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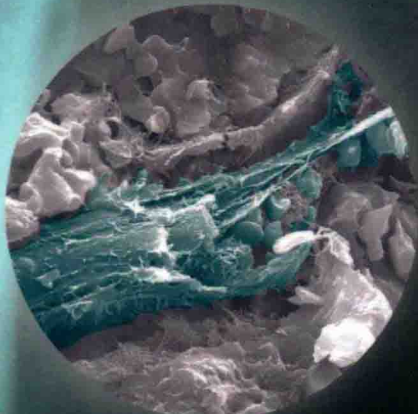
Characterization of Biomaterials



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Characterization of Biomaterials

Preface

The field of biomaterials is inherently multidisciplinary involving materials science, physical, engineering, biological and clinical sciences. Therefore, it is important for biomaterials researchers to understand what to and how to characterise different biomaterials. In recent years, there are quite a few good books published on introduction to biomaterials topic, however, no specific book is available towards how to characterise different biomaterials. The aim to develop this book was to focus primarily on biomaterials characterisation, something that can help graduate students and biomaterials professionals to learn specifically what techniques are good for testing certain biomaterial properties based on applications and how to do it. Moreover, what properties are good to test during materials development versus which properties should be tested during device development? These questions may be simple to some experienced biomaterials scientists, but many times hard to find answers for others. Considering these issues, this book is developed with specific emphasis towards characterisation of biomaterials and biomedical devices for their physical, mechanical, surface, *in vitro* and *in vivo* biological properties. Special attention was given towards device level characterisation for orthopaedic and cardiovascular implants. Chapters dealing with physical, mechanical and surface properties of biomaterials are developed by researchers from physical and engineering sciences. These chapters are focused on techniques that can reveal basic properties such as atomic structures, bonding, chemical interactions, phase identification and transformation, strength and toughness measurements, and property measurements at the surface level. Most of these techniques are followed by biomaterials researchers during early stage of materials development towards certain applications. The following chapters include *in vitro* and *in vivo* testing of biomaterials including microbial interactions and biofilm characterisation. These levels of testing are needed before a biomaterial can be considered for clinical trials or in actual device manufacturing. The final part of the book deals with device level characterisation with special emphasis on orthopaedic and cardiovascular devices. Researchers with industrial product development background contributed towards these chapters.

Apart from all the contributing authors, we also like to thank many of our students for their support towards developing this book particularly Mr Solaiman Tarafder, Mr Gary Fielding, Mr Himanshu Sahasrabudhe and Ms Sahar Vahabzadeh. We are also grateful to our boys, Shohom and Aditya,

without their cooperation we could not have completed this work. We hope that better understanding of biomaterials and biomedical device will not only save time but also will make them safer to use, a dream that resonates with every biomaterials researcher.

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Pullman, WA, USA
February 2013.

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Chapter 1

Introduction to Biomaterials

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Chapter Outline

1.1. INTRODUCTION

With the evolution of human civilization, the field of biomaterials evolved involving different materials at multiple length scales from nano- to micro- to macrolevel with a simple focus to extend human life and improve the quality of life. Over 1000 years back, silver in different forms was used as an antimicrobial agent to prevent infection. Different types of surgical procedures can also be found during early stages of civilization. However, probably the most significant developments took place in the field of biomaterials over the years 1901–2000. Artificial joints improved the quality of life for millions of people over the past 60 years, resorbable sutures simplified surgical procedures, and different cardiovascular devices saved millions of lives, just to name a few. The advent of tissue engineering and organ regeneration is pushing the frontiers of science today to make the years 2001–2100 more exciting in the field of biomaterials. However, to appreciate the benefits, it is not just the design of biomaterials that is important, but sound engineering design and appropriate materials and device characterization are also needed. Moreover, for a biomedical device to see the commercialization light, it is also important to carry out testing following appropriate standards to get regulatory approval. Overall, benefits of biomaterials research can only be appreciated when these

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materials are characterized well at both the materials level and the device level following regulatory guidelines. Considering the multidisciplinary nature of the field, it is also not easy to carry out large variety of experiments using different techniques. Realizing this problem in biomaterials characterization, we have developed this book to offer an insight on various characterization tools focusing on biomaterials and biomedical devices.

1.2. TYPES OF MATERIALS

Materials can be classified into different groups based on their crystal structure, bonding, and macrostructures. Each subgroup of materials shows somewhat similar properties and then those materials can be clubbed together to study their performance for different applications. If we look at types of bonding, materials can be classified into three broad categories—metals, ceramics and polymers. Materials that are bonded via metallic bonds are called *metals*. Due to abundance of free electrons in metallic bonds, metals are both thermally and electrically conductive, and show malleability in terms of their mechanical properties. Materials that are primarily ionic and/or covalently bonded are called *ceramics*. Since ionic and covalent bonds do not offer any free electrons, ceramics are generally nonconducting materials both thermally and electrically. However, due to the movements of defects, some ceramics show conductivity at higher temperature. Materials that are based on long carbon chain and covalently bonded with some secondary bonding are polymers, where "mers" or units are connected in the long range. Due to covalent bonding, most polymers are nonconducting. When any three of these main materials are mixed together without losing its inherent characteristics, then we form a new class of materials, called *composites*. Some examples of natural composites are wood and bone.

When we look at the unit cell, the basic building block of any material, we can classify materials into three groups—crystalline, semicrystalline and amorphous. If the unit cell is repeated in all three directions and maintains a long-range order, then those materials are called a crystalline material such as iron, titanium, chromium or polycrystalline ceramics. The basic unit cell, defined by the three-dimensional shape and atom positions, can be for example body centered cubic or face centered cubic or hexagonal close packed (hcp), where "cubic" or "hexagonal" are crystal systems defined by the shape of the unit cell and "body centered" or "face centered" are specific atom positions that defines the Bravais lattice of the unit cell. These kinds of simple structures are common for most metallic systems, which are mainly crystalline in nature. For many materials, unit cell does not repeat itself in three dimension for long range, but only shows short-range repetition. Those materials with short-range ordering of unit cells are called amorphous materials or glass. Due to lack of ordering, glassy materials show unique properties such as glass transition temperature (T_g), where a liquid phase transforms to a solid rubbery phase. There are also a group of materials that are partially glassy and partially crystalline. Those materials are called semicrystalline materials. Among others, many polymeric materials show semicrystalline nature.

Materials can also be classified as natural or synthetic. Natural materials are those which are available in nature such as wood, rocks, corals and bones. Most natural materials are ceramics, polymers and their composites. Mother Nature designed these materials for a variety of purposes such as sensors, reservoirs, structural support or energy converters. Most of these materials have complex chemistry and structure and the mankind is still exploring those to enrich their learning. Synthetic materials are man-made materials designed for specific functionality. These materials include metallic materials such as steels for fracture management devices, to titanium and its alloys for implant, to polymers for ocular lenses and to ceramics for bone-tissue engineering. Synthetic materials are tailored for specific chemistry and structure for properties that can be utilized to improve our everyday life. Once processed, their physical, chemical, mechanical and sometimes biological property determination is necessary based on application need.

Materials can also be classified based on their macrostructures such as dense or porous. Most natural materials such as rocks, tissues, wood are porous materials. Porosity in these materials can serve various purposes. Most ceramic materials have residual porosity. Porosity can be nonuniform and vary in size and distribution. Porosity in materials can vary from 1% to 10% such as in cortical bone to as high as >70% in some cancellous bones. Because of porosity, these materials are lighter weight, and many times show nonuniform properties at different directions. However, it is very difficult to mimic such natural materials in terms of composition, structure and properties. When materials do not show any porosity, those are called dense materials. Most metallic materials are dense in nature with residual porosity <1%. Dense materials are typically isotropic in nature and can be shaped easily by various forming techniques.

Figure 1.1 schematically shows different types of materials. Any one material can also fall into many of these categories. For example, bone is a natural material, that is porous, and a ceramic–polymer composite.

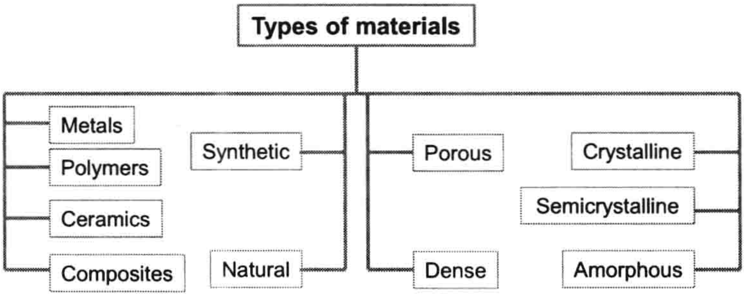

FIGURE 1.1 Different types of materials.

1.3. BIOMATERIALS AND BIOCOMPATIBILITY

A biomaterial is a material, synthetic or natural, that can be used in medical applications to perform a body function or replace a body part or tissue. A biomaterial is intended to interact at the interface of biological systems. It may also be used as a delivery system for drug or biological factor. Biomaterials are designed based on application needs. Reaching back to the beginnings of civilization, the Romans, Aztecs and Chinese used gold in dental applications. The Mayans were found to have fashioned dental implants out of sea shells with results indicating actual bone integration. A biomaterial must be biocompatible, i.e., it should be friendly to biological system and not do any harm to the system, whether at the cellular level or at the system level. A biocompatible material should elicit appropriate host response or able to perform its intended function in a specific application without the presence of adverse reactions. This is an emerging paradigm that requires and pushes unique multidisciplinary boundaries based on understanding and integration of concepts from various broad fields, but not limited to, chemistry, biology, materials science, mechanical, chemical and electrical engineering as well as medicine.

Biomaterials are used to augment, repair or replace any tissue, organ, or function of the body that has been lost through trauma, disease or injury. Recent practice in medicine often times uses tissue reconstruction using autograft, where tissue graft or organ transplant from one point to another of the same individual takes place. However, limited availability, donor site morbidity and above all, the need for a second surgery restrict their application. On the other hand, potential alternative is the use of allograft, i.e. tissue graft or organ transplant from a donor of the same species as the recipient. The other alternative could be xenograft, which is tissue graft or organ transplant from a donor of a different species from the recipient. Both allograft and xenograft use are somewhat restricted due to the immunogenic response and they may impose adverse biocompatibility in patients' body. These reasons draw our attention to the biomaterials that are available from other sources, which could be synthetic or natural. It was not until the turn of the twentieth century, modern biomaterials and their potential applications began to take shape. These first-generation modern biomaterials are mainly focused on basic functionality and biocompatibility.

Since early 1900s, metal plates were used to stabilize long bone fractures with the hopes of faster and more functional healing. By the 1930s, full joint replacement surgeries were being performed with varying degrees of success. The invention and widespread use of synthetic plastics created a boom in the biomaterials industry resulting in devices such as synthetic heart valve (metal cage surrounding a silicone elastomer ball) and total hip arthroplasty systems (ultrahigh molecular weight polyethylene). Some other important inventions in this era include the intraocular lenses (poly(methyl methacrylate)—PMMA) and the desk-sized pacemaker.

Further understanding of the complexities of biology ushered in the next generation of biomaterials beginning in the 1960s. Scientists and engineers began to design materials specifically for use in biomedical applications. The focus began to shift from materials that were simply biocompatible to technologies that took into consideration the specific needs of the specific biology. Many bioresorbable materials, those biomaterials resorbed in biological system, were also created during this time. Some of the major advances in materials came in the form of synthetic polymers such as Teflon, which is still widely used today in various vascular grafting and surgical applications. Hydrogels lead to the invention of the soft contact lenses. Poly(lactic–glycolic acid) (PLGA) was developed for resorbable sutures. Plastic materials were not the only advances made during this time period. Ceramics such as calcium phosphate synthetic bone analogs were also developed. Today, these synthetic materials are used more often than autografts (bone taken from another source on the patient's body) or allografts (processed cadaver bones). Titanium alloys with better biocompatibility were developed as a lighter alternative to traditional stainless steel orthopedic implants.

1.4. TYPES OF BIOMATERIALS

Like any other materials, biomaterials can be grouped into four major categories: (1) polymers, (2) metals, (3) ceramics, and (4) composites. Polymers can be used in both soft and hard tissue applications, and comprise the largest class of biomaterials. Polymers are also widely used in drug delivery applications. Polymers could be natural (examples: collagen, sodium alginate, and cellulose) or synthetic (examples: silicone rubber, PMMA, poly(vinyl chloride), and co-PLGA). Metals are mostly used for dental and orthopedic applications. Most commonly used metals are Ti and its alloy, stainless steels and Co–Cr alloy. Ceramics are mainly used in hard tissue repair, regeneration and augmentation, especially in nonload-bearing applications or as coatings on metal implants. Most widely used ceramic biomaterials are calcium phosphates (CaP), alumina (Al_2O_3), and bioglass. Polymer–ceramic composite represents the major part of composite biomaterials.

Biomaterials–tissue responses can be divided into four different types. (1) Toxic: toxic materials cause death to surrounding tissue. (2) Bioinert: this type of response is caused by nontoxic but biologically inactive materials. Fibrous tissue encapsulation of the bioinert material is caused *in vivo*, which leads to the loosening and ultimate failure of the implant. This is most commonly seen in metallic implants. A bioactive material coating on metallic implant may prevent fibrous tissue encapsulation. (3) Bioactive: this type of response is seen if the material is nontoxic and biologically active. The term biologically active means that an interfacial bond forms between the material and host tissue. Bioactive glasses, many types of polymers and