# Biomaterial Course

# Introduction to Biomaterials

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## Final Year Bachelor of Chemical Engineering

**Dr. Ratnesh Jain**
**UGC Assistant Professor**

# BACKGROUND

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

Early biomaterials :

- Gold: Malleable, inert metal (does not oxidize); used in dentistry by Chinese, Aztecs and Romans--dates 2000 years
- Iron, brass: High strength metals; rejoin fractured femur (1775)
- Glass: Hard ceramic; used to replace eye (purely cosmetic)
- Wood: Natural composite; high strength to weight; used for limb prostheses
- and artificial teeth
- Bone: Natural composite; uses: needles, decorative piercings
- Sausage casing: cellulose membrane used for early dialysis (W Kolff)
- Other: Ant pincers. Central American Indians used to suture wounds

Biomaterials are defined by their application, NOT chemical make-up

# INTRODUCTION

A biomaterial

- is a nonviable material used in a medical device, intended to interact with biological systems.[1]
- is used to make devices to replace a part of a function of the body in a safe, reliable, economic, and physiologically acceptable manner.
- is any substance (other than a drug), natural or synthetic, that treats, augments, or replaces any tissue, organ, and body function.

The need for biomaterials stems from an inability to treat many diseases, injuries and conditions with other therapies or procedures :

- replacement of body part that has lost function (total hip, heart)
- correct abnormalities (spinal rod)
- improve function (pacemaker, stent)
- assist in healing (structural, pharmaceutical effects: sutures, drug release)

[1] Williams, D.F. (1987) Definitions in Biomaterials. Proceedings of a Consensus Conference of the European Society For Biomaterials, England, 1986, Elsevier, New York.

# HISTORY

Important dates

- 1860's: Lister develops aseptic surgical technique
- early 1900's: Bone plates used to fix fractures
- 1930's: Introduction of stainless steel, cobalt chromium alloys
- 1938 : first total hip prosthesis (P. Wiles)
- 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 valves
- 1970's: PEO (polyethyleneoxide) protein resistant thin film coating
- 1976: FDA ammendment governing testing & production of biomaterials /devices
- 1976: Artificial heart (W. Kolff, Prof. Emeritus U of U)

# MOTIVATION

Improve quality of life...

$$$ Biomaterials is a $100 billion + market, increasing at 5-7% / yr

- Consider diabetes, which afflicts over 10 million Indians (4% of population)
    - An artificial pancreas, if it existed, and were given to 10% of diabetics would generate over 2.3 billion/yr

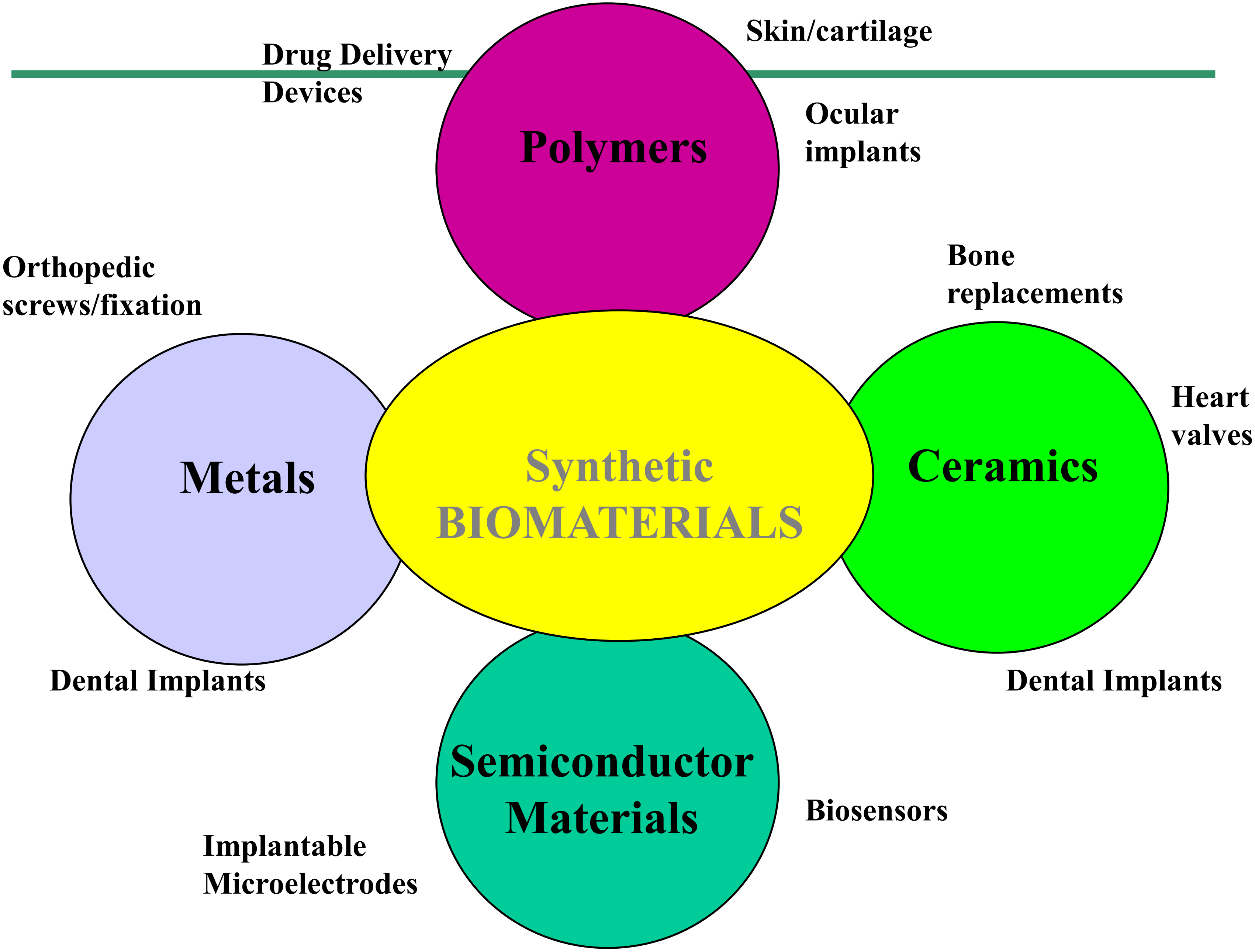
Devices currently on the market[2]

| Device | patient cost | cost of biomaterial | annual revenue (US Data, Indian Data NA) |
|---|---|---|---|
| hemodialyzer | $18 | $6 | $110M |
| pacemaker | $6,000 | $75 | $6.75M |
| hip | $3,000 | $100 | $0.5M |
| stent and catheter | $3,000 | $30 | $1.75M |

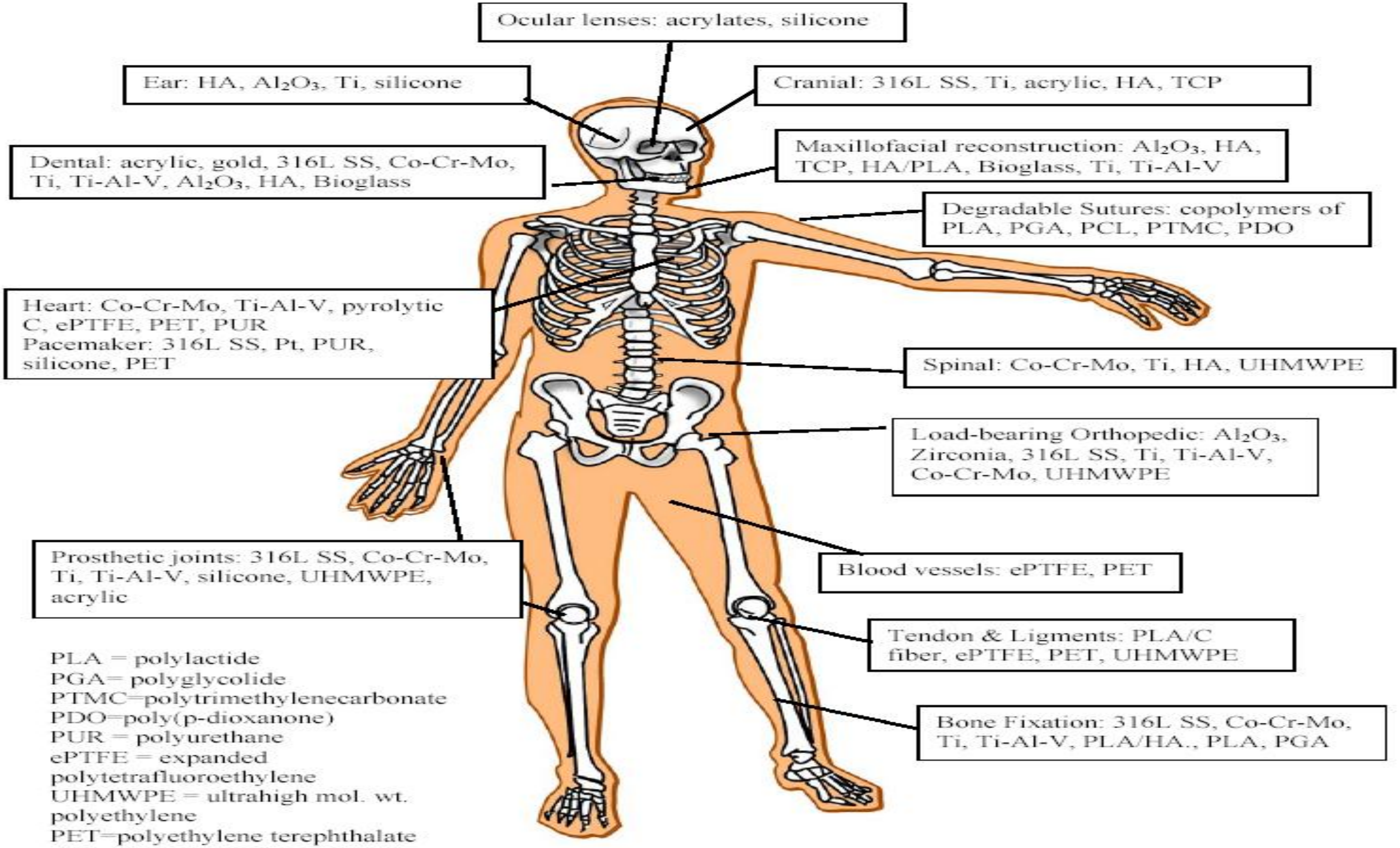
[2] The Economical Impact of Biomaterials

# EXAMPLES OF USES OF BIOMATERIALS

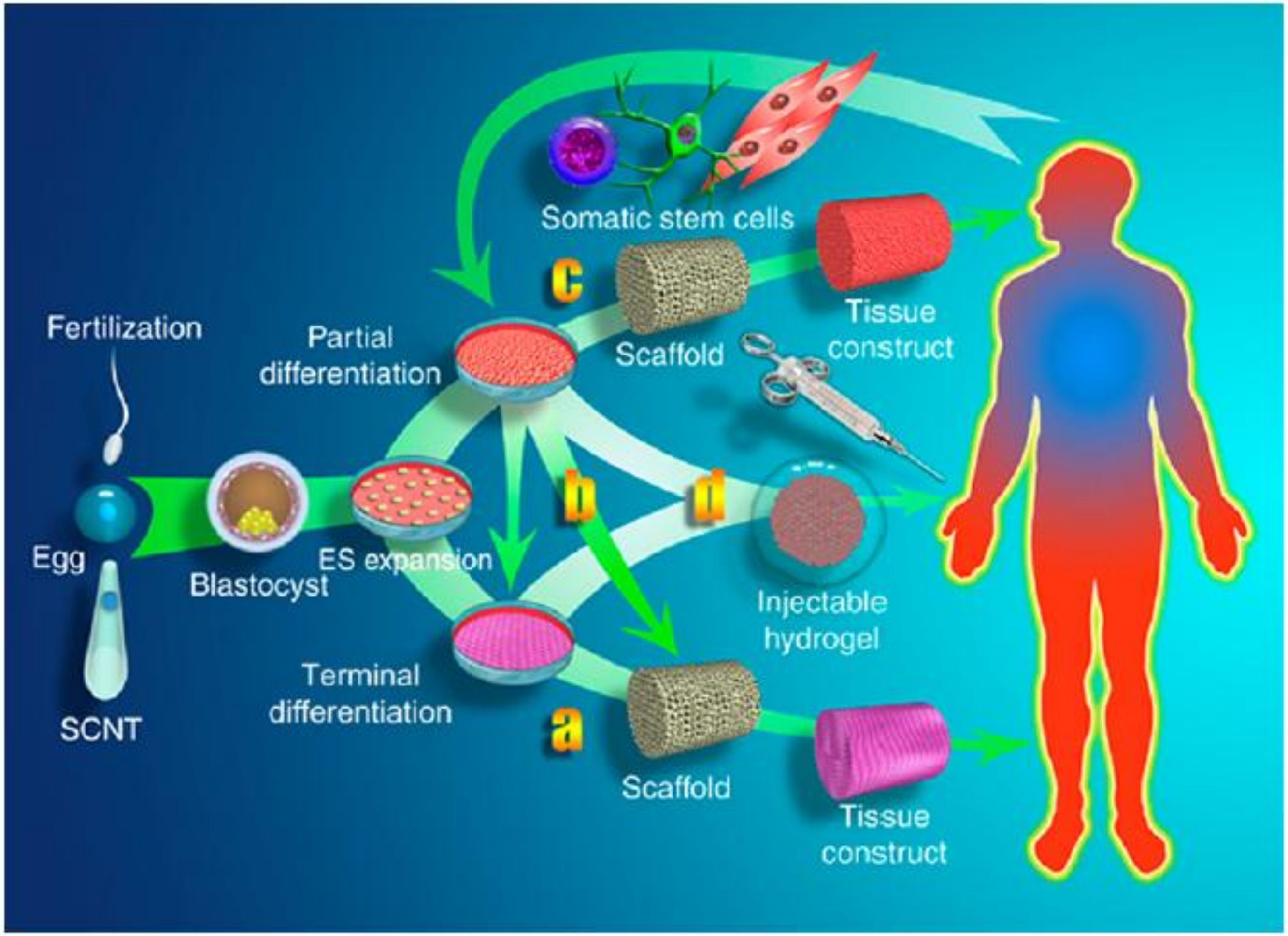
| Organ/Tissue | Examples |
|---|---|
| heart | pacemaker, artificial valve, artificial heart |
| eye | contact lens, intraocular lens |
| ear | artificial stapes, cochlea implant |
| bone | bone plate, intramedullary rod, joint prosthesis, bone cement, bone defect repair |
| kidney | dialysis machine |
| bladder | catheter and stent |
| muscle | sutures, muscle stimulator |
| circulation | artificial blood vessels |
| skin | burn dressings, artificial skin |
| endocrine | encapsulated pancreatic islet cells |


Skin/cartilage
Drug Delivery
Devices
Polymers
Ocular
implants
Orthopedic
screws/fixation
Bone
replacements
Heart
valves
Metals
Synthetic
BIOMATERIALS
Ceramics
Dental Implants
Dental Implants
Semiconductor
Materials
Biosensors
Implantable
Microelectrodes

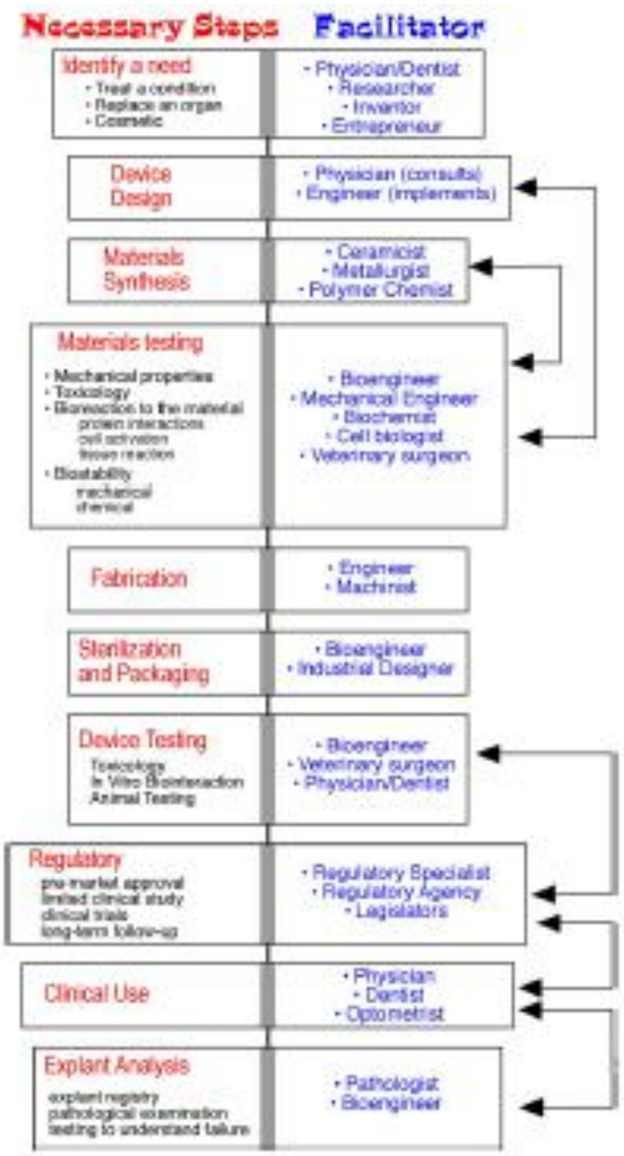
# Biomaterial Science




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


Somatic stem cells
Fertilization
Partial differentiation
c
Scaffold
Tissue construct
Egg
ES expansion
Blastocyst
b
d
Injectable hydrogel
Terminal differentiation
SCNT
a
Scaffold
Tissue construct

# Need


Necessary Steps
Facilitator
Identify a need
• Treat a condition
• Replace an organ
• Cosmetic
• Physician/Dentist
• Researcher
• Inventor
• Entrepreneur
Device Design
• Physician (consults)
• Engineer (implements)
Materials Synthesis
• Ceramicist
• Metallurgist
• Polymer Chemist
Materials testing
• Mechanical properties
• Toxicology
• Bioreaction to the material
protein interactions
cell activation
tissue reaction
• Biostability
mechanical
chemical
• Bioengineer
• Mechanical Engineer
• Biochemist
• Cell biologist
• Veterinary surgeon
Fabrication
• Engineer
• Machinist
Sterilization and Packaging
• Bioengineer
• Industrial Designer
Device Testing
Toxicology
In Vitro Biointeraction
Animal Testing
• Bioengineer
• Veterinary surgeon
• Physician/Dentist
Regulatory
pre-market approval
limited clinical study
clinical trials
long-term follow-up
• Regulatory Specialist
• Regulatory Agency
• Legislators
Clinical Use
• Physician
• Dentist
• Optometrist
Explant Analysis
explant registry
pathological examination
testing to understand failure
• Pathologist
• Bioengineer

# MATERIAL ATTRIBUTES FOR BIOMEDICAL APPLICATIONS

| Property | Desirables |
| --- | --- |
| Biocompatibility | Noncarcinogenic, nonpyrogenic, nontoxic, nonallergenic, blood compatible, non-inflammatory |
| Sterilizability | Not destroyed by typical sterilizing techniques such as autoclaving, dry heat, radiation, ethylene oxide |
| Physical characteristics | Strength, elasticity, durability |
| Manufacturability | Machinable, moldable, extrudable |

# BIOCOMPATIBILITY

*There is no general set of criteria, that if met, qualify a material as being biocompatible*

- The time scale over which the host is exposed to the material or device must be considered

| material | contact time |
|---|---|
| syringe needle | 1-2 s |
| tongue depressor | 10 s |
| contact lens | 12 hr - 30 days |
| bone screw / plate | 3-12 months |
| total hip replacement | 10-15 yrs |
| intraocular lens | 30 + yrs |

“Biocompatibility” is strongly determined by primary chemical structure !

# Classes of Biomaterials

- Metals
  - stainless steel, cobalt alloys, titanium alloys
- Ceramics
  - aluminum oxide, zirconia, calcium phosphates
- Polymers
  - silicones, poly(ethylene), poly(vinyl chloride), polyurethanes, polylactides
- Natural polymers
  - collagen, gelatin, elastin, silk, polysaccharides

# Material Properties

## OBJECTIVES

To introduce the fundamental mechanical and surface chemistry properties of biomaterials

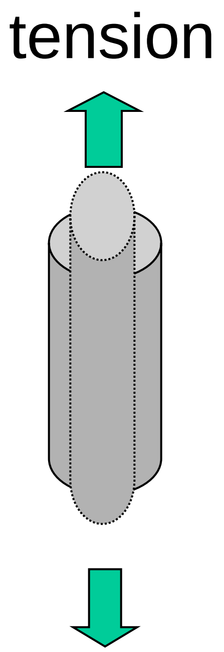
## OUTLINE

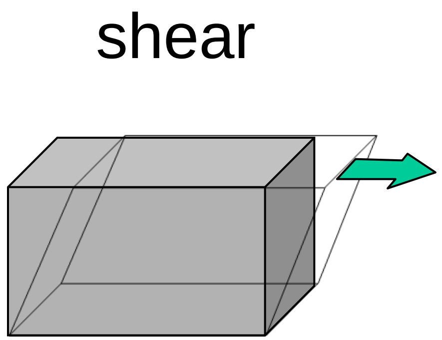
- Mechanical Properties
  - elasticity, viscoelasticity, brittle fracture, fatigue

- Surface chemistry

# Mechanical Properties

Many applications require the biomaterial to assume some of the applied **load** on the body part.



# Viscoelasticity

The response of materials to an imposed stress may under certain conditions resemble the behavior of a solid or a liquid.

Stress Relaxation (application of a sudden strain to the sample and following the stress as a function of time as the strain is held constant).

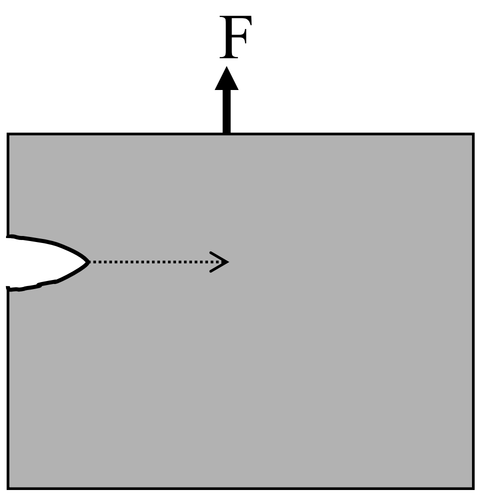
Creep (a constant stress is instantaneously applied to the material and the resulting strain is followed as a function of time)

Creep is function of crystallinity: As % crystallinity increases, creep decreases

# Brittle Fracture

Calculated ultimate tensile strengths are large compared to measured ultimate tensile strengths.

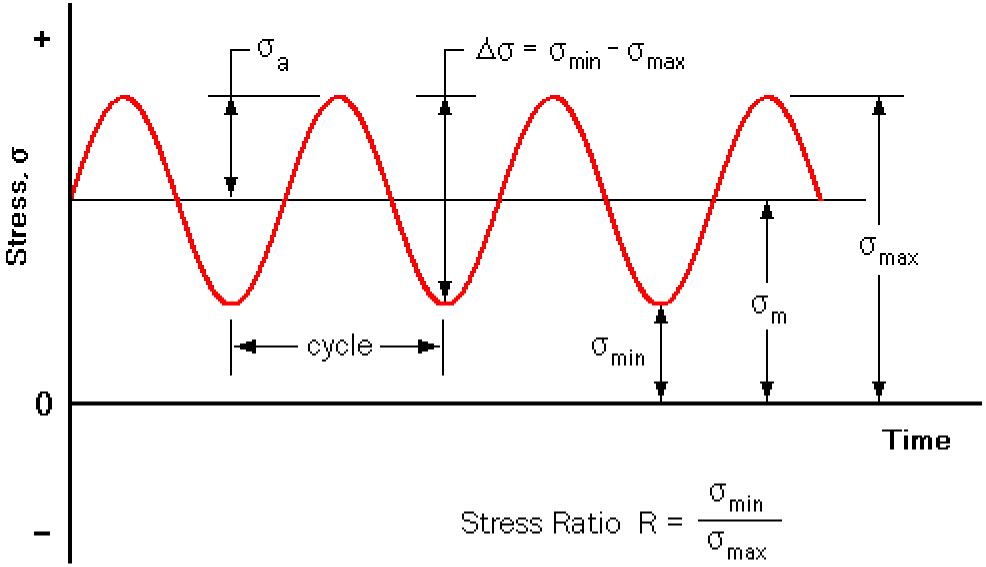
$$K_{Ic} = Y\sigma_f\sqrt{\pi c}$$



# Fatigue

The progressive deterioration of the strength of a material or structural component during service such that failure can occur at much lower stress levels than the ultimate stress of the material.

Cyclic Fatigue



# Surface Energy

Interface

- boundary between 2 layers

significance

- protein adsorption to materials
- blood coagulation/thrombosis due to material contact
- cellular response to materials

# Surface Chemistry

*Primary*

- Ionic: $e^-$ donor, $e^-$ acceptor *ceramics, glasses (inorganic)*
- Covalent: $e^-$ sharing *glasses, polymers*
- Metallic: $e^-$ "gas" around lattice of + nuclei

*Secondary/Intermolecular*

- Electrostatic
- H-bonding
- Van der Waals (dipole-dipole, dipole-induced dipole, London dispersion)
- Hydrophobic Interactions (entropy-driven clustering of nonpolar gps in $H_2O$)
- Physical Entanglement (high MW polymers)

Ex. 1: alumina $Al_2O_3$ (corundum) — used for hard tissue replacement – e.g., dental implants

Properties:

- corrosion resistant
- high strength
- wear resistant
- "biocompatible"

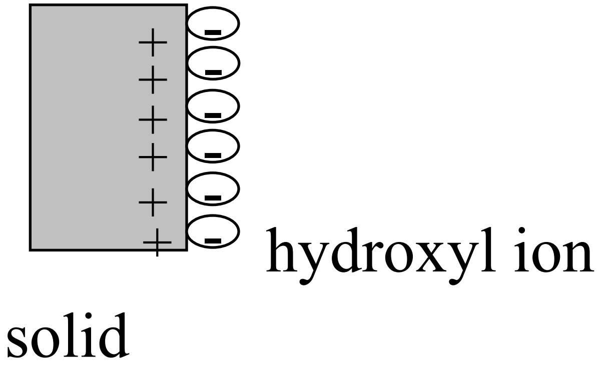
} derived from ionic bonding

"biocompatible" → Electrostatic interactions w/ charges on proteins ⇒ non-denatured adsorbed protein layer ⇒ "camouflage"

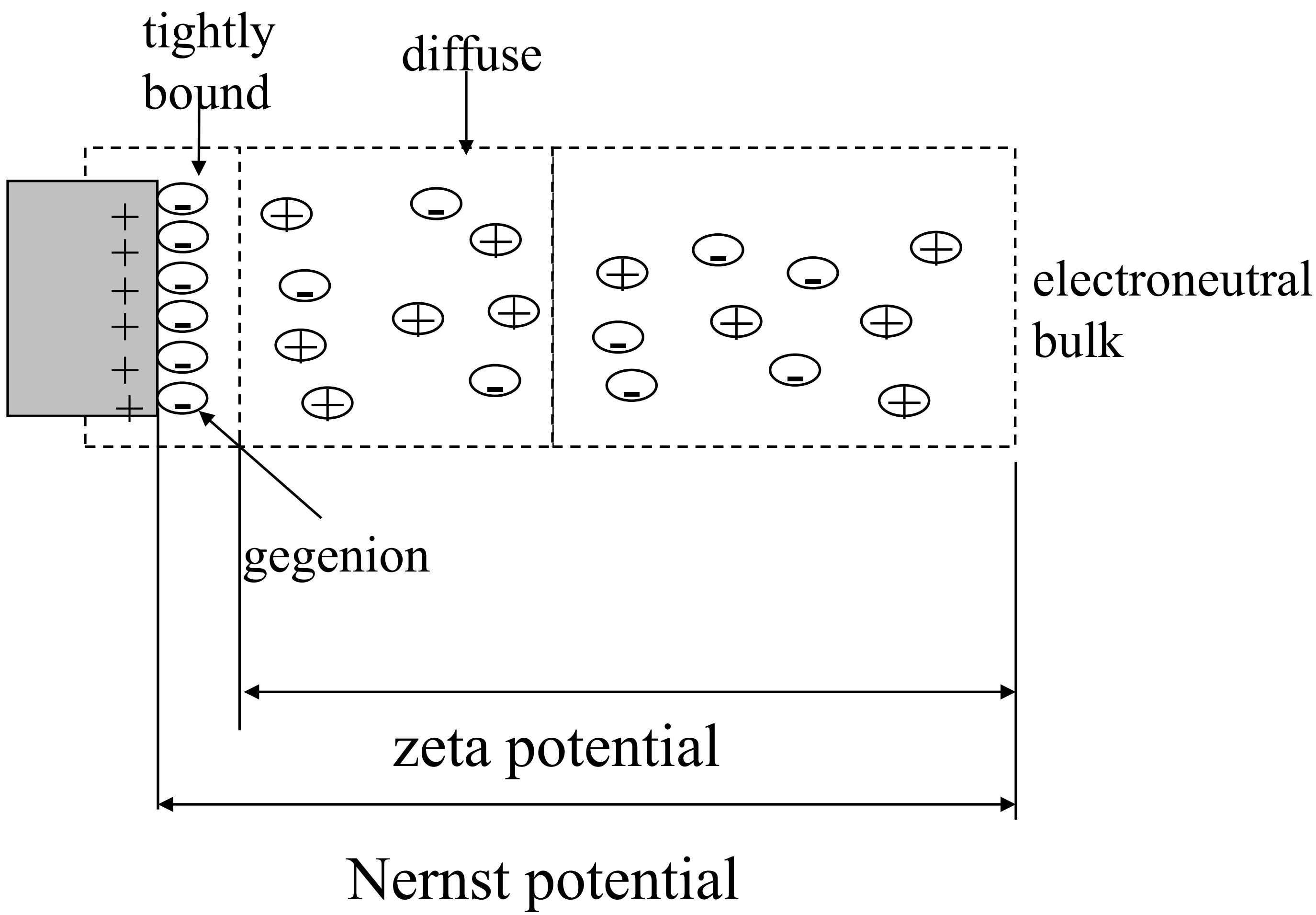
# Surface Electrical Properties

surface may become charged by

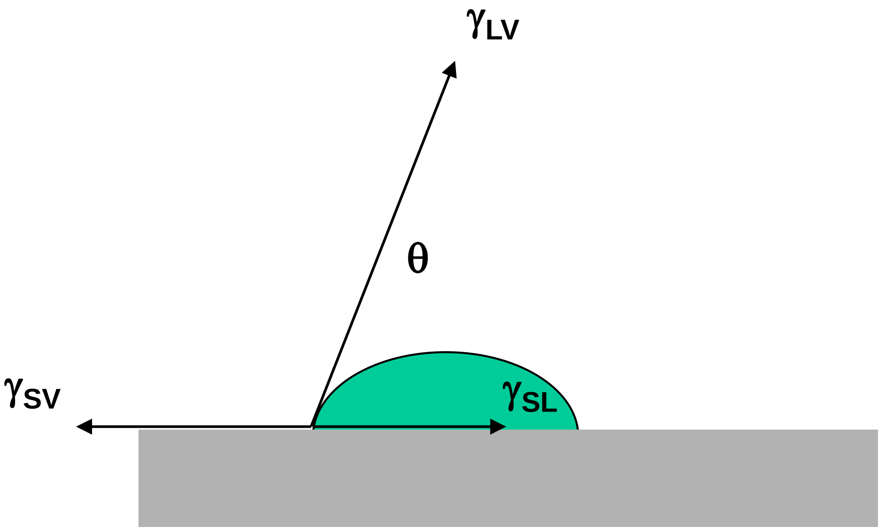
- adsorption of ionic species present in sol'n or preferential adsorption of $OH^-$
- ionization of -COOH or $-NH_2$ group



# Electric Double Layer



# Surface Energy and the Contact Angle

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TIFF (Uncompressed) decompressor
are needed to see this picture.

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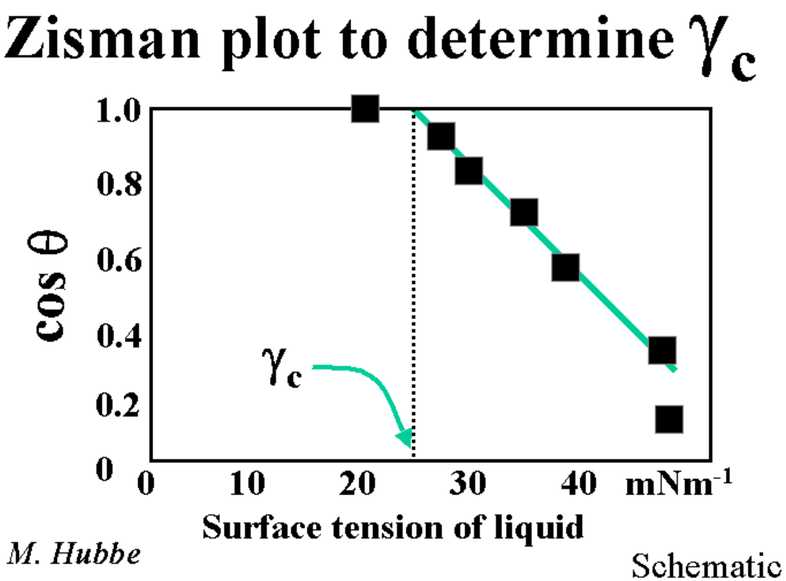
# Critical Surface Tension, $\gamma_c$

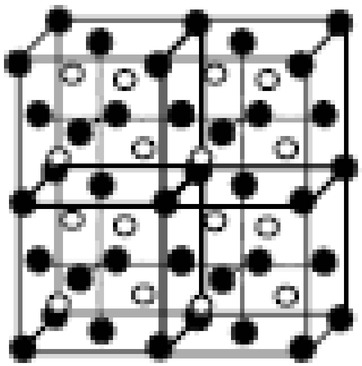
The critical surface tension is the surface tension of a liquid that would completely wet the solid of interest.




| Material | $\gamma_c$ (dyne/cm) |
|---|---|
| Co-Cr-Mo | 22.3 |
| Pyrex glass | 170 |
| Gold | 57.4 |
| poly(ethylene) | 31-33 |
| poly(methylmeth acrylate) | 39 |
| Teflon | 18 |

# Higher Order Structures

**Crystals:** 3D periodic arrays of atoms or molecules



*metals, ceramics,*
*polymers (semicrystalline)*

crystallinity decreases solubility and bioerosion
(biogradable polymers & bioresorbable ceramics)

**Networks:** exhibit short range order & characteristic lengths

*inorganic glasses, gels*

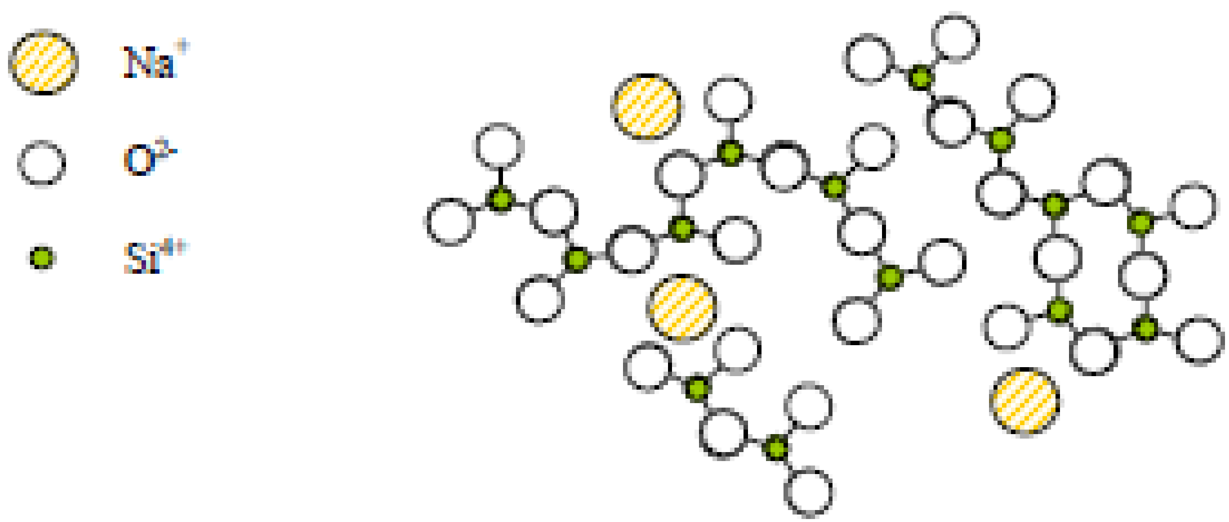
Ex. 1: Bioactive Glasses — used for hard connective tissue replacement

Network formers (~50wt%): $SiO_2$, $P_2O_5$
Network modifiers (high! ~50wt%): $Na_2O$, CaO

Properties:

- partially soluble *in vivo* (facilitates bone bonding)
- easily processed (complex shapes)

} derived from loose ionic network




Other Ex. Hydrogel, Self assemblies, micelles, liposomes

# Microstructures

Ex. 1: Porous Bioresorbable Scaffolds
polylactide (PLA)

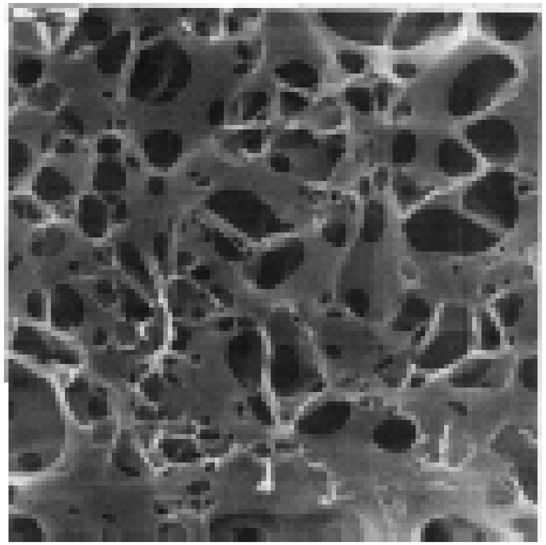
used for tissue regeneration

Properties:

- Penetrable to body fluids, cells
- Structurally stable

derived from pore microstructure

Pore dimensions:
10-100 μm



Other: crystal grain, spherulites etc.

# Thank You