**Biomaterials**

Biomaterials is an exciting and rapidly developing interdisciplinary field involving elements of materials science, engineering, biology, chemistry, and medicine. The biomaterials topic is designed to provide a broad basis in the fundamentals of biomaterials science and engineering.

**Definition**

Biomaterial - Any material of natural or synthetic origin that comes in contact with tissue, blood or biological fluids, and intended for use in prosthetic, diagnostic, therapeutic or storage application.

**Factors that govern biomaterial choice**

* Bulk properties: The use of biomaterial in particular applications is often dictated by bulk properties; Mechanical (Eg. modulus, strength & toughness for load-bearing applications, wear resistance for articulating surfaces, flexibility & compliance for vascular and soft tissues.), Chemical (Eg. degradation) and Optical (Eg. whiteness, clarity) matched to those of natural organs.
* Ability to Process

**Requirements of Biomaterials**

A biomaterial should broadly satisfy the following requirements;

* Biocompatibility - the ability of a material to perform with an appropriate host response in a specific application. The biomaterials must neither degrade in its properties within the body (unless this is wanted), nor biomaterials/devices (and any degradation product) must cause any adverse reaction within the host´s body. Biocompatibility is strongly determined by the primary chemical structure of the material.
* Biofunctionality - The material must satisfy its design requirements. Eg: Articulation to allow movement (e.g. artificial knee joint), load transmission and stress distribution etc.
* Inert or specifically interactive
* Mechanically and chemically stable - tensile strength, yield strength, elastic modulus, corrosion and fatigue resistance, surface finish, creep, and hardness.
* Processable (for manufacturability) - should be machinable, moldable and extrudable
* Sterilizable

**Types of Biomaterials**

The biomaterials are divided into four classes: – Metals, Ceramics (including glasses), Composites and Polymers. The properties and safety of materials must be carefully assessed with respect to the specific application. Metals are susceptible to degradation by corrosion, a process that can release by-products that may cause adverse biological responses. Ceramics are attractive as biological implants for their biocompatibility. The availability of a wide range of polymers significantly influenced the growth of tissue engineering and controlled drug delivery technologies. Innovations in the composite material design and fabrication processes are raising the possibility of realizing implants with improved performance.

1. ***Metals and alloys***

Metals are widely used as biomaterials due to their favorable mechanical properties like strength and toughness, especially fracture toughness and fatigue strength. The type of bonding (closely packed crystal structure) in metals and metal alloys render them valuable exclusively for load- bearing implants, such as hip and knee prostheses and fracture fixation wires, pins, screws, and plates. Their properties depend on the processing method and purity of the metal. When processed suitably they contribute high tensile, fatigue and yield strengths; low reactivity and good ductility. Although pure metals are sometimes used, alloys frequently provide an improvement in material properties, such as strength and corrosion resistance. The main considerations in selecting metals and alloys for biomedical applications are their excellent electrical and thermal conductivity, biocompatibility, appropriate mechanical properties, corrosion resistance, and reasonable cost.

The human body is an aggressive medium for inducing corrosion in metals: water, dissolved oxygen, proteins, chloride and hydroxide. The biocompatibility of the metallic implant is of considerable concern because these implants can corrode in an *in vivo* environment. The corrosion of the implant material will weaken the implant, and the corrosion products induce a toxic effect on the surrounding tissues and organs. Hence to avoid corrosion, the composition of the biological environment (ions, pH, oxygen pressure, etc.) should be considered. Choice of appropriate metals, avoiding implantation of dissimilar metals and minimizing pits and crevices on the metal surface can reduce corrosion. Three material groups dominate biomedical metals: Stainless steel, titanium and titanium alloys and cobalt-chromium-molybdenum alloy.

*Stainless steel* (most common 316L) used in orthopedics (Eg. Joint replacements, screws) and dental implants has 60-65% Fe, 17-19% Cr, 12-14% Ni, > 0.030% C and minor amounts of N, Mn, Mo, P, Si, and S. The low carbon content enables better resistance to *in vivo* corrosion, chromium for corrosion resistance by formation of surface oxide and nickel improves strength. Due to the potential long-term release of Ni2+, Cr3+ and Cr6+ restricted to temporary devices.

*Ti alloys* due to the combination of its excellent characteristics such as high strength, low density, lightweight, high specific strength, good resistance to corrosion, complete inertness to body environment, enhanced biocompatibility, good mechanical properties are a suitable choice for implantation. TiO2 layer provides good corrosion resistance to stress corrosion cracking and corrosion fatigue in body fluids. But, titanium has unsatisfactory wear. Eg. heart pacemakers, artificial heart valves, Bone and Joint Replacements

*Co-Cr-Mo alloy-* Cobalt-based alloys are highly resistant to corrosion even in chloride environment due to spontaneous formation of passive oxide layer within the human body environment. The thermal treatments used to Co-Cr-Mo alloys modify the microstructure of the alloy alters the electrochemical and mechanical properties of the biomaterial. The corrosion products of Co-Cr-Mo are more toxic than those of stainless steel 316L.

1. ***Ceramics***

Inorganic polycrystalline compounds that contain metallic and non-metallic elements. High oxidized state and inter-atomic ionic/covalent bonding in ceramics make them resistant to oxidation, increasingly stable and non-conducting. Ceramic biomaterials have been used less extensively than either metals or polymers. The bioceramics are highly chemically inert in the body, hard, possess excellent corrosion resistance, high wear resistance, high modulus (stiffness) & compressive strength and fine aesthetic properties (for dental applications), but they are difficult to fabricate. Ceramics are used in several areas like dentistry, orthopedics, and as medical sensors.

Eg: Alumina, Zirconium, Calcium phosphate, Silica, hydroxyapatite

Bioceramics are of three basic types: bioinert, bioactive and bioresorbable ceramics.

1. *Bioinert* refers to a material that retains its structure in the body after implantation and does not induce any immunologic host reactions.

Eg. Alumina (Al2O3) is used in loadbearing hip prostheses and dental implants, because of its combination of excellent corrosion resistance, good biocompatibility, high wear resistance and high strength. These properties are attributed to ionic bonding/electrostatic interactions with the charges on the proteins. The reasons for the excellent wear and friction behavior of alumina are associated with the surface energy and surface smoothness of this ceramic.

1. *Bioactive* refers to materials that form direct chemical bonds with bone or even with the soft tissue of a living organism.

Eg. Bioglass and glass-ceramics widely used for filling bone defects permit modification of the surface that occurs upon implantation. Bonding to bone is due to specific amounts of ionic network formers: SiO2 and P2O5 and network modifiers: Na2O and CaO. They are partially soluble *in vivo*, which facilitates direct chemical bond with bone, which includes a slight solubility of the glass ceramic and a solid state reaction between the stable apatite crystals in the glass ceramic and the bone. The porosity of bioglass is beneficial for resorption and bioactivity.

1. *Bioresorbable* refers to materials that degrade by a hydrolytic breakdown in the body, while they are being replaced by regenerating natural tissue; the chemical byproducts of the degrading materials are absorbed and released via metabolic processes of the body.

Eg. Calcium phosphate ceramics have ideal pore size similar to that of spongy bone, and hence bond to living the bone-like apatite layer on their surface.

Ceramics typically fail due to little plastic deformation, and they are sensitive to the presence of cracks or other defects, has low tensile strength and poor fatigue resistance. They are brittle and relatively difficult to process.

1. ***Polymers***

Polymers are the most widely used materials in biomedical applications. The unique properties of the polymeric biomaterials compared to metal or ceramic materials are flexibility, ease of manufacture to produce various shapes (latex, film, sheet and fibers), ease of secondary processability, surface modification, reasonable cost, resistance to biochemical attack, good biocompatibility, light weight, availability in a wide variety of compositions with tailorable physical and mechanical properties. But they are leachable, absorb water and proteins, allows surface contamination, wear and tear and difficult to sterilize.

Eg: Polymethylmethacrylate (PMMA) is used as intraocular lenses due to its high refractive index, easily processability, environmental stability (relatively inert) and good mechanical properties.

Surfaces of materials are high-energy regions and thereby facilitate chemical reactions that influence the performance of biomaterials. Eg. Some biopolymers are susceptible to chemical reactions that lead to degradation through hydrolysis. However, in some cases, a polymer is specifically chosen for its ability to degrade *in vivo*.

Polymer hydrolysis involves the scission of susceptible molecular groups by reaction with H2O, catalyzed by acid, base or enzyme.

Molecular and structural factors influencing hydrolysis are

1. Bond Stability - Susceptible linkages at bonds where resonance stabilized intermediates are possible.
2. Hydrophobicity: ↑ hydrophobicity ⇒ ↓ hydrolysis
3. MW & architecture: higher MW ⇒ ↓ hydrolysis
4. Morphology: crystallinity ↓ hydrolysis

crystallinity ↓ solubility

porosity ↑ hydrolysis

1. Tg: less mobility ⇒ ↓ hydrolysis

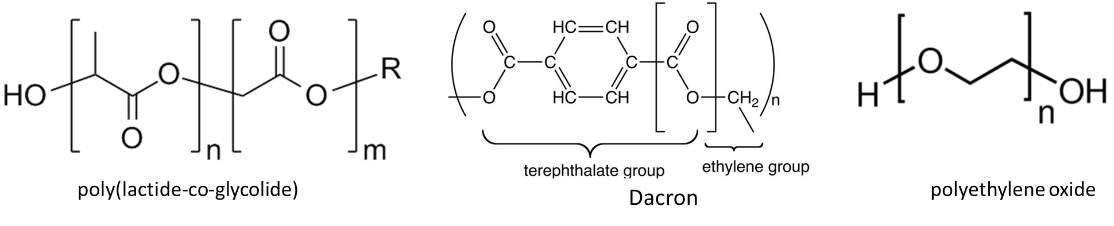
Rates of Hydrolysis: anhydride > ester > amide > ether

Esters: R-COO-R’ + H2O → R-COOH + HO-R’

An amorphous poly(lactide-co-glycolide) with rapid degradation property is used as bioresorbable sutures, controlled release matrices, tissue engineering scaffolds etc. Whereas, semicrystalline polyethylene terephthalate (Dacron) with very slow hydrolysis property find application in vascular grafts, arterial patches, heart pumps etc.

Ethers: R-O-R’ + H2O → R-CH2-OH + HO-CH2-R’

Semicrystalline polyethylene oxide (PEO) used for protein resistant coatings and hydrogels is flexible, hydrolyzable, water soluble and bioinert. These properties are derived from both primary and strong secondary H-bonding.



However, some olefins (e.g., Ultrahigh molecular weight polyethylene-UHMWPE: joint cup liners), halogenated hydrocarbons (e.g., PVC: catheters; PTFE: vascular grafts), siloxanes (e.g., PDMS: soft tissue prostheses) and sulfones (e.g., PSF: renal dialysis membranes) exhibit stable polymer chemistry

1. ***Composites***

Natural biocomposites include bone, wood, dentin, cartilage, and skin. Bone achieves most of its mechanical properties as a natural composite material composed of calcium phosphate ceramics in a highly organized polymeric collagen matrix. Biocomposites are composite materials composed of a biodegradable matrix and biodegradable natural fibers as reinforcement in order to obtain properties that improve every one of the components. Composite materials allow a flexible design since their structure and properties can be optimized and tailored to specific applications. Eg. fiberglass with a polymeric matrix is used in the current synthetic casting materials. The use of composite materials for biomedical applications offers many new options and possibilities for implants design. The implant structure and its interactions with the surrounding tissues can be optimized by varying the constituents, the type, and distribution of the reinforcing phase and adding coupling agents. The composite materials and components can be designed to obtain a wide range of mechanical and biological properties.