# Lecture 1: Intro. to Biomaterials: Structural Hierarchy in Materials & Biology

What are "biomaterials"?

A good working definition from the text is: *"A nonviable material used in a medical device, intended to interact with biological systems."**

| MEDICAL DEVICE EXAMPLES | ANNUAL # (U.S.)* |
|---|---|
| Sutures (temporary or bioresorbable) | 250 M** |
| Catheters (fluid transport tubes) | 200 M |
| Blood Bags | 40 M |
| Contact Lenses | 30 M |
| Intraocular Lenses | 2.5 M |
| Coronary Stents | 1.2 M*** |
| Knee and Hip Prostheses | 0.5 M |
| Breast Prostheses (cancer or cosmetic) | 0.25 M |
| Dental Implants | 0.9 M |
| Renal Dialyzers (patients) | 0.3 M |
| Oxygenators/CPB's (cardiopulmonary bypass system—facilitates open heart surgery) | 0.3 M |
| Vascular Grafts | 0.3 M |
| Pacemakers (pulse generators) | 0.4 M |

Biomaterials are defined by their <u>application</u>, NOT chemical make-up

Ex. *Intraocular lenses*

Composition: poly(methyl methacrylate)
PMMA, a.k.a. "acrylic"

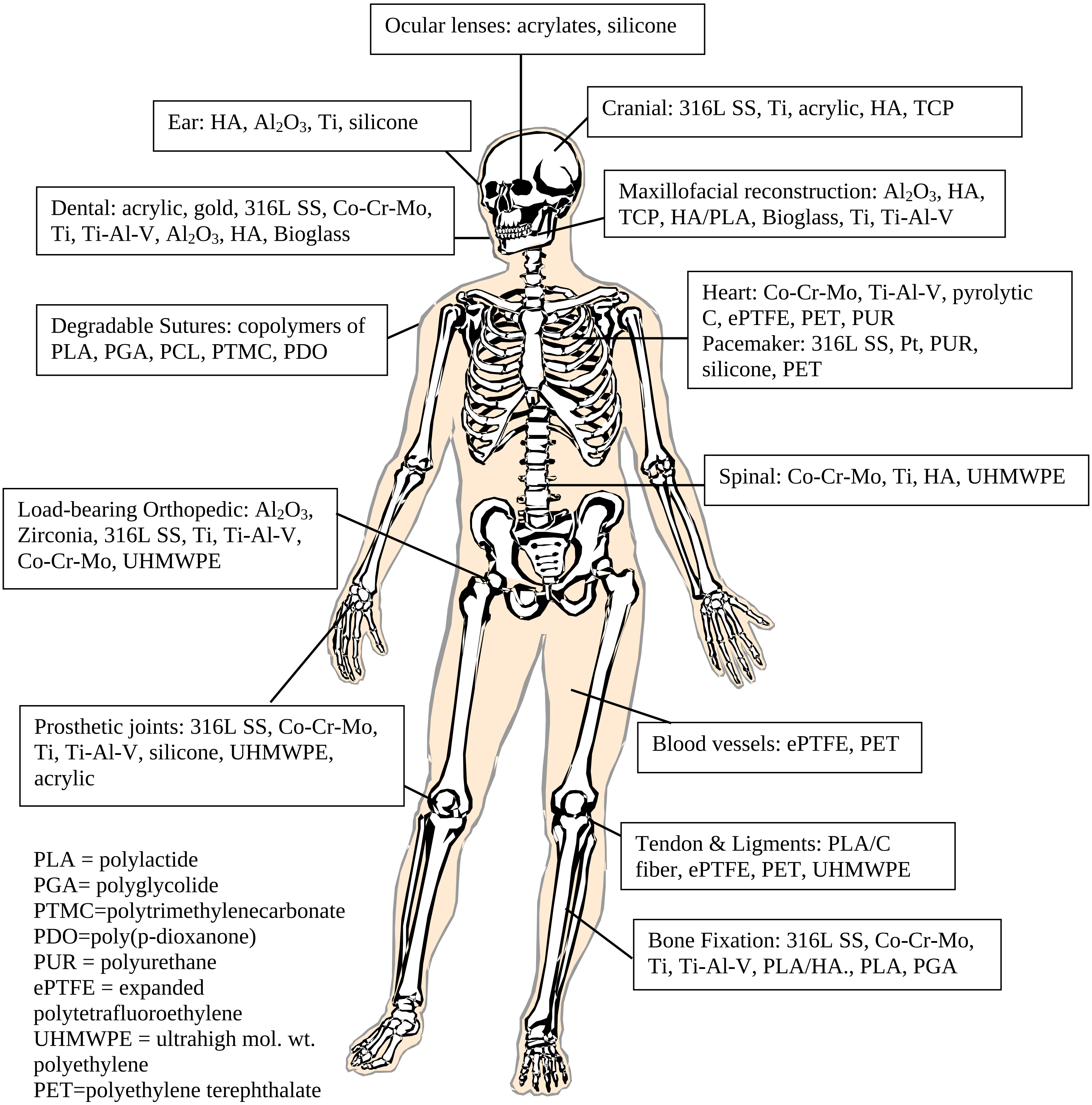
Properties:

- High refractive index
- Easily processed
- Environmentally stable (relatively inert)
- Good mechanical properties

Used as auto taillight covers for the same reasons!

*from Biomaterials Science: An Introduction to Materials in Medicine, 2nd ed., B.D. Ratner et al., eds., Elsevier, NY 2004
**from Biomaterials Science: An Introduction to Materials in Medicine, 1st ed., B.D. Ratner et al., eds., Elsevier, NY 1996
***from Introduction to Biomedical Engineering, 2nd ed., J. Enderle et al,, eds., Elsevier, NY 2005

Biomaterials cover all classes of materials – metals, ceramics, polymers




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

Figure by MIT OCW

## What governs materials choice?

<u>Historically ⇒ Today</u>

1. Bulk properties: matched to those of natural organs

- Mechanical (ex., modulus)
- Chemical (ex., degradation)
- Optical (ex., whiteness, clarity)

2. Ability to Process

3. Federal Regulations:
Medical Device Amendment of '76 → ?
(all new biomaterials must undergo premarket approval for safety and efficacy)

<u>Today ⇒ Future</u>

Rational design of biomaterials based on better understanding of natural materials and the material/biological organism interface

Adoption of the Materials Engineering Paradigm

Application (Performance)
⇑
Properties
⇑
Structure
⇑
Processing

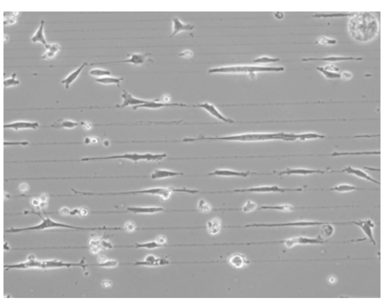
What is "structure"? *the arrangement of matter*

Both synthetic materials & biological systems have <u>many length scales</u> of structural importance.

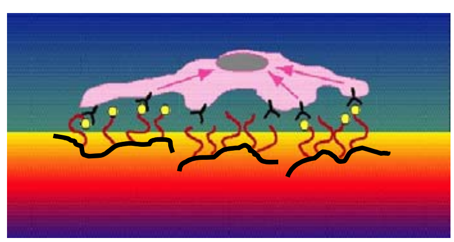
# *Structural Hierarchies*

| <u>Synthetic Materials</u> | | <u>Living Organisms</u> |
|---|---|---|
| Chemical Primary Structure | $10^{-10}$m | Molecules (H$_2$O, peptides, salts…) |
| Higher Order Structure | The realm of biomaterials engineering | Organelles (lysosomes, nucleus, mitochondria) |
| Microstructure | | Cells |
| Composites | $10^{-3}$m | Tissues |
| Parts | | Organs |
| Devices | | Individuals |

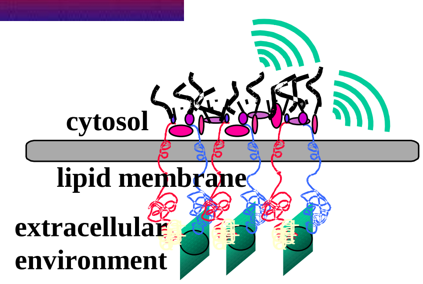
**Biomaterials Engineering spans ~8 orders of magnitude in structure!**



Fibroblast cells aligned on micro-patterned surface
Engineered length scale: $10^{-3}$ to $10^{-6}$ m



Cell adheres to RGD peptide clusters linked to comb copolymer chain ends
Engineered length scale: $10^{-7}$ to $10^{-8}$ m




Cell adhesion receptors embedded in membrane interact with RGD sequence
Engineered length scale: $10^{-9}$ to $10^{-10}$ m

# LENGTH SCALES OF STRUCTURE

## 1. Primary Chemical Structure
(Atomic & Molecular: 0.1–1 nm)

Length scale of ***bonding*** – strongly dictates biomaterial performance

*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)

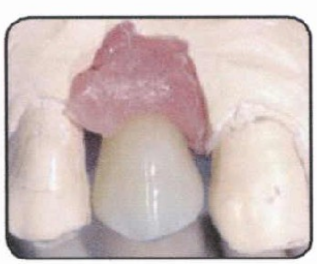
Ex. 1: alumina $Al_2O_3$ (corundum) — used for hard tissue replacement – e.g., dental implants

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

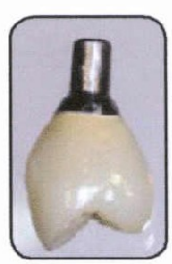
derived from ionic bonding

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

from Biocon, Inc. website: www.biocon.com



Integrated Abutment Crown™ on soft-tissue model.



Integrated Abutment Crown™.

Insertion of Integrated Abutment Crown™ into implant well.

Ex. 2: polyethylene oxide (PEO)
$(CH_2CH_2O)_n$

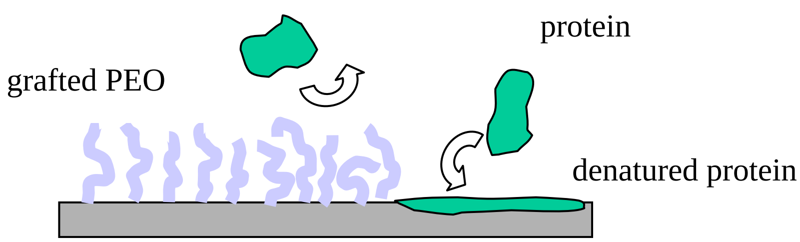
used for protein resistant coatings, hydrogels

Properties:

- flexible
- hydrolysable
- water soluble
- bioinert

Derived from primary & secondary bonding

Strong H-bonding, unique 3 n.n. coordination w/ $H_2O \Rightarrow$ water-like layer $\Rightarrow$ "camouflage"



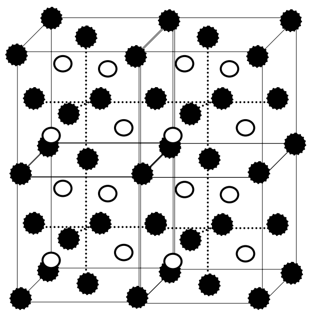

**Take Home Message:**
***"Biocompatibility" is strongly determined by primary chemical structure!***

Biocompatibility: "ability of a material to perform with an appropriate host response"

Chemical Structure
⇩
Protein Adsorption
⇩
Cell Attachment
⇩
Cell Secretion
⇩
Host Response

## 2. Higher Order Structure (1 – 100 nm)

**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*

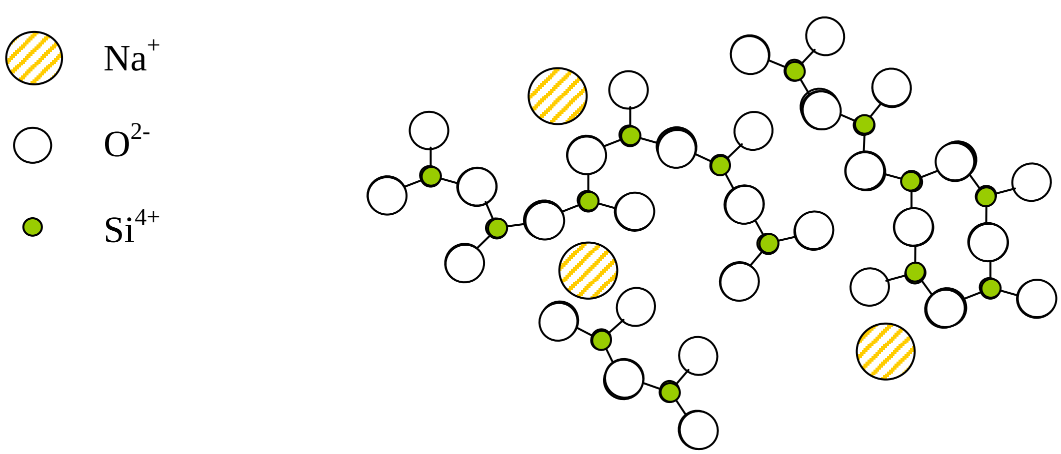
Ex. 1: Bioactive Glasses — used for hard connective tissue replacement

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)

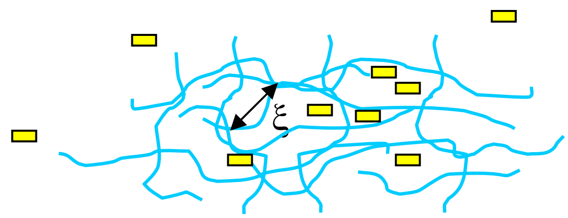
} derived from loose ionic network



Ex. 2: Hydrogels

used for contact lenses, drug delivery matrices, synthetic tissues

x-linked, swollen polymer network




crosslink density $\sim 1/\xi^3$

Properties:

- shape-retaining
- flexible
- slow release of entrapped molecules

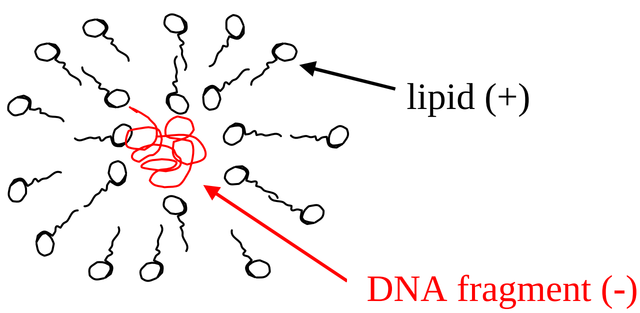
} derived from crosslinked network

**Self-Assemblies:** aggregates of amphiphilic molecules

*micelles, lyotropic liquid crystals, block copolymers*

Ex.: Cationic Liposomes

used for gene therapy



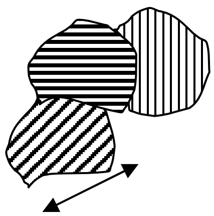

Properties:

- water dispersible
- can contain/release DNA
- can penetrate cell membrane (-)

} derived from supramolecular assembly

## 3. Microstructure (1μm + )

**Crystal "grains":** crystallites of varying orientation



10 μm

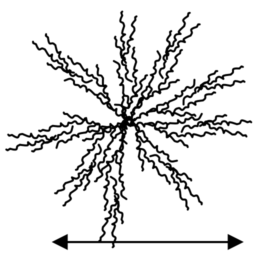
Ex: Stainless steels Fe-Ni-Cr

Depletes at grain boundaries causing corrosion

used for fracture fixation plates,etc., & angioplasty stents

**Spherulites:** radially oriented crystallites interspersed w/ amorphous phase

*semicrystalline polymers, glass-ceramics*



10 μm

**Precipitates:** secondary phases present as inclusions

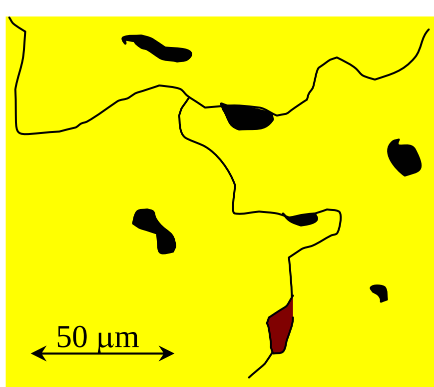
*metals, ceramics, polymers*

Ex: Carbides in Co-Cr alloys

Properties:

- Hardness
- Corrosion resistance (form at grain boundaries)

} derived from precipitates



**Porosity:** often desirable in biomaterials applications

Ex. 1: Porous Bioresorbable Scaffolds

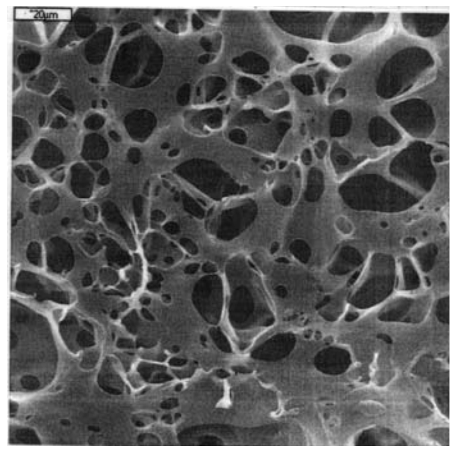
polylactide (PLA)

used for tissue regeneration

Properties:

- Penetrable to body fluids, cells
- Structurally stable

derived from pore microstructure



Pore dimensions: 10-100 μm

Ex. 2: Porous Metal Coatings

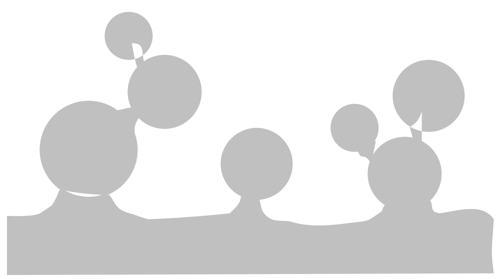
Ti or Co-Cr-Mo

used on hard tissue replacemt implants

Properties:

- Enhanced cell adhesion
- Tissue ingrowth

derived from pore microstructure



Pore dimensions: 10-100 μm

**Take Home Message:**

***Higher order structure & microstructure strongly dictate kinetic processes & mechanical response.***