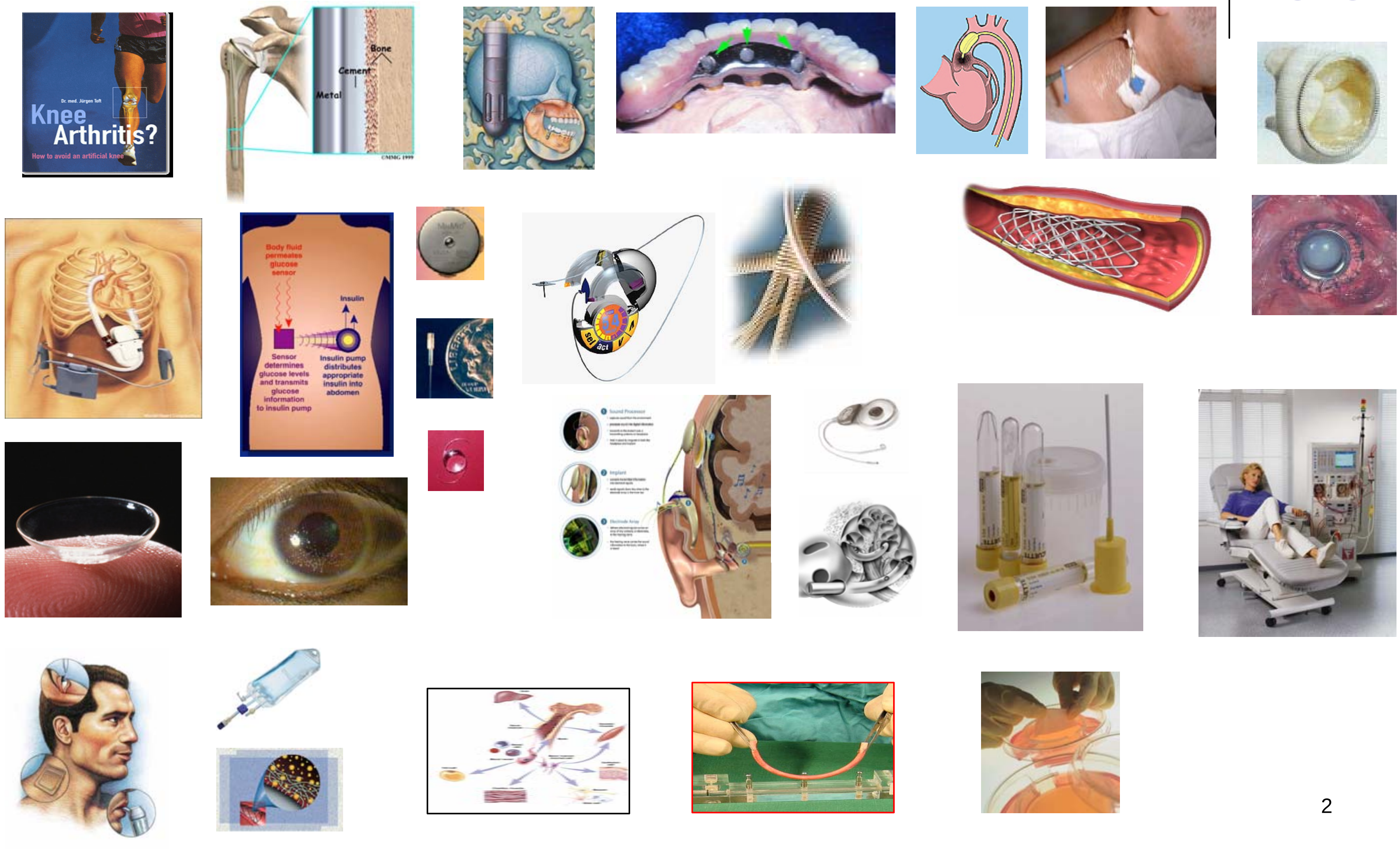
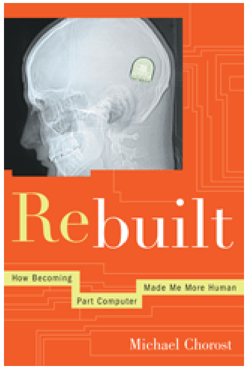
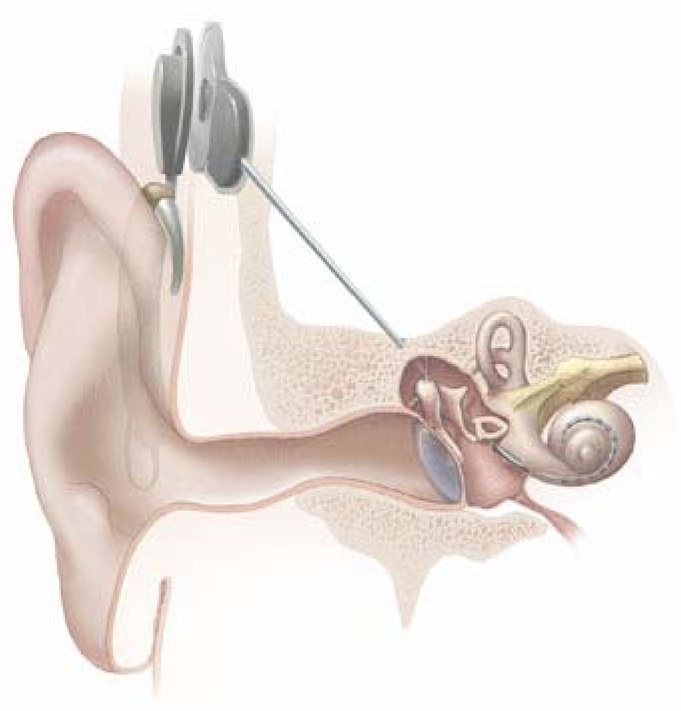
"Ask courageous questions. Do not be satisfied with superficial answers."

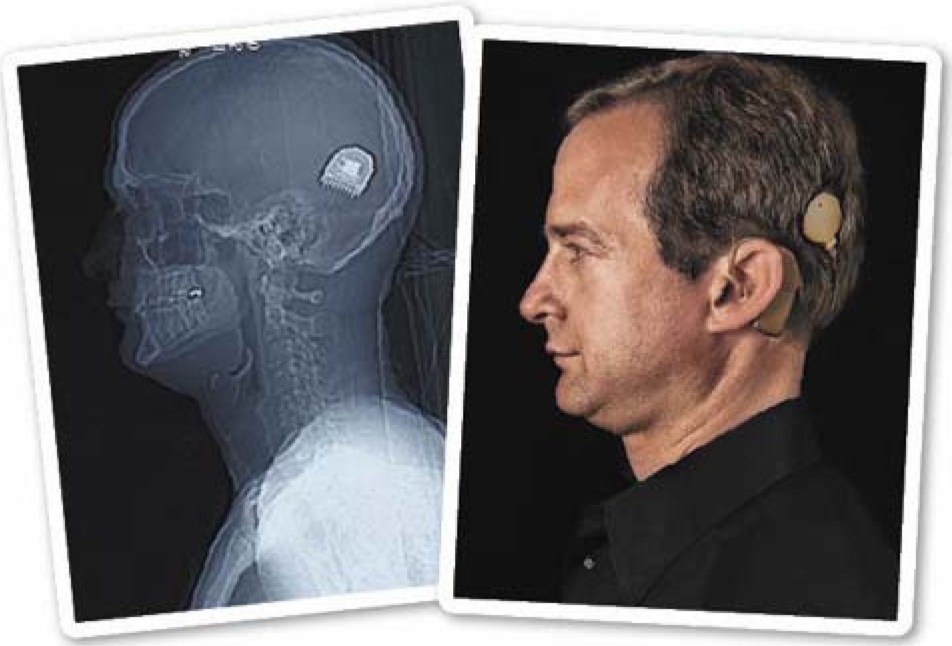
-- Carl Sagan

Examples of Biomaterials Applications



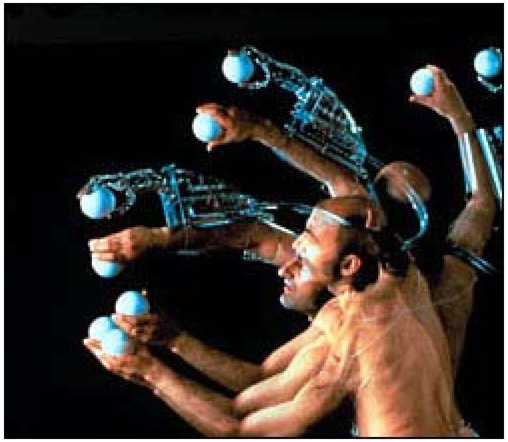

Rebuilt
How Becoming
Part Computer
Made Me More Human
Michael Chorost

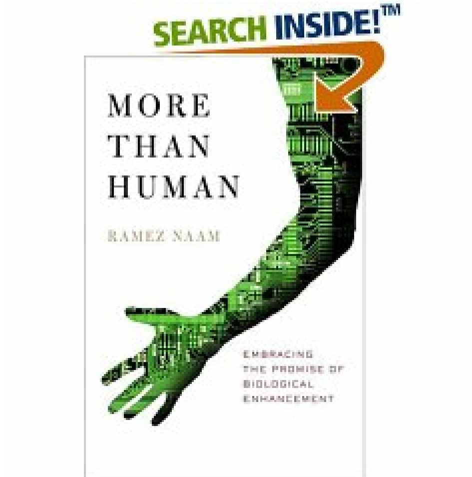


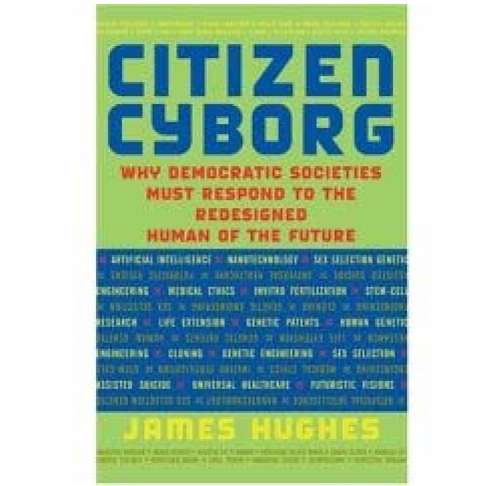


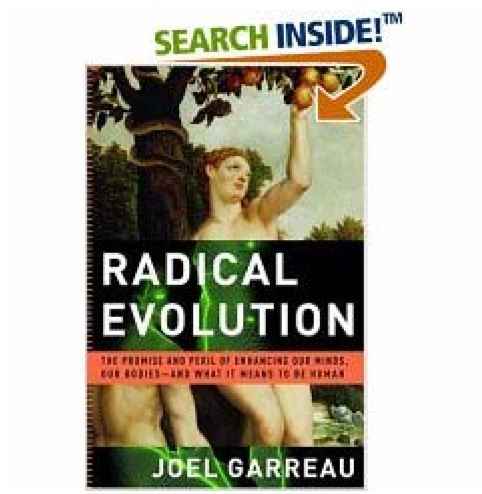

KSL
TV

The upgrade

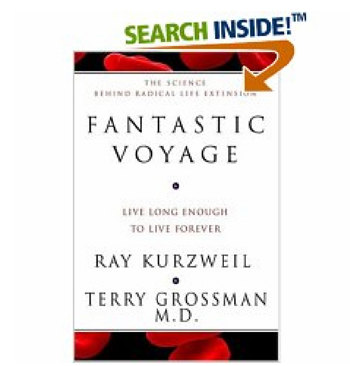



SEARCH INSIDE!™
MORE THAN HUMAN
RAMEZ NAAM
EMBRACING THE PROMISE OF BIOLOGICAL ENHANCEMENT


CITIZEN CYBORG
WHY DEMOCRATIC SOCIETIES MUST RESPOND TO THE REDESIGNED HUMAN OF THE FUTURE
JAMES HUGHES

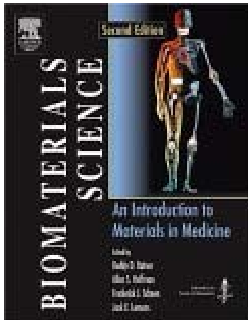

SEARCH INSIDE!™
RADICAL EVOLUTION
THE PROMISE AND PERIL OF ENHANCING OUR MINDS, OUR BODIES—AND WHAT IT MEANS TO BE HUMAN
JOEL GARREAU


SEARCH INSIDE!™
The Scientific Conquest of Death
Essays on Infinite Lifespans
THE IMMORTALITY INSTITUTE 2004


SEARCH INSIDE!™
THE SCIENCE BEHIND RADICAL LIFE EXTENSION
FANTASTIC VOYAGE
LIVE LONG ENOUGH TO LIVE FOREVER
RAY KURZWEIL
TERRY GROSSMAN M.D.

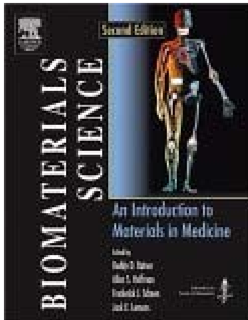
Are medical devices monolithic?

- No
- Composites
- Many diverse materials
- Dependent on applications



Biomaterials Research in Industry

- is dominated as much by the regulatory approval process and submission requirements as by the physical, mechanical, and chemical properties of the medical device.



Definition: Biomaterial -FDA

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of it's primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

The Food and Drug Administration (www.fda.gov)

Regulates:

- Food
- Drugs-*Prescription, Over-the-Counter, Generic*….
- Medical Devices
- Animal Feed and Drugs-*Livestock, Pets* …
- Cosmetics-*Safety, Labeling*…..
- Radiation Emitting Products-*Cell Phones, Lasers, Microwaves*…..

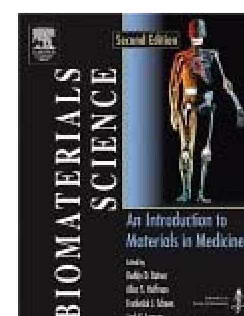
Center for Devices and Radiologic Health- (CDRH)

(www.fda.gov/cdrh/)

- Responsible for regulating firms who manufacture, repackage, relabel, and/or import medical devices sold in the United States.

BIOMATERIAL OR MEDICAL DEVICE?

- FDA neither approves materials nor maintains a list of approved materials
- the properties and safety of materials must be carefully assessed with respect to the specific application in question and its degree of patient contact.
- the final assessment must be performed on the finished product, under actual use conditions.

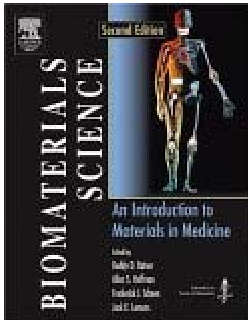


Manufacture of a Medical Device

1. materials selection;
2. types of tests required for evaluation depend on the physical and chemical nature of its materials and the nature of the device's exposure to the body;
3. its physical properties, cost, and availability may be acceptable, but might contain toxic chemical components;
4. screen the candidate materials at an early stage to eliminate those that are toxic, and select those that are sufficiently biocompatible or nontoxic for their intended use.
5. Chemical constituents and potential extractables should be identified and quantitated for overall safety assessment of the device.

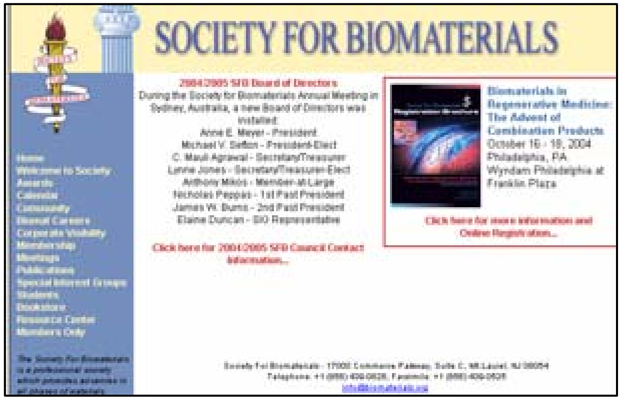
Biomaterials Science is an Interdisciplinary Affair

Biomaterialists include physical scientists, engineers, dentists, biological scientists, surgeons, and veterinary practitioners in industry, government, clinical specialties, and academic settings.



The Society For Biomaterials

A professional society which promotes advances in all phases of materials research and development by encouragement of cooperative educational programs, clinical applications, and professional standards in the biomaterials field. (www.biomaterials.org)



Relevant Biomaterials Journals

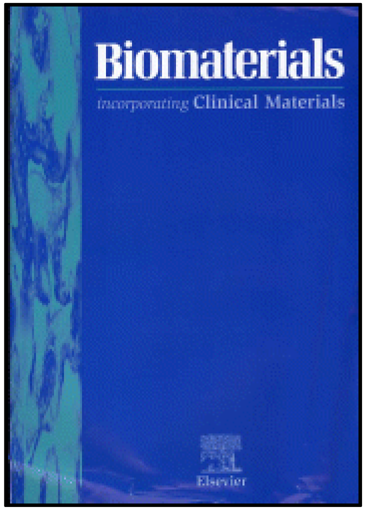
Journal of Biomedical Materials Research

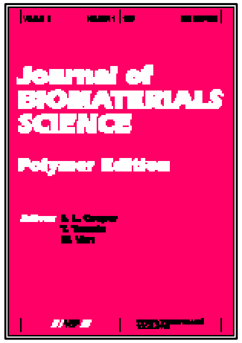
Biomaterials

Journal of Biomaterials Science. Polymer Edition

Journal of Biomaterials Applications

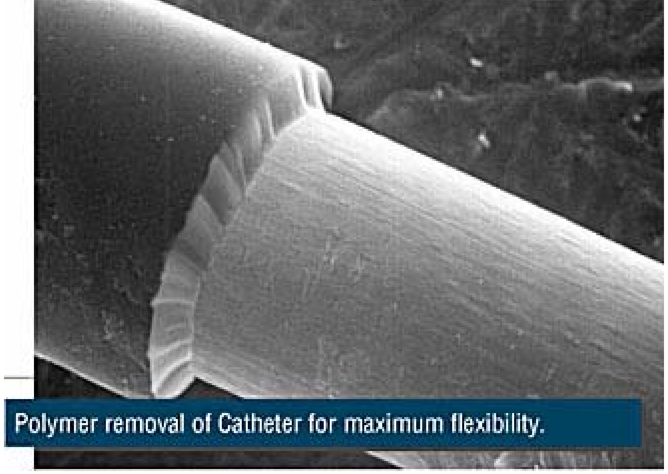
Journal of Materials Science: Materials in Medicine

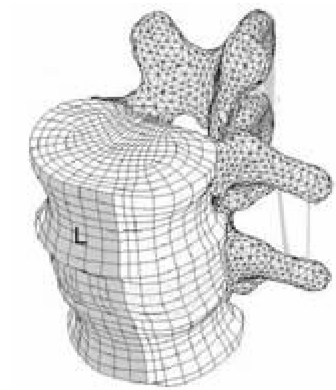


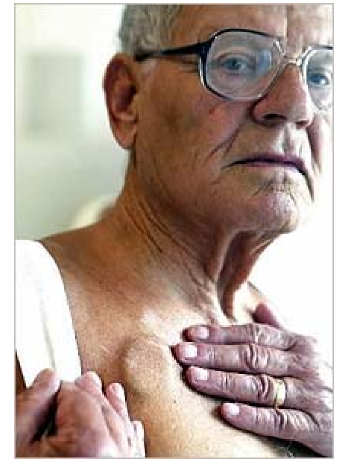


Relevant Websites

- Biomaterials Network (www.biomat.net)
- Medical Device Information (www.devicelink.com)
- Medical Materials Engineering reference (www.engineeringreference.com)
- United States Patents and Trademarks Office (www.uspto.gov)
- MEDLINE-(www.ncbi.nih.gov/entrez/query.fcgi)







Classes of Materials Used in Medicine

Requirements of Biomaterials

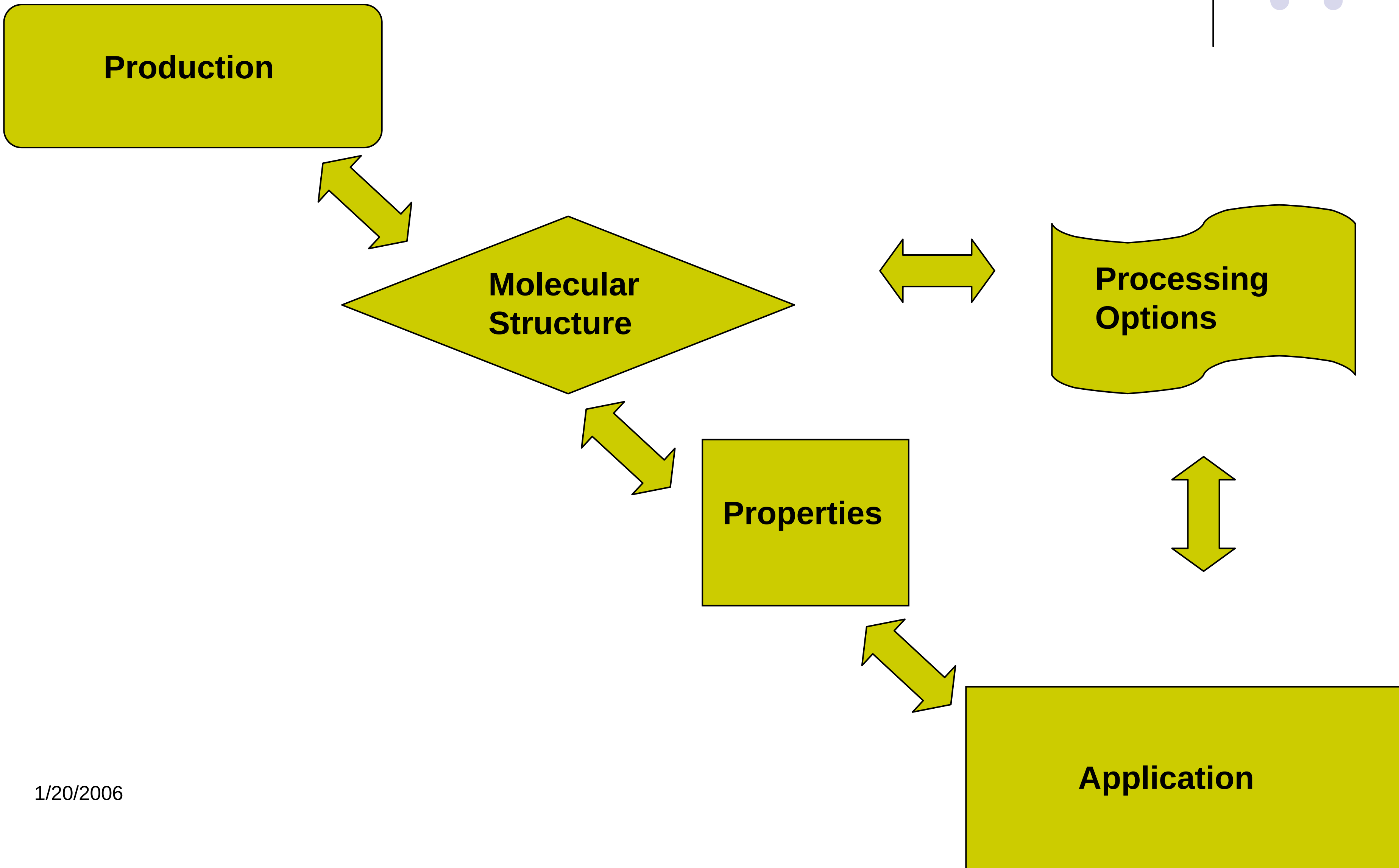
A biomaterial must be:

- Biocompatible
- Nonthrombogenic (if blood-contacting)
- Processable (for manufacturability)
- Sterilizable
- Affordable

Syllabus

23 Jan	Hlady	Surface Properties of Biomaterials
25 Jan	Hlady	Surface Characterization
27 Jan	Hlady	Surface & Protein Interactions

Processing Technology

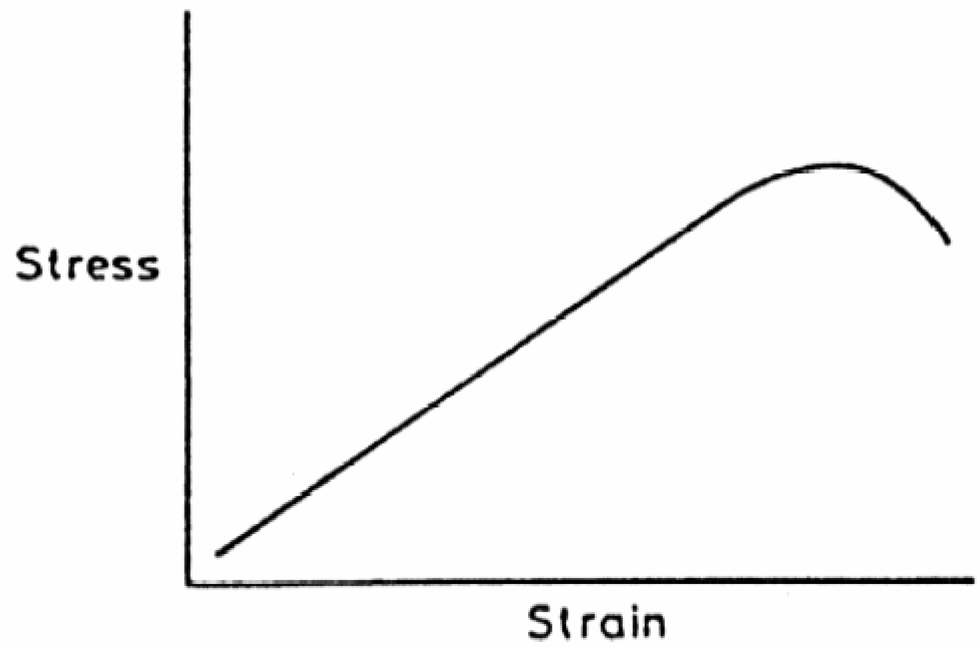


Processing Technology

Successful product design requires a knowledge of:

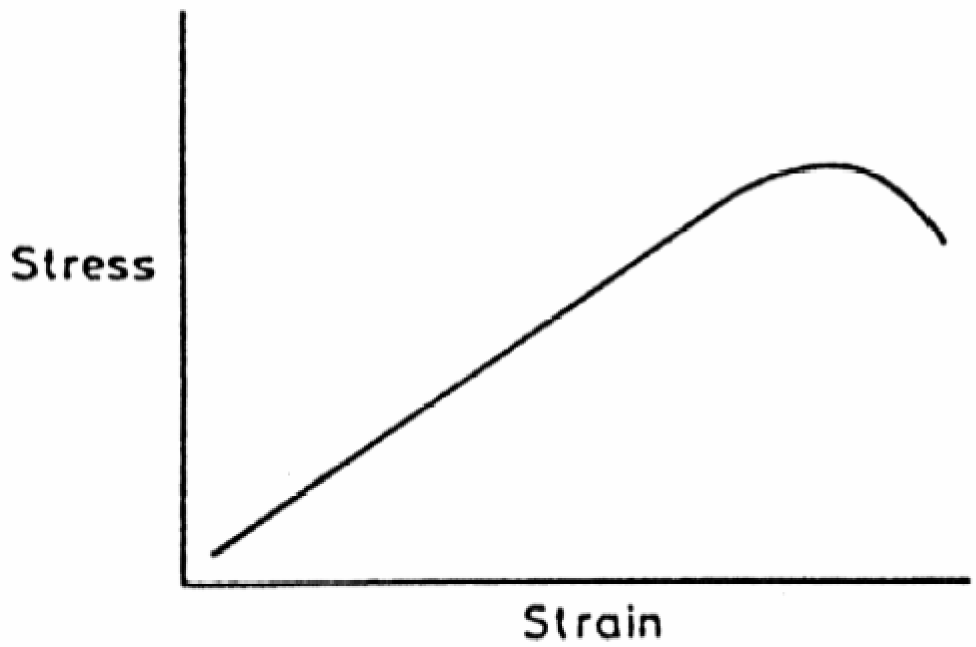
- the requirements of the final product;
- the behavior of the materials; and,
- commercial processing and fabrication technology.

Stress- Strain Curves



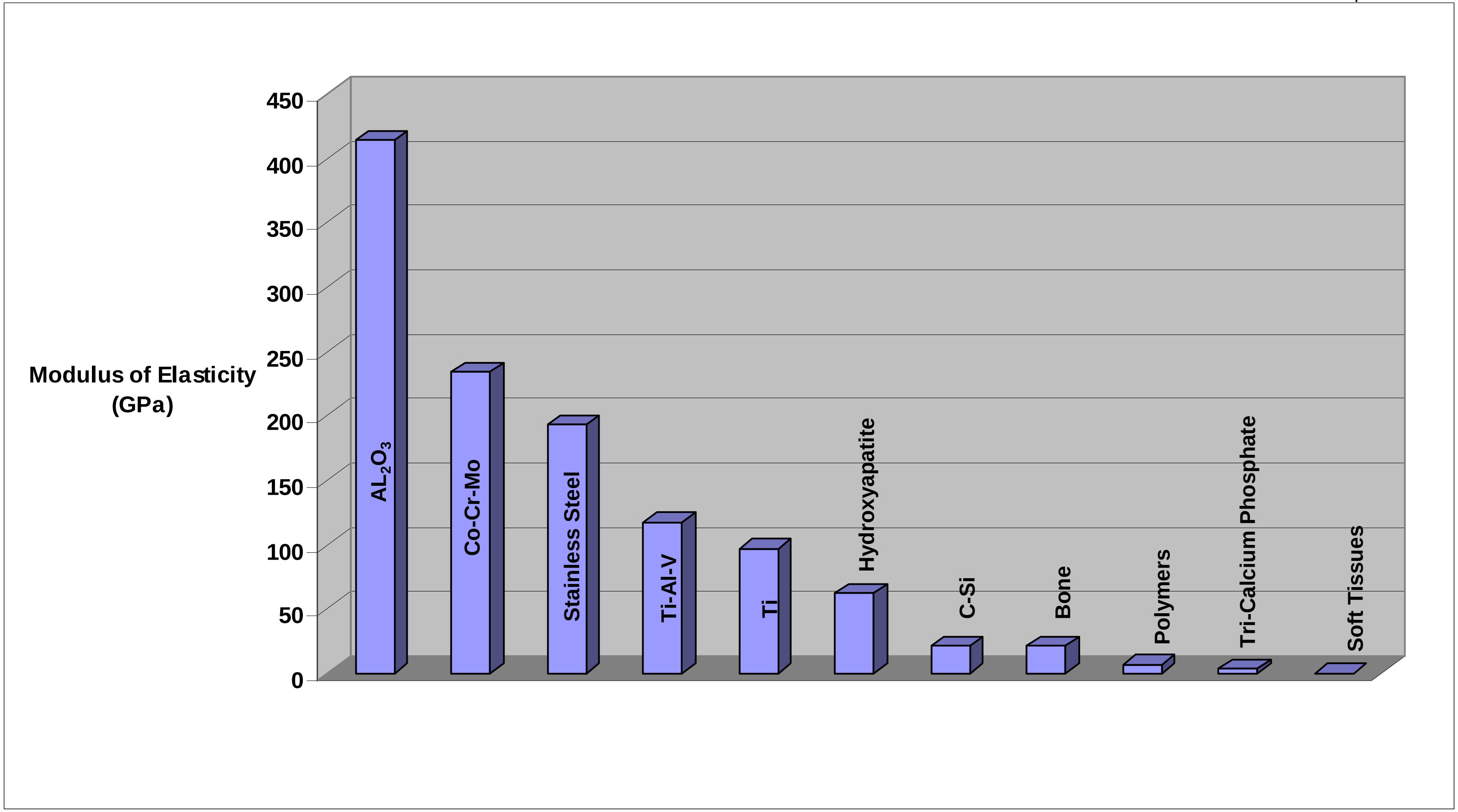
Stress- Strain Curves

Young's modulus, Ultimate tensile strength, % Elongation at failure

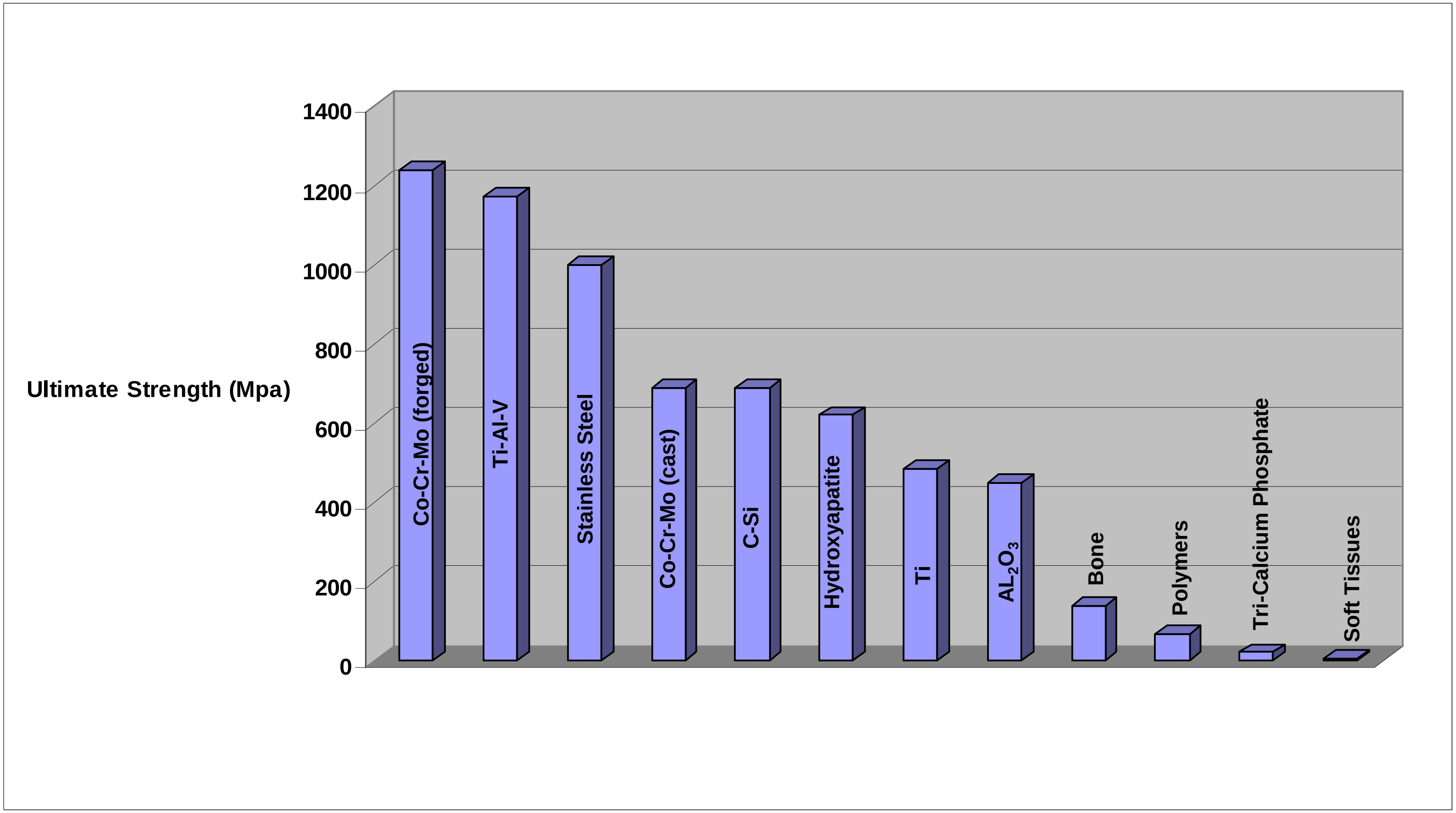


Comparison of Moduli of Elasticity:

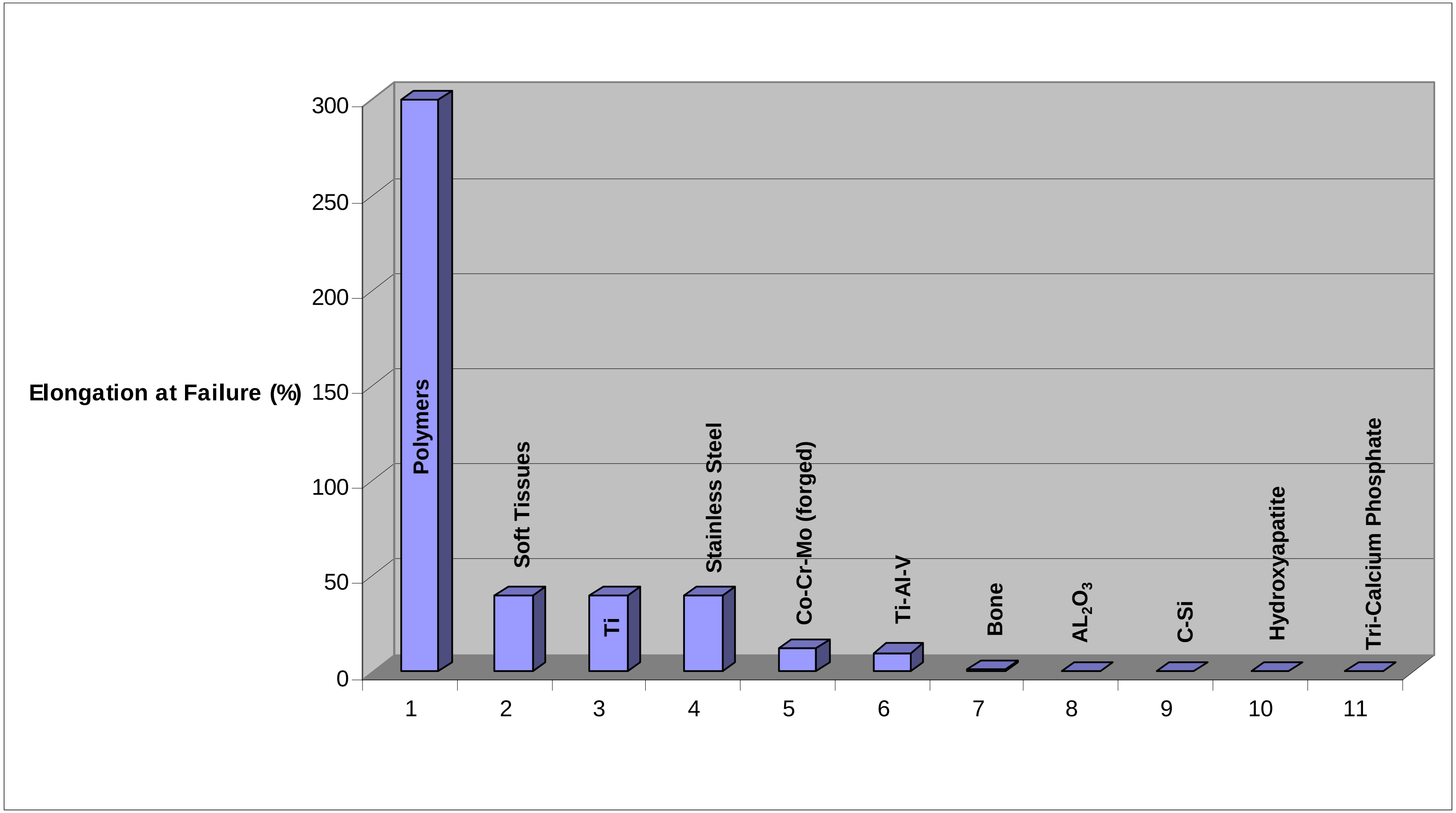
Note the very high values for ceramics and metals



Comparison of Ultimate Tensile Strength: **Note the very high values for metals which make them candidates for load bearing applications**



Comparison of Elongation at Failure: Note that polymers have exceptional elongation



Ceramics

Inorganic compounds that contain metallic and non-metallic elements, for which inter-atomic bonding is ionic or covalent, and which are generally formed at high temperatures

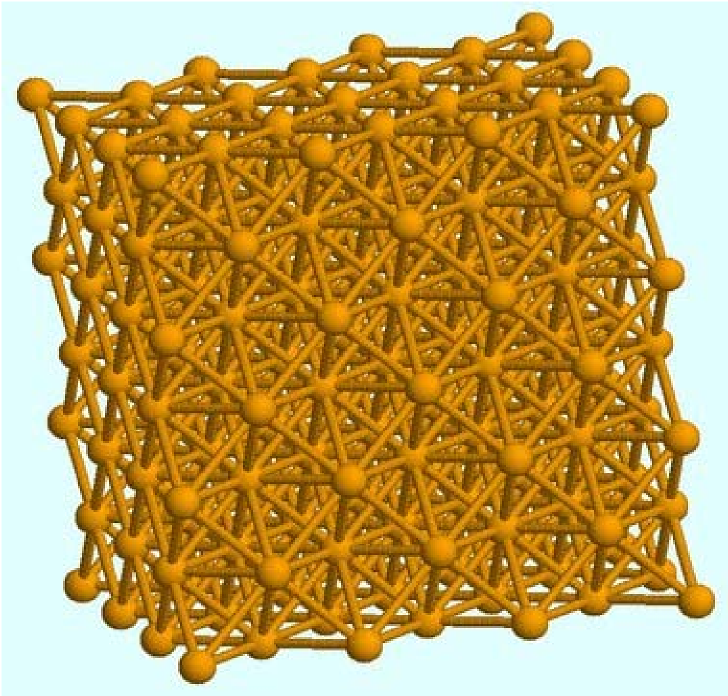
Minerals

Composition of *Earth's Crust*:

O = 50% Fe = 5% K = 2.5%

Si = 26% Ca = 3% Mg = 2%

Al = 8% Na = 2.5% H = 1%



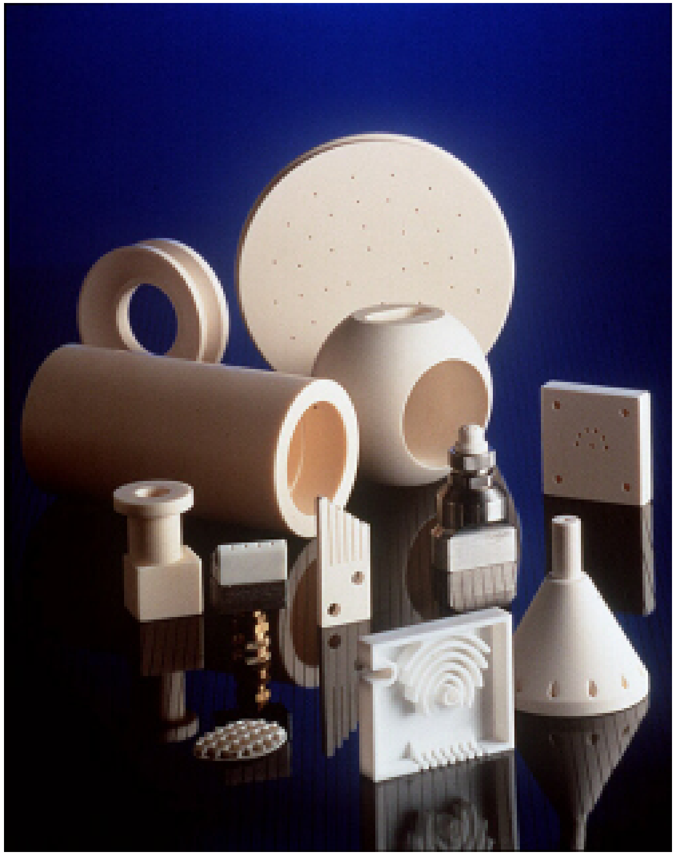
Ceramics

Advantages:

- high modulus (stiffness) & compressive strength
- high wear resistance
- inert in body
- fine esthetic properties for dental applications

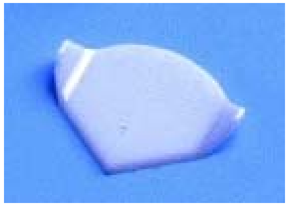
Disadvantages:

- brittle
- poor fatigue resistance



Ceramic Applications

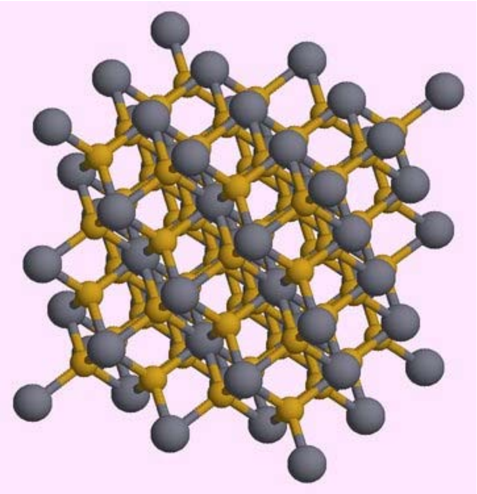
- artificial hip;
- knee prostheses;
- spinal fusion devices;
- dental-crowns, bridges, implants and caps;
- inner ear and cochlear implants (cochlear implants);
- drug delivery devices; and,



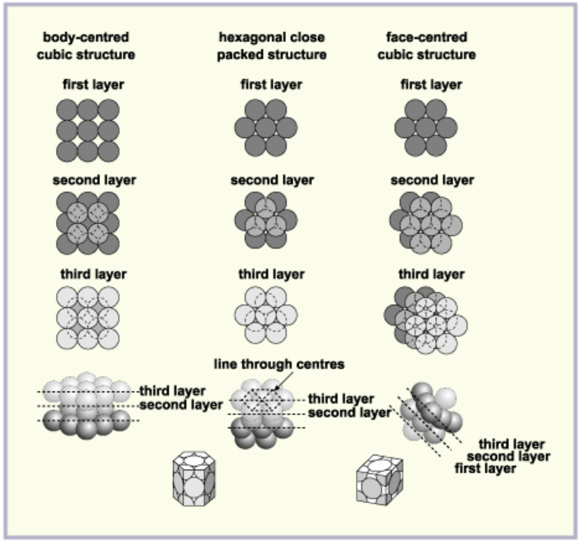
Leaflet of heart valve

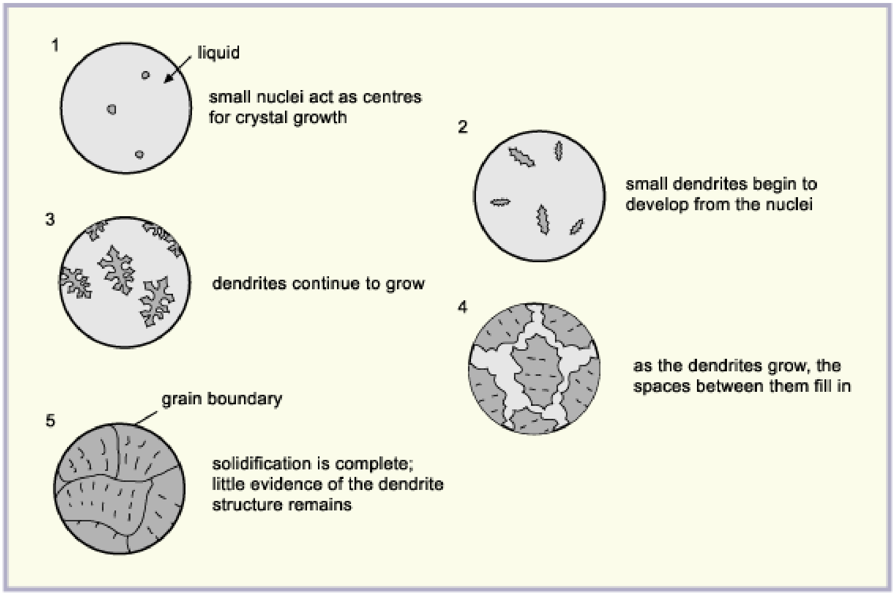
Metals

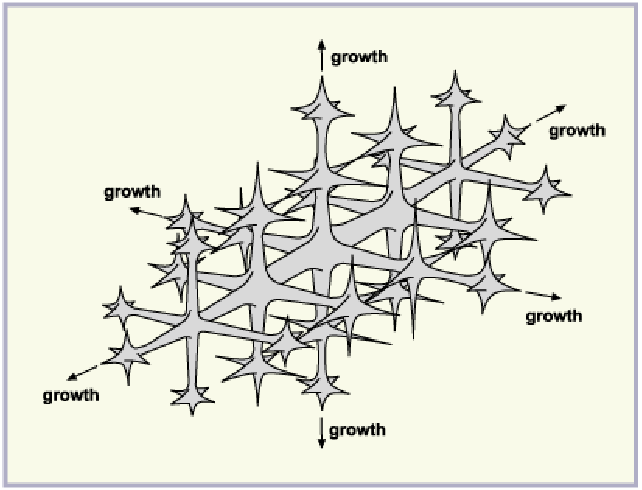
- closely packed crystal structure;
- the type of bonding in metals and metal alloys render them valuable as load bearing implants as well as internal fixation devices used for orthopedic applications as well as dental implants



Metals Manufacturing

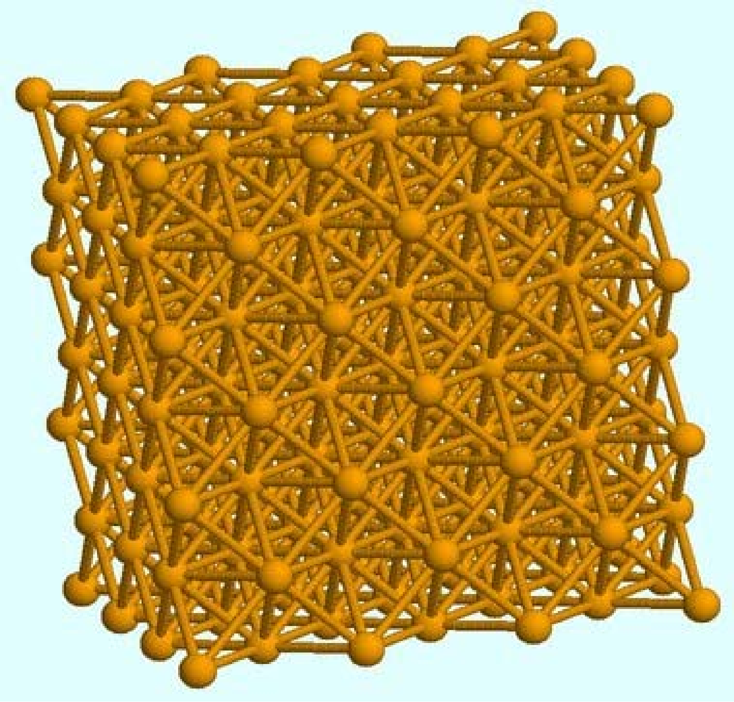


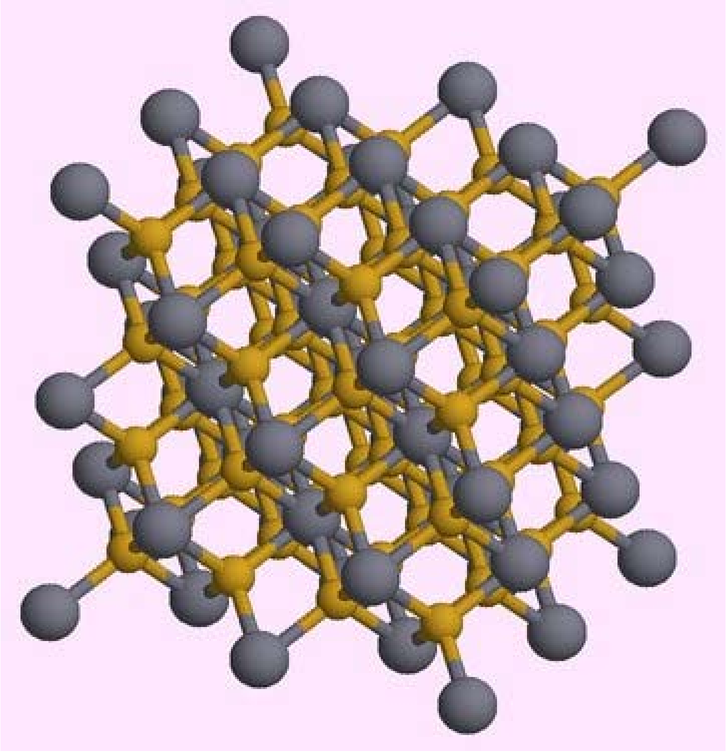


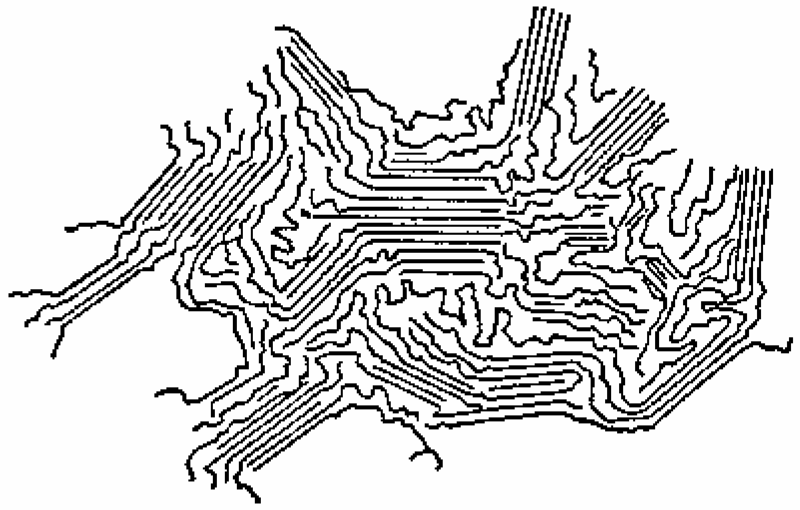


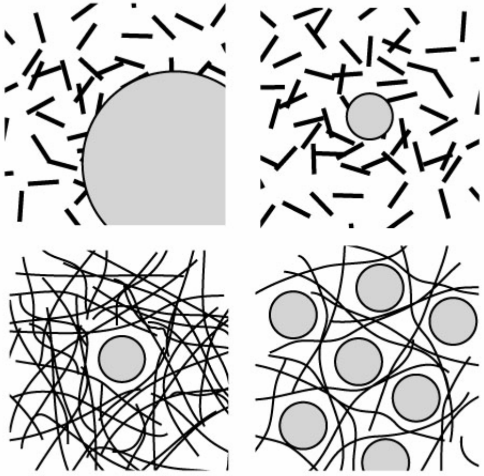
Ceramics

Metals

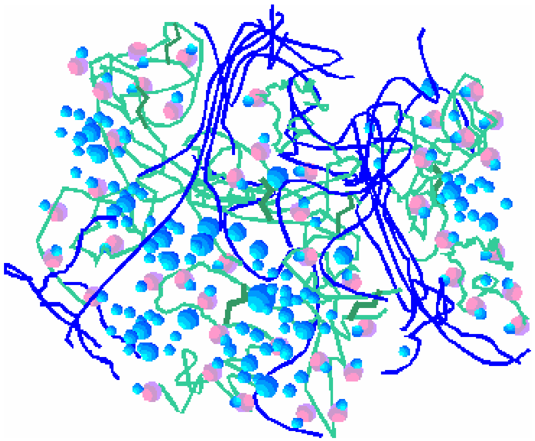


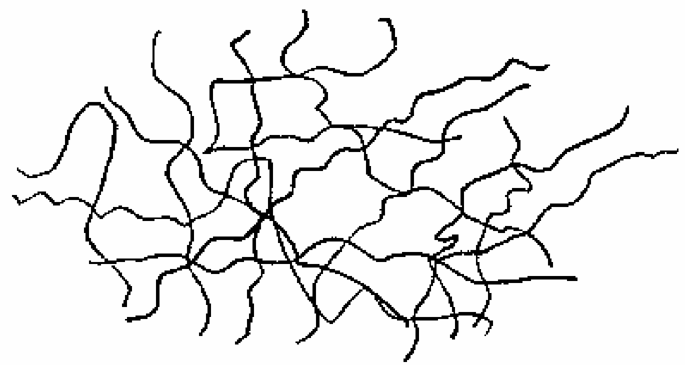






Polymeric Materials



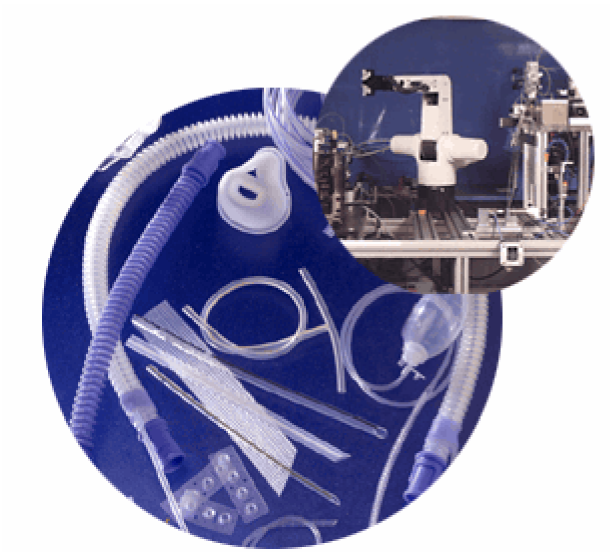


Polymers

- Greek root “poly” meaning many and “meros” meaning parts
- Macromolecule
- If we disregard metals and inorganic compounds, we observe that practically everything else in the world is polymeric.
- Most items in living and built world.

MEDICAL PLASTIC MARKET FORECAST TO CROSS 2.6 BILLION POUNDS BY 2006- Worldwide

- Disposable market (50% volume)
- Nondisposable
- Packaging



Medical Plastics Market

- Major nondisposable markets
  - testing/diagnostic equipment,
  - surgical instruments and related equipment,
  - prostheses/implants,and,
  - dental/ophthalmic devices;
- Disposable products
  - syringes, kits,
  - labware,
  - tubing,
  - blood bags,
  - gloves, trays, catheters, thermometers, etc.

Polymeric Biomaterials are used in a Broad Range of Products

Learning Resource

The Macrogalleria

www.psrc.usm.edu/macrog/index.htm

Read through levels 2-5

Types of Polymers

- Thermosets
- Thermoplastics

Classification based on Processing

- Elastomers – Classification based on mechanical properties
- Hydrogels- Classification based on chemical properties
- Polyelectrolytes-Classification based on chemical properties
- Natural-Classification based on origin
- Biodegradable-Classification based on biostability

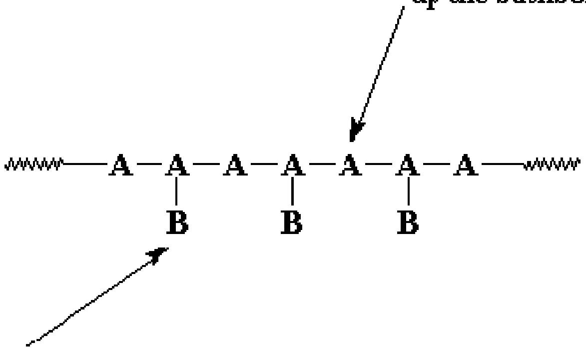
Polymers

- linear macromolecules.

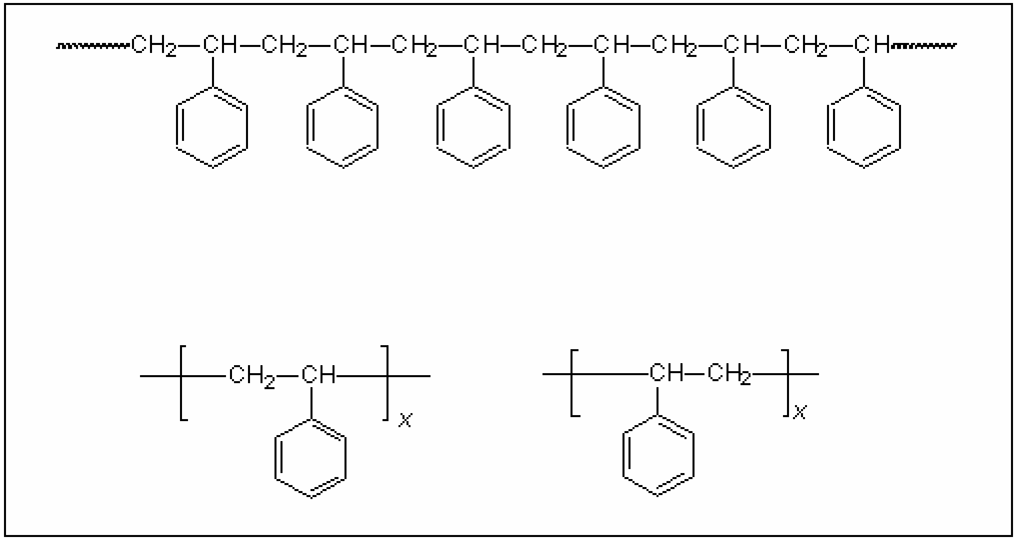
a linear polymer made of "A" atoms

- *backbone*.
- *pendant groups.*

These "A" atoms make up the backbone chain

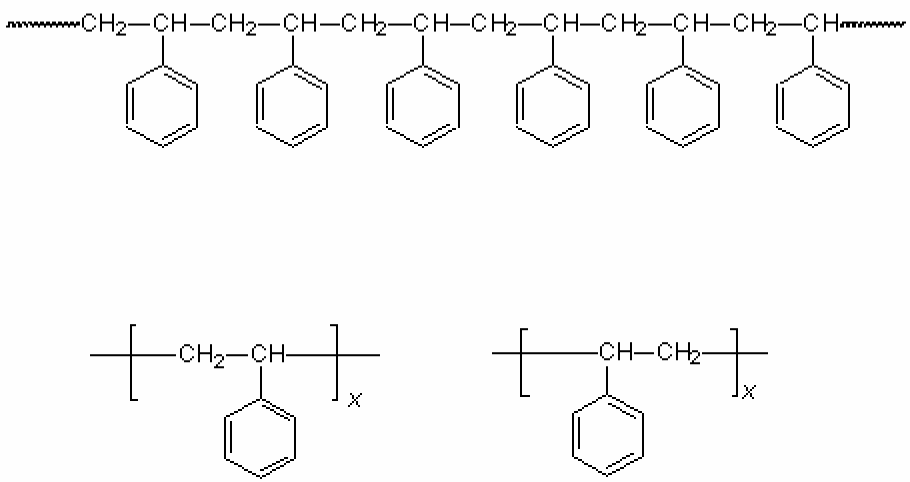


The "B" atoms are pendant groups



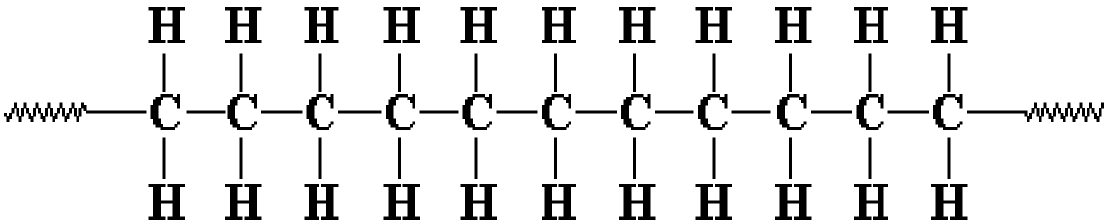
-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-

Homopolymer



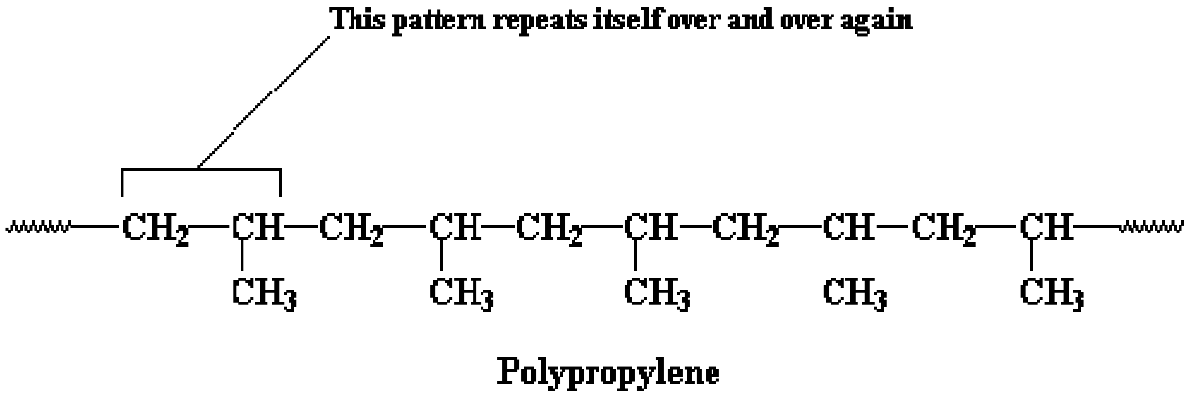
The Structure of Polymers

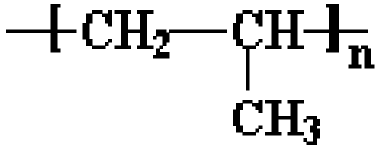
- the simplest polymer structure



- hydrocarbons

Polypropylene





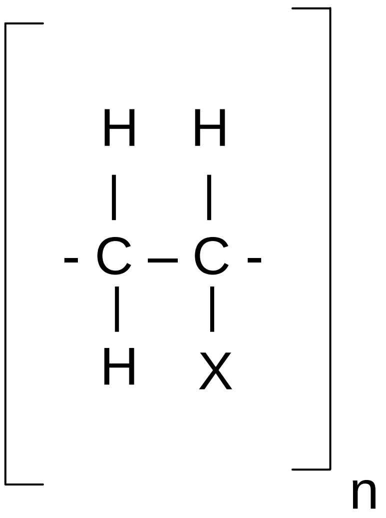
The Structure of Polymers

- The basic makeup of many polymers is carbon and hydrogen;
- Other elements can also be involved.
  - Oxygen, chorine, fluorine, nitrogen, silicon, phosphorous, and sulfur are other elements found in the molecular makeup of polymers.
- Polyvinyl chloride (PVC) contains chlorine.
- Nylon contains nitrogen.
- Teflon contains fluorine.
- Polyester and polycarbonates contain oxygen.

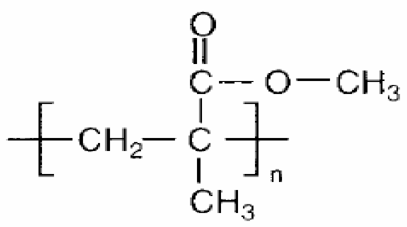
Carbon Chain Polymers

Homopolymer

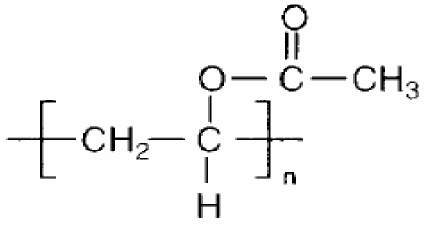
- If X=H then polyethylene
- If X = CH3 then polypropylene
- If X = Cl then polyvinylchloride
- If X = Benzene ring then polystyrene



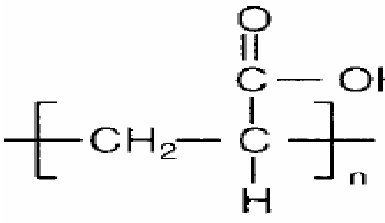
Chemical Structure of Some Common Polymers



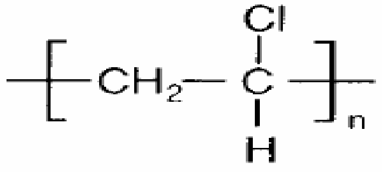
Poly(methylmethacrylate) “PMMA”



Poly(vinylacetate) “PAVc”

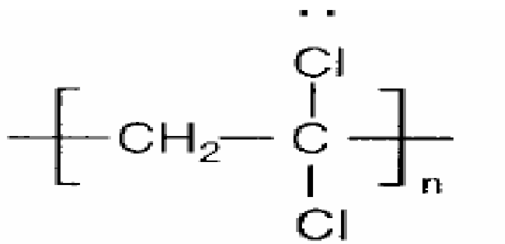


Poly(acrylate) “PAA”

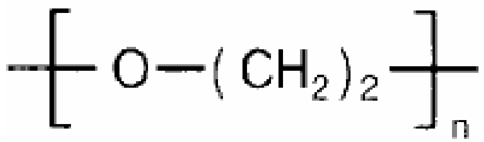


Poly(vinylchloride) “PVC”

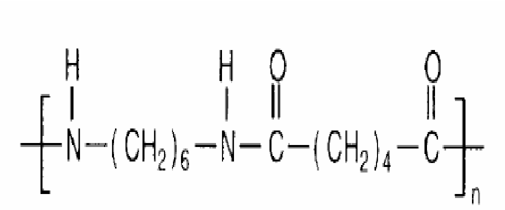
Chemical Structure of Some Common Polymers



Poly(vinylidene chloride)“PAVc”

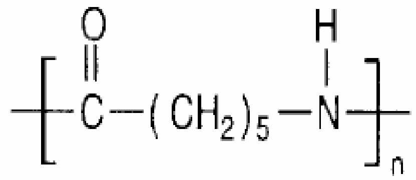


Poly(ethylene oxide)“PEO”



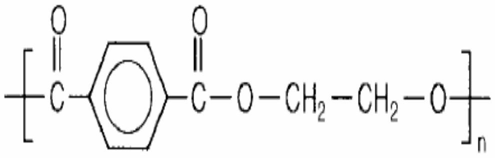
Poly(hexamethylene adipamide)

“Nylon 6,6”

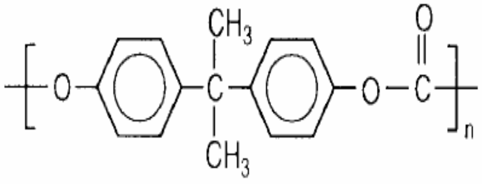


Poly(caprolactam) or “Nylon”

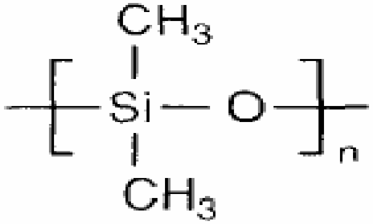
Chemical Structure of Some Common Polymers



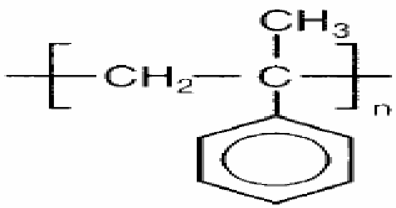
Poly(ethylene terephthalate)“PET”



Poly(carbonate)

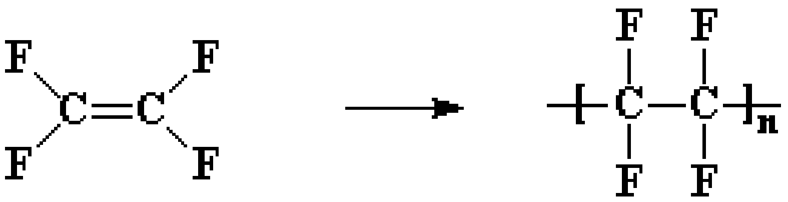


Poly(dimethyl siloxane)



Poly(methyl styrene)

PTFE

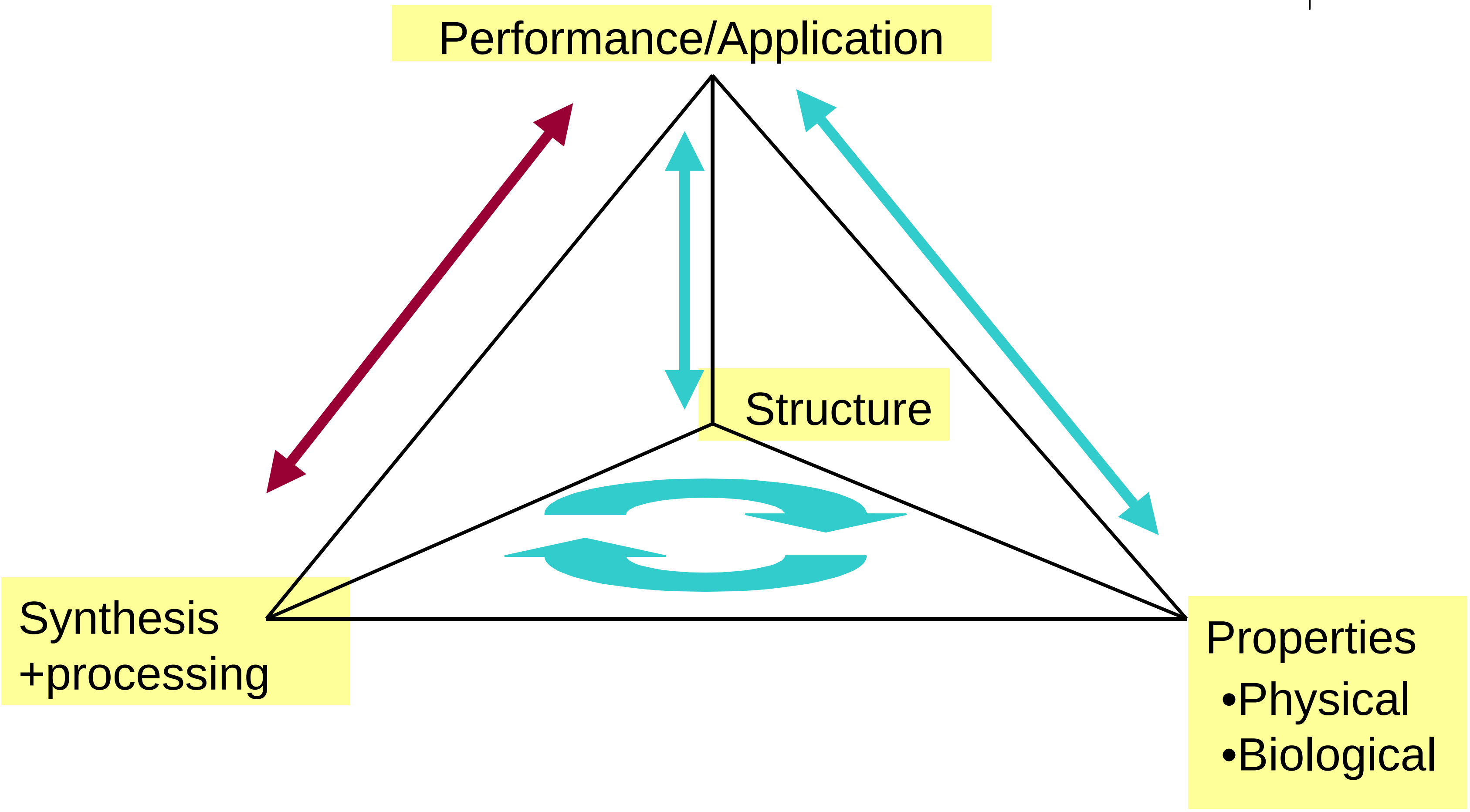


polytetraflouroethylene

Medical Plastics Market

- Almost 80% of polymers used:
  - **PVC,**
  - **Polypropylene**
  - **Polystyrene.**
- Thermoplastics currently dominate the market with a little under 50% of total volume.

Material Science Logic



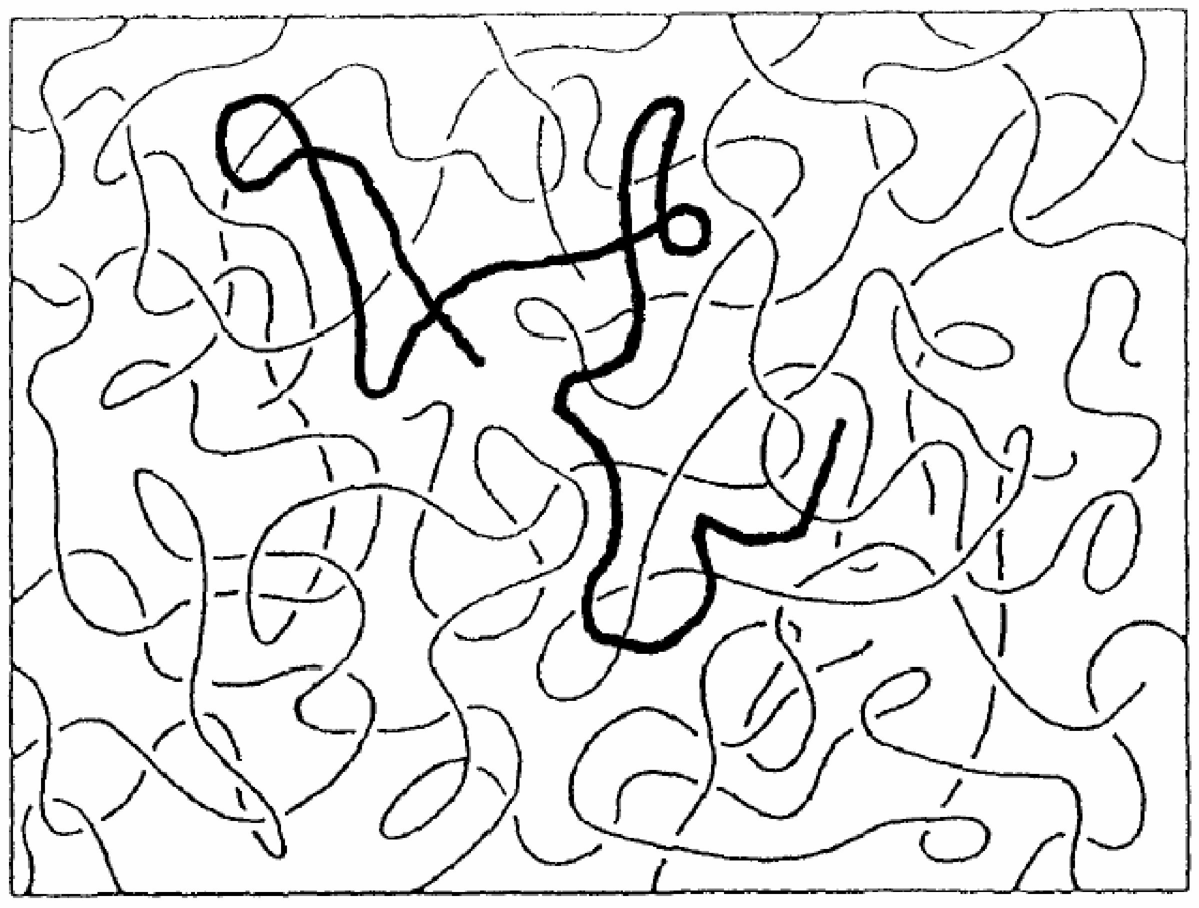
Basics of Polymer Structure

- What distinguishes polymers from other organic compounds is molecular weight and dimension?

TABLE 1.1 Properties of the Alkane Series

Number of Carbons in Chain	State and Properties of Material	Use, Dependent on Chain Length
1–4	Simple gas	Bottled gas for cooking
5–11	Simple liquid	Gasoline
9–16	Medium-viscosity liquid	Kerosene
16–25	High-viscosity liquid	Oil and grease
25–50	Simple solid	Paraffin wax candles
1000–3000	Tough plastic solid	Polyethylene bottles and containers

Illustration of the random coil model. One chain is marked in bold.

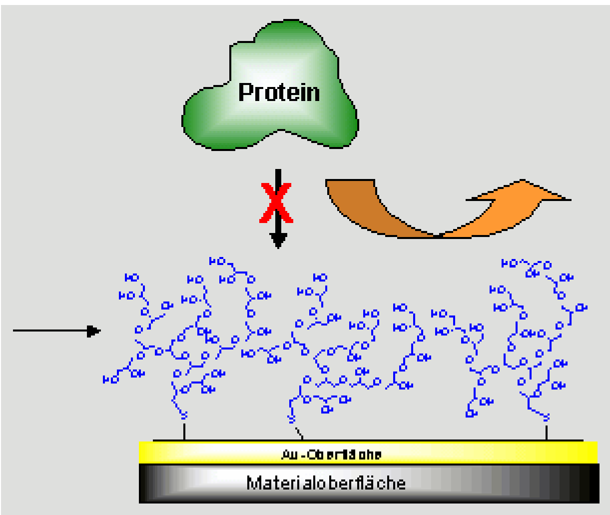


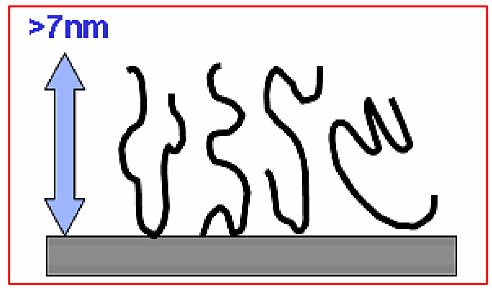
What makes One Polymer Different from Another?

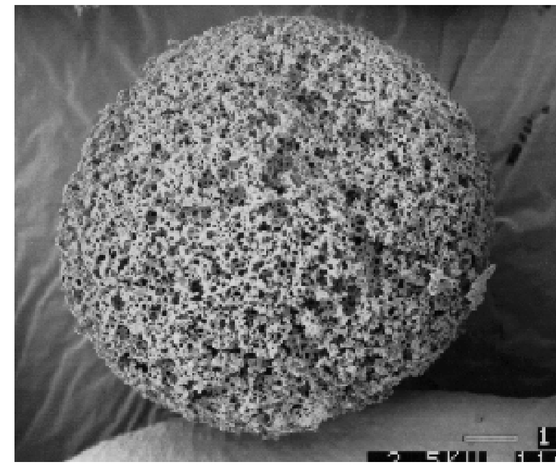
- Strength of intermolecular forces and their sum over long polymer chains.
- Molecular weight and entanglement, which slow down motion of polymers.
- Crystallinity.
- Crosslinking.

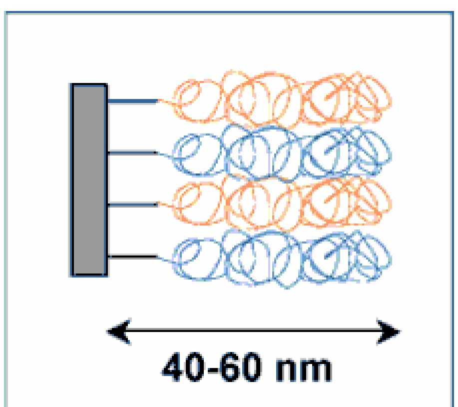
All these properties determine the diverse states of macromolecular aggregation that polymers show.

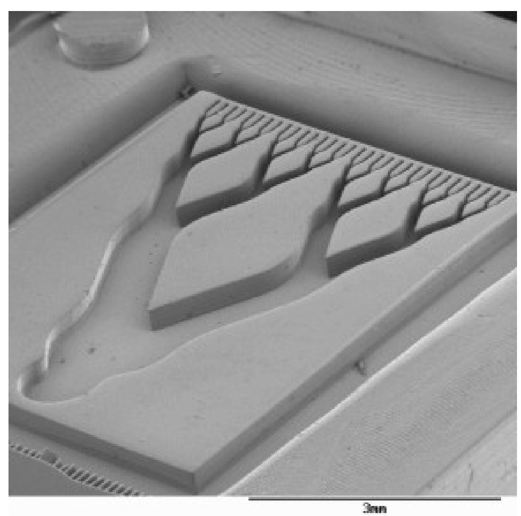
Interesting Properties when Presented at Interfaces

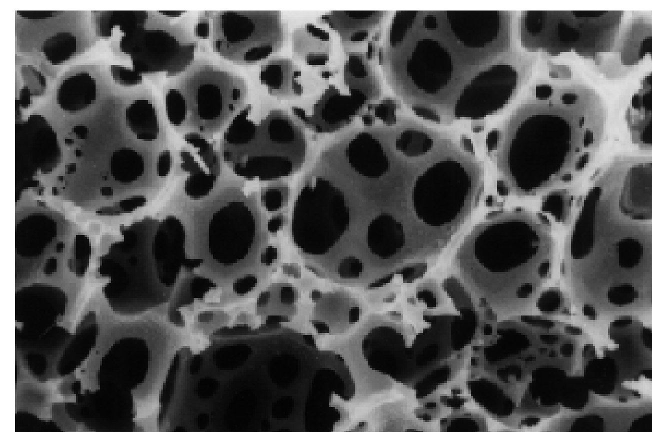












Structure Determines Properties

- differences
  - intramolecular and intermolecular forces that exist
- functional groups
- length of molecule
- branching
- conformations

Binding and Structure of Polymers

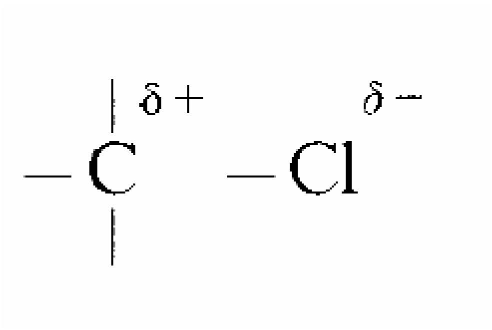
Interchain bonding: covalent

Intermolecular binding

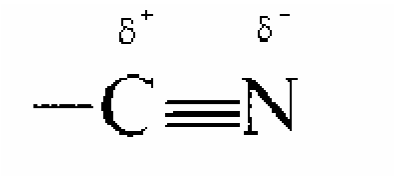
- permanent dipole (polar groups)
- induction forces: induced dipole
- hydrogen bonds
- repulsive forces (Pauli principle)
- Van der Waals interaction

Intermolecular Interactions

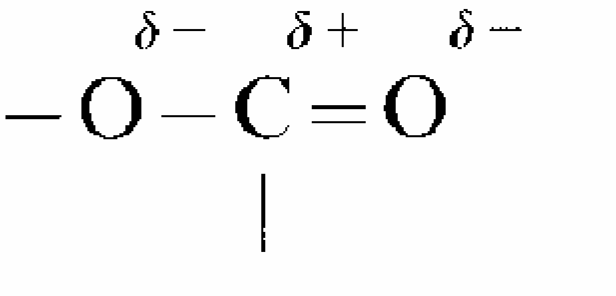
- Forces between permanent dipoles
- Different electronegativity of partners
- permanent dipole moment
- Examples of “polar groups“: e.g., in PVC



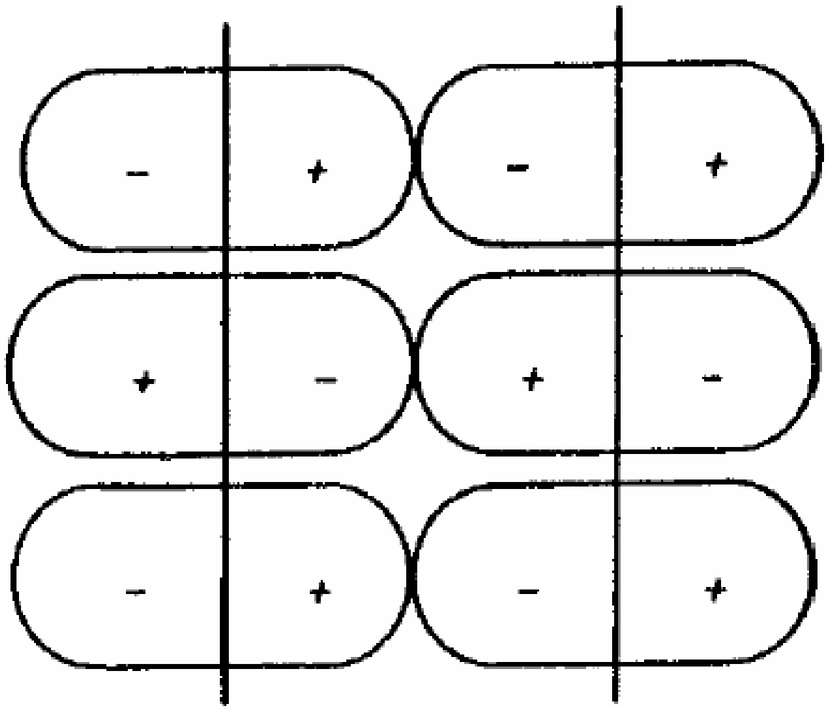
- nitrite group (less polar)

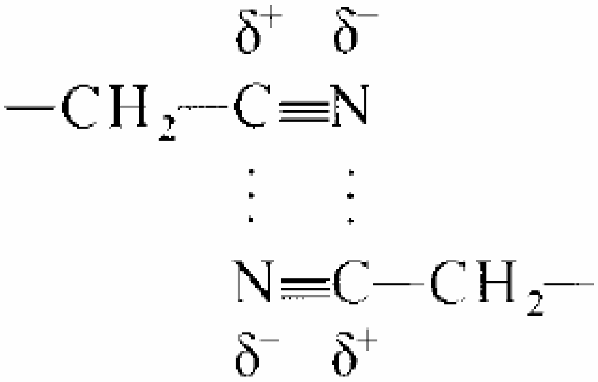


- ester group (less polar)



Dipole forces in a polymer.



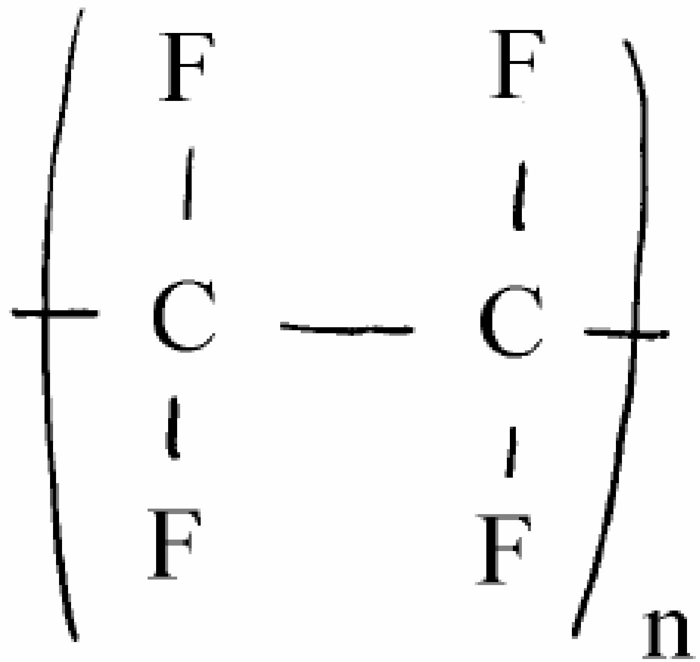


Effect of Polar Groups:

- lower solubility (except in strongly polar solvents)
- higher softening temperature (glass temperature *T*g).

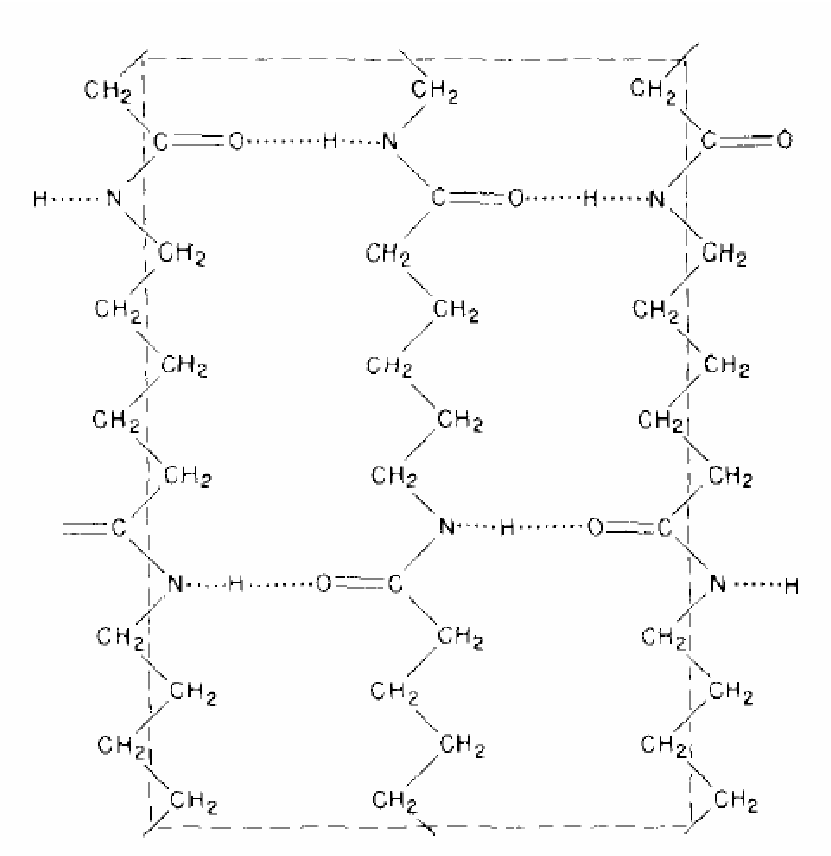
Almost no external dipole moment for symmetrical arrangement of dipoles!

PTFE

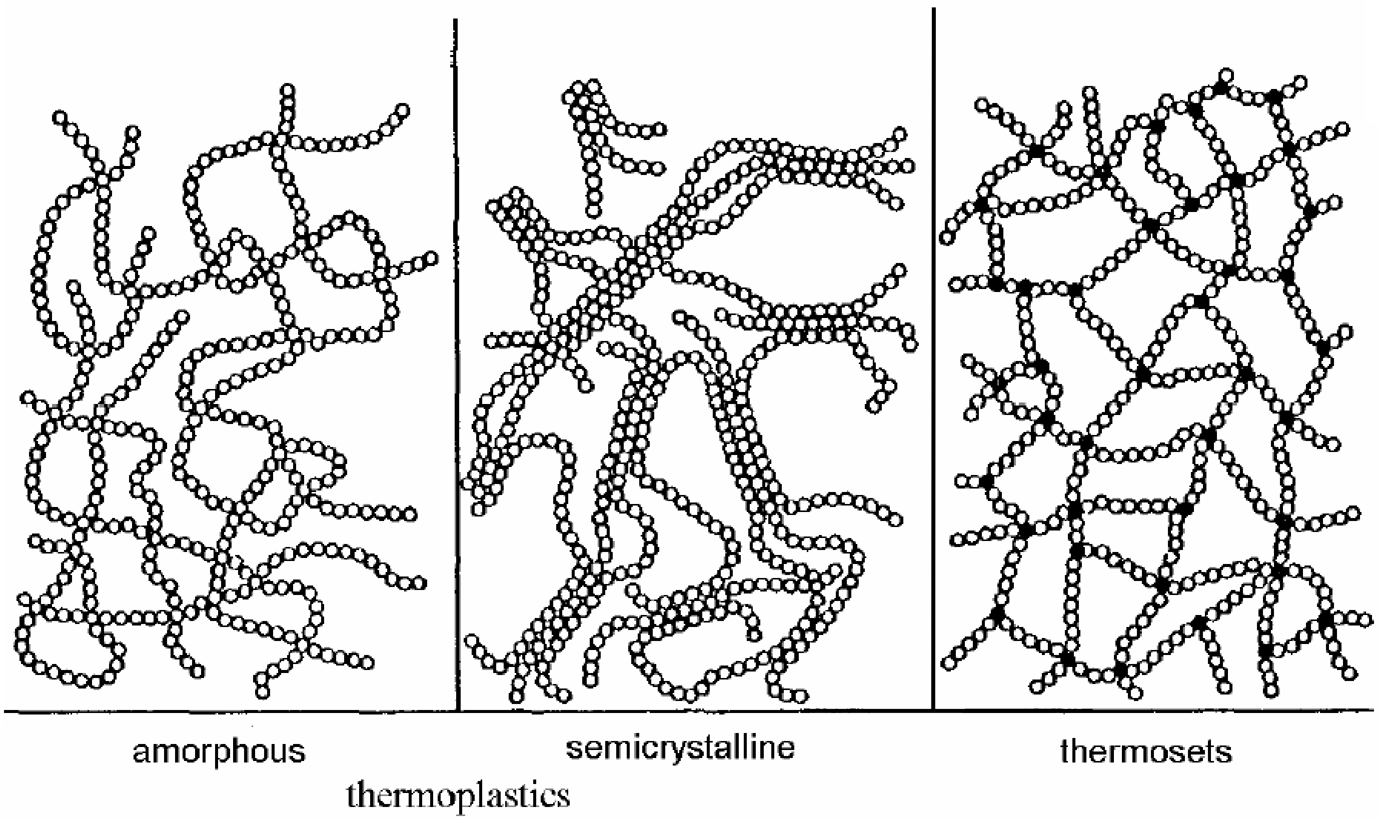


Hydrogen bonds
only for F, O, N as strongly electronegative partner

- Illustration of hydrogen bonds in polyamid 6 (PA6)
- Particularly strong in polyamides and polyurethanes



Schematic sketch of thermoplastics and thermosets. Thermoplastics are amorphous or a semicrystalline with no covalent crosslinks.



Thermoplastics

- thermoplastic polymers are defined as materials that soften, melt, and flow when heat is applied; the adhesives solidify when cooled.
- Majority of familiar plastics
- Can be reprocessed

Thermoplastics

Amorphous

- Random structure
- Good clarity
- Broad melt temperature
- Low mold shrinkage (<0.005 in./in.)
- Acrylic, polycarbonate, PETG,polystyrene, PVC, TPU,

Thermoplastics

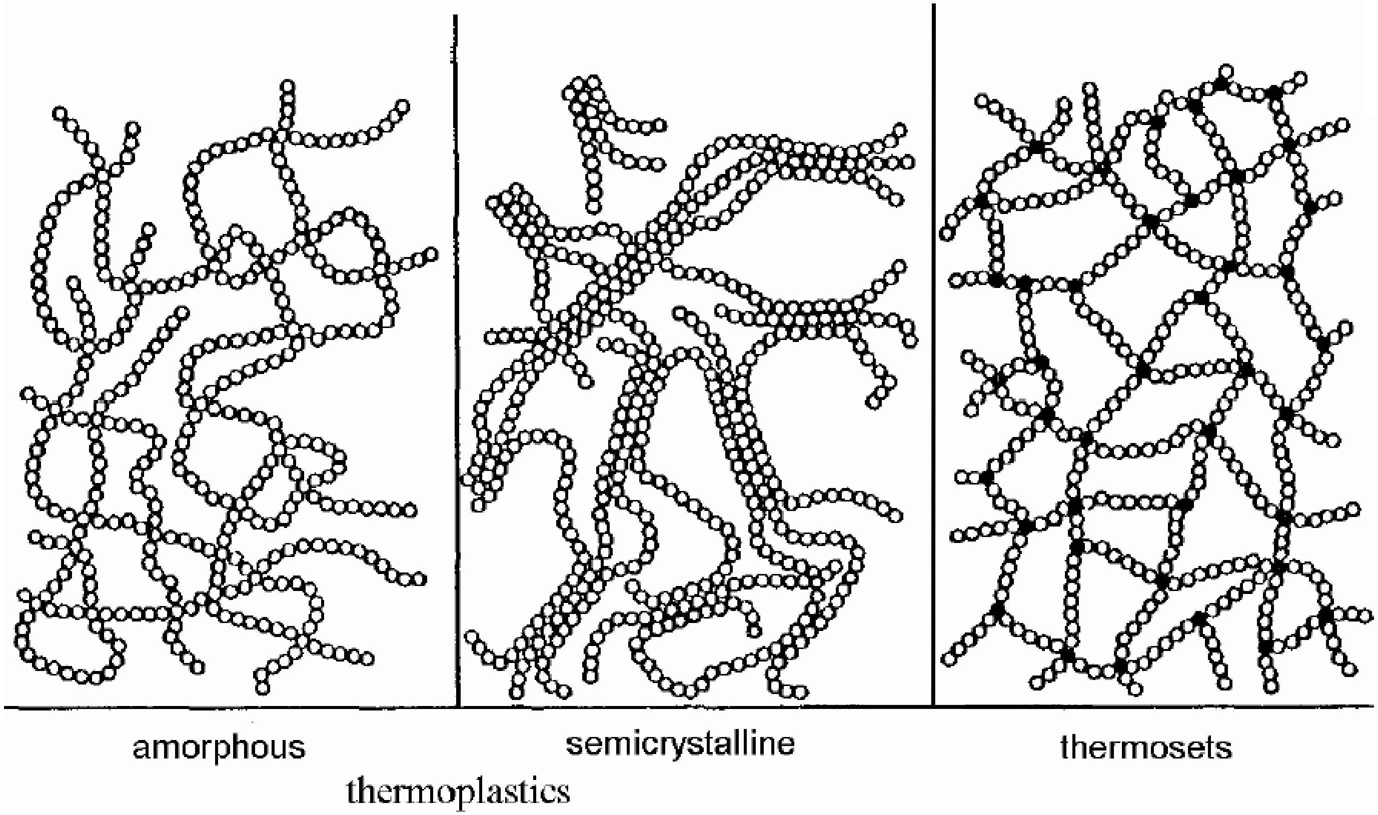
Semi-crystalline

- Linear alignment of chains
- Harder, less flexible
- Unique melting point
- High mold shrinkage (>0.01 in./in.)
- Polyethylene (LDPE / MDPE /HDPE), polypropylene, PTFE, Polyamide, PEK, TPU

(Thermo)plastics

- Glass transition at *T*g: onset of long-range chain mobility
- If semicrystalline plastics: melting intervall of crystallites at *T*m
- - *T* > *T*g: mouldable into any shape
- - *T* < *T*g: range of usage
- ·Soluble

Schematic sketch of thermosets and thermoplastics. The latter can be amorphous or a structure similar to thermosets but a lower crosslink density.



Thermosets

- A thermosettingpolymer, as the name suggests, becomes set into a given network, normally through the action of a catalyst—heat, radiation, or a combination of these factors—during the process of cross-linking.
- As the name suggests, *cross-linking* is the process of forming cross-links between linear polymer molecules (*curing* is another term commonly used).
- As a result of this process, thermosets become infusible and insoluble.
- Thermosetting resins (e.g., epoxies, polyesters, and phenolics) are the basis of many structural adhesives for load-bearing medical applications, as well as for the precision joining of electronic parts.

Thermosets

- Hard, strong, rigid
- Excellent heat resistance
- Cannot be reprocessed

Crystalline

- Epoxy, phenolic, polyester,

Amorphous

- Rubber, silicone, polyurethane

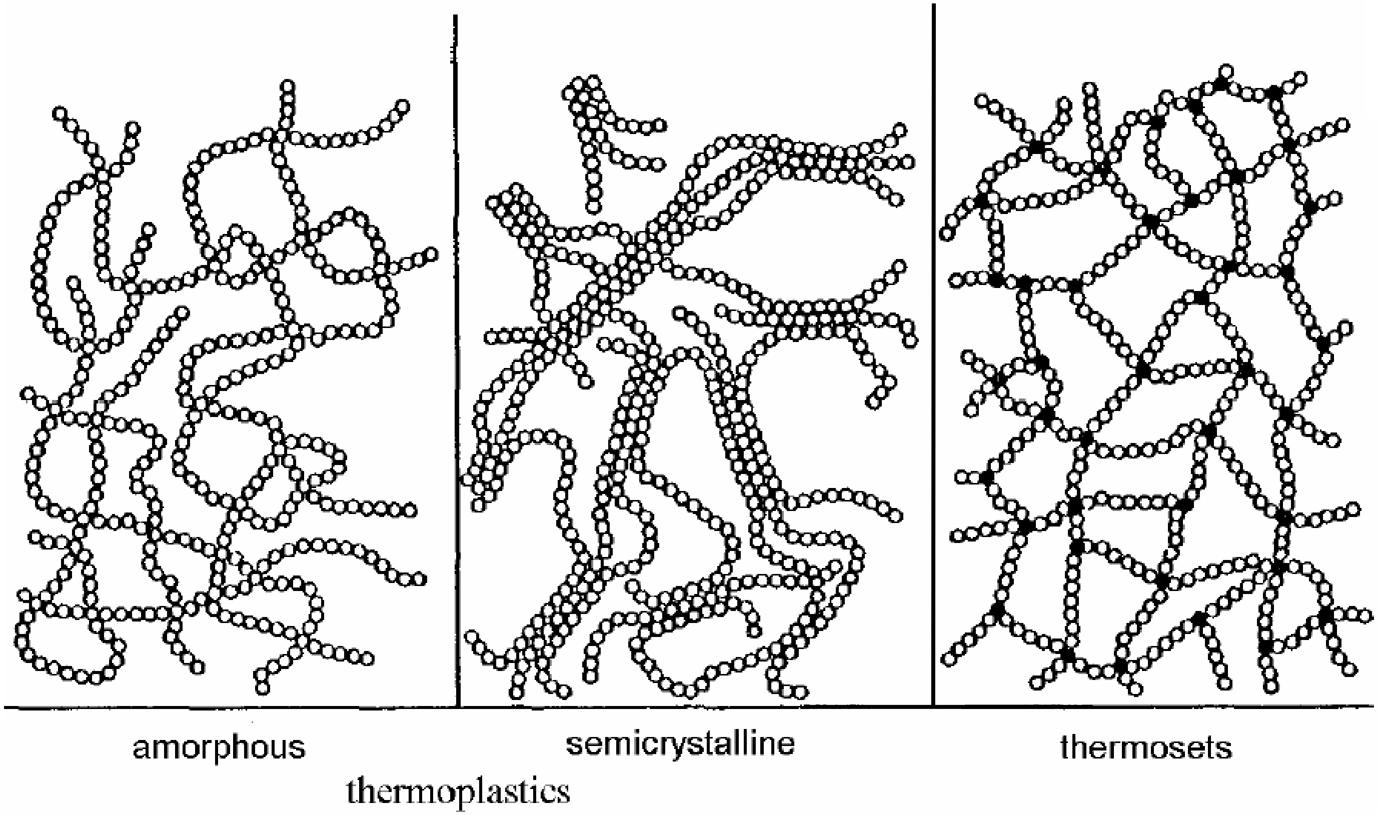
Thermosets

- Not meltable
- Not soluble
- Not swellable
- Processing generally prior to crosslinking

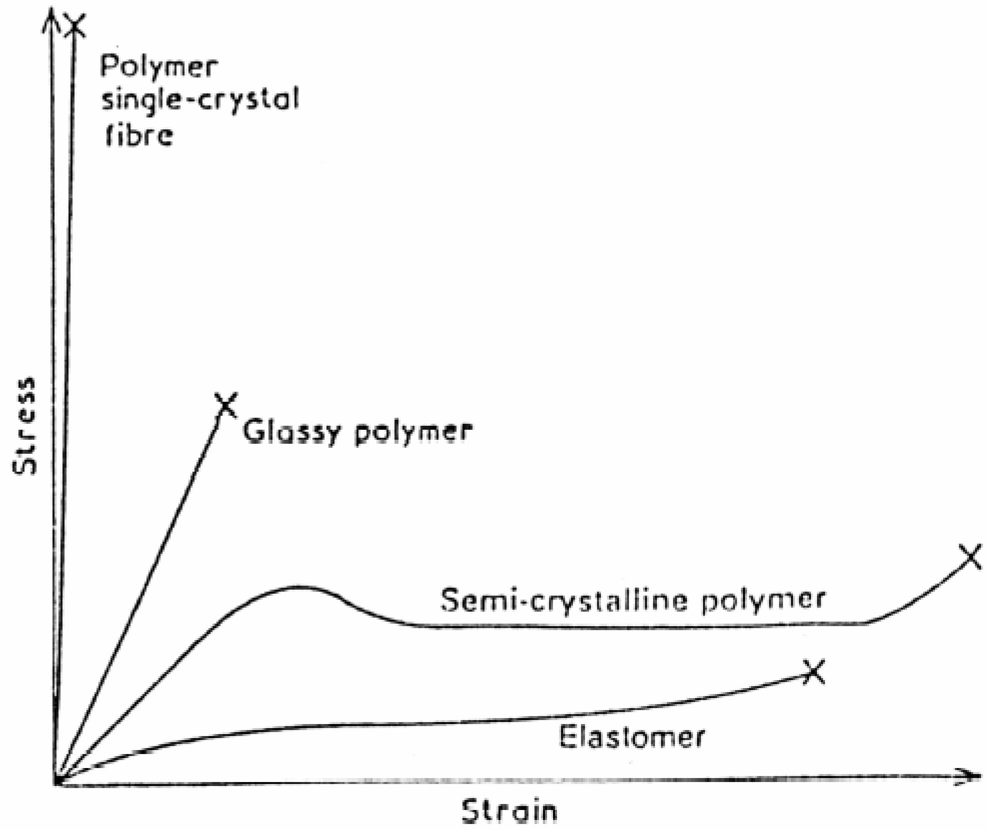
Elastomers

- Not meltable
- Not soluble
- Swellable
- Used at $T > T$g (Tg often reduced by plasticizers).

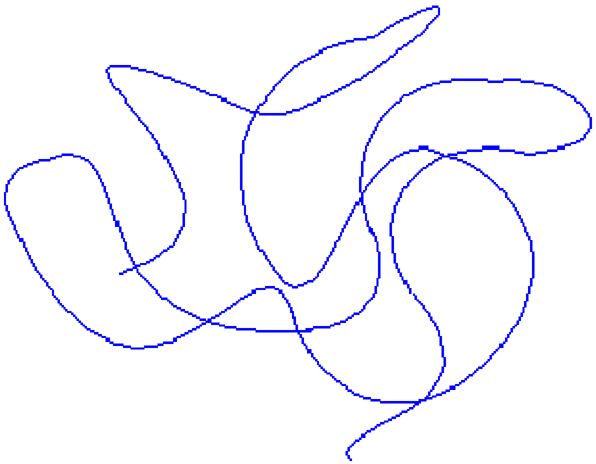
Schematic sketch of thermosets and thermoplastics. The latter can be amorphous or a structure similar to thermosets but a lower crosslink density.



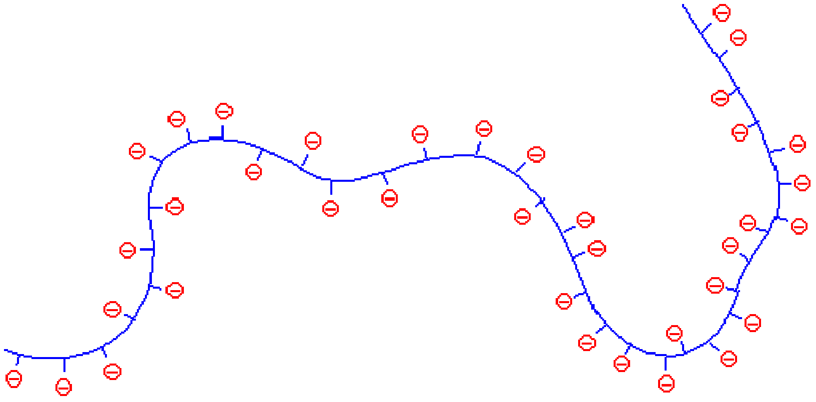
Idealized Stress-Strain Curves for Different Types of Polymers



Polyelectrolytes



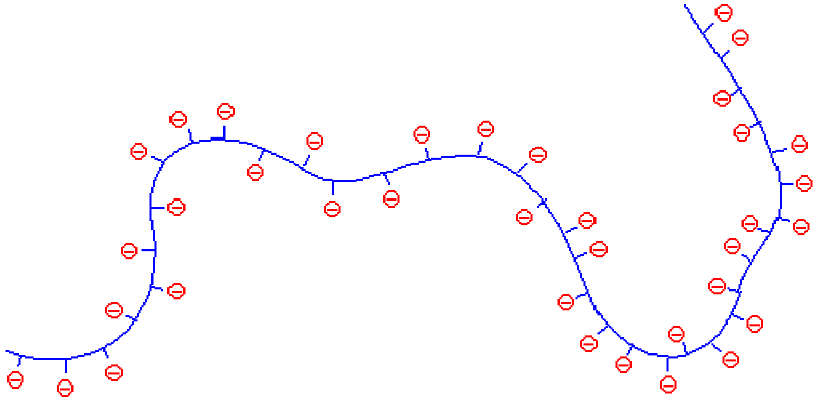
A polymer molecule tangled in a random coil.



A polyelectrolyte expands because it's like charges repel each other

Polyelectrolytes

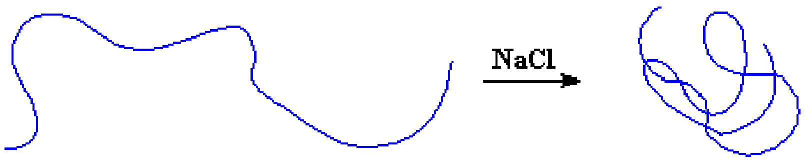
- But when the polymer chain is covered with negative charges (which repel each other), the polymer can't be bunched in on itself. So the chain stretches out, like this.
- This makes the solution (remember we're talking about polyelectrolytes *in solution*) more viscous.
- Think about it.
- When the polyelectrolyte chain stretches out it takes up more space, and is more effective at resisting the flow of the solvent molecules around it.



A polyelectrolyte expands because it's like charges repel each other

Reversibility of the Process

- If one take a solution of a polyelectrolyte in water, and throws in a lot of salt.
- The NaCl will separate into Na+ and Cl- ions.
- In the case of a negatively charged polyelectrolyte like poly(acrylic acid), the positively charged Na+ ions will get in between the negative charges on the polymer, and cancel them out in effect. When this happens, the polymer chain collapses back into random coil again.



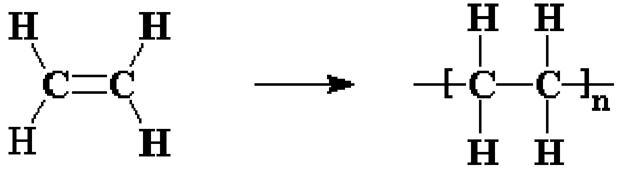
Salt makes polyelectrolytes in solution collapse into random coils.

Polymerization

- Starts with monomers
- The Addition-Condensation System

Addition Polymerization

- polymerization where the entire monomer molecule becomes part of the polymer.
- ethylene is polymerized to make polyethylene.

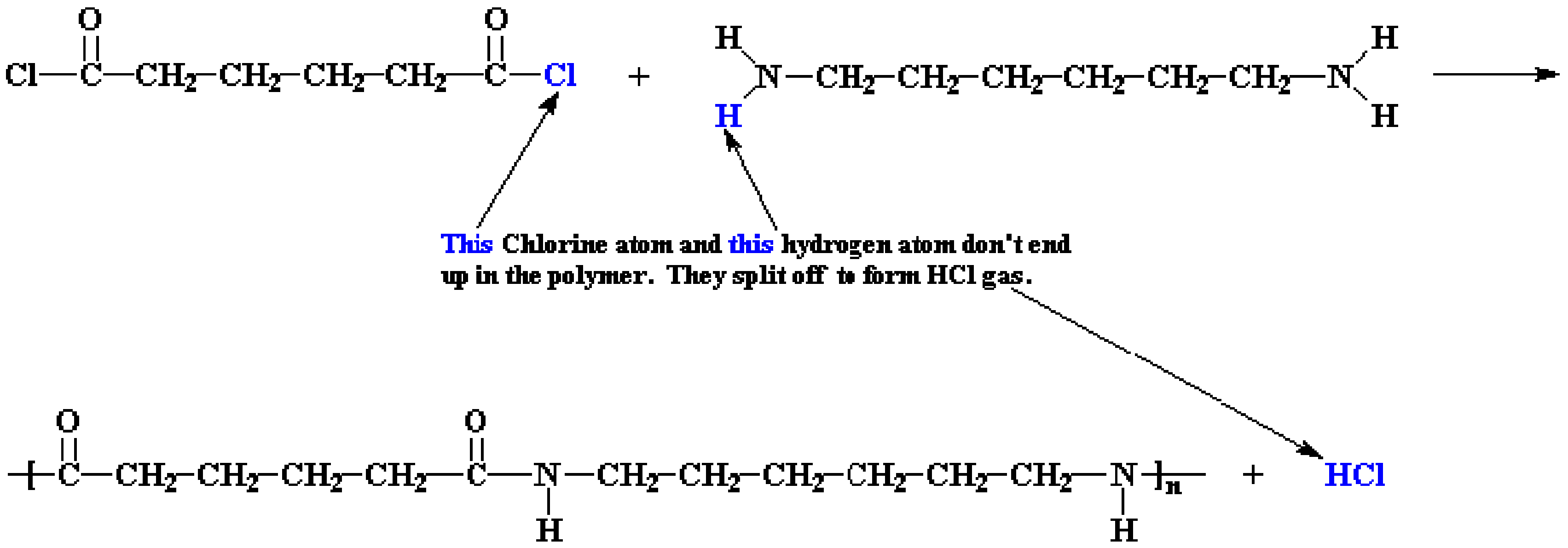


Ethylene has two carbon atoms and four carbon atoms, and the polyethylene repeat structure has two carbon atoms and four hydrogen atoms. None gained, none lost.

Condensation Polymerization

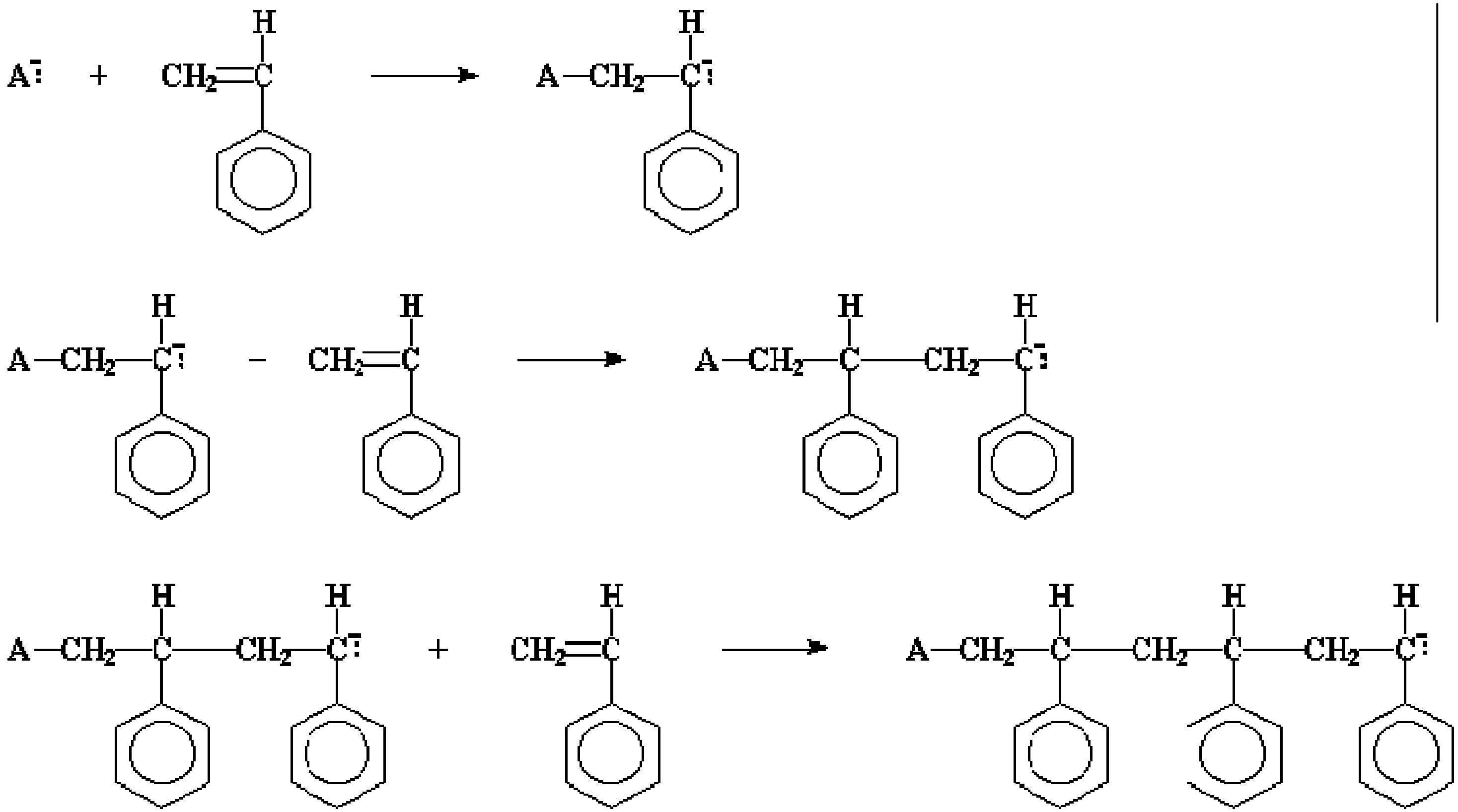
- Reaction where part of the monomer molecule is kicked out when the monomer becomes part of the polymer.
- The part that gets kicked out is usually a small molecule like water, or HCl gas.
- The polymerization of Nylon 6,6
- Because there is less mass in the polymer than in the original monomers, we say that the polymer is *condensed* with regard to the monomers.

Nylon 6,6 is made from adipoyl chloride and hexamethylene diamine

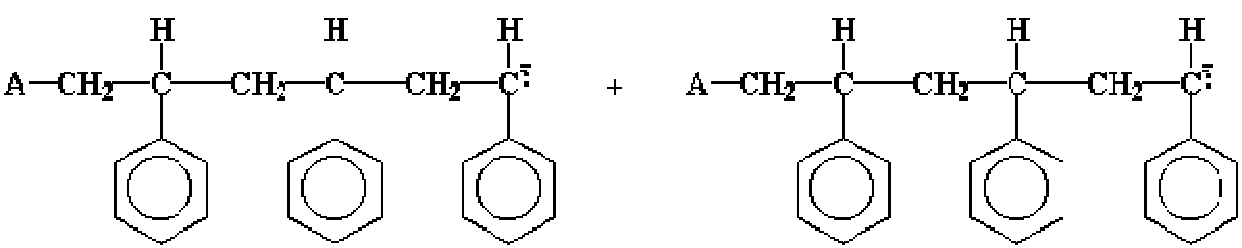


Chain Growth Polymerizations

- monomers become part of the polymer one at a time.



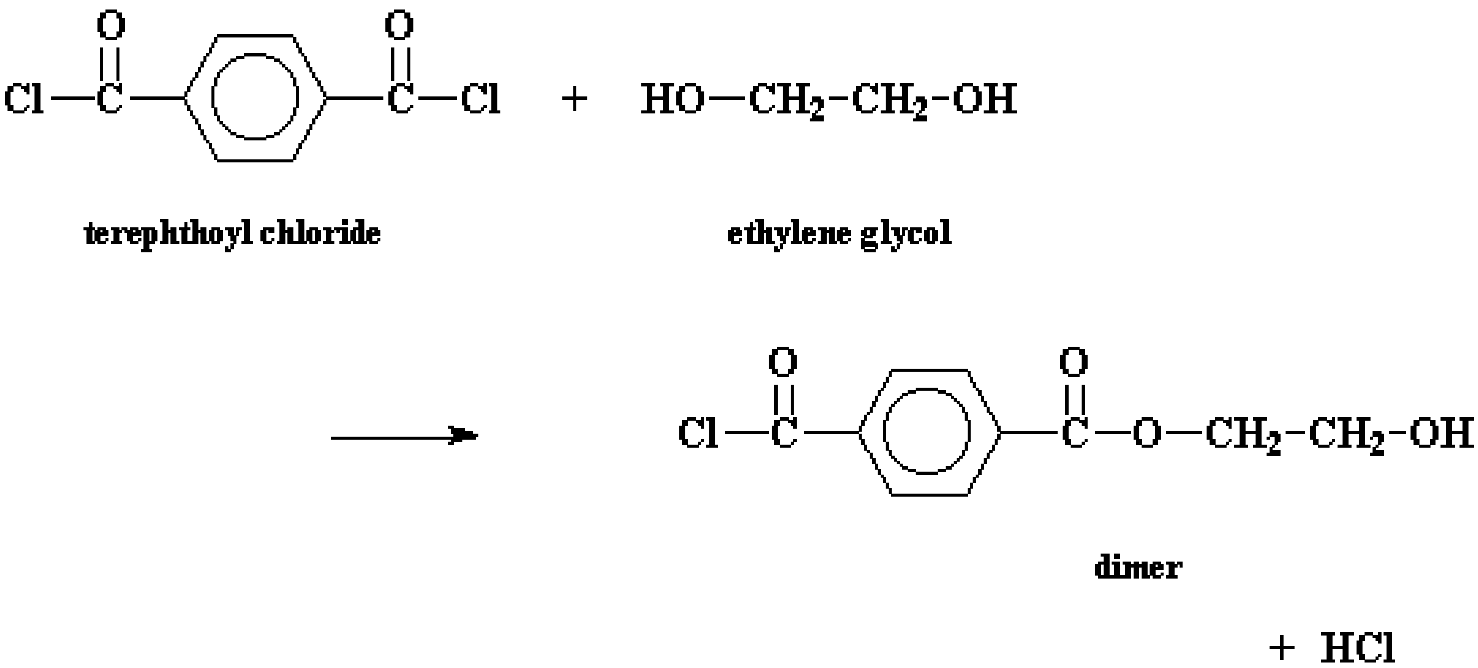
***A chain growth polymerization*: in the anionic polymerization of styrene, only styrene monomer can react with the growing polystyrene chain. Two growing chains won't react with each other.**



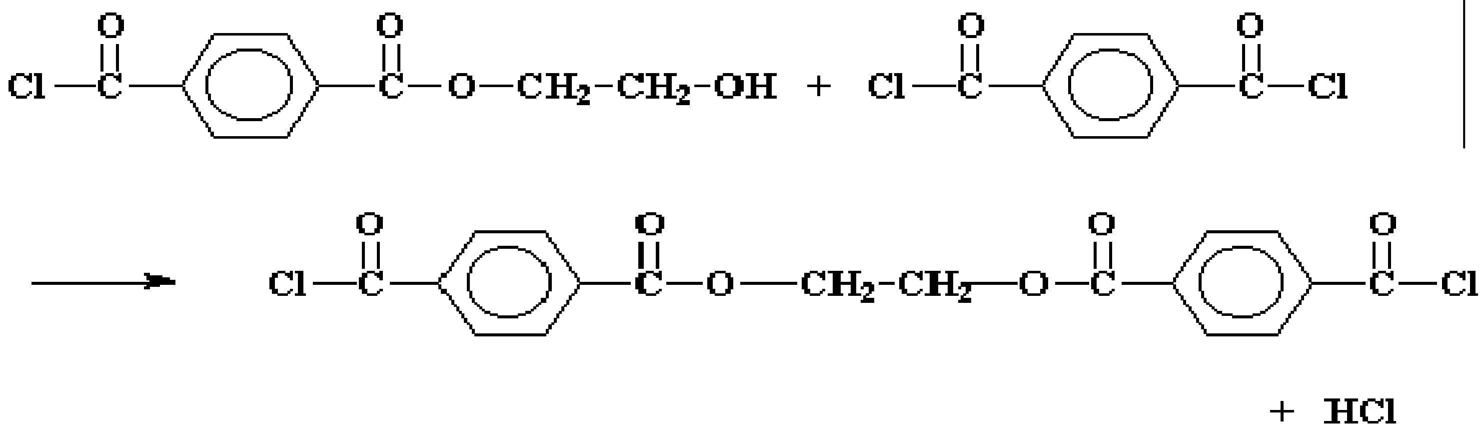
Step Growth Polymerizations

- This is a little more complicated, whereas chain growth polymerizations add one monomer at a time; multiple reaction products are possible.
- Let's take a look at the step growth polymerization of two monomers, terephthoyl chloride and ethylene glycol, to make a polyester called poly(ethylene terephthalate).

Terephthoyl chloride and ethylene glycol react to form an ester dimer

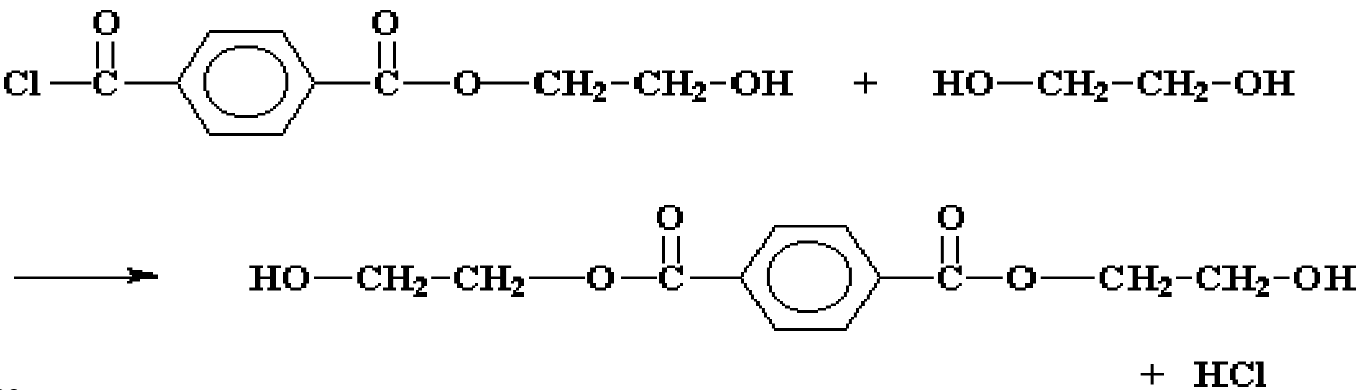


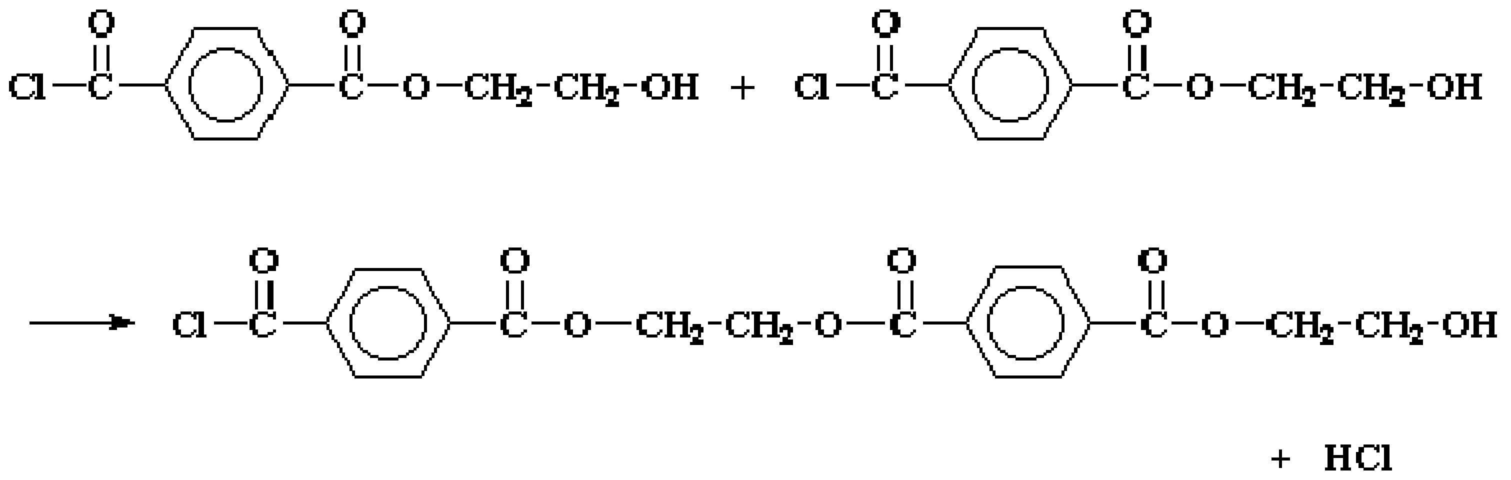
Our little dimer can react with a molecule of terephtoyl chloride...



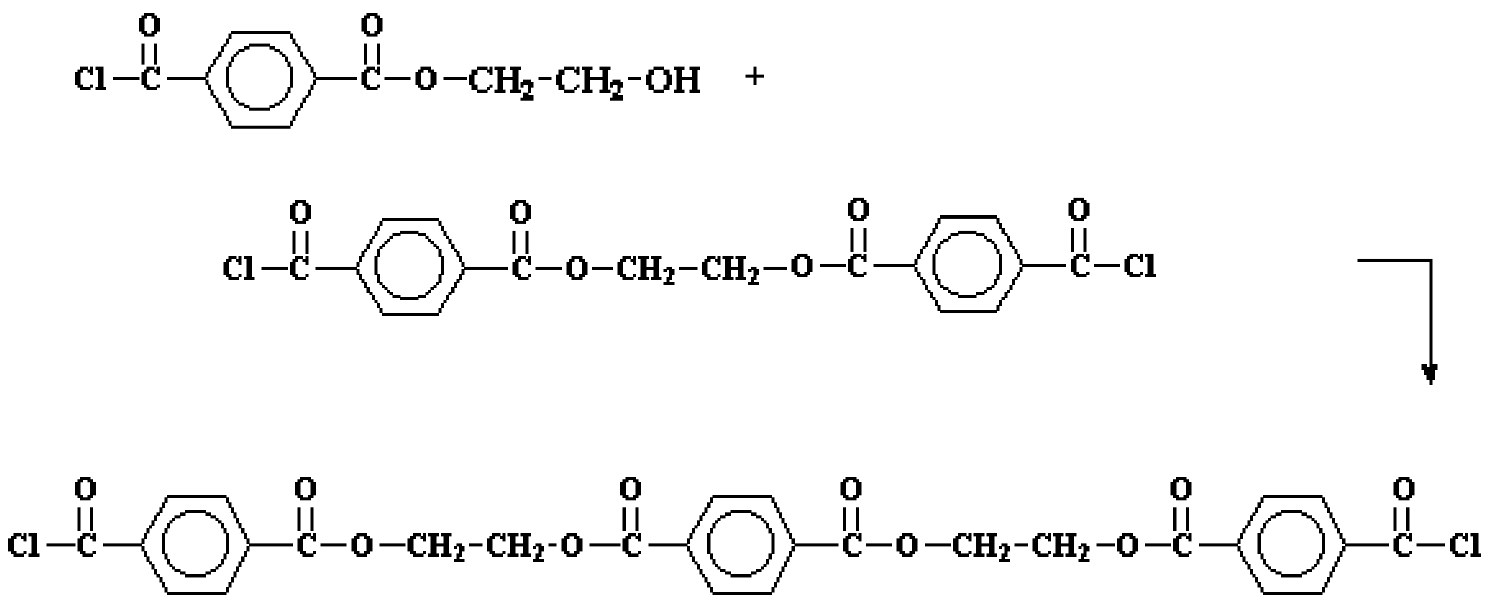
Or...

It can react with a molecule of ethylene glycol.





Two of our dimers are ganging up to form a tetramer.

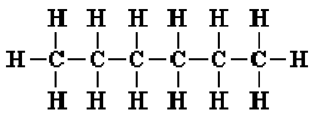


Merger Mania!

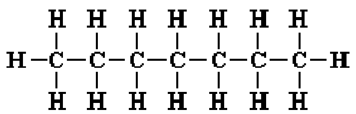
The dimer joins the trimer to form a pentamer. Will the madness never stop?

Molecular Weight

- Let's think about a small molecule, say, hexane. Hexane has a molecular weight of 86.
- Every hexane molecule has a molecular weight of 86.
- Now if we add another carbon to our chain, and the appropriate amount of hydrogen atoms, we've increased our molecular weight to 100.



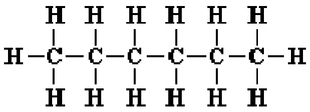
Hexane has one molecular weight, 86.



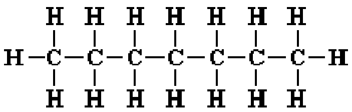
Lengthening the carbon chain by one carbon turns hexane into a completely different compound, heptane, molecular wieght = 100.

Molecular Weight

- That's fine, but the molecule is no longer hexane. It's heptane!
- If we have a mixture of some molecules of hexane and some of heptane, the mixture won't act like pure heptane, nor will it act like pure hexane.
- The properties of the mixture, say its boiling point, vapor pressure, etc., will be neither those of pure hexane nor pure heptane.



Hexane has one molecular weight, 86.



Lengthening the carbon chain by one carbon turns hexane into a completely different compound, heptane, molecular wieght = 100.

Dispersity

- Consider a protein-a protein in a polymer of amino acids linked a linear sequence, and like classic small molecules, it has a specific molecular weight and can be said to be monodisperse.
- However, commercial synthetic polymers, such as HDPE, are made up of molecules of different molecular weight.
- The numerical number for n, or the degree of polymerization (DP).
- Thus, the average molecular weight of a polydisperse polymer is equal to the product of the DP and the molecular weight of the repeating unit or mer.

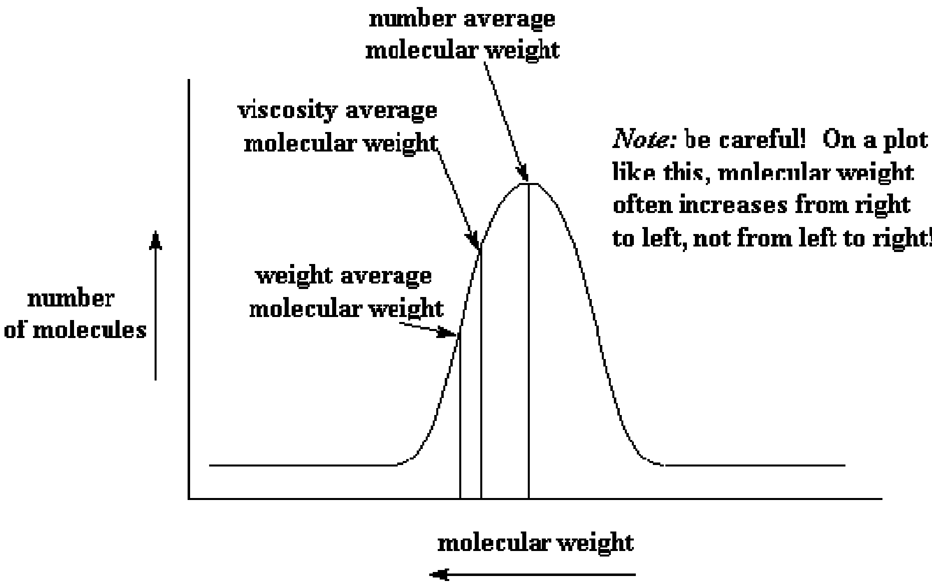
But Polymers are Different.

- Imagine polyethylene.
- If we have a sample of polyethylene, and some of the chains have fifty thousand carbon atoms in them, and others have fifty thousand and two carbon atoms in them, this little difference isn't going to amount to anything.
- If you really want to know the truth, one almost never finds a sample of a synthetic polymer in which all the chains have the same molecular weight.
- Instead, we usually have a bell curve, a *distribution* of molecular weights.

Molecular Weight

The Number Average Molecular Weight, *Mn*

- the total weight of all the polymer molecules in a sample, divided by the total number of polymer molecules in a sample



The Weight Average Molecular Weight, *Mw*

$$M_w = \frac{\sum_i N_i M_i^2}{\sum_i N_i M_i}$$

Where N is the number of moles in the sample with mass M, and N*M is the mass of the sample.

Molecular Weight

1. Number Average Molecular Weight (Mn)

$$Mn = \frac{\text{weight}}{\text{molecules}} = \frac{\sum NxMx}{\sum Nx}$$

2. Weight Average Molecular Weight (Mw)

$$Mw = \frac{\sum CxMx}{\sum Cx} = \frac{\sum (NxMx)(Mx)}{\sum NxMx} = \frac{\sum NxMx^2}{\sum NxMx}$$

3. Polydispersity

Polydispersity = Mw/Mn

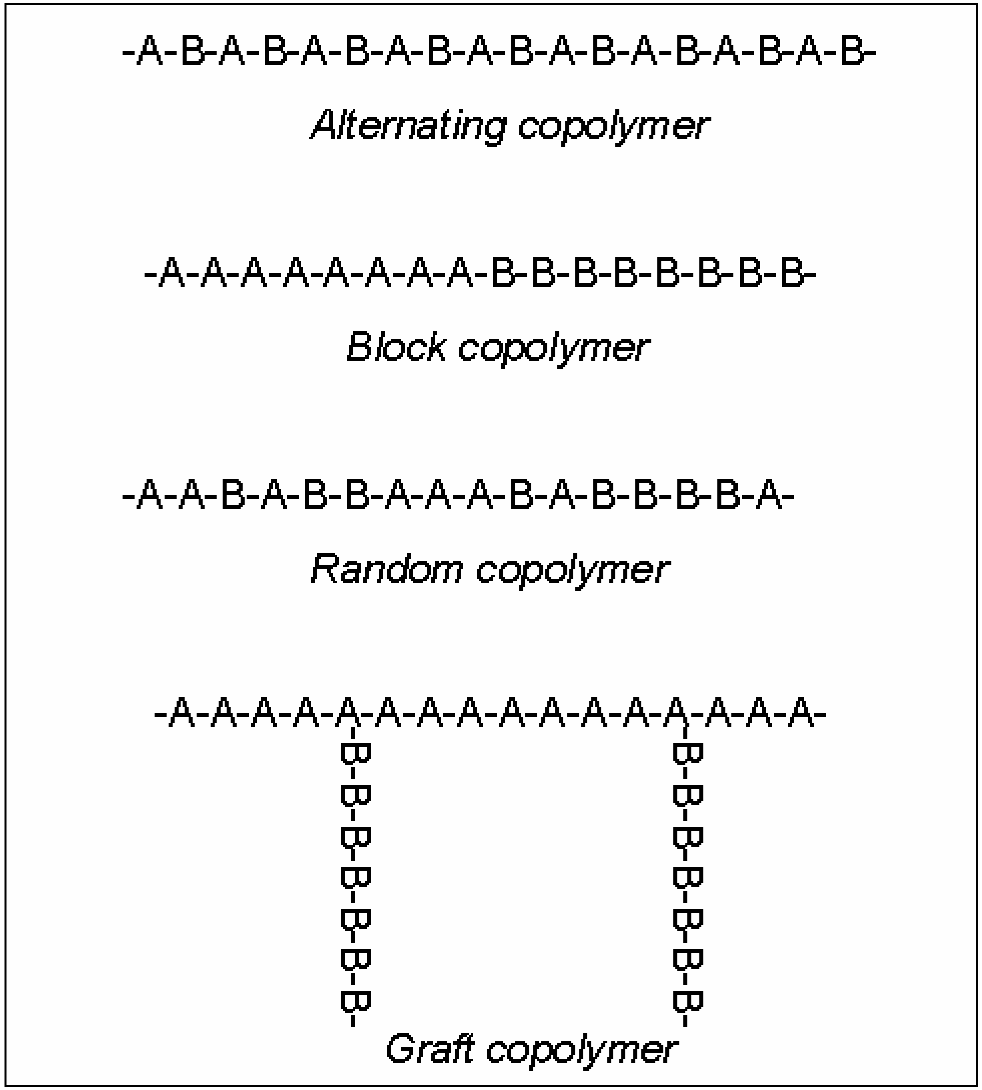
Influence of Increasing Molar Mass on Properties

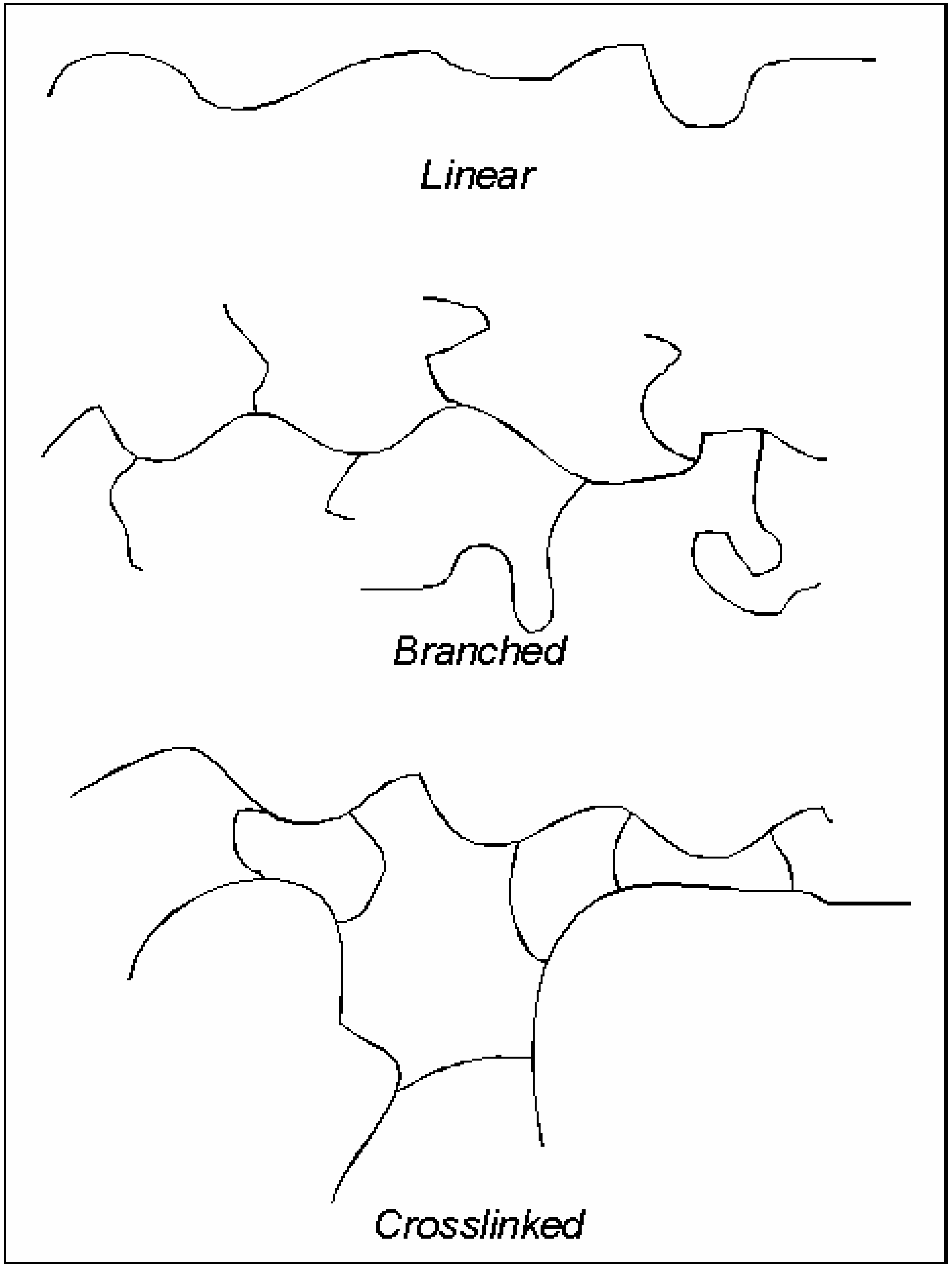
Increasing molar mass leads to			
higher strength	higher impact strength	higher chemical resistivity	reduction in flowability and resistance to melt fracture

Reasons			
higher interchain forces, more entanglements	lower degree of crystallization at higher chain length, more entanglements	higher interchain forces, degradation not so detrimental since high level	more entanglements

Experimental Determination of Molecular Weight

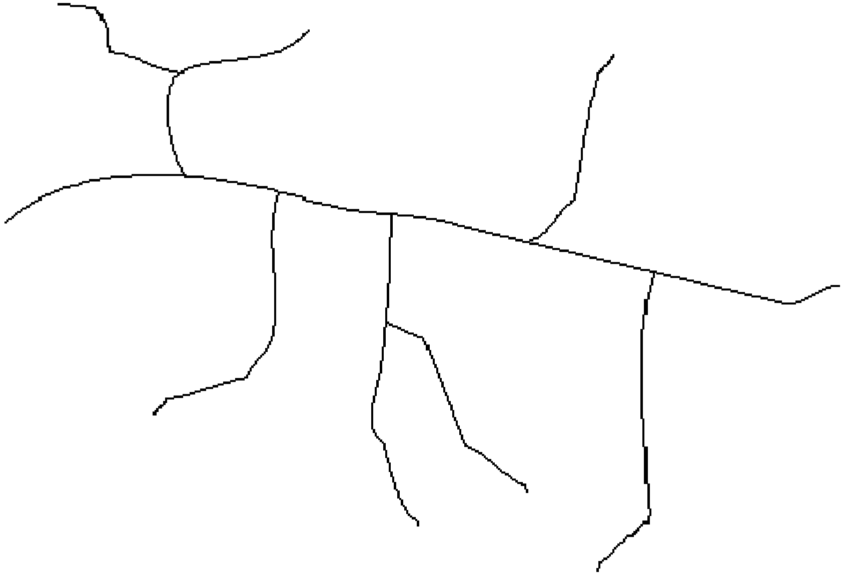
- Gel Permeation Chromatography
- Laser Light Scattering
- Viscometry


-A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-B-A-B-
Alternating copolymer
-A-A-A-A-A-A-A-A-B-B-B-B-B-B-B-B-
Block copolymer
-A-A-B-A-B-B-A-A-A-B-A-B-B-B-B-A-
Random copolymer
-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-A-
-B-B-B-B-B-B-B-
-B-B-B-B-B-B-B-
Graft copolymer


Linear
Branched
Crosslinked

Branched Polymers

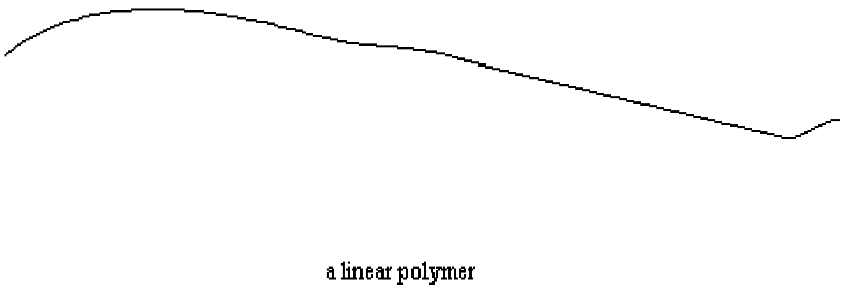
- Not all polymers are linear
- Some thermoplastic polymers, like polyethylene, can be made in linear or branched versions.



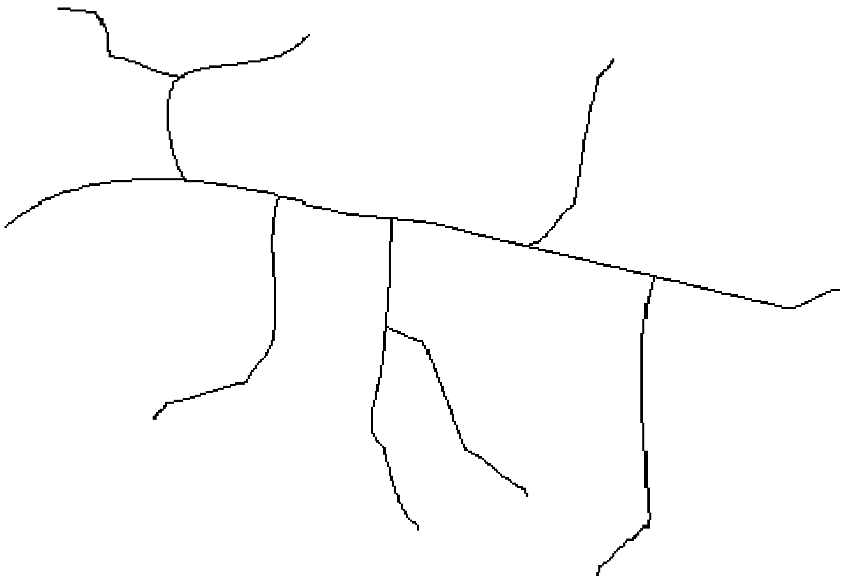
a branched polymer

HDPE vs LDPE

HDPE



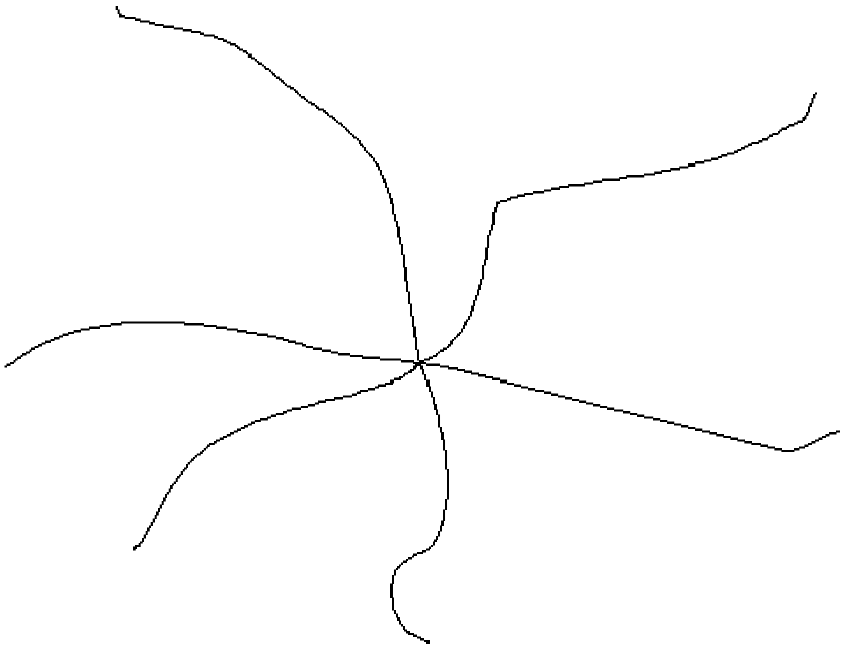
LDPE



The branching increases the volume and thus reduces the density of the polymer.

Star Polymers

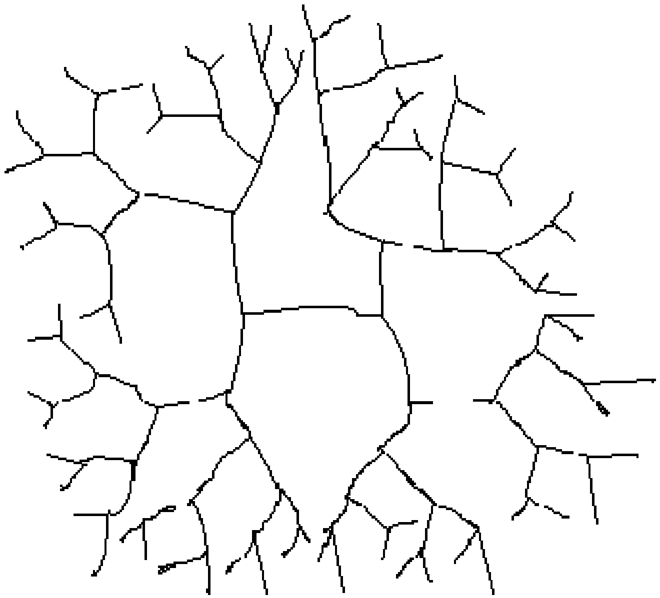
- Sometimes the ends of several polymer chains are joined together at a common center.
- Polymers like this are called *star polymers*.
- They're often used as additives or as coating materials.



a star polymer

Dendrimer

- Sometimes there is no backbone chain at all.
- Sometimes a polymer is built in such a way that branches just keep growing out of branches and more branches grow out of those branches.
- These are called *dendrimers*, from the ancient Greek word for "tree".



a dendrimer

Learning Resources

www.msm,cam.ac.uk/

University of Cambridge

Department of Materials Science and Metallurgy

Teaching: DoITPoMS Project

Library of Teaching and Learning Packages for Materials Science

www.msm.cam.ac.uk/doitpoms/tlplib/index.php

THE GLASS TRANSITION IN POLYMERS (required reading)