

# Biomaterial

A **biomaterial** is a substance that has been engineered to interact with biological systems for a medical purpose, either a therapeutic (treat, augment, repair, or replace a tissue function of the body) or a diagnostic one. As a science, **biomaterials** is about fifty years old. The study of biomaterials is called **biomaterials science** or **biomaterials engineering**. It has experienced steady and strong growth over its history, with many companies investing large amounts of money into the development of new products. Biomaterials science encompasses elements of medicine, biology, chemistry, tissue engineering and materials science.



A hip implant is an example of an application of biomaterials

Note that a biomaterial is different from a biological material, such as bone, that is produced by a biological system. Additionally, care should be exercised in defining a biomaterial as biocompatible, since it is application-specific. A biomaterial that is biocompatible or suitable for one application may not be biocompatible in another.<sup>[1]</sup>

## IUPAC definition

*Material exploited in contact with living tissues, organisms, or microorganisms.*<sup>[2][a][b][c]</sup>

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## Introduction

Biomaterials can be derived either from nature or synthesized in the laboratory using a variety of chemical approaches utilizing metallic components, polymers, ceramics or composite materials. They are often used and/or adapted for a medical application, and thus comprise whole or part of a living structure or biomedical device which performs, augments, or replaces a natural function. Such functions may be relatively passive, like being used for a heart valve, or maybe bioactive with a more interactive functionality such as hydroxy-apatite coated hip implants. Biomaterials are also used every day in dental applications, surgery, and drug delivery. For example, a construct with impregnated pharmaceutical products can be placed into the body, which permits the prolonged release of a drug over an extended period of time. A biomaterial may also be an autograft, allograft or xenograft used as a transplant material.

## Bioactivity

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The ability of an engineered biomaterial to induce a physiological response that is supportive of the biomaterial's function and performance is known as bioactivity. Most commonly, in bioactive glasses and bioactive ceramics this term refers to the ability of implanted materials to bond well with surrounding tissue in either osseoconductive or osseoproductive roles.<sup>[4]</sup> Bone implant materials are often designed to promote bone growth while dissolving into surrounding body fluid.<sup>[5]</sup> Thus for many biomaterials good biocompatibility along with good strength and dissolution rates are desirable. Commonly, bioactivity of biomaterials is gauged by the surface biomineralisation in which a native layer of hydroxyapatite is formed at the surface. These days, the development of clinically useful biomaterials is greatly enhanced by the advent of computational routines that can predict the molecular effects of biomaterials in a therapeutic setting based on limited *in vitro* experimentation.<sup>[6]</sup>

## Self-assembly

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Self-assembly is the most common term in use in the modern scientific community to describe the spontaneous aggregation of particles (atoms, molecules, colloids, micelles, etc.) without the influence of any external forces. Large groups of such particles are known to assemble themselves into thermodynamically stable, structurally well-defined arrays, quite reminiscent of one of the seven crystal systems found in metallurgy and mineralogy (e.g. face-centered cubic, body-centered cubic, etc.). The fundamental difference in equilibrium structure is in the spatial scale of the unit cell (lattice parameter) in each particular case.

Molecular self assembly is found widely in biological systems and provides the basis of a wide variety of complex biological structures. This includes an emerging class of mechanically superior biomaterials based on microstructural features and designs found in nature. Thus, self-assembly is also emerging as a new strategy in chemical synthesis and nanotechnology. Molecular crystals, liquid crystals, colloids, micelles, emulsions, phase-separated polymers, thin films and self-assembled monolayers all represent examples of the types of highly ordered structures, which are obtained using these techniques. The distinguishing feature of these methods is self-organization.<sup>[7][8][9]</sup>

## Structural hierarchy

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Nearly all materials could be seen as hierarchically structured, since the changes in spatial scale bring about different mechanisms of deformation and damage. However, in biological materials, this hierarchical organization is inherent to the microstructure. One of the first examples of this, in the history of structural biology, is the early X-ray scattering work on the hierarchical structure of hair and wool by Astbury and Woods.<sup>[10]</sup> In bone, for example, collagen is the building block of the organic matrix, a triple helix with diameter of 1.5 nm. These tropocollagen molecules are intercalated

with the mineral phase (hydroxyapatite, calcium phosphate) forming fibrils that curl into helicoids of alternating directions. These "osteons" are the basic building blocks of bones, with the volume fraction distribution between organic and mineral phase being about 60/40.

In another level of complexity, the hydroxyapatite crystals are mineral platelets that have a diameter of approximately 70 to 100 nm and thickness of 1 nm. They originally nucleate at the gaps between collagen fibrils.<sup>[11]</sup>

Similarly, the hierarchy of abalone shell begins at the nanolevel, with an organic layer having a thickness of 20 to 30 nm. This layer proceeds with single crystals of aragonite (a polymorph of  $\text{CaCO}_3$ ) consisting of "bricks" with dimensions of 0.5 and finishing with layers approximately 0.3 mm (mesostructure).<sup>[12]</sup>

Crabs are arthropods, whose carapace is made of a mineralized hard component (exhibits brittle fracture) and a softer organic component composed primarily of chitin. The brittle component is arranged in a helical pattern. Each of these mineral 'rods' (1  $\mu\text{m}$  diameter) contains chitin–protein fibrils with approximately 60 nm diameter. These fibrils are made of 3 nm diameter canals that link the interior and exterior of the shell.

## Applications

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Biomaterials are used in:

1. Joint replacements
2. Bone plates <sup>[13]</sup>
3. Intraocular lenses (IOLs) for eye surgery
4. Bone cement
5. Artificial ligaments and tendons
6. Dental implants for tooth fixation
7. Blood vessel prostheses
8. Heart valves
9. Skin repair devices (artificial tissue)
10. Cochlear replacements
11. Contact lenses
12. Breast implants
13. Drug delivery mechanisms
14. Sustainable materials
15. Vascular grafts
16. Stents
17. Nerve conduits
18. Surgical sutures, clips, and staples for wound closure<sup>[14][15]</sup>
19. Pins and screws for fracture stabilisation<sup>[16]</sup>
20. Surgical mesh<sup>[17][18]</sup>

Biomaterials must be compatible with the body, and there are often issues of biocompatibility, which must be resolved before a product can be placed on the market and used in a clinical setting. Because of this, biomaterials are usually subjected to the same requirements as those undergone by new drug therapies.<sup>[19][20]</sup> All manufacturing companies are also required to ensure traceability of all of their products, so that if a defective product is discovered, others in the same batch may be traced.

## Heart valves

In the United States, 49% of the 250,000 valve replacement procedures performed annually involve a mechanical valve implant. The most widely used valve is a bileaflet disc heart valve or St. Jude valve. The mechanics involve two semicircular discs moving back and forth, with both allowing the flow of blood as well as the ability to form a seal against backflow. The valve is coated with pyrolytic carbon and secured to the surrounding tissue with a mesh of woven fabric called Dacron (du Pont's trade name for polyethylene terephthalate). The mesh allows for the body's tissue to grow, while incorporating the valve.<sup>[21]</sup>

## Skin repair

Most of the time, "**Artificial' tissue**" is grown from the patient's own cells. However, when the damage is so extreme that it is impossible to use the patient's own cells, artificial tissue cells are grown. The difficulty is in finding a scaffold that the cells can grow and organize on. The characteristics of the scaffold must be that it is biocompatible, cells can adhere to the scaffold, mechanically strong and biodegradable. One successful scaffold is a copolymer of lactic acid and glycolic acid.<sup>[21]</sup>

## Compatibility

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Biocompatibility is related to the behavior of biomaterials in various environments under various chemical and physical conditions. The term may refer to specific properties of a material without specifying where or how the material is to be used. For example, a material may elicit little or no immune response in a given organism, and may or may not be able to integrate with a particular cell type or tissue. Immuno-informed biomaterials that direct the immune response rather than attempting to circumvent the process is one approach that shows promise.<sup>[22]</sup> The ambiguity of the term reflects the ongoing development of insights into "**how biomaterials interact with the human body**" and eventually "**how those interactions determine the clinical success of a medical device (such as pacemaker or hip replacement)**". Modern medical devices and prostheses are often made of more than one material, so it might not always be sufficient to talk about the biocompatibility of a specific material.<sup>[23]</sup> Surgical implantation of a biomaterial into the body triggers an organism-inflammatory reaction with the associated healing of the damaged tissue. Depending upon the composition of the implanted material, the surface of the implant, the mechanism of fatigue, and chemical decomposition there are several other reactions possible. These can be local as well as systemic. These include immune response, foreign body reaction with the isolation of the implant with a vascular connective tissue, possible infection, and impact on the lifespan of the implant. Graft versus host disease is an auto- and alloimmune disorder, exhibiting a variable clinical course. It can manifest in either acute or chronic form, affecting multiple organs and tissues and causing serious complications in clinical practice, both during transplantation and implementation of biocompatible materials.<sup>[24]</sup>

## Biocompatible plastics

Some of the most commonly-used biocompatible materials (or biomaterials) are polymers due to their inherent flexibility and tunable mechanical properties. Medical devices made of plastics are often made of a select few including: cyclic olefin copolymer (COC), polycarbonate (PC), polyetherimide (PEI), medical grade polyvinylchloride (PVC), polyethersulfone (PES), polyethylene (PE), polyetheretherketone (PEEK) and even polypropylene (PP). To ensure biocompatibility, there are a series of regulated tests that material must pass to be certified for use. These include the United States Pharmacopoeia IV (USP Class IV) Biological Reactivity Test and the International Standards Organization 10993 (ISO 10993) Biological Evaluation of Medical Devices. The main objective of

biocompatibility tests is to quantify the acute and chronic toxicity of material and determine any potential adverse effects during use conditions, thus the tests required for a given material are dependent on its end-use (i.e. blood, central nervous system, etc.).<sup>[25]</sup>

## Mechanical properties

In addition to a material being certified as biocompatible, biomaterials must be engineered specifically to their target application within a medical device. This is especially important in terms of mechanical properties which govern the way that a given biomaterial behaves. One of the most relevant material parameters is the Young's Modulus,  $E$ , which describes a material's elastic response to stresses. The Young's Moduli of the tissue and the device that is being coupled to it must closely match for optimal compatibility between device and body, whether the device is implanted or mounted externally. Matching the elastic modulus makes it possible to limit movement and delamination at the biointerface between implant and tissue as well as avoiding stress concentration that can lead to mechanical failure. Other important properties are the tensile and compressive strengths which quantify the maximum stresses a material can withstand before breaking and may be used to set stress limits that a device may be subject to within or external to the body. Depending on the application, it may be desirable for a biomaterial to have high strength so that it is resistant to failure when subjected to a load, however in other applications it may be beneficial for the material to be low strength. There is a careful balance between strength and stiffness that determines how robust to failure the biomaterial device is. Typically, as the elasticity of the biomaterial increases, the ultimate tensile strength will decrease and vice versa. One application where a high-strength material is undesired is in neural probes; if a high-strength material is used in these applications the tissue will always fail before the device does (under applied load) because the Young's Modulus of the dura mater and cerebral tissue is on the order of 500 Pa. When this happens, irreversible damage to the brain can occur, thus the biomaterial must have an elastic modulus less than or equal to brain tissue and a low tensile strength if an applied load is expected.<sup>[26][27]</sup>

For implanted biomaterials that may experience temperature fluctuations, e.g. dental implants, ductility is important. The material must be ductile for a similar reason that the tensile strength cannot be too high, ductility allows the material to bend without fracture and also prevents the concentration of stresses in the tissue when the temperature changes. The material property of toughness is also important for dental implants as well as any other rigid, load-bearing implant such as a replacement hip joint. Toughness describes the material's ability to deform under applied stress without fracturing and having a high toughness allows biomaterial implants to last longer within the body, especially when subjected to large stress or cyclically-loaded stresses, like the stresses applied to a hip joint during running.<sup>[26]</sup>

For medical devices that are implanted or attached to the skin, another important property requiring consideration is the flexural rigidity,  $D$ . Flexural rigidity will determine how well the device surface can maintain conformal contact with the tissue surface, which is especially important for devices that are measuring tissue motion (strain), electrical signals (impedance), or are designed to stick to the skin without delaminating, as in epidermal electronics. Since flexural rigidity depends on the thickness of the material,  $h$ , to the third power ( $h^3$ ), it is very important that a biomaterial can be formed into thin layers in the previously mentioned applications where conformality is paramount.<sup>[28]</sup>

## Biopolymers

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**Biopolymers** are polymers produced by living organisms. Cellulose and starch, proteins and peptides, and DNA and RNA are all examples of biopolymers, in which the monomeric units, respectively, are sugars, amino acids, and nucleotides.<sup>[29]</sup> Cellulose is both the most common biopolymer and the most common organic compound on Earth. About 33% of all plant matter is

cellulose.<sup>[30][31]</sup> On a similar manner, silk (proteinaceous biopolymer) has garnered tremendous research interest in a myriad of domains including tissue engineering and regenerative medicine, microfluidics, drug delivery.<sup>[32][33]</sup>

## See also

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- [Bionics](#)
- [Hydrogel](#)
- [Polymeric surface](#)
- [Surface modification of biomaterials with proteins](#)
- [Synthetic biodegradable polymer](#)
- [List of biomaterials](#)

## Footnotes

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1. The notion of exploitation includes utility for applications and for fundamental research to understand reciprocal perturbations as well.<sup>[2]</sup>
2. The definition “non-viable material used in a medical device, intended to interact with biological systems” recommended in ref.<sup>[3]</sup> cannot be extended to the environmental field where people mean “material of natural origin”.<sup>[2]</sup>
3. This general term should not be confused with the terms *biopolymer* or *biomacromolecule*. The use of “polymeric biomaterial” is recommended when one deals with polymer or polymer device of therapeutic or biological interest.<sup>[2]</sup>

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