Biomaterials

Materials used to safely replace or interact with biological systems

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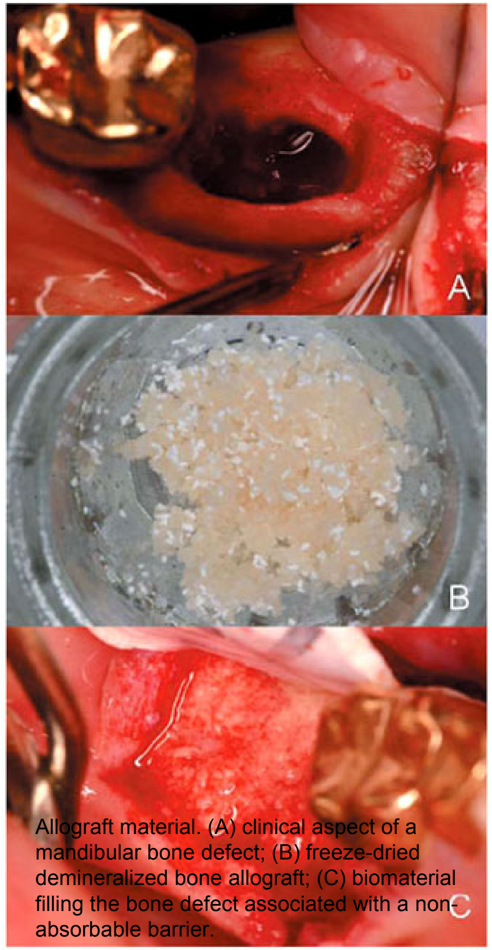
Vorlesungsunterlagen: IGB Homepage
Education, Biomaterials

Recommended literature:

“Biomaterials, an introduction” J. Park and R.S. Lakes 2007 Springer Science

and

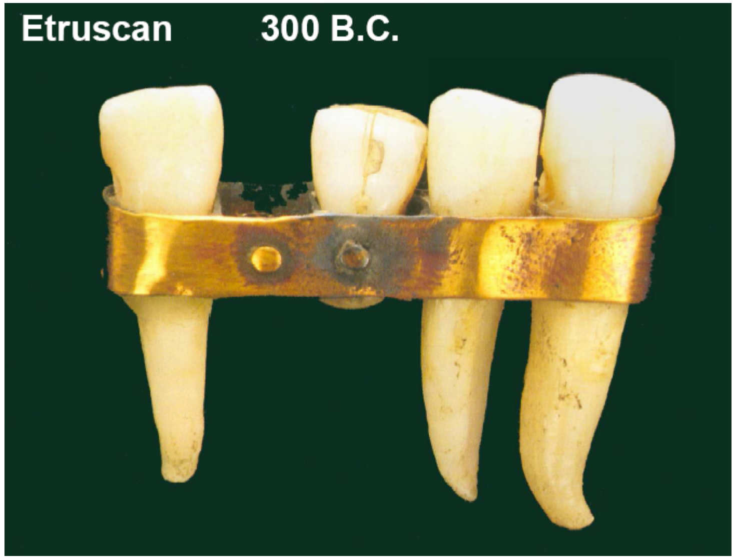
“Biomaterials Science” BD. Rafner 2004 Elsevier Academic Press (available from the TUG-Bib in e-version)



Allograft material. (A) clinical aspect of a mandibular bone defect; (B) freeze-dried demineralized bone allograft; (C) biomaterial filling the bone defect associated with a non-absorbable barrier.

A very short history of biomaterials

- The Romans, Chinese, and Aztec used gold in dentistry more than 2000 years ago.
- Glass eyes and wooden teeth have been used trough much of the recorded history.



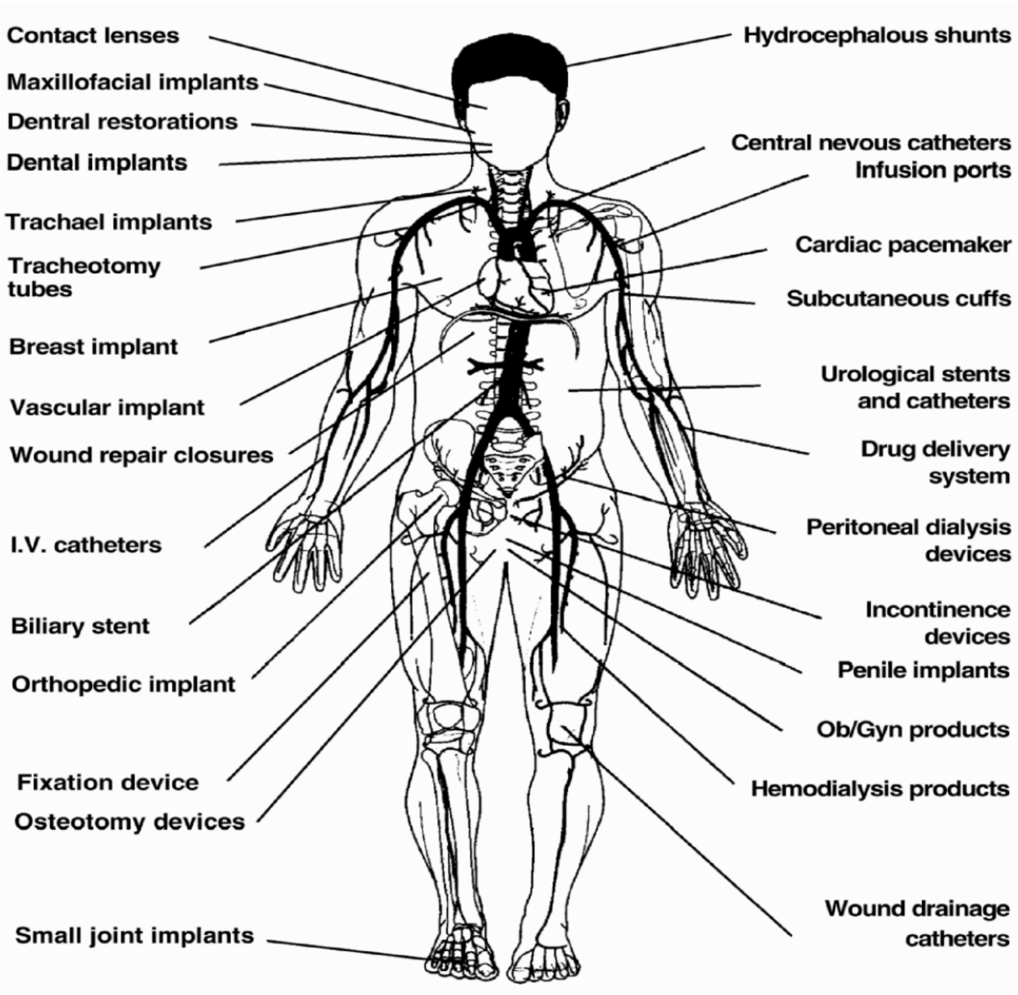
A very short history of biomaterials

- Synthetic plastics became available at the turn of last century.
- PMMA (Polymethyl methacrylate) was intoduced in dentistry in 1937.
- Experiments with parachute cloth (Vinyon N) as vascular prosthesis after world war II.
- In the early 1960s total hip replacement made of PMMA, ultrahigh-molecular-weight polyurethan, and stainless steel.

Notable Developments Relating to Implants

Year	Investigator	Development
Late 18th–19th century		Various metal devices to fix fractures; wires and pins from Fe, Au, Ag, and Pt
1860–1870	J. Lister	**Aseptic** surgical techniques
1893–1912	W.A. Lane	Steel screws and plates for fracture fixation
1909	A. Lambotte	Brass, Al, Ag, and Cu plate
1912	Sherman	Vanadium steel plate, **first alloy** developed exclusively for medical use
1926	E.W. Hey-Groves	Used carpenter's screw for femoral neck fracture
1931	M.N. Smith-Petersen	Designed first femoral neck fracture fixation nail made originally from stainless steel, l ater changed to Vitallium®
1938	P. Wiles	First total **hip replacement**
1946	J. and R. Judet	First **biomechanically** designed hip prosthesis; first **plastics** used in joint replacement
1940s	M.J. Dorzee, A. Franceschetti	**Acrylics** for corneal replacement
1952	A.B, Voorhees, A. Jaretzta, A.H. Blackmore	First blood vessel replacement made of parachute cloth
1958	S. Furman, G. Robinson	First successful direct stimulation of heart
1960	A. Starr, M.L. Edwards	Heart valve
1970s	W.J. Kolff	**Experimental total heart replacement**
1990s		**Refined implants** allowing bony ingrowth
1990s		Controversy over silicone mammary implants
2000s		**Tissue engineering**
2000s		**Nanoscale materials**

Various implants and devices for replacement or enhancement



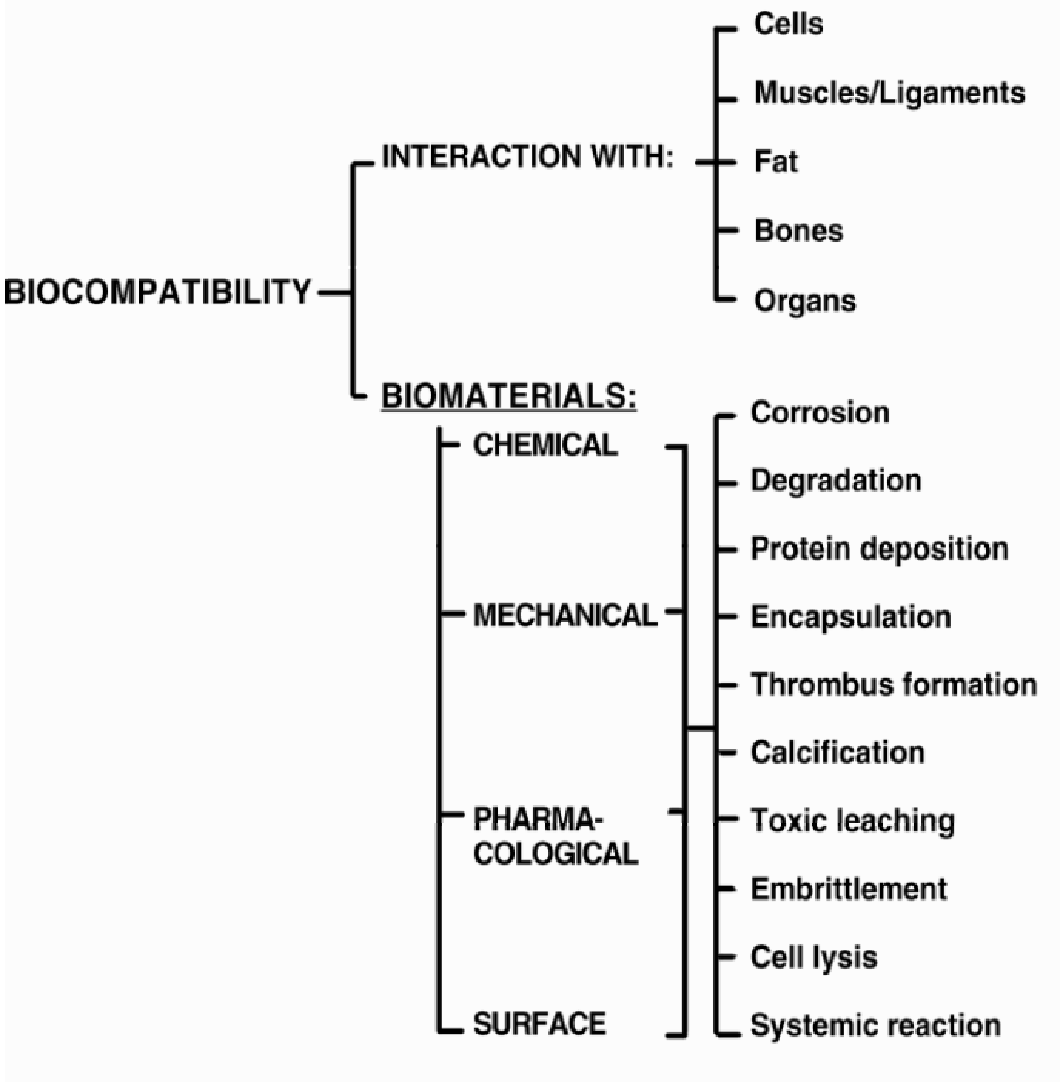
Courtesy R. Zenz

Biomaterial science - definitions

- Biomaterial — A biomaterial is a nonviable material used in a (medical) device intended to interact with biological systems (Williams 1987).
- Biocompatibility — The ability of a material to perform with an appropriate host response in a specific application (Williams 1987).
- Host Response — The response of the host organism (local and systemic) to the implanted material or device.

E.g.: A hemodialysis system serving as an artificial kidney requires materials that must function in contact with the patients`s blood and exhibit appropriate membrane permeability and mass transport characteristics.

Biocompatibility



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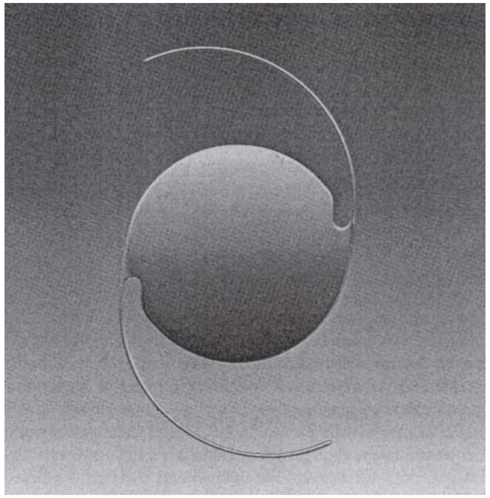
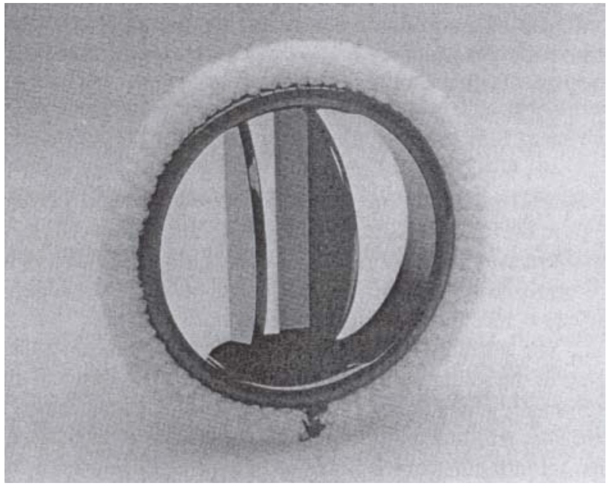
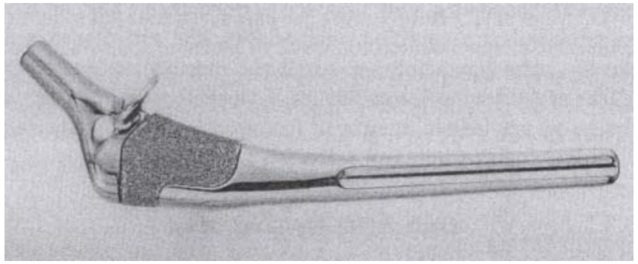
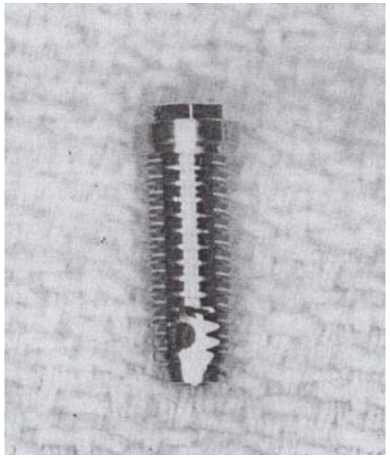
Examples of biomaterial applications (USA)

- Substitute heart valves (45,000/year)
- Artifical hips (90,000/year)
- Dental implants (275,000/year)
- Intraocular lenses (1.4 millions/year)









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Examples of biomaterial applications (USA)

Numbers of devices:	
Intraocular lenses	1,400,000[a]
Contact lenses:	
Extended wear soft lens users	4,000,000[a]
Daily wear soft lens users	9,000,000[a]
Rigid gas-permeable users	2,600,000[a]
Vascular grafts	250,000[b]
Heart valves	45,000[a]
Pacemakers	460,000[a]
Blood bags	30,000,000[b]
Breast prostheses	544,000[a]
Catheters	200,000,000[b]
Oxygenators	500,000[b]
Renal dialyzers	16,000,000[b]
Orthopedic (knee, hip)	500,000[b]
Knee	816,000[a]
Hip	521,000[a]

[a]1990 estimate for United States.
[b]1981 estimate for western countries and Japan.

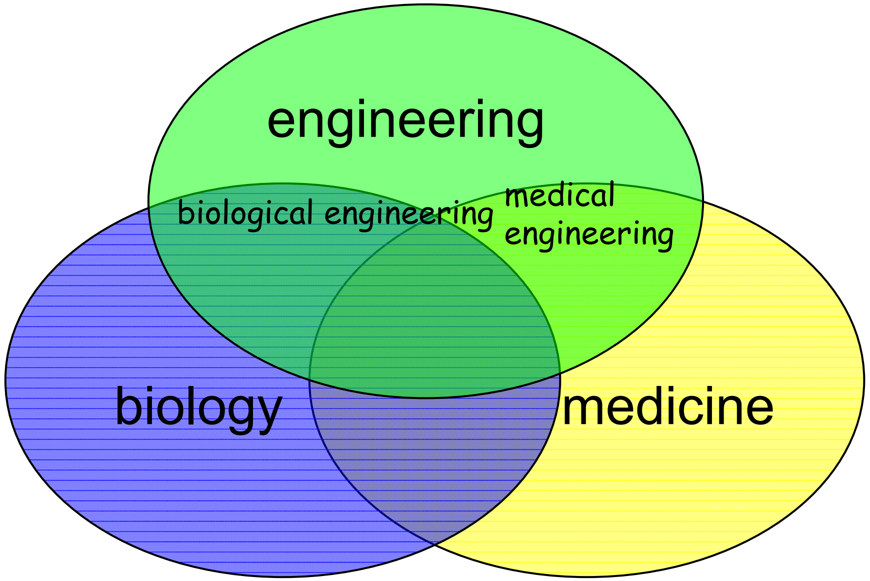
Many materials are used

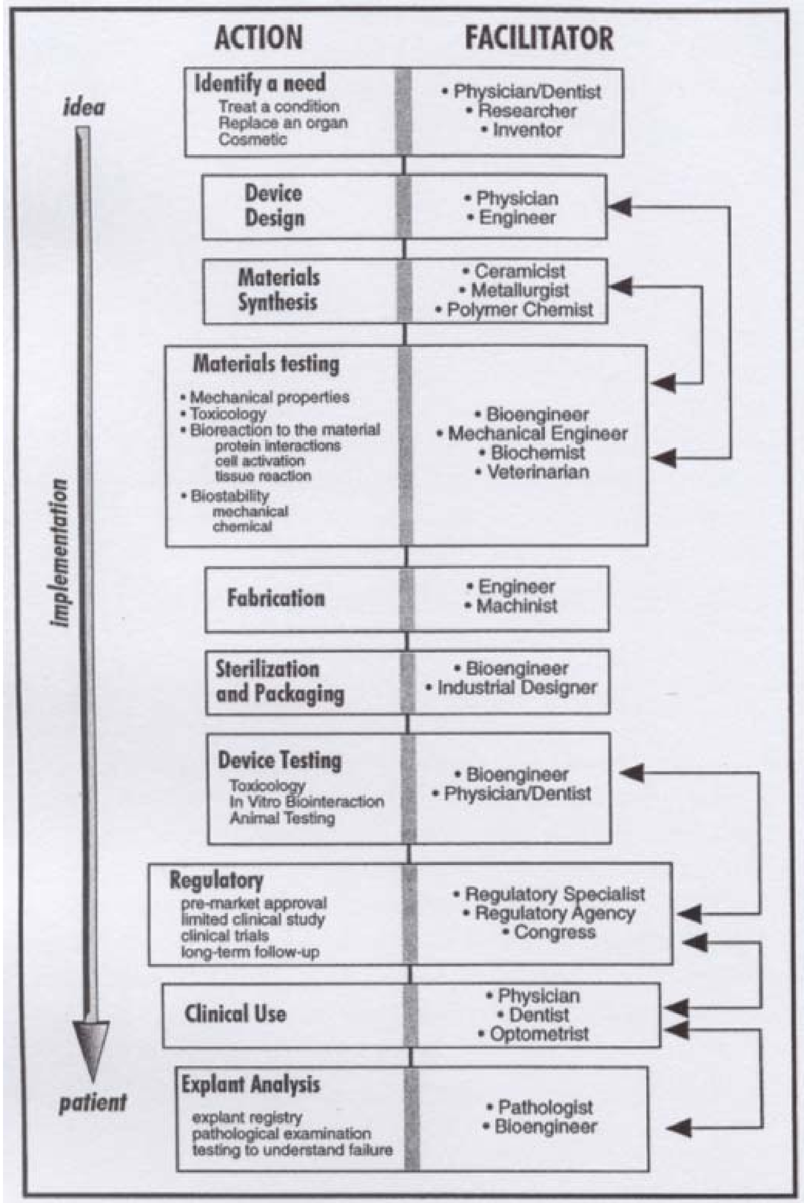
TABLE 1 Some Applications of Synthetic Materials and Modified Natural Materials in Medicine

Application	Types of materials
Skeletal system	
Joint replacements (hip, knee)	Titanium, Ti–Al–V alloy, stainless steel, polyethylene
Bone plate for fracture fixation	Stainless steel, cobalt–chromium alloy
Bone cement	Poly(methyl methacrylate)
Bony defect repair	Hydroxylapatite
Artificial tendon and ligament	Teflon, Dacron
Dental implant for tooth fixation	Titanium, alumina, calcium phosphate
Cardiovascular system	
Blood vessel prosthesis	Dacron, Teflon, polyurethane
Heart valve	Reprocessed tissue, stainless steel, carbon
Catheter	Silicone rubber, Teflon, polyurethane
Organs	
Artificial heart	Polyurethane
Skin repair template	Silicone–collagen composite
Artificial kidney (hemodialyzer)	Cellulose, polyacrylonitrile
Heart–Lung machine	Silicone rubber
Senses	
Cochlear replacement	Platinum electrodes
Intraocular lens	Poly(methyl methacrylate), silicone rubber, hydrogel
Contact lens	Silicone–acrylate, hydrogel
Corneal bandage	Collagen, hydrogel

Interdisciplinary interactions are needed

Different disciplines have to work together, starting from the identification of a need for a biomaterial through development, manufacture, implantation, and removal from the patient.



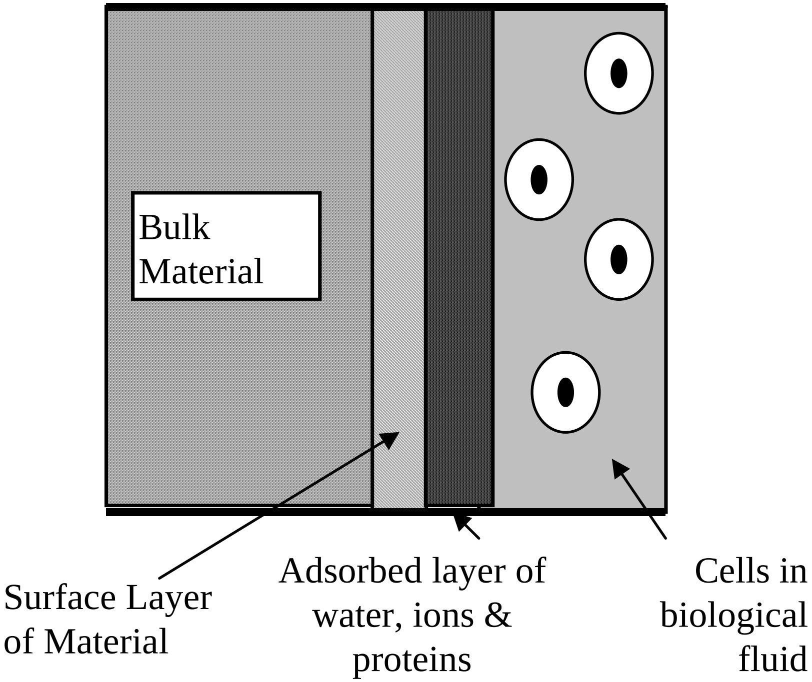


Subjects integral to biomaterials science

- Toxicology
  - Biomaterials should not be toxic.
  - „smart bombs“ (drug release systems that seeks out cancer cells and destroy them)
  - A biomaterial should not give off anything from its mass (problem with many low-molecular-weight polymers).
- Biocompatibility
  - Non tumorigenic
  - Normal wound healing, no infections
  - No hypersensitivity
- Mechanical and performance requirements
  - Hip prothesis: strong and rigid,
  - Articular cartilage substitute: soft and elastomeric
  - Dialysis membrane: strong and flexible
  - ....

Properties of materials

- Bulk properties
- Suface properties
  – Synthetic materials have specific bulk and surface characteristics.
  – They must be known prior to any medical application.
  – Do they change over time in vivo?



This information must be evaluated within the context of the intended biomedical use, since applications and host tissue responses are quite specific within areas (e.g. Cardiovascular: flowing blood contact; orthopedic: functional load bearing).

Properties and structure

- Structure can be viewed at many levels:
  - Atomic or molecular
  - Ultrastructural
  - Microstructural

- Each level of structure in a material affects the overall properties of that material in different, and sometimes conflicting, ways.

 Courtesy R. Zenz

Atomic or molecular level

- Types of bonding
  - Almost all the physical properties depend on the nature and strenght of the interatomic bonds:
    - Shape, density, ect.
    - Heat conduction
    - Electrical conduction
    - Biochemical reactivity
    - Surface properties
    - Load-deformation behavior

Bulk properties of materials

Solids are held together by strong interatomic forces.

- Metallic bonding
- Covalent bonding
- Ionic bonding
- Weak bonding

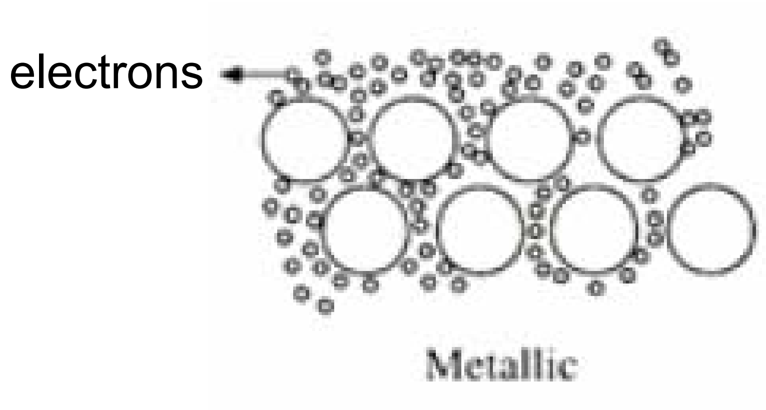
Courtesy R. Zenz

Metallic bonding

- Positively charged ion cores with negative electrons circulate around the core.
  - Free valence electrons which can "travel" about the material.
  - Electrical charge is neutralized on average.
  - Bonds are non-directional (isotropic).

- Allow plastic deformation
  - Atom position is non discriminative

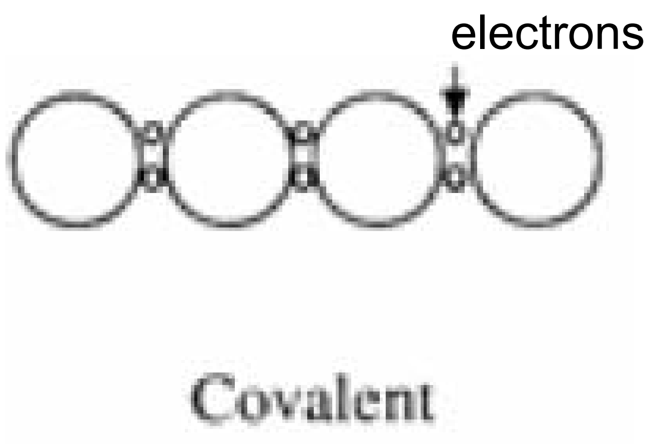
- Good electrical and heat conductance



Covalent bonding

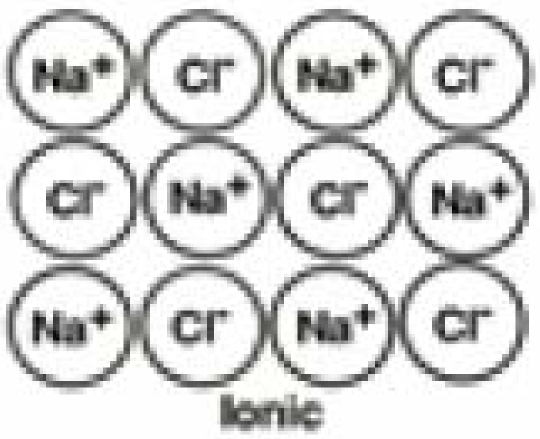
- Formed between non-metallic atoms when the valence electrons are shared to fill each outer valence orbital.
  - Carbon atoms sharing pairs of electrons.
  - Highly directional, allowing chains of monomers to be formed.

- Poor electrical and heat conductance.



Ionic bonding

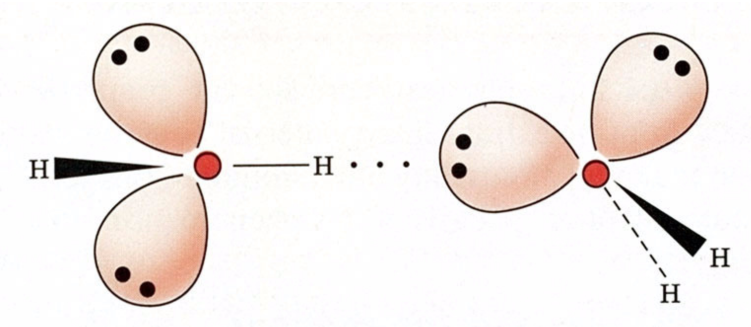
- Metallic atom shares one or more electrons with the non-metallic atom.
  - Cation is surrounded by as many anions as possible.
  - Reduces mutual repulsion of cations.
  - Packing is a function of relative atomic sizes.
- Forms a crystalline structure.
- Results in low electrical and head conductivity and low chemical reactivity.



Weak or secondary bonding

- Van Waals bonds:
  - Form among hydrogen, oxygen and other atoms.
  - Not highly directional.
  - High number of possible bonds results in strength.

- Hydrogen bonds Hydrogen bonds:
  - Formed when hydrogen is covalently bonded to an electronegative atoms.



Relative bond strenght

- Heat of vaporization (KJ/mol)

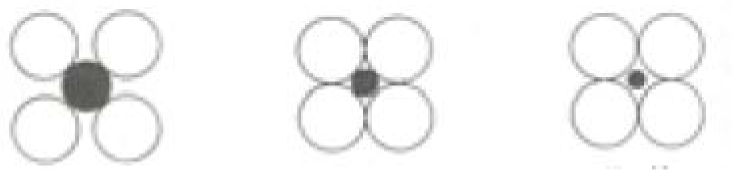
– Van der Waals	He	0.14
	N_2	13
– Hydrogen	Phenol	31
	HF	47
– Metallic	Na	180
	Fe	652
– Ionic	NaCl	1062
	MgO	1880
– Covalent	Diamond	1180
	SiO_2	2810

Ultra-structual level

- Atomic structures defined by bonding:
  - Crystalline
    - Form organized three dimensional lattices with only minor defects.
  - Non- crystalline (amorphous)
    - Form random patterns of connections.
  - Mixed

Metals-Crystalline

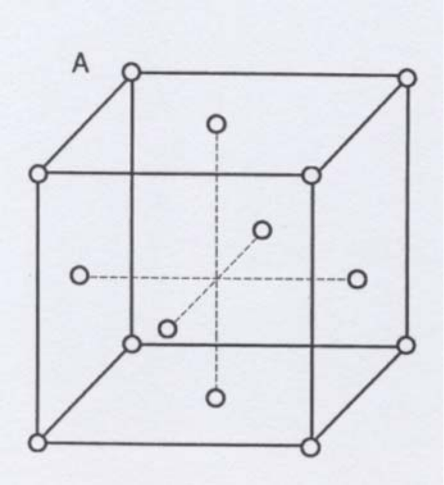
- Materials containing only metallic atoms:
  - Single elements
  - In combination (alloys)
- Single elements can closely pack.
- Alloys will pack due to relative sizes of the atoms:
  - Could be stable or unstable packing of interstitial atoms.



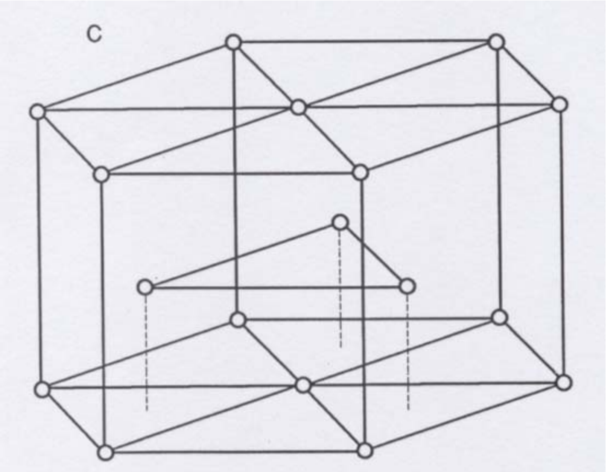
- Packing efficiency:
  - Defined by the coordination number.

Metals

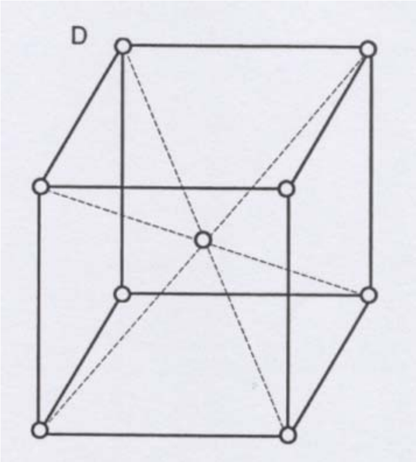
- Exhibit metallic bonding in the solid state.
- Mixtures or solutions of different metals are alloys.
- 85% have one of these crystal structures:



FCC (face centered cubic)



HCP (hexagonal close packed)



BCC (body centered cubic)

Every atom (ion) is surounded by 12 (FCC, HCP) or 8 (BCC) neighbors.

 Courtesy R. Zenz

Polymers-Amorphous

- Material behavior is more a factor of molecular features than inter-atomic bonds.

- Very long chain molecules:
  - The mer (monomer) is the basic unit.
  - Molecule containing one or more atoms that can each participate in two or more covalent bonds.

Polymers

- Covalent bonding forms the chain structure:
  - Fixed bond length.
  - Permits rotation of adjacent atoms about its axis.
  - When atoms (carbon) forms multiple covalent bonds, the sizes of the angles between the bonds involving a particular atom is fixed.

- Other covalent, hydrogen or van der Waals bonds link between chains:
  - Wide variety of conformations possible.

Polymers

- Two (3) classes of polymers:
  - Thermoplastic
    - “Straight” - have little or no branching
    - Can be melted and remelted
    - Will reform into similar structure
  - Thermosetting
    - Side chains are present
    - Side chains form links between chains
    - Will not reform equally upon remelting
  - Elastomers

Ceramics-Crystalline

- Inorganic, non-metallic materials:
    - Those materials that aren't metals or polymers

  - Most contain one or more metallic oxides along with other compounds.

  - May have varied phases:
    - Crystalline, single or poly crystalline, or amorphous

Ceramics

- Combinations of ionic and covalent bonding.

  – Must be electrically neutral:
    - Requires specific organization of covalently bonded atoms.
    - Leads to complex crystal or mixed structures.

  – Combined cation anion structure results in mechanical and thermal/electrical properties:
    - Good thermal and electrical insulator.
    - Resistant to high temperatures and severe environment.

Ceramics

- Nearly inert ceramics:
  - Alumina (Al_2O_3)
  - Carbon (diamond)
- Surface reactive ceramics:
  - Sites for oxidation or protein bonding on surfaces.
- Highly reactive:
  - Can be resorbed by exposure to biological environment:
    - Calcium phosphate

Inorganic glasses-amorphous

- To make:
  - Take ceramic material and melt.
  - With cooling the material does not return to a crystal structure.
- Form structures that do not repeat throughout the aggregates:
  - Silicates and phosphates
    - Brittle
    - Low heat and electrical conduction

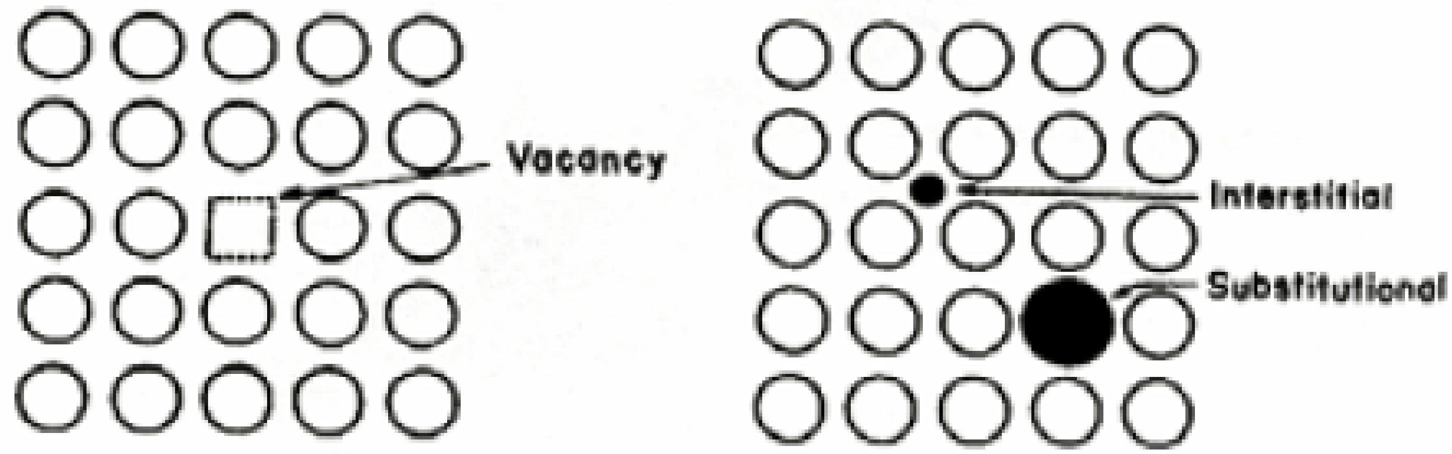
Ultra-structural level in crystalline materials

- Imperfections in crystalline structures:
    - Defects play a major role in determining the physical properties of a material.

  - Point defects
  - Line defects
  - Grain boundaries

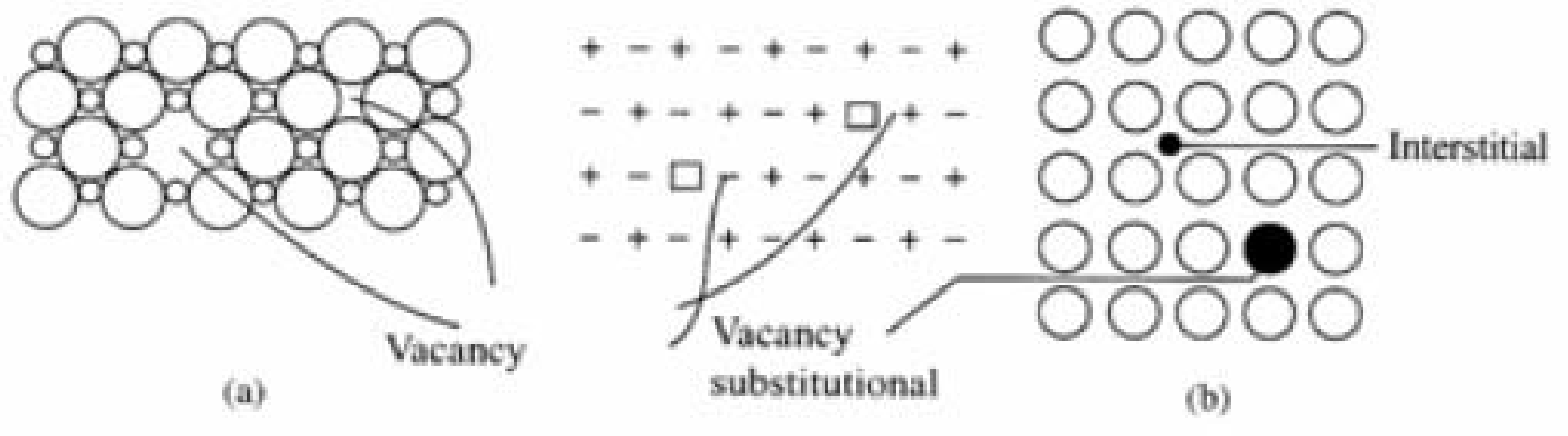
Point defects

- Vacancies:
  - Empty sites in the crystal formation.
  - Allow for increased atomic diffusion.
  - Maintains charge balance.
  - Relative size of atoms controls.



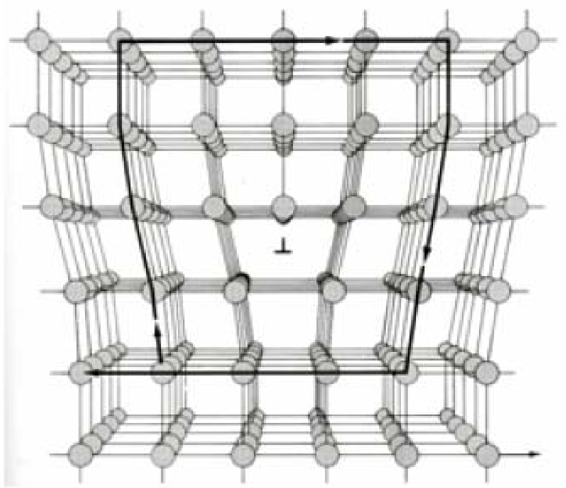
Point defects

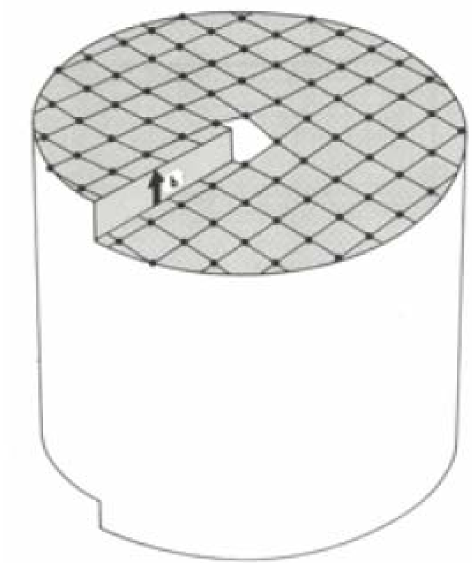
- Substitutional atoms:
  - Sites filled by differing atoms.
  - Result in atomic distortion if atomic radii differ.
- Interstitial atoms:
  - Atoms fitted into the crystal formation.
  - Less frequent in closely packed structures.



Line defects

- Plane of atoms is displaced or dislocated from its regular lattice space.





Courtesy R. Zenz

Line defects

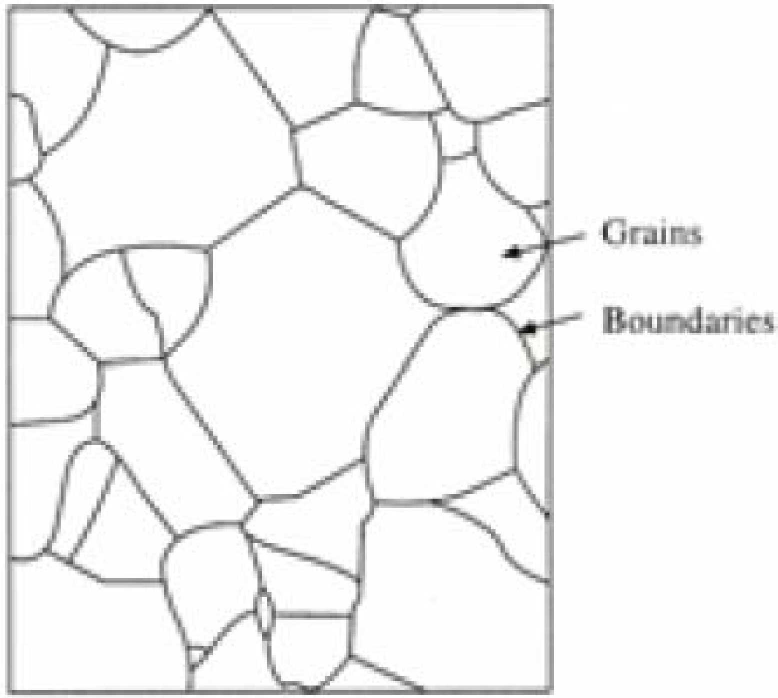
- Act to reduce the strength and stiffness of the solid:
  - An increase in energy along the dislocation.
    - Less energy must be added to move the planes or break the bonds at this location.
  - Effect is concentration dependent.
    - Many line defects will act to strengthen a material as they interfere with the progression of dislocations.

Grain boundaries

- Planar defect between crystals in a polycrystalline material.

  - Typically 1 to 2 atomic distances wide.

  - Within a grain, all crystalline unit cells are aligned.



  - At grain boundaries, there is a transition zone where atoms are not aligned with either grain.

Grain boundaries

- Less efficient atomic packing at grain boundaries:
  - Allows for diffusion of gases or liquids.
- Increases chemical reactivity.
- Can prevent progression of line defects:
  - Alignment of grains.
  - Strengthening material.

Microstructural level in crystalline materials

- Grain structure can vary in:
  - Grain size
  - Preferred orientation
  - Grain shape

Grain size

- A larger grain size number (GS#) indicates a higher number of grains and grain boundaries per unit volume.
  - Fine grained structure is stronger than a coarse one at normal temperatures.
    - Grain boundaries interfere with the movement of atoms during deformation.
- A fine-grained structure is weaker and softer than a coarse one at elevated temperatures.
  - Grain boundaries are a source of weakness above temperatures where atoms start to move significantly.

Grain shape

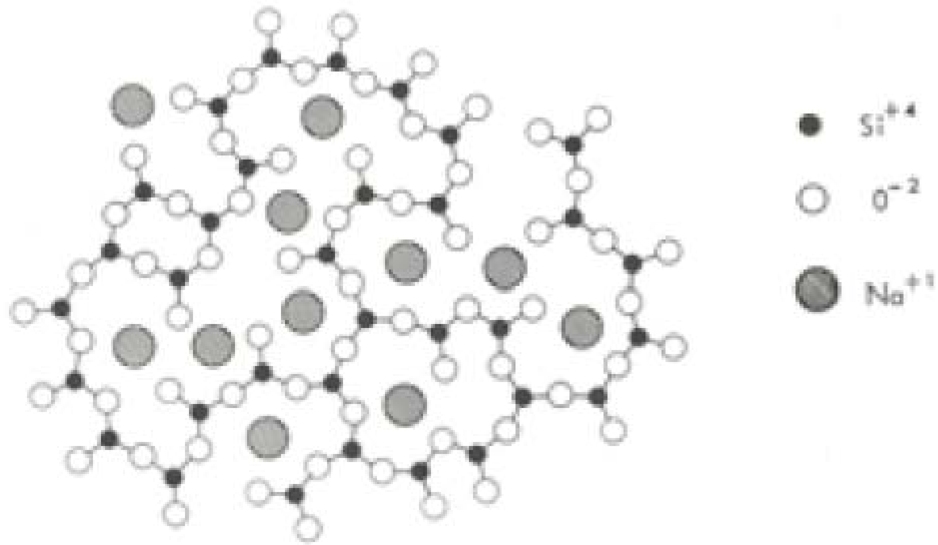
- Equiaxed
  - Approximately equal dimensions in 3 directions
- Plate-like
  - One dimension smaller than other two
- Columnar
  - One dimension larger than other two
- Dendritic (tree-like)

Grain orientation

- Description of the crystal orientation within grains:
  - Typically random orientation within metals.
    - Ferric metals align to Earth's magnetic field.
- Preferred orientation can be manipulated to obtain improved material properties.

Ultra-structural level in amorphous materials

- In network materials:
  - Vacancies
  - Substitutional atoms
  - Interstitial atoms



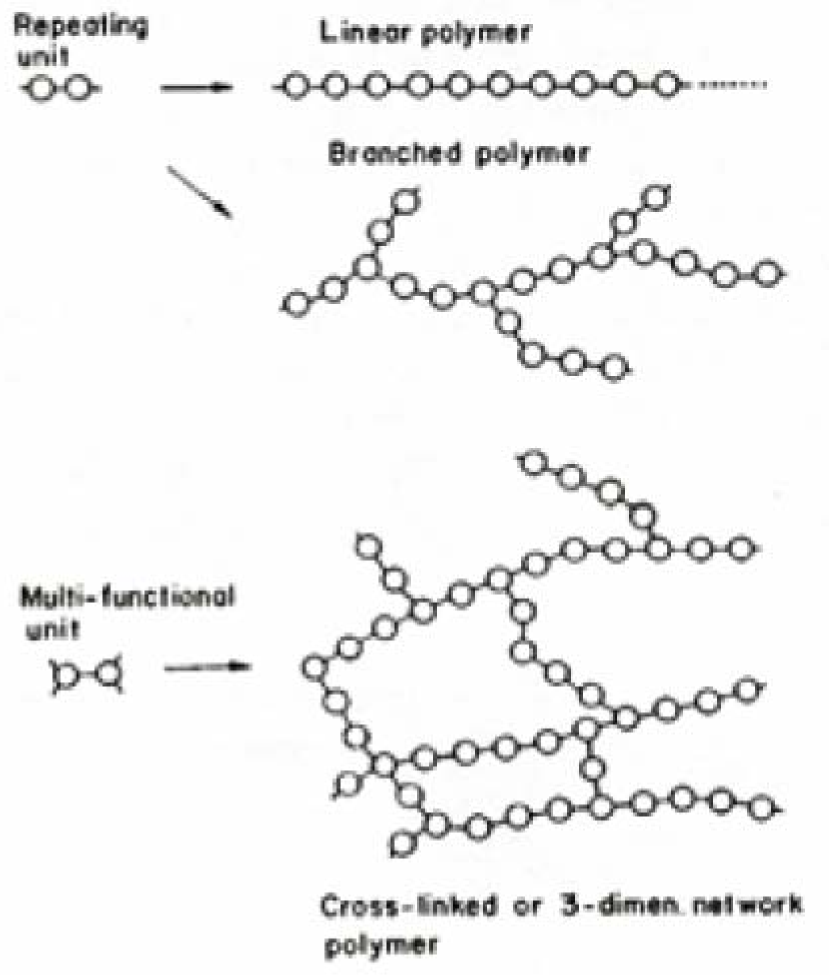
  - SiO_2 with Na^+
  - With more O, network is broken, becomes crystalline.

Ultra-structural level in polymers

- Polymer material behavior is a function of:
  - Linearity, branching and cross-linking of polymer chain(s).
  - Symmetry of chain.
  - Degree of crystallinity.

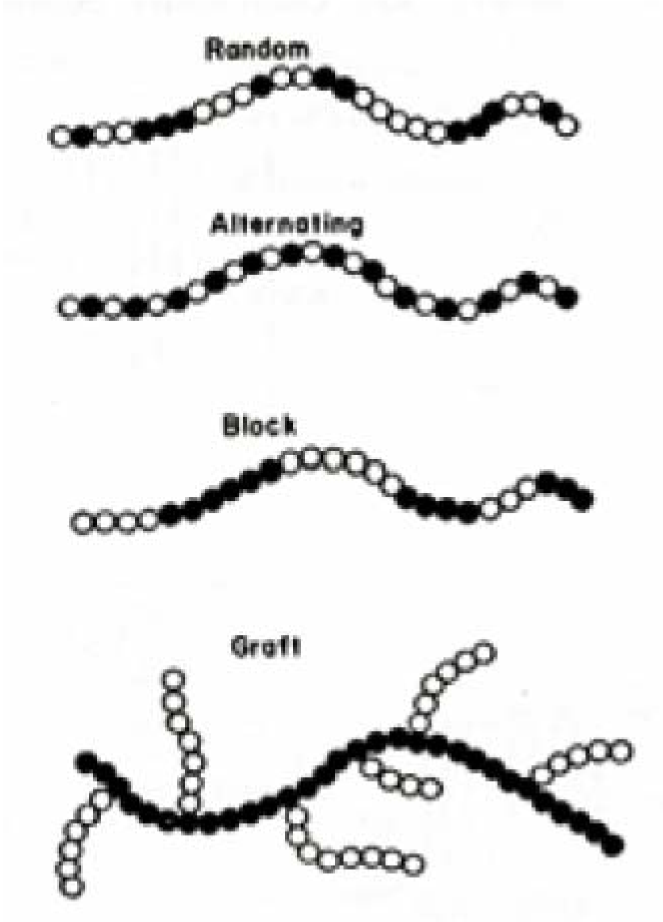
Polymers

- Organization of chain molecules within the polymer.
  - Linear
  - Branched
  - Cross-linked



Ultra-structural level in polymers

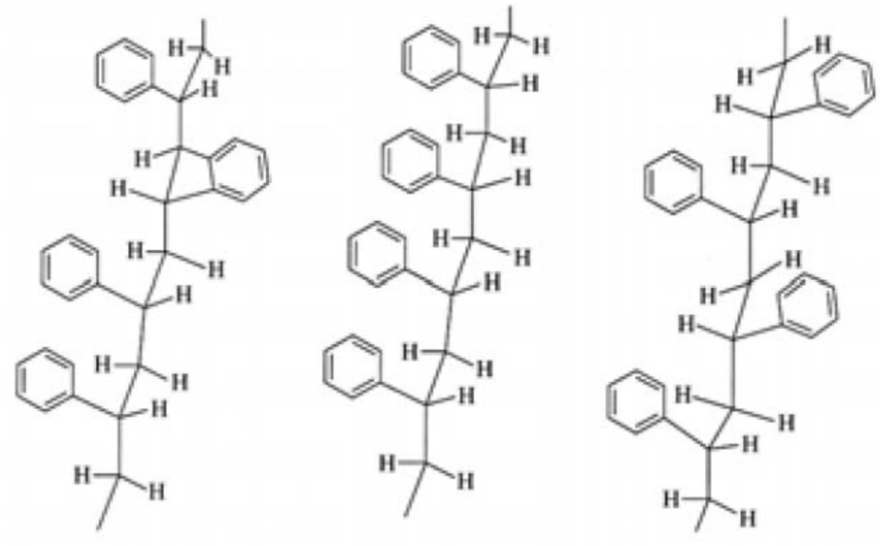
- Co-polymer can form (similarly as substitutional atoms) in the polymer chain:
  - Random
  - Alternating
  - Block
  - Graft



Side elements of polymers

- Structural molecules along the chains:
  - Atactic molecules:
    - Elements not all facing the same way.
  - Isotactic molecules:
    - Elements are facing same direction.
  - Syndiotactic molecules:
    - Elements alternate perfectly.

Polystyrene



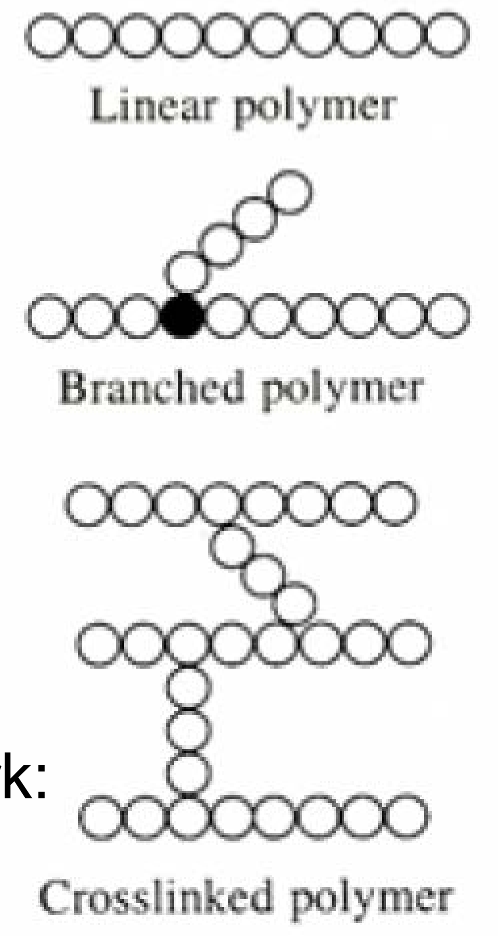
atactic isotactic syndiotactic

Polymers

- Effects of linearity, branching and symmetry on structure:
  - Unbranched isotactic or syndiotactic polymers can form highly crystalline denser materials.
  - More branched, cross - linked or atactic chains form amorphous, lower density materials.

- Degree of polymerization:
  - The average number of monomers or repeating units per molecule or chain.
  - Longer chains result in less mobility of the polymer
  - Higher molecular weight results in:
    - Higher strength.
      - More interweaving of the chains.
    - Greater thermal stability.

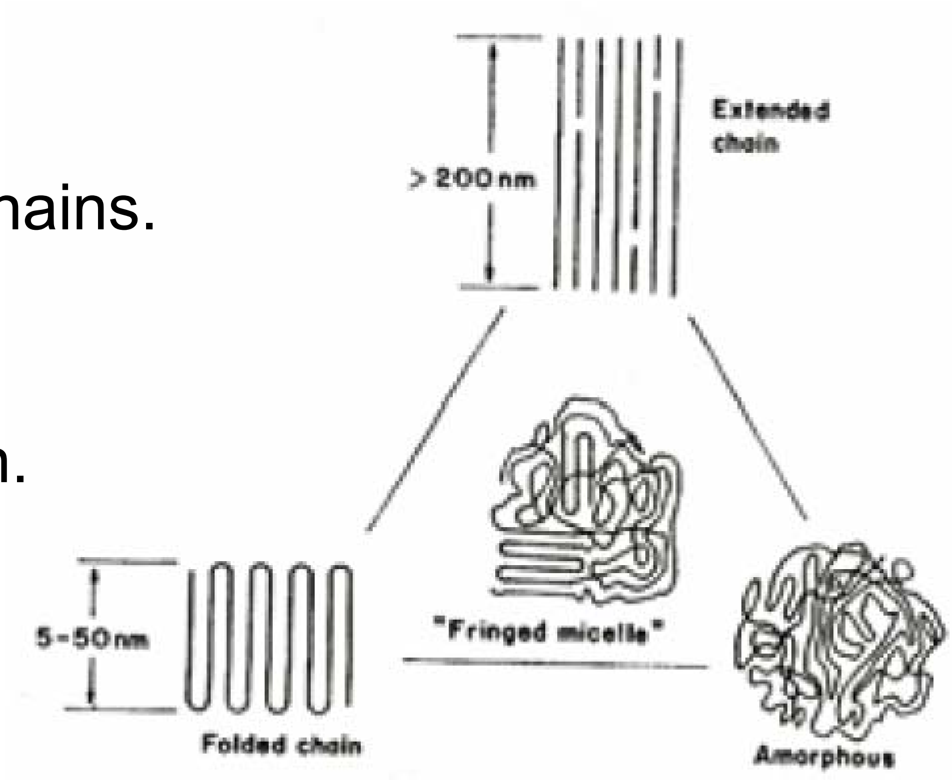
Micro-structural levels in polymers



- Linear:
  - No branches, most easily crystallizes.
- Branched:
  - Single back-bone allows minimal crystallization.
- Cross-linked or three dimensional network:
  - Forms only amorphous structures.

Micro-structural levels in polymers

- Crystalline regions:
  - Extended chains:
    - Linear regions of chains.
  - Folded chains:
    - Chains wrapping forth back and forth.
- Amorphous region:
  - Totally random structure.
- Fringed micelle:
  - Coexistence of all three structures.



Surface properties

- The surface of the material should be fully characterized in terms of its chemistry (elemental/molecular composition), physical morphology, and structure.
- The interactions of macromolecules in the biological system with the characterized surface should be studied.
- The cellular response to the material should be evaluated by performing in vitro and in vivo experiments.

Surface characterization

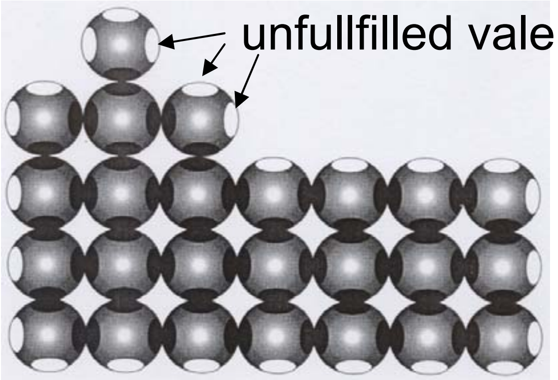
- The surface will always be different than the bulk material:
  - Reactive to its environment
  - Has reacted with its environment
  - Has been modified during formation
  - Contamination or impurities
  - Forced atomic or molecular orientations
  - Energy variations

Courtesy R. Zenz

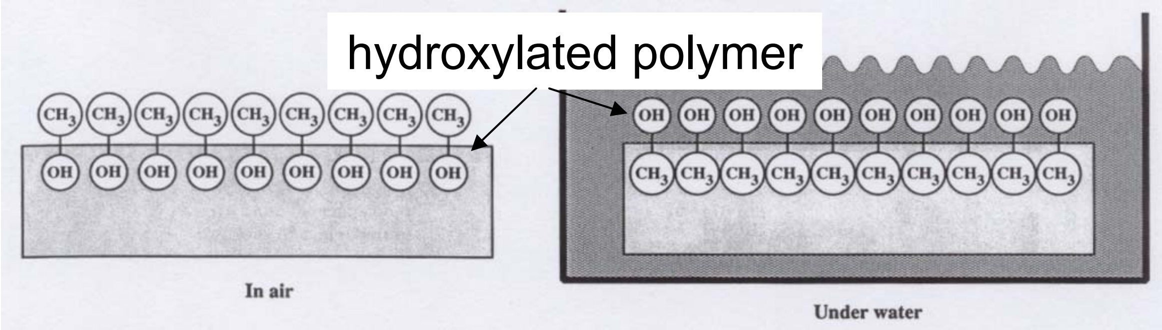
Surface properties of materials

The surface region of a material is uniquely reactive.

- The surface is inevitably different from the bulk.
- Surfaces readily contaminates.



- The surface structure of a material is often mobile (movement of atoms and molecules near the surface).



The body „reads“ the surface structure of devices and materials and responds.

Surface properties of materials

- Implant surface
  - Dense and inert:
    - Implant movement and loosening is possible.
  - Porous:
    - Ingrowth of tissue (bone) stabilizes the implant.
    - Blood supply is needed (pore size >100µm for vascularization).
    - Large porosity degrades strenght of the material.
    - Micromovement of implant:
      - Cut off of blood supply - tissue will die – inflammation – interfacial stability will be destroyed.

Surface properties of materials

- Porous metals:
  - Large increase of surface area provides focus for corrosion of the implant and loss of metal ions into the tissue.
    - Surface coating with bioactive ceramic such as HA (hydroxyapatite).

- Porous ceramics:
  - Advant.: inert + bone ingrowth
  - Disadvant.: weaker → restricted to non-load bearing applications.

Surface characteization

- Interactions of macromolecules in the biological system with the biomaterial:
  - Reactivity
  - Protein adhesion
  - Absorption
  - Permeability
  - Corrosion
  - Degradation

Courtesy R. Zenz

Surface characterization

- The cellular response to the material should be evaluated by performing in vitro and in vivo experiments.
  - Cell adhesion
  - Cell motility
  - Protein or enzyme production
  - Gene expression
  - Cell death or toxicity