CHAPTER

1

Biomedical Engineering: A Historical Perspective

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OUTLINE

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

- Identify the major role that advances in medical technology have played in the establishment of the modern health care system.
- Define what is meant by the term *biomedical engineering* and the roles biomedical engineers play in the health care delivery system.
- Explain why biomedical engineers are professionals.

In the industrialized nations, technological innovation has progressed at such an accelerated pace that it has permeated almost every facet of our lives. This is especially true in the area of medicine and the delivery of health care services. Although the art of medicine has a long history, the evolution of a technologically based health care system capable of providing a wide range of effective diagnostic and therapeutic treatments is a relatively new phenomenon. Of particular importance in this evolutionary process has been the establishment of the modern hospital as the center of a technologically sophisticated health care system.

Since technology has had such a dramatic impact on medical care, engineering professionals have become intimately involved in many medical ventures. As a result, the discipline of *biomedical engineering* has emerged as an integrating medium for two dynamic professions—medicine and engineering—and has assisted in the struggle against illness and disease by providing tools (such as biosensors, biomaterials, image processing, and artificial intelligence) that health care professionals can use for research, diagnosis, and treatment.

Thus, biomedical engineers serve as relatively new members of the health care delivery team that seeks new solutions for the difficult problems confronting modern society. The purpose of this chapter is to provide a broad overview of technology's role in shaping our modern health care system, highlight the basic roles biomedical engineers play, and present a view of the professional status of this dynamic field.

1.1 THE EVOLUTION OF THE MODERN HEALTH CARE SYSTEM

Primitive humans considered diseases to be "visitations"—the whimsical acts of affronted gods or spirits. As a result, medical practice was the domain of the witch doctor and the medicine man and medicine woman. Yet even as magic became an integral part of the healing process, the cult and the art of these early practitioners were never entirely limited to the supernatural. Using their natural instincts and learning from experience, these individuals developed a primitive science based upon empirical laws. For example, through acquisition and coding of certain reliable practices, the arts of herb doctoring, bone setting, surgery, and midwifery were advanced. Just as primitive humans learned from observation that certain plants and grains were good to eat and could be cultivated, the healers and shamans observed the nature of certain illnesses and then passed on their experiences to other generations.

Evidence indicates that the primitive healer took an active, rather than simply intuitive, interest in the curative arts, acting as a surgeon and a user of tools. For instance, skulls with holes made in them by trephiners have been collected in various parts of Europe, Asia, and South America. These holes were cut out of the bone with flint instruments to gain access to the brain. Although one can only speculate the purpose of these early surgical operations, magic and religious beliefs seem to be the most likely reasons. Perhaps this procedure liberated from the skull the malicious demons that were thought to be the cause of extreme pain (as in the case of migraines) or attacks of falling to the ground (as in epilepsy). That this procedure was carried out on living patients, some of whom actually survived, is

evident from the rounded edges on the bone surrounding the hole, which indicate that the bone had grown again after the operation. These survivors also achieved a special status of sanctity so that, after their death, pieces of their skull were used as amulets to ward off convulsive attacks. From these beginnings, the practice of medicine has become integral to all human societies and cultures.

It is interesting to note the fate of some of the most successful of these early practitioners. The Egyptians, for example, have held Imhotep, the architect of the first pyramid (3000 BC), in great esteem through the centuries, not as a pyramid builder but as a doctor. Imhotep's name signified "he who cometh in peace" because he visited the sick to give them "peaceful sleep." This early physician practiced his art so well that he was deified in the Egyptian culture as the god of healing.

Egyptian mythology, like primitive religion, emphasized the interrelationships between the supernatural and one's health. For example, consider the mystic sign *Rx*, which still adorns all prescriptions today. It has a mythical origin: the legend of the Eye of Horus. It appears that as a child Horus lost his vision after being viciously attacked by Seth, the demon of evil. Then Isis, the mother of Horus, called for assistance to Thoth, the most important god of health, who promptly restored the eye and its powers. Because of this intervention, the Eye of Horus became the Egyptian symbol of godly protection and recovery, and its descendant, Rx, serves as the most visible link between ancient and modern medicine.

The concepts and practices of Imhotep and the medical cult he fostered were duly recorded on papyri and stored in ancient tombs. One scroll (dated c. 1500 BC), which George Elbers acquired in 1873, contains hundreds of remedies for numerous afflictions ranging from crocodile bites to constipation. A second famous papyrus (dated c. 1700 BC), discovered by Edwin Smith in 1862, is considered to be the most important and complete treatise on surgery of all antiquity. These writings outline proper diagnoses, prognoses, and treatment in a series of surgical cases. These two papyri are certainly among the outstanding writings in medical history.

As the influence of ancient Egypt spread, Imhotep was identified by the Greeks with their own god of healing: Aesculapius. According to legend, the god Apollo fathered Aesculapius during one of his many earthly visits. Apparently Apollo was a concerned parent, and, as is the case for many modern parents, he wanted his son to be a physician. He made Chiron, the centaur, tutor Aesculapius in the ways of healing (Figure 1.1). Chiron's student became so proficient as a healer that he soon surpassed his tutor and kept people so healthy that he began to decrease the population of Hades. Pluto, the god of the underworld, complained so violently about this course of events that Zeus killed Aesculapius with a thunderbolt and in the process promoted Aesculapius to Olympus as a god.

Inevitably, mythology has become entangled with historical facts, and it is not certain whether Aesculapius was in fact an earthly physician like Imhotep, the Egyptian. However, one thing is clear: by 1000 BC, medicine was already a highly respected profession. In Greece, the Aesculapia were temples of the healing cult and may be considered the first hospitals (Figure 1.1). In modern terms, these temples were essentially sanatoriums that had strong religious overtones. In them, patients were received and psychologically prepared, through prayer and sacrifice, to appreciate the past achievements of Aesculapius and his physician priests. After the appropriate rituals, they were allowed to enjoy "temple sleep." During

FIGURE 1.1 A sick child brought to the Temple of Aesculapius. *Courtesy of http://www.nouveaunet.com/images/art/84.jpg.*

the night, "healers" visited their patients, administering medical advice to clients who were awake or interpreting dreams of those who had slept. In this way, patients became convinced that they would be cured by following the prescribed regimen of diet, drugs, or bloodletting. On the other hand, if they remained ill, it would be attributed to their lack of faith. With this approach, patients, not treatments, were at fault if they did not get well. This early use of the power of suggestion was effective then and is still important in medical treatment today. The notion of "healthy mind, healthy body" is still in vogue today.

One of the most celebrated of these "healing" temples was on the island of Cos, the birthplace of Hippocrates, who as a youth became acquainted with the curative arts through his father, also a physician. Hippocrates was not so much an innovative physician as a collector of all the remedies and techniques that existed up to that time. Since he viewed the physician as a scientist instead of a priest, Hippocrates also injected an essential ingredient into medicine: its scientific spirit. For him, diagnostic observation and clinical treatment began to replace superstition. Instead of blaming disease on the gods, Hippocrates taught that disease was a natural process, one that developed in logical steps, and that symptoms were reactions of the body to disease. The body itself, he emphasized, possessed its own means of recovery, and the function of the physician was to aid these natural forces. Hippocrates treated each patient as an original case to be studied and documented. His shrewd

descriptions of diseases are models for physicians even today. Hippocrates and the school of Cos trained many individuals, who then migrated to the corners of the Mediterranean world to practice medicine and spread the philosophies of their preceptor. The work of Hippocrates and the school and tradition that stem from him constitute the first real break from magic and mysticism and the foundation of the rational art of medicine. However, as a practitioner, Hippocrates represented the spirit, not the science, of medicine, embodying the good physician: the friend of the patient and the humane expert.

As the Roman Empire reached its zenith and its influence expanded across half the world, it became heir to the great cultures it absorbed, including their medical advances. Although the Romans themselves did little to advance clinical medicine (the treatment of the individual patient), they did make outstanding contributions to public health. For example, they had a well-organized army medical service, which not only accompanied the legions on their various campaigns to provide "first aid" on the battlefield but also established "base hospitals" for convalescents at strategic points throughout the empire. The construction of sewer systems and aqueducts were truly remarkable Roman accomplishments that provided their empire with the medical and social advantages of sanitary living. Insistence on clean drinking water and unadulterated foods affected the control and prevention of epidemics and, however primitive, made urban existence possible. Unfortunately, without adequate scientific knowledge about diseases, all the preoccupation of the Romans with public health could not avert the periodic medical disasters, particularly the plague, that mercilessly befell its citizens.

Initially, the Roman masters looked upon Greek physicians and their art with disfavor. However, as the years passed, the favorable impression these disciples of Hippocrates made upon the people became widespread. As a reward for their service to the peoples of the Empire, Julius Caesar (46 BC) granted Roman citizenship to all Greek practitioners of medicine in his empire. Their new status became so secure that when Rome suffered from famine that same year, these Greek practitioners were the only foreigners not expelled from the city. On the contrary, they were even offered bonuses to stay!

Ironically, Galen, who is considered the greatest physician in the history of Rome, was himself a Greek. Honored by the emperor for curing his "imperial fever," Galen became the medical celebrity of Rome. He was arrogant and a braggart and, unlike Hippocrates, reported only successful cases. Nevertheless, he was a remarkable physician. For Galen, diagnosis became a fine art; in addition to taking care of his own patients, he responded to requests for medical advice from the far reaches of the empire. He was so industrious that he wrote more than 300 books of anatomical observations, which included selected case histories, the drugs he prescribed, and his boasts. His version of human anatomy, however, was misleading because he objected to human dissection and drew his human analogies solely from the studies of animals. However, because he so dominated the medical scene and was later endorsed by the Roman Catholic Church, Galen actually inhibited medical inquiry. His medical views and writings became both the "bible" and "the law" for the pontiffs and pundits of the ensuing Dark Ages.

With the collapse of the Roman Empire, the Church became the repository of knowledge, particularly of all scholarship that had drifted through the centuries into the Mediterranean. This body of information, including medical knowledge, was literally scattered through the monasteries and dispersed among the many orders of the Church.

The teachings of the early Roman Catholic Church and the belief in divine mercy made inquiry into the causes of death unnecessary and even undesirable. Members of the Church regarded curing patients by rational methods as sinful interference with the will of God. The employment of drugs signified a lack of faith by the doctor and patient, and scientific medicine fell into disrepute. Therefore, for almost a thousand years, medical research stagnated. It was not until the Renaissance in the 1500s that any significant progress in the science of medicine occurred. Hippocrates had once taught that illness was not a punishment sent by the gods but a phenomenon of nature. Now, under the Church and a new God, the older views of the supernatural origins of disease were renewed and promulgated. Since disease implied demonic possession, monks and priests would treat the sick through prayer, the laying on of hands, exorcism, penances, and exhibition of holy relics—practices officially sanctioned by the Church.

Although deficient in medical knowledge, the Dark Ages were not entirely lacking in charity toward the sick poor. Christian physicians often treated the rich and poor alike, and the Church assumed responsibility for the sick. Furthermore, the evolution of the modern hospital actually began with the advent of Christianity and is considered one of the major contributions of monastic medicine. With the rise in 335 AD of Constantine I, the first of the Roman emperors to embrace Christianity, all pagan temples of healing were closed, and hospitals were established in every cathedral city. (The word *hospital* comes from the Latin *hospes,* meaning "host" or "guest." The same root has provided *hotel* and *hostel*.) These first hospitals were simply houses where weary travelers and the sick could find food, lodging, and nursing care. The Church ran these hospitals, and the attending monks and nuns practiced the art of healing.

As the Christian ethic of faith, humanitarianism, and charity spread throughout Europe and then to the Middle East during the Crusades, so did its "hospital system." However, trained "physicians" still practiced their trade primarily in the homes of their patients, and only the weary travelers, the destitute, and those considered hopeless cases found their way to hospitals. Conditions in these early hospitals varied widely. Although a few were well financed and well managed and treated their patients humanely, most were essentially custodial institutions to keep troublesome and infectious people away from the general public. In these establishments, crowding, filth, and high mortality among both patients and attendants were commonplace. Thus, the hospital was viewed as an institution to be feared and shunned.

The Renaissance and Reformation in the fifteenth and sixteenth centuries loosened the Church's stronghold on both the hospital and the conduct of medical practice. During the Renaissance, "true learning," the desire to pursue the true secrets of nature including medical knowledge, was again stimulated. The study of human anatomy was advanced, and the seeds for further studies were planted by the artists Michelangelo, Raphael Durer, and, of course, the genius Leonardo da Vinci. They viewed the human body as it really was, not simply as a text passage from Galen. The painters of the Renaissance depicted people in sickness and pain, sketched in great detail and, in the process, demonstrated amazing insight into the workings of the heart, lungs, brain, and muscle structure. They also attempted to portray the individual and to discover emotional as well as physical qualities. In this stimulating era, physicians began to approach their patients and the pursuit of medical knowledge in similar fashion. New medical schools, similar to the most famous of such institutions at

Salerno, Bologna, Montpelier, Padua, and Oxford, emerged. These medical training centers once again embraced the Hippocratic doctrine that the patient was human, disease was a natural process, and commonsense therapies were appropriate in assisting the body to conquer its disease.

During the Renaissance, fundamentals received closer examination, and the age of measurement began. In 1592, when Galileo visited Padua, Italy, he lectured on mathematics to a large audience of medical students. His famous theories and inventions (the thermoscope and the pendulum, in addition to the telescopic lens) were expounded upon and demonstrated. Using these devices, one of his students, Sanctorius, made comparative studies of the human temperature and pulse. A future graduate of Padua, William Harvey, later applied Galileo's laws of motion and mechanics to the problem of blood circulation. This ability to measure the amount of blood moving through the arteries helped to determine the function of the heart.

Galileo encouraged the use of experimentation and exact measurement as scientific tools that could provide physicians with an effective check against reckless speculation. Quantification meant theories would be verified before being accepted. Individuals involved in medical research incorporated these new methods into their activities. Body temperature and pulse rate became measures that could be related to other symptoms to assist the physician in diagnosing specific illnesses or diseases. Concurrently, the development of the microscope amplified human vision, and an unknown world came into focus. Unfortunately, new scientific devices had little impact upon the average physician, who continued to blood-let and to disperse noxious ointments. Only in the universities did scientific groups band together to pool their instruments and their various talents.

In England, the medical profession found in Henry VIII a forceful and sympathetic patron. He assisted the doctors in their fight against malpractice and supported the establishment of the College of Physicians, the oldest purely medical institution in Europe. When he suppressed the monastery system in the early sixteenth century, church hospitals were taken over by the cities in which they were located. Consequently, a network of private, nonprofit, voluntary hospitals came into being. Doctors and medical students replaced the nursing sisters and monk physicians. Consequently, the professional nursing class became almost nonexistent in these public institutions. Only among the religious orders did "nursing" remain intact, further compounding the poor lot of patients confined within the walls of the public hospitals. These conditions were to continue until Florence Nightingale appeared on the scene years later.

Still another dramatic event was to occur. The demands made upon England's hospitals, especially the urban hospitals, became overwhelming as the population of these urban centers continued to expand. It was impossible for the facilities to accommodate the needs of so many. Therefore, during the seventeenth century two of the major urban hospitals in London—St. Bartholomew's and St. Thomas—initiated a policy of admitting and attending to only those patients who could possibly be cured. The incurables were left to meet their destiny in other institutions such as asylums, prisons, or almshouses.

Humanitarian and democratic movements occupied center stage primarily in France and the American colonies during the eighteenth century. The notion of equal rights finally began, and as urbanization spread, American society concerned itself with the welfare of many of its members. Medical men broadened the scope of their services to include the

"unfortunates" of society and helped to ease their suffering by advocating the power of reason and spearheading prison reform, child care, and the hospital movement. Ironically, as the hospital began to take up an active, curative role in medical care in the eighteenth century, the death rate among its patients did not decline but continued to be excessive. In 1788, for example, the death rate among the patients at the Hotel Dru in Paris, thought to be founded in the seventh century and the oldest hospital in existence today, was nearly 25 percent. These hospitals were lethal not only to patients but also to the attendants working in them, whose own death rate hovered between 6 and 12 percent per year.

Essentially the hospital remained a place to avoid. Under these circumstances, it is not surprising that the first American colonists postponed or delayed building hospitals. For example, the first hospital in America, the Pennsylvania Hospital, was not built until 1751, and the city of Boston took over two hundred years to erect its first hospital, the Massachusetts General, which opened its doors to the public in 1821.

A major advancement in the history of modern medicine came in the mid-nineteenth century with the development of the now well-known Germ Theory. Germ Theory simply states that infectious disease is caused by microorganisms living within the body. A popular example of early Germ Theory demonstration is that of John Snow and the Broad Street pump handle. When Cholera reached epidemic levels in the overcrowded Industrial Era streets of London, local physician John Snow was able to stop the spread of the disease with a street map. Snow plotted the cases of Cholera in the city, and he discovered an epicenter at a local water pump. By removing the handle, and thus access to the infected water supply, Snow illustrated Germ Theory and saved thousands of lives at the same time. French chemist Louis Pasteur is credited with developing the foundations of Germ Theory throughout the mid-nineteenth century.

Not until the nineteenth century could hospitals claim to benefit any significant number of patients. This era of progress was due primarily to the improved nursing practices fostered by Florence Nightingale (Figure 1.2) on her return to England from the Crimean War. She demonstrated that hospital deaths were caused more frequently by hospital conditions than by disease. During the latter part of the nineteenth century, she was at the height of her influence, and few new hospitals were built anywhere in the world without her advice. During the first half of the nineteenth century, Nightingale forced medical attention to focus once more on the care of the patient. Enthusiastically and philosophically, she expressed her views on nursing: "Nursing is putting us in the best possible condition for nature to restore and preserve health.... The art is that of nursing the sick. Please mark, not nursing sickness."

Although these efforts were significant, hospitals remained, until the twentieth century, institutions for the sick poor. In the 1870s, for example, when the plans for the projected Johns Hopkins Hospital were reviewed, it was considered quite appropriate to allocate 324 charity and 24 pay beds. Not only did the hospital population before the turn of the century represent a narrow portion of the socioeconomic spectrum, but it also represented only a limited number of the types of diseases prevalent in the overall population. In 1873, for example, roughly half of America's hospitals did not admit contagious diseases, and many others would not admit incurables. Furthermore, in this period, surgery admissions in general hospitals constituted only 5 percent, with trauma (injuries incurred by traumatic experience) making up a good portion of these cases.

FIGURE 1.2 A portrait of Florence Nightingale. *Courtesy of http://ginnger.topcities.com/cards/computer/nurses/765x525nightengale.gif.*

American hospitals a century ago were rather simple in that their organization required no special provisions for research or technology and demanded only cooking and washing facilities. In addition, since the attending and consulting physicians were normally unsalaried, and the nursing costs were quite modest, the great bulk of the hospital's normal operating expenses were for food, drugs, and utilities. Not until the twentieth century did "modern medicine" come of age in the United States. As we shall see, technology played a significant role in its evolution.

1.2 THE MODERN HEALTH CARE SYSTEM

Modern medical practice actually began at the turn of the twentieth century. Before 1900, medicine had little to offer the average citizen, since its resources were mainly physicians, their education, and their little black bags. At this time physicians were in short supply, but for different reasons than exist today. Costs were minimal, demand was small, and many of the services provided by the physician could also be obtained from experienced amateurs residing in the community. The individual's dwelling was the major site for treatment and recuperation, and relatives and neighbors constituted an able and willing nursing staff.

Midwives delivered babies, and those illnesses not cured by home remedies were left to run their fatal course. Only in the twentieth century did the tremendous explosion in scientific knowledge and technology lead to the development of the American health care system, with the hospital as its focal point and the specialist physician and nurse as its most visible operatives.

In the twentieth century, the advances made in the basic sciences (chemistry, physiology, pharmacology, and so on) began to occur much more rapidly. Discoveries in the physical sciences enabled medical researchers to take giant strides forward. For example, in 1903, William Einthoven devised the first electrocardiograph and measured the electrical changes that occurred during the beating of the heart (Figure 1.3). In the process, Einthoven initiated a new age for both cardiovascular medicine and electrical measurement techniques.

Of all the new discoveries that followed one another like intermediates in a chain reaction, the most significant for clinical medicine was the development of x-rays. When W. K. Roentgen described his "new kinds of rays," the human body was opened to medical inspection. Initially these x-rays were used in the diagnosis of bone fractures and dislocations. In the United States, x-ray machines brought this "modern technology" to most urban hospitals. In the process, separate departments of radiology were established, and the influence of their activities spread with almost every department of medicine (surgery, gynecology, and so forth) advancing with the aid of this new tool. By the 1930s, x-ray visualization

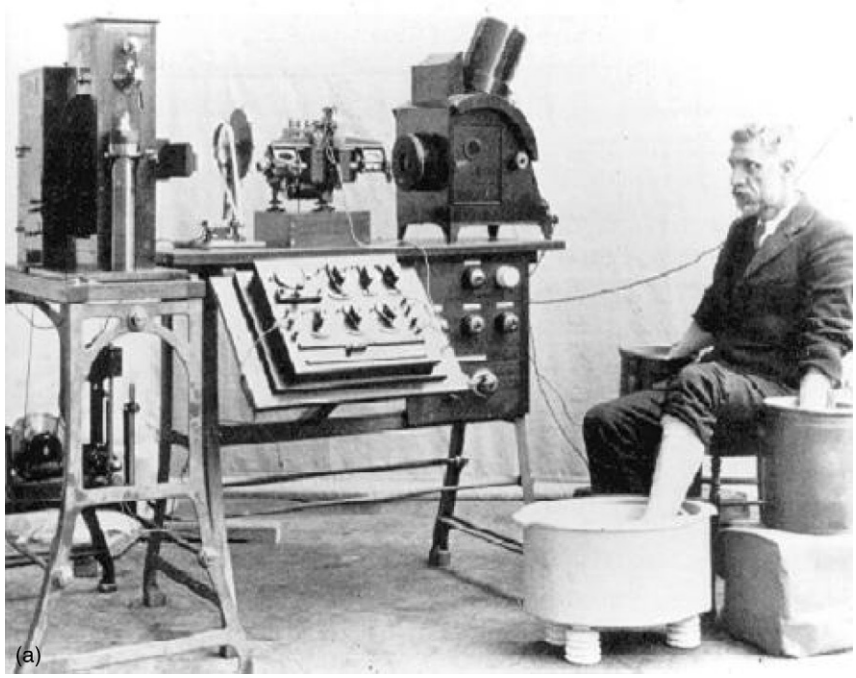

FIGURE 1.3 (a) An early electrocardiograph machine and

Continued

FIGURE 1.3, cont'd (b) a modern ECG setup. Computer technology and electronics advances have greatly simplified and strengthened the ECG as a diagnosis tool.

of practically all the organ systems of the body was possible by the use of barium salts and a wide variety of radiopaque materials.

The power this technological innovation gave physicians was enormous. The x-ray permitted them to diagnose a wide variety of diseases and injuries accurately. In addition, being within the hospital, it helped trigger the transformation of the hospital from a passive receptacle for the sick poor to an active curative institution for all the citizens of American society.

The introduction of sulfanilamide in the mid-1930s and penicillin in the early 1940s significantly reduced the main danger of hospitalization: cross-infection among patients. With these new drugs in their arsenals, surgeons were able to perform their operations without prohibitive morbidity and mortality due to infection. Also, despite major early-twentieth-century advancements in the field of hematology (including blood type differentiation and the use of sodium citrate to prevent clotting), blood banks were not fully developed until the 1930s, when technology provided adequate refrigeration. Until that time, "fresh" donors were bled, and the blood was transfused while it was still warm.

As technology in the United States blossomed, so did the prestige of American medicine. From 1900 to 1929, Nobel Prize winners in physiology or medicine came primarily from Europe, with no American among them. In the period 1930 to 1944, just before the end of World War II, 19 Americans were honored as Nobel Prize Laureates. During the postwar period (1945–1975), 102 American life scientists earned similar honors, and from 1975 to 2009, the number was 191. Thus, since 1930 a total of 312 American scientists, including some born abroad, have performed research that was significant enough to warrant the

distinction of a Nobel Prize. Most of these efforts were made possible by the technology that was available to these clinical scientists.

The employment of the available technology assisted in advancing the development of complex surgical procedures. The Drinker respirator was introduced in 1927, and the first heart-lung bypass was performed in 1939. In the 1940s, cardiac catheterization and angiography (the use of a cannula threaded through an arm vein and into the heart with the injection of radiopaque dye for the x-ray visualization of lung and heart vessels and valves) were developed. Accurate diagnoses of congenital and acquired heart disease (mainly valve disorders due to rheumatic fever) also became possible, and a new era of cardiac and vascular surgery began. The development and implementation of robotic surgery in the first decade of the twenty-first century have even further advanced the capabilities of modern surgeons. Neurosurgery, both peripheral and central, and vascular surgery have seen significant improvements and capabilities with this new technology (Figure 1.4).

Another child of this modern technology, the electron microscope, entered the medical scene in the 1950s and provided significant advances in visualizing relatively small cells. Body scanners using early PET (positron-emission tomography) technology to detect tumors arose from the same science that brought societies reluctantly into the atomic age. These "tumor detectives" used radioactive material and became commonplace in newly established departments of nuclear medicine in all hospitals.

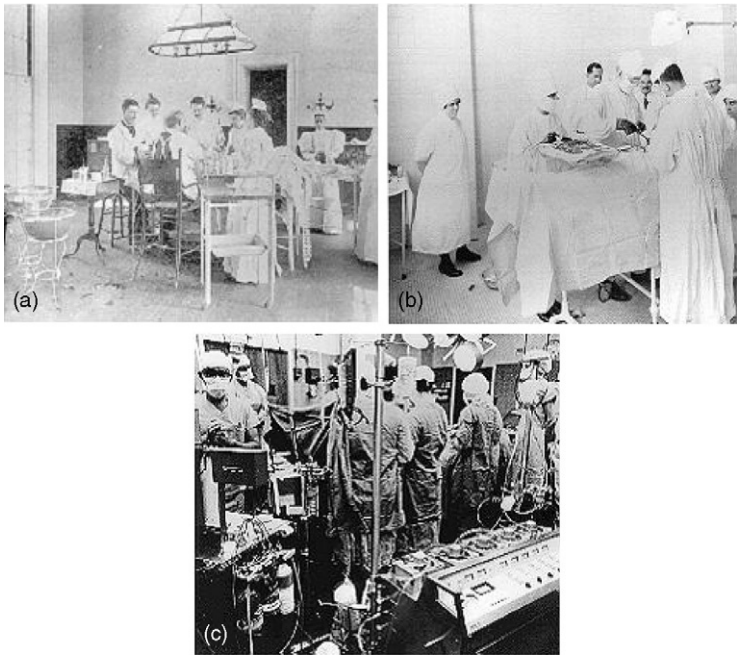

FIGURE 1.4 Changes in the operating room: (a) the surgical scene at the turn of the century, (b) the surgical scene in the late 1920s and early 1930s, and (c) the surgical scene today *From J. D. Bronzino,* Technology for Patient Care, *St. Louis: Mosby, 1977;* The Biomedical Engineering Handbook, *CRC Press, 1995; 2000; 2005.*

The impact of these discoveries and many others was profound. The health care system that consisted primarily of the "horse and buggy" physician was gone forever, replaced by the doctor backed by and centered around the hospital, as medicine began to change to accommodate the new technology.

Following World War II, the evolution of comprehensive care greatly accelerated. The advanced technology that had been developed in the pursuit of military objectives now became available for peaceful applications, with the medical profession benefiting greatly from this rapid surge of technological "finds." For instance, the realm of electronics came into prominence. The techniques for following enemy ships and planes, as well as providing aviators with information concerning altitude, air speed, and the like, were now used extensively in medicine to follow the subtle electrical behavior of the fundamental unit of the central nervous system—the neuron—or to monitor the beating heart of a patient.

The Second World War also brought a spark of innovation in the rehabilitation engineering and prosthetics fields. With advances in medical care technologies, more veterans were returning home alive—and disabled. This increase in need, combined with a surge in new materials development in the late 1940s, assisted the growth of assistive technologies during the post-WWII era.

Science and technology have leapfrogged past each other throughout recorded history. Anyone seeking a causal relation between the two was just as likely to find technology the cause and science the effect, with the converse also holding true. As gunnery led to ballistics and the steam engine transformed into thermodynamics, so did powered flight lead to aerodynamics. However, with the advent of electronics this causal relation has been reversed; scientific research is systematically exploited in the pursuit of technical advancement.

Just as World War II sparked an advancement in comprehensive care, the 1960s enjoyed a dramatic electronics revolution, compliments of the first lunar landing. What was considered science fiction in the 1930s and 1940s became reality. Devices continually changed to incorporate the latest innovations, which in many cases became outmoded in a very short period of time. Telemetry devices used to monitor the activity of a patient's heart freed both the physician and the patient from the wires that previously restricted them to the four walls of the hospital room. Computers, similar to those that controlled the flight plans of the *Apollo* capsules, now completely inundate our society.

Since the 1970s, medical researchers have put these electronic brains to work performing complex calculations, keeping records (via artificial intelligence), and even controlling the very instrumentation that sustains life. The development of new medical imaging techniques such as computerized tomography (CT) and magnetic resonance imaging (MRI) totally depended on a continually advancing computer technology. New imaging developments include functional MRI (Figure 1.5), a tool capable of illustrating active neural areas by quantifying oxygen consumption and blood flow in the brain. The citations and technological discoveries are so myriad that it is impossible to mention them all.

"Spare parts" surgery is now routine. With the first successful transplantation of a kidney in 1954, the concept of "artificial organs" gained acceptance and officially came into vogue in the medical arena (Figure 1.6). Technology to provide prosthetic devices, such as artificial heart valves and artificial blood vessels, developed. Even an artificial heart program to develop a replacement for a defective or diseased human heart began.

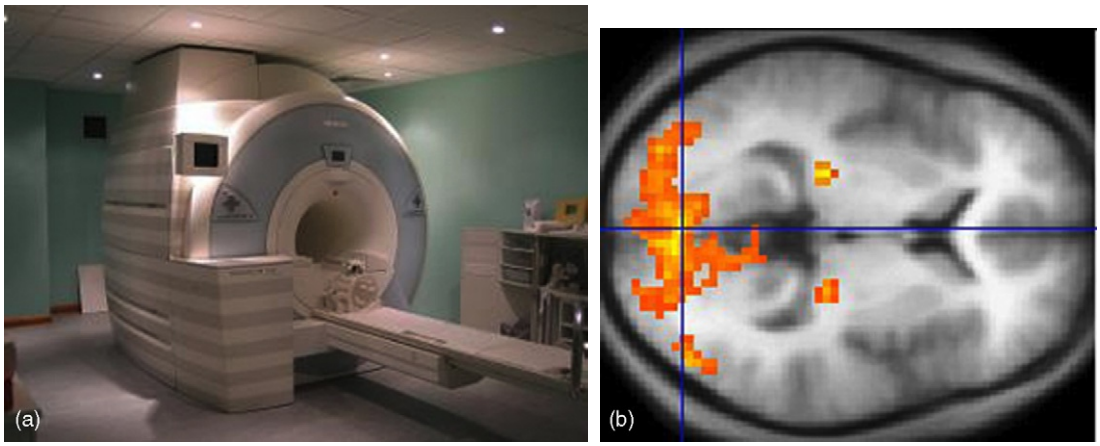

FIGURE 1.5 (a) A modern fMRI medical imaging facility and (b) an fMRI scan image. *http://neurophilosophy.wordpress.com*.

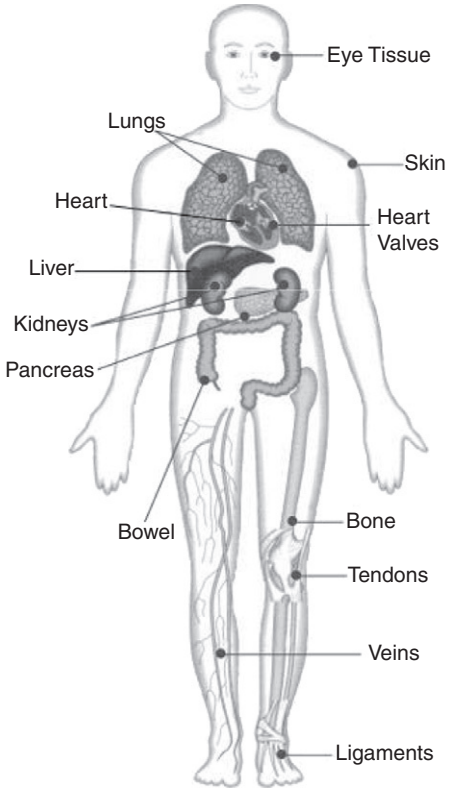

FIGURE 1.6 Transplantations performed today. *http://www.transplant.bc.ca/images/what_organs.gif*.

With the neural function, resilience, and incredible mechanical strength and endurance of the human heart, complete replacement prosthetics have been only marginally successful. Left ventricular assist devices (LVAD), however, have seen success as a replacement for the "workhorse" region of the heart and are a popular temporary option for those waiting on a full heart transplant. Future directions for heart failure solutions will most likely involve more tissue and cellular level treatments, as opposed to macromechanical systems. These technological innovations have vastly altered surgical organization and utilization, even further enhancing the radical evolution hospitals have undergone from the low-tech institutions of just 100 years ago to the modern advanced medical centers of tomorrow.

In recent years, technology has struck medicine like a thunderbolt. The Human Genome Project was perhaps the most prominent scientific and technological effort of the 1990s. Some of the engineering products vital to the effort included automatic sequencers, robotic liquid handling devices, and software for databasing and sequence assembly (See Figure 1.7). As a result, a major transition occurred, moving biomedical engineering to focus on the cellular and molecular level rather than solely on the organ system level. With the success of the "genome project," completed in 2003 after a 13-year venture, new vistas have been opened. Stem cell research highlights this chemical and molecular level focus and has been on the

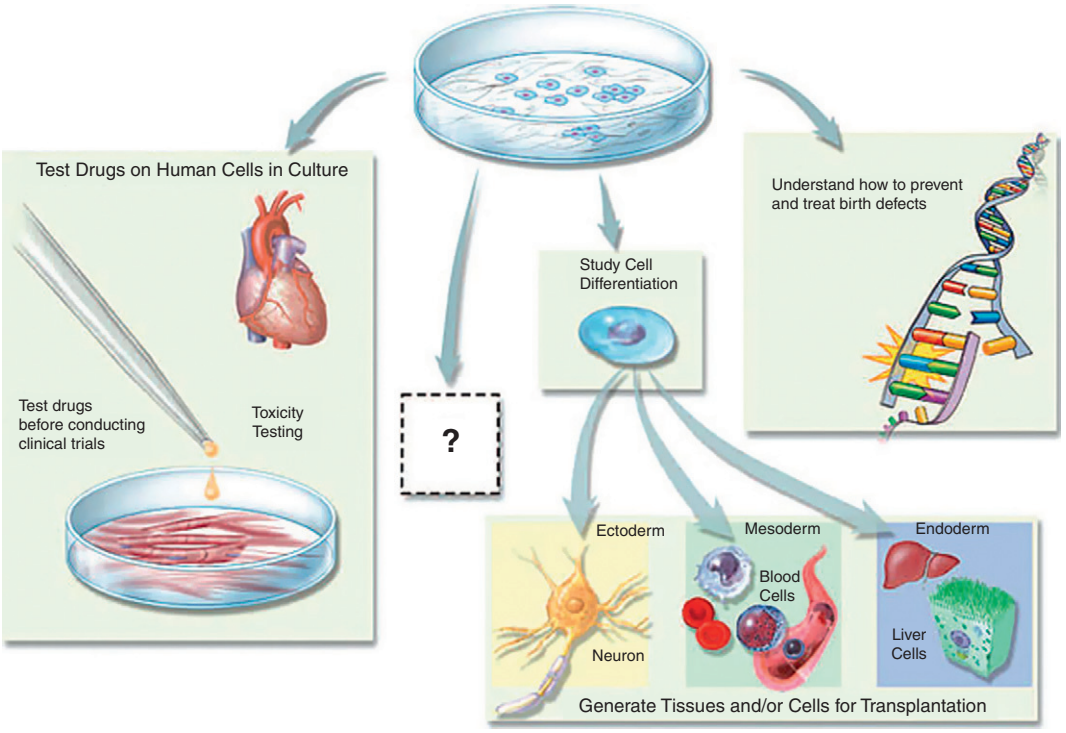

FIGURE 1.7 Stem cell research—potential applications made possible. *http://stemcells.nih.gov/info/media/promise.htm.*

FIGURE 1.8 Robotic surgery—a new tool in the arsenal of the physician. *http://library.thinkquest.org/03oct/00760/steve.jpg*.

forefront of controversial scientific research since its conception. While the multitudes of possibilities defy imagination, the moral issues accompanying stem cells have received equal attention in recent years.

Furthermore, advances in nanotechnology, tissue engineering, and artificial organs are clear indications that science fiction will continue to become reality. However, the social and economic consequences of this vast outpouring of information and innovation must be fully understood if this technology is to be exploited effectively and efficiently.

As one gazes into the crystal ball, technology offers great potential for affecting health care practices (Figure 1.8). It can provide health care for individuals in remote rural areas by means of closed-circuit television health clinics with complete communication links to a regional health center. Development of multiphasic screening systems can provide preventative medicine to the vast majority of our population and restrict hospital admissions to those requiring the diagnostic and treatment facilities housed there. With the creation of a central medical records system, anyone moving or becoming ill away from home can have records made available to the attending physician easily and rapidly. These are just a few of the possibilities that illustrate the potential of technology in creating the type of medical care system that will indeed be accessible, high quality, and reasonably priced for all. (For an extensive review of major events in the evolution of biomedical engineering, see Nebeker, 2002.)

1.3 WHAT IS BIOMEDICAL ENGINEERING?

Many of the problems confronting health professionals today are of extreme importance to the engineer because they involve the fundamental aspects of device and systems analysis, design, and practical application—all of which lie at the heart of processes that are fundamental to engineering practice. These medically relevant design problems can range

from very complex large-scale constructs, such as hospital information systems, to the creation of relatively small and "simple" devices, such as recording electrodes and transducers used to monitor the activity of specific physiological processes.

The American health care system, therefore, encompasses many problems that represent challenges to certain members of the engineering profession, called biomedical engineers. Since biomedical engineering involves applying the concepts, knowledge, and approaches of virtually all engineering disciplines (e.g., electrical, mechanical, and chemical engineering) to solve specific health care–related problems, the opportunities for interaction between engineers and health care professionals are many and varied.

Although what is included in the field of biomedical engineering is considered by many to be quite clear, many conflicting opinions concerning the field can be traced to disagreements about its definition. For example, consider the terms *biomedical engineering*, *bioengineering*, *biological engineering*, and *clinical* (or *medical*) *engineer*, which are defined in the *Bioengineering Education Directory*. While Pacela defined *bioengineering* as the broad umbrella term used to describe this entire field, bioengineering is usually defined as a basic-research-oriented activity closely related to biotechnology and genetic engineering—that is, the modification of animal or plant cells or parts of cells to improve plants or animals or to develop new microorganisms for beneficial ends. In the food industry, for example, this has meant the improvement of strains of yeast for fermentation. In agriculture, bioengineers may be concerned with the improvement of crop yields by treatment plants with organisms to reduce frost damage. It is clear that bioengineers for the future will have tremendous impact on the quality of human life. The full potential of this specialty is difficult to image. Typical pursuits include the following:

- The development of improved species of plants and animals for food production
- The invention of new medical diagnostic tests for diseases
- The production of synthetic vaccines from clone cells
- Bioenvironmental engineering to protect human, animal, and plant life from toxicants and pollutants
- The study of protein-surface interactions
- Modeling of the growth kinetics of yeast and hybridoma cells
- Research in immobilized enzyme technology
- The development of therapeutic proteins and monoclonal antibodies

The term *biomedical engineering* appears to have the most comprehensive meaning. Biomedical engineers apply electrical, chemical, optical, mechanical, and other engineering principles to understand, modify, or control biological (i.e., human and animal) systems. When a biomedical engineer works within a hospital or clinic, he or she is more properly called a *clinical engineer*. However, this theoretical distinction is not always observed in practice, since many professionals working within U.S. hospitals today continue to be called biomedical engineers.

The breadth of activity of biomedical engineers is significant. The field has moved significantly from being concerned primarily with the development of medical devices in the 1950s and 1960s to include a more wide-ranging set of activities. As shown in Figure 1.9, the field of biomedical engineering now includes many new career areas:

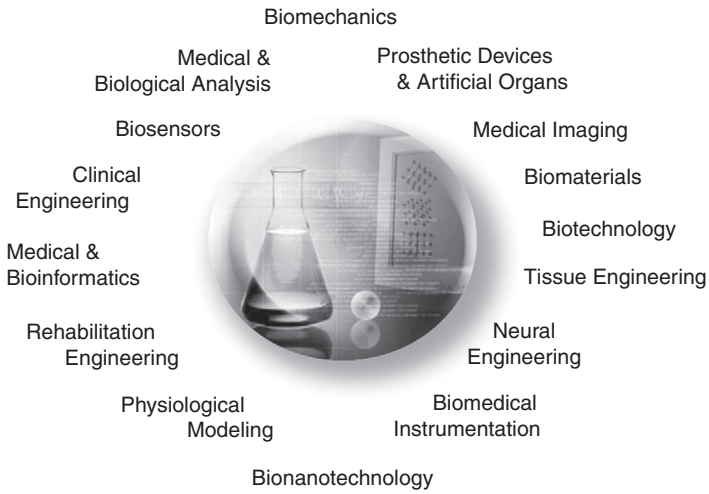

FIGURE 1.9 The world of biomedical engineering.

- Application of engineering system analysis (physiologic modeling, simulation, and control to biological problems)
- Detection, measurement, and monitoring of physiologic signals (i.e., biosensors and biomedical instrumentation)
- Diagnostic interpretation via signal-processing techniques of bioelectric data
- Therapeutic and rehabilitation procedures and devices (*rehabilitation engineering*)
- Devices for replacement or augmentation of bodily functions (*artificial organs*)
- Computer analysis of patient-related data and clinical decision making (i.e., medical informatics and artificial intelligence)
- Medical imaging—that is, the graphical display of anatomic detail or physiologic function
- The creation of new biologic products (i.e., biotechnology and tissue engineering)

Typical pursuits of biomedical engineers include the following:

- Research in new materials for implanted artificial organs
- Development of new diagnostic instruments for blood analysis
- Writing software for analysis of medical research data
- Analysis of medical device hazards for safety and efficacy
- Development of new diagnostic imaging systems
- Design of telemetry systems for patient monitoring
- Design of biomedical sensors
- Development of expert systems for diagnosis and treatment of diseases
- Design of closed-loop control systems for drug administration
- Modeling of the physiologic systems of the human body
- Design of instrumentation for sports medicine
- Development of new dental materials
- Design of communication aids for individuals with disabilities

- Study of pulmonary fluid dynamics
- Study of biomechanics of the human body
- Development of material to be used as replacement for human skin

The preceding list is not intended to be all-inclusive. Many other applications use the talents and skills of the biomedical engineer. In fact, the list of activities of biomedical engineers depends on the medical environment in which they work. This is especially true for the clinical engineers—biomedical engineers employed in hospitals or clinical settings. Clinical engineers are essentially responsible for all the high-technology instruments and systems used in hospitals today, the training of medical personnel in equipment safety, and the design, selection, and use of technology to deliver safe and effective health care.

Engineers were first encouraged to enter the clinical scene during the late 1960s in response to concerns about electrical safety of hospital patients. This safety scare reached its peak when consumer activists, most notably Ralph Nader, claimed, "At the very least, 1,200 Americans are electrocuted annually during routine diagnostic and therapeutic procedures in hospitals." This concern was based primarily on the supposition that catheterized patients with a low-resistance conducting pathway from outside the body into blood vessels near the heart could be electrocuted by voltage differences well below the normal level of sensation. Despite the lack of statistical evidence to substantiate these claims, this outcry served to raise the level of consciousness of health care professionals with respect to the safe use of medical devices.

In response to this concern, a new industry—hospital electrical safety—arose almost overnight. Organizations such as the National Fire Protection Association (NFPA) wrote standards addressing electrical safety specifically for hospitals. Electrical safety analyzer manufacturers and equipment safety consultants became eager to serve the needs of various hospitals that wanted to provide a "safety fix" and of some companies, particularly those specializing in power distribution systems (most notably isolation transformers). To alleviate these fears, the Joint Commission on the Accreditation of Healthcare Organizations (then known as the Joint Commission on Accreditation of Hospitals) turned to NFPA codes as the standard for electrical safety and further specified that hospitals must inspect all equipment used on or near a patient for electrical safety at least every six months. To meet this new requirement, hospital administrators considered a number of options, including (1) paying medical device manufacturers to perform these electrical safety inspections, (2) contracting for the services of shared-services organizations, or (3) providing these services with in-house staff. When faced with this decision, most large hospitals opted for in-house service and created whole departments to provide the technological support necessary to address these electrical safety concerns.

As a result, a new engineering discipline—clinical engineering—was born. Many hospitals established centralized clinical engineering departments. Once these departments were in place, however, it soon became obvious that electrical safety failures represented only a small part of the overall problem posed by the presence of medical equipment in the clinical environment. At the time, this equipment was neither totally understood nor properly maintained. Simple visual inspections often revealed broken knobs, frayed wires, and even evidence of liquid spills. Many devices did not perform in accordance with manufacturers'

specifications and were not maintained in accordance with manufacturers' recommendations. In short, electrical safety problems were only the tip of the iceberg. By the mid-1970s, complete performance inspections before and after equipment use became the norm, and sensible inspection procedures were developed. In the process, these clinical engineering pioneers began to play a more substantial role within the hospital. As new members of the hospital team, they did the following:

- Became actively involved in developing cost-effective approaches for using medical technology
- Provided hospital administrators with advice regarding the purchase of medical equipment based on their ability to meet specific technical specifications
- Started using modern scientific methods and working with standards-writing organizations
- Became involved in the training of health care personnel regarding the safe and efficient use of medical equipment

Then, during the 1970s and 1980s, a major expansion of clinical engineering occurred, primarily due to the following events:

- The Veterans Administration (VA), convinced that clinical engineers were vital to the overall operation of the VA hospital system, divided the country into biomedical engineering districts, with a chief biomedical engineer overseeing all engineering activities in the hospitals in that district.
- Throughout the United States, clinical engineering departments were established in most large medical centers and hospitals and in some smaller clinical facilities with at least three hundred beds.
- Health care professionals—physicians and nurses—needed assistance in utilizing existing technology and incorporating new innovations.
- Certification of clinical engineers became a reality to ensure the continued competence of practicing clinical engineers.

During the 1990s, the evaluation of clinical engineering as a profession continued with the establishment of the American College of Clinical Engineering (ACCE) and the Clinical Engineering Division within the International Federation of Medical and Biological Engineering (IFMBE). Clinical engineers today provide extensive engineering services for the clinical staff and serve as a significant resource for the entire hospital (Figure 1.10). Possessing in-depth knowledge regarding available in-house technological capabilities as well as the technical resources available from outside firms, the modern clinical engineer enables the hospital to make effective and efficient use of most if not all of its technological resources.

Biomedical engineering is thus an interdisciplinary branch of engineering heavily based in both engineering and the life sciences. It ranges from theoretical, nonexperimental undertakings to state-of-the-art applications. It can encompass research, development, implementation, and operation. Accordingly, like medical practice itself, it is unlikely that any single person can acquire expertise that encompasses the entire field. As a result, there has been an explosion of biomedical engineering specialties to cover this broad field. Yet, because of the interdisciplinary nature of this activity, there are considerable interplay and overlapping of interest and effort between them. For example, biomedical engineers engaged in the

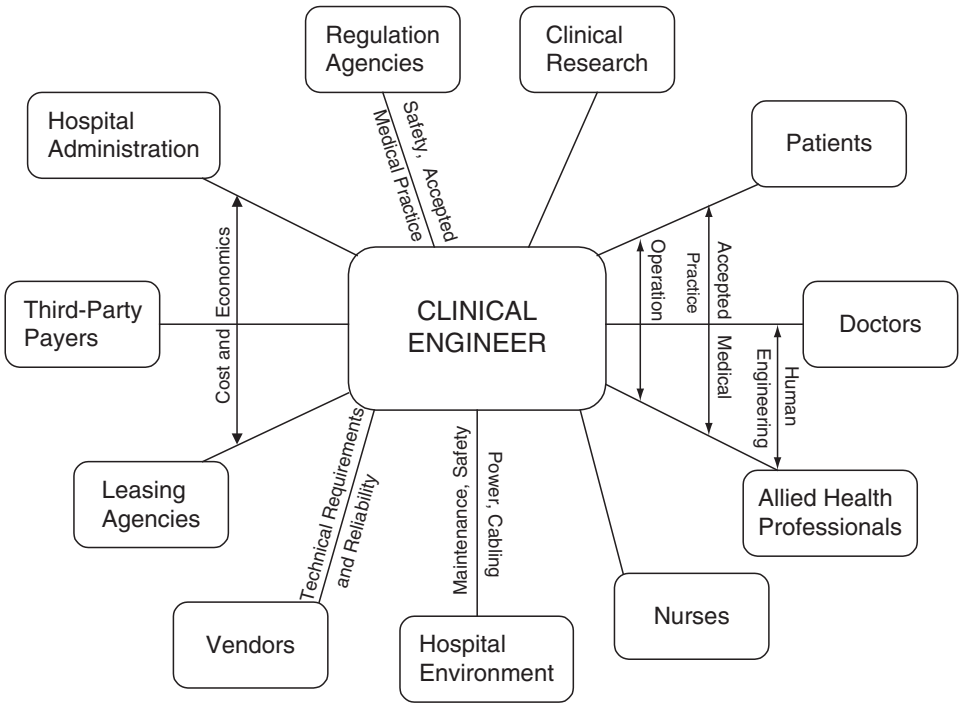

FIGURE 1.10 The range of interactions that a clinical engineer may be required to engage in a hospital setting.

development of biosensors may interact with those interested in prosthetic devices to develop a means to detect and use the same bioelectric signal to power a prosthetic device. Those engaged in automating the clinical chemistry laboratory may collaborate with those developing expert systems to assist clinicians in making clinical decisions based upon specific laboratory data. The possibilities are endless.

Perhaps an even greater benefit of the utilization of biomedical engineers lies in the potential for implementing existing technologies to identify and solve problems within our present health care system. Consequently, the field of biomedical engineering offers hope in the continuing battle to provide high-quality health care at a reasonable cost. If properly directed toward solving problems related to preventative medical approaches, ambulatory care services, and the like, biomedical engineers can provide the tools and techniques to make our health care system more effective and efficient.

1.4 ROLES PLAYED BY THE BIOMEDICAL ENGINEERS

In its broadest sense, biomedical engineering involves training essentially three types of individuals: the clinical engineer in health care, the biomedical design engineer for industry, and the research scientist. Presently, one might also distinguish among three specific roles these biomedical engineers can play. Each is different enough to merit a separate

description. The first type, the most common, might be called the "problem solver." This biomedical engineer (most likely the clinical engineer or biomedical design engineer) maintains the traditional service relationship with the life scientists who originate a problem that can be solved by applying the specific expertise of the engineer. For this problem-solving process to be efficient and successful, however, some knowledge of each other's language and a ready interchange of information must exist. Biomedical engineers must understand the biological situation to apply their judgment and contribute their knowledge toward the solution of the given problem, as well as to defend their methods in terms that the life scientist can understand. If they are unable to do these things, they do not merit the "biomedical" appellation.

The second type, which is less common, could be called the "technological entrepreneur" (most likely a biomedical design engineer in industry). This individual assumes that the gap between the technological education of the life scientist or physician and the present technological capability has become so great that the life scientist cannot pose a problem that will incorporate the application of existing technology. Therefore, technological entrepreneurs examine some portion of the biological or medical front and identify areas in which advanced technology might be advantageous. Thus, they pose their own problem and then proceed to provide the solution, at first conceptually and then in the form of hardware or software. Finally, these individuals must convince the medical community that they can provide a useful tool because, contrary to the situation in which problem solvers find themselves, the entrepreneur's activity is speculative at best and has no ready-made customer for the results. If the venture is successful, however, whether scientifically or commercially, then an advance has been made much earlier than it would have been through the conventional arrangement. Because of the nature of their work, technological entrepreneurs should have a great deal of engineering and medical knowledge as well as experience in numerous medical systems.

The third type of biomedical engineer—the "engineer-scientist" (most likely found in academic institutions and industrial research labs)—is primarily interested in applying engineering concepts and techniques to the investigation and exploration of biological processes. The most powerful tool at their disposal is the construction of an appropriate physical or mathematical model of the specific biological system under study. An example of this relationship can be found in the study of cardiac function. The engineer-scientist may be exploring the complexities of fluid flow through the incredible pump that is the human heart. Mathematical models may be created to model the kinematics of the heart during contraction and equations to define the behavior of fluid flow. Through simulation techniques and available computing machinery, they can use this model to understand features that are too complex for either analytical computation or intuitive recognition. In addition, this process of simulation facilitates the design of appropriate experiments that can be performed on the actual biological system. The results of these experiments can, in turn, be used to amend the model. Thus, increased understanding of a biological mechanism results from this iterative process.

This mathematical model can also predict the effect of these changes on a biological system in cases where the actual experiments may be tedious, very difficult, or dangerous. The researchers are thus rewarded with a better understanding of the biological system,

and the mathematical description forms a compact, precise language that is easily communicated to others. In the example of the cardiac researcher, the engineer must at all times consider the anatomical and physiological causes for the macro-model results—in this case, why the heart is pumping the way it is. The activities of the engineer-scientist inevitably involve instrument development because the exploitation of sophisticated measurement techniques is often necessary to perform the biological side of the experimental work. It is essential that engineer-scientists work in a biological environment, particularly when their work may ultimately have a clinical application. It is not enough to emphasize the niceties of mathematical analysis while losing the clinical relevance in the process. This biomedical engineer is a true partner of the biological scientist and has become an integral part of the research teams being formed in many institutes to develop techniques and experiments that will unfold the mysteries of the human organism. Each of these roles envisioned for the biomedical engineer requires a different attitude, as well as a specific degree of knowledge about the biological environment. However, each engineer must be a skilled professional with a significant expertise in engineering technology.

Therefore, in preparing new professionals to enter this field at these various levels, biomedical engineering educational programs are continually being challenged to develop curricula that will provide an adequate exposure to and knowledge about the environment, without sacrificing essential engineering skills. As we continue to move into a period characterized by a rapidly growing aging population, rising social and economic expectations, and a need for the development of more adequate techniques for the prevention, diagnosis, and treatment of disease, development and employment of biomedical engineers have become a necessity. This is true not only because they may provide an opportunity to increase our knowledge of living systems but also because they constitute promising vehicles for expediting the conversion of knowledge to effective action.

The ultimate role of the biomedical engineer, like that of the nurse and physician, is to serve society. This is a profession, not just a skilled technical service. To use this new breed effectively, health care practitioners and administrators should be aware of the needs for these new professionals and the roles for which they are being trained. The great potential, challenge, and promise in this endeavor offer not only significant technological benefits but humanitarian benefits as well.

1.5 RECENT ADVANCES IN BIOMEDICAL ENGINEERING

Biomedical engineering is a vast field with a multitude of concentrations and research initiatives. While the technicians affiliated with clinical engineering and a number of other concentrations focus mainly on preexisting technologies, researchers enjoy the exhilaration of innovating the new. Biomedical engineering has grown exponentially since its acceptance as a field less than a century ago, to the extent that today there is not a branch of medicine untouched by the problem-solving skill set of the engineer. The objective of this section is not to make the reader aware of every cutting-edge technology in development today but rather to provide an introduction to a sample of these new adventures.

1.5.1 Prosthetics

Prosthetics are one of the oldest innovations of biomedical engineering. The assistive technology field, prosthetics especially, became a true engineering discipline in itself in the period following World War II, when an unprecedented number of veterans returned home alive, but disabled, due to advances in medicine.

Prosthetics are defined as any "internal or external device(s) that *replace* lost parts or functions of the neuroskeletomotor system" and may be either orthopedic or externally controlled. Externally controlled devices may be powered by the body itself through myoelectricity or a separate power supply. Neural prosthetics represent the newest field in prosthetics and one of the fastest-developing topics in biomedical engineering today.

Orthopedic Prosthetics

In designing a "replacement" limb for the human body, an engineer is buried under an obscene amount of considerations and design constraints. The appendage must be functionally sufficient, a design unique to each individual, depending on the activities to be accomplished. It must be comfortable, aesthetically pleasing, convenient, and simple in attachment. Prosthetics and orthoses seeking to imitate the human body piece by piece tend to have a great amount of difficulty in development and implementation. Instead, the general application of the device should always be considered, with the user in mind. An example of this design strategy can be found in the flex foot, a prosthetic foot with no real resemblance to the natural appendage. Instead of struggling to recreate the biomechanics of the ankle, tarsals, metatarsals, and phalanges of the lower leg, designers created a prosthetic with a single contact piece, no joint, and consisting of only one material. The Cheetah Leg shown in Figure 1.11, is one type of such a prosthetic and has

FIGURE 1.11 Paralympic sprinter Oscar Pistorius with a prosthetic leg. Designing for overall function, as opposed to mirroring the human body, is often the more practical approach. *Compliments of http://www.thefinalsprint.com/images/2008/05/oscar-pistorius-double-amputee-sprinter.jpg.*

allowed paralympians like Oscar Pistorius to compete at a scale approaching that of able-bodied athletes. Actually, the Cheetah Leg allowed Pistorius, a double amputee, to compete at a level that became subject to controversy. In 2008, the South African sprinter battled courts for the opportunity to race with able-bodied athletes in the Beijing Olympic Games. While Pistorius ultimately did not qualify, his efforts fueled a debate as to whether his engineered prosthetics functioned better than a human leg, actually giving him an advantage over runners in the standard Olympic Games.

Externally controlled prosthetics use external motors to power their operation. The C-Leg is an example of such a device. This prosthetic leg has a microprocessor-controlled knee; has force sensors throughout for angle, swing, and velocity; and lasts 25 to 30 hours without charging. Uneven terrain is tackled with the C-Leg, as are changes in walking pace and direction. In recent years, sensor and minimally sized motor developments have made devices such as the C-Leg possible.

Neural Prosthetics

Neural prosthetics present one of the newest and perhaps most exciting concentrations of biomedical engineering. These devices may be powered by the human body—that is, they operate from electrical signals sent via electrodes from an external source to the peripheral muscle neuron—or they may be powered externally. These systems that use functional electrical stimulation (FES) to "restore sensory or motor function"are the definition of neural prostheses. These NPs have the potential to assist victims of spinal cord or cervical column injury (SCI and CI), restoring function to the muscle and lower extremities.

Stimulation via electrodes must reach a threshold frequency to achieve tetanization, or the smooth motion contraction of muscle. Stimulation below this frequency results in isolated twitches and muscle fatigue. Electrodes may be implanted transcutaneously (on the surface), percutaneously (stimulator outside the body connects to a stimulation point inside), or implanted.

As opposed to the leg, where a series of fairly simple joints and large motor units provide sufficient function, the upper extremities prove a significant challenge in fine-tuned control requirements. The incredible strength and flexibility of complex hand function are difficult to reproduce. The newest in prosthetic design hopes to overcome some of these challenges. The Luke Arm (Figure 1.12) is the brainchild of Segway inventor Dean Kamen. The arm has just as many degrees of freedom as the human arm and is capable of lifting above the user's head. The arm uses myoelectric signals originating from residual nerves in the upper body. Fine-tuned control is assisted by controls in the user's shoe; by activating different "pedals," the user can rotate the wrist or grasp or release an object. Sensory feedback, a constant issue with mechanical prosthetics, is provided via a pressure sensor on the fingertips, which feed back to a vibrating patch worn on the user's back. Increased pressure is felt by the user by changes in vibration intensity. Clinical trials are underway.

The design of prosthetics involves an intensive materials engineering background, as well as an in-depth understanding of kinematics modeling and physiology. The American Board for Certification in Orthotics, Prosthetics, and Pedorthics provides guidelines for certification as a licensed prosthetist. Those in the field are required to complete an accredited

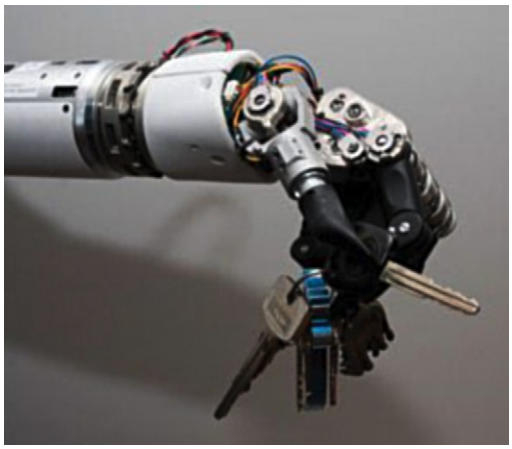

FIGURE 1.12 Dean Kamen's Luke Arm, the most advanced neural prosthetic to date, which uses myoelectric signals. Clinical trials are presently underway. *Courtesy of http://medgadget.com.*

undergraduate program in prosthetics or a graduate program specializing in the field with an appropriate undergraduate degree. Neural prosthetic development involves a team of members from various backgrounds, including biomechanics, electronics, and mathematical modeling.

While prosthetics provide a strong example of the evolution of assistive technology and present a number of interesting design innovations, in recent years the field of biomedical engineering has shifted from a focus on mechanical systems to biological and organic solutions. Whereas decades ago the primary objectives of the biomedical engineer consisted of device design, modern feats are more likely to involve biochemistry and gene therapy than screws, nuts, and bolts. Two prime examples of this shift in focus are tissue engineering and stem cell research.

1.5.2 Tissue Engineering

Tissue engineering, a relatively new field in biomedical engineering, consists of the manufacture of biological tissue either ex vivo or in vitro (outside the body), or the incorporation of new advancements to aid in the repair and growth of existing tissues in vivo (inside the body). In ex vivo applications, bioartificial tissues (those composed of both synthetic and natural materials) are used as an alternative to organ transplant or developed to study tissue behavior in vitro. Some important issues within the field include cell isolation, control of cell organization and function, upscaling to full bioartificial tissues, and biomaterial fabrication.

While the most well-known tissue engineering feats have been in epithelial tissues, clinical trials are also currently under way for reconstruction of cartilage, bone, neural, and liver tissues. Grafts are used for treatment of every type of skin damage, including burns, pressure sores, venous stasis ulcers, and diabetic ulcers. Polymeric tubes are implanted to assist in nerve regeneration due to central and peripheral nervous system damage or disorders.

Tissue engineering also covers joint replacements, including connective tissue recreation and bone grafts. Artificial heart valves implement bovine and porcine tissues along with bioartificial substances. Organ failure is treated with innovations in the field as well, with treatment for everything from liver cancer to breast reconstruction. Blood transfusions and dental surgery advancements are just two more examples of the wide range of applications of tissue engineering technologies.

Bone marrow transplantation works to regenerate the most prolific organ of the body. Marrow is responsible for the production of blood cells and is often damaged by myeloablative treatment regimens, such as chemotherapy and radiation. Modern methods involve harvesting patient samples of marrow prior to the therapy regimen and reinjecting them following treatment. The body regenerates its marrow supply, causing a temporary immunodeficiency.

In the case of pancreatic and liver tissue development, a bioreactor model is used. Bioreactors are systems consisting of a large number of cells that take in an input of reactants and output a set of products. Bioreactors have also been implemented for blood cell production from hematopoietic tissue. The two types of bioreactor systems are hollow fiber and microcarrier-based systems. In the hollow fiber system, a large number of small-diameter, hollow tubes are bundled together by a larger shell tube. The small tubes are injected with organ-specific cells that are suspended in a collagen-based matrix. The matrix will contract, leaving space within the small tubes. The patient's own blood or plasma is injected into the larger, encompassing tube and is allowed to nourish the hepatopoietic cells by flowing through the newly emptied space in the smaller tubes. In microcarrier-based systems, small beads (less than 500 μm) with surfaces specially treated for cell attachment are either positioned in a packed or fluidized bed or incorporated in hollow fiber cartridges. In the packed bed method, a column is filled with the beads and capped at each end with porous plates to allow perfusion. Success rates rely on fluid flow rate through the column, as well as the density of packed beads and dimension ratios of the column.

Biomaterials play a significant role in tissue engineering. In each of the previous examples, biomaterials prove an integral component of tissue regeneration and reconstruction. From the obvious application of artificial valve design to the less apparent role of injection needle design in bone marrow transplantation, biomaterial development is a necessary step in the advancement of tissue engineering. Devices must provide mechanical support, prevent undesirable tissue interactions, and potentially allow for timely biodegradation. Biomaterial devices can be broken down into two types, each existing on a scale as small as a few hundred microns. Immunoprotective devices contain semipermeable membranes that prevent specific host immune system elements from entering the device. Open devices, in contrast, are designed for systems to be fully integrated with the host and have large pores (greater than 10 μm), allowing for free transport of cells and molecules.

Pore sizes within a biomaterial directly correlate to the functions of the device. The structure of a pore is determined by the continuity of individual pores in the device, as well as the size and size distribution. The three classifications of porous materials are microporous, mesoporous, and macroporous. Microporous materials have pores with a diameter less than 2 nm and allow for transport of small molecules, including gases. Mesoporous materials allow for transport of small proteins and have pores with diameters ranging from 2 to 50 nm. Macroporous materials have pores with diameters greater than 50 nm and allow

for large proteins, and possibly even cells, to pass through. Fibrovascular tissue will pass through any material with pores greater than 10 nm. Pore size and distribution are rarely regular, and abnormalities will both change general material properties as well as fluid flow rate across the device.

A major focus in tissue engineering is controlling cell organization and regeneration. The more control the researcher has over cell development, the greater the capabilities and the wider the range of applications of the bioartificial tissue. Stem cells provide an opportunity for researchers to develop tissues essentially from scratch. Stem cells both build and maintain cells in vivo and possess the ability to be used for tissue generation ex vivo. Some background information on this new technology is provided following, and specific applications to tissue engineering are available in later chapters.

1.5.3 Stem Cell Research

In recent years, stem cells have become the topic of both intense controversy and incredible excitement within the research community. The potential for stem cell technology is apparently limitless, with some known possibilities shown in Figure 1.7. Cells may be used to test drugs on different types of tissues, to understand how to prevent birth defects, and to potentially replace and regenerate damaged tissue in the body. The possibilities truly seem endless.

In actuality there are two different types of stem cells. *Embryonic stem cells* come from embryos, which are mostly supplied by in vitro fertilization clinics four to five days following fertilization. At this point, stem cells will either self-regenerate or commit and differentiate. *Self-renewal* or *regeneration* means that the stem cell will reproduce with no developmental commitment. Essentially, the stem cell remains a stem cell. *Differentiation* is the expression of tissue or cell-specific genes.

For the majority of tissues in the human body, cells will differentiate terminally. In some cases, however, dynamic operation is required, and, as such, a population of *adult stem cells* is maintained for regeneration purposes. The two most common types of adult stem cells are those of the hematopoietic system (blood renewal) and the intestinal epithelia. These cell types are similar in that they both occur in very large numbers and have short life spans. Stem cells are required to maintain this dynamic population.

Researchers control stem cell development and differentiation within cultures by a number of means. For embryonic stem cells, the difference between self-regeneration and differentitation, surprisingly enough, is the concentration of a single essential protein, or growth factor. Leukemia inhibitory factor (LIF), in high enough concentrations, will cause embryonic stem cells to regenerate indefinitely in cultures. This is an interesting fact, because it proves that stem cell development is not an intrinsic predetermined state but rather is induced by extrinsic factors.

With an executive order in 2009, President Barack Obama lifted an eight-and-a-half-year ban on government-funded stem cell research, earning praise from the science community for opening the door to potential cures for some of mankind's most debilitating diseases. Both tissue engineering and stem cell research represent just a sampling of the breakthrough biologically focused ventures currently being explored by today's biomedical engineers.

1.6 PROFESSIONAL STATUS OF BIOMEDICAL ENGINEERING

Biomedical engineers are *professionals,* which are defined as an aggregate of people finding identity in sharing values and skills absorbed during a common course of intensive training. Whether individuals are professionals is determined by examining whether they have internalized certain given professional values. Furthermore, a professional is someone who has internalized professional values and is licensed on the basis of his or her technical competence. Professionals generally accept scientific standards in their work, restrict their work activities to areas in which they are technically competent, avoid emotional involvement, cultivate objectivity in their work, and put their clients' interests before their own.

The concept of a profession that is involved in the design, development, and management of medical technology encompasses three primary occupational models: science, business, and profession. Consider initially the contrast between science and profession. *Science* is seen as the pursuit of knowledge, its value hinging on providing evidence and communicating with colleagues. *Profession*, on the other hand, is viewed as providing a service to clients who have problems they cannot handle themselves. Scientists and professionals have in common the exercise of some knowledge, skill, or expertise. However, while scientists practice their skills and report their results to knowledgeable colleagues, professionals, such as lawyers, physicians, and engineers, serve lay clients. To protect both the professional and the client from the consequences of the layperson's lack of knowledge, the practice of the profession is often regulated through such formal institutions as state licensing. Both professionals and scientists must persuade their clients to accept their findings. Professionals endorse and follow a specific code of ethics to serve society. On the other hand, scientists move their colleagues to accept their findings through persuasion.

Consider, for example, the medical profession. Its members are trained in caring for the sick, with the primary goal of healing them. These professionals not only have a responsibility for the creation, development, and implementation of that tradition, but they are also expected to provide a service to the public, within limits, without regard to self-interest. To ensure proper service, the profession closely monitors the licensing and certification process. Thus, medical professionals themselves may be regarded as a mechanism of social control. However, this does not mean that other facets of society are not involved in exercising oversight and control of physicians in their practice of medicine.

A final attribute of professionals is that of integrity. Physicians tend to be both permissive and supportive in relationships with patients and yet are often confronted with moral dilemmas involving the desires of their patients and social interest. For example, how to honor the wishes of terminally ill patients while not facilitating the patients' deaths is a moral question that health professionals are forced to confront. A detailed discussion of the moral issues posed by medical technology is presented in Chapter 2.

One can determine the status of professionalization by noting the occurrence of six crucial events: the first training school, the first university school, the first local professional association, the first national professional association, the first state license law, and the first formal code of ethics. The early appearances of the training school and the university affiliation underscore the importance of the cultivation of a knowledge base. The strategic innovative role of the universities and early teachers lies in linking knowledge to practice and creating

a rationale for exclusive jurisdiction. Those practitioners pushing for prescribed training then form a professional association. The association defines the tasks of the profession: raising the quality of recruits; redefining their function to permit the use of less technically skilled people to perform the more routine, less involved tasks; and managing internal and external conflicts. In the process, internal conflict may arise between those committed to previously established procedures and newcomers committed to change and innovation. At this stage, some form of professional regulation, such as licensing or certification, surfaces because of a belief that it will ensure minimum standards for the profession, enhance status, and protect the layperson in the process.

The last area of professional development is the establishment of a formal code of ethics, which usually includes rules to exclude the unqualified and unscrupulous practitioners, rules to reduce internal competition, and rules to protect clients and emphasize the ideal service to society. A code of ethics usually comes at the end of the professionalization process.

In biomedical engineering, all six critical steps have been clearly taken. The field of biomedical engineering, which originated as a professional group interested primarily in medical electronics in the late 1950s, has grown from a few scattered individuals to a very well-established organization. There are approximately 48 international societies throughout the world serving an increasingly expanding community of biomedical engineers. Today, the scope of biomedical engineering is enormously diverse. Over the years, many new disciplines such as tissue engineering, artificial intelligence, and so on, which were once considered alien to the field, are now an integral part of the profession.

Professional societies play a major role in bringing together members of this diverse community to share their knowledge and experience in pursuit of new technological applications that will improve the health and quality of life. Intersocietal cooperation and collaborations, at both the national and international levels, are more actively fostered today through professional organizations such as the Biomedical Engineering Society (BMES), the American Institute for Medical and Biological Engineering (AIMBE), Engineering in Medicine and Biology Society (EMBS), and the Institute of Electrical and Electronic Engineers (IEEE).

1.7 PROFESSIONAL SOCIETIES

1.7.1 The American Institute for Medical and Biological Engineering

The United States has the largest biomedical engineering community in the world. Major professional organizations that address various cross sections of the field and serve biomedical engineering professionals include the American College of Clinical Engineering, the American Institute of Chemical Engineers, the American Medical Informatics Association, the American Society of Agricultural Engineers, the American Society for Artificial Internal Organs, the American Society of Mechanical Engineers, the Association for the Advancement of Medical Instrumentation, the Biomedical Engineering Society, the IEEE Engineering in Medicine and Biology Society, an interdisciplinary Association for the Advancement of

Rehabilitation and Assistive Technologies, and the Society for Biomaterials. In an effort to unify all the disparate components of the biomedical engineering community in the United States as represented by these various societies, the American Institute for Medical and Biological Engineering (AIMBE) was created in 1992. The primary goal of AIMBE is to serve as an umbrella organization in the United States for the purpose of unifying the bioengineering community, addressing public policy issues, and promoting the engineering approach in society's effort to enhance health and the quality of life through the judicious use of technology. (For information, contact AIMBE, 1701 K Street, Suite 510, Washington, DC, 20036; http://www.aimbe.org/; e-mail: aimbeoffice@gmail.com.)

1.7.2 IEEE Engineering in Medicine and Biology Society

The Institute of Electrical and Electronic Engineers (IEEE) is the largest international professional organization in the world and accommodates 37 different societies and councils under its umbrella structure. Of these 37, the Engineering in Medicine and Biology Society (EMBS) represents the foremost international organization, serving the needs of over 8,000 biomedical engineering members around the world. The major interest of the EMBS encompasses the application of concepts and methods from the physical and engineering sciences to biology and medicine. Each year, the society sponsors a major international conference while cosponsoring a number of theme-oriented regional conferences throughout the world. Premier publications consist of a monthly journal (*Transactions on Biomedical Engineering*), three quarterly journals (*Transactions on Neural Systems and Rehabilitation Engineering*, *Transactions on Information Technology in Biomedicine*, and *Transactions on Nanobioscience*), as well as a bimonthly magazine (*IEEE Engineering in Medicine and Biology Magazine*). Secondary publications, authored in collaboration with other societies, include *Transactions on Medical Imaging*, *Transactions on Neural Networks*, and *Transactions on Pattern Analysis and Machine Intelligence*. (For more information, contact the IEEE EMBS Executive Office, IEEE, 445 Hoes Lane, Piscataway, NJ, 08855-1331; http://www.embs.org/; e-mail: emb-exec@ieee.org.)

1.7.3 The Biomedical Engineering Society

Established in 1968, the Biomedical Engineering Society (BMES) was founded in order to address a need for a society that afforded equal status to representatives of both biomedical and engineering interests. With that in mind, the primary goal of the BMES, as stated in their Articles of Incorporation, is "to promote the increase of biomedical engineering knowledge and its utilization." Regular meetings are scheduled biannually in both the spring and fall. Additionally, special interest meetings are interspersed throughout the year and are promoted in conjunction with other biomedical engineering societies such as AIMBE and EMBS. The primary publications associated with the BMES include *Annals of Biomedical Engineering*, a monthly journal presenting original research in several biomedical fields; *BMES Bulletin*, a quarterly newsletter presenting a wider array of subject matter relating both to biomedical engineering as well as BMES news and events; and the *BMES Membership Directory*, an annual publication listing the contact information of the society's

individual constituents. (For more information, contact the BMES directly: BMES, 8401 Corporate Drive, Suite 140, Landover, MD 20785-2224; http://www.bmes.org/default.asp; e-mail: info@bmes.org.)

The activities of these biomedical engineering societies are critical to the continued advancement of the professional status of biomedical engineers. Therefore, all biomedical engineers, including students in the profession, are encouraged to become members of these societies and engage in the activities of true professionals.

1.8 EXERCISES

1. Select a specific "medical technology" from the historical periods indicated. Describe the fundamental principles of operation and discuss their impact on health care delivery: (a) 1900–1939; (b) 1945–1970; (c) 1970–1980; (d) 1980–2003.
2. Provide a review of the effect that computer technology has had on health care delivery, citing the computer application and the time frame of its implementation.
3. The term *genetic engineering* implies an engineering function. Is there one? Should this activity be included in the field of biomedical engineering?
4. Discuss in some detail the role the genome project has had and is anticipated having on the development of new medical technology.
5. Using your crystal ball, what advances in engineering and/or life science do you think will have the greatest impact on clinical care or biomedical research?
6. The organizational structure of a hospital involves three major groups: the Board of Trustees, the administrators, and the medical staff. Specify the major responsibilities of each. In what group should a Department of Clinical Engineering reside? Explain your answer.
7. Based on its definition, what attributes should a *clinical engineer* have?
8. List at least seven (7) specific activities of clinical engineers.
9. Provide modern examples (i.e., names of individuals and their activities) of the three major roles played by biomedical engineers: (a) the problem solver; (b) the technological entrepreneur; and (c) the engineer scientist.
10. Do the following groups fit the definition of a *profession*? Discuss how they do or do not. (a) registered nurse; (b) biomedical technician; (c) respiratory therapist; (d) hospital administrator.
11. List the areas of knowledge necessary to practice biomedical engineering. Identify where in the normal educational process one can acquire knowledge. How best can administrative skills be acquired?
12. Prosthetic limbs are often created for specialized activities, such as mountain biking or driving. Create a design for an upper- or lower-extremity prosthetic for a particular specialty activity.
13. What steps must be taken to become a licensed prosthetician?
14. What are the two means of powering a neural prosthetic?
15. What is the difference between an adult stem cell and an embryonic stem cell? Where does each come from?

16. While stem cell research has recently been granted federal funding, limitations on the types of research allowed are decided by the state. Research your home state's policies on stem cell research, and provide a summary paragraph.
17. Provide a copy of the home page for a biomedical engineering professional society and a list of its major activities for the coming year.
18. Research a biomedical engineering professional society and provide three benefits of joining the society.
19. What is your view regarding the role biomedical engineers will play in the health care system of tomorrow?
20. Discuss the trade-offs in health care that occur as a result of limited financial resources.
21. Discuss whether medical technology is an economic cost factor, a benefit, or both.

Suggested Readings

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