UNIVERSITÁ DEGLI STUDI DI TERAMO

Biomaterials in Tissue Engineering

INTRODUCTION TO BIOMATERIALS

Biomaterials Sciences

- The properties and applications of materials (synthetic vs. natural) that are used in contact with biological system (Ratner and Hoffman, 2004)
- The combination of several advance fields including medical, biology, materials science and chemistry in developing a medical device/apparatus/implant

INTRODUCTION TO BIOMATERIALS

1980's

Any *systemically, pharmacologically inert* substance (other than drugs) or combination of substances of synthetic or natural origin, *used for implantation within or incorporation with a living system* for any period of time, to **treats, augments, or replaces any tissues, organ, or function of the body** **(Consensus Development Conference, Chester, UK, 1982)**

1990's

Bio-material *is a* ***non viable material*** *used in a medical device, intended to interact with biological system.* ***(Williams)***

Application of Biomaterials

Tissue Engineering

- Study of the growth of new connective tissues, or organs, from cells and a scaffold to produce a fully functional organ for implantation back into the donor host or by injecting/applying hydrogel.
- Hydrogel = self Healing Biomaterial.

Drug Delivery

- Refers to approaches, formulations, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effect. It is typically concerned with both quantity and duration of drug presence.

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Need for Biomaterials

- Millions of patients suffer end stage organ and tissue failure annually.

- 8 millions surgical procedures.

- Treatment options include transplantation, reconstruction, mechanical devices.

- Transplantation:
    - Clinical donor shortage
        - ✓ 3000 livers annually for 30000 people in need.
    - Disease transmission
        - ✓ HIV
        - ✓ Hepatitis
        - ✓ Other transmissible disease.

- Surgical Reconstruction
    - Not always possible
    - Complications

- Mechanical Device
  - Engineering approach – engineer new tissues, systems.
  - Limited by:
    - ✓ Complexity of the human body
    - ✓ Multiple functions
    - ✓ Living components *vs.* non-living components.

In the biomedical field, the goal is to develop and characterize artificial materials, or in other words, “spare parts” for use in the human body to **measure, restore** and **improve** <u>physical functions and enhance survival and quality of life.</u>

Biomaterials Properties

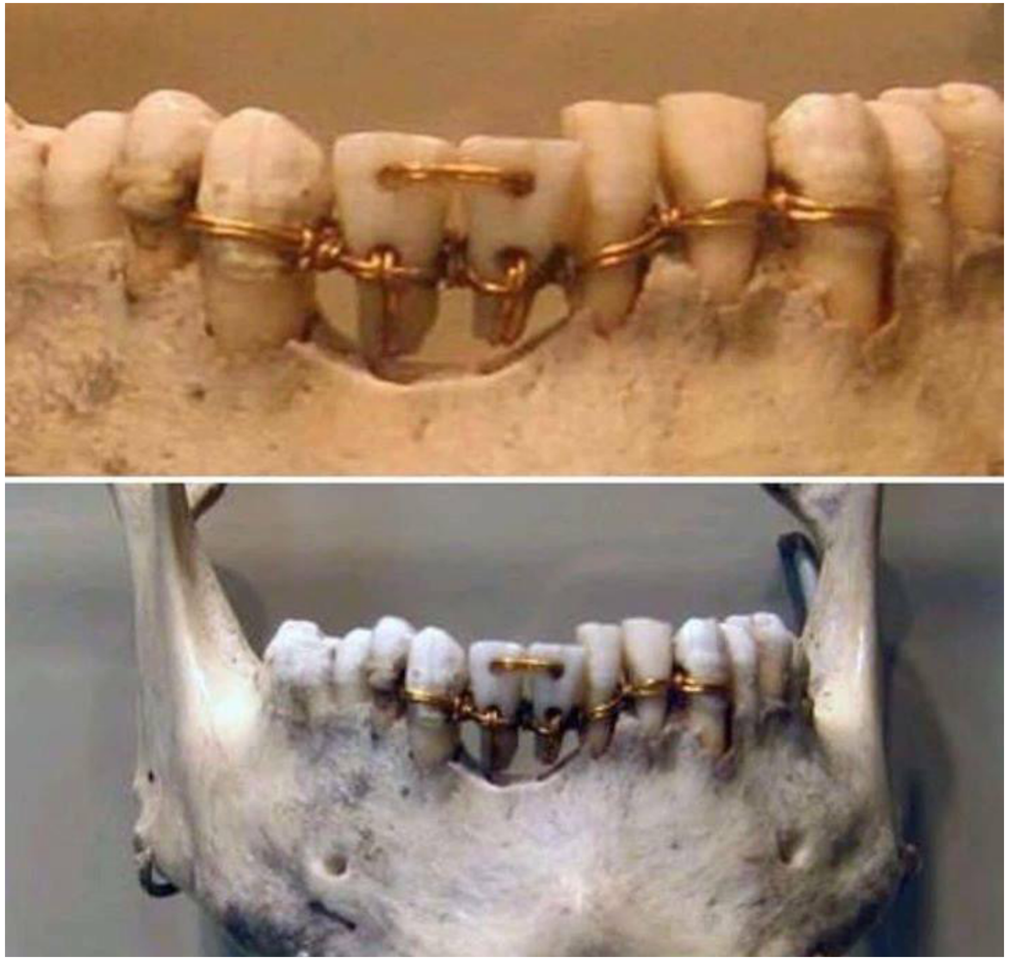
Biocompatible	• Able to perform within appropriate host response without having toxic or injurious effects on biological system
Adequate mechanical performance	• Has appropriate mechanical performance suitable for its application
Application design	• Structure design and selection of materials are compatible with its area of application
Repeatable fabrication	• Relatively inexpensive, reproducible, easy to fabricate and process for large-scale production

HISTORICAL DEVELOPMENT OF BIOMATERIALS

- Some of the earliest biomaterial applications were as far back as ancient Phoenicia where loose teeth were bound together with gold wires for tying artificial ones to neighboring teeth.

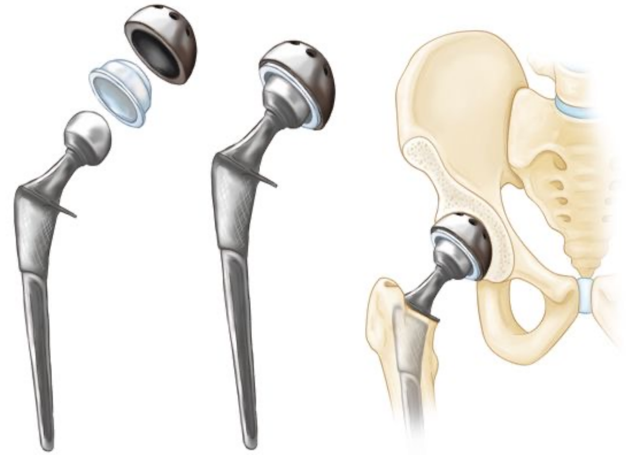
- Ancient Egyptians and Romans used vegetable fibers to sew skin lesions, and they were able to model wooden limb prostheses.

- In the early 1900’s bone plates were successfully implemented to stabilize bone fractures and to accelerate their healing.



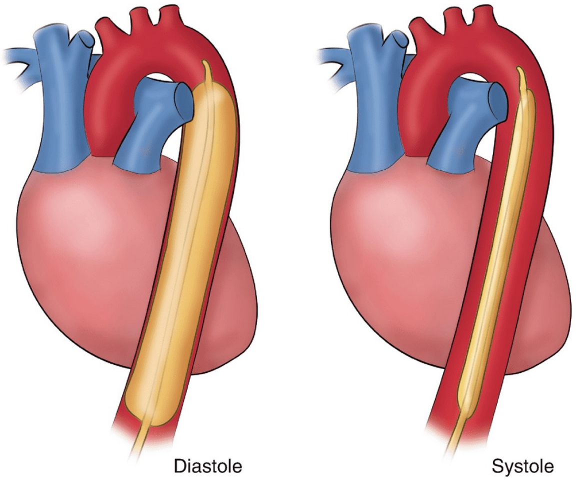
HISTORICAL DEVELOPMENT OF BIOMATERIALS

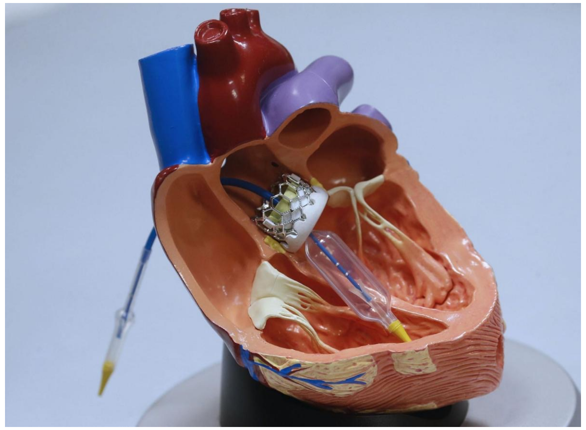
600 B.C	Samhita	Nose construction
1893-1912	W.A. Lane	Steel screws for fixation
1912	W.D. Sherman	Use of Vanadium steel plate
1938	P. Wiles	First total hip replacement



HISTORICAL DEVELOPMENT OF BIOMATERIALS

1952	A.B. Voorhees	Blood Vessel
1953	A. Kantrowitz	Intraortic balloon pumping
1960	M.I. Edwards	Heart valve
1980	W.J. Kolff	Artificial Heart





MATERIAL CLASSIFICATION

❑ First generation: INERT

- Do not tigger any reaction in the host: neither rejection nor recognition.
- "do not bring any good results"

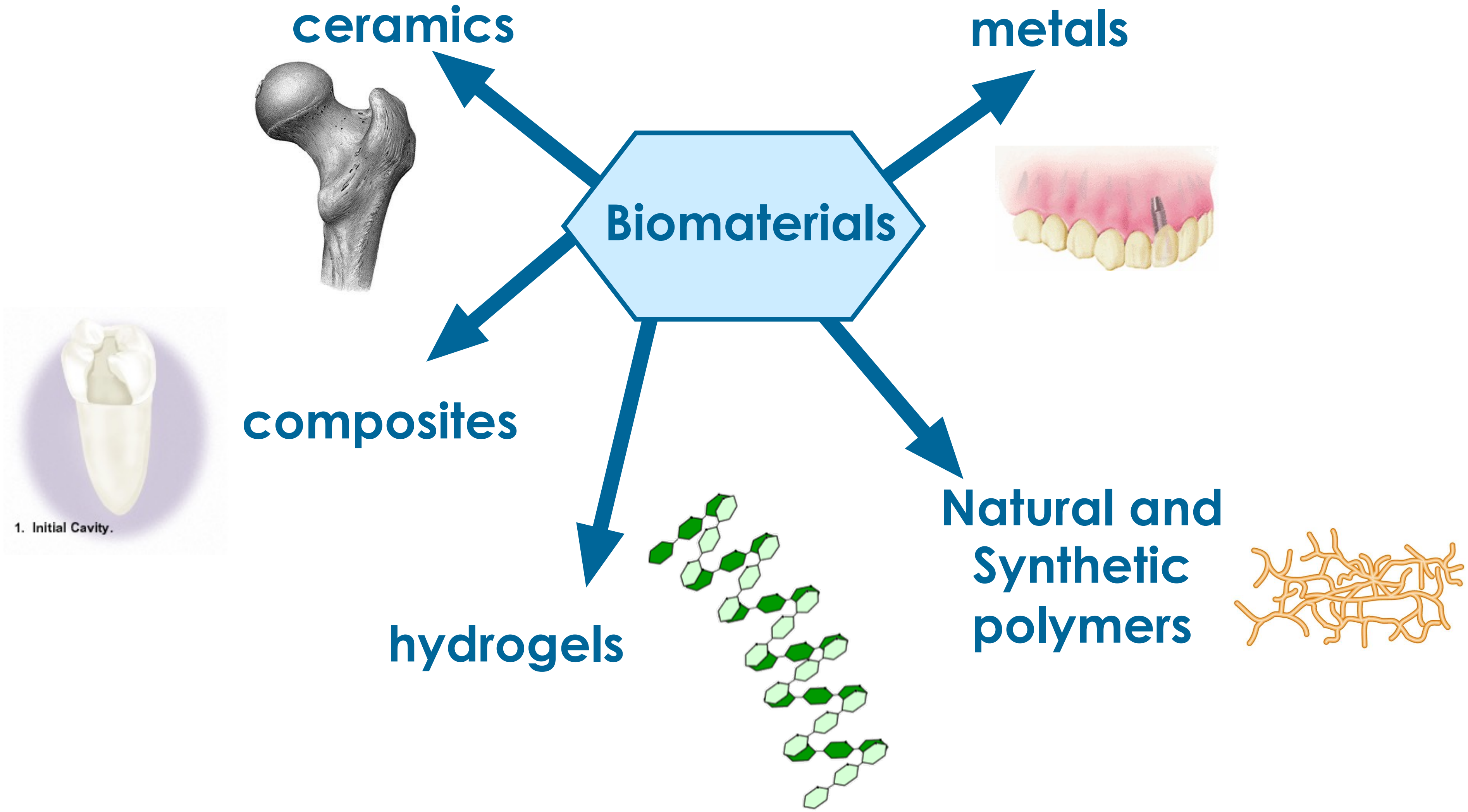
❑ Second generation: BIOACTIVE

- Ensure a more stable performance in a long time or for the period you want.

❑ Third generation: BIODEGRADABLE

- It can be chemically degraded or decomposed by natural effectors (temperature, environment, pH, enzyme)

MATERIAL CLASSIFICATION

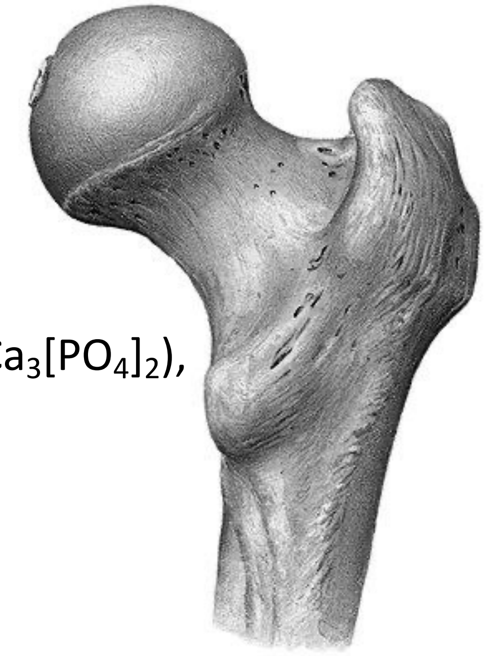


ceramics

- Inorganic compounds of natural or synthetic origin (metallic of nonmetallic elements).

- There are three categories based on their characteristics
  - Bio-inert ceramics
  - Resorbable materials
  - Bioactive ceramics

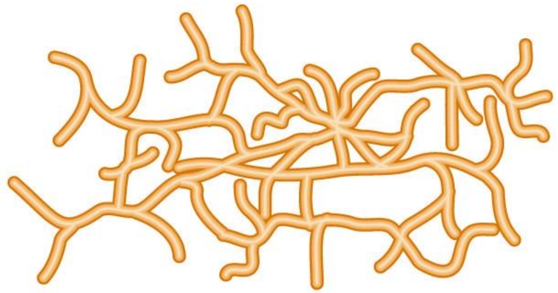
- Most common ceramics biomaterials are:
  - CaP, including hydroxyapatite (HA) ($Ca_{10}[PO_4]_6[OH]_2$), beta-tricalcium phosphate (BTF) ($Ca_3[PO_4]_2$), biphasic calcium phosphate (mixture of HA and BTF)
  - Bioactive glass: 45 wt% SiO_2, 24.5 wt% CaO, 24.5 wt% Na_2O, and 6.0 wt% P_2O_5.
  - Alumina (Al_2O_3),
  - Zirconia oxide (ZrO_2)



Natural and Synthetic Polymers

- Natural polymers:
  - Low mechanical properties.
  - Coupled with other materials to increase their mechanical properties.
  - Batch-to-batch variation.
  - Hybrid materials can be used to mimic ECM.

- Eight major classes based on their chemical structure:
  - Polysaccharides: Alginate, Chitosan obtained from Chitin, Hyaluronic acid from hyaluronan.
  - Proteins and other polyamides.
  - Polyhydoxyalkanoates (PHA) are polyoxoesters
  - Polythioesters
  - Polyanhydrides (polyphosphate)
  - Polysoprenoids
  - Lignin
  - Nucleic acid



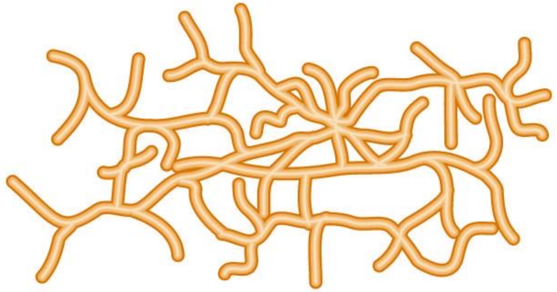
Collagen
Alginate
Cellulose
Proteoglycans
Chitin and chitosan
Hyaluronic acid

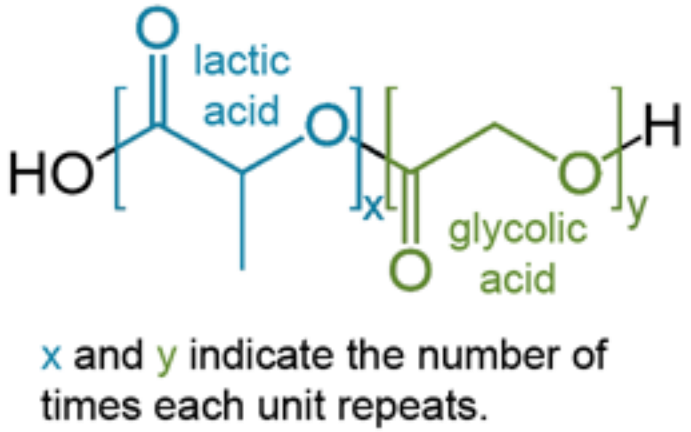
Natural and Synthetic Polymers

- Synthetic polymers are high molecular weight compounds composed of a series of monomeric units.

  - Form of fibers, films, bars, and viscous liquids,
  - Important advantage to modulate their mechanical properties and biodegradation by varying synthesis process and reactants used.
  - Classification: **Biodegradable** and **non-biodegradable**.

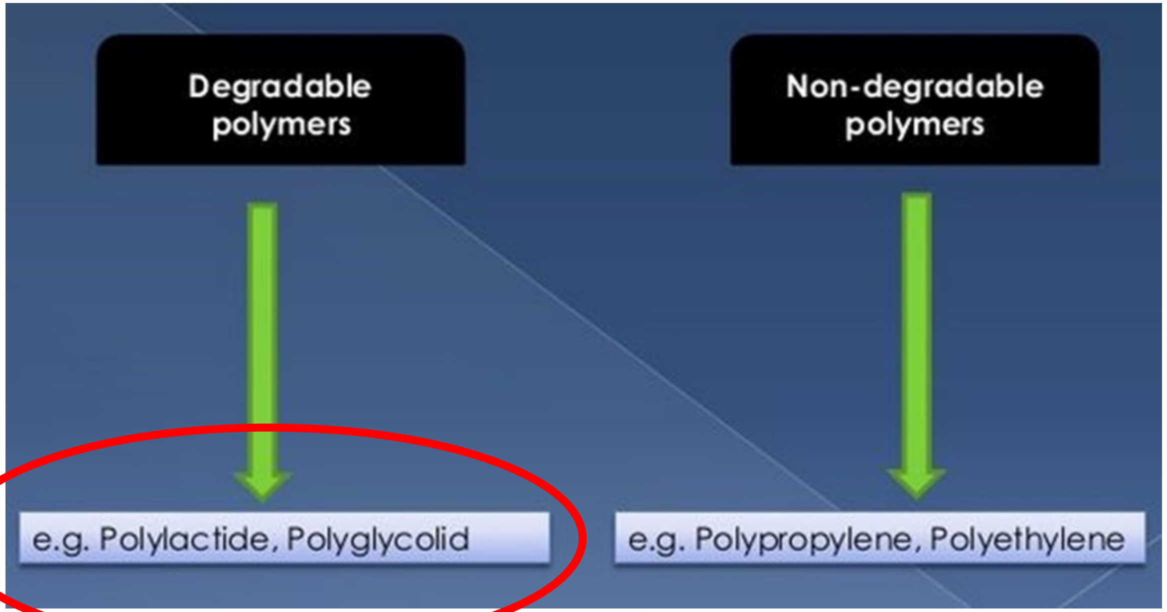
  - polystyrene, thermoplastic aromatic polymer with a linear structure;
  - poly-l-lactic acid (PLA), hydrophobic polymer with slow degradation rate,
  - polyglycolic acid (PGA), hydrophilic polymer with good mechanical properties and fast degradation;
  - poly-dl-lactic-co-glycolic acid (PLGA), biocompatible copolymers with regulated degradation rate;
  - polycaprolactone (PCL), highly hydrophobic polymer with good permeability.
  - polyethylene glycol (PEG) is not biodegradable, but below a certain molecular weight, it can be excreted through your kidney.
  - Poly(vinyl alcohol) (PVA), and polyacrylic acid (PAA) are some of the examples of non-biodegradable materials, which have been tried out for tissue engineering applications.





PLGA

Polymers Used for Biomimetic Scaffolds



Polyester family

Degradable polymers

Natural polymers	Fibrin	Collagen	Chitosan	Hyaluran	**Artificial biomimetic scaffolds**
Synthetic polymers	PLA, PGA, PLGA, PCL, Polyorthoesters …	Poly(dioxanone)	Poly(anhydrides)	Poly(trimethylene carbonate)	**Artificial biomimetic scaffolds**

…Why choose synthetic biocompatible polymers?

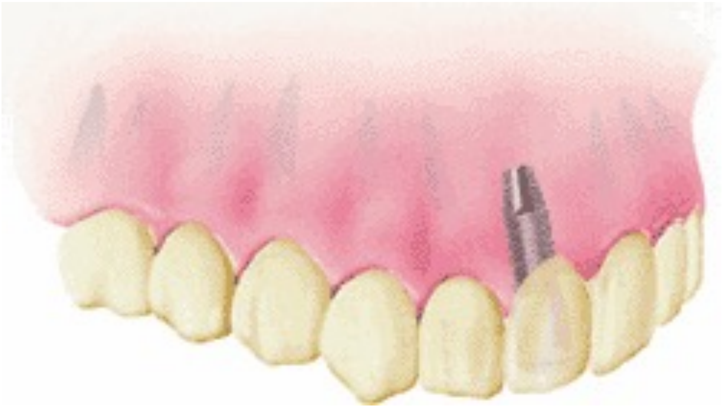
- Synthetic polymers are often cheaper than biologic ones.
- They can be produced in large uniform quantities and have a long shelf time.
- Many commercially available synthetic polymers show physicochemical and mechanical properties comparable to those of biological tissues.

Metals

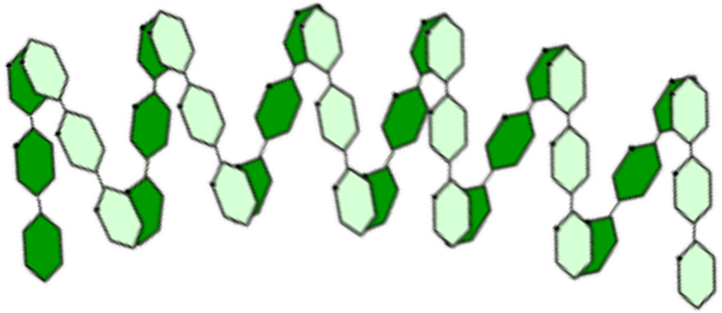
- Metals are particularly suitable for tissue engineering strategies for their good mechanical properties such as high elastic module, yield strength, and high ductility allowing them to bear a load without being deformed.

- If mechanical resistance makes them excellent candidates for scaffold production, however, the reduced cell adhesion to their surface could be a considerable limit to their use.

- Among the different metals used for scaffold production, there are stainless steel, cobalt, and titanium alloys.



Hydrogels

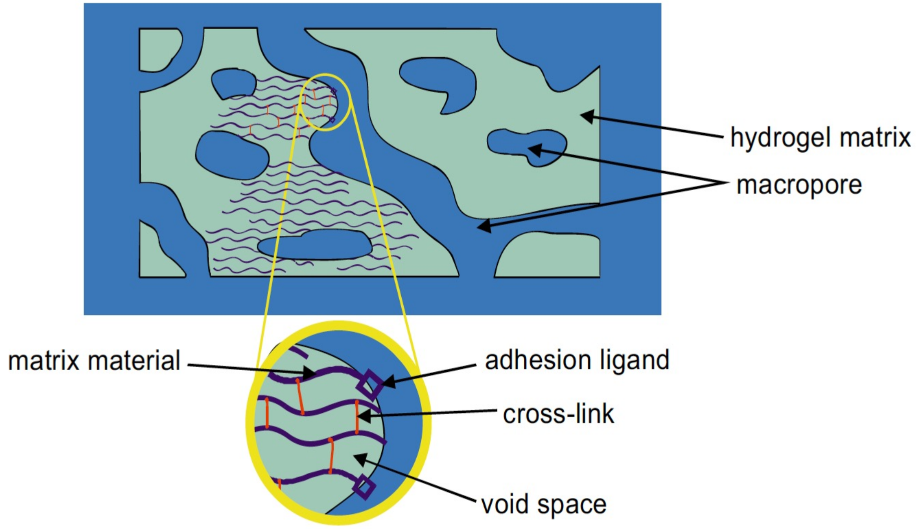


- Hydrogels are hydrophilic polymers rich of polar moieties such as carboxyl, amide, amino, and hydroxyl groups, held together by chemical bounds or physical intra-molecular and inter-molecular attractions.

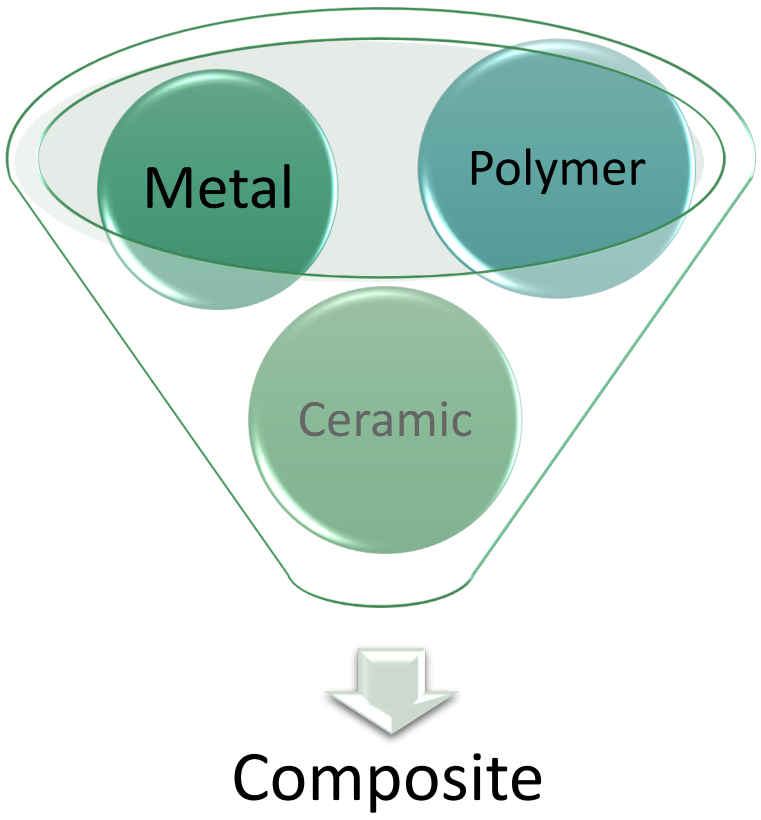
- Their main feature is the ability to absorb enormous amounts of water or biological fluids and swell without dissolving.

- Hydrogel can be classified into natural (made of polypeptides and polysaccharides), synthetic (obtained by traditional polymerization), and semi-synthetic.

- Depending on their stability in a biological system, they can be considered durable if they do not undergo chemical-physical modification or biodegradable if they degrade into oligomers, which are subsequently eliminated from the body.

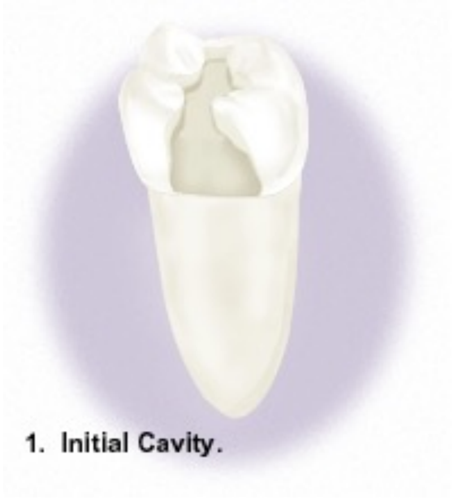


Composites



Composite : Combination of two materials with different physical and chemical properties that will produces different properties from its original parent.

Metal + Polymer
Metal + Ceramic
Polymer + Ceramic
Polymer + Polymer
Ceramic + Ceramic



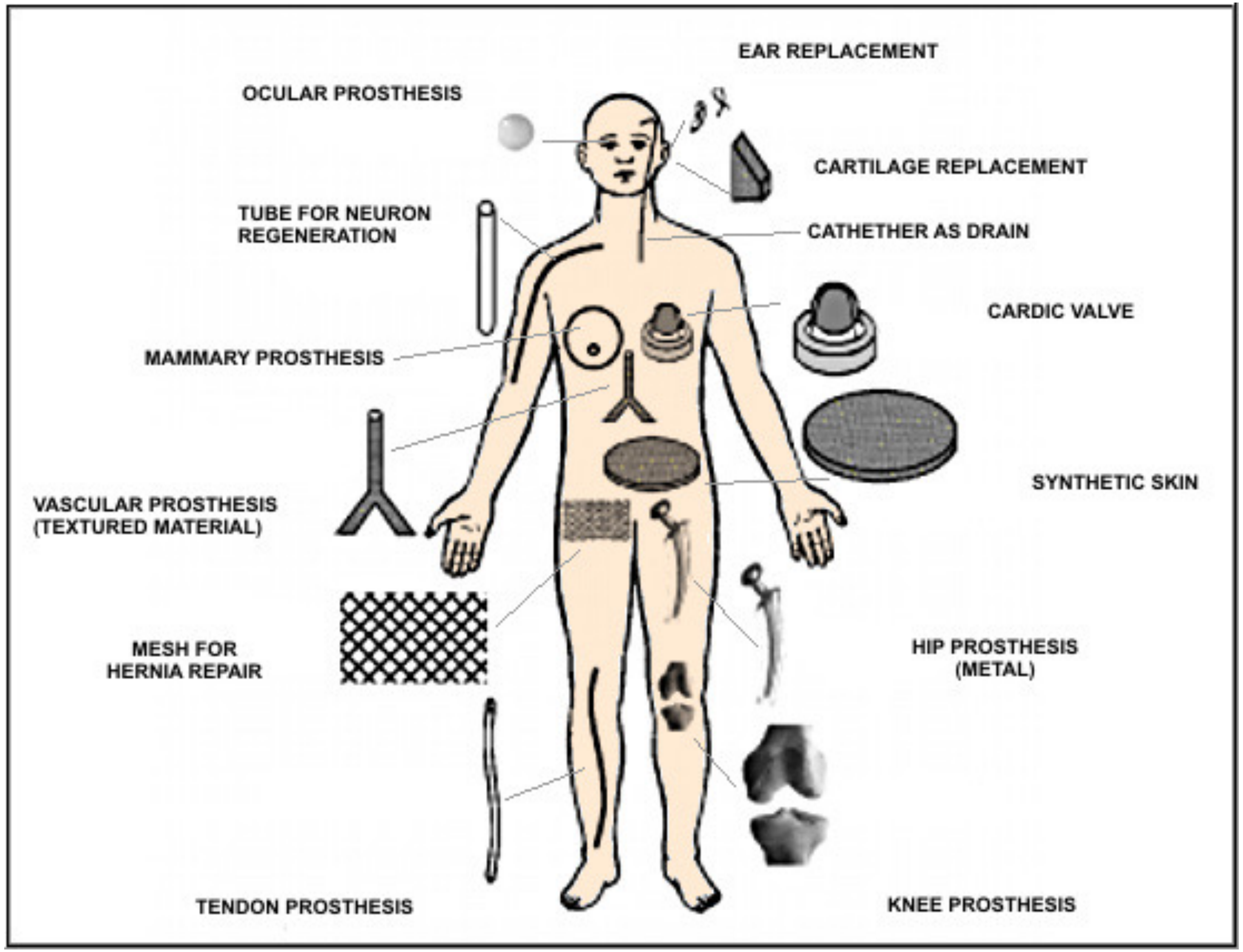
but

Metal + Metal → Commonly known as Alloy

PRO AND CON

	Advantages	Disadvantages	Clinical Uses
Ceramics	- Hard surface - High mechanical stiffness - Chemical-physic refractoriness - High biocompatibility - Osteoinductivity	- Brittleness - Slow degradation - Processing difficulties	- Hip prosthesis - Dental prosthesis - Bone and cartilage
Natural polymers	- Biocompatibility - Bioactivity	- Poor mechanical properties - Fast biodegradation - Risk of immunogenecity	- Bone and cartilage - Tendon and ligaments
Synthetic polymers	- Possibility of modulating porosity and mechanical properties during the synthesis process - Good biocompatibility	- Possible release of ions and other residual particles of polymerization - Low mechanical strength	- Sutures - Catheters - Cardiovascular prostheses - Bone cements - Bone and cartilage - Tendon and ligaments
Metals	- Good mechanical properties: high elastic modulate, yield strength, and high ductility	- Reduced cell adhesion to their surface - Possible corrosion mediated by biological fluid	- Dentistry and orthopaedic prostheses
Hydrogels	- Biocompatibility - Controlled biodegradation in vivo - Possibility to modulate their parameters (cross-linking density, porosity, pore size and interconnectivity)	- Complexity associated with purification and immunogenecity	- Hard and soft tissues
Composites	- Biocompatibility - Good mechanical properties	- Processing difficulties	- Hard and soft tissues

Biomaterials in Human



http://mitr.p.lodz.pl/biomat/old_site/raport/1_radiation_hydrogels.html