1

Concepts of Biomedical Engineering

1.1 Introduction

Biomaterials technology is one newly emerging biomedical form to create new device and induce the regeneration of detective and injured body tissues and organs as well as to substitute the biological functions of damaged organs. To this end, the cells of high proliferation and differentiation potentials are being combined with some cell scaffolds and biological signals of growth factor and gene. Since there are some cases in which cells are genetically innovated to produce the growth factors inducible angiogenesis and tissue regeneration, the technology of gene delivery is also necessary for tissue engineering. Current developments in the technological fields of biomedical and tissue engineering, bioengineering, biomechanics, microfabrication, and microfluidics have led to highly complex and pertinent new tools for *in vitro* and *in vivo* applications. The purpose of biomaterials technology is to mimic organ tissues *in vitro* in order to partially reduce the amount of *in vivo* testing. These types of systems can enhance functionality of cells by mimicking the tissue architecture complexities when compared to *in vitro* analysis and at the same time present a more rapid and simple process when compared to *in vivo* testing procedures. The development of new technology for analysis of engineered tissues can be achieved through the combination of these research domains. Combining these advanced research domains, we then present a new area of technology that allows analysis *in vitro* on engineered tissues. An extension of the biomaterials technology has also allowed tissue and organ development, which can be considered as a first step toward the replacement of animal testing using a combined organ model.

1.2 Frontiers in Biomedical Engineering

Nowadays, pharmaceutical technology and research for new drugs and formulations is of great importance, as scientists attempt to discover even more revolutionary and efficient methods to treat various diseases. At the same time the correct dosing and the side targeting are equally important for clinical success. Research in sustained drug-release systems is very promising toward such direction, while it offers advantages and potential rewards contrary to the traditional therapy. The

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drug plasma concentrations remain inside the therapeutic range for a longer time period compared to the conventional formulations. In addition, sustained-release formulations may increase the likelihood for the patient to respond to therapy, since drug formulations are generally characterized as once-daily given dose. The rate at which a drug is released from a sustained-release formulation depends on many factors, while excipients play the most important role. Most of sustained-release formulations are based on biodegradable polymers in the form of a drug-encapsulating matrix or membrane. Examples range from monolithic devices, polymer-coated capsules and implant devices, hydrogels, to injectable systems based on suspensions of microspheres, nanospheres, or polymer solutions. The advantages and disadvantages of these different formulation systems are being extensively discussed in this book.

Administration forms, capable of sustained-drug release, became an important part of medication in terms of improved treatment effect, reduction of side effects, and patients' convenience. Sustained release of active drug provides many therapeutic advantages, the most important of which is that the drug blood levels can be maintained for a long time with minimal fluctuation. The problem with each dose of an immediate-release drug is that the concentration of drug available to the body immediately peaks and then declines rapidly. When the drug concentration reaches very high levels, it contributes to adverse side effects, while when it remains at lower levels, it is not possible to provide therapeutic benefit. Thus, it is desirable to release drugs at a constant rate, therefore maintaining drug concentration within the therapeutic range and eliminating the need for frequent dosages. Other advantages of sustained-release devices can include delivery to the required site, reduced dangers of overdose or side effects, and economic advantages by virtue of more efficient dosage, at the expense of possibly more complicated fabrication.

Sustained-release devices with sophisticated design, along with the used polymers, are considered important for the efficient control of the drug release. Modern sustained-release dosage forms require reliable excipients to ensure a release rate of the active drug, which is reproducible in a narrow range. Since a limited number of polymers fulfill this requirement, there is an interest in either modulating drug release via addition of common excipients or developing new polymers, designed for the specific application. Frequently, the approaches used to achieve adequate control of drug release include hydrophilic and lipophilic matrix systems, in which the mechanism of drug release is based on a combination of diffusion and erosion processes. Waxes or other hydrophobic materials, swellable hydrophilic excipients, and lipid combination of hydrophobic and hydrophilic excipients are the most common applications in order to achieve the desired release rate. Most of them are insoluble and permeable biocompatible polymers. For sensitive drugs, such as proteins, excipients are required for drug stabilization during manufacturing process, storage, and release. In general, controlled-release preparations appear mainly in three forms: a dosage having an internal matrix typically based on polymers, a dosage wherein active drug-containing particles are coated (mainly tablets or microparticles), and a dosage relying on osmotic pressure. From those three types, the matrix form tablet is the one that has achieved the greatest popularity, mainly due to its ease of manufacturing process. From all these formulations, the delivery mechanism should control the rate of release.

The ideal release mechanism should be at a constant rate (zero order) and can be broadly classified into physical and chemical mechanisms.

The physical mechanisms include diffusion of drug molecules through a polymer layer, dissolution or degradation of polymer matrix controlling the drug-release rate, osmotic pressure for drug release (solvent-activated release), and use of ion exchange for ionized drugs. One of the main advantages of using physical mechanisms is that the drug-release kinetics can be controlled by the drug-delivery system itself. Each drug-delivery system has predetermined drug-release kinetics that can be adjusted by varying simple parameters, e.g. the type of a polymer used, the thickness of the polymer membrane, and the surface area. In a diffusion system, the drug is either encapsulated in a polymer membrane or suspended within a polymer matrix. The procedure of the release mechanism from such a system can be described as follows: water diffuses into the membrane or matrix, the drug dissolves, and finally the dissolved drug diffuses out of the polymer. In a membrane system, diffusion of water through the polymer is the rate-limiting step. Furthermore, the rate of release remains constant, and it is proportional to the concentration of the initially appeared drug. Solvent-activated systems use several mechanisms. The most common one employs a semipermeable membrane that contains a small, laser-drilled hole. Within the membrane there is a high concentration of an osmotic agent, either the drug itself or a salt, which causes water to enter through the membrane. The drug is then forced out through the hole because of the increased pressure (osmotic pumps). Polymeric degradation is perhaps the most interesting method of drug release. As with the diffusion method, the drug is contained within a polymer membrane or matrix. The polymer is designed to degrade and release the drug at a specific location in the body. As the polymer degrades, the drug is freed and it is then available to the body.

The chemical mechanisms are based on breaking the covalent bonds that connect drug molecules to a delivery vehicle, such as polymer chains, through the implementation of either chemical or enzymatic degradation. The main disadvantage of using the chemical mechanisms is that drug molecules have to be chemically modified for grafting to the delivery vehicle. Such a situation leads to the development of new chemical entities, which are called prodrugs. For this reason, the physical mechanisms have been widely implemented.

Drug control release can be accomplished in numerous ways: intravenously, transdermally, or orally. The present review will focus first on the different sustained-release formulations administered orally, second on the materials used for their preparation, and third on the mechanisms that have been developed and patented during the past years in order to control the drug release. The examples mostly used, focus on innovative formulations and are being investigated during the last 5–7 years.

From the viewpoint of designing a biomaterial, understanding materials' characteristics is critical for predicting what function the material can exhibit as a biomaterial. For example, the design of a ceramic or metal implant emphasizes the mechanical functions, such as the geometric shape, surface, and mechanical properties, to bear and transmit loading. The metal stent serves as mechanical supports to prevent localized flow constriction by its rigid structure. The contact lenses made by polymer provide optical function to allow visible light to precisely transmit and refract into pupil. Cochlear implant using electrical impulses stimulates cochlear nerves that can create a perception of sound. The electric function such as cardiac pacemaker stimulates muscle to induce rhythmical pulses. Also, piezoelectric implant transfers mechanical stress into electric current to improve bone growth.

From the viewpoint of safety, in general, toxic reaction is directly associated with chemical or electrochemical properties of biomaterials interacting with body fluid. The passive characteristic is the basic and important requirement for invaded biomaterials. Accordingly, the physical interactions between biomaterials and the living body rather than chemical interactions should be particularly concerned. From several clinical cases, failures also occur when utilizing biomaterials with unfavorable physical properties. For instance, comparing with bone, a relatively higher elastic modulus of titanium alloy that served as an artificial hip joint may induce the stress-shielding effect and may result in implant loosening after a long-term implantation. The main reason for stress-shielding effect is an unsymmetrical loading-stress transfer from implant to neighboring bone due to their mismatch stiffness.

According to above-mentioned two viewpoints of safety and design, understanding physical properties of materials is an important step to improve or further develop novel biomedical devices. The physical properties of material including electric, thermal, and optical properties will be introduced in this book while deducing how to apply these specific properties to make a material to replace functions of living tissues.

Electronic biomaterials can be divided into two classifications. The first is using nonbiological electronic materials to serve as biomedical devices due to their particular electronic properties, such as conducting wire, lithium battery, and pulse generator, contained cardiac pacemaker to provide electronic properties. The second is utilizing biologicals or biologically derived materials as templates. For instance, a template made by DNA is used to link electrodes with nanoparticles. This book highlights the electronic conductivity and resistance of these materials.

Recently, the optical properties of materials have been widely applied in biomedical field, including medical image and biological spectrum to obtain image of biological body by combining many techniques such as radiology, thermography, nuclear medicine, medical photography, and microscopy . The medical images consisted of X-ray radiography, ultrasound, computed topography, nuclear medicine, magnetic resonance image, and positive emission tomography created by different radiation. On the other hand, the biological spectrum techniques, used to detect the biochemical, structural, and functional changes of biological molecules, such as atomic absorption spectroscopy, X-ray diffraction spectroscopy, fluorescence spectroscopy and nuclear medicine, magnetic resonance spectroscopy, will be introduced in this book.

The thermal properties for polymers are relatively important for biomedical applications as compared with metals and ceramics because their thermal properties directly affect their mechanical properties. For example, biodegradable synthetic polymers show that the lower the glass transition temperature, the weaker the mechanical properties. Hence, this book introduces three kinds of thermal properties, i.e. thermal expansion, conductivity, and capacity of materials.

A variety of materials, such as metals, ceramics, polymers, and composites, are used in bioengineering. The understanding and measurement of the mechanical properties and failure processes of these biomaterials are quite important for their successful and safe applications. Mechanical behavior of a material reflects its response to the applied load or force. It is necessary to know the mechanical behavior of materials to have a suitable design for their applications and to prevent the occurrence of fracture when in use. In this chapter, the fundamentals in mechanics of materials, methods of mechanical testing, and failure processes are demonstrated. The basic knowledge in this chapter is applicable to various materials, certainly including most of the biomaterials.

The basic mechanics of materials are introduced in this book. All solid materials can be deformed when subjected to external loads. The deformation may be elastic, viscoelastic, and/or plastic ones. The mechanics of materials mainly ascertain the relationship between the responsive deformation and applied load. A variety of vocabularies and several important phenomena related to the mechanics of materials, such as engineering stress–strain, true stress–strain, modulus of elasticity, shear modulus, yielding, necking, and dislocation slip, have to be clearly demonstrated in discussing the mechanical properties of materials.

A number of mechanical tests are demonstrated in this book. The tensile test is widely used to measure the strength of materials. An engineering stress–strain curve is constructed from the load–elongation measurements. Yield strength is the stress required to produce a small specified amount of plastic deformation. Hardness testing is a measure of a material's resistance to localized plastic deformation. A small indenter is forced into the surface of a tested material, under controlled conditions of load and rate of application. Thereafter, the depth or size of the resulting indentation is measured, which in turn is related to a hardness index number. The softer the material, the larger and deeper the indentation, and the lower the hardness index number is. Impact tests are established to ascertain the characteristics of material fracture at high loading rates. Charpy and Izod are two standardized impact tests to measure the impact energy or as called notch toughness. The toughness of a material is the ability to absorb energy in the plastic range without fracturing.

Several fracture behaviors of materials, such as ductile and brittle fracture, fatigue failure, and wear, are discussed in this book. Ductile materials exhibit substantial plastic deformation with high energy absorption before fracture. Brittle fracture normally has little or no plastic deformation with low energy. The material fracture includes two steps, crack initiation and propagation, in response to the applied stress. The fracture mode is highly dependent on the mechanism of crack propagation. Ductile fracture is characterized by extensive plastic deformation in the vicinity of an advancing crack. For brittle fracture, cracks may spread quite rapidly, with a little or even no accompanying plastic deformation. Fatigue is a failure that occurs for materials subjected to dynamic and fluctuating stresses. The failure of metals involves alternating stresses of which maximum stress is lower than the materials strength. A stress–cycle (S—N) curve is an important parameter that characterizes a material's fatigue behavior. The fatigue limit or endurance limit and fatigue strength are defined in the S—N curves for a variety of materials. The fatigue fracture is characterized by three distinct steps: crack initiation, crack propagation, and final fracture. The initiation of fatigue crack always occurs on the surface of a component at some sites with stress concentration. The macroscopic fatigue failure surface is divided into two areas with different appearances. The polished or burnished area decorated with clamshell marking or beach marks is associated with slow crack growth when the cracks rub each other as the specimen is deformed back and forth through each stress cycle. The rough or granular area fractured as a result of overload when the crack propagates rapidly. The fatigue behavior of engineering materials is highly sensitive to a number of variables, such as the mean stress level, geometrical design, metallurgical variables, surface effects, and environment. Commercially, the processes of shot peening, carburizing, or nitriding are often executed on the surfaces to improve the material's fatigue properties. Wear is an important factor in the deterioration of components that move over each other. This phenomenon often limits both the using life and the performance of these components. Wear loss of material from the surface is mainly by transfer to another surface or the creation of wear debris. Besides the wear loss, some surface defects may be created in the surface. These surface defects may exacerbate other types of damage, such as fatigue and stress corrosion. Adhesive wear and abrasive wear are two primary wear mechanisms. These two wear mechanisms are mainly ascribed to the sliding wear. Sliding wear could be affected by various conditions, such as lubrications, materials, loading, sliding speed, hardness, and surface roughness.

Metallic materials, ceramic materials, and polymeric materials represent a versatile class of biomaterials being extensively applied in multitude of biomedical applications. An in-depth understanding and valid modification of physical, chemical, biological, and engineering properties is highly relevant to the performance and development of medical devices. Surface properties of biomaterials play a major role in determining biocompatibility. They have a significant influence on biological response and also determine the long-term performance. The main goal in designing biomaterials is therefore to ensure that they exhibit appropriate surface properties as well as desired physical and mechanical characteristics, which would enable them to function properly in the biological environment. It is hard to satisfy all of these characteristics. In order to improve surface properties, the surface treatment techniques should be applied. However, it is still a highly challenging task to modify surface properties – producing hemocompatible surfaces of an ECMO film, for example. Biological response to biomaterials is very complex and still not fully investigated. For the ECMO, the surface of the biomaterial is responsible for initiating the primary interaction with blood fluids due to the mechanism of blood coagulation. Therefore, the effective control of the surface structure and properties of biomaterials would be very beneficial for getting insights into physicochemical properties and their corresponding applications.

The surface treatments of biomaterials could be simply separated into interchange of surface species and directly cover compounds. It is of vital importance to ensure that the surface of the materials is suitably conditioned to ensure an appropriate biocompatibility. For that reason, if the surface structures of the materials can be properly modified to improve their biological reaction properties with keeping their original natural functions, the surface treatment is viable. This definitely requires advanced instrumentation and characterization techniques to understand surface structure properties and functional performance relationships of various materials and further to open the way toward more efficient medical devices, therapies, and other biomedical applications.

The surface treatments of materials by chemical methods, electrochemical methods, plasma methods, and ion beam implantation are principally explained and recommended in this book. Those methods can provide an improvement of surface properties to greatly expand the biomedical applications of materials. For an evaluation of the surface properties of materials, image technologies such as scanning electron microscope (SEM), atomic force microscope (AFM), near-field scanning optical microscope (NSOM), and tip-enhanced Raman scattering (TERS) imaging and spectroscopy methods such as surface-enhanced Raman scattering (SERS), X-ray absorption near-edge spectroscopy (XANES), and extended X-ray absorption fine structure (EXAFS) are also interpreted.

Cell therapy using biomaterials technology will only be a topic of the future rather than the present and is based on combinational technology of materials science, stem cells technology, and reconstructive surgery that aim to regenerate natural tissues as well as to create biological substitutes for defective or lost organs and tissues. The design of materials that can regulate cell behavior such as proliferation and differentiation is a key component for the fabrication of tissue engineering scaffolds. From the viewpoint of immune system response of the body, the implanted biomaterials should mimic the structure and biological function of native extracellular matrix (ECM), both in terms of chemical composition and physical properties. Therefore, in order to mimic the biological function of ECM proteins, the scaffold materials used in tissue engineering need to be chemically functionalized to provide appropriate niches for cell proliferation and differentiation and ultimately tissue regeneration as ECM does. Fabricated tissue-engineered scaffolds used in regenerative medicine have micron dimensions that fail to mimic the structure of natural ECM. Nanotechnology and the use of new nanomaterials underpin the race for tissue-engineered products because of the strong biological activity that current researches appear to indicate for these materials. It is no doubt that tissue engineering and regenerative medicine using nanomaterials will be the novel innovation of the future. Remarkably, the recent identification of nanotechnology with enhanced ability to mimic natural ECM proteins such as collagen structure has led to the discovery of a class of nanomaterials with specific properties for tissue engineering applications and regenerative medicine therapy. One of the common approaches is to produce fibers similar to ECM proteins is self-assembly of collagen. This technique is sufficient to cause its rapid transduction into a variety of different tissues *in vitro* as well as *in vivo*. Moreover, this novel technique for proteins and peptides appears to circumvent many problems associated with cells and drug-based methods. This review will consider the self-assembled systems and the recent developments for their potential applications in regenerative medicine. The self-assembling proteins and peptides for designing novel biomimetic nanomaterials and their potential applications in regenerative medicine and biomedical applications will be also discussed in detail from the viewpoint of their biological applications.

Many three dimensional (3D) models currently in practice require expensive equipment, large sample volumes, long incubation times, and/or extensive expertise, and their greatest disadvantage is that they are too far from the nature of human organs. Because of the above problems, research and development on drug discovery, regenerative medicine, biotech, and pharmaceutical industries is very costly and takes several years to bring a single drug/product to the market. The goal of biomedical engineering is to merge biomaterials science, nanotechnology, and biological principles to generate 3D *in vitro* living organs to mimic organ/tissues in order to partially reduce the amount of *in vitro* and *in vivo* animal testing and clinical trials, and to solve the above problems; to sum up, the final goal is to jump from the lab bench to the market. It is proposed to do all the above costly and timely tests in a rapid and cost-affordable way. At the nanoscale, chemistry and materials help us to fabricate novel type of hydrogels that are similar to human organs, infusing the cell-laden hydrogels with ECM molecules and gradients of signaling molecules to influence cell development and aggregation. At microscale, fabrication technologies adopted from the semiconductor industry, such as photolithography, will help us to mass produce identical building blocks in a variety of shapes and sizes. These products will have to mimic the physical, chemical, and biological properties of natural organs and tissues at different scales, from molecules to cells to building blocks to organized clusters to reach the final device. It is envisioned that the proposed method can be used to generate vascularized organs and tissues with controlled cell–cell and cell–matrix interactions that will be useful as *in vitro* diagnostics tools and drug screening applications as well as for transplantation.

We anticipate that elucidation of the preceding goals will open many doors and lead to significant improvements in biological tools, drug discovery process, lead identification as well as therapeutic approaches. The miniaturization of this approach allows one to perform many more experiments than previously possible in a simpler manner. Biomaterials technology aims to develop set of tools that are simple, inexpensive, portable, and robust that could be commercialized and used in various fields of biomedical sciences such as drug discovery, diagnostic tools, and therapeutic approaches in regenerative medicine. It will build up interdisciplinary critical and experimental research media aimed at overcoming the fundamental limits to information processing. It will enhance graduate education in the local universities and produce high-quality researchers among local students and encourage them to pursue research careers by creating new knowledge in selected areas of focus. Also, it will consist of a top academic and high-tech objective to fabricate, investigate, and implement novel advanced microstructures, nanostructures, and superstructures based on ordered highly functionalized materials to meet the demands of maximum efficient, active hydrogel materials of high and sustained reactivity as well as long-term stability. It will also enable new fundamental research and development for the next generation of biomedical materials as well as exploit such novel structures to develop novel biomedical devices, and transfer the knowledge to academia and industry for a future implementation of novel knowledge and technology to the world. In turn, it should increase the international competitiveness of the world into a knowledge-intensive micro- and bioengineering organ-based biosensors by focusing on high-impact research to generate new breakthroughs aimed at solving significant practical problems of biomedical sciences while seeking to extend the boundaries of understanding. It aims to raise research profile of bioengineering as a vibrant center for medical and technological applications through a bottom-up approach that embraces both elements of basic and applied research to enhance the competencies in existing technologies, to seek out promising new areas, and to develop an integrated, cutting-edge research program by growing a pool of top research talent and developing the platforms on which local universities could create research breakthroughs of importance to the world. Since advancement in device development technologies is a significant indicator of the developed societies, rapidly growing market for biomedical devices provides competitive advantage in R&D and commercialization for this field. Such advancement can be reached by means of setting up and helping local universities to establish their own facilities using our technology created in local universities.

1.3 Impact of Biomedical Engineering

Biodegradable materials such as collagen, gelatin, dextran, and carbohydrate derivatives are traditionally used as coating biomaterials for the clinical preparation of nanoparticles. Cross-linked iron oxide nanoparticles have also been developed as a result of the amination or carboxylation of dextran; they have improved conjugation capacity for more complex, integrative applications. The polymer-encapsulated method is very flexible, since it allows the preparation of iron oxide nanoparticles that can carry a wide variety of stabilizers. Various proteins, antibodies, peptides, and aptamers have been attached to the surface of the iron oxide nanoparticle. These act as targeting agents for specific biomarkers on target cells, providing a more exciting avenue to modulate nanotoxicity *in vivo*. The surface charge also plays a role in nanotoxicity, as it influences the adsorption of molecules and ions that may change organism/cellular responses toward nanoparticles. The surface charge is a major determinant of nanoparticle colloidal behavior that influences the organism response by changing the shape and size of nanoparticle through aggregate/agglomerate formation. Generally, neutral surfaces are the most biocompatible, whereas cationic surfaces are more likely to induce hemolysis and platelet aggregation. This may be as a result of the affinity of cationic nanoparticles to the negative phospholipid head groups or protein domains on cellular membranes. In addition, the surface charge can influence plasma protein binding. Hence, it affects the *in vivo* biodistribution and the clearance of the iron oxide nanoparticles from the circulation. The surface roughness is one of the main factors involved in the nonspecific binding forces that promote cellular uptake (similar to hydrophobicity and cationic charge). Small radii surface coarseness greatly minimizes electrostatic or hydrophobic–hydrophilic repulsive interactions, therefore promoting cell–nanoparticle interactions. However, significant nanotoxicities can also be caused by the enhancement of certain physicochemical properties of nanoparticles.

1.3.1 Target Drug Delivery

It is becoming clear that due to its instability and degradability, naked drug is rarely applied in systemic delivery; accordingly, this section will deal primarily with drug-loaded carriers, such as nanospheres, nanocapsules, liposomes, micelles, microemulsions, conjugates, and other nanoparticles. Polymeric biomaterials are classically biodegradable and positively charged (e.g. cationic-cell-penetrating peptides, cationic polymers, dendrimers, and cationic lipids) that are widely used as drug (gene, growth factor) carrier [1–20]. Conjugation of drugs with a variety of small molecules (e.g. cholesterol, bile acids, and lipids), polymers, peptides, proteins (e.g. antibodies), as well as aptamers (e.g. RNAs), and encapsulating drugs in nanoparticulate formulations improves the stability, cellular internalization, or cell-specific active targeted delivery synthetic polymers that have been widely investigated for drug delivery. These synthetic polymers may enhance intracellular delivery by facilitating endosomal escape and inducing lysosomal disruption, endosomal release, and drug protection from lysosomal degradation by way of buffering the endosomes [21–30]. Biodegradable polymers have been reported to undergo hydrolytic degradation and yielding nontoxic and neutral pH degradation products, thereby providing sustained gene delivery [22, 31–44].

1.3.2 Early Stage Detection

The initial interaction between cells and solid substrates is important for designing biomaterials to a variety of biological applications such as tissue engineering and cell-based biochip. Microfluidic devices have been recently used to fabricate vascularized tissue-engineered constructs and miniaturized bioreactors. Microscale technologies, which were traditionally used in the microelectronics industry to fabricate computer chips, have recently emerged as a useful approach to control the various aspects of the cellular microenvironment. In particular, the development of techniques such as soft lithography that can be cheaply and easily used to fabricate micro- and nano-devices, without the need for microfabrication facilities, has greatly enhanced the widespread application of microscale technologies in drug discovery. Microscale technologies have emerged as a powerful tool to pattern cells on substrates. In this approach, techniques such as microcontact printing and micromolding are used to generate adhesive micropatterns on substrates. These techniques have been used to create arrays of cells as well as to control the shape of individual cells. Furthermore, by using these techniques novel biological insights have been gained regarding the effects of cell shape on apoptosis and differentiation. Micropatterning techniques are a powerful method in standardizing *in vitro* drug discovery assays since they can be easily incorporated within the microwell systems used currently for drug screening.

1.3.3 Personalized Medicine

Therapies based on drugs are entering clinics, especially for diseases requiring locoregional treatments, including age-related macular degeneration, diabetic macular edema, respiratory virus infection, pachyonychia congenital, hepatitis, human immunodeficiency virus infection, and cancer. There are a number of obstacles and concerns that should be overcome before personalized medicine will be used as a new therapeutic technique.

1.4 General Applications of Biomedical Engineering

The initial interaction between cells and solid substrates is important for designing biomaterials to a variety of biological applications such as tissue engineering and cell-based biochip. On the contrary, nanoparticles have many potential applications ranging from imaging to drug-delivery systems. Therefore, design of an advanced *in vitro* culture system that can analyze the interaction of particles with cells may be beneficial.

1.4.1 Pharmaceutic

One of the future approaches with stem cells is the combinational therapies with gene. The cells can not only function as the carrier vehicle to target genes to the site of action but can also positively participate in the process of tissue repairing. Therefore, several researches have been investigated on the therapy of tissue regeneration by genetically engineered stem cells. Over the last decade gene therapy has captured the scientific and public interest with the promise to deliver genes and proteins to specific tissues or to replace deficient host cell populations. In planning gene therapy strategies for tissue engineering, the aim is to deliver a therapeutic gene of a growth factor or cytokine, into the target tissue. However, considering the immunological and safety issues of viral vectors, necessity in the development of nonviral vector systems has been increasingly magnified. Better understanding of molecular mechanism on the differentiation of stem cells will eventually allow us to properly manipulate stem cells both *in vivo* and *in vitro* for the regeneration of tissues and organs. This paradigm provided a proof of principle for the use of tissue engineering techniques as a means to improve methods of gene transduction. Tissue-engineered cell construct can be potentially used as therapeutic cell-based gene delivery or as an *in vitro* model system for testing of genetic manipulations in order to understand the effects of gene expression on tissue development.

1.4.2 Medicine

Materials technology aims to develop a technique that draws from microscale engineering, novel biomaterials, and biological principles to overcome the limitations of the current approaches to generate 3D *in vitro* living organs. These include the inability to generate 3D constructs that mimic the complexity of native tissue structure as well as to generate vascularized structures within 3D tissue culture system. The success of hydrogels as tissue implants or biomedical devices is strongly dependent on their bulk properties. The ability to directly seed cells within macroporous hydrogels will be important for overcoming challenges associated with uniform cell-seeding density and vascularization. In general, hydrogels from natural sources can be derived from polymers such as collagen, hyaluronic acid (HA), fibrin, alginate, agarose, or chitosan. Depending on their origin and composition, various natural polymers have specific utilities and properties. Many natural polymers, such as collagen, HA, and fibrin, are derived from various components of the mammalian ECM. The advantages of natural polymers include low toxicity and biocompatibility.

1.4.3 Consumer Goods

Metallic materials, ceramic materials, and polymeric materials represent versatile class of biomaterials being extensively applied in multitude of biomedical applications. An in-depth understanding and valid modification of physical, chemical, biological, and engineering properties is highly relevant to the performance and development of medical devices. Surface properties of biomaterials play a major role in determining biocompatibility. They have a significant influence on biological response, and they also determine the long-term performance. The main goal in designing biomaterials is therefore to ensure that they exhibit appropriate surface properties as well as desired physical and mechanical characteristics, which would enable them to function properly in the biological environment. It is hard to satisfy all of these characteristics. In order to improve surface properties, the surface treatment techniques should be applied. Biological response to biomaterials is very complex and still not fully investigated. Therefore, the effective control of the surface structure and properties of biomaterials would be very beneficial for getting insights into physicochemical properties and their corresponding applications.

1.5 Summary and Challenges

The surface treatments of biomaterials could be simply separated into interchange of surface species and directly cover compounds. It is of vital importance to ensure that the surface of the materials is suitably conditioned to ensure an appropriate biocompatibility. For that reason, if the surface structures of the materials can be properly modified to improve their biological reaction properties while keeping their original natural functions, the surface treatment is viable [4, 12, 14–18, 22, 31, 37, 38, 45–78]. This definitely requires advanced instrumentation and characterization techniques to understand surface structure properties and functional performance relationships of various materials and further to open the way toward more efficient medical devices, therapies, and other biomedical applications. Cell therapy using biomaterials technology will only be a topic of the future rather than the present and is based on combinational technology of materials science, stem cells technology, and reconstructive surgery that aim to regenerate natural tissues as well as to create biological substitutes for defective or lost organs and tissues [13, 19–21, 39–42, 78–100]. The design of materials that can regulate cell behavior such as proliferation and differentiation is a key component for the fabrication of tissue engineering scaffolds [9, 27, 28, 65, 101–126]. From the viewpoint of immune system response of the body, the implanted biomaterials should mimic the structure and biological function of native ECM, in terms of both chemical composition and physical properties [127–144]. Therefore, in order to mimic the biological function of ECM proteins, the scaffold materials used in tissue engineering need to be chemically functionalized to provide appropriate niches for cell proliferation and differentiation and ultimately tissue regeneration as ECM does.

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