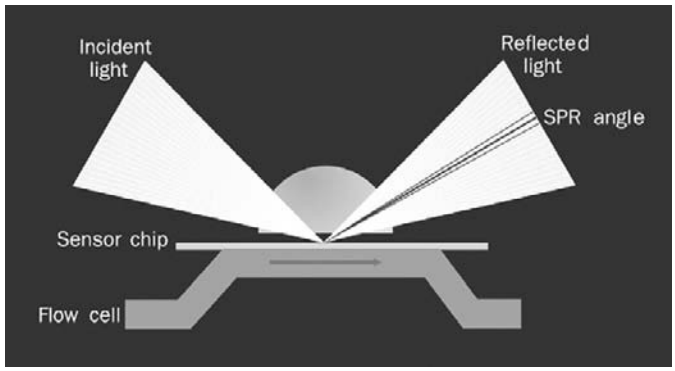

FIGURE 10.43 Principle of a surface plasmon resonance (SPR) detection system. *Courtesy of Biacore AB, Uppsala, Sweden.*

SPR is generally used for sensitive measurement of variations in the refractive index of the medium immediately surrounding the metal film. For example, if an antibody is bound to or absorbed into the metal surface, a noticeable change in the resonance angle can be readily observed because of the change of the refraction index at the surface if all other parameters are kept constant. The advantage of this concept is the improved ability to detect the direct interaction between antibody and antigen as an interfacial measurement.

10.7 EXERCISES

1. Give an example of a biomedical transducer that is used to monitor patients in the intensive care unit.
2. Discuss the important considerations in the selection of materials for packaging of an implantable biosensor.
3. Estimate the response time of an airflow transducer to monitor changes in breathing rate.
4. Explain why low drift is an important specification for implantable sensors.
5. The calibration tests of a new pressure transducer produced the readings in Table 10.4.
   (a) Plot the input-output calibration for this transducer.
   (b) Find the offset for readings between 0 to 200 mmHg.
   (c) Find the sensitivity for readings between 0 to 200 mmHg.
   (d) Estimate the average sensitivity for readings ranging between 200 to 300 mmHg.
   (e) State whether the response of this transducer over the entire measurement range is linear or nonlinear.
6. Suggest a method to measure hysteresis in a blood flow transducer.
7. Discuss the problem of using a pressure transducer with hysteresis to monitor blood pressure.
8. Explain how the accuracy of a new temperature sensor can be determined.
9. Two identical silver electrodes are placed in an electrolyte solution. Calculate the potential drop between the two electrodes.

TABLE 10.4 Sample Calibration Data for a Pressure Sensor

Pressure (mmHg)	Reading (μV)
20	0
40	20
60	40
80	60
100	80
120	100
140	120
160	135
180	150
200	165
220	180
240	190
260	200
280	210
300	220
320	225
340	230
360	235
380	237
400	239
420	240
440	240

10. Cadmium and zinc electrodes are placed in an electrolyte solution. Calculate the current that will flow through the electrodes if the equivalent resistance of the solution is equal to 14 kΩ.

11. Explain what will happen when the Ag/AgCl gel of an ECG electrode used to monitor a patient in the ICU dries out over time.

12. By how much would the inductance of an inductive displacement transducer coil change if the number of coil turns is decreased by a factor of 6?

Continued

13. Determine the ratio between the cross-sectional areas of two blood vessels assuming that the voltage ratio induced in identical magnetic flow probes is equal to 2:3 and the ratio of blood flows through these vessels is 1:5.
14. A 4.5 kΩ linear rotary transducer is used to measure the angular displacement of the knee joint. Calculate the change in output voltage for a 165° change in the angle of the knee. Assume that a constant current of 14 mA is supplied to the transducer.
15. Provide a step-by-step derivation of Eq. (10.11).
16. An elastic resistive transducer with an initial resistance, R_o, and length, l_o, is stretched to a new length. Assuming that the cross-sectional area of the transducer changes during stretching, derive a mathematical relationship for the change in resistance ΔR as a function of the initial length, l_o; the change in length, Δl; the volume of the transducer, V; and the resistivity, ρ.
17. The area of each plate in a differential capacitor sensor is equal to 5.6 cm^2. Calculate the equilibrium capacitance in air for each capacitor assuming that the equilibrium displacement for each capacitor is equal to 3 mm.
18. Plot the capacitance (y-axis) versus displacement (x-axis) characteristics of a capacitance transducer.
19. Calculate the sensitivity of a capacitive transducer (i.e., $\Delta C/\Delta d$) for small changes in displacements.
20. A capacitive transducer is used in a mattress to measure changes in breathing patterns of an infant. During inspiration and expiration, the rate of change (i.e., dV/dt) in voltage across the capacitor is equal to ±1V/s, and this change can be modeled by a triangular waveform. Plot the corresponding changes in current flow through this transducer.
21. Derive the relationship for the current through the capacitor-equivalent piezoelectric crystal as a function of V and C.
22. Two identical ultrasonic transducers are positioned across a blood vessel, as shown in Figure 10.44. Calculate the diameter of the blood vessel if it takes 380 ns for the ultrasonic sound wave to propagate from one transducer to the other.
23. Discuss the advantages of MEMS-type sensors.

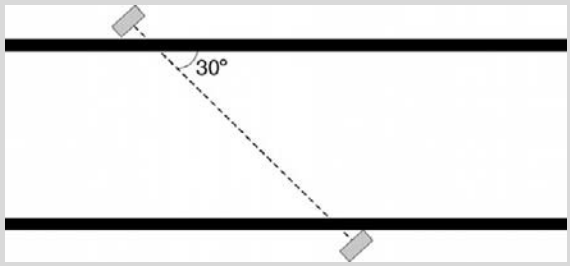

FIGURE 10.44 Two identical ultrasonic transducers positioned across a blood vessel.

24. Calculate the resistance of a thermistor at 98°F assuming that the resistance of this thermistor at 12°C is equal to 7.0 kΩ and $\beta = 4{,}600$.

25. The resistance of a thermistor with a $\beta = 5{,}500$ measured at 18°C is equal to 250 Ω. Find the temperature of the thermistor when the resistance is doubled.

26. Calculate the β of a thermistor assuming that it has a resistance of 4.4 kΩ at 21°C (room temperature) and a resistance of 2.85 kΩ when the room temperature increases by 20 percent.

27. A Chromel/Constantan thermocouple has the following empirical coefficients:

$C_0 = -2.340 \times 10^{-2}$

$C_1 = 4.221 \times 10^{-2}$

$C_2 = 3.284 \times 10^{-5}$

Find the EMF generated by this thermocouple at a temperature of 250°C.

28. Find the Seebeck coefficient for the Chromel/Alumel thermocouple at a temperature of 200°C.

29. Explain why the temporal artery thermometer is not used to measure core body temperature over the radial artery.

30. Compare and contrast the temporal artery and tympanic thermometers.

31. Compare and contrast a temperature pill with a temporal artery thermometer.

32. Sketch the current (*y*-axis) versus pO_2 (*x*-axis) characteristics of a typical polarographic Clark electrode.

33. Explain why the value of the normalized ratio (*R*) in a pulse oximeter is independent of the volume of arterial blood entering the tissue during systole.

34. Explain why the value of the normalized ratio (*R*) in a pulse oximeter is independent of skin pigmentation.

35. Explain the difference between a potentiometric and amperometric sensor.

36. Explain the difference between intravascular fiber optic pO_2 and SvO_2 sensors.

37. A pH electrode is attached to a sensitive voltmeter that reads 0.652 V when the electrode is immersed in a buffer solution with a pH of 6.7. After the pH electrode is moved to an unknown buffer solution, the reading of the voltmeter is decreased by 20 percent. Calculate the pH of the unknown buffer solution.

38. Plot the optical density, OD, of an absorbing solution (*y*-axis) as a function of the concentration of this solution (*x*-axis). What is the slope of this curve?

39. An unknown sample solution whose concentration is 1.55×10^{-3} g/L is placed in a 1 cm clear holder and found to have a transmittance of 44 percent. The concentration of this sample is changed such that its transmittance has increased to 57 percent. Calculate the new concentration of the sample.

40. Calculate the angle of the refracted light ray if an incident light ray passing from air into water has a 75-degree angle with respect to the normal.

41. Explain why fiber optic sensors typically require simultaneous measurements using two wavelengths of light.

42. Plot the fluorescence intensity of a fiber optic pO_2 sensor (*y*-axis) as a function of oxygen concentration (*x*-axis).

Continued

43. A chemical sensor is used to measure the pH of a dye with an absorbance spectrum shown in Figure 10.45. Assume that the absorbance of each form of the dye is linearly related to its pH. Devise a method to measure the pH of the dye.

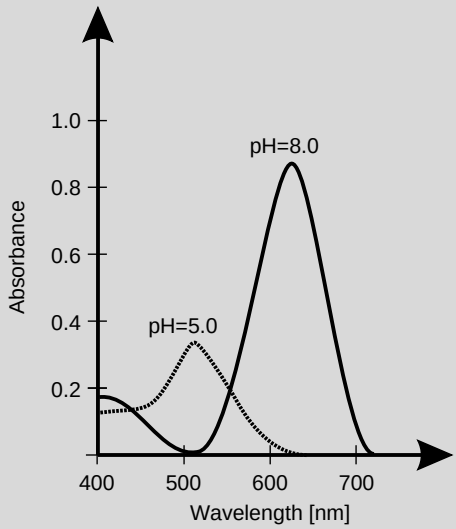

FIGURE 10.45 Optical absorbance spectra of a dye in its acid (pH = 5.0) and base (pH = 8.0) forms.

44. Explain the difference between absorption-based and fluorescence-based measurements.

Suggested Readings

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