BIOMEDICAL ENGINEERING

Biomedical engineering is the collective term for the disciplines that bring the concepts and principles of engineering to the field of medicine. The integration of chemical, mechanical, electrical, and computer engineering fundamentals with biology and medical science has a relatively recent history that began in the mid-1900s. Technological and scientific advances in the twentieth century created the opportunity for biomedical engineering innovations, such as physiological simulation and modeling, designing of implants and drug delivery systems, and development of instrumentation and diagnostic tools.

The emergence of biomedical engineering followed the movement of primary medical care from the home to the hospital in the 1930s and 1940s. Until this time, hospitals were used mainly for care of the poor. Home care by physicians, midwives, and family was the predominant form of health care. The hospital, however, became the center of modern medical care after the discovery of X rays and antibiotics. By the 1930s, the use of barium salts and radio-opaque materials allowed X-ray visualization of practically all organ systems (1). Because of its cost, the improved diagnostic capability that radiation equipment provided was available only at hospitals. The advent of antibacterial agents and antibiotics, for example, sulfanilamide in the mid-1930s and penicillin in the early 1940s (1), helped prevent cross-infection among patients and staff, a previous deterrent to hospital care.

Electronic innovations developed for the military effort in World War II provided the basis for advances in medical electronics in the post-war era. These advances made it possible to measure low-level biosignals, which lead to a better understanding of electrical impulses and the central nervous system. The biologists who had been recruited for radar work during the war were prepared for these developments. However, the next generation of biologists was without this benefit, and now technology was advancing rapidly. The need for a bridge between the gap of technical knowledge and biology resulted in the emergence of the biomedical engineer (2).

The areas in which engineering blends with medicine are abundant and diverse. Biomedical engineers design imaging and diagnostic instrumentation, drug delivery systems, medical sensors, prostheses, rehabilitative devices, and artificial organs. They develop biocompatible materials, model physiological systems, or create patient information databases that assist in making clinical decisions. Some biomedical engineers work in hospitals where they design clinical systems and procedures and others work as consultants in the field of rehabilitation engineering to help restore mobility and other functions for disabled individuals. In recent years, some biomedical engineers have begun to work in the areas of genetic and tissue engineering. Some of the disciplines within biomedical engineering include the following (3):

- Biological effects of electromagnetic fields
- Biomaterials
- Biomechanics
- Biomedical instrumentation
- Biomedical sensors
- Biomedical signal analysis
- Biotechnology (including tissue engineering)
- Clinical engineering
- Medical imaging
- Medical informatics
- Physiological modeling, simulation, and control
- Prostheses and artificial organs
- Rehabilitation engineering

The challenges facing biomedical engineers do not necessarily fall solely into one category. For example, the design of an artificial heart involves knowledge of design requirements for the artificial organ and the appropriate biomaterials. Given the broad range of problems studied in biomedical engineering, it is rare for a single person to have expertise in all facets of the field.

BIOLOGICAL EFFECTS OF ELECTROMAGNETIC FIELDS

A biomedical engineer involved in the study of the biologic effects of electromagnetic fields studies a variety of diagnostic and therapeutic applications of electromagnetic fields and the adverse effects of such fields. The diagnostic uses of extremely low-frequency (ELF) magnetic fields include magnetic resonance imaging (MRI), which also uses a radiofrequency (RF) field, and neural stimulation by strong magnetic pulses. Bone and cartilage repair, soft-tissue healing, and nerve repair or regeneration are among the therapeutic applications under investigation for applications of low-frequency, pulsed electromagnetic fields (PEMF). There is considerable concern in today's society regarding the bioeffects of electromagnetic fields, but no deleterious effects have been shown to be associated with long-term exposure to low-level electromagnetic fields.

In cancer treatment, heat generated by radio-frequency energy (3 kHz to 300 GHz) or microwave energy (300 MHz to 300 GHz) kills radiation-resistant tumor cells. This therapeutic use of electromagnetic energy is termed hyperthermia. Another use of electromagnetic energy, called electroporation, involves the use of an electrical pulse to disrupt the membranes of cells. This is a common DNA transformation technique used in biotechnology. There is additional interest in electroporation that stems from its possible use in drug delivery systems.

BIOMATERIALS

Biomedical engineers working in this area are concerned with researching and designing safe and reliable synthetic materials that can intimately contact living systems and tissues. This contact makes it essential that these materials are physiologically acceptable and pharmacologically inert, that is, nontoxic and noncarcinogenic. Additional requirements include (1) adequate mechanical strength, (2) adequate fatigue life, (3) proper weight and density, and (4) usable in reproducible and cost effective large-scale fabrication (4). Examples of biomaterials range from replacement parts to sutures, diagnostic aids, and tooth fillings. The three main classes of biomaterials are metals, ceramics, and polymers.

Metallic Biomaterials

Metals in the body can corrode and possibly cause damage to an implant and harmful interactions with its corrosion products. Some metals, such at iron (Fe) and cobalt (Co), are required by the body for normal function but are still harmful if available in more than minute quantities. Implants consisting of stainless steels, cobalt-chromium (CoCr) alloys, and titanium (Ti) and titanium alloys are corrosion resistant and biocompatible. Stainless steels with molybdenum (Mo), types 316 and 316L, have increased salt-water corrosion resistance and are commonly found in temporary implants like fracture plates or screws. Type 316L, which differs from type 316 only in carbon content, is more widely recommended. Cobalt-chromium alloys are used in dentistry and artificial joints (castable CoCrMo) and in knee and hip prostheses (wrought CoNiCrMo). Titanium is a strong, lightweight metal that is ideal for implants. However, its poor shear strength precludes it from being used in bone screws and plates. Titanium-nickel alloys (TiNi) have the uncommon property of shape memory effect (SME). This is involved when, after deformation, a material returns to its previous shape when heat is applied. Attempts to take advantage of this property include research into intracranial aneurysm clips, contractile artificial muscles for an artificial heart, and orthopedic implants. There are other specialized uses for metals, such as platinum alloys for electrodes and tantalum for wire sutures. In dentistry, gold provides durable, corrosion-resistant fillings, and gold alloys are implemented in cast restorations, inlays, crowns, and cusps. Dental amalgam for cavities is a mixture of liquid mercury with silver, tin, copper, and zinc (5).

Ceramic Biomaterials

Ceramics are primarily inorganic, polycrystalline compounds, such as silicates and metal oxides. However, the covalently bonded forms of carbon, such as graphite and diamonds, are also considered ceramics. Improvements in ceramic formation in the late twentieth century have resulted in materials without the characteristic brittleness and low impact and tensile strengths that previously limited the use of ceramics. Ceramics are typically used in bone replacement and dental crowns. The three general classifications of ceramic biomaterials are (1) nonabsorbable, (2) bioactive or surface reactive, and (3) biodegradable or resorbable. Ceramics are also designated as relatively inert, semi-inert, and noninert.

Common nonabsorbable or relatively inert ceramics include alumina (Al_2O_3), zirconia (ZrO_2), and carbonaceous ceramics. Implant uses for nonabsorbable ceramics are generally for structural support, such as bone plates, bone screws, and femoral heads. This class of ceramics has also been used in ventilation tubes and in sterilization and drug delivery devices. Carbon ceramics are primarily for coating surfaces of devices that are used to repair diseased heart valves and blood vessels because of their high compatibility with tissue and blood.

Surface-reactive ceramics are primarily used to coat metal prostheses. When implanted, these ceramics actually form strong bonds with surrounding tissue. Dense, nonporous glass-ceramics, formed by controlled crystallization of glasses, fall into this category.

Resorbable or noninert ceramics are used to make both implants and drug delivery devices. The implants, predominantly variations of calcium phosphate, typically act as a substitute for bone. After implantation, resorbable ceramics degrade while endogenous tissue replaces it (6,7).

Polymeric Biomaterials

Various medical supplies, devices, and implants consist of polymers. The biocompatibility, ease of processing into diverse shapes, and the relatively low cost make polymers ideal biomaterials. Out of the multitude of polymers, only about twenty are used as biomaterials. Polyvinylchloride (PVC) tubing, sheets and films form IVs, catheters, cannulae, blood and solution bags, and surgical packaging. Pharmaceutical bottles, pouches and bags, and orthopedic implants are made from polyethylene (PE) of varying densities. Artificial vascular grafts, suture, and packaging of devices are among the medical uses of polypropylene (PP). Soft contact lenses, implantable ocular lenses, dentures, bone cement for joint prostheses fixation, blood pumps and reservoirs, membranes for blood dialyzers, and IV systems contain polymethylmethacrylate (PMMA). Sutures, including resorbable sutures, and artificial vascular graft applications involve polyesters. Nylon thread is a common surgical material. Other polymeric biomaterials include polystyrene (PS) and polystyrene copolymers; rubbers, such as silicone rubber; polyurethane; polyacetal; polysulfone; polycarbonate; and fluorocarbon polymers (primarily for coatings), such as Teflon® (7).

Composite Biomaterials

Materials consisting of two distinct phases or components are called composites. Various biological materials, such as bone and skin, are naturally occurring composite materials. Research and development in the field of biomaterials includes implants formed from composites. Composites offer a means to manipulate properties, such as strength-to-weight ratios and stiffness, in ways not possible with homogeneous materials.

The shape of the inclusion material of a composite can be classified in three ways: (1) particulate, (2) fiber, and (3) platelet or lamina. These consist of none, one, or two long dimensions, respectively. Polymeric biomaterials can contain particulates or fibers to improve stiffness. Examples include inclusion of bone particles or metal fibers in PMMA to improve the stiffness and fatigue life of bone cement and silica (SiO_2) particles in rubber to strengthen catheters and rubber gloves (8). Honeycombs and foams are composite materials and voids that are filled with either air or a liquid. Some porous composites have been used as a support for tissue growth.

BIOMECHANICS

Materials can be classified as either solids or fluids based on the response of the material to a constant force. A solid gives a discrete, finite time-independent response whereas a fluid responds with a continuous, time-independent response. Whether a material behaves as a solid or fluid has much to do with its thermodynamic state. At a given temperature and pressure, some materials, called viscoelastic, display both responses depending on the rate at which the force is applied. Biomechanics deals with determining the time and space characteristics of biological solids, fluids, and viscoelastic materials in response to imposed systems of internal and external forces (9).

The knowledge gained by mechanical analysis of biological materials has a significant impact on understanding the mechanisms of failure and requirements for replacement devices, such as prostheses and artificial organs. Biomechanics assists in designing orthopedic prosthetics by evaluating surface motion and lubrication of joints to provide information about joint wear, stability, and degeneration. Models have been developed which account for the viscoelastic behavior of weight-bearing long bone and assist in evaluating design specifications for lower limb prostheses. One active area of research involves accurately modeling porous bone to study the effects of aging, such as osteoporosis. Analysis of blood vessels has led to an understanding of vascular mechanics, which is useful when designing vascular grafts (10). This type of information is necessary for accurate modeling of physiological systems, for example, determining the forces generated by skeletal muscles (11) and those that act on muscles through tendons (12).

In addition to quantifying forces, biomechanics provides information about mechanisms of failure or injury needed to modify the environment of individuals. Head and neck injuries are studied to help in designing better support systems, for example air bags, that are important in the event of a car accident. Ergonomics is a field in which work conditions are analyzed to help determine methods for preventing back injuries or discomfort.

BIOMEDICAL INSTRUMENTATION

Biomedical instrumentation provides the necessary tools for measuring physiological variables and parameters (13–17). Great advances in biomedical instrumentation have resulted from developments in electronics and from the advent of the computer age. Biomedical instrumentation includes equipment that is used to diagnose disease in a patient, devices that are used to improve or maintain the health and well-being of a patient, and instruments that are used to continuously monitor the current physiological state of a patient. While developments in electronics have contributed much to the increased capabilities and sophistication of biomedical instrumentation, the proliferation of medical and nonmedical electronic devices has also contributed to radio frequency interference (RFI), which can affect the performance of some medical equipment.

The electrocardiograph (ECG), which first appeared in hospitals in 1910, measures the electrical activity of the heart (18). Devices that measure the electrical activity in other parts of the body also contribute to current diagnostic capabilities. In addition to the ECG, bioelectric phenomena that are measured for research and diagnostic purposes include electroencephalography (EEG), electromyography (EMG), electroretinography (ERG), and electrogastrography (EGG), which measure the electrical activity of brain, muscle, eye, and stomach, respectively. The measurement of propagated neural impulses that result from electrical stimulation is used to assess nerve damage.

Biomagnetic fields arise from the electrical activity of tissue. The magnetocardiogram (MCG), or magnetic measurement of the electric activity of the heart, has the highest amplitude of biomagnetic signals (50 pT) and was first detected in 1963 by Baule and McFee. The MCG, unlike the other lower amplitude biomagnetic signals, does not require a magnetically shielded room. Comparisons between the MCG and the ECG have revealed similar capabilities for diagnosing myocardial disorders with 50% improvement when combined as an electromagnetocardiogram (EMCG) (19). The ECG is still much more widely used than the MCG.

Other biomagnetic measurements, for example, the electrical activity of the brain which is called a magnetoencephalogram (MEG), are limited in location by the need for a room with magnetic shielding because of the very low amplitude of the signals. The development of the superconducting quantum interference device (SQUID) in 1970 made it possible to record these low biomagnetic signals with good signal quality. There are thought to be two advantages of MEG over the EEG: (1) the ability to measure smaller regions of the brain and (2) fundamental differences in the sensitivity distribution between the two methods.

Implantable pacemakers help patients who cannot maintain a steady heartbeat by supplying a controlled, rhythmic electric stimulus to the heart. This stimulus mimics the action of the sinoatrial node (SA node) of a healthy heart, the heart's natural pacemaker. With modern implantable pacemakers, clinicians use telemetry to program and monitor functions externally.

Ventricular fibrillation (VF) is a type of cardiac arrhythmia that is lethal. Death occurs in minutes during VF if the condition is not corrected. Because self-correction is rarely possible, defibrillation, typically by the application of an electrical shock to the heart, resets the heart to normal beating. Defibrillators are used externally, as in emergency rooms or ambulances, or are implanted into patients who are at constant risk of developing VF. Some commercial airlines are now equipped with automatic defibrillators that will trigger a shock if the device determines that the patient is having VF. These devices do not have to be operated by clinically trained personnel.

Bioelectric impedance analysis (BIA) of tissue provides information about the small pulsatile impedance changes that occur during heart and respiratory action. BIA is used to determine body characteristics (e.g., percent body fat) or to reconstruct tomographical images of the body (20,21) by measuring conductivity and permittivity at different frequencies.

BIOMEDICAL SENSORS

Biomedical sensors, or biosensors, convert biologically significant signals into electrical signals (13,15,17,18,22,23). These sensors have both diagnostic and therapeutic applications, and can be active or passive devices. Two major classes of biomedical sensors, which are based on the variable measured, are physical and chemical sensors. Bioanalytic sensors are a special class of chemical sensors that take advantage of biochemical binding reactions to identify complex biomolecules with high specificity and selectivity. One of the earliest and most clinically relevant biosensor applications was developed for measuring blood gases (O_2, CO_2) and pH. Measuring blood gases and pH continues to be an important use of biomedical sensors. Other aspects of blood chemistry, for example, glucose and lactate, can now be measured. Another method of classification, involving the method of application of the sensor, is divided into four categories: (1) noncontacting, (2) skin surface, (3) indwelling (minimally invasive), and (4) implantable. Indwelling and implantable devices involve carefully selecting inert biomaterials for the sensing interface and packaging. Implantable sensing devices need to maintain long-term calibration and function.

BIOMEDICAL SIGNAL ANALYSIS

Biomedical signals, signals that contain information about a biological system, often need processing so that the physiologically meaningful parts of the signal are extracted (24–30). Processing involves enhancement that reduces noise or transformation to obtain hidden information. Typical digital signal processing techniques include filtering, averaging, and spectral estimations. Signal enhancement to remove noise in frequency domain signals is achieved through optimal and adaptive filtering. Optimal filtering is for stationary signals whereas adaptive filtering adjusts to perform under changing circumstances. In general, adaptive filters are more appropriate for biomedical signals.

Sources of biomedical signals include (1) bioelectrical signals generated by nerve cells and muscle cells; (2) bioimpedance signals from the impedance of tissue; (3) bioacoustic signals from the flow of blood and air and sounds in the digestive tract, the joints, and contracting muscle; (4) biomagnetic signals from various organs, such as the brain and heart; (5) biomechanical signals resulting from mechanical function, such as motion, displacement, pressure, tension, and flow; (6) biochemical signals arising from chemical measurements; and (7) biooptical signals by both natural and induced optical functions.

For analysis, the main concern is the signal characteristics, not the origin of the signal. Therefore, another classification system involves identifying the signal as either continuous or discrete. Continuous signals are transformed into discrete signals by sampling. Additionally, biomedical signals are generally stochastic, which means they cannot be described exactly graphically or by an equation but rather in terms of probability.

BIOTECHNOLOGY

Biotechnology is not considered a discipline but rather a collection of procedures and techniques by which a scientist or engineer attempts to modify biological organisms for the benefit of humanity. These attempts include improving plants and animals for agricultural and food production, genetic engineering of organisms to produce therapeutic proteins, and biological fuel generation (31–36).

A predominant area of biotechnology is manipulating biological organisms to produce proteins, including industrial enzymes, therapeutic proteins, and animal feed supplements. These proteins are found naturally in the organism (e.g., bacterial amylases used in food production and biological detergents) or are introduced by gene transfer techniques (e.g., insulin production in bacteria). Therapeutic proteins produced through genetic engineering are termed recombinant therapeutic proteins. This comes from the term recombinant DNA, which means a combination, not possible in nature, of DNA from two organisms through genetic engineering. Examples of recombinant therapeutic proteins include insulin (with about 100 amino acids it is technically a polypeptide), the growth hormone somatostatin, and immunity-enhancing lymphokines.

Human Genome Project

The human genome project (HGP) represents an area of great possibilities for biotechnology in medicine (31,32,34,37). The term genome refers to the entire genetic material of an organism. Begun in 1990, the HGP will sequence the approximately 100,000 genes on the 22 homologous chromosomes and the two sex chromosomes of a human by the year 2005. The HGP has already begun to provide valuable information on single-gene defects (diseases caused by a mutation in a single gene) and to improve possibilities for gene therapy. Engineers have contributed to the HGP by developing equipment that can rapidly sequence large segments of DNA or produce large quantities of a single DNA strand.

Tissue Engineering

Tissue engineering is separated into two main categories: (1) in vitro and (2) in vivo. In vitro methods in tissue engineering involve the use of bioartificial tissues, which are hybrids of synthetic and living material. A typical use of in vitro tissue engineering is in organ replacement in lieu of an organ transplant. In vivo applications attempt to alter the growth and function of cells. A typical in vivo application would use implanted polymeric tubes to promote nerve regeneration by reconnecting damaged nerves in the peripheral nervous system (38). Generally mammalian cells need a support or attachment surface (substrate) to proliferate. Extracellular protein influences how cells interact with the surface and surrounding cells, especially cell adhesion. The seeding density of cells on these supports is a primary concern for the necessary interaction and communication between cells. Therefore, the three main determining factors in the ultimate morphology of the tissue are cell–substrate adhesion, cell–cell adhesion, and the rigidity of the substrate. Cultures can be seeded in a three-dimensional matrix, on single surfaces, or in a sandwich configuration. The seeding support is typically composed of collagen. Other considerations in tissue engineering involve types of cells selected (typically differentiated cells, such as hepatocytes and pancreatic islets cells), metabolic requirements for the cells (oxygen tends to be limiting), and control of tissue organization.

CLINICAL ENGINEERING

Biomedical engineers who work within hospitals or clinics are called *clinical engineers.* Clinical engineers support and maintain all biomedical instrumentation within the hospital and provide recommendations for and assessments of new instrumentation. This involves managing equipment inspections and preventive maintenance schedules, modifying or repairing instrumentation, and overseeing medical technician training on the safe and proper use of the equipment. Clinical engineers play a role in the design of medical instrumentation and new clinical or hospital facilities. Additionally, equipment inventory and computer support fall within the scope of clinical engineering (39).

MEDICAL IMAGING

Medical imaging provides vital information about a body's structures and functions. Examples of medical imaging modalities include X rays, magnetic resonance imaging (MRI), positron emission tomography (PET), single-photon emission computed tomography (SPECT), ultrasound, and computed tomography (CT). These areas have advanced rapidly with the computer age. However, challenges still exist to reduce the cost of common imaging equipment.

The discovery of X rays by Wilhelm Roentgen in 1895 provided the first technique for seeing inside the human body (40). The theory behind the images involves the exposure of the body to X rays which pass through to a detector or interact by being absorbed or scattered. When scattered, the X rays may still reach the detector and cause a loss in image quality. When there is not enough variation in the absorption of X rays between the area of interest and the surrounding tissues, contrast is provided by barium salts (strong X-ray absorbers). Radiopaque materials, such as iodine compounds, provide the contrast in X-ray angiography (serial radiographs of the circulatory system). Standard X-ray imaging is used to detect disease or injury in bones or other body structures, while mammograms are used to diagnose breast cancer (41,42). The X-ray tube for mammograms is different from the one used to detect changes in bony structures.

Computed tomography (CT), which was developed in the 1970s and is based on the same principles as X-rays, provided the first cross-sectional images of internal body structures (43). CT images are produced by reconstructing a large number of X-ray transmission measurements, called projection data, into tomographic maps of the X-ray linear attenuation coefficient. Now a standard procedure in most hospitals, practically all parts of the body are imaged by CT technology. One of the problems associated with both CT and X-ray imaging is that tissue damage can occur if single exposures or the accumulated life-time exposures to X rays exceed safe levels.

Magnetic resonance imaging (MRI) uses a strong magnetic field to align the weak nuclear moments of materials with atoms containing an odd number of protons or neutrons (e.g., ^{1}H, ^{13}C, and ^{31}P) (44,45). Typically, MRI images the protons (^{1}H) of water because the body is two-thirds water. However, it is not possible to directly measure the weak signals of the protons that are aligned with the strong applied magnetic field. Therefore, resonance techniques are employed to measure the collection of the nuclear moments, called spins. To distinguish the locations of spins, the magnetic field that is imposed in MRI has spatial variations. Primarily, MRI images provide diagnostic information. Recently, research efforts on blood flow and brain perfusions, termed functional magnetic resonance imaging (fMRI) have been aided by using MRI. In addition to diagnostic capabilities and research, an interest has developed in using MRI in image-guided surgical procedures. Future developments will include open MRI, real-time MRI, and continuous MRI during surgery.

A new form of microscopy, magnetic resonance microscopy, allows studying biological samples noninvasively and nondestructively, unlike electron and optical microscopy. This extension of magnetic resonance imaging provides three-dimensional images with spatial resolution better than 100 μm (46). Magnetic resonance microscopy is used in histologic studies, toxicologic studies, and developmental biology.

In nuclear medicine, the patient is given a small dose of radionuclide either intravenously or by rebreathing or ingestion. The low doses of radioactivity are safe for the patient and allow external imaging without interaction with the organ of interest. Single-photon emission computed tomography (SPECT) is the result of combining nuclear medicine and computed tomography. SPECT uses radioactive pharmaceuticals, which undergo differential distribution based on the type of tissue or organ, in lieu of the conventional X rays used in CT scans. SPECT is generally the primary imaging technique for the brain (47).

In positron emission tomography (PET), tracers are injected into the patient (48). These tracers are metabolically active biomolecules with positron-emitting isotopes, such as ^{11}C, ^{13}N, ^{15}O, and ^{18}F. An array of detectors captures simultaneous recordings of two photons that travel in opposite directions. These pairs of photons result from the annihilation of an electron and an emitted positron (positive electron) from the tracer. Because the annihilation event occurs along the line that connects the locations of the recorded pair of photons, the PET image is reconstructed from a collection of these recordings. The use of tracers makes PET a powerful research tool. Examples of its uses include the study of neurotransmitters, tumors, and Alzheimer's disease.

In ultrasonic imaging, high-frequency mechanical waves are reflected and scattered by the soft tissues of the body and the echoes of backscattering are captured and displayed as real-time moving images (49,50). Better resolution of images is achieved at higher frequencies. However, the depth of penetration decreases. Therefore, the choice of frequency depends on the application. Typical ultrasonic frequencies are 2 MHz to 5 MHz for deep penetration, 20 MHz to 50 MHz for shallow penetration with high resolution, and up to 200 MHz for examining subcellular structures with ultrasonic microscopy. Some ultrasound applications are based on transmission of the ultrasound waves rather than on backscattering. Advantages of ultrasonic imaging include lower cost of equipment, portability of equipment, minimal use of expendables, and the absence of harmful side effects.

Virtual reality is beginning to play a part in medicine that will only expand as advances are made in computing techniques and less expensive equipment becomes available. Virtual surgeries, used as a teaching aid in lieu of cadavers or animals and as a tool for practicing professionals to improve skills or preplan procedures, can improve performance in surgery by providing a risk-free method for training surgeons to deal with possible complications. Virtual reality can also play an important role in medical informatics, including telemedicine and telesurgery (remote surgery) (51).

MEDICAL INFORMATICS

Biomedical engineers working in medical informatics develop computer databases and networks that contain patient-related information (52–55). This information facilitates healthcare delivery and assists in clinical decision making. Two prime examples are the hospital information systems (HIS) and computer-based patient medical records (CBPMR). The HIS database encapsulates all of the information regarding patients, not just a limited departmental or clinical view. A modern HIS database includes (1) the entire clinical record of a patient, including all inpatient and outpatient procedures; (2) all patient charges and financial information; (3) admission, transfer, and release information (hospital bed control); (4) patient management (prescribed therapy) information; and (5) clinical decision making functions. The CBPMR is an electronic form of a patient's medical record that includes radiological and pathological images. It has advantages of accessibility and ease in information retrieval over the typical paper medical record. The CBPMR database supports clinical decision-making functions by assisting in patient treatment with suggestions for diagnosis and further testing and by providing therapeutic protocols and alerts for possible drug interactions. Confidentiality of patient information is protected by having different layers of access available to users with different privileges.

The technological advances in computers and telecommunications have brought about the field of telemedicine. The CBPMR contains the entire patient's record, including images, which can be transferred electronically to consulting physicians in distant locations. The benefit of telemedicine becomes apparent when considering patients in areas without major hospitals and medical universities who need the expertise of the medical profession to analyze digital images, such as magnetic resonance images. One area of concern involves the quality of digital representations, such as scanned X-rays.

PHYSIOLOGICAL MODELING, SIMULATION, AND CONTROL

Modeling attempts to find the most simplified method for accurately defining a system. Physiological modeling, or biomodeling, assists in (1) research by verifying hypotheses or indicating areas needing further study, (2) teaching and training in medical schools, and (3) clinical applications by aiding in such areas as diagnosis, determination of drug regimens, or design of biomedical devices, including prostheses or drug delivery systems (56). Typically, these models are continuous models and some use artificial intelligence and neural modeling.

Biomedical engineers who model physiological systems must have (1) an in-depth understanding of the physiology, anatomy, biochemistry and biophysics of the physiological system being modeled; (2) knowledge of instrumentation, methods of measurement, and sources of data for important parametric and system variables; (3) a background in applied mathematics, such as ordinary differential equations (ODEs), partial differential equations (PDEs), and statistics; and (4) experience with computer hardware and software, including differential equation solving and compiler languages (56).

Models of physiological systems need to consider transport phenomenon associated with the system under consideration.

Transport mechanisms in the body include momentum, mass, energy, and information transport. Momentum transport is considered when modeling blood flow. Mass transport deals with the flow of various substances, such as oxygen, carbon dioxide, and pharmaceuticals, that are carried in the blood, air, food and digestive juices, and urine, and with the diffusion of these substances into and out of air, blood, and tissues. Energy transport refers to the mechanisms the body uses to deal with heat energy. Energy transformation and transport need to be considered when models involve muscle tissue. The transmission of information through nerves or hormones is what is meant by information transport.

A typical modeling method for quantifying the kinetics of materials in the body via production, distribution, transport, utilization, or substrate–hormone control interactions involves compartmental analysis (57). One example of compartmental analysis is a model of the kinetics of a pharmaceutical in the blood stream. These models treat any part of the physiological system which can be considered homogeneous, as a compartment, and the system that is being modeled is segmented into a finite number of these compartments. The direction of flow of material between these compartments is determined and then modeled with differential equations. Unlike modeling, simulation attempts to reproduce the experimental data without trying to identify the mechanisms responsible for the experimental observations (58).

Closed-loop drug delivery (CLDD) systems represent a practical application of control (59). CLDD systems are used for therapeutic and diagnostic purposes. For example, an infusion pump administers a drug to the patient, the patient's response is sent to a monitor, and the monitor feeds the information to a controller which determines the next infusion rate for the patient and adjusts the pump accordingly. The control laws typically applied to CLDDs are proportional-integration-derivative (PID), adaptive, and fuzzy control. Adaptive is the most prevalent. In the clinical use of these systems, a supervisor is present to override control in case of unphysiological disturbances, such as a change in drug concentration.

PROSTHESES AND ARTIFICIAL ORGANS

A device that is an artificial substitute for a body part, whether it is a limb or a heart valve, is called a prosthesis. When the prosthesis replaces all or part of an organ, it is called an artificial organ. Though replacement of organs from donor transplants is a more straightforward and reliable method, the supply of donor organs and thus their use is limited. Artificial organs have been designed because they can be produced in sufficient quantities to meet demand and they eliminate the possibility of transferring infections, for example, HIV and hepatitis, from the donor to the recipient. When designing an artificial organ, function is of primary concern and can result in a device that bears little resemblance to its natural counterpart. Typically, artificial organs are made from synthetic materials not found in nature and use mechanisms different from those of the natural organ to achieve the same function. Disadvantages of artificial organs include the relative inability to adapt to growth, which limits their use in children, the mechanical and chemical wear due to use, and the body's environment, which can limit the life of the device. Recently the design of artificial organs has included combining biological material, such as organelles, cells, or tissues, with synthetic, engineered devices. These hybrids are called bioartificial organs (60).

Artificial hearts are primarily used as a "bridge-to-transplant," that is, a temporary replacement used until a donor organ donor is transplanted. Research continues in developing long-term, completely implanted heart replacements. The heart-lung machine is a short-term artificial organ used for patients undergoing transplant operations. It allows the patient to survive the removal of the heart until the replacement organ is surgically implanted. Common prostheses for the circulatory system are cardiac valve prostheses and vascular grafts. Concerns with these prosthetics include the formation of fibrous blood clots inside the circulatory system (thrombi), tissue overgrowth, hemorrhage from anticoagulants, and infection (61).

The artificial lung must provide a mechanism for the uptake of O_2 by the blood and the removal of CO_2. It can be used to completely replace the function of the lung temporarily during surgery or to assist with gas exchange temporarily until the lung can heal. Artificial lungs also replace or assist lung function permanently, if necessary. Typically, artificial lungs are not placed where the natural lung is located so the blood in the pulmonary system must be diverted to the artificial lung and pumped to return it to the heart and systemic circulation. Gas is commonly exchanged by using membrane oxygenators. Difficulties in design include developing membranes as thin as the walls of the alveoli and finding a blood distribution method that mimics the branching achieved in a short distance by the lung (62).

One kidney can sustain function for a lifetime which makes live kidney donation possible: however, donors are typically cadavers. The artificial kidney provides a common intermittent treatment for renal failure during diminishing function of the kidneys or for patients who are waiting for a donor kidney. Dialysis, the mechanism of the artificial kidney, performs the necessary functions of the kidneys. These involve regulating (1) the volume of the blood plasma (contributing significantly to the regulation of blood pressure), (2) the concentration of waste products in the blood, (3) the concentration of electrolytes (Na^+, K^+, HCO_3^-, and other ions) in the plasma, and (4) the pH of plasma (63). More aggressive dialysis of the peritoneum, the membrane surrounding the body cavity and covering some of the digestive organs, is a recently developed treatment for irreversible end-stage kidney failure (64).

The main concern with the loss of liver function is loss of the ability to detoxify the blood. Therefore, devices which augment liver function focus on methods of detoxification. Some procedures currently in practice or under investigation involve dialysis, filtration, absorbent materials, and immobilized enzymes to convert specific toxins to less harmful substances. Currently, temporary replacement of the liver involves systems with mammalian hepatocytes (liver parenchymal cells which remove most of the carbohydrates, amino acids, and fat from the digestive products absorbed from the intestines by the blood) attached to a synthetic support, where input from the host is separated from the device by a semipermeable membrane. Bioartificial livers using functional hepatocytes in a device immersed in body fluids are being investigated as an alternative to organ replacement (65).

Partial or complete removal of the pancreas can occur due to polycystic disease, trauma, or tumors. The replacement artificial pancreas focuses on the hormonal or endocrinal activity of the pancreas (i.e., insulin and glucagon secretion), which regulates the uptake and release of glucose. Devices have not yet been developed that can replace the exocrine function of the pancreas, namely, the secretion of proteolytic and lypolytic enzymes in the gastrointestinal tract. Other artificial organs for the digestive system include trachea replacements, electrical and pneumatic larynxes, which replace only the phonation function of the larynx because a complete artificial organ that restores respiration and protection of the lower airway during swallowing has yet to be designed, and extracorporeal and intraesophageal stents (66).

Skin replacement following loss from events, such as a fire or mechanical accident, or through conditions, such as skin ulcers, is achieved by using autographs of the patient's skin, allographs from cadavers, xenographs from animals, or artificial skin. The risk of viral infection and rejection are concerns when using allographs and xenographs. Artificial skin is a bilayer membrane whose top layer is a silicone film that controls moisture and prevents infection and whose bottom layer consists of a porous, degradable copolymer. The top layer is removed and replaced by an autograph after about two weeks, and the bottom layer is removed by complete degradation after it induces the synthesis of new dermis. Clinical studies have shown that autographs take better than artificial skin, but donor sites in which the top layer has artificial skin instead of silicone film heal faster and appear more like the patient's skin than donor sites that used autographs (67).

REHABILITATION ENGINEERING

A rehabilitation engineer designs and develops technologies that augment or replace impaired sensory, communication, or motor systems. A device that augments an impaired function is called an orthosis, and a replacement device is called a prosthesis. Rehabilitation engineering is concerned with restoring the ability to perform activities of daily living (ADL), such as (1) eating, brushing teeth, and reading; (2) public transportation and building accessibility; (3) personal mobility; (4) sensory disabilities, such as impaired sight or hearing; and (4) communications. In addition to the biology, physiology, and engineering involved in design, a rehabilitation engineer needs to consider the social, financial, and psychological impacts of a device or technology. One particular difficulty in rehabilitation engineering is the variation in retained ability and needs of patients. Even if a standard device exists, individual modifications are expected because of differences among patients (68).

Traditional orthoses for sensory impairments are eyeglasses or contacts and hearing aids. The retention of some function in the sensory system is required for these devices to work. If vision has been completely impaired through damage to the retina, optic nerve, or cerebral cortex, other methods for restoring ADL have been developed. An example of this is the development of Braille to allow the visually impaired to read. Advances in computing make scanning text and conversion into either voice or Braille (by the movement of a matrix of pins) available as other possible reading methods. Many deaf individuals use their vision and sign language as a substitute for speech. If deafness results from damage only to the cochlea, implants are available which do not usually completely restore hearing but give the ability to sense environmental sounds. Advances in computing with translation aids that are marketed to travelers could assist the deaf by capturing and displaying spoken phrases in a language known to the individual.

The wheelchair provides a primary replacement for loss of motor skills in the lower body. Although wheelchairs provide great mobility, they also require special access, such as ramps and elevators in lieu of stairs, and terrain amenable to rolling. Increased mobility has resulted from development of hand controls for most major methods of transportation (cars, vans, airplanes, etc.). Artificial limbs commonly replace lost limbs. The design of these orthopedic prostheses involves selecting materials that provide weight and strength similar to those of the limb that is being replaced along with a slow yielding mode of failure, determining the method of attachment to the body for stability and appropriate load distribution, including the appropriate mobility or motion for the limb, and making it cosmetically acceptable to the recipient. A prime example of an orthopedic orthotic is the brace for such areas as the neck, limbs, and feet. The use of external power and control has led to improvements in orthotics and prosthetics by restoring hand functions and providing active limbs which assist in ease and speed of locomotion.

Communication disorders that result from damage to the larynx are currently relieved only through the use of an external artificial larynx or through a device which converts typing to speech. An implantable artificial larynx was recently used to restore speech to a man who had lost his larynx due to injury. For individuals with impaired motor skills, words and concepts can be communicated through the use of symbol or letter boards. There is active research to determine if information may be obtained from the speech of individuals who produce sound that is difficult to understand.

CONCLUSION

A very brief overview of many of the areas that are currently important in biomedical engineering has been presented. However, this is a very diverse field that is constantly expanding. Future developments will occur in nanofabrication, microelectromechanical (MEM) technology, sensory replacements (e.g., the artificial retina), engineered tissues, molecular electronics, low-cost medical devices that will help improve health care without increasing health care costs, and other emerging areas.

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