

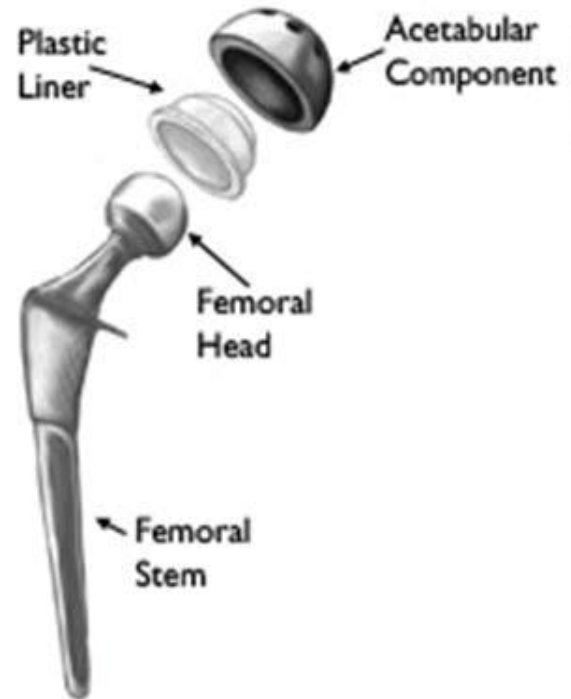
Classes of Materials Used in Medicine:

Polymers

THE POLYMER MOLECULE

- Polymer materials possess an array of unique properties which make them useful in a wide variety of biomaterial applications such as;

✓ Orthopedics



✓ Dental



- Denture bases and teeth
- Soft liners
- Cementing materials

- ✓ hard and soft tissue replacements
- ✓ cardiovascular devices.



Heart valve

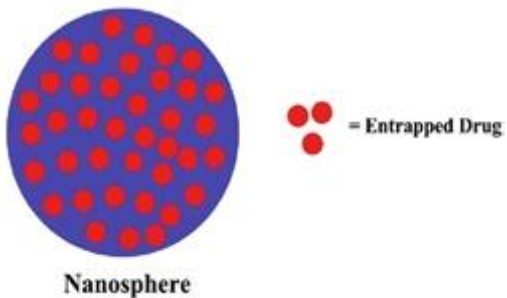


blood vessel



Artificial skin

- ✓ Drug release systems



- ✓ Scaffolds



❑ Molecular Structure of Single Polymer Molecules

- A single polymer molecule could have a molecular weight of 200,000 Da compared to a water molecule, which has a molecular weight of 18 Da.
- Polymer molecules are organized into different architectures.

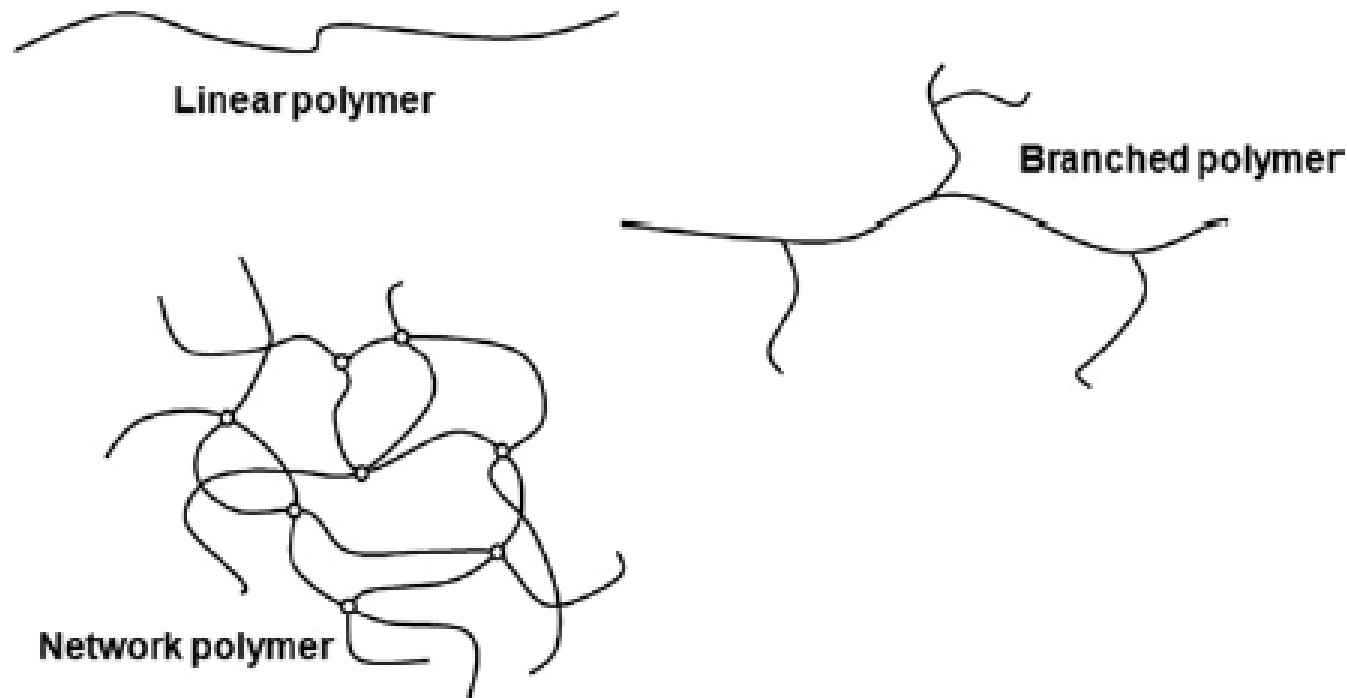
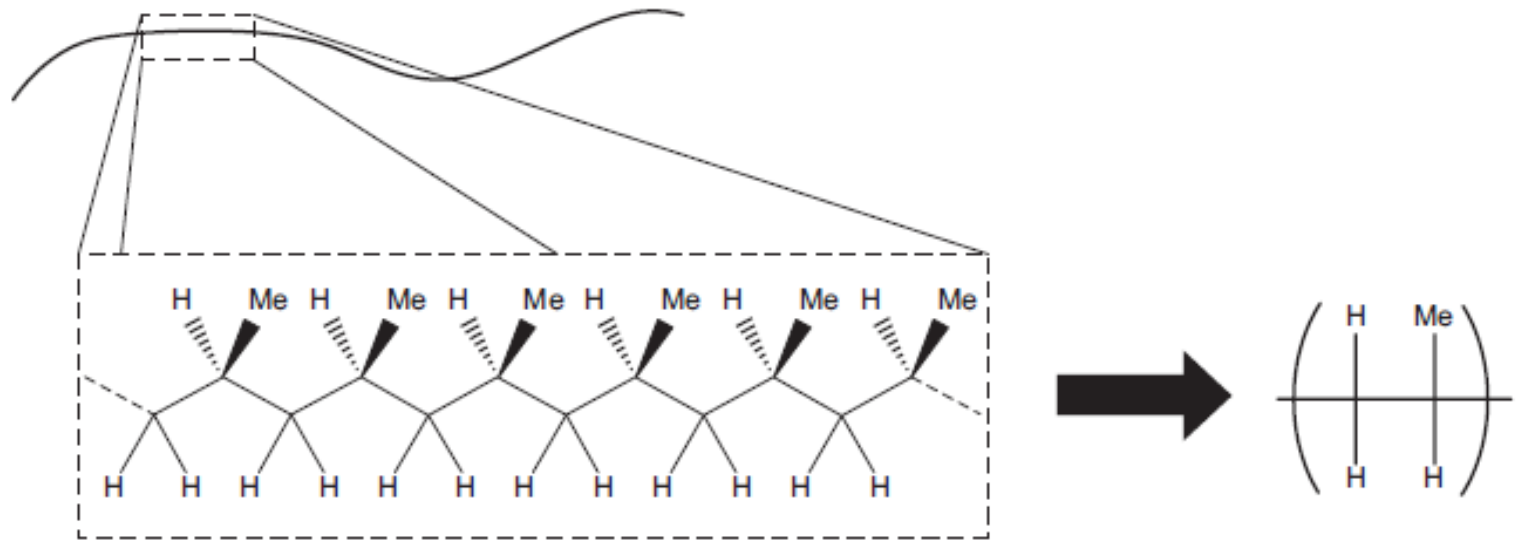


FIGURE 1.2.2.1 Some of the molecular structures available for polymer molecules. In the schematic of the network, polymer open circles indicate cross-link sites.

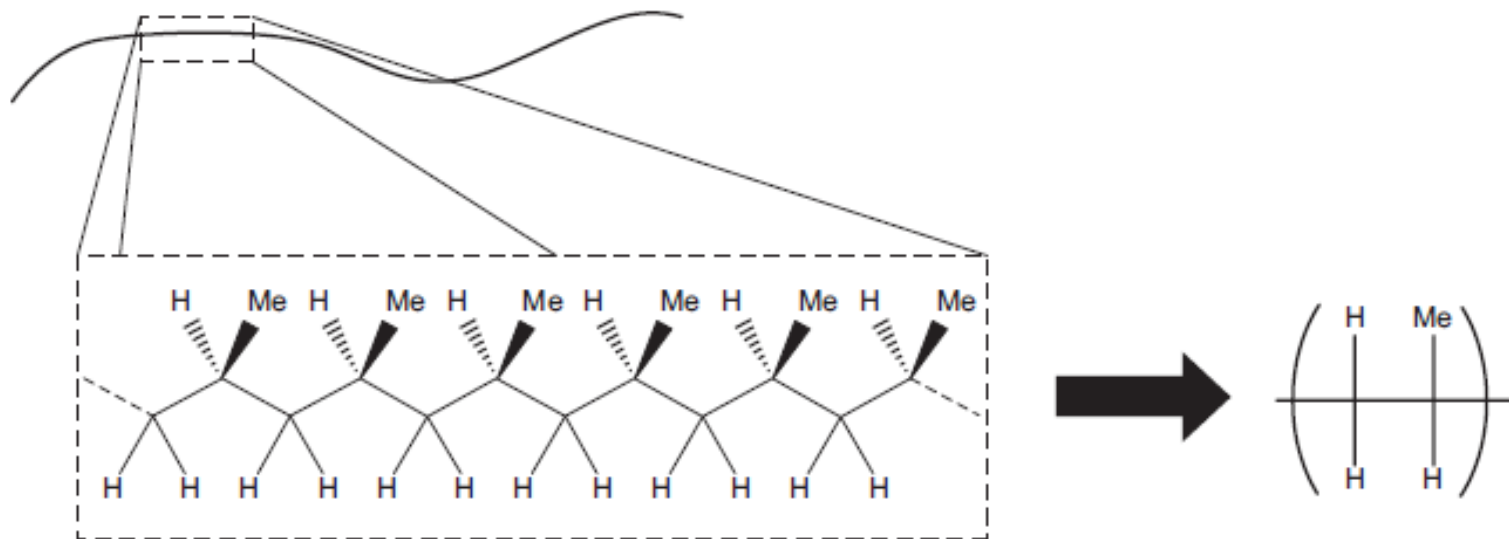
- When **linear chains** of two different composition polymers (e.g., A and B) are linked together, the resultant polymer is called an A–B block copolymer. If another chain is added to the second chain, it may be called an A–B–C triblock copolymer, or more simply, an A–B–C block copolymer .
- **Branched structures** are also possible where a central polymer backbone has smaller side chains extending from it.
- If you took a linear polymer molecule and covalently bond it to the backbone of another linear chain and repeat this act many times, you would eventually link all of the polymer chains together into one very large **network polymer**.
- This is also possible by using “cross-linker” molecules to react with terminal reactive groups on linear polymer chains, eventually yielding a network polymer.

□ Chemical Structure of Single Polymer Molecules

- If you were able to see the individual atoms making up a polymer molecule, you would notice the same basic structure repeats over and over again.

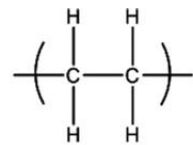


schematic of a linear polypropylene molecule.

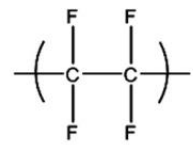


- The polymer backbone is a series of carbon–carbon single bonds, while the hydrogen atoms and methyl group are ***pendant groups***.
- The polymer chain is composed of many $\text{-(CH}_2\text{-CHMe)-}$ groups covalently linked end-to-end. This structure is called the ***repeat unit*** of a polymer molecule.

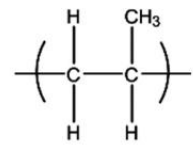
- Repeat unit of common polymer biomaterials.



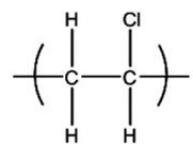
**Polyethylene
(PE)**



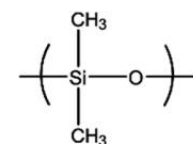
**Polytetrafluoroethylene
(PTFE)**



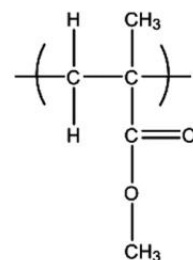
**Polypropylene
(PP)**



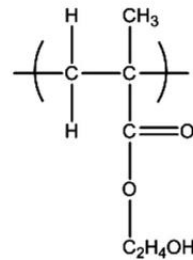
**Polyvinylchloride
(PVC)**



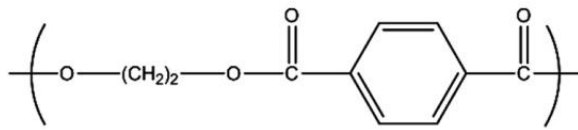
**Polydimethylsiloxane
(PDMS)**



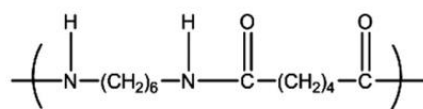
**Poly(methyl methacrylate)
(PMMA)**



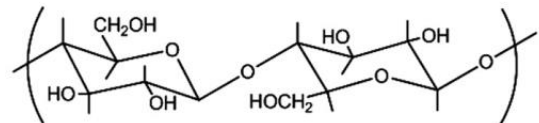
**Poly(hydroxyethyl methacrylate)
(PHEMA)**



**Polyethyleneterephthalate
(PET)**



Nylon 6,6



Cellulose

The repeat unit can be controlled through polymer synthesis and plays a large role in the macroscopic behavior of the polymer

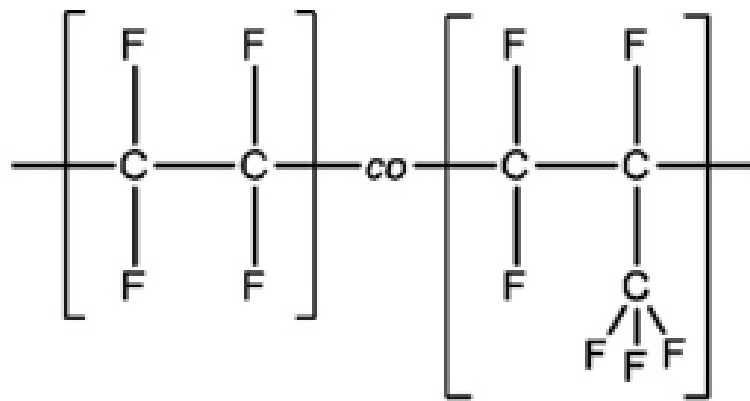
□ Copolymers

- Copolymers contain more than one chemically distinct repeat unit polymer which contains repeat units “A” and “B.”
- There are many different ways the repeat units could be organized such as:
 - Random
 - Alternating
 - Block
 - Graft

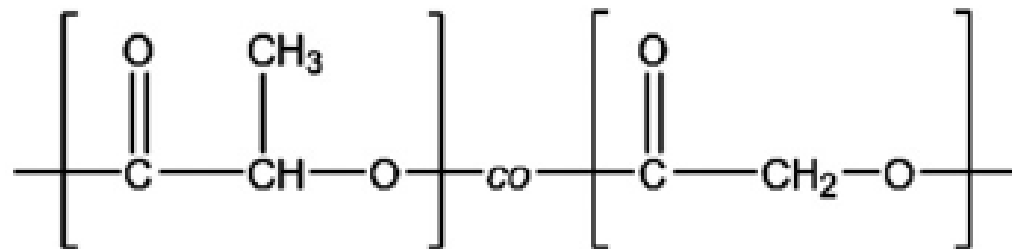


FIGURE I.2.2.4 Some of the molecular structures available for copolymers.

the arrangement of repeat units affects the physical behavior of the biomaterial.



Poly(tetrafluoroethylene-co-hexafluoropropylene)random copolymer

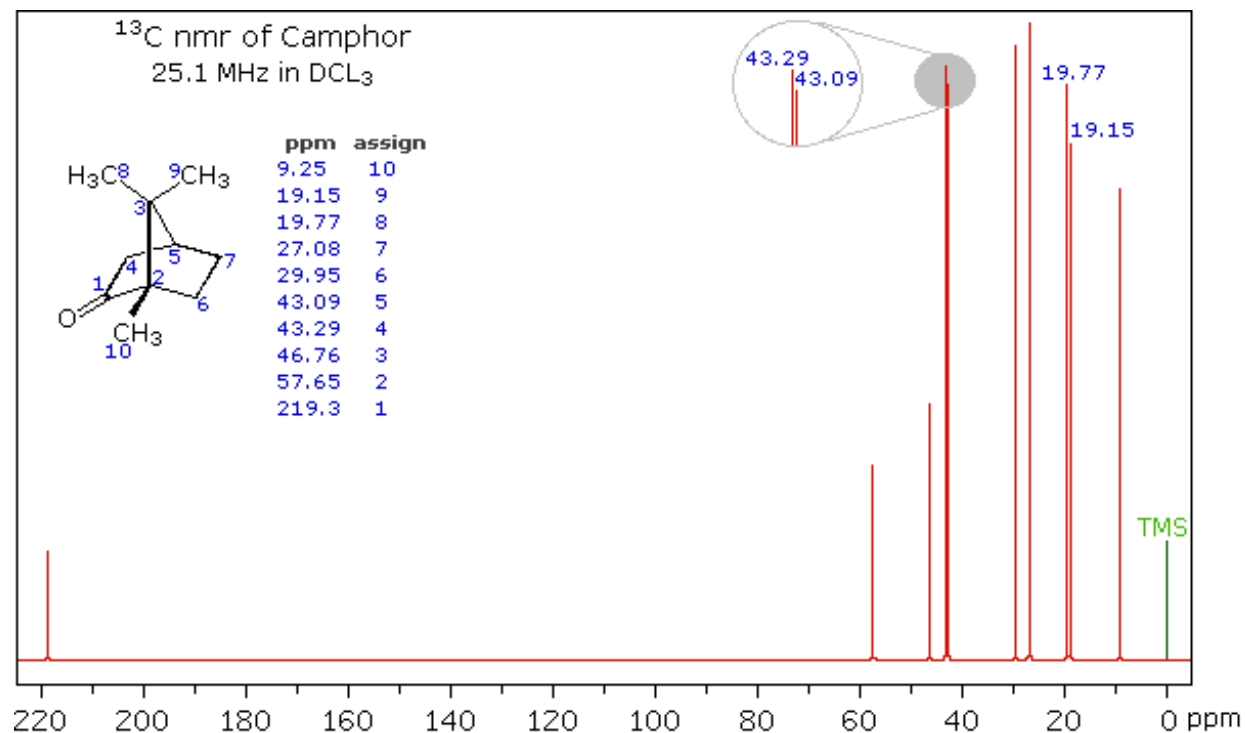
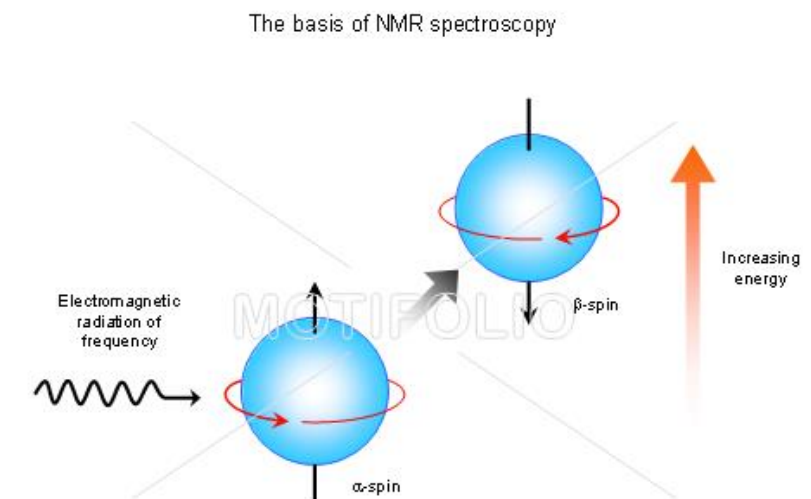
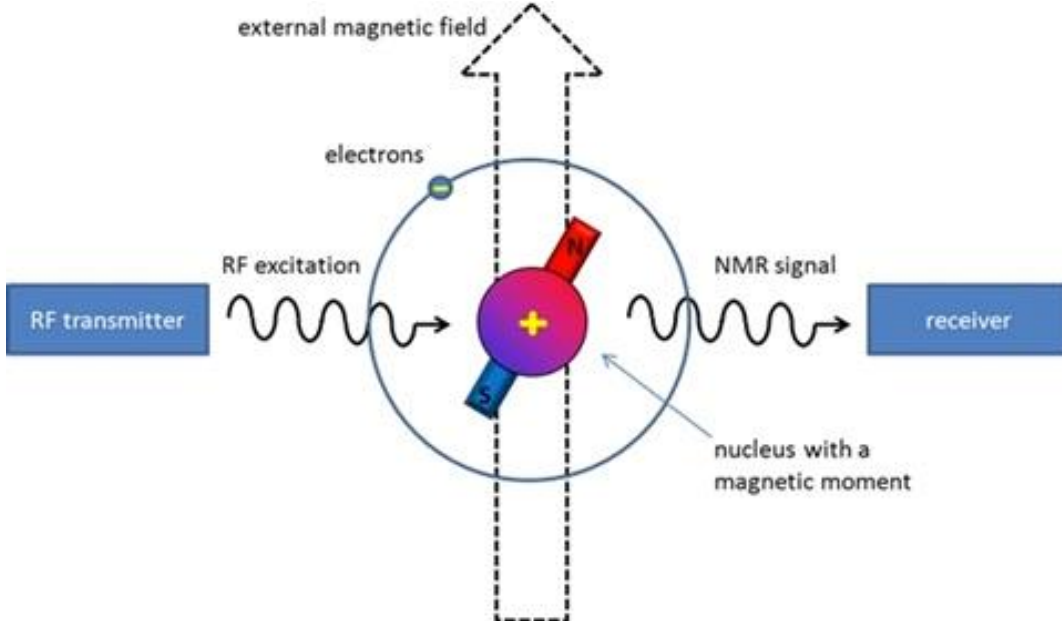


Poly (lactide-co-glycolide)random copolymer

FIGURE I.2.2.5 Repeat unit of two common copolymer biomaterials.

❑ **Determination of Chemical Composition**

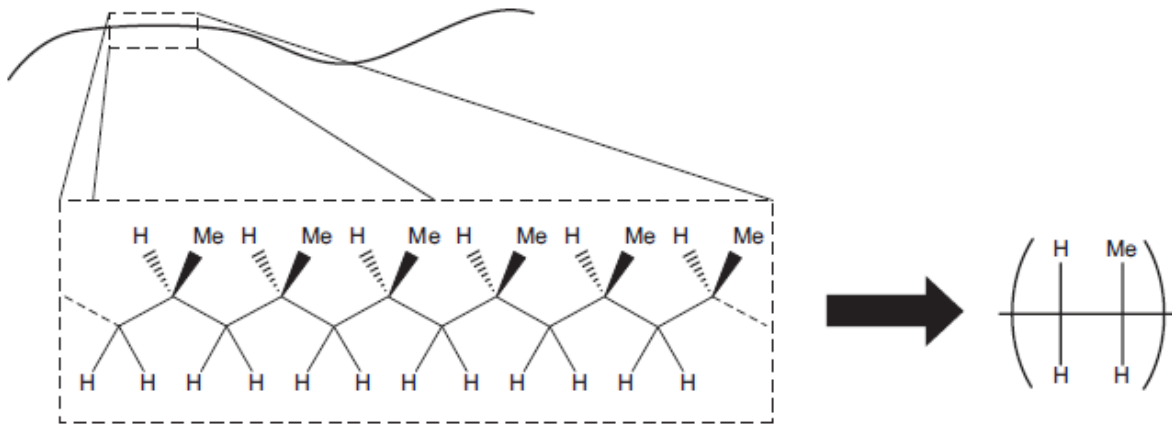
- A researcher will often need to verify the chemical structure of polymers or determine the composition of copolymer systems.
- Common techniques a scientist would use are **nuclear magnetic resonance spectroscopy (NMR)**, **infrared spectroscopy (IR)**, and **X-ray photoelectron spectroscopy (XPS)** .
- NMR is an analytical technique which exploits the magnetic moments associated with nuclei containing an odd number of protons (most commonly the ^1H and ^{13}C isotopes). These protons are excited to a higher energy state through a burst of radiofrequency radiation. Then the nuclei relax to a lower energy state which is measured as an electric signal.
- Due to shielding, protons attached to different structural units will display chemical shifts, meaning their peaks in the NMR spectrum will be at different frequencies.
- Through analysis of the peak placement and intensity, the chemical structure of molecules can be determined .



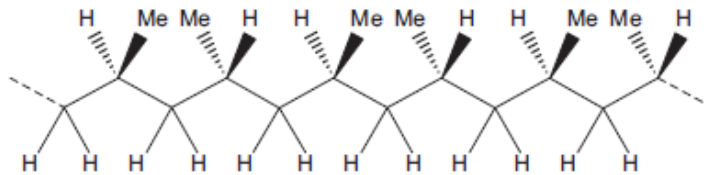
- **Infrared spectroscopy (IR)**; the sample of interest is irradiated with infrared radiation and the sample adsorbs certain wavelengths, resulting in specific molecular motion (such as C–H stretching).
- **X-ray photoelectron spectroscopy (XPS)** – also known as electron spectroscopy for chemical analysis (ESCA) – is a common technique.
- A sample is bombarded with X-rays which results in the ejection of inner shell electrons from the atoms displayed on the material surface.
- The kinetic energies of the ejected electrons are measured and interpreted into information about the chemical composition of the surface

Tacticity

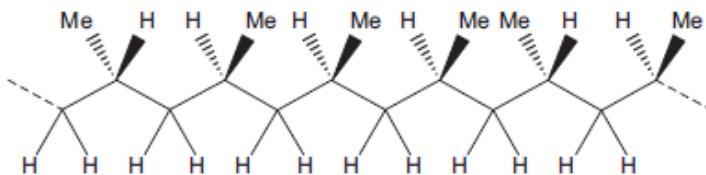
- Tacticity describes the stereochemistry of the repeat units in polymer chains.



Isotactic PP



Syndiotactic PP



Atactic PP

- sometimes the methyl groups are all on one side of the backbone, sometimes they alternate from side to side, and sometimes they are randomly distributed.

FIGURE I.2.2.2 Polypropylene repeat unit and different tactic isomers. In the schematic Me indicates a methyl group.

□ Molecular Weight

- During polymerization, polymer chains are built up from low molecular weight monomers. The number of monomer repeat units in each polymer chain is called the ***degree of polymerization***.
- Degree of polymerization may change for each polymer chain.
- For instance, in the polymerization of polyethylene, one polymer chain may add 3000 monomers, a second may add 4500 monomers, and a third may only add 1500. Therefore, most polymer systems have a ***distribution of molecular weights***.

CONNECTING PHYSICAL BEHAVIOR WITH CHEMICAL CHARACTERISTICS

- Key characteristics of polymer molecules are:
 - molecular architecture
 - chemical composition
 - Tacticity
 - molecular weight.

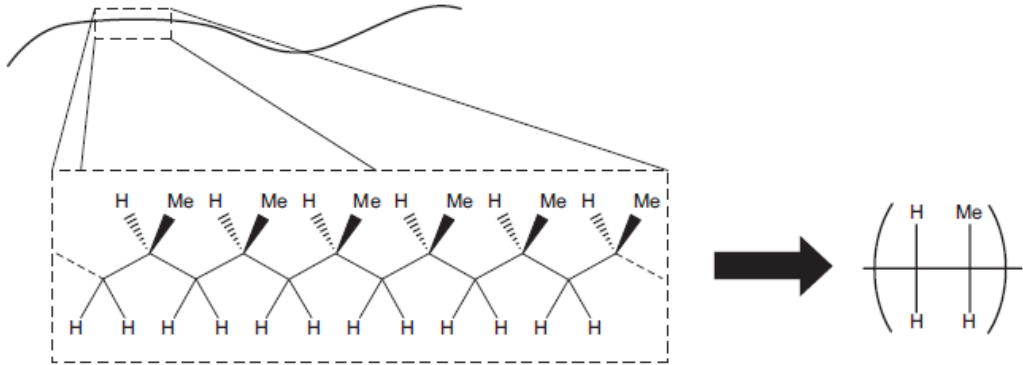
How these molecular characteristics are related with to macroscopic properties?

How these characteristics can be manipulated to create a polymer system with the desired behavior?

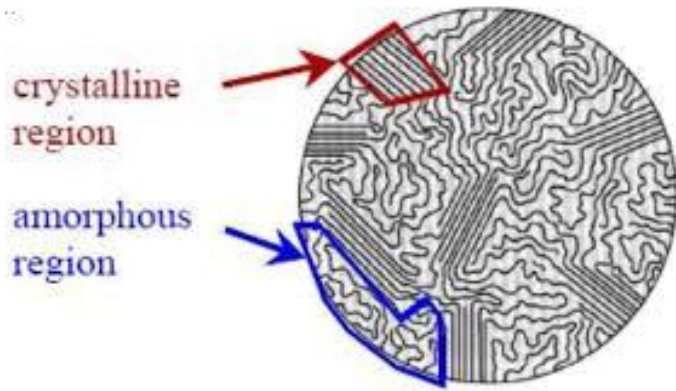
□ Physical States of Linear Polymers.

- When designing a biomaterial, physical behavior is a key feature.
 - if you were creating a cement for use in loadbearing bones (tibia or femur) you would have to ensure the material is both strong enough to act as a cement, but not so brittle that it would fail due to low fracture toughness .
- The four most fundamental molecular characteristics of polymer chains which determine the physical behavior of a polymer are
 - ① chain stiffness
 - ② chain composition
 - ③ chain architecture
 - ④ molecular weight.
- Physical states of linear polymers are:
 - Rubbery State
 - Glassy State
 - Semi crystalline State

- Polypropylene molecules extended into planar zigzags shown in the figure but this type of extended structure is rarely seen in nature



- More often, polymer molecules are found as unorganized and three-dimensional structures called the **random coil**.
- In an **amorphous structure**, each random coil is highly interpenetrated with its neighbors.



- Polymers in the rubbery state or the glassy state have this amorphous molecular arrangement.
- Under certain conditions, some polymers will arrange themselves into highly organized crystalline domains resulting in a semi-crystalline material.

➤ The Rubbery State.

- Rubbery polymers are amorphous
- Macroscopically these materials are soft, flexible, and extensible

➤ The Glassy State

- As the polymer system is cooled, main chain bonds in a polymer chain gets stiffer and stiffer. Eventually, at a low enough temperature, random coils become frozen in space. This is called the **glassy state**.
- The temperature where single bond rotation ceases is called the glass transition temperature (T_g).
- A material below its T_g is called a glass because it is hard, stiff, and brittle.
- Molecules in the glassy state can no longer rearrange themselves under applied stress, so deformation results.
- The opposite occurs when an amorphous polymer is heated: the amorphous region goes from hard and glassy, to rubbery, and if the material is not cross-linked, it will eventually flow as a viscous fluid and can be processed into shapes.

Glass Transition Temperature (T_g)

- Hard, brittle

Soft, rubbery

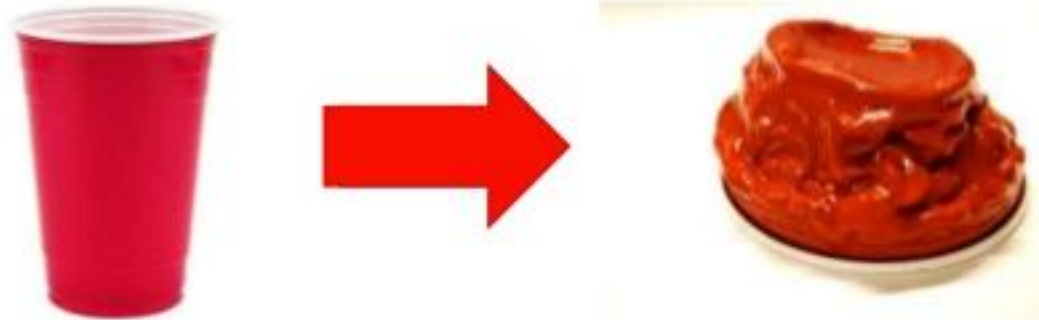


Figure 6 – Visual representation of polymers' actions at T_g .

➤ The Semi-Crystalline State.

- All polymer systems form glasses at sufficiently low temperatures. However, as a melt is cooled, certain polymers have the ability to pack into a regular lattice, leading to the formation of stable **crystalline** domains.
- If only a portion of the long polymer chains crystallize (some segments will not be able to pack into the crystallites), this state is called **semi-crystalline**.
- The temperature above which such crystalline regions will melt is called the crystalline melting point (T_m).
- Crystallites act to **stiffen and reinforce the bulk material**, and extend the stiffness and strength properties of a material well above the glass transition temperature

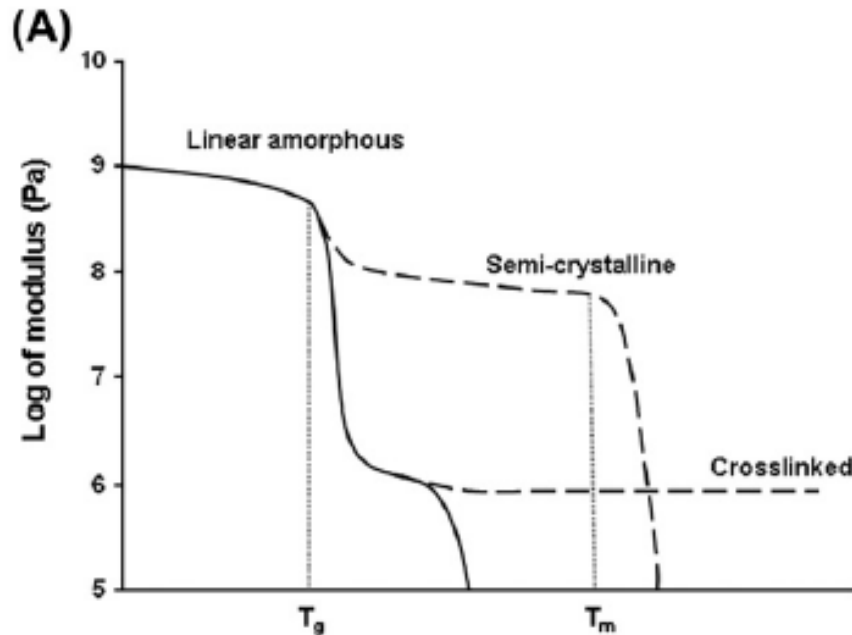
❑ The Physical Behavior of Linear and Amorphous Polymers

- Unlike metals which are held together by metallic bonds and atomic crystals which are held together by covalent bonds, polymer materials are held together by secondary interactions such as Van der Waals, and hydrogen bonding. For this reason, **polymers are often mechanically weaker than other classes of materials**; however, they can display physical behavior more similar to native tissue.
- When **rubbery materials (amorphous)** are strained, the polymer molecules are able to deform and extend resulting in a material which is macroscopically soft and weak, yet highly extensible. However, as the T_g of the material approaches and exceeds the environmental conditions, the material becomes a glass and is much stronger yet stiffer.



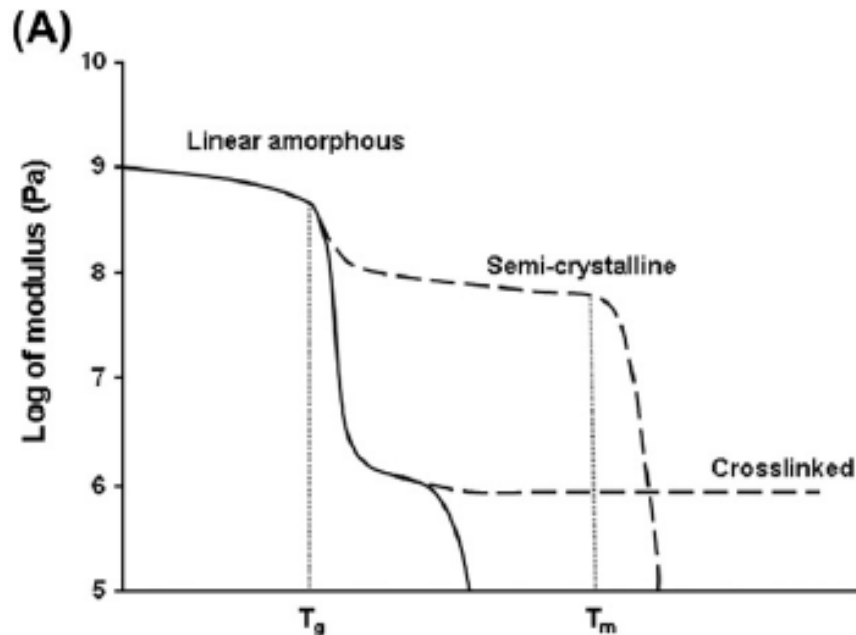
□ The Physical Behavior of Other Physical States

- Cross-linking, crystallinity, and copolymerization greatly affect the physical behavior of polymer systems, and controlling these parameters gives a polymer scientist ways of specifying the physical behavior of a polymer system.



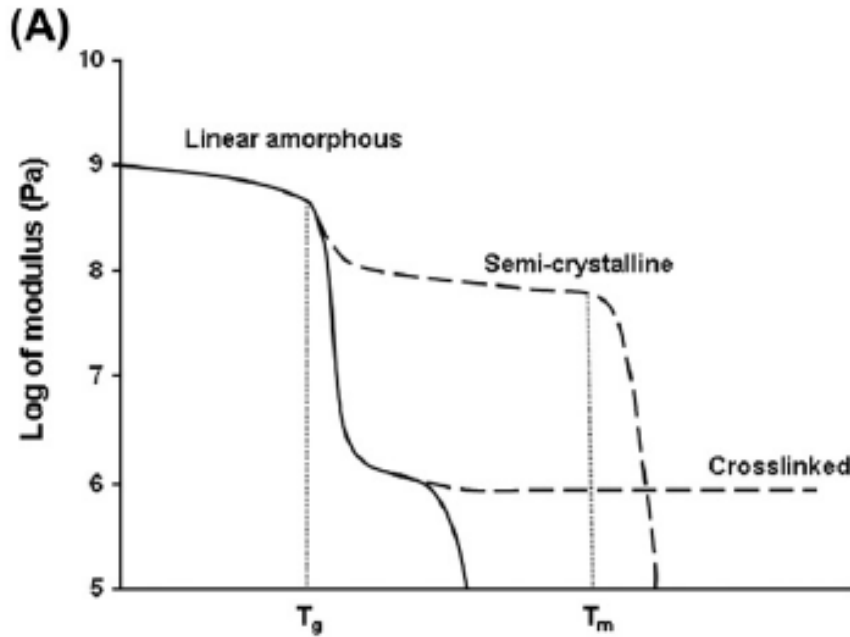
standard modulus–temperature behavior of a linear and amorphous polymer system (solid line).

- Below the T_g , the material is a glass and has a high modulus.
- However, at the glass transition temperature we see a dramatic drop in modulus due to the increased mobility within the polymer structure.
- At temperatures just higher than the T_g , we see a plateau on the curve where modulus declines more slowly with temperature. This is called the rubbery plateau, and in this region the polymer is still solid-like but soft, flexible, and extensible.
- Eventually, as the temperature is increased more, we see the modulus curve take another drop corresponding to the material beginning to flow.
- Notice that amorphous materials do not have a melting temperature. Melting refers to the loss of crystallinity, and since these materials are non-crystalline they never truly melt.



modulus–temperature behavior of a semi-crystalline material

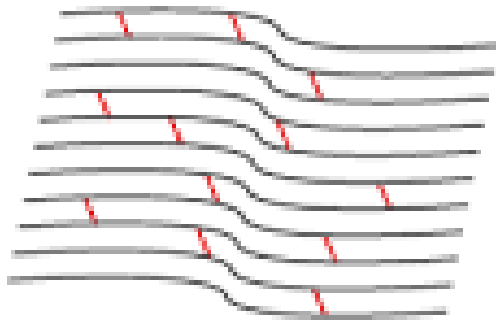
- a small drop in the modulus at the glass transition temperature, due to the amorphous regions of the polymer. Since crystallites are unaffected by the T_g , the magnitude of this drop is greatly affected by the amount of crystallinity in the system.
- After the T_g we see that the modulus holds steady until the melting point, illustrating that crystallinity is a way to increase the window of temperatures in which a polymer can be employed.
- At T_m the crystallites melt and the polymer begins to flow.



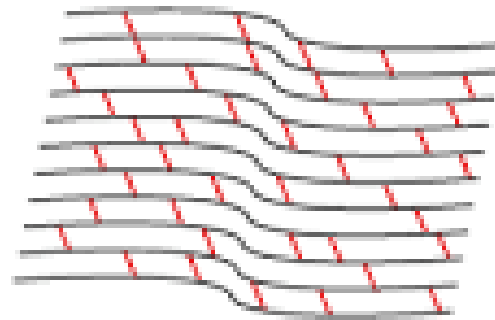
modulus– temperature behavior of a cross-linked polymer.

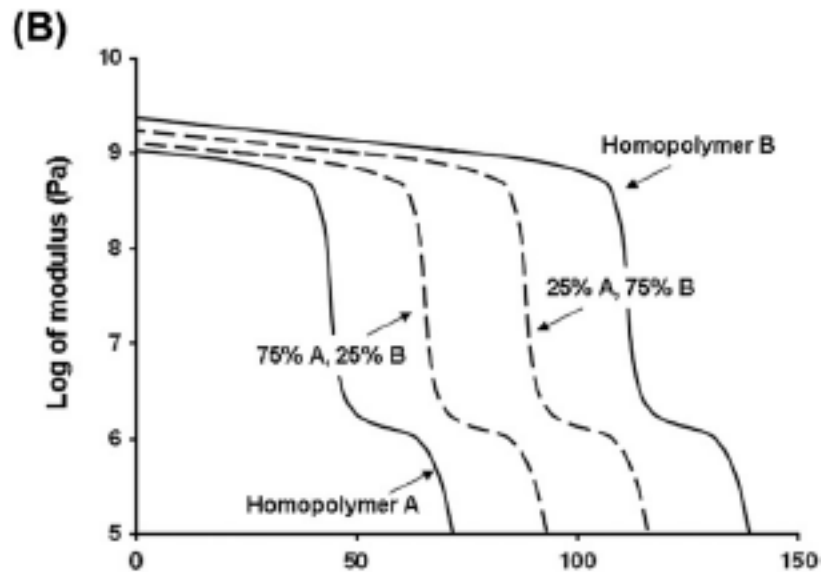
- at the glass transition temperature a decrease in modulus, however, above the T_g the modulus is relatively independent of temperature because the cross-links act to tether the polymer chains in place.
- In fact, the cross-linked polymer will not experience a large decrease in modulus until the temperature is high enough to begin thermally degrading the bonds holding the structure together.

Less Cross-linking (weaker)



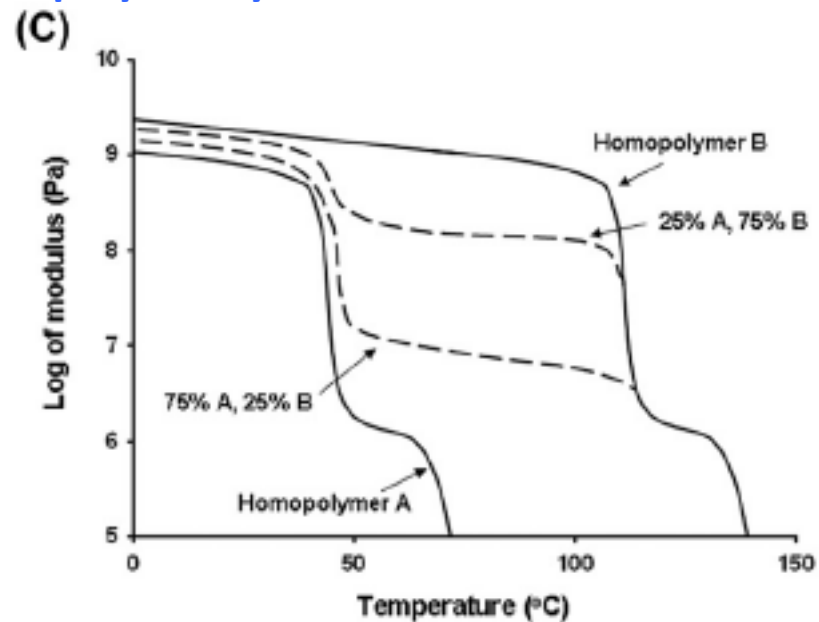
More Cross-linking (stronger)





- the shape of the curve is maintained, but shifted laterally.

modulus–temperature curves for a random copolymer system

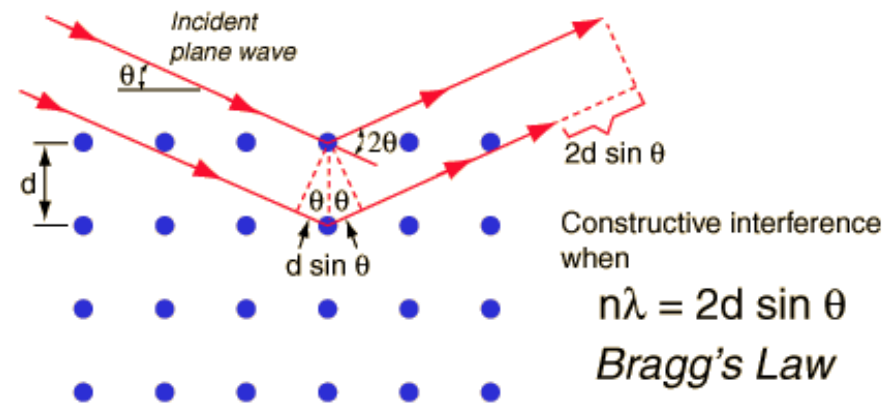
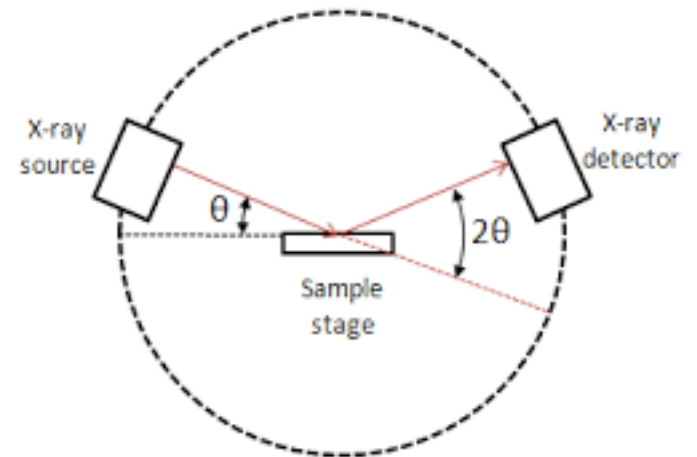
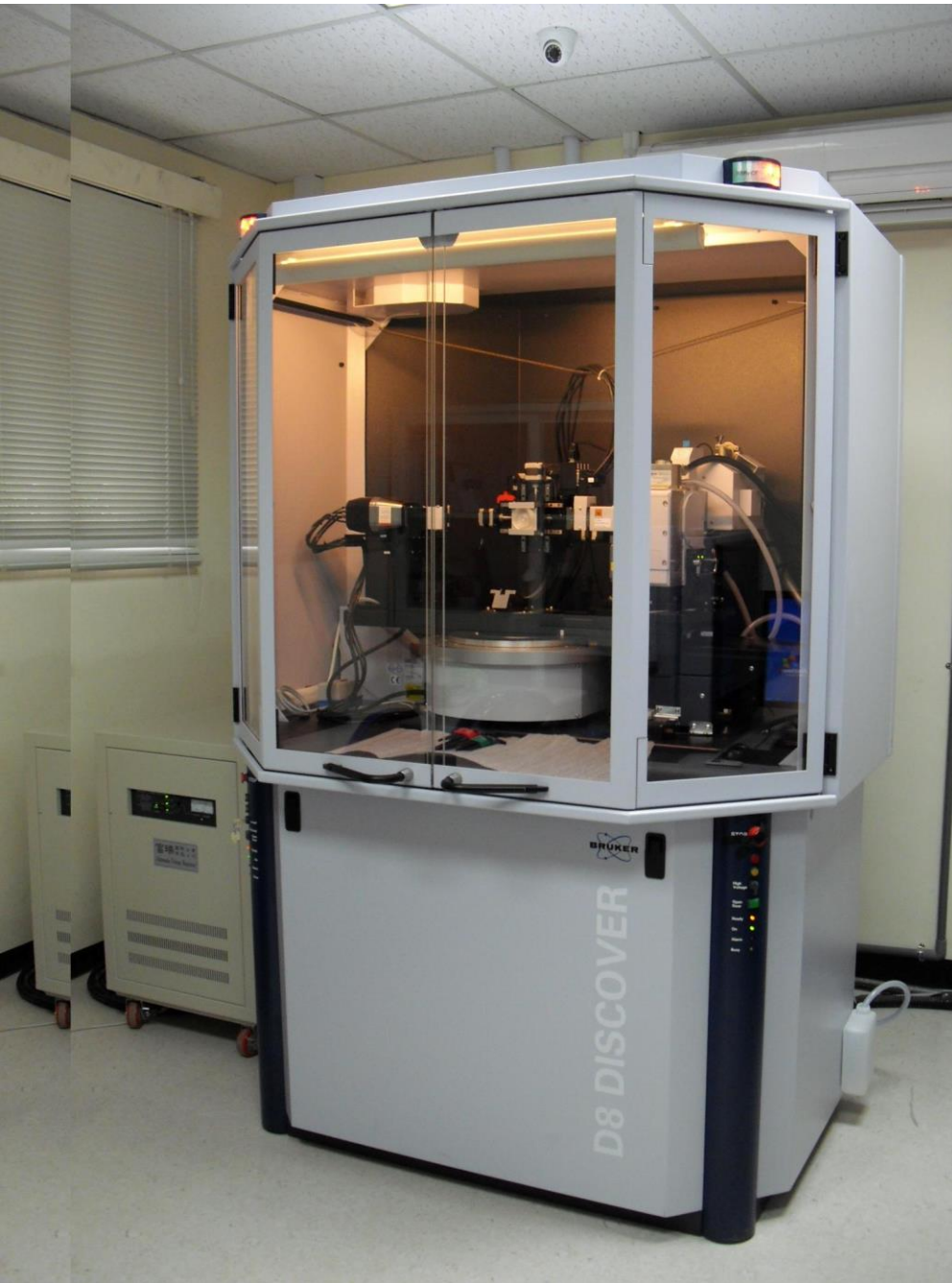


- distinct transition of both materials used to generate the copolymer

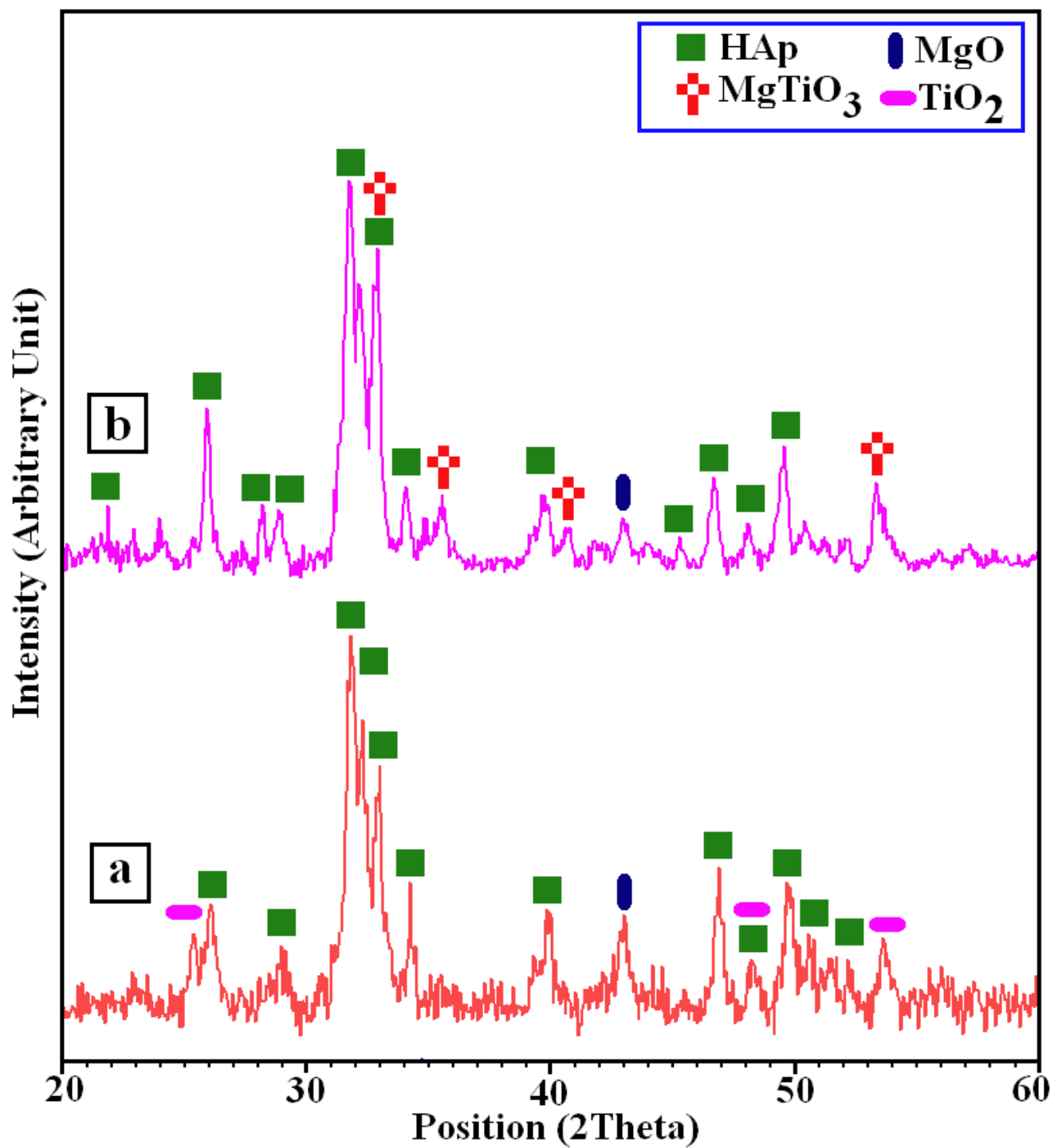
modulus–temperature curves for block copolymers

❑ Characterizing a Polymer's Physical State and Behavior

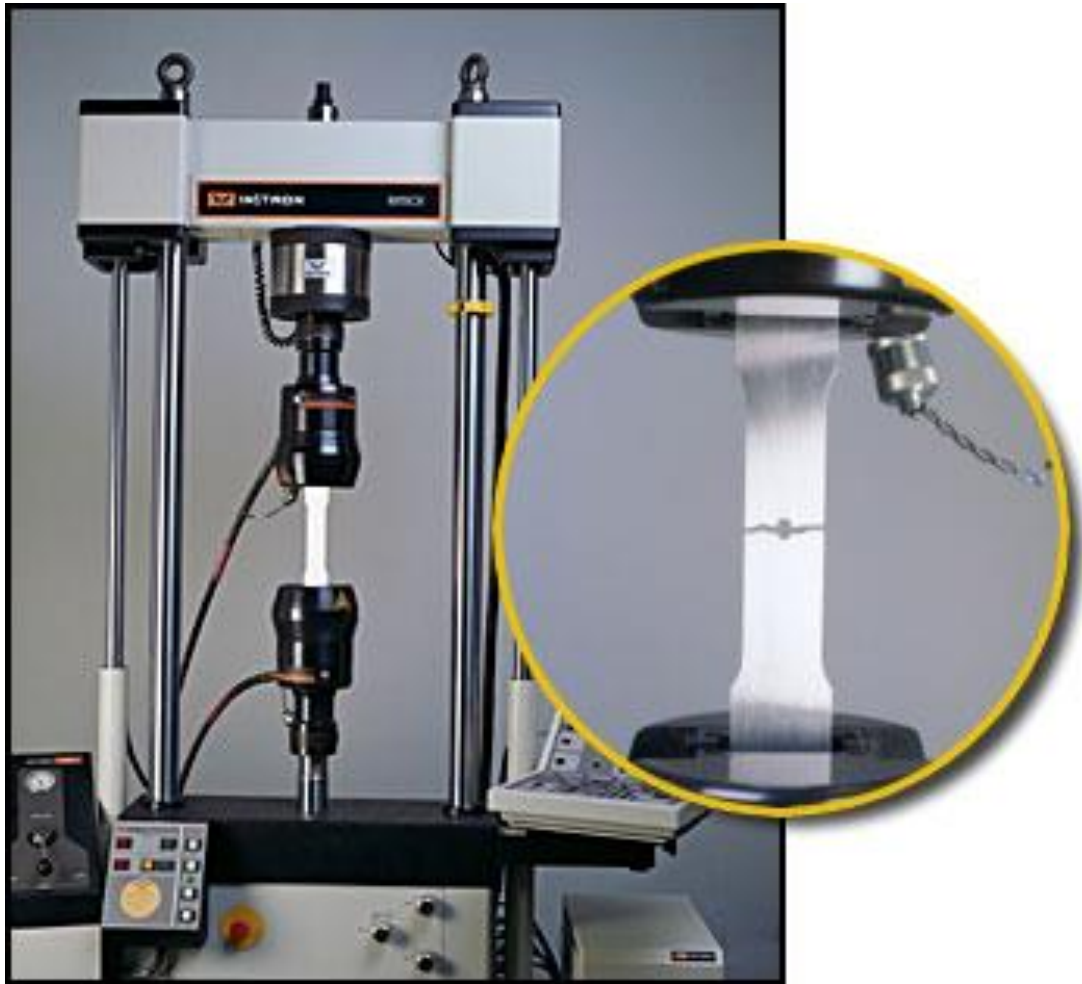
- **Crystallinity** plays a large role in determining polymer behavior.
- The ***degree of crystallinity*** – a measurement of how much of the polymer is incorporated into crystalline regions – can be studied with techniques such as measurement of density, **X-ray diffraction (XRD)**, and **infrared spectroscopy**.
- In **XRD experiments** a polymer sample is bombarded with X-ray radiation and the intensity of the scattered X-rays is measured as a function of scattering angle.
- A fully amorphous material would produce a very broad peak, covering all scattering angles. However, crystalline materials will produce sharp peaks at specific angles.
- The placement of these peaks corresponds to a particular crystalline structure.



Video # 1



- **Stress-strain analysis** provides information about the mechanical behavior of a polymeric biomaterial. In this test a polymer sample of known dimensions is deformed at a given rate, and the force needed to cause the deformation is recorded.



Video # 2

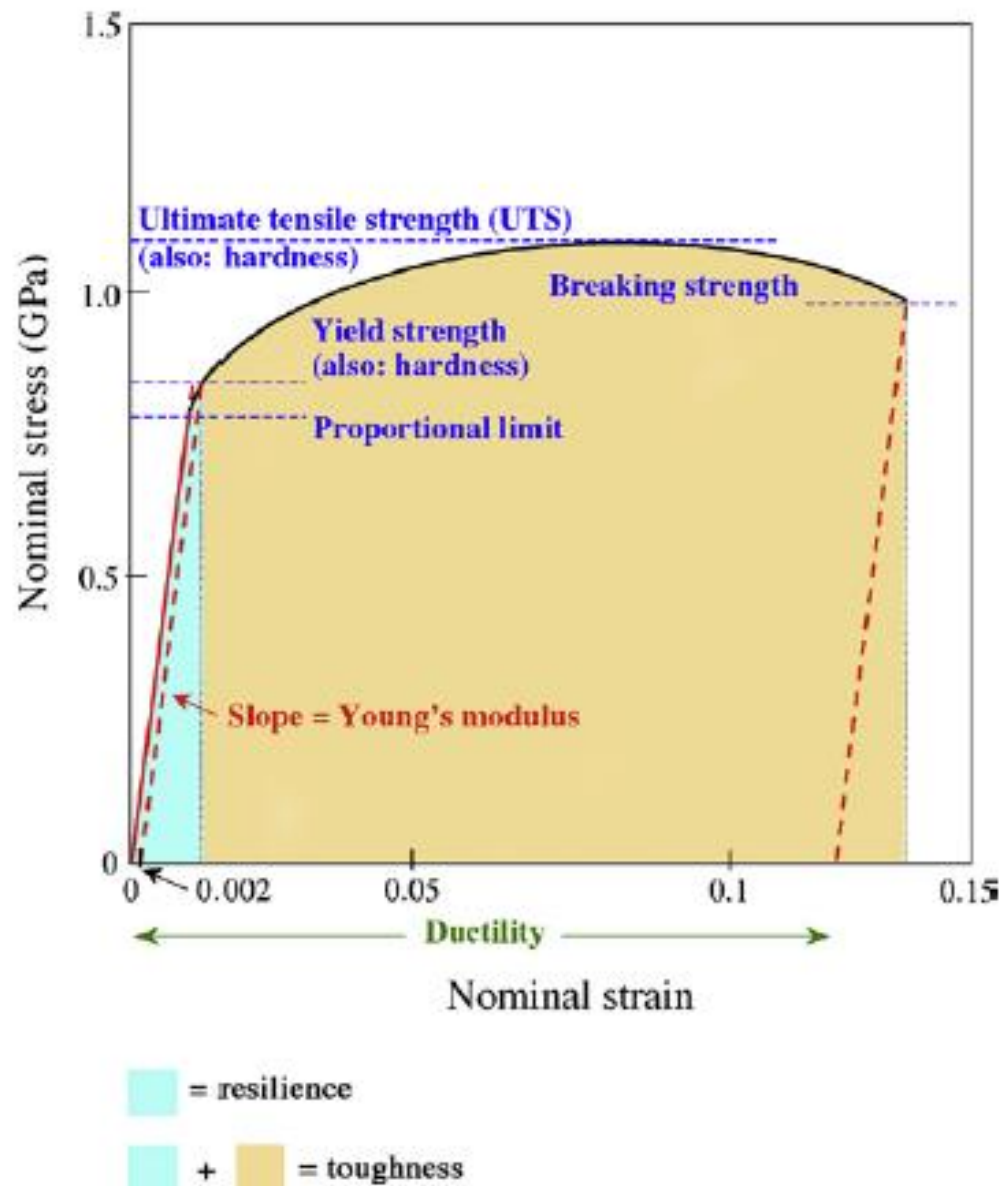


FIGURE I.1.3.3 Schematic nominal stress versus nominal strain plot for a ductile metal, emphasizing the features that relate to specific mechanical properties.

- From this analysis several key material properties can be determined:
 - modulus (a measurement of material stiffness)
 - tensile strength (the stress at failure)
 - percent elongation (the amount of deformation at failure).

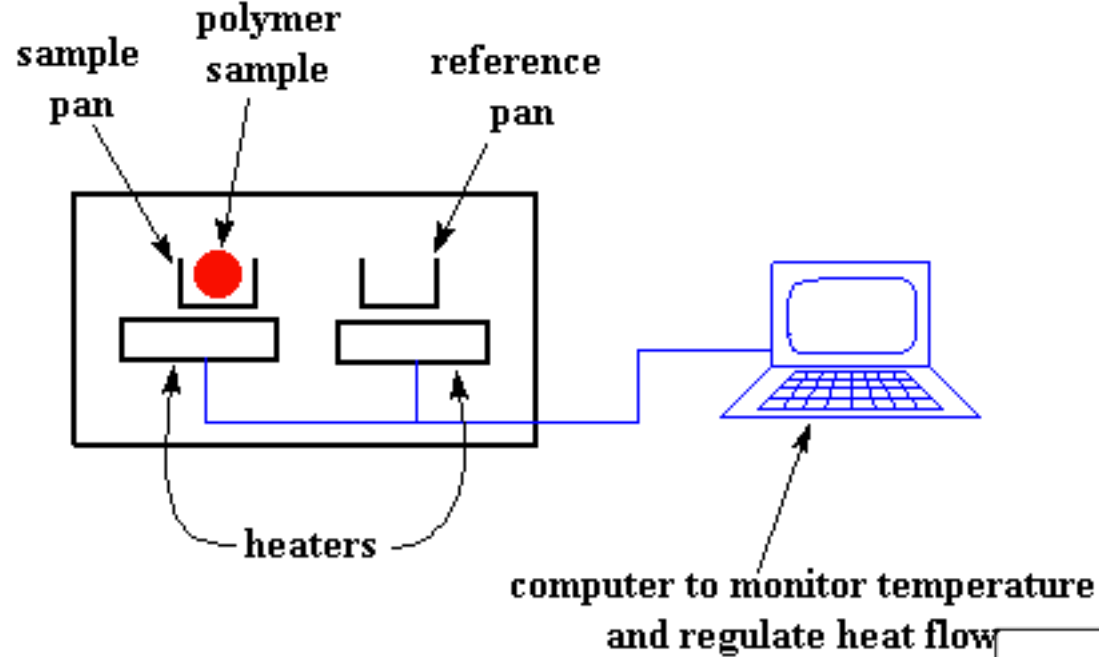
The room temperature mechanical properties of several polymeric biomaterials

TABLE 1.2.2.1 Physical Properties and Equilibrium Water Absorption of Common Polymeric Biomaterials				
Material	Tensile Modulus (GPa)	Tensile Strength (MPa)	Elongation at Break (%)	Water Absorption (%)
Polyethylene (PE)	0.8–2.2	30–40	130–500	0.001–0.02
Poly(methyl methacrylate) (PMMA)	3–4.8	38–80	2.5–6	0.1–0.4
Polytetrafluoroethylene (PTFE)	1–2	15–40	250–550	0.1–0.5
Poly(lactide) (PLA)	3.4	53	4.1	<0.5
Poly(hydroxyethyl methacrylate) [†] (PHEMA)	0.29	0.15	71	40
Polypropylene (PP)	1.6–2.5	21–40	100–300	0.01–0.035
Poly(ethylene terephthalate) (PET)	3–4.9	42–80	50–500	0.06–0.3

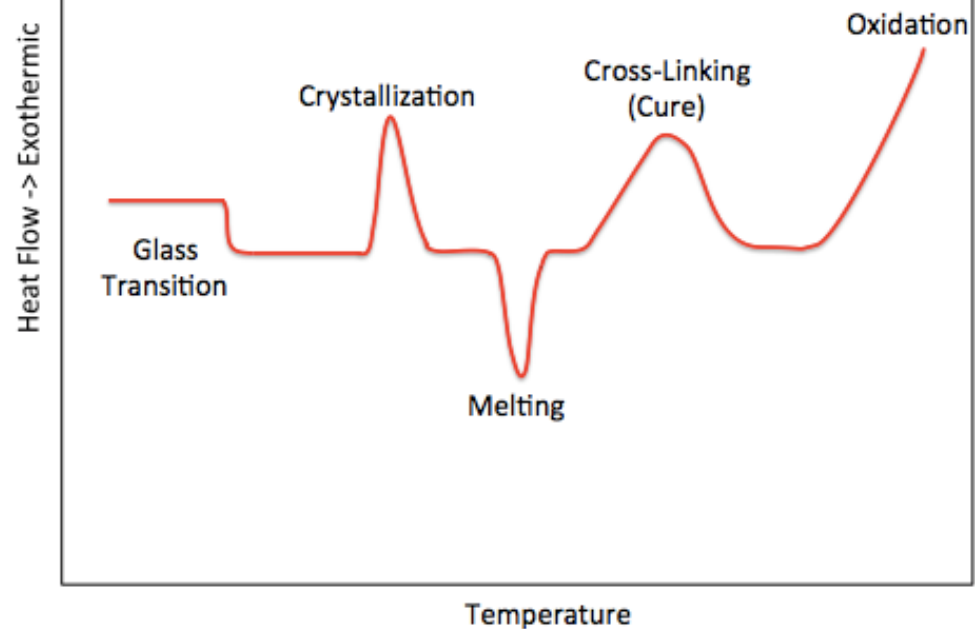
[†]Tensile properties were measured after the polymer was equilibrated with water.

❑ Measuring the Transition Temperatures Between States

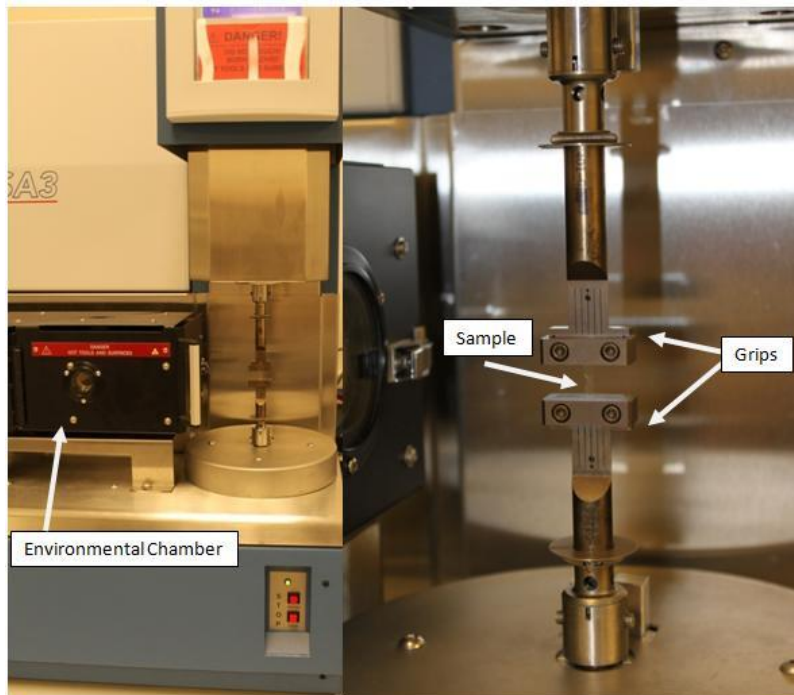
- Measuring transition temperatures (T_g and T_m) is important to understanding how a material will behave in a certain application.
- Two common methods for determining the transition temperatures in polymer systems are **differential scanning calorimetry (DSC)** and **dynamic mechanical analysis (DMA)**
- **In DSC experiments** a polymer sample is heated at a constant temperature rate (generally 10–20°C/min) and the amount of heat supplied to the sample to obtain the temperature increase is recorded.
- The output from this experiment is a plot of supplied heat versus temperature.



Video # 3



- When performing a **dynamic mechanical analysis (DMA) experiment**, one measures the modulus (stiffness) of the material over a temperature range.
- The glass transition temperature of the material is physically observed as the softening point of the material.
- In a DMA study the modulus drops by approximately three orders of magnitude at the T_g .
- At the T_m another drop is observed, associated with the softening due to melting of the polymer crystalline units and the onset of flow behavior.



❑ Interactions with Water

- Biomaterials are often employed in highly hydrated environments, so their interaction with water is an important design characteristic
- Relatively non-polar and electrically neutral polymers such as polyethylene or poly(methylmethacrylate) are very hydrophobic and absorb <1 wt% water. However, as polarity is incorporated into the polymer, it will imbibe more water due to polar (and coulombic) interactions.
- One can tailor the interaction of a polymer with water in several ways, such as by controlling the ratio of hydrophobic and hydrophilic monomers in a copolymer.
- Crystalline regions in polymers usually resist infiltration of water molecules.
- If a polymer is processed in a way to control the degree of crystallization, the swelling character of the polymer can thereby be controlled.
- Cross-linked hydrophilic polymers generate hydrogels that can imbibe upwards of 200 wt% water.

Measuring the Hydrophilicity of Polymer Materials?

- The surface hydrophilicity is probed through either static or dynamic contact angle experiments

❑ Degradation Characteristics

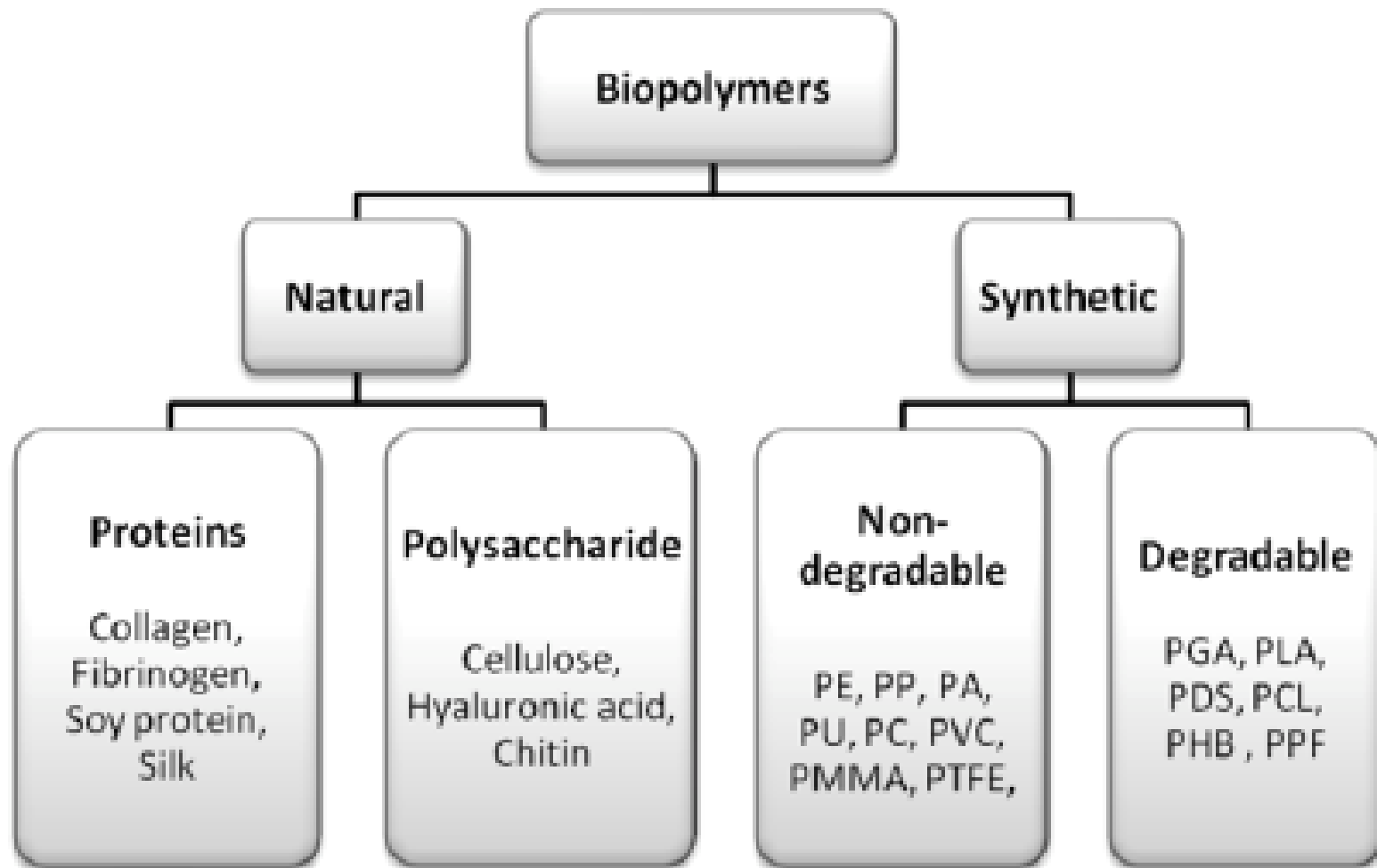
- Depending on the application, one may desire a polymer material that is either **biodegradable** or **biostable**.
 - For instance, a polymer that will be used for a tissue engineered scaffold needs to be biodegradable, and to “disappear” as functioning tissue is regenerated by cells. However, some biomaterials, such as dental implants, vascular grafts, and intraocular lenses need to be biostable so that they retain their function for the lifetime of the patient.
- The main type of polymer degradation reaction occurring in the body is **hydrolysis**
 - the reaction of the polymer backbone bonds with water, which results in the hydrolysis of those bonds and loss of the polymer’s mechanical properties.
- The ultimate stability of polymers in the body depends on **two key factors**: water absorption and the susceptibility of main chain bonds to hydrolysis.
 - The **carbon–carbon single bond** is very stable and those materials with main chain C–C bonds, such as polyethylene, polypropylene or PMMA, do not lose their properties due to degradation of the backbone.
 - the presence of other bonds in the polymer backbone (**heterochain polymers**) can lead to hydrolytic breakdown, and the rate of this hydrolysis is greatly affected by the polymer’s molecular structure.

Chemical Characteristics Of Several Polymeric Biomaterials, and Their Clinical Applications.

TABLE 1.2.2.4 Common Polymeric Biomaterials with Their Applications and the Properties That Make Them Useful in the Medical Field

Material	Characteristics	Uses
Poly(methyl methacrylate) (PMMA)	Hydrophobic polymer which is hard, rigid, and biostable. The amorphous material is clear allowing light transmittance	Bone cement Intraocular lenses Hard contact lenses
Polyacrylamide (PA)	Cross-linking produces a hydrogel with molecular-sized pores and allows the gel to be used as a separation medium	Separation gel used in electrophoresis
Poly(acrylic acid) (PAA)	The liquid monomer can be cured with a photo-initiator. If inorganic salts are added, ionic cross-linking can occur. The material is glassy and rigid, and has the potential to bond to enamel	Glass ionomer cement used in dental restoration
Polyethylene (high density) (PE)	Low density PE cannot withstand sterilization temperatures; however, high density PE has good toughness and wear resistance	Tubing for drains and catheters Prosthetic joints
Poly(vinyl chloride) (PVC)	PVC is plasticized to make flexible materials. This material is used for short-term applications since plasticizers can be leached resulting in embrittlement of the material	Tubing Blood storage bags
Polypropylene (PP)	Isotactic PP is semi-crystalline, has high rigidity and tensile strength, and good biostability	Non-degradable sutures Hernia repair
Polydimethylsiloxane (PDMS)	Due to its silicone backbone, this material has a very low T_g making it extremely flexible and providing it with good fatigue resistance at physiological conditions	Finger joints Heart valves Breast implants Ear, chin, and nose reconstruction
Poly(ethylene terephthalate) (PET)	The aromatic rings in the backbone generate a polymer with a high melting point ($T_m = 267^\circ\text{C}$). It is semi-crystalline and possesses excellent tensile strength	Vascular grafts Fixation of implants Hernia repair Ligament reconstruction
Cellulose acetate (CA)	Unique transport properties make it excellent for use in the separation of complex biological mixtures	Dialysis membranes Osmotic drug delivery devices

Classification of biopolymers



NATURAL POLYMERS VERSUS SYNTHETIC POLYMERS

Natural polymers are polymer compounds that can be found naturally in our environment

Occur naturally

Produced from biological processes

Most polymers are easily degraded by biological processes

Synthetic polymers are polymer compounds that are produced artificially by humans

Do not occur naturally

Produced from chemical processes

Most polymers are hard to degrade naturally by biological processes