Introduction to Biomaterials
Objective

- To introduce the different biomaterials used in Biomedical Engineering
- To provide some fundamentals properties of these materials,
- And to indicate how they are used.
What is a biomaterial?

- A biomaterial is a nonviable material used in a medical device, intended to interact with biological systems (Williams, 1987)

[OR]

- Any material of natural or of synthetic origin that comes in contact with tissue, blood or biological fluids, and intended for use in prosthetic, diagnostic, therapeutic or storage application without adversely affecting the living organism and its components.
Need for biomaterials

- Millions of patients suffer end stage organ and tissue failure annually.
  - $400 billion annually for treatment.
  - 8 million surgical procedures.
- Treatment options include transplantation, reconstruction, mechanical devices.
Need for biomaterials

- Statistics in the US in 2002
  - Total hip joint replacement: 448,000
  - Knee joint replacement: 452,000
  - Shoulder joint replacement: 24,000
  - Dental implants: 854,000
  - Coronary stents: 1,204,000
  - Coronary catheters: 1,328,000
Background

- Mechanical Devices
  - Engineering approach – engineer new tissues, systems
- Limited by
  - Complexity of the human body
  - Multiple functions
  - Living components versus non-living components
  - Materials?
Background

- Historically, biomaterials consisted of materials common in the laboratories of physicians, with little consideration of materials properties.

- Early biomaterials:
  - Gold: Malleable, inert metal (does not oxidize), used in dentistry.
  - Iron, Brass: High Strength Metals, rejoin fractured femur
  - Glass: Hard ceramic, used to replace eye [cosmetic]
  - Wood: Natural composite, high strength to weight, used for limb prostheses.
  - Bone: Natural composite.
History

- 1860’s – Lister develops aseptic surgical technique
- Early 1900’s: Bone plates used to fix fractures.
- 1938: First total hip prosthesis
- 1940’s: Polymers in medicine: PMMA bone repair, cellulose for dialysis, nylon sutures.
- 1952: Mechanical heart valve
- 1953: Dacron [polymer fiber] vascular grafts
- 1958: Cemented [PMMA] joint replacement
- 1960: first commercial heart valve
- 1970’s: PEO protein resistant thin film coating
- 1976: FDA amendment governing testing & production of biomaterials / devices
- 1976: Artificial heart
Biomaterials

- Polymeric biomaterials
- Bioceramics
- Metallic biomaterials
- Biocomposite
- Biologically based (derived) biomaterials
Where do the differences between (bio-)materials come from?

- Primary bonds

**Ceramics**
(Ionic & covalent bonding):

- Large bond energy
- Large $T_m$
- Large $E$
- Small $\alpha$

**Metals**
(Metallic bonding):

- Variable bond energy
- Moderate $T_m$
- Moderate $E$
- Moderate $\alpha$

**Polymers**
(Covalent & Secondary):

- Directional Properties
- Secondary bonding dominates
- Small $T$
- Small $E$
- Large $\alpha$
Biocompatibility

- **Biocompatibility**: The ability of a material to perform with an appropriate host response in a specific application.

- **Host response**: The reaction of a living system to the presence of a material.

- Biocompatibility is a function of several factors:
  - \( B = f(X_1, X_2, \ldots, X_n) \)
  - Where \( X \): material, design, application etc.
Polymeric biomaterials

- PMMA
- PVC
- PLA/PGA
- PE
- PP
- PA
- PTFE
- PET
- PUR
- Silicones
Exercise: find the meaning of these acronyms:

- PMMA
- PVC
- PLA/PGA
- PE
- PP
- PA
- PTFE
- PET
- PUR
- Silicones
Polymeric biomaterials

- **Advantages**
  - Easy to make complicated items
  - Tailorable physical & mechanical properties
  - Surface modification
  - Immobilize cell etc.
  - Biodegradable

- **Disadvantages**
  - Leachable compounds
  - Absorb water & proteins etc.
  - Surface contamination
  - Wear & breakdown
  - Biodegradation
  - Difficult to sterilize
Bioceramics

- Alumina
- Zirconia (partially stabilized)
- Silicate glass
- Calcium phosphate (apatite)
- Calcium carbonate
Exercise: find the composition of the following bioceramics

• Alumina
• Zirconia (partially stabilized)
• Silicate glass
• Calcium phosphate (apatite)
• Calcium carbonate
Bioceramics

- **Advantages**
  - High compression strength
  - Wear & corrosion resistance
  - Can be highly polished
  - Bioactive/inert

- **Disadvantages**
  - High modulus (mismatched with bone)
  - Low strength in tension
  - Low fracture toughness
  - Difficult to fabricate
Metallic biomaterials

- Stainless steel (316L)
- Co-Cr alloys
- Ti6Al4V
- Au-Ag-Cu-Pd alloys
- Amalgam (AgSnCuZnHg)
- Ni-Ti
- Titanium
Metallic biomaterials

- **Advantages**
  - High strength
  - Fatigue resistance
  - Wear resistance
  - Easy fabrication
  - Easy to sterilize
  - Shape memory

- **Disadvantages**
  - High elastic modulus
  - Corrosion
  - Metal ion sensitivity and toxicity
  - Metallic looking
Deterioration of biomaterials

- Corrosion
- Degradation
- Calcification
- Mechanical loading
- Combined
General criterion for biomaterial selection

- Mechanical and chemicals properties
- No undesirable biological effects
  - carcinogenic, toxic, allergenic or immunogenic
- Possible to process, fabricate and sterilize with a good reproducibility
- Acceptable cost/benefit ratio
Host Reactions to Biomaterials

- Thrombosis
- Hemolysis
- Inflammation
- Infection and Sterilization
- Carcinogenesis
- Hypersensitivity
- Systemic Effects
Cell/tissue reaction to implant

- Soft tissue
- Hard tissue
- Blood cells
Various biological levels

- Atomic scale
- Molecular scale
- Cellular level
- Tissue
- Organ
- System
- Organism
pH in humans

- Gastric content 1.0
- Urine 4.5 - 6.0 (sometimes 8 according to the diet)
- Intracellular 6.8
- Interstitial 7.0
- Blood 7.17 - 7.35
Soft tissue response to an implant

- Injury
- Acute inflammation
- Granulation tissue
- Foreign body reaction
- Fibrosis
Soft tissue response to an implant

- **Acute (mins to hrs)**
  - Cell type: Leukocytes
  - Function: Recognition, engulfment and degradation (killing)

- **Chronic (days to months)**
  - Cell types: Macrophages, monocytes and lymphocytes.

- **Granulation tissue formation (3-5 days)**
  - Cell types: Endothelial cells (forming blood vessels), fibroblasts (forming connective issue)

- **Foreign body reaction (days to life time)**
  - Cell types: Foreign body giant cells, Macrophages, fibroblasts

- **Fibrosis & Fibrous encapsulation**
  - Cell type: Fibroblasts
Osteointegration

• A chemical bonding between bone and material will be formed. (Bioactive, Hydroxylapatite)
• A direct contact between bone and implant under light microscope. (Osteointegration, titanium)
Blood-material interaction

- Hemolysis (red cells)
- Coagulation (Platelets)
Applications of biomaterials

- Skeletel system
  - Joint replacement (Hip, knee)
  - Bone plate
  - Bone cement
  - Artificial tendon and ligment
  - Dental implant

- Cardiovascalar sysem
  - Blood vessel prosthesis
  - Heart valve
  - Catheter

- Organs
  - Artificial heart
  - Skin repair template
  - Artificial kidney
  - Heart-lung machine

- Senses
  - Cochlear replacement
  - Intraocular lens
  - Contact lens
  - Corneal bandage

- Biomaterials
  - Titanium, Stainless steel, PE
  - Stainless steel, Co-Cr alloy
  - PMMA
  - Hydroxylapatie Teflon, Dacron
  - Titanium, alumina, calcium phosphate
  - Dacron, Teflon, Polyurethane
  - Reprocessed tissue, Stainless steel, Carbon
  - Silicone rubber, teflon, polyurethane
  - Polyurethane
  - Silicone-collage composite
  - Cellulose, polyacrylonitrile
  - Silicone rubber
  - Platinum electrodes
  - PMMA, Silicone rubber, hydrogel
  - Silicone-acrylate. Hydrogel
  - Collagen, hydrogel
Applications of biomaterials

Ocular lenses: acrylates, silicone

Ear: HA, Al₂O₃, Ti, silicone

Cranial: 316L SS, Ti, acrylic, HA, TCP

Maxillofacial reconstruction: Al₂O₃, HA, TCP, HA/PLA, Bioglass, Ti, Ti-Al-V

Degradable Sutures: copolymers of PLA, PGA, PCL, PTMC, PDO

Spinal: Co-Cr-Mo, Ti, HA, UHMWPE

Load-bearing Orthopedic: Al₂O₃, Zirconia, 316L SS, Ti, Ti-Al-V, Co-Cr-Mo, UHMWPE

Blood vessels: ePTFE, PET

Tendon & Ligaments: PLA/C fiber, ePTFE, PET, UHMWPE

Bone Fixation: 316L SS, Co-Cr-Mo, Ti, Ti-Al-V, PLA/HA, PLA, PGA

Dental: acrylic, gold, 316L SS, Co-Cr-Mo, Ti, Ti-Al-V, Al₂O₃, HA, Bioglass

Heart: Co-Cr-Mo, Ti-Al-V, pyrolytic C, ePTFE, PET, PUR

Pacemaker: 316L SS, Pt, PUR, silicone, PET

Prosthetic joints: 316L SS, Co-Cr-Mo, Ti, Ti-Al-V, silicone, UHMWPE, acrylic

PLA = polylactide
PGA = polyglycolide
PTMC = polytrimethylene carbonate
PDO = poly(p-dioxanone)
PUR = polyurethane
ePTFE = expanded polytetrafluoroethylene
UHMWPE = ultrahigh mol. wt. polyethylene
PET = polyethylene terephthalate
HA = hydroxyapatite
SS = stainless steel
Evolution of biomaterials

• 1\textsuperscript{st} generation (since 1950s)
  – Goal: Bioinertness

• 2\textsuperscript{nd} generation (since 1980s)
  – Goal: Bioactivity

• 3\textsuperscript{rd} generation (since 2000s)
  – Goal: Regenerate functional tissue
First Generation Implants

- Ad-hoc’ (unplanned) Implants
- Specified by physicians using common and borrowed materials
- Most successes were accidental rather than by design
- Examples – First generation Implants
  - Gold fillings, wooden teeth, PMMA dental prosthesis
  - Steel, gold, ivory, bone plates etc.
  - Glass eyes and other body parts
Intraocular Lens

- 3 basic materials – PMMA, Acrylic, silicone
Vascular graft
Second generation Implants

- Engineered implants using common and borrowed materials
- Developed through collaborations of physicians and engineers
- Built on first generation experiences
- Used advances in materials science
- Examples – Second generation implants
  - Titanium alloy dental and orthopedic implants
  - Cobalt-chromium implants
  - UHMW polyethylene bearing surfaces for total joint replacements
  - Heart valves and Pacemakers.
Artificial Hip Joints
Third Generation Implants

- Bioengineered implants using bioengineered materials
- Few examples on the market
- Some modified and new polymeric devices
- Many under development
- Example – Third generation implants
  - Tissue engineered implants designed to re-grow rather than replace tissues
  - Some resorbable bone repair cements
  - Genetically engineered ‘biological’ components.
Heart valves

Biological valve (human or porcine)
Synthetic Polymer Scaffolds

- In the shape of a nose (left) is seeded with cells called chondrocytes that replace the polymer with cartilage over time (right) to make a suitable implants.
Evolution of biomaterials

• Structural → Soft tissue replacement → Functional tissue engineered construct
Advances in biomedical technology

- Cell matrices for 3-D growth and tissue reconstruction
- Biosensors, Bio-mimetic and Smart devices
- Controlled Drug Delivery / Targeted Delivery
- Bio-hybrid organs and Cell Immuno-isolation
- New biomaterials – bioactive, biodegradable, inorganic
- New processing techniques
Biomaterials for tissue replacement

- Bioresorbable Vascular Graft
- Biodegradable nerve guidance channel
- Skin Grafts
- Bone Replacements
• Material properties
Properties of biomaterials

• Bulk Properties
• Surface Properties
• Characterization
Exercise: provide a definition of the following material properties

- Compressive strength
- Tensile strength
- Bending strength
- E-Modulus
- Coefficient of thermal expansion
- Coefficient of thermal conductivity
- Surface tension
- Hardness and density
- Hydrophobic/philic
- Water sorption/solubility
- Surface friction
- Creep
- Bonding properties
Material properties

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- Bonding properties
Elastic behavior

- Hooke’s law
- Materials extend depending on the load

*FIG. 3.* Initial extension is proportional to load according to Hooke’s law.
Stress and strain

- Normalized load and deformation
- Stress: N/m²
- Strain: adimensional

\[ \varepsilon = \frac{l_f - l_o}{l_o} = \frac{\Delta l}{l_o} \]

**FIG. 4.** Tensile stress and tensile strain.
Shear

• In case with applied load parallel to the area supporting it
• Shear stress
• Shear strain

\[
\tau = \frac{F}{A_\parallel} \quad \text{Shear stress}
\]
\[
\gamma = \frac{\Delta l}{l_\perp} \quad \text{Shear strain}
\]

**FIG. 5.** Shear stress and shear strain.
Elastic constants

- Inherent properties of the material
  - $E$: Young's modulus
  - $G$: shear modulus
Mechanical testing

- Push
- Pull
- Bend
- Rotate
Brittle fracture

- Elastic behavior does not persist indefinitely.
- Due to microscopic defects, materials eventually break.
- Fracture stress
Plastic deformation

- Non recoverable deformation
- Only possible with the presence of metallic bonds
- Useful for shaping the materials
- Offset yield strength
- UTS: maximum load experienced
- Shaded area: work required until the materials fail. (Toughness)

*FIG. 8.* Stress versus strain for a ductile material. (Toughness)
Creep and viscous flow

- Time varying response of materials to the applied load or strain
- Creep w/ constant load
- Viscous flow (stress relaxation) w/ constant strain
Fatigue

- Failure as a result of cyclic stresses
- Important for total hip implant, artificial heart valve, pacemaker lead
- Number of cycles varies (probability)
Finite Element Analysis

- Complexity of biomaterials or their structures
  - Non-elastic behavior
  - Geometrical nonlinearity
  - Mixed boundary conditions

- FEM
- Computational approach by dividing a structure into a large number of small parts with interconnecting nodes
- Each element with simple geometry
- Linking elements by considering adjacent or sharing nodes
FIG. 2. 3D FE representations of the human femur. (A) Tetrahedral elements; (B) hexahedral elements. (From Middleton et al., 1996, p. 125. Reproduced with permission of Gordon and Breach Publishers, Overseas Publishers Assn., Amsterdam.)
Some overview
Surface properties

- Surface is important because this is the place where biological reactions occur.
  - Protein adsorption
  - Cell adhesion
  - Cell growth
  - Blood compatibility
- Importance in surface
  - Unique reactivity
  - Different from the inner structure
  - Not much of total mass
  - Readily contaminated
  - Mobile
Contact angle methods

FIG. 5. Four possibilities for contact angle measurement: (A) sessile drop, (B) captive air bubble method, (C) capillary rise method, (D) Wilhelmy plate method.
Scanning electron microscopy
Scanning electron microscopy
Atomic force microscopy

- Piezo drive mechanism
- Attraction and repulsion between the tip and the surface
- Contact and tapping modes
Confocal fluorescent microscopy
Confocal fluorescent microscopy