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 application, 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!

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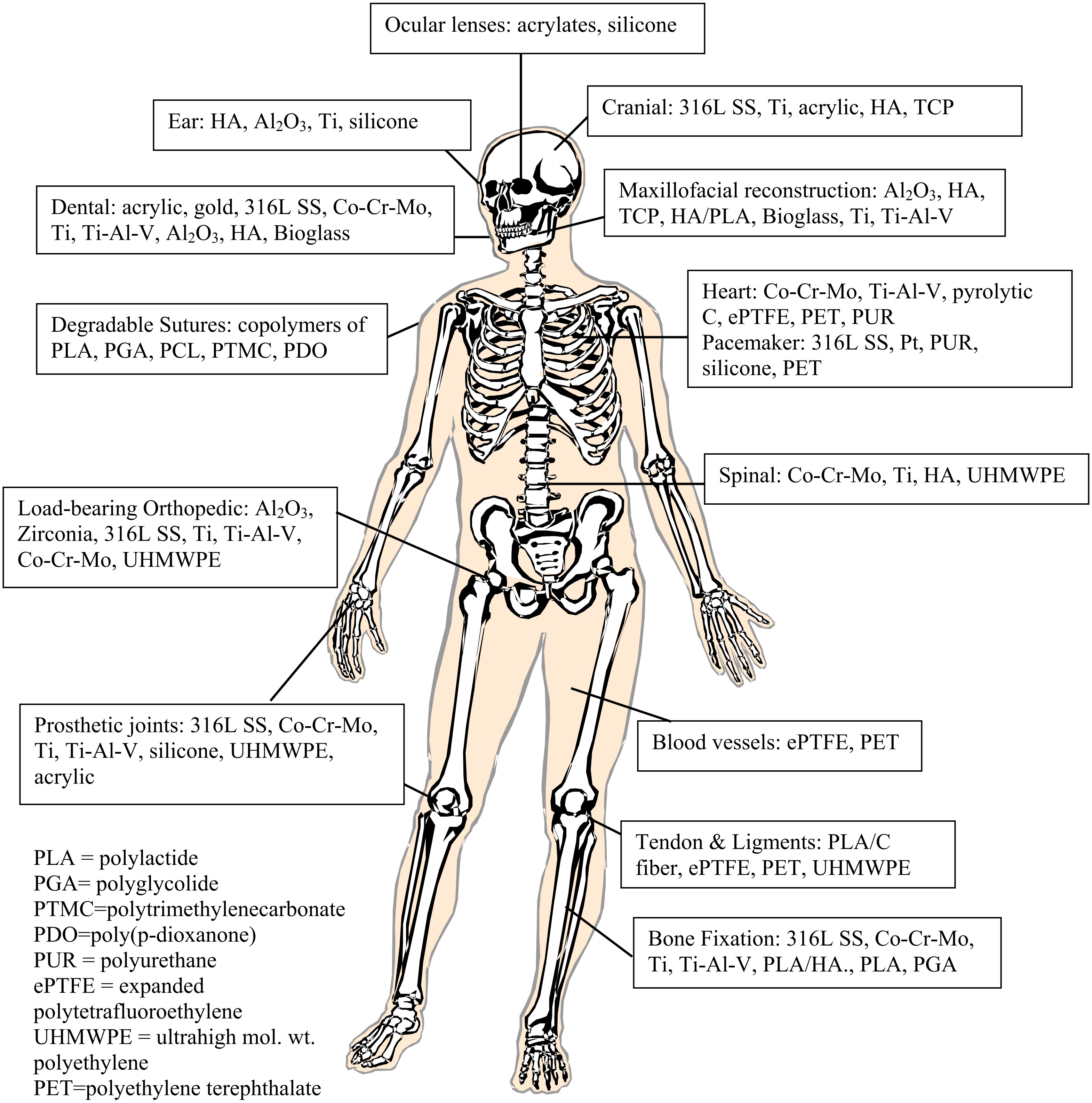
*from Biomaterials Science: An Introduction to Materials in Medicine, 2nd ed., B.D. Ratner et al., eds., Elsevier, NY 2004
**from Biomaterials Science: An Introduction to Materials in Medicine, 1st ed., B.D. Ratner et al., eds., Elsevier, NY 1996
***from Introduction to Biomedical Engineering, 2nd ed.,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

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



Ocular lenses: acrylates, silicone

Ear: HA, Al_2O_3, Ti, silicone

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

Dental: acrylic, gold, 316L SS, Co-Cr-Mo, Ti, Ti-Al-V, Al_2O_3, HA, Bioglass

Maxillofacial reconstruction: Al_2O_3, HA, TCP, HA/PLA, Bioglass, Ti, Ti-Al-V

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

Heart: Co-Cr-Mo, Ti-Al-V, pyrolytic C, ePTFE, PET, PUR
Pacemaker: 316L SS, Pt, PUR, silicone, PET

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

Load-bearing Orthopedic: Al_2O_3, Zirconia, 316L SS, Ti, Ti-Al-V, Co-Cr-Mo, UHMWPE

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

Blood vessels: ePTFE, PET

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

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

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

What governs materials choice?

Historically ⇒ Today

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)

Today ⇒ Future

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

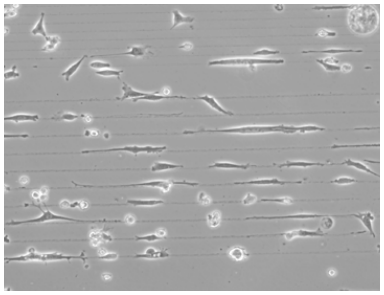
What is “structure”? *the arrangement of matter*

Both synthetic materials & biological systems have many length scales of structural importance.

Structural Hierarchies

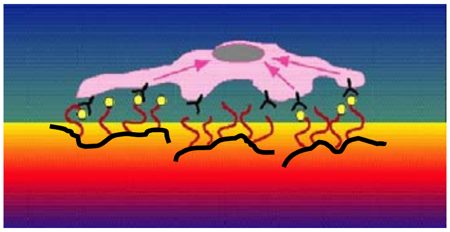
Synthetic Materials		Living Organisms
Chemical Primary Structure	10^{-10}m	Molecules (H$_2$O, peptides, salts…)
Higher Order Structure	The realm of biomaterials engineering	Organelles (lysosomes, nucleus, mitochondria)
Microstructure	Ce	
Composites	10^{-3}m	Tissues
Parts		Organs
Devices	Individual	s

Biomaterials Engineering spans ~8 orders of magnitude in structure!

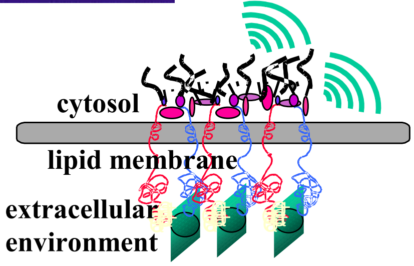


Fibroblast cells aligned on micro-patterned surface
Engineered length scale: 10^{-3} to 10^{-6} m

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

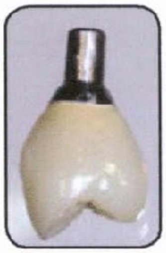
Properties:
- corrosion resistant
- high strength
- wear resistant
- "biocompatible"

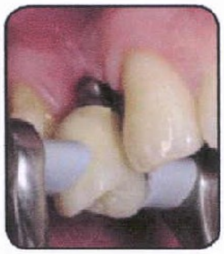
derived from ionic bonding

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

from Bicon, Inc. website:
www.bicon.com


Integrated Abutment Crown™ on soft-tissue model.


Integrated Abutment Crown™.


Insertion of Integrated Abutment Crown™ into implant well.

Courtesy of BICON, LLC. (http://www.bicon.com). Used with permission.

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

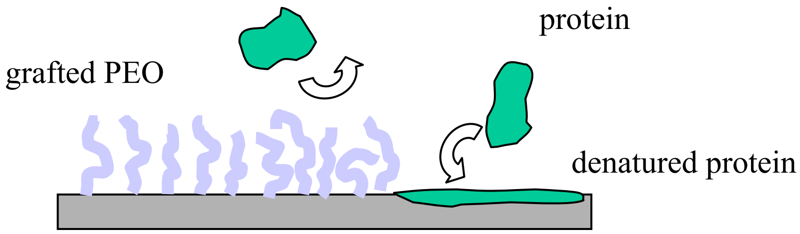
used for protein resistant coatings, hydrogels

Properties:

- flexible
- hydrolysable
- water soluble
- bioinert

Derived from primary & secondary bonding

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



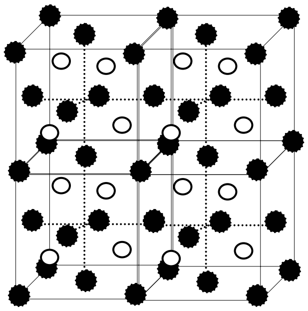
Take Home Message:
"Biocompatibility" is strongly determined by primary chemical structure!

Biocompatibility: "ability of a material to perform with an <u>appropriate</u> 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

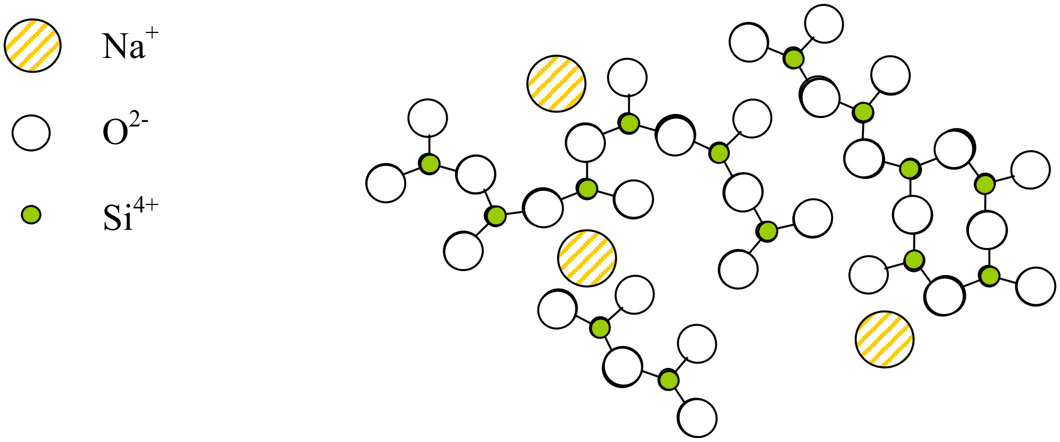
Ex. 1: Bioactive Glasses — used for hard connective tissue replacement

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)

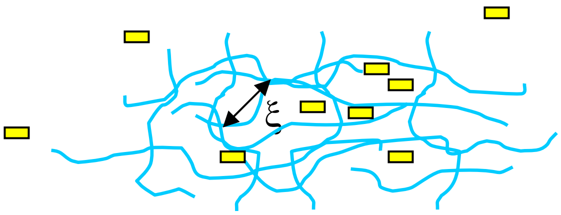
} derived from loose ionic network



Ex. 2: Hydrogels

used for contact lenses, drug delivery matrices, synthetic tissues

x-linked, swollen polymer network



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

Properties:

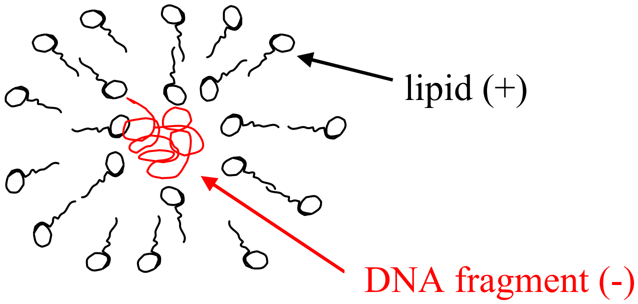
- shape-retaining
- flexible
- slow release of entrapped molecules

} derived from crosslinked network

Self-Assemblies: aggregates of amphiphilic molecules

micelles, lyotropic liquid crystals, block copolymers

Ex.: Cationic Liposomes used for gene therapy



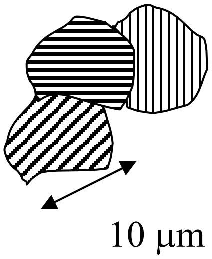
Properties:

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

} derived from supramolecular assembly

3. Microstructure (1 µm +)

Crystal “grains”: crystallites of varying orientation



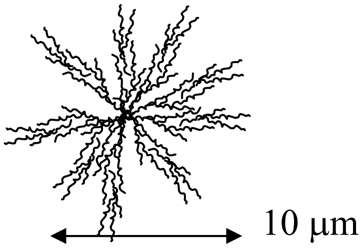
Ex: Stainless steels Fe-Ni-Cr

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



Precipitates: secondary phases present as inclusions

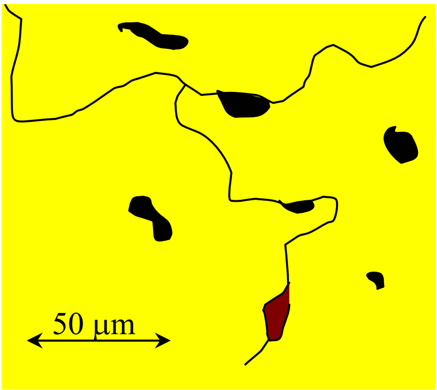
metals, ceramics, polymers

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

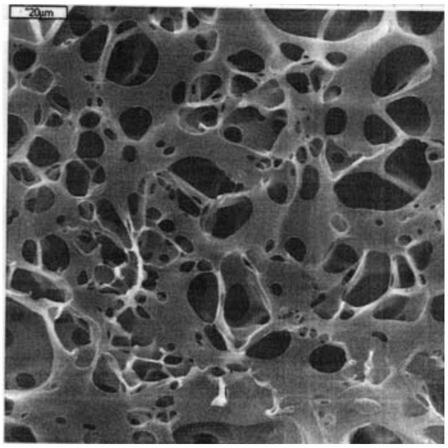
polylactide (PLA)

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

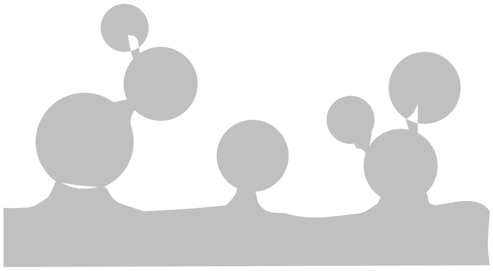
Ti or Co-Cr-Mo

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.