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Chapter 4
Biomaterials: Basic principles

4.1 Introduction

Human tissues and organs sometimes fail to perform their regular actions due to genetic defects, age, illness, trauma, degeneration, or injuries. Some of these conditions are handled with the use of day-to-day medication, i.e., drugs. However, some cannot be repaired/rectified by providing medicines and require the use of unique materials and devices. These then bring about the inevitability of surgical repair, which encompasses anatomical sections such as knee joints, elbow joints, vertebrae, teeth, and other crucial organs such as heart, skin, kidney, etc. In the broadest sense, the unique materials (other than drugs) or combinations of materials that are primarily expected to be used inside a mammal or human to treat, repair, augment or replace any tissue is referred to as biomaterials. These biomaterials can either be formed from nature or physically manufactured by utilizing a wide range of physical and chemical methods.

The field of biomaterials is multidisciplinary (Figure 4.1). The design of a simple biomaterial (for example, a bone screw or bone plate) necessitates knowledge and ideas from multiple disciplines. It needs the synergistic integration of materials, biology, medicine, mechanical sciences, and chemistry. The number of medical devices used annually by humans is significant, estimated at 1.5 million by the World Health Organization, with around 10,000 forms of standardized device classes available worldwide.

The term "*biomaterials*" is often described as any material that comes into contact with humans or animals to fulfil their intended function without causing any toxic reaction. This is the single most crucial aspect that differentiates a biomaterial from any other material, i.e., its capacity to be in

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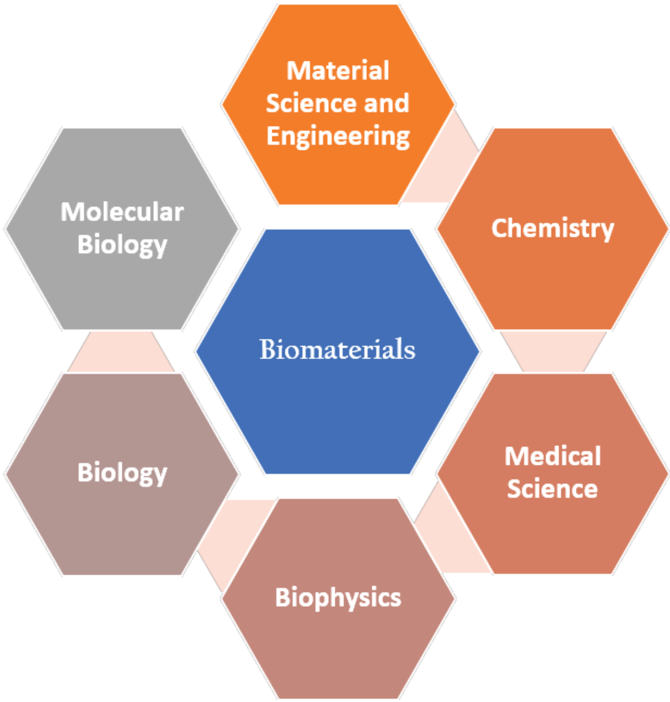

Figure 4.1: Interdisciplinary system of biomaterials (Cooke *et al*., 1996; Marin *et al*., 2020; Ramakrishna *et al*., 2010; Ratner, 1996).

contact with human body tissues without instigating an undesirable degree of response. For thousands of years, humans have inevitably used or at least attempted to use materials to make devices and instruments of practical value by converting basic available substances into materials. Biomaterials have a long history of medical use, and at various times they were seen in a different way. Based on the development and its uses, the broad definition has evolved over the years and could be further expanded as new applications in medicine emerge. Nevertheless, the meaning of biomaterials attained a harmony of opinion by scientists worldwide and is now defined now as "*a material designed to take a form that can direct, through interactions with living systems, the course of any therapeutic or diagnostic procedure*." In most cases, a biomaterial is any natural or synthetic *biocompatible* material that is used to replace or assist part of an organ or a tissue while maintaining close contact with living tissue. They may be produced from

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materials including solid, liquid, and gel substances (metallic components, polymers, ceramics or composite materials). It should be noted that the *bio* prefix of biomaterials applies to biocompatible, rather than *biological* or *biomedical*, as many would intuitively assume.

Biomaterials, a fascinating and highly interdisciplinary area, have grown to become an integral component in the modern-day improvement of human condition and quality of life. It is accomplished by addressing numerous health-related issues that come from several sources. Over the past few decades, biomaterials have broadened their applications from diagnostics (gene arrays and biosensors) and medical equipment (blood bags, surgical tools) to therapeutic medications (medical implants and devices) and emerging regenerative drugs (tissue-engineered skin and cartilage), and more. Many uses of synthetic and naturally occurring medicinal materials can be classified by their place and role in the human body: skeletal system (joint replacements, bone fractures and defects, artificial tendons and ligaments, dental implants), cardiovascular system (blood vessel prosthesis, heart valves), organs (artificial heart, skin repair), etc. The vital applications are presented in Figure 4.2 and tabulated in Table 4.1.

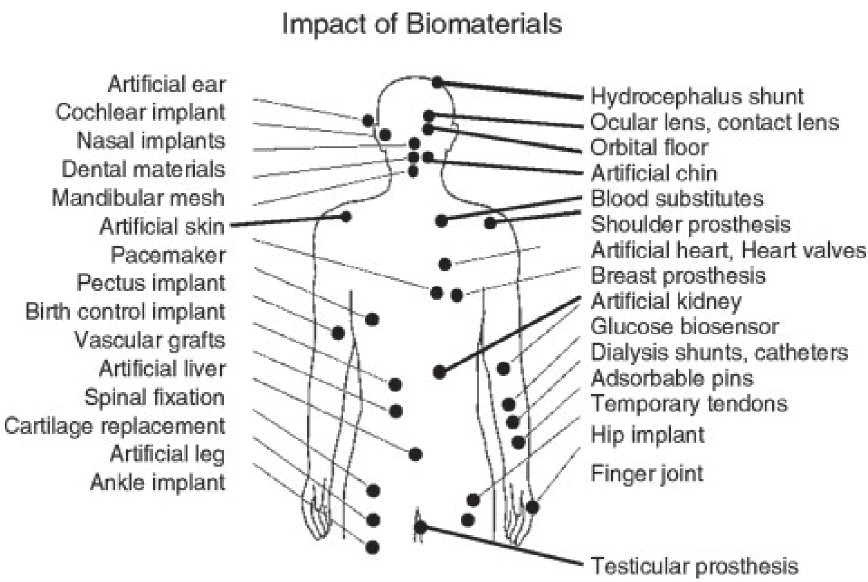

Figure 4.2: Biomaterials have made an enormous impact on the treatment of injury and disease and are used throughout the body (Cooke *et al*., 1996; Kuhn, 2005; Ratner *et al*., 2020).

Table 4.1: Applications of biomaterials.

Organ/Tissue	Examples
Heart	Biventricular pacemakers, artificial valves, artificial heart
Eye	Contact lens, artificial intraocular lens
Ear	Hair-clip artificial stapes, cochlear implants
Muscle	Sutures
Kidney	Dialysis machines
Skin	Skin wound repair, burn dressings, skin substitutes, artificial skin
Circulation	Synthetic blood vessels
Bone	Bone screws, plates, pins, intramedullary rods, bone cement to repair defects
Teeth	Fillings and replacements

4.2 Desired properties of biomaterials

As discussed earlier, the ultimate goal of biomaterials in medicine is to treat, improve, or substitute tissue organs (e.g., bone, muscle, skin) or body function. Such goals can be accomplished by integrating the properties of materials, nature of the system, device architecture, and physiological specifications. The biomaterial application method must combine the chemical and mechanical features of the biological system in order to achieve the required functional results (Figure 4.3). For the processing of biomaterials and related medical items, different elements from science and social parameters are also considered.

4.2.1 *Biocompatibility*

From a biological point of view, biocompatibility is nothing but the acceptability of non-living materials (synthetic or natural) in a living body (mammal/human). This acceptance is broadly defined as the "*ability of a material to perform its desired functions with respect to a medical therapy, to induce an appropriate host response in a specific application and to interact with living systems without having any risk of injury, toxicity, or rejection by the immune system and undesirable or inappropriate local or systemic effects*". Since a biomaterial is intended to be used in intimate contact with living tissues, it is important that the implanted material does

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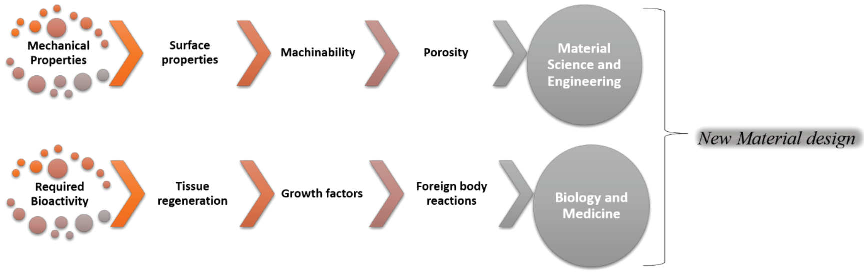

Figure 4.3: Primary requirements of new material design.

not cause any undesired reactions to the surrounding tissues and host organs. Apart from that, the implanted material is expected not to subdue the activity of normal cells or provoke any unwanted local or systemic reactions in the recipient, but is encouraged to generate positive cellular or tissue response.

Usually, the criteria for this biocompatibility are dynamic and detailed and differ with individual specific medical applications. For example, a specially designed material (screw or plate) may possibly be biocompatible in bone implant surgery, but the same components may not be biocompatible in skin applications.

4.2.2 *Host response*

Host response is defined as the "*response of the host organism (local and systemic) to the implanted material or device*". Most of the materials are never inert, and a biomaterial's clinical success depends significantly on the host tissue's reaction with the foreign material. For material establishment-host tissue interaction, these reactions depend heavily on the time-length, purpose, and site of implantation.

4.2.3 *Non-toxicity*

Toxicity of biomaterials deals with elements that migrate out of the biomaterials. A carefully designed biomaterial should serve its purpose in the

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living body's environment without negatively influencing other cells, organs, or the whole organism. It is logical to assume that, unless specifically designed to do so, a biomaterial should not release or generate anything from its bulk.

4.2.4 *Mechanical properties*

In addition to biocompatibility, mechanical properties are embedded in biomaterial design prior to implementation and will majorly contribute to the outcome. Materials undergo several forces which are primarily stress, strain, shear, and a mixture of these. The tensile strength, yield strength, elastic modulus, corrosion, creep, and hardness are some of the most important properties of biomaterials that should be carefully studied and evaluated before implantation. For hard tissue applications, the mechanical properties are of top priority.

4.2.5 *Corrosion, wear, and fatigue properties*

Wear is often considered as one of the leading causes of implant failure. In some cases, wear has also been shown to accelerate the corrosion of biomedical devices and implants. The fatigue resistance is related to the material's reaction to repeated cyclic loads.

4.2.6 *Design and manufacturability*

Appropriate material design is also one of the critical factors to consider for biomaterials. For example, in the early 1900s, bone plates were utilized to assist in fixing long bone fractures. Many of these experimental plates broke because of their primitive mechanical design where they were too narrow and had a stress-focusing corner. Manufacturability is the ability to manufacture the item with relative ease that is ideal for its intended use at minimal cost and high reliability. Concerning biomaterials, the manufacturability, in a broader sense, incorporates the potential of the material to be sterilized by a validated sterilization technique which is deemed appropriate for biomedical applications. The material is

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expected to not get impaired by standard sterilizing techniques such as autoclaving, dry heat, radiation, ethylene oxide, etc. (see Chapter 8 for more details).

In summary, for any material to qualify as a biomaterial, it should

- Be biocompatible, i.e., non-toxic, non-carcinogenic, non-allergenic, etc.
- Have required/suitable physical and chemical properties
- Have suitable mechanical properties
- Have stable durability for the period it is intended for, i.e., hours to years
- Be easy to process with the available techniques
- Be sterilizable with current facilities without any difficulty
- Be cost-effective and accessible

4.3 Types of biomaterials

Depending on the chemical bonding, materials can be categorized into three broad groups. These are (i) polymers, (ii) ceramics, and (iii) metals. Because these material structures vary by their nature of bonding (covalent, ionic or metallic), they have different properties, and hence different uses in the body (Table 4.2). Different kinds of biomaterials and chemical bonds associated with it are shown in Figure 4.4. Metals and ceramics are differentiated in the field of materials engineering, although they are both

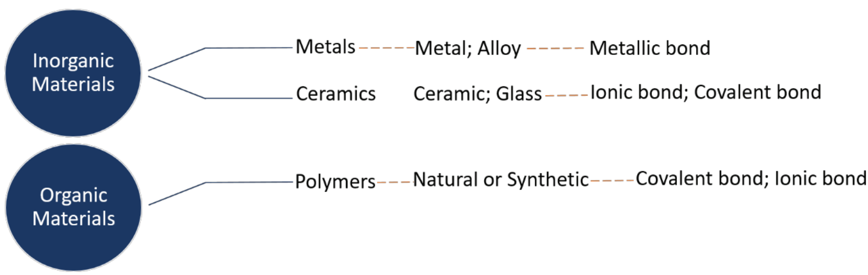

Figure 4.4: Different kinds of biomaterials and chemical bonds associated with them (Gul *et al*., 2020; He *et al*., 2017; Zindani *et al*., 2019).

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Table 4.2: Classification of biomaterials and typical properties associated with them (Wagner, 2020).

Attributes	Polymers	Metals & Alloys	Ceramics
Type of bonds present	Covalent & van der Waals forces	Metallic	Ionic/Covalent
Melting point	Low	Intermediate	High
Chemical stability	Poor	Good	Very high
Electrical conductivity	Very low	High	Very low, but varies
Thermal conductivity	Very low to intermediate	High	Low
Properties and advantages	Degradable, inert, similar density to soft tissues and ease of processing	High strength and hardness	Non-conductive and inert; closely mimic biological properties of bone
Mechanical deformation	Very high, plastic (can be easily shaped and processed)	High (ductile)	Low (brittle)
Major issues	Thermally unstable; low strength	Wear and corrosion	High density and brittle
Biomedical applications	Soft tissue implants; drug delivery systems; tissue engineering	Hard tissue applications (Orthopedic and dental implants)	Tissue engineering

inorganic compounds. Each material has its own benefits and drawbacks, and its biomedical applications are decided according to its individual properties and intended place substitution.

4.3.1 *Metals*

Metals are the most widely known biomedical materials and are indispensable in the medical field. Nearly all of the metal biomaterials are crystalline in nature, i.e., with regular atomic arrangements. Metals have great strength, resistance to fracture toughness, better elasticity, and rigidity compared with ceramics and polymers. Their outstanding

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mechanical reliability properties are controlled by dislocation and crystallization. For this reason, metals are extensively employed for load-bearing implant applications such as orthopaedic, dental, and maxillofacial surgery. Apart from these, metals are also used in making stents and stent-grafts for cardiovascular surgeries. The most common metals and alloys used for biomedical applications are stainless steel, titanium, titanium-based alloys, cobalt-based alloys, magnesium-based alloys, and tantalum-based alloys.

4.3.2 *Ceramics*

Ceramics are inorganic solid materials consisting of metallic and non-metallic elements that are predominantly bound together by ionic bonds. They exist as both crystalline and non-crystalline (amorphous) compounds. Ceramics are typically characterized by excellent biocompatibility, high corrosion resistance, high wear, high strength, extremely high stiffness, and hardness. The advancement of ceramic material applications in the biomedical industry has focused mostly on orthopaedics and dentistry. Bioinert ceramics such as alumina (Al_2O_3), zirconia (Zr_2O_3) and pyrolytic carbon, and bioresorbable ceramics such as calcium phosphates are some of the widely employed bioceramics.

4.3.3 *Polymers*

Polymers are macromolecules and they represent a major and versatile class of biomaterials being widely applied in biomedical applications due to their low toxicity in biological fluids, easy pre/post-processing, sterilization, better shelf life, lightweight nature, and remarkable physical and chemical properties.

Biomaterial use is primarily dependent on the need, function, and environment of the intended application. In a variety of implants, metal, polymers, ceramics, and composites are being used. The specific material or material combinations for use in a device will significantly affect both its patient performance and marketing potential. The next three chapters will discuss in detail each of the material types.

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4.4 Multiple choice questions

1. Biomaterials
   (a) are always synthetic materials; natural materials are not employed
   (b) are always natural materials; synthetic materials are not employed
   (c) can be natural or synthetic materials
   (d) are always polymeric materials

2. Select the statement which correctly relates to biocompatibility.
   (a) a biocompatible material should provide healing characters
   (b) a biocompatible material should have therapeutic characteristics
   (c) a material is considered as a biocompatible material as long as it causes no harm to the host body
   (d) a biocompatible material should have the exact dimensions as the damaged tissue or part

3. Select the option(s) which do(es) NOT come under the class of biocompatible materials.
   (a) eyeglasses; wheelchair
   (b) contact lenses; dental implants
   (c) orthopedic implant; stents
   (d) external hip prosthesis; massage footwear

4. Which of the following has the best osteointegration properties?
   (a) SS316
   (b) porous titanium
   (c) Co-Cr alloys
   (d) all of the above

5. Which of the following is/are biomaterial(s)?
   I. materials used for tooth filling
   II. materials used for cardiovascular repairs
   III. glucose meters and stethoscopes
   IV. materials used for hip implants
      (a) only I
      (b) only I, II and IV
      (c) only I, III and IV
      (d) only III

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6. Select the option(s) which is/are TRUE about biodegradation.
   (a) it depends on the molecular architecture
   (b) it is a precise breakdown of the material over time
   (c) metals biodegrade faster than polymeric materials
   (d) all of the above

7. Which class of biomaterials has chemical structures similar to bone?
   (a) polymeric biomaterials
   (b) ceramic biomaterials
   (c) metallic biomaterials
   (d) all of the above

8. Which class of biomaterials encourages bonding with surrounding tissues and stimulates new bone growth?
   (a) bioinert ceramics
   (b) bioactive ceramics
   (c) Co-Cr alloys
   (d) all of the above

9. Which of the following is TRUE?
   (a) ceramics possess excellent wear and friction properties
   (b) SS316, Co-Cr and Ti alloys form a protective oxide layer on their surfaces
   (c) bioceramics are more reactive then certain metallic implants
   (d) all of the above

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