

Introduction to Biomaterials & Biocompatibility Lecture 5

Synthetic Polymer Biomaterials

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Consider...

For polymers, the term “molecular weight” is ambiguous because every molecule does not have the same number of monomer units. This non-uniform molecular size situation arises from the chemical processes in the synthesis of the polymer.

Quantifying Polymer Molecular Weight

The possible values of M make up a set of numbers with discrete values labeled M_i . Let N_i be the number of polymers with molecular weight M_i . Then the total weight of all polymers is

$$\text{Total Weight} = \sum_{i=1}^{\infty} N_i M_i$$

and the total number of polymer molecules is

$$\text{Total Number} = \sum_{i=1}^{\infty} N_i$$

As discussed above, the number average molecular weight is

$$\overline{M}_N = \frac{\sum_{i=1}^{\infty} N_i M_i}{\sum_{i=1}^{\infty} N_i} = \frac{\text{Total Weight}}{\text{Number of Polymers}} = \frac{\text{Weight}}{\text{Polymer}}$$

The term $N_i / \sum N_i$ is physically the number fraction of polymers with molecular weight M_i . If we denote number fraction as X_i (*i.e.*, mole fraction) the number average molecular weight is

$$\overline{M}_N = \sum_{i=1}^{\infty} X_i M_i$$

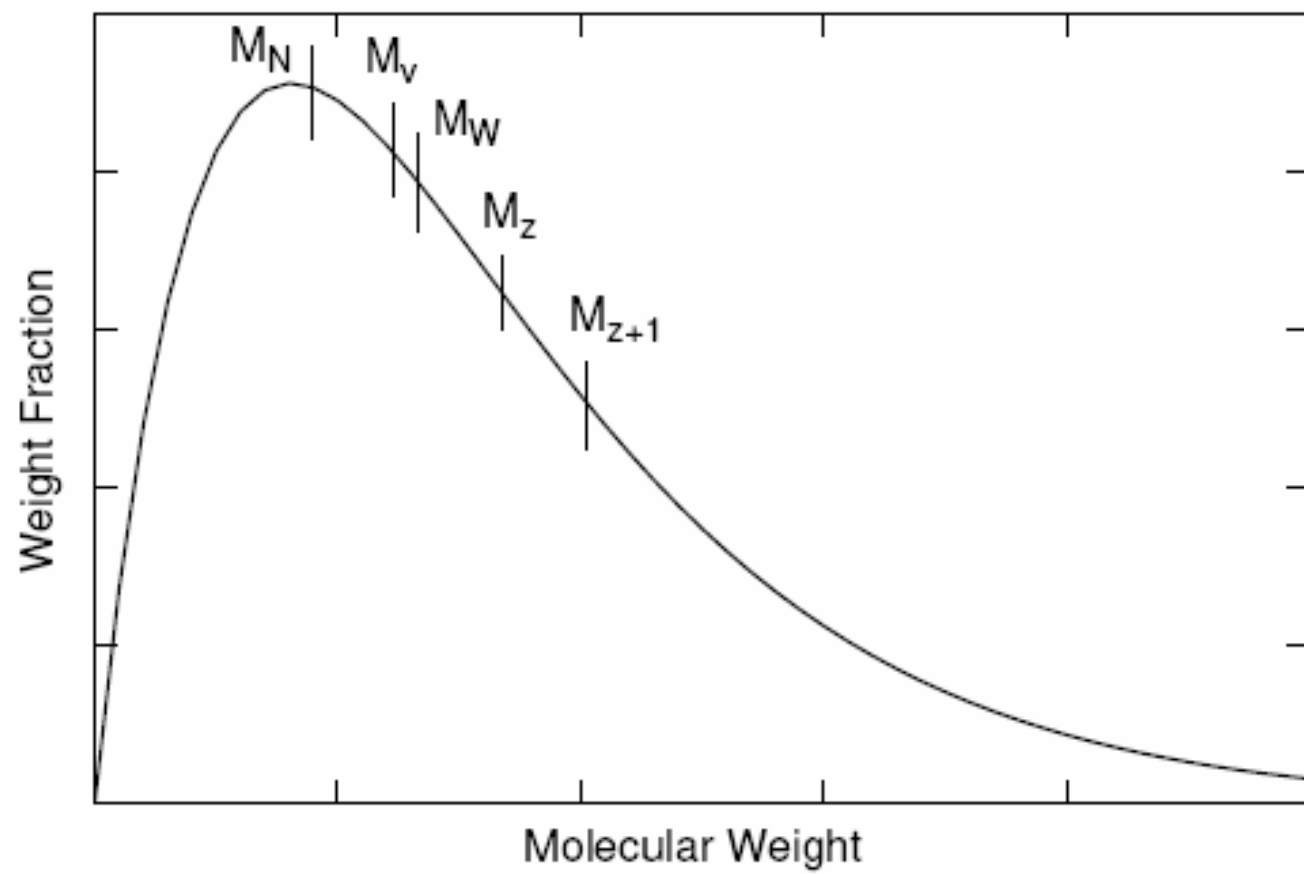
Consider of polymer property which depends not just on the number of polymer molecules but on the size or weight of each polymer molecule. A classic example is light scattering. For such a property we need a weight average molecular weight. To derive the weight average molecular weight, replace the appearance of the number of polymers of molecular weight i or N_i in the number average molecular weight formula with the weight of polymer having molecular weight i or $N_i M_i$. The result is

$$\overline{M_W} = \frac{\sum_{i=1}^{\infty} N_i M_i^2}{\sum_{i=1}^{\infty} N_i M_i}$$

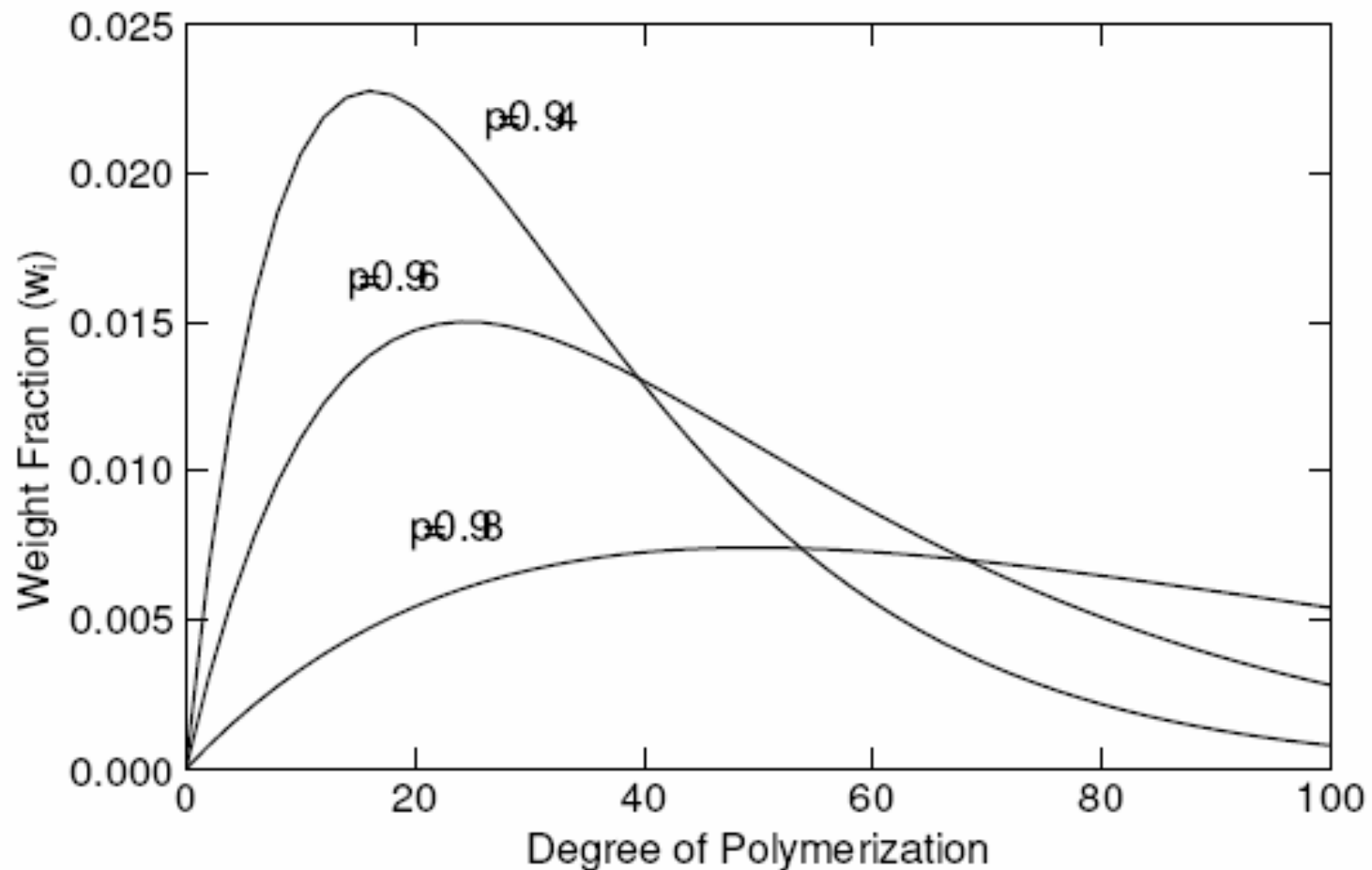
By noting that $N_i M_i / \sum N_i M_i$ is the weight fraction of polymer with molecular weight i , w_i , an alternative form for weight average molecular weight in terms of weight fractions

$$\overline{M_W} = \sum_{i=1}^{\infty} w_i M_i$$

Comparing this expression to the expression for number average molecular weight in terms of number fraction (see Eq. (3.7)) we see that $\overline{M_N}$ is the average M_i weighted according to number fractions and that $\overline{M_W}$ is the average M_i weighted according to weight fractions. The meanings of their names are thus apparent.

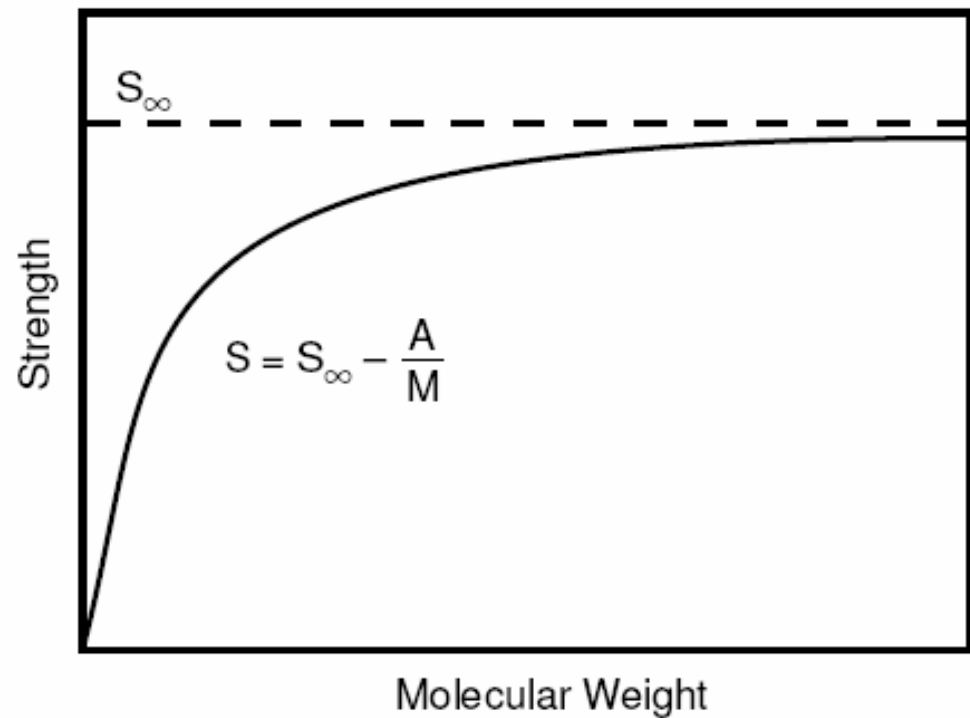


The molecular weight distribution changes during the course of the polymerization reaction.



Effect of Polymer Molecular Weight

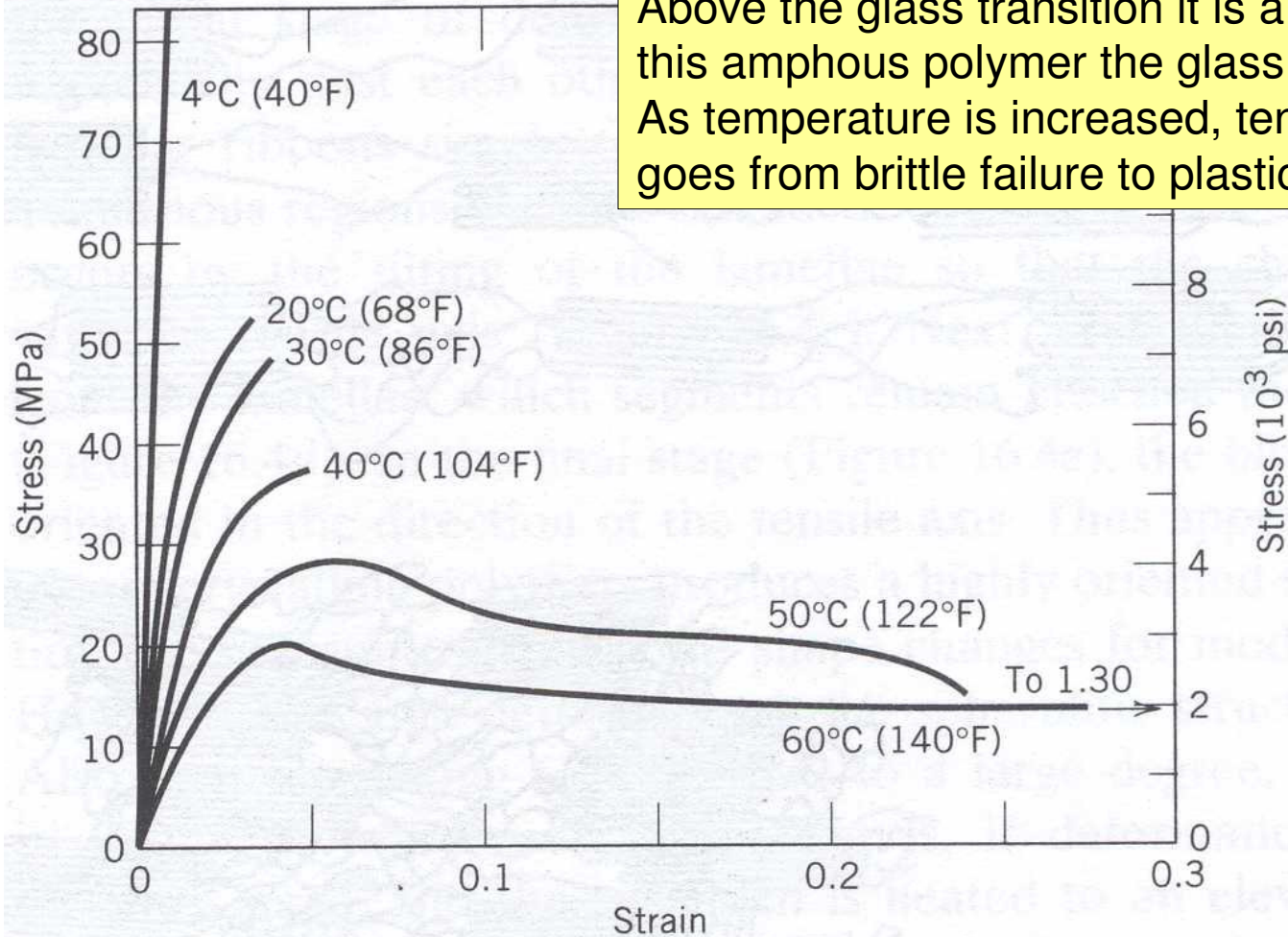
Unlike small molecules, the molecular weight of a polymer is not one unique value. Rather, a given polymer will have a distribution of molecular weights. The distribution will depend on the way the polymer is produced. For polymers we should not speak of a molecular weight, but rather of the distribution of molecular weights, or of the average molecular weight. Polymer physical properties will be functions of the molecular weight distribution function.



Consider...

The ability of polymer chains to rearrange by segmental relaxation processes allows polymer properties to change over time or with sufficient temperature. Polymers have a wide range of possibilities for aggregation states in the solid. In addition, a single chain can have a trajectory that passes through multiple states of aggregation. These factors can make polymer solid state behavior very complex.

Temperature can have a profound effect on polymer properties. Below the glass transition an amorphous PMMA polymer is a rigid glass. Above the glass transition it is a plastic solid. For this amorphous polymer the glass transition is 4°C. As temperature is increased, tensile behavior goes from brittle failure to plastic deformation.

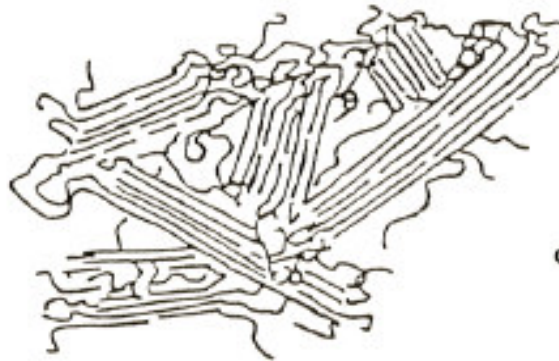


The primary chain structure of polymers allow different types of internal morphology to develop. These different morphologies strongly influence physical behavior. Control of these morphologies allow control of physical behavior.

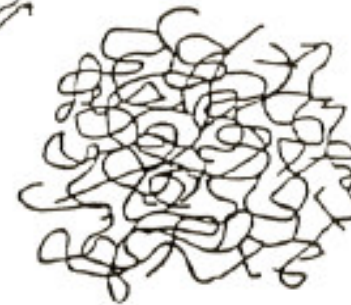
Crystalline



Semicrystalline

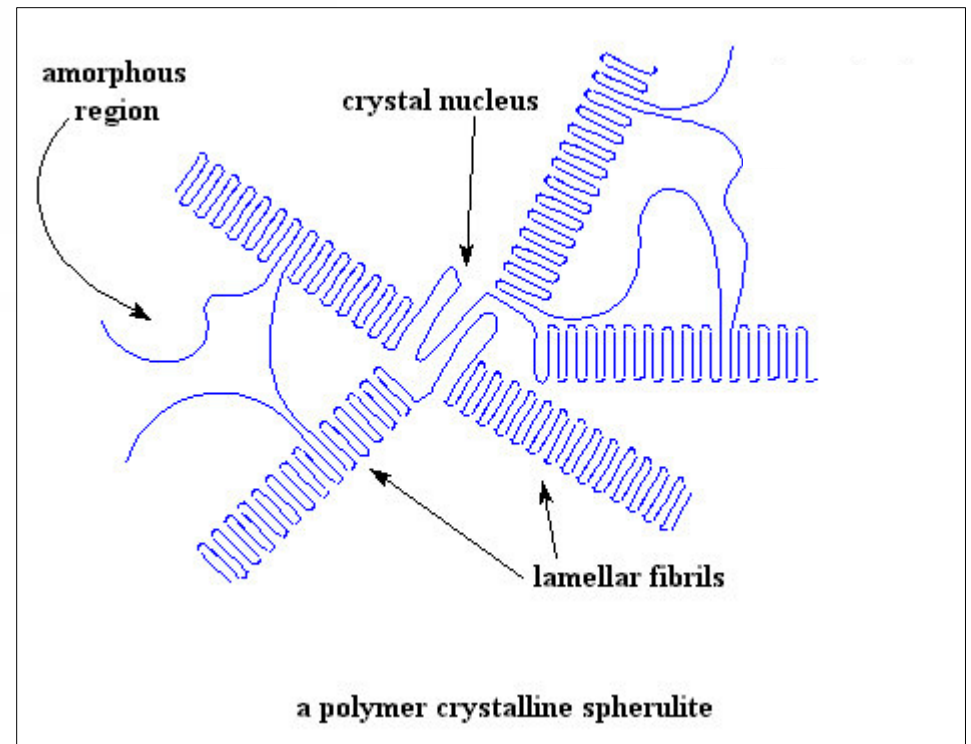
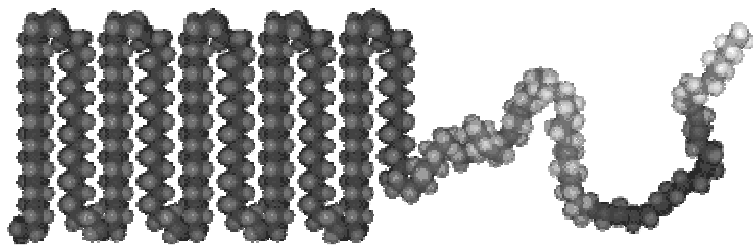
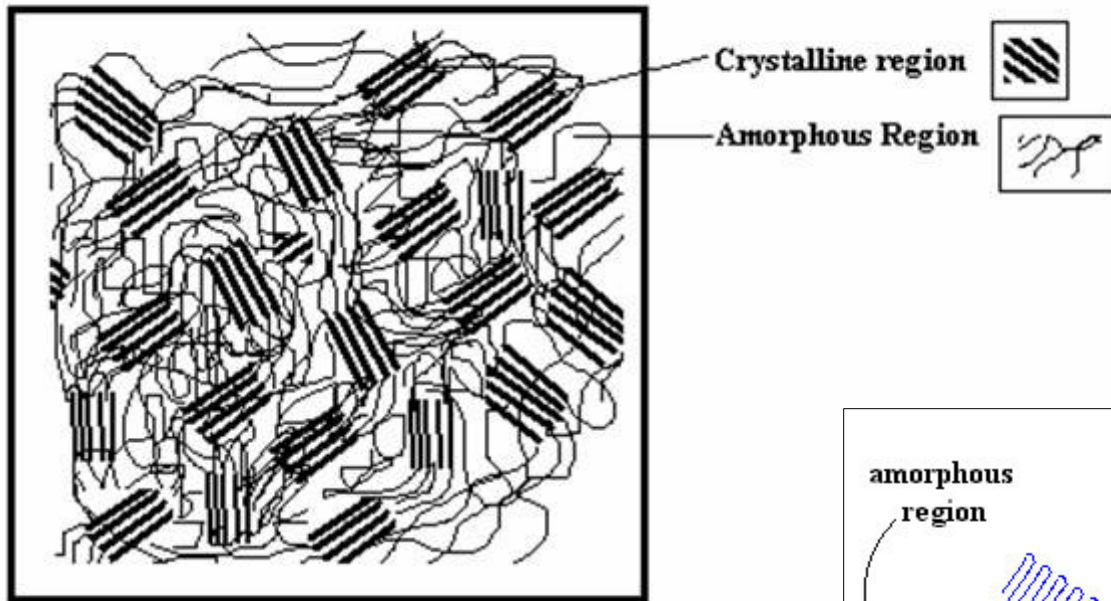


Amorphous

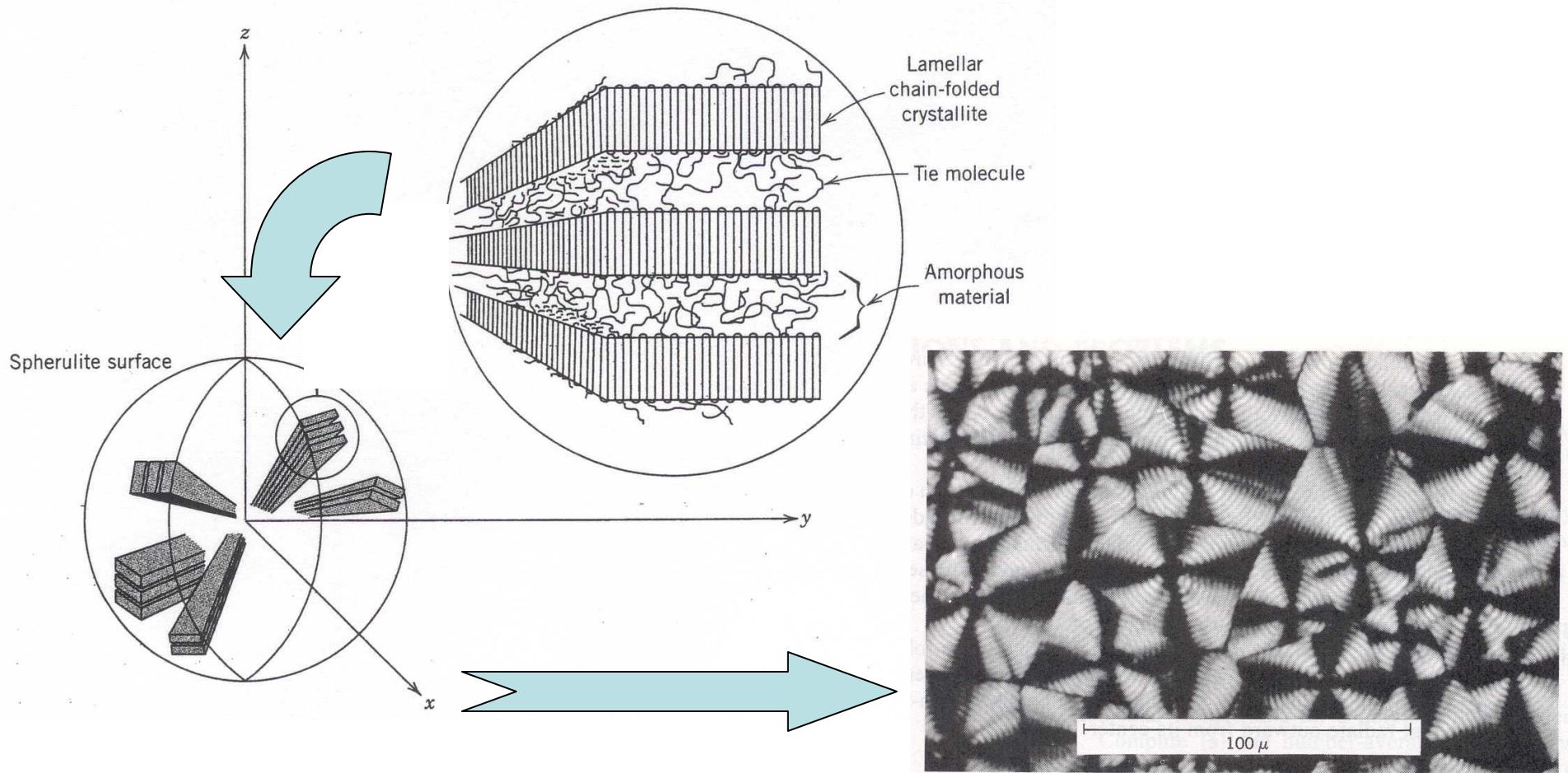


Melting @ T_m
Heat of Fusion
Stronger Forces
Correlated Structure

Glass Transition
No Heat of Fusion
Free Volume
Amorphous Form



Semicrystalline Polymers



Microscopic Mechanism of Deformation

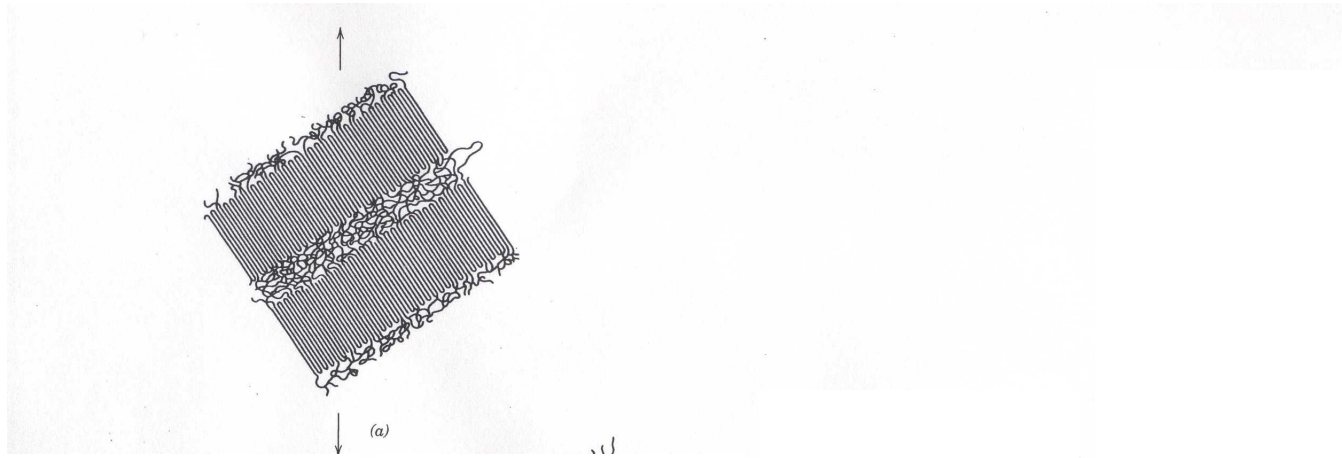


FIGURE 16.4 Stages in the deformation of a semicrystalline polymer. (a) Two adjacent chain-folded lamellae and interlamellar amorphous material before deformation. (b) Elongation of amorphous tie chains during the first stage of deformation. (c) Tilting of lamellar chain folds during the second stage. (d) Separation of crystalline block segments during the third stage. (e) Orientation of block segments and tie chains with the tensile axis in the final deformation stage. (From Jerold M. Schultz, *Polymer Materials Science*, copyright © 1974, pp. 500–501. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, NJ.)

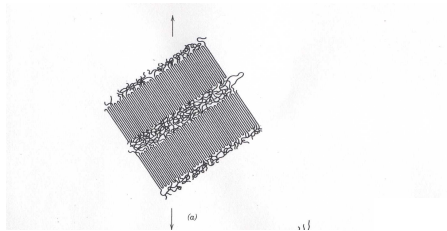


FIGURE 16.4 Stages in the deformation of a semicrystalline polymer. (a) Two adjacent chain-folded lamellae and interlamellar amorphous material before deformation. (b) Elongation of amorphous tie chains during the first stage of deformation. (c) Tilting of lamellar chain folds during the second stage. (d) Separation of crystalline block segments during the third stage. (e) Orientation of block segments and tie chains with the tensile axis in the final deformation stage. (From Jerold M. Schultz, *Polymer Materials Science*, copyright © 1974, pp. 500–501. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, NJ.)

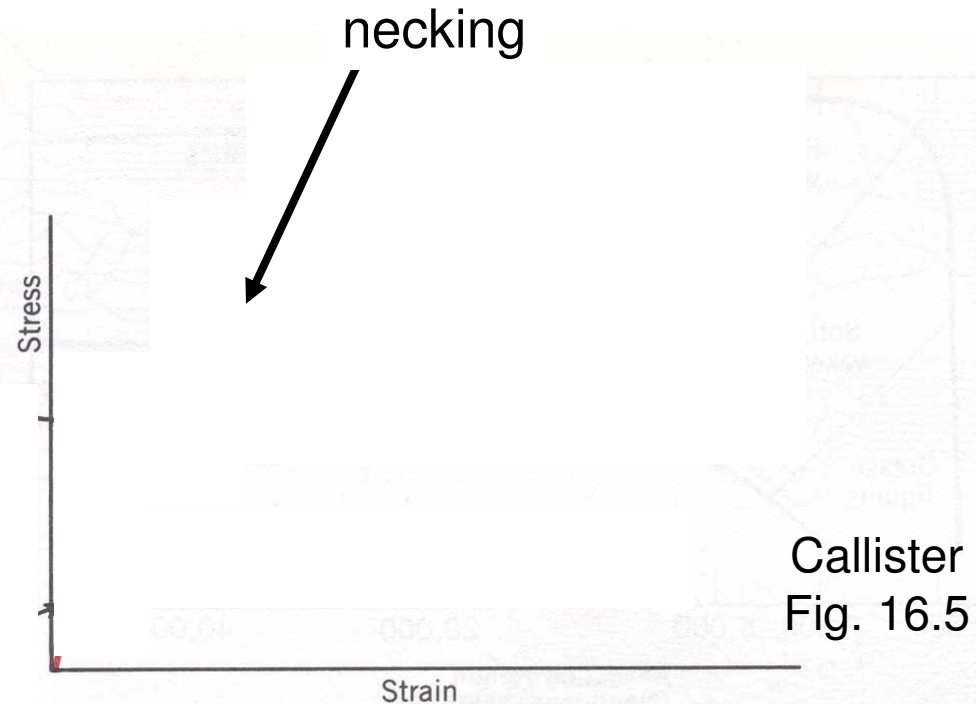
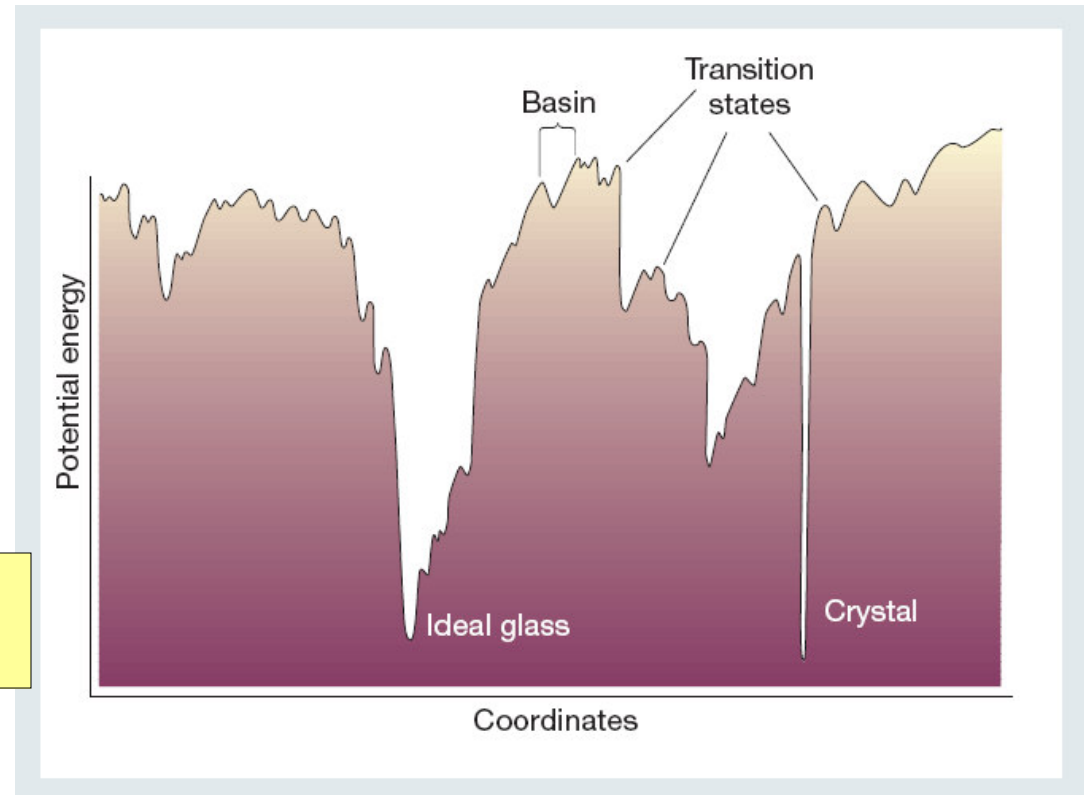
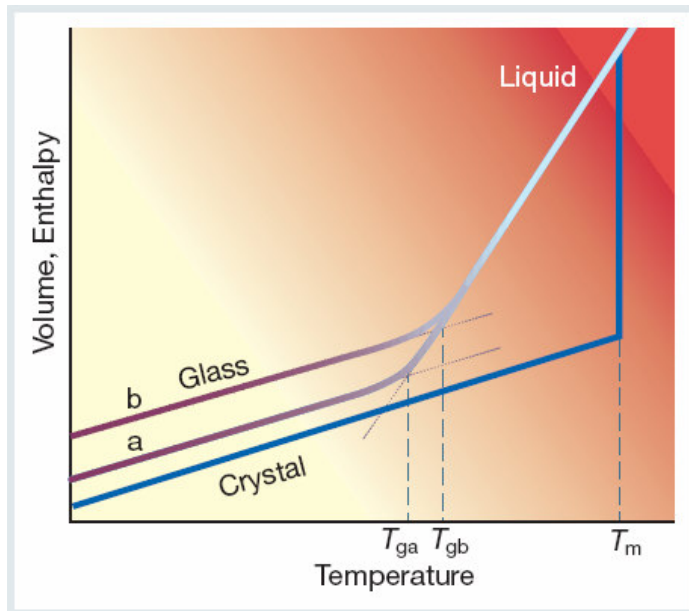
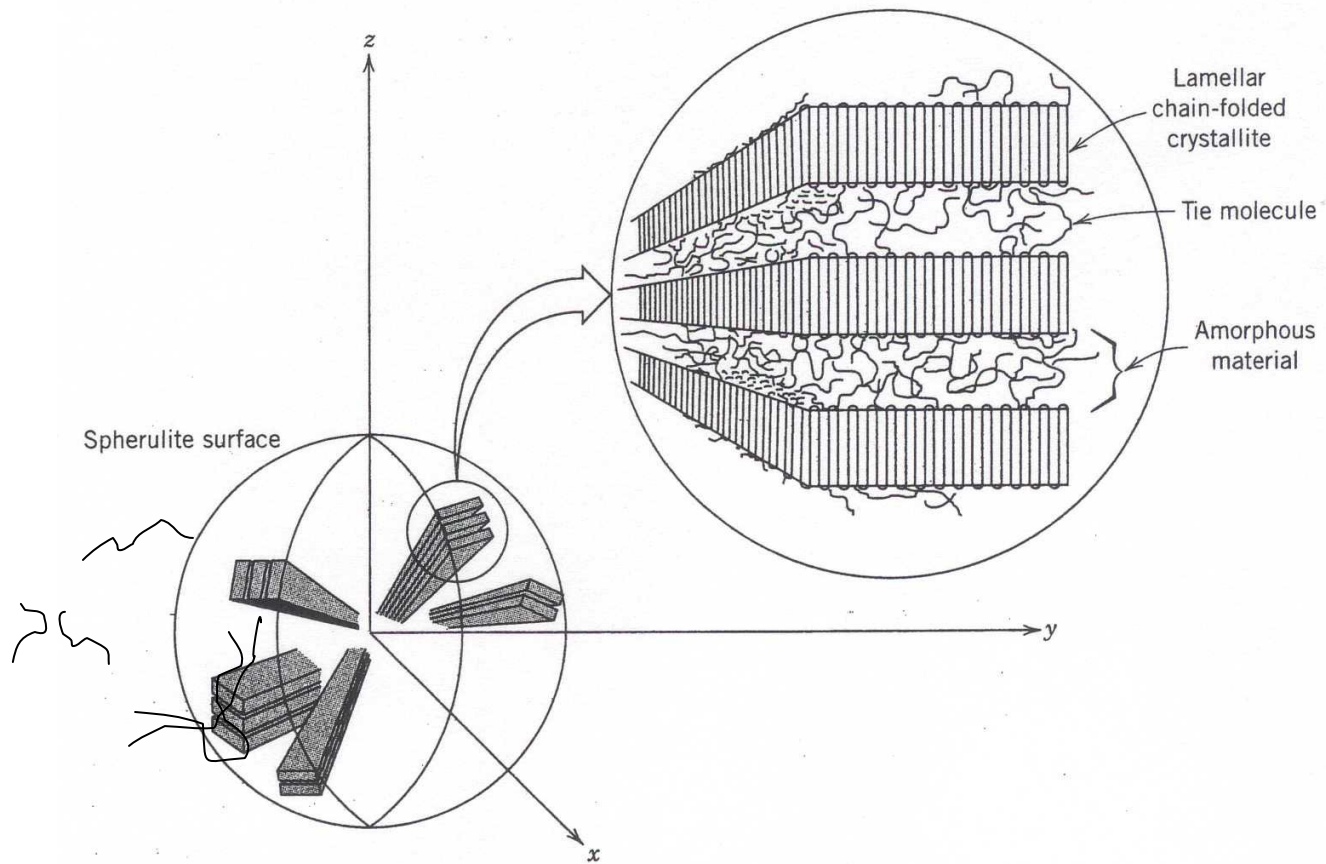


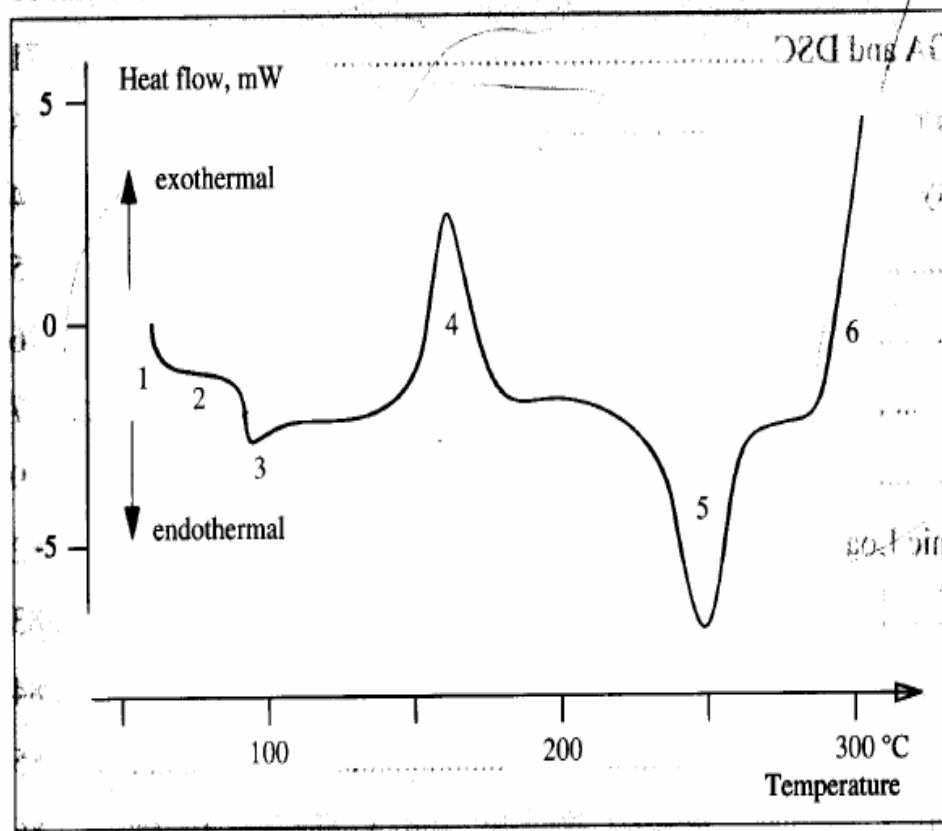
Figure 16.5 Schematic tensile stress–strain curve for a semicrystalline polymer. Specimen contours at several stages of deformation are included. (From Jerold M. Schultz, *Polymer Materials Science*, copyright © 1974, p. 488. Reprinted by permission of Prentice-Hall, Inc., Englewood Cliffs, NJ.)

Amorphous polymers are typically not in their lowest thermodynamic state when they are vitrified. Because non-crystalline polymer chains can undergo temperature and time dependent relaxations, they will continue to relax towards a lower thermodynamic state which is more dense. If this is done deliberately, it is called annealing. If it occurs spontaneously, it is called ageing.



Supercooled liquids and the glass transition,
Pablo G. Debenedetti & Frank H. Stillinger
NATURE, VOL 410, MARCH 8, 2001, p. 259





<http://centrum.vslib.cz/centrum/itsapt/Summer2005/files/manich.pdf>

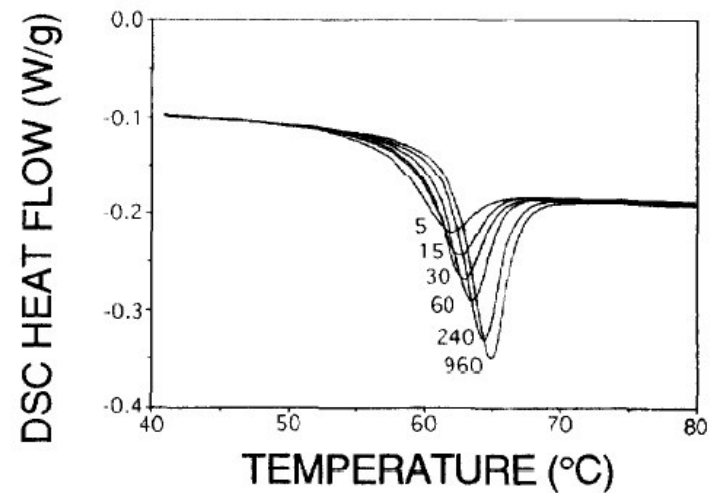


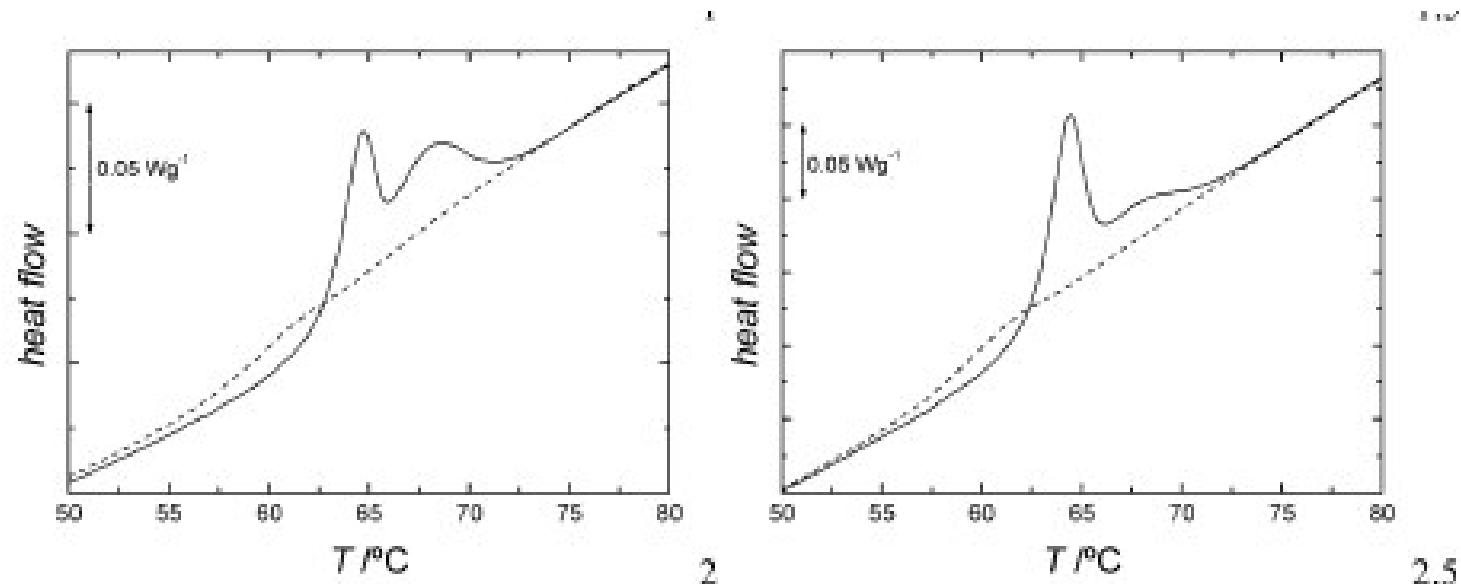
Fig. 3 - Effect of the aging time on the size and location of enthalpy relaxation peaks. Numbers are aging times (min).

<http://ieeexplore.ieee.org/iel2/3195/9096/00404381.pdf?arnumber=404381>

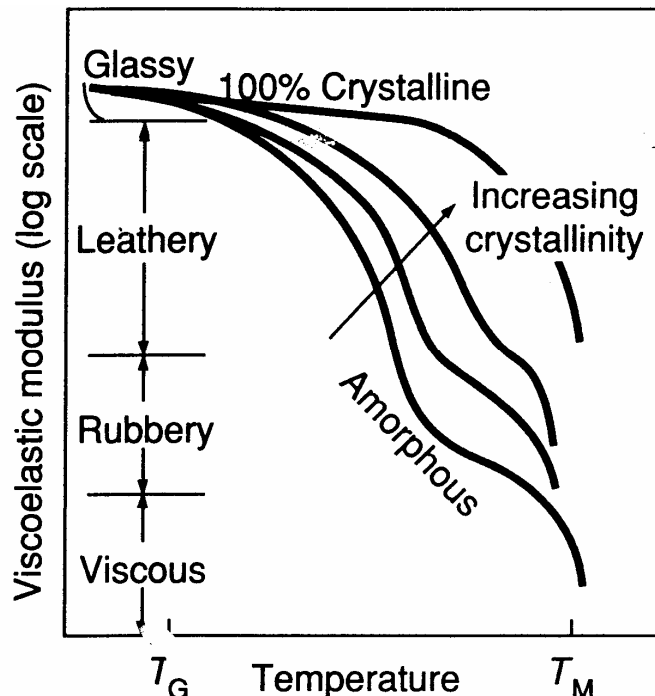
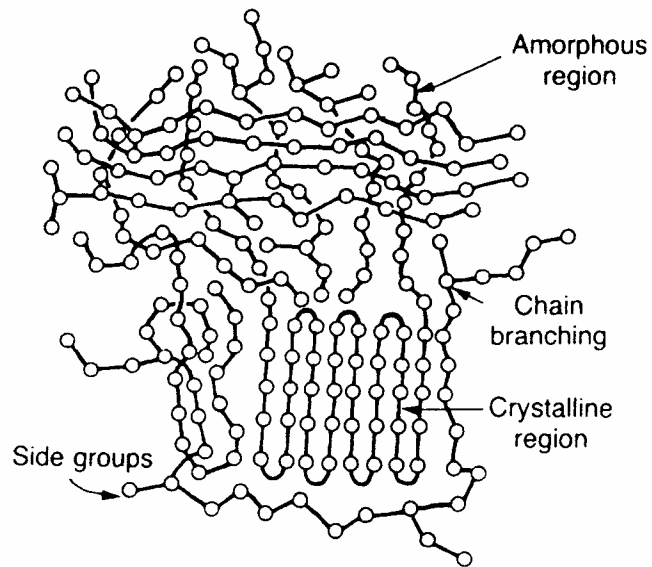
Morphological Contributions to Glass Transition in Poly(L-lactic acid)

Y. Wang,^{1,†} J. L. Gómez Ribelles,[‡] M. Salmerón Sánchez,[‡] and J. F. Mano^{*,†,‡}

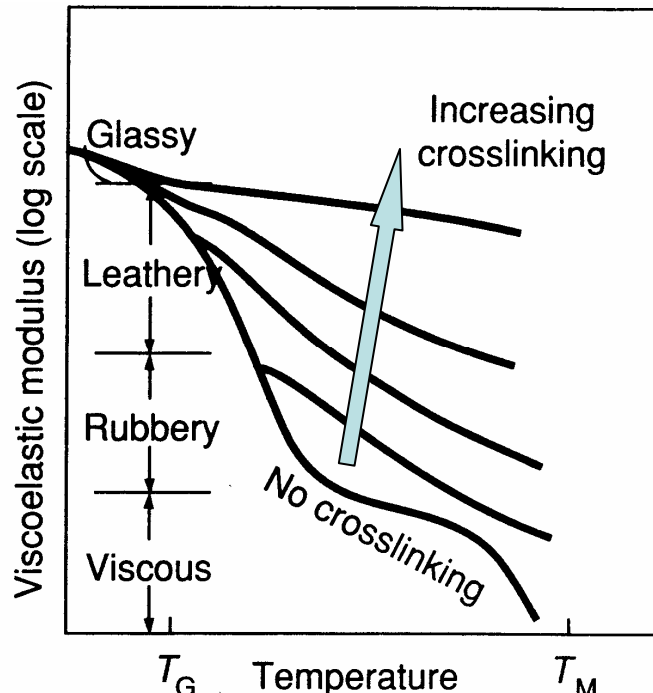
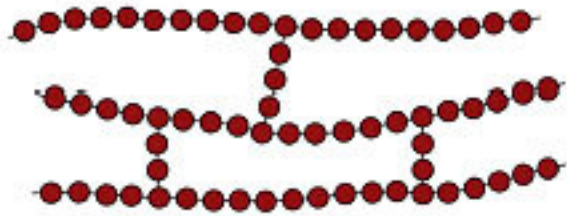
Polymer Engineering Department, University of Minho, Campus de Azurém, 4800-058 Guimarães, Portugal; 3B's Research Group—Biomaterials, Biodegradables and Biomimetics, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal; and Center for Biomaterials, Universidad Politécnica de Valencia, P.O. Box 22012, E-46071 Valencia, Spain



Enthalpy recovery of two distinct amorphous regions can be observed. One represents the noncrystalline interlamellar region, while the other represents the bulk amorphous region.



In some cases it is possible for portions of the polymer chain to crystallize forming a two phase, semi-crystalline material. The crystalline phase is rigid with a high modulus, while the amorphous phase has a much lower modulus. Increasing the crystallinity will increase the modulus of the material.



The ability of a polymer chain to move can be constrained by crosslinking. There are several modes of crosslinking (entanglements, chemical bonding, physical interaction). As crosslinking increases, chain mobility decreases and the stiffness of the material increases. Thermosets are highly crosslinked three dimensional polymer chain networks (Bakelite, Plexiglas, Epoxy Resins)

Polymers as Materials

The term “plastics” is often used to refer to polymer materials. The term is used because it refers to wide category of synthetic materials that can be relatively easily molded or formed into various shapes.

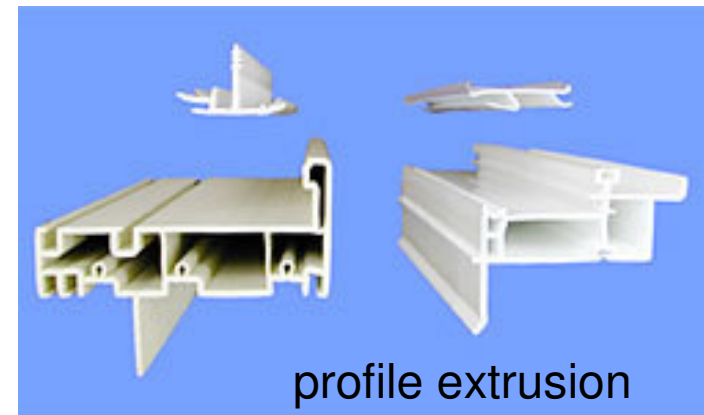
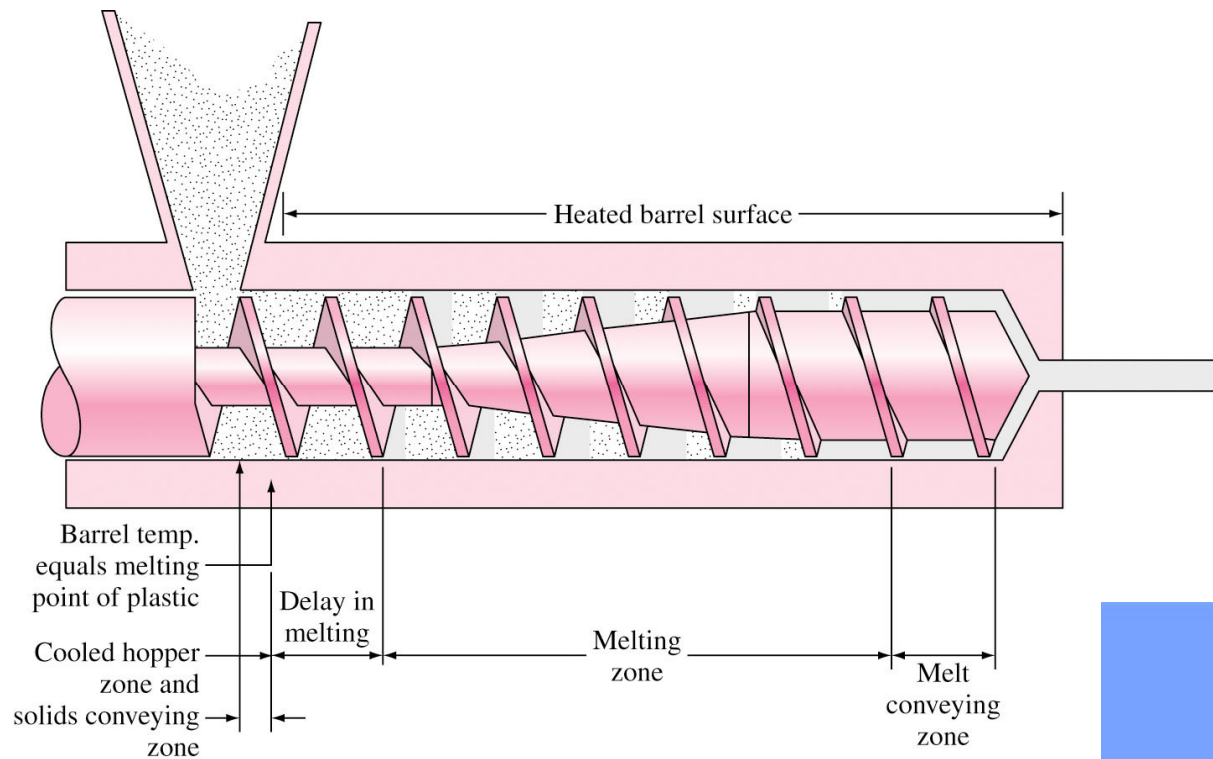
Thermoplastics: polymer materials that will flow into a mold or form on a mold under the influence of heat and will hold the shape of the mold on cooling. The shape of the mold is loss on reheating.

Thermosets: polymer materials that will form on a mold under the influence of heat and will crosslink to permanently fix the molded shape.

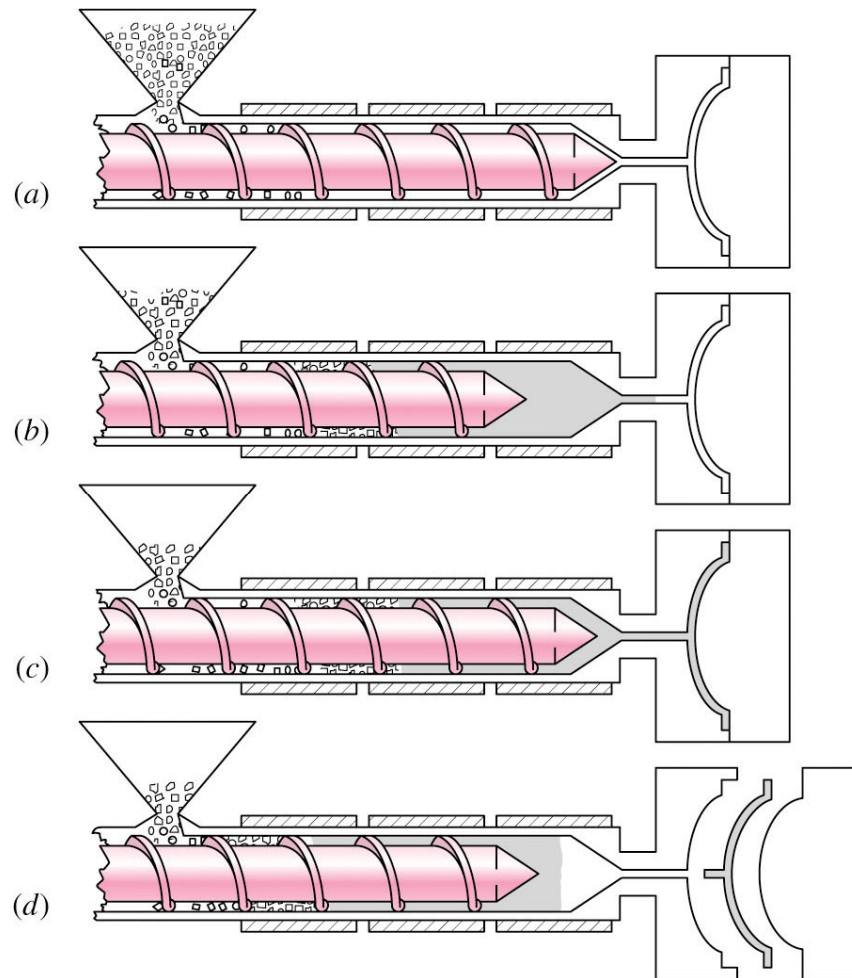
Generally, polymer products are formed *near-net-shape* and do not require further finishing. This one-step processing gives polymer processing a cost advantage over metal processing.

Processing Thermoplastics

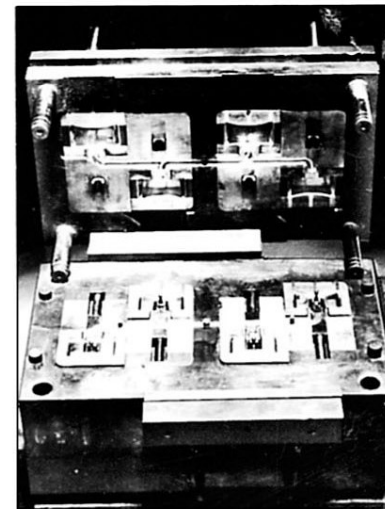
Extrusion



Processing Thermoplastics



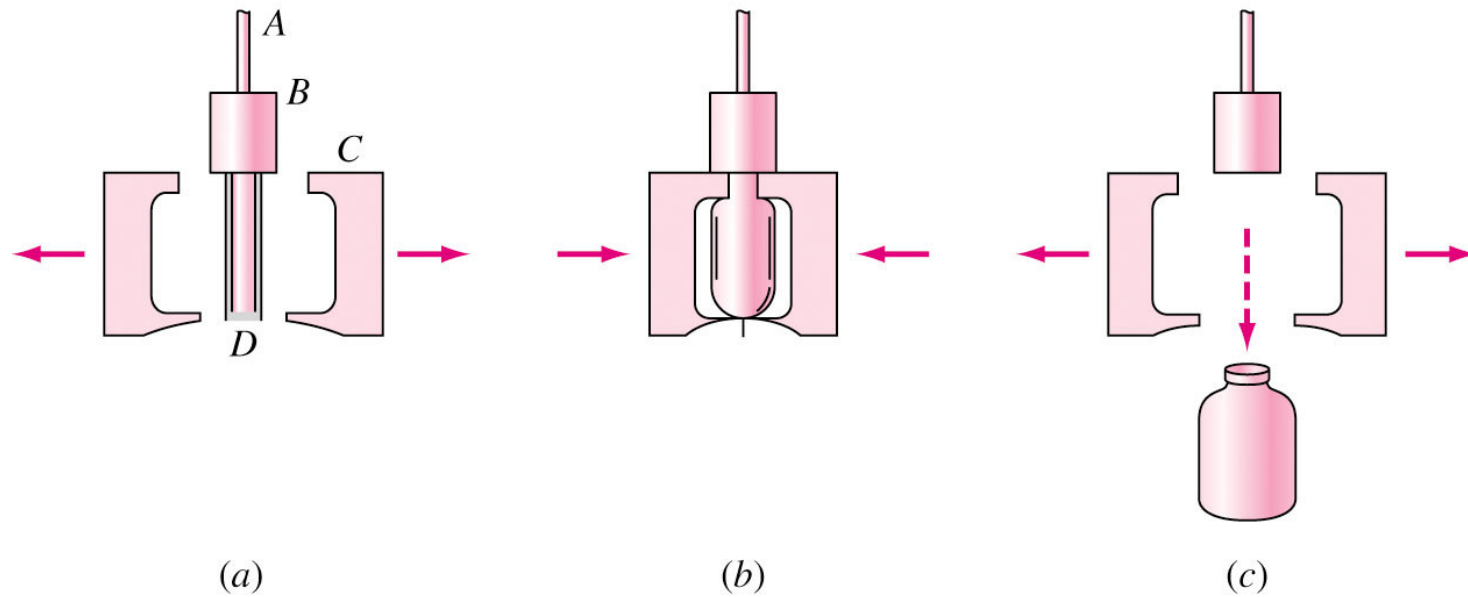
Injection Molding



(e)

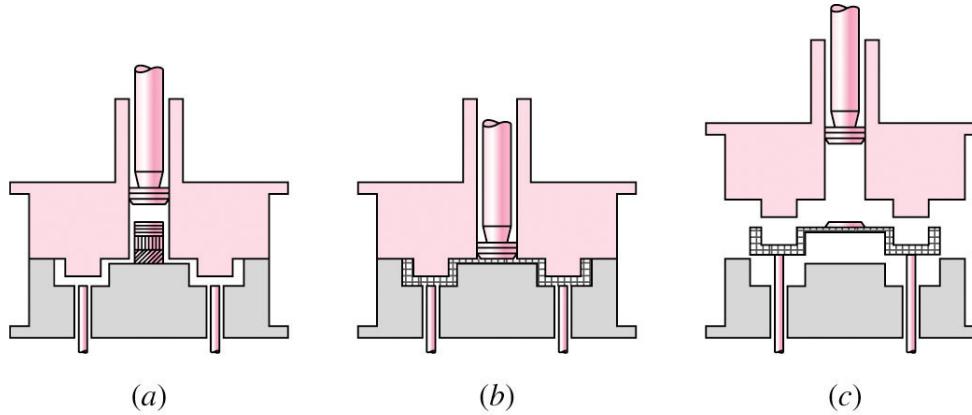
Processing Thermoplastics

Blow Molding



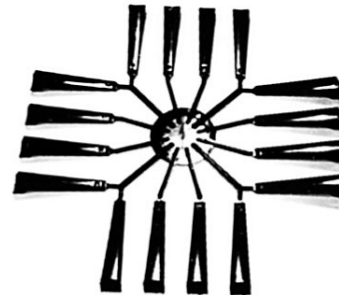
Industrial Scale Blow Molding

Processing Thermosets



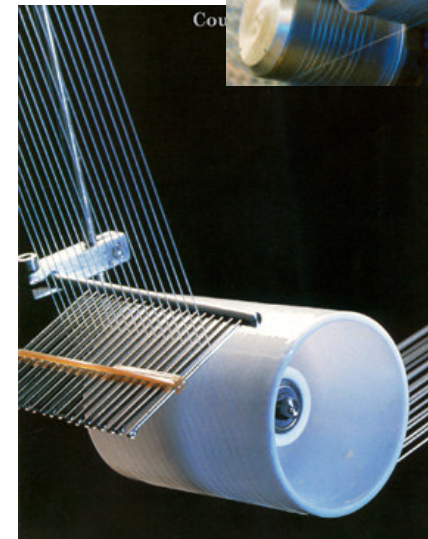
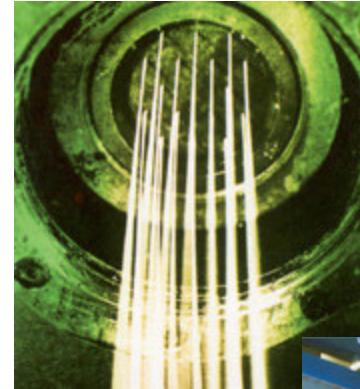
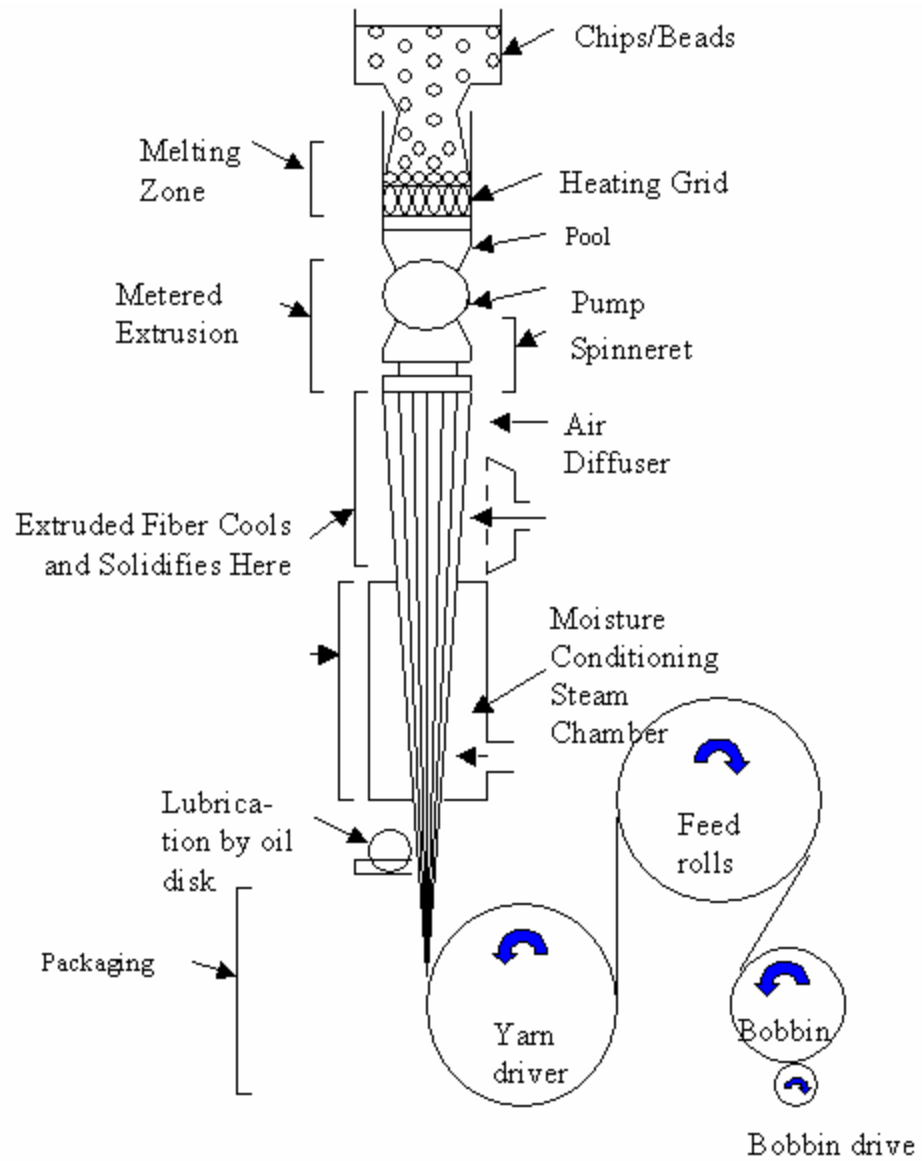
(d)

Transfer Molding



(e)

Melt Spinning



Polymeric Biomaterials

The majority of biomaterials used in humans are synthetic polymers such as the polyurethanes or Dacron (trademark; chemical name polyethylene terephthalate), rather than polymers of biological origin such as proteins or polysaccharides. The properties of common synthetic biomaterials vary widely, from the soft and delicate water-absorbing hydrogels made into contact lenses to the resilient elastomers found in short- and long-term cardiovascular devices or the high-strength acrylics used in orthopedics and dentistry. The properties of any material are governed by its chemical composition and by the intra- and intermolecular forces that dictate its molecular organization. Macromolecular structure in turn affects macroscopic properties and, ultimately, the interfacial behaviour of the material in contact with blood or host tissues.

Polymeric Biomaterials Criteria for Use

For use as biomaterials, synthetic polymers must possess the appropriate physical and mechanical properties for the intended application and must be free of residual monomer and other leachables. Above all, the polymers must be “biocompatible”. This refers both to the effects of the material on the biological environment and of this environment on the material. In essence, the polymer must not: (a) induce any clinically significant changes in the tissues or fluids of the body, (b) undergo significant changes in mechanical, physical or chemical properties during the period of implantation, and (c) degrade with the liberation of harmful substances into the biological environment. In the case of biodegradable and fully resorbable polymers, the degradation must occur at an optimum rate and not produce products that are toxic or carcinogenic. Finally, the polymers must be sterilizable (usually by ethylene oxide or high energy radiation); they must withstand various processing conditions, and be available at a reasonable cost.

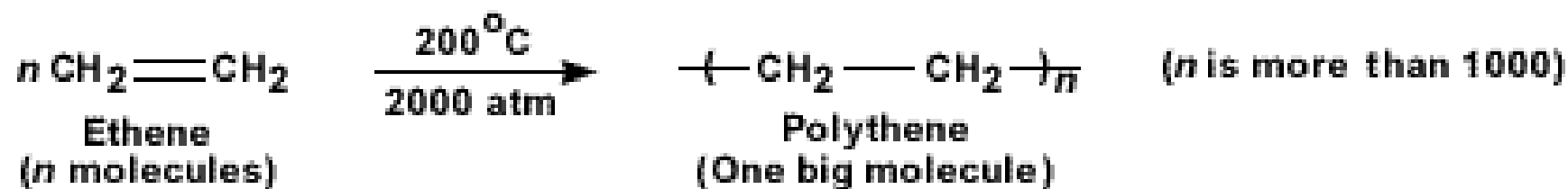
Some Common Polymers Used as Biomaterials

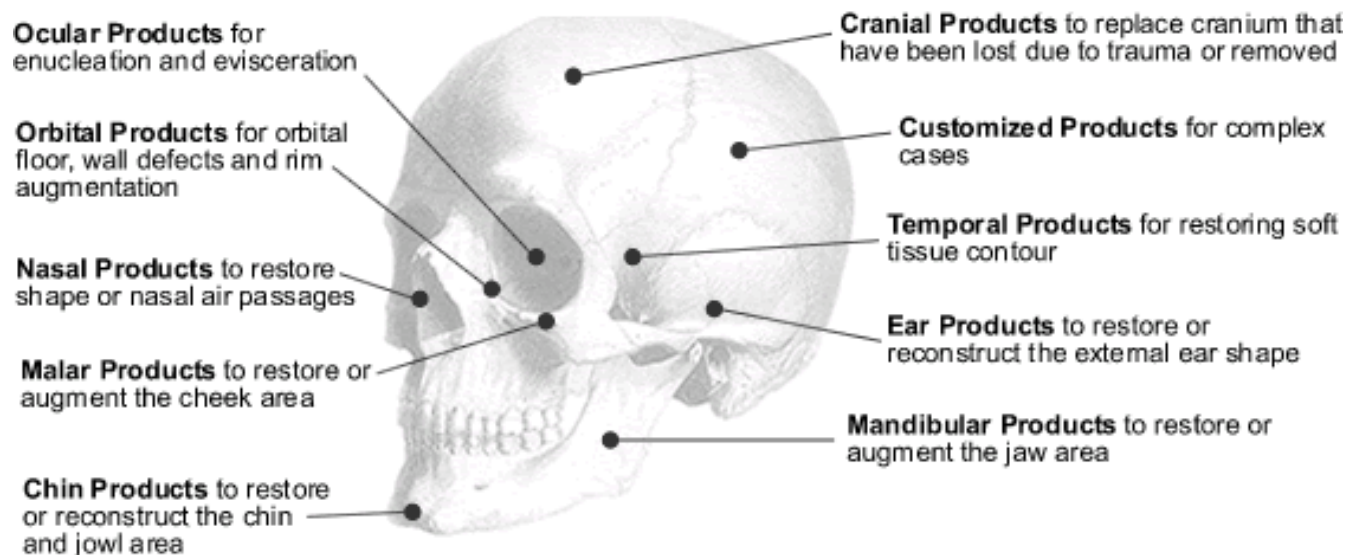
- ***Polyethylene***
- ***Polymethylmethacrylate (PMMA)***
- ***Polytetrafluoroethylene (PTFE)***
- ***Polyurethane***
- ***Polyvinylchloride (PVC)***
- ***Polydimethylsiloxane (Silicone)***
- ***Nylons***
- ***Polyesters***

Polyethylene

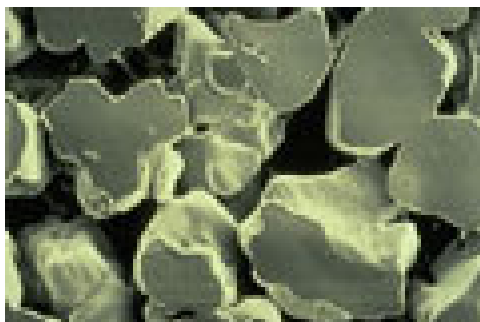
Polyethylene, as the name implies, is produced by the polymerization of ethylene gas ($\text{CH}_2=\text{CH}_2$) and hence has the simple composition of CH_2CH_2 repeating units. Different methods of synthesis, however, can produce different grades which vary mainly in the degree of branching of the polymer chains. A high degree of branching results in polymers of lower density increased softness and easier processing. Commercially, polyethylene is available in five major grades: very low density, low density, linear low density, high density, and ultra high molecular weight. The first four grades are used in medicine as catheters, pharmaceutical bottles, non-woven fabrics, flexible tubing, pouches and bags. The grade of polyethylene that has made the greatest impact is that with ultra high molecular weight. In this, the polymer chains are composed of around 150,000 CH_2 units linked together, compared to the 5,000-10,000 of the other grades. This gives the polymer extraordinary load-bearing capacity as well as low friction and high durability. As such, it is used extensively for orthopedic implant fabrication especially for knee and hip joint prostheses.

Polyethylene Chemistry





MEDPOR Surgical Implants are manufactured from linear high-density polyethylene. Polyethylene has a long history of use in surgical implants. MEDPOR Biomaterial allows for tissue ingrowth because of its interconnecting open pore structure. The porosity of MEDPOR Biomaterial is maintained large with average pore sizes greater than 100 micro-meters and a pore volume in the 50 percent range. The firm nature of the material allows carving with a sharp instrument without collapsing the pore structure.



MEDPOR® Biomaterial

ORBITAL RIM ONLY IMPLANTS



Designed with:
Robert A. Goldberg, M.D.

The MEDPOR Orbital Rim Onlay Implants are designed to support the lower eyelid and lateral canthus in patients who have inadequate support due to congenital variation or changes with aging. The implant augments the inferior and lateral orbital rims and moderately increases the anterior rim projection. This mimics the normal orbital rim anatomy and provides support to the eyelid and canthal structures.

RZ EXTENDED CHIN IMPLANTS



Designed with:
Oscar M. Ramirez, M.D.

The RZ Extended Chin Implants are available in designs with square or round anterior projections. Three sizes are provided in each design with anterior projections of 3mm (small), 5mm (medium), and 7mm (large). The Extended Chins contain a notch for mental nerve passage and provide tri-dimensional projection (anterior, lateral and inferior).



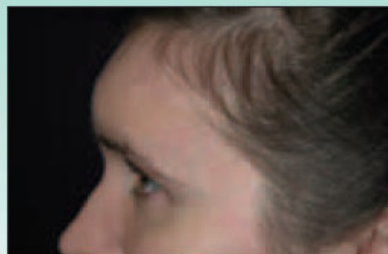
Immediate Pre-Op



Fixation of Implant

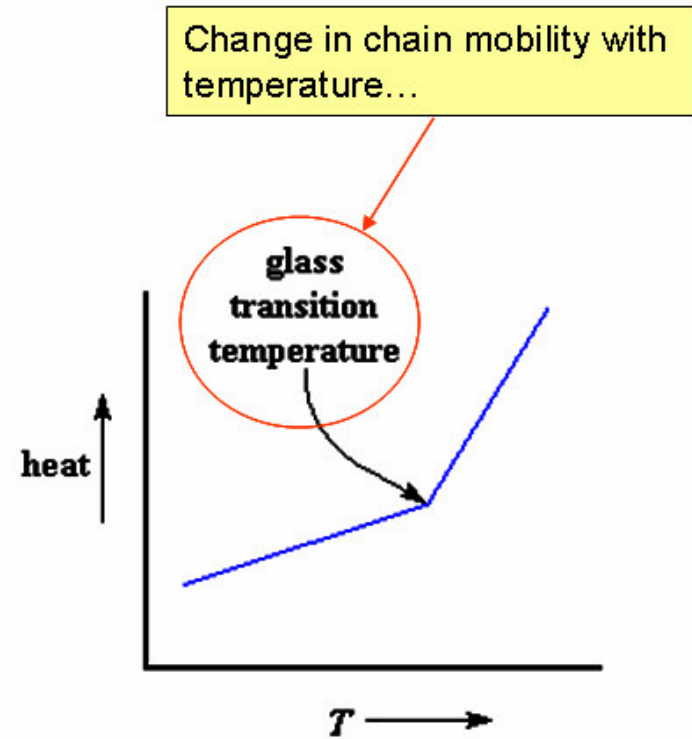
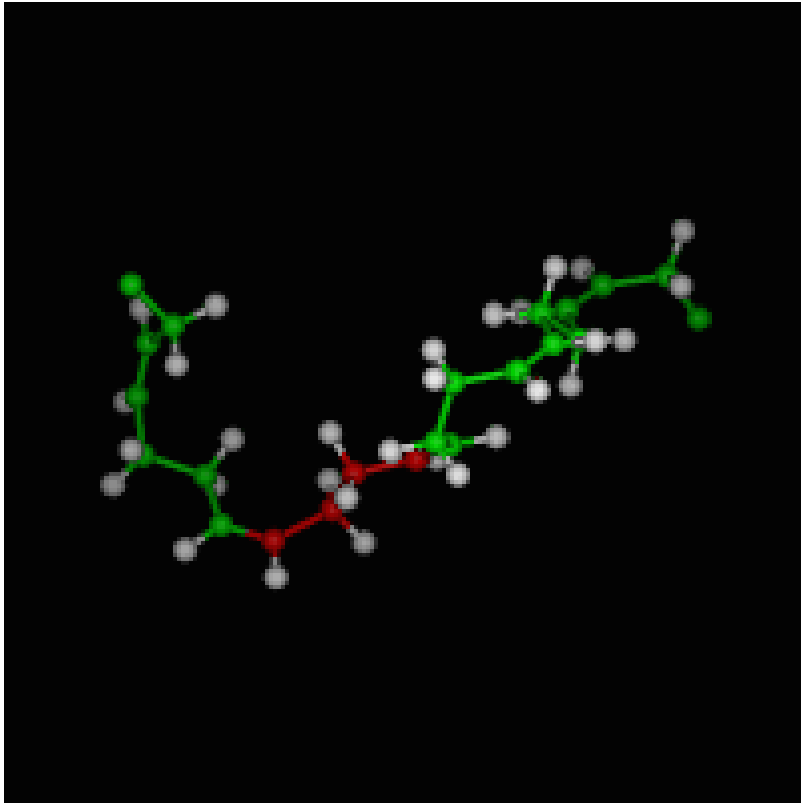


Feathering of the Implant

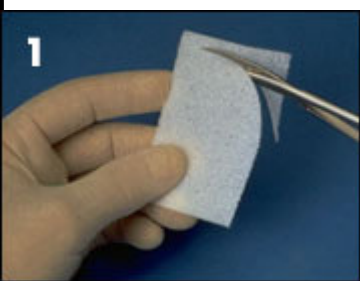

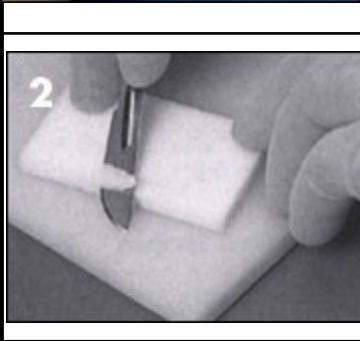
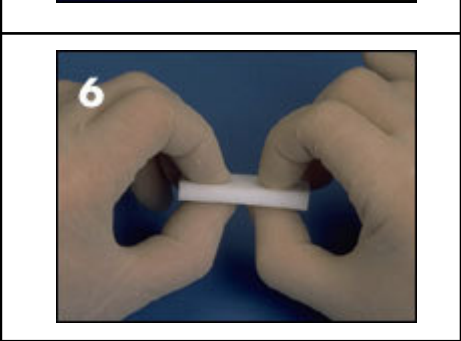
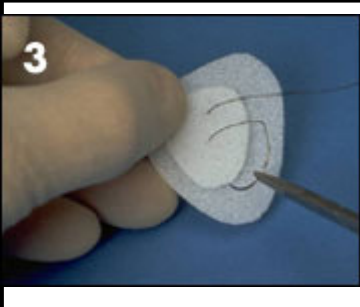
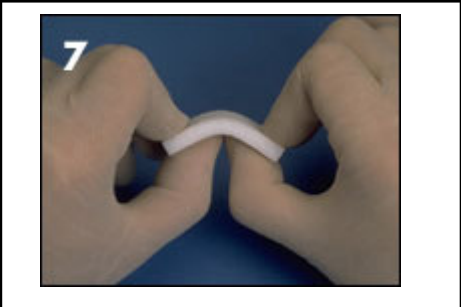
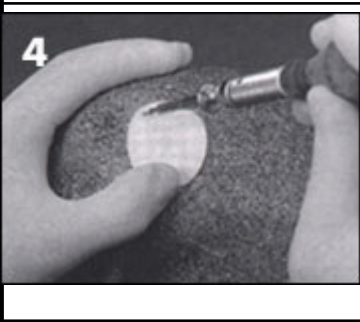


Twenty-One Month Post-Op

Photos courtesy of Robert D. Wallace, MD



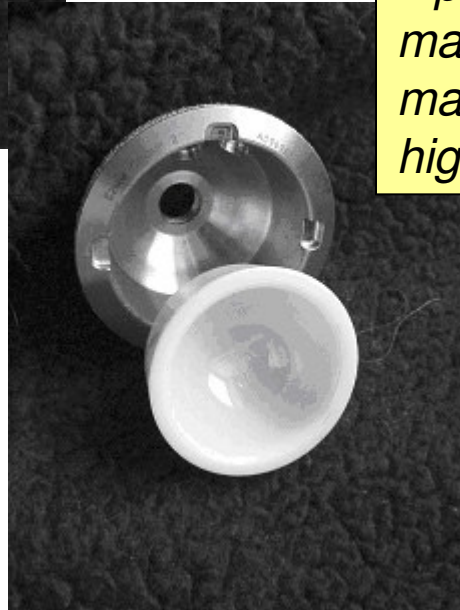
The temperature at which the polymer chains become mobile will determine the temperature at which the material will soften...

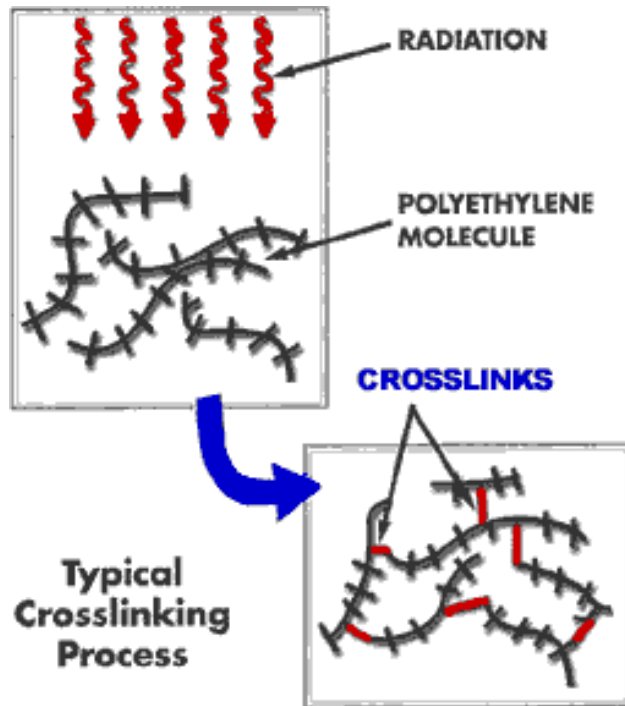
	<p><i>Sheets and blocks trim easily with surgical scissors or a small scalpel blade.</i></p>		<p><i>Submerge the implant in a hot, sterile saline bath (180 °F) to softens.</i></p>
	<p><i>Thicker implants may be shaped with large scalpels.</i></p>		<p><i>Gently bend the implant to the desired shape.</i></p>
	<p><i>Multiple pieces of implant material may be stacked and sutured together.</i></p>		<p><i>Hold the implant in the final shape and allow to cool.</i></p>
	<p><i>Proper rigid fixation techniques allow for stabilization of the implant.</i></p>		

Photograph of femoral stem and femoral head. The head may be made out of metal or ceramic, and the finish of the head may vary.

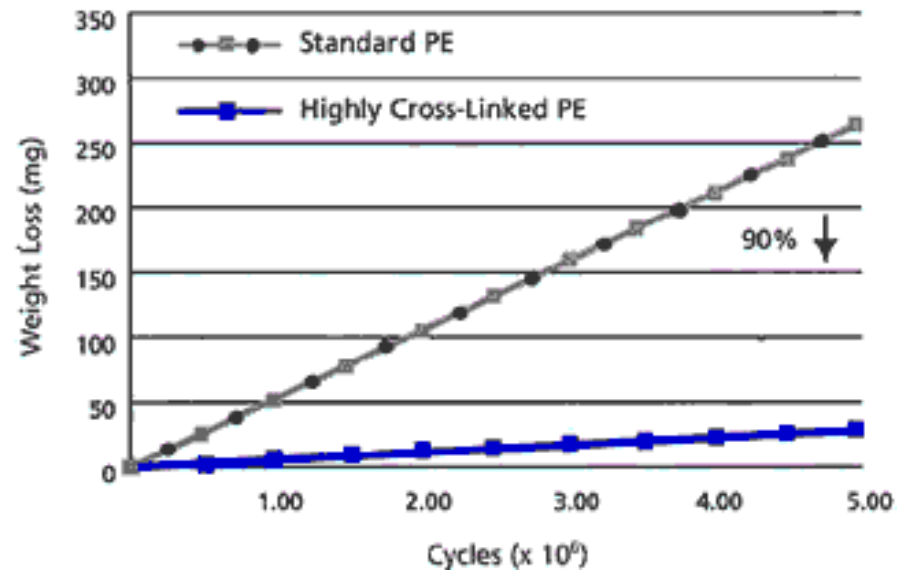


Photograph of the acetabular components of a contemporary total hip replacement. The shell is usually made out of metal, and the liner may be ceramic, metal, or ultra-high-molecular weight polyethylene.





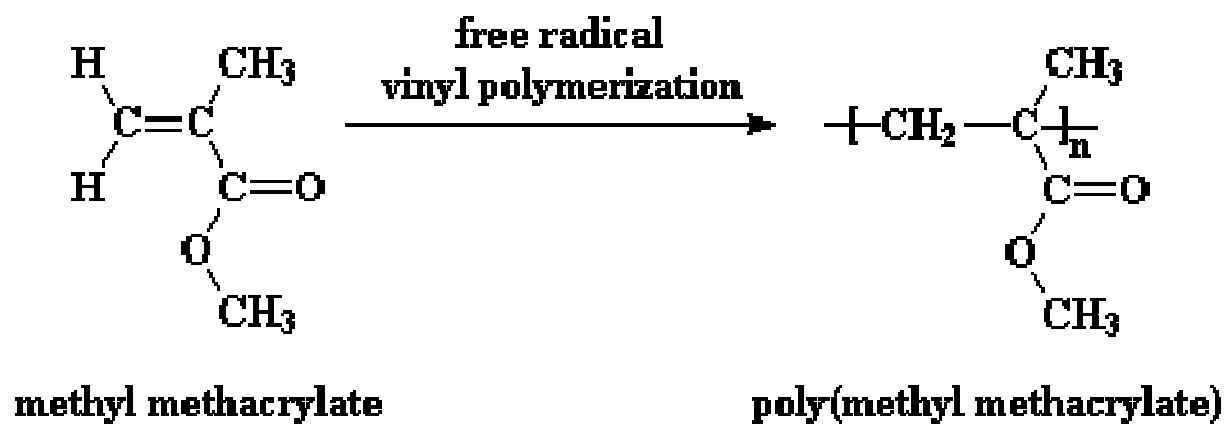
Modification of UHMW polyethylene wear behavior by crosslinking.



Poly(methyl methacrylate)

PMMA belongs to the family of acrylics. It is a glassy polymer with exceptional light transparency, high refractive index, good chemical resistance, and a very high level of biocompatibility. PMMA is used broadly in biomedical applications such as implantable ocular lenses, dentures, bone cement for fixation of hip and knee prostheses, blood pumps, and membranes for blood dialysers. The related hydrophilic (water loving) acrylic polymer, poly(hydroxymethyl methacrylate), is used in soft contact lenses as it forms a transparent hydrogel when lightly crosslinked.

Poly(Methyl Methacrylate) Chemistry



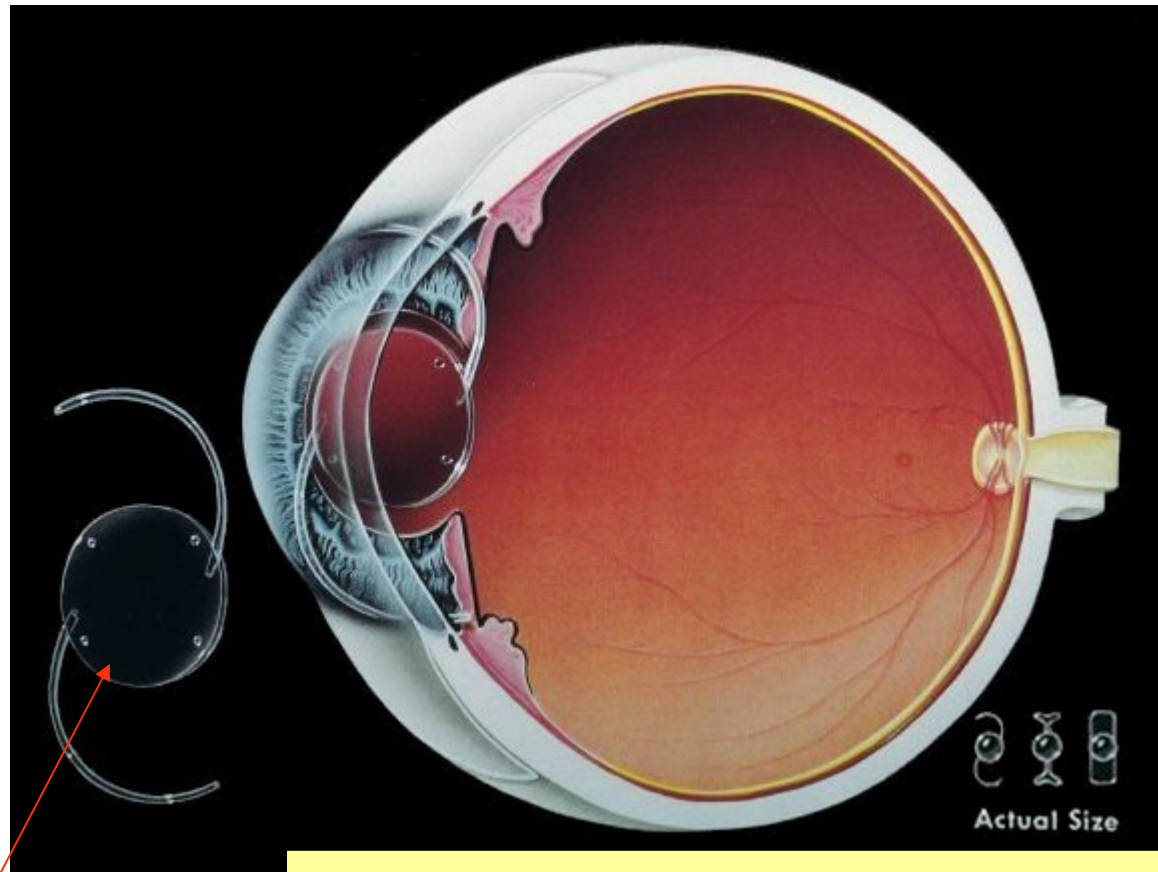
THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS

BULLETIN

Volume 49, No.1 ■ February 2001

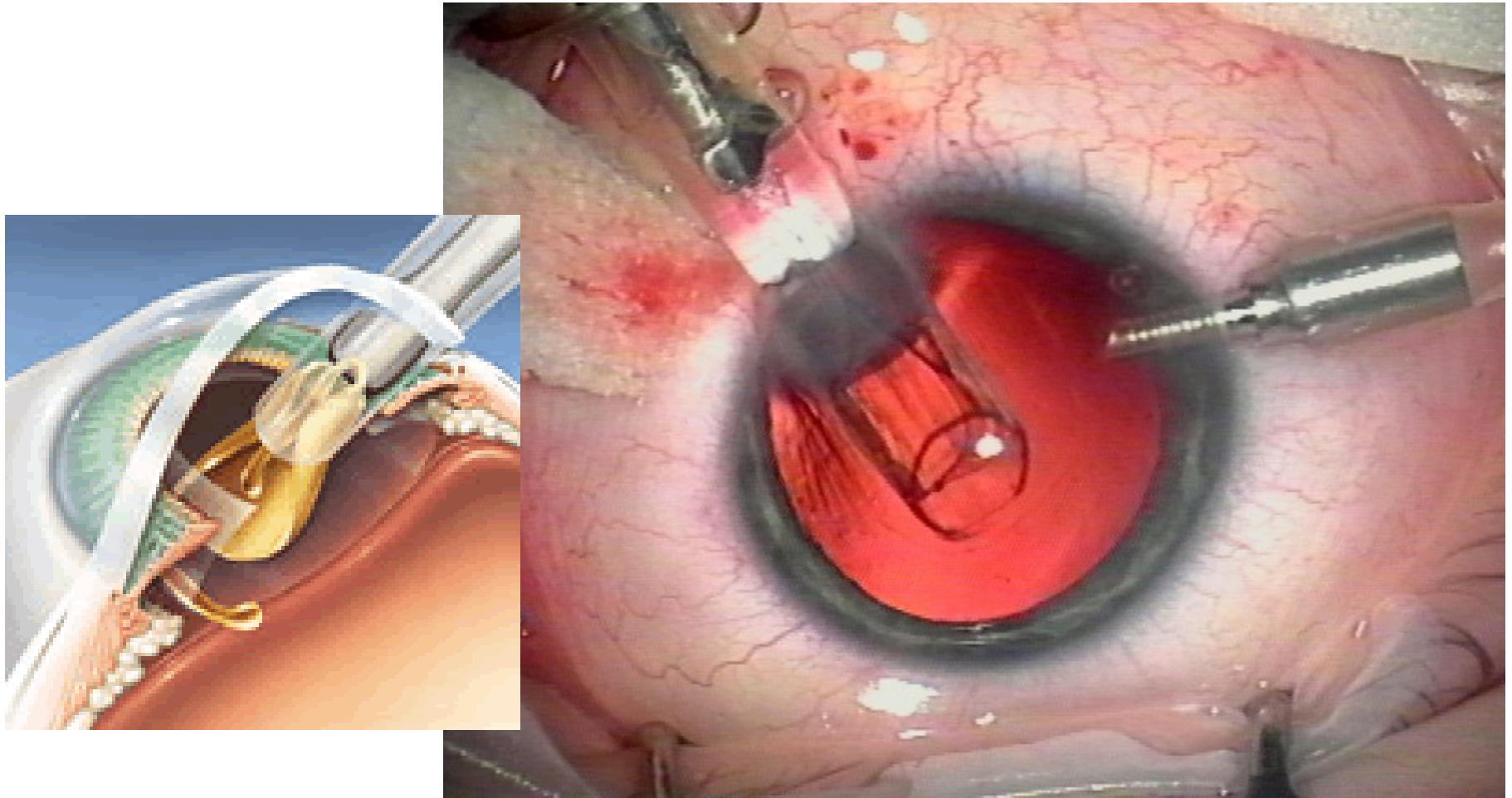
FDA concerned about use of PMMA cement in spine

The U.S. Food and Drug Administration (FDA) has expressed concern about potential serious patient care issues involved with the use of polymethylmethacrylate (PMMA) bone cement in the spine. A physician might insert the PMMA bone cement into vertebrae by various procedures, including vertebroplasty and kyphoplasty. Orthopaedic surgeons should be alert to possible complications. PMMA bone cement is considered a device for FDA purposes. In October 1999, the FDA reclassified PMMA bone cement as a Class II device for its intended use "in arthroplastic procedures of the hip, knee and other joints for the fixation of polymer or metallic prosthetic implants to living bone." The use of a device for other than its FDA-cleared indication is an off-label use. Physicians may use a device off-label if they believe, in their best medical judgment, that its use is appropriate for a particular patient (e.g., tumors). The use of PMMA bone cement in the spine is described in Academy educational courses, videotapes and publications for educational purposes only. As is the Academy's policy regarding all of its educational offerings, the fact that the use of PMMA bone cement in the spine is discussed does not constitute an Academy endorsement of this use.

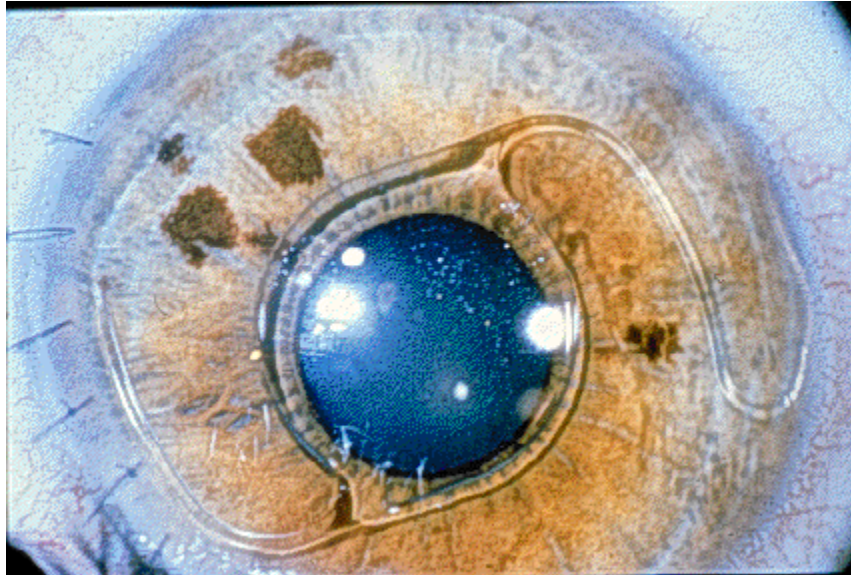


Intraocular Lense

Modern cataract operation in the 1990's involved sophisticated technology utilizing microsurgery on the cataract with delicate, controlled ultrasound removal of the cataract and the placement of a foldable intraocular lens made of acrylic or silicone. Amazingly, this is accomplished through a very small incision with special wound construction that has, essentially, eliminated the need for sutures except on infrequent occasions.

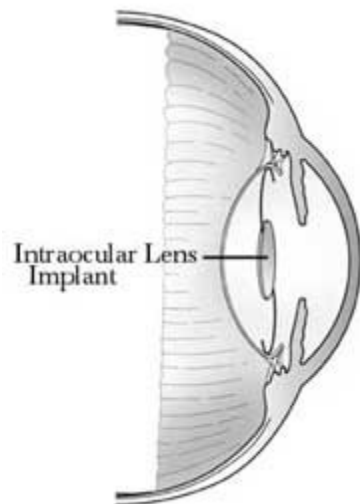


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PHAKIC INTRAOCULAR LENS (PIOL)

involves placement of a lens implant inside the eye for the correction of either nearsightedness or farsightedness. This lens becomes in effect an internal contact lens inside the eye rather than on the surface of the eye. At the present time this lens is being studied outside the United States.

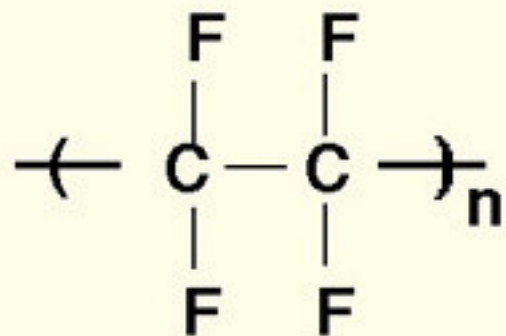


Polytetrafluoroethylene

Polytetrafluoroethylene is composed of CF_2 repeating units. This polymer is very inert, it is dense and crystalline, has moderate strength, and very low surface tension and friction coefficient. Its very high melting point and melt viscosity makes it unsuitable for injection moulding or melt extrusion and hence articles or implants are produced by sintering powders of the polymer at high temperature and pressure. PTFE is widely used for catheters and for artificial ligaments and tendons. It is relatively easy to foam and in this form has found use in the production of porous vascular grafts

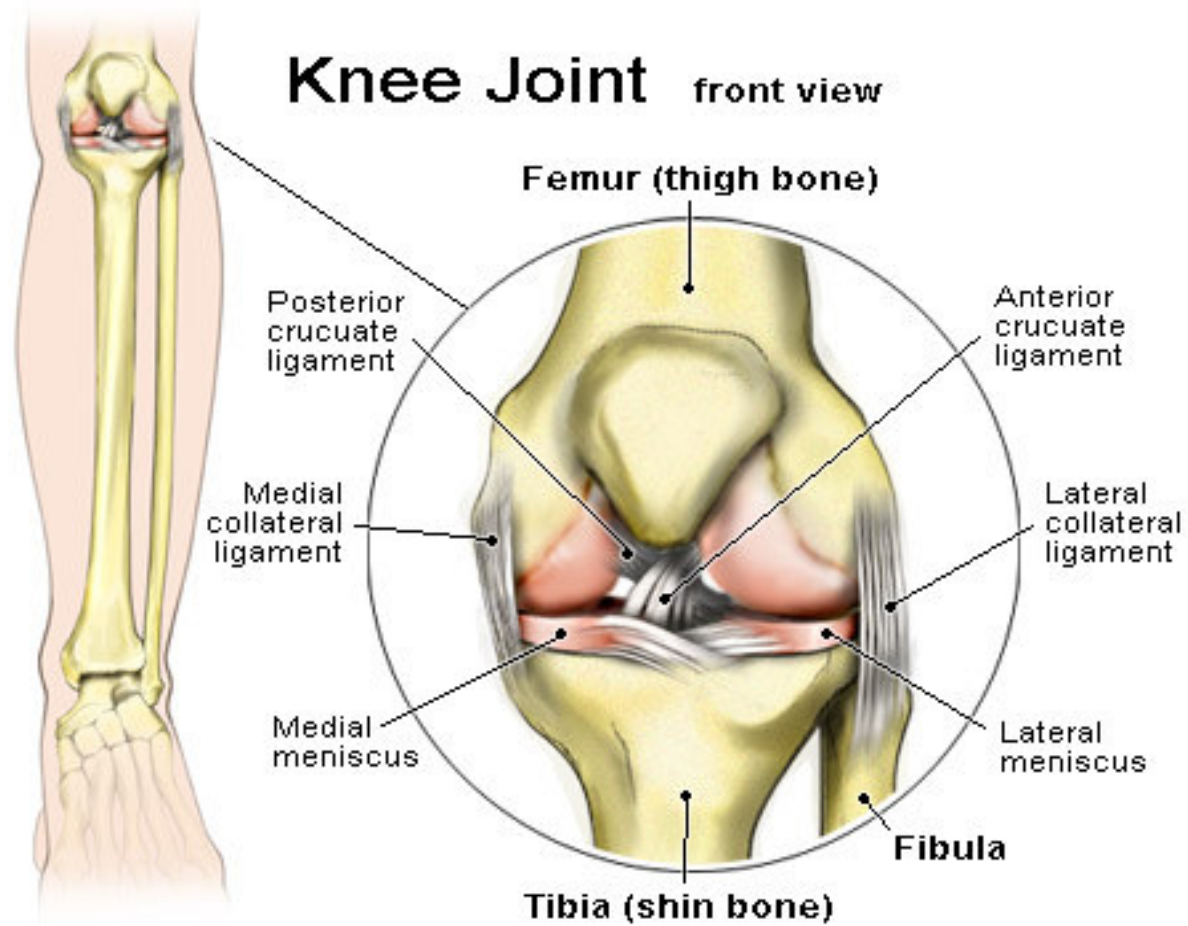
Polytetrafluoroethylene, Teflon

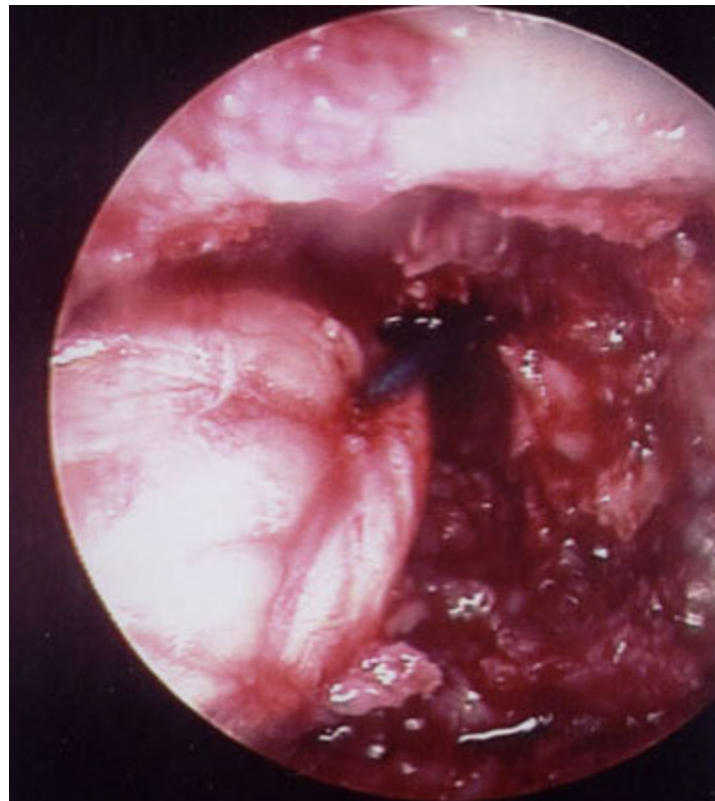
From 1,1,2,2,-tetrafluoro-1-ethene





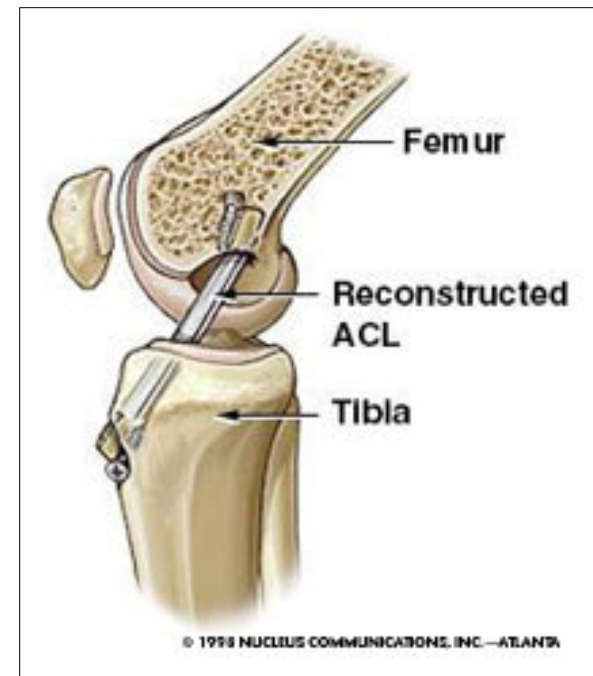
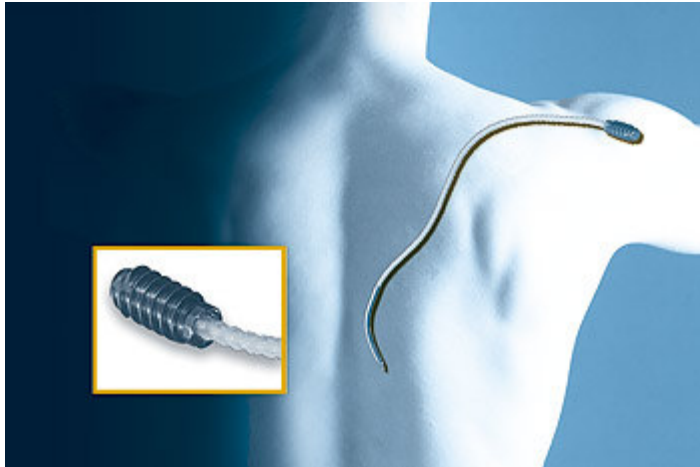
The Advanta SST is nothing short of revolutionary and is the only PTFE graft that pulses and performs like nature intended, with little or no needle hole bleeding or weeping. Using state-of-the-art membrane technology Atrium has crafted a perfect blend of biomaterial science into the world's most pulsatile vascular graft. It is constructed from an amazing hydrostatic protection membrane developed and patented by Atrium. Our proprietary trilaminate construction has been engineered to meet or exceed all surgical and performance strength requirements, with the benefit of being extraordinarily supple with incredible "vein-like" handling qualities.





DynaMesh - LFX

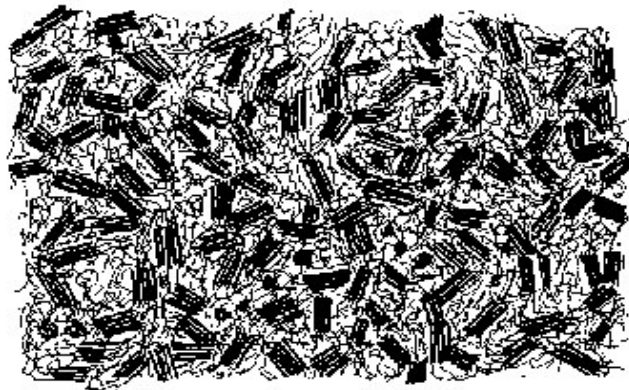
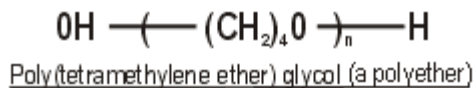
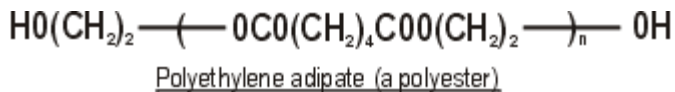
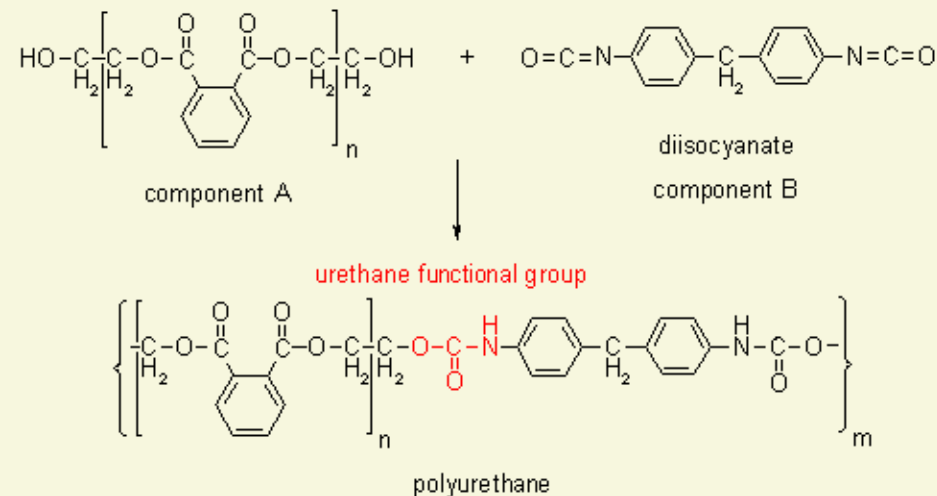
PVDF Ligament with Fixation Screw



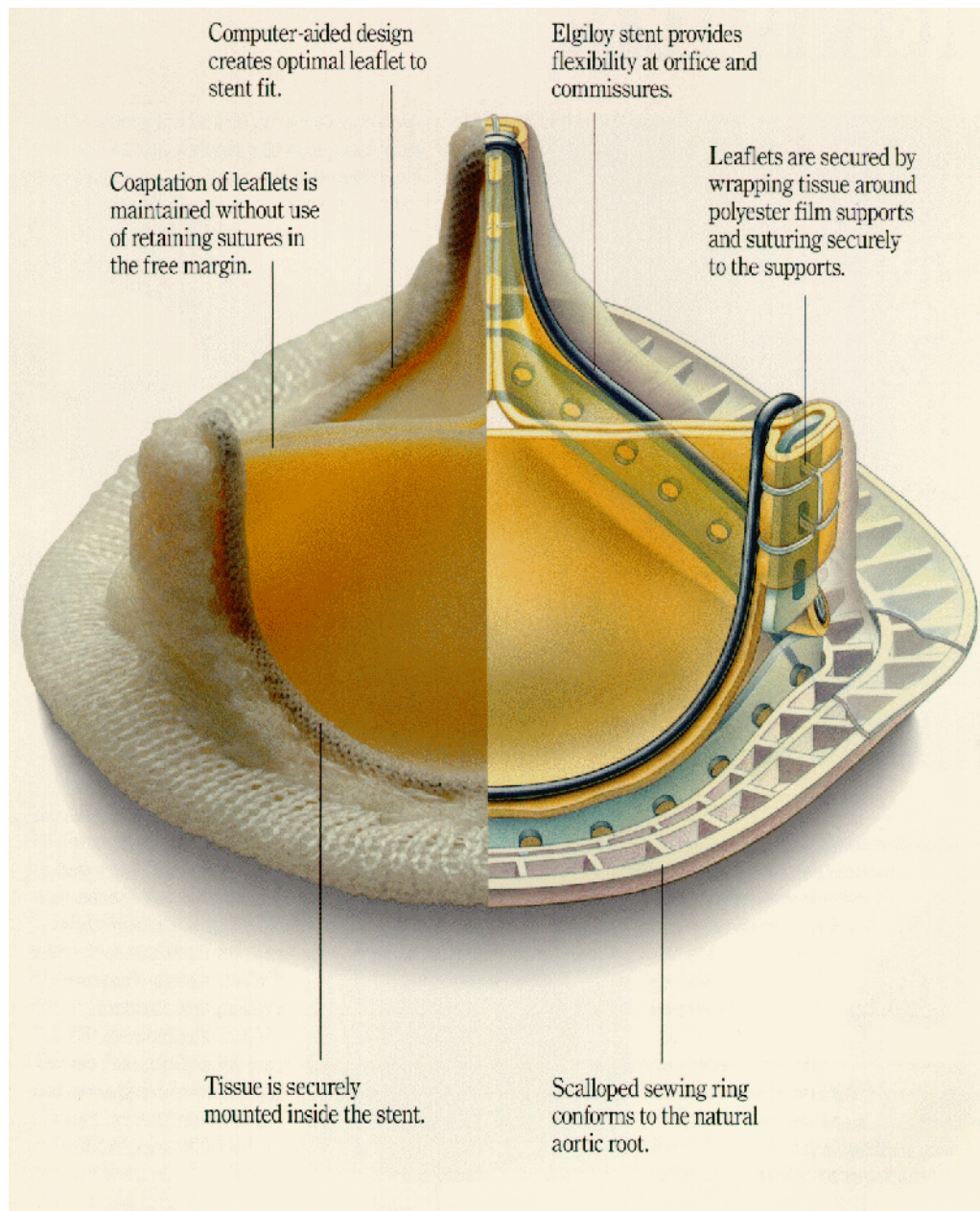
- Optimal ligament material: 100% PVDF braided monofilaments
- Highest ligament stability > 500 N
- Superb biocompatibility: PVDF-ligament / titanium-screw
- Newly designed connection between screw and ligament (patented adhesive connection)
- Optimal handling: Integrated fixation screw and application needle
- Tension free ligament fixation

Polyurethane

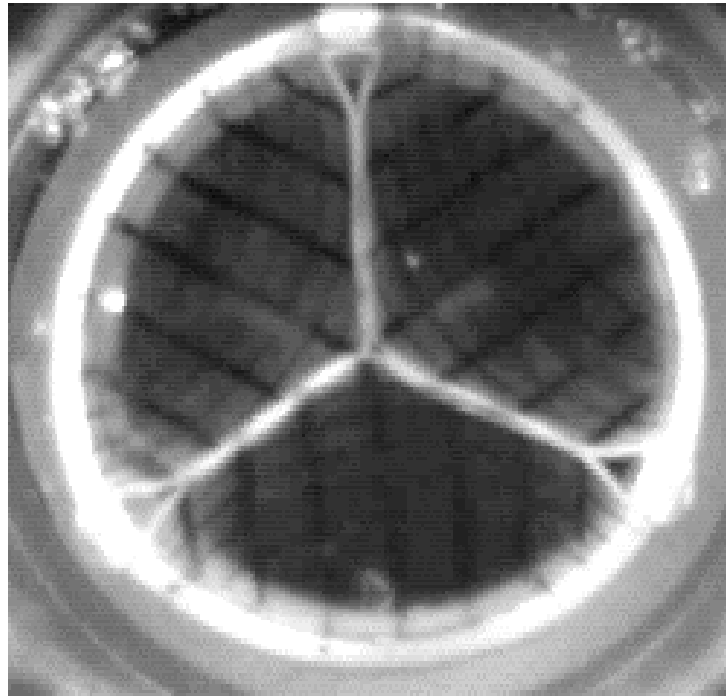
Polyurethane is the generic name for a very large family of polymers that can be synthesised in a wide range of compositions and properties. Biomedical applications rely mainly on the sub class referred to as polyurethane thermoplastic elastomers. These are produced by the reaction of diisocyanates with pre-prepared short chain polymeric diols (called polyols or macrodiols) and monomeric diol chain extenders. With several commercially available choices for each of the three components, a wide range of materials can be produced. The outstanding feature of polyurethane thermoplastic elastomers is that they can be melt-processed (extruded, injection moulded, etc.) but when returned to normal temperature they exhibit the properties of a tough rubber. Other important properties include high resistance to abrasion, tear, and fatigue, good biocompatibility and, for some applications, an acceptable degree of resistance to degradation in the biological environment. As such, polyurethanes have found use in vascular prostheses, intra-aortic balloons, pacemaker lead insulation, cardiac valves, wound dressings, breast implants, facial reconstruction, and both male and female condoms.

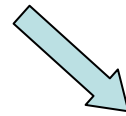
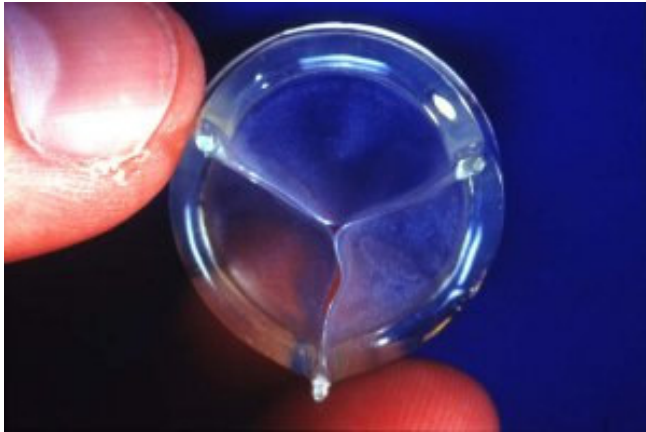


A PU is made by mixing together the ingredient chemicals (isocyanate and polyol) in predetermined proportions, which then react to form the polymer. Uniquely, PUs utilise simultaneous polymerisation and shaping of the part. The production of consistent end products depends on mixing, in precise ratio, the ingredient chemicals and maintenance of the appropriate processing temperatures. As the liquid isocyanate and polyol react to form the PU, the liquid mix becomes increasingly viscous eventually forming a solid mass.



Polyurethane Cardiac Valve
Carpentier-Edwards Pericardial





The fully developed foreign body reaction can debilitate the functional utility of a medical device.



Polyvinylchloride (PVC)

Polyvinylchloride Chemistry





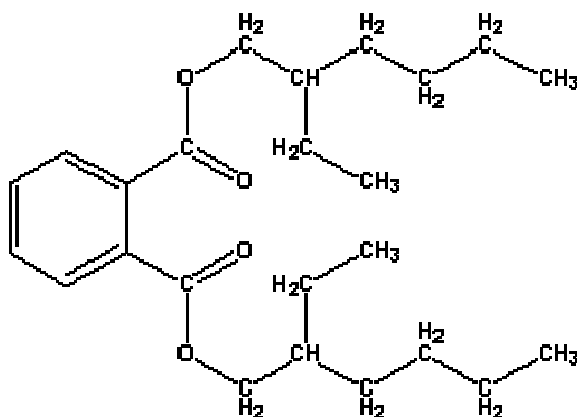
Unplasticized PVC has a T_g of 85°C , making it a rigid solid at room temperature suitable for plastic pipes. Adding a small amount of *plasticizer* to PVC can lower the T_g to -40°C . This addition renders the PVC a soft, flexible material at room temperature, ideal for applications such as garden hoses. A plasticized PVC hose can, however, become stiff and brittle in winter. In this case, as in any other, the relation of the T_g to the ambient temperature is what determines the choice of a given material in a particular application.

Polyvinylchloride (PVC)

Changes in some hormones by low doses of di (2-ethyl hexyl) phthalate (DEHP), a commonly used plasticizer in PVC blood storage bags & medical tubing

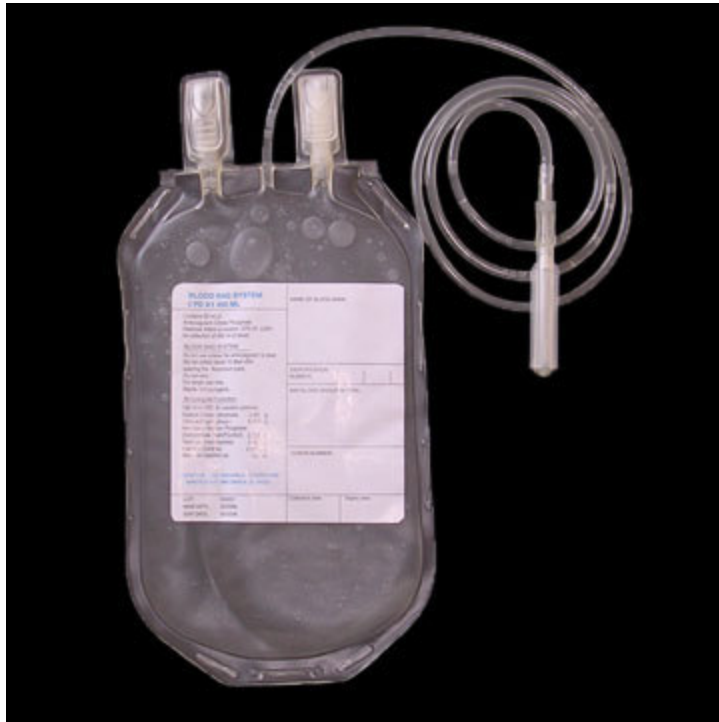
[INDIAN JOURNAL OF MEDICAL RESEARCH](#), [Apr 2004](#) by [Gayathri, N S](#), [Dhanya, C R](#), [Indu, A R](#), [Kurup, P A](#)

The results indicated decrease in serum insulin, cortisol and liver glycogen, and increase in blood glucose, serum T_3 and T_4 in rats receiving DEHP. These changes were reversed when administration of DEHP was stopped. Similar changes in hormones were also observed in the blood stored in DEHP plasticized blood bags.



Also evidence of carcinogenicity at this [link](#)

Jiaxing Tianhe Pharmaceutical Co., Ltd.



This blood bag is made with medical grade PVC rolled film and filled with anticoagulation solution, comes with 16G needle. For blood collection, preservation and transfusion



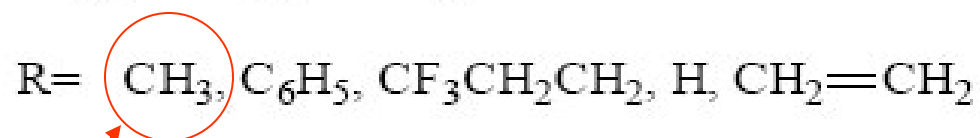
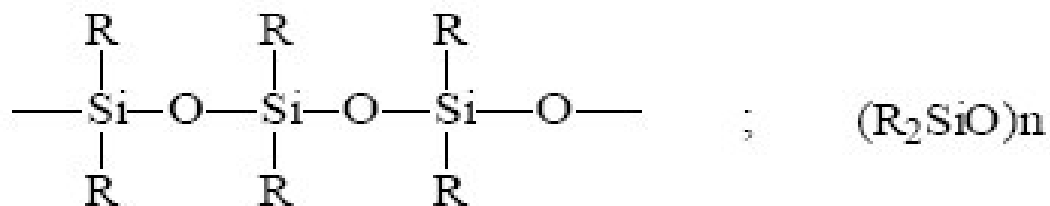
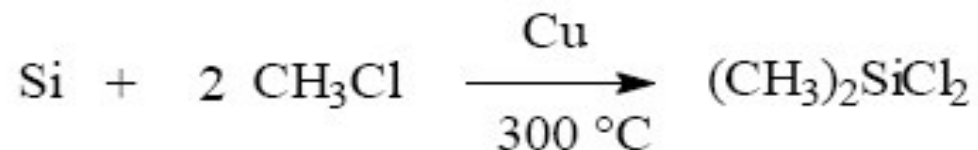
Il PVC plastificato o semirigido è il materiale maggiormente utilizzato per la produzione di sacche e tubi per trasfusioni di sangue grazie alle eccellenti proprietà meccaniche, la bassa tendenza alla formazione di fish eyes, l'elevata purezza e la resistenza agli agenti chimici. Questi manufatti sono prodotti per calandratura o estrusione.



Polydimethylsiloxane (Silicone)

Silicone based rubbers have excellent biocompatibility, flexibility, resistance to degradation, and oxygen permeability. A limitation for biomedical applications is their relatively poor tear and abrasion resistance. The main use of polysiloxanes is in cosmetic and reconstructive surgery but in conjunction with other polymers they have also been applied to dental, eye and ear prostheses, in materials to aid the healing of damaged skin, and in extended wear contact lenses.

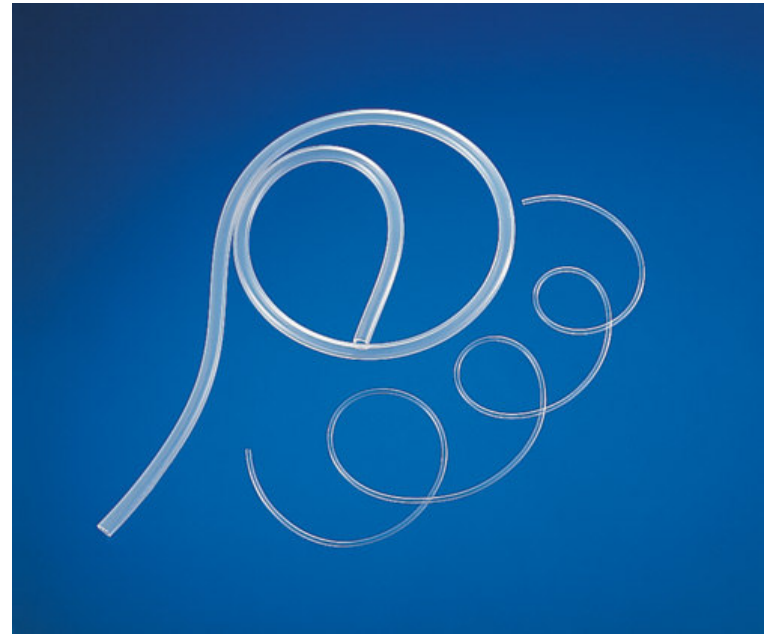
Polydimethylsiloxane Chemistry



methyl



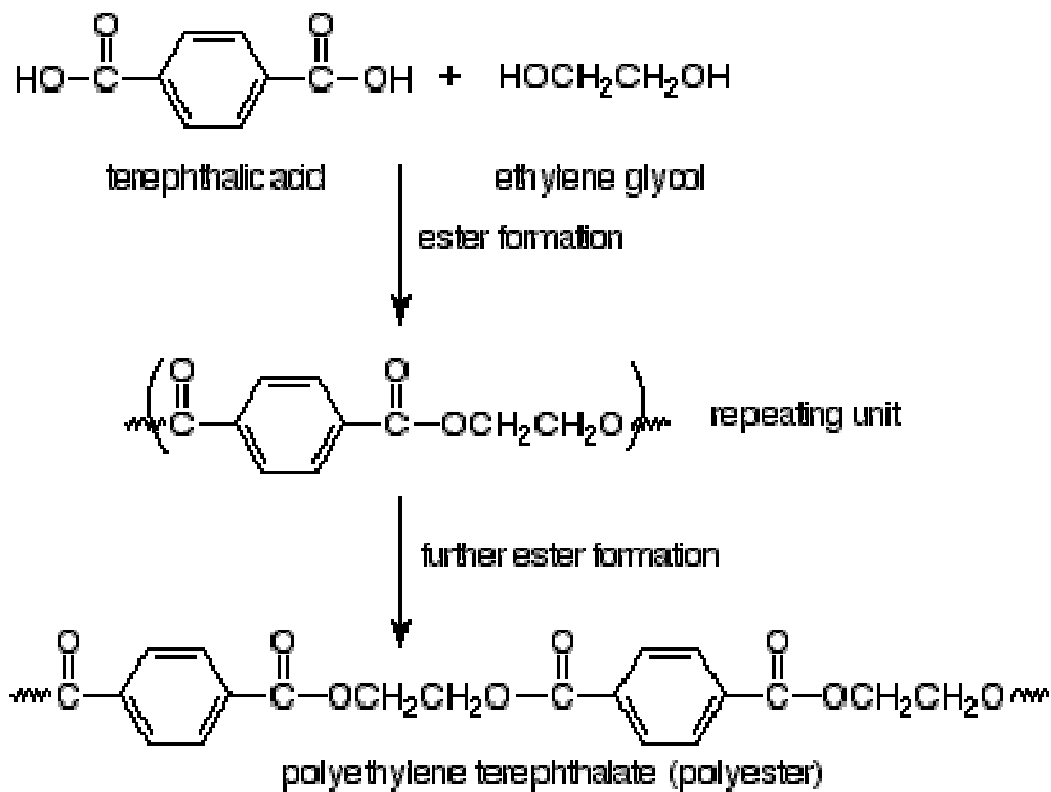
In a narrow decision, the Food and Drug Administration (FDA) decided against allowing silicone gel breast implants back on the market. This debate was sparked by the worries of the medical community that the implants could cause cancer, autoimmune and connective tissue disorders among other problems.



Poly(ethylene terephthalate) PET

PET belongs to the family of polyesters and is the most important of this group of polymers for biomedical applications. It is a rigid crystalline and high melting polymer that can be relatively easily processed into various shapes including fibres. Its good mechanical properties, chemical resistance, and excellent biocompatibility make it suitable for a range of biomedical implants. These include woven vascular grafts, braided artificial heart valves, sutural materials, ligament and tendon prostheses, and supporting meshes.

Polyester Chemistry



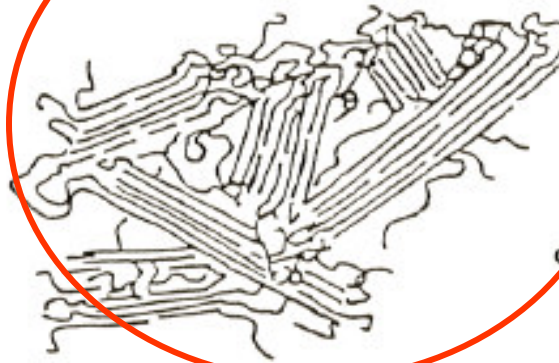
The primary chain structure of polymers allow different types of internal morphology to develop. These different morphologies strongly influence physical behavior.

Polyesters

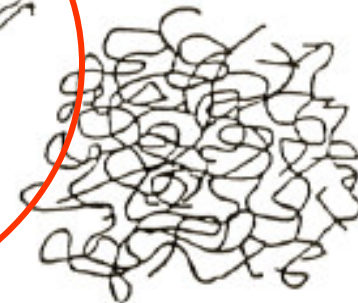
Crystalline



Semicrystalline



Amorphous



Melting @ T_m
Heat of Fusion
Stronger Forces
Correlated Structure

Glass Transition
No Heat of Fusion
Free Volume
Amorphous Form



Precision parts such as injection-molded winged luers are among the many medical products made from polyester resins. Photo: Eastman Chemical Co.

CHAD
THERAPEUTICS

**PURITAN
BENNETT**

GORE POLYESTER VASCULAR PRODUCTS

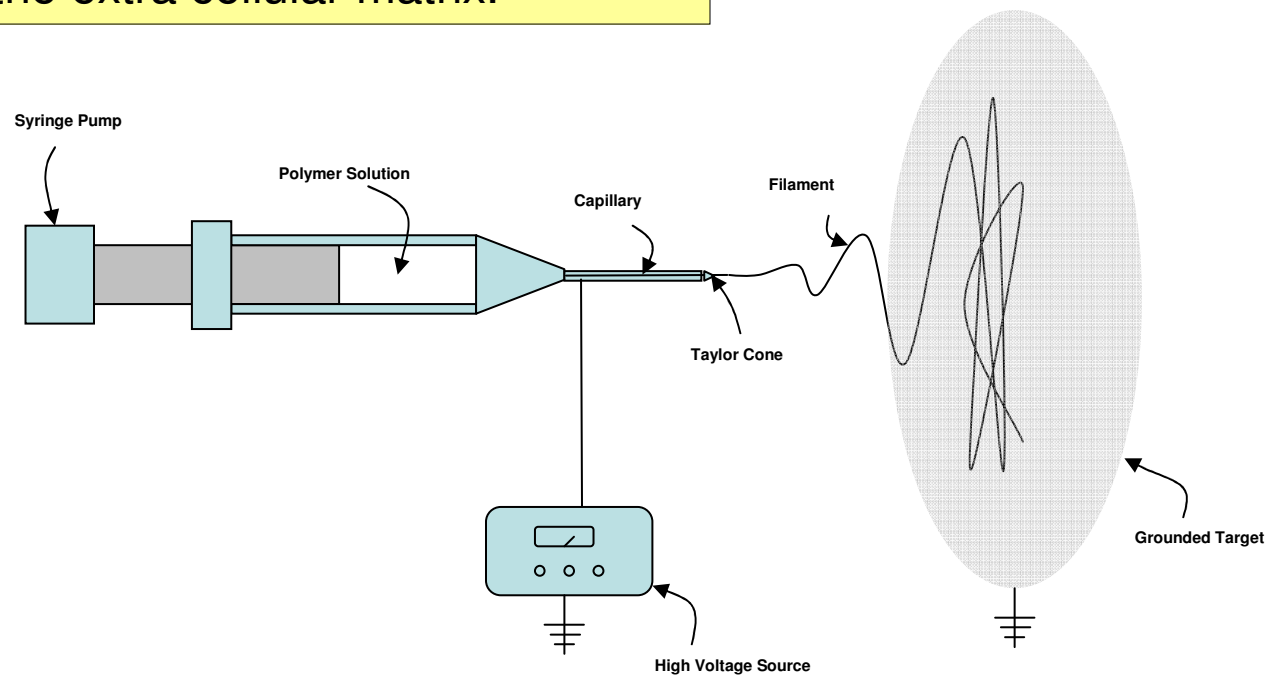


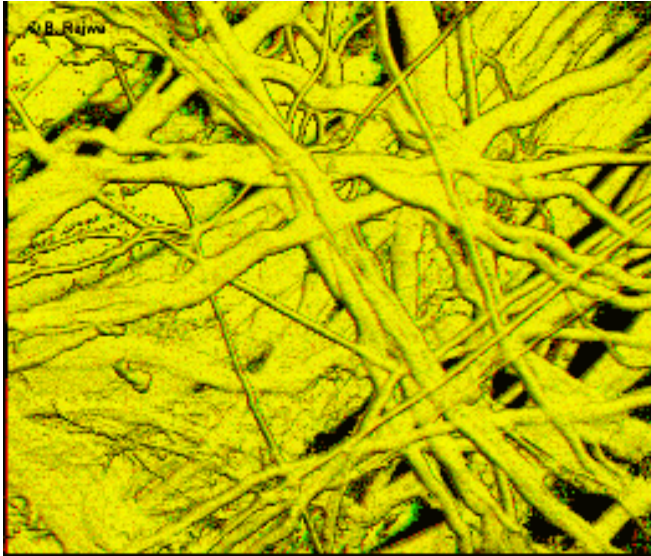
Polyester/Spandex Leg Bag Holder

Biodegradable Devices

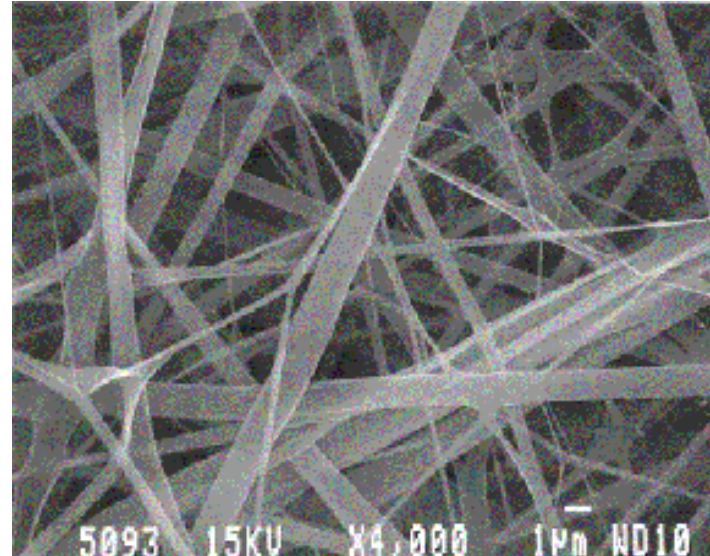
A synthetic tissue scaffold provides the framework on which native tissue cells can regenerate after injury. As the healing proceeds the need for the scaffold is progressively diminished. A biodegradable scaffold material will disintegrate in vivo, and eliminate the need for surgical removal.

Electrospinning is a technique for producing nanofiber non-woven mats from dilute polymer solutions. These mats can serve as scaffold devices for tissue engineering applications. These materials mimic the structure of the extra cellular matrix.





**A. Small Intestinal
Submucosa - Natural ECM**



**B. Electrospun Type I, II
Collagen and Elastin**

THE EFFECT OF VARYING THE ARCHITECTURE OF SCAFFOLDS ON MESENCHYMAL STEM CELL OSTEOGENESIS AND CHONDROGENESIS

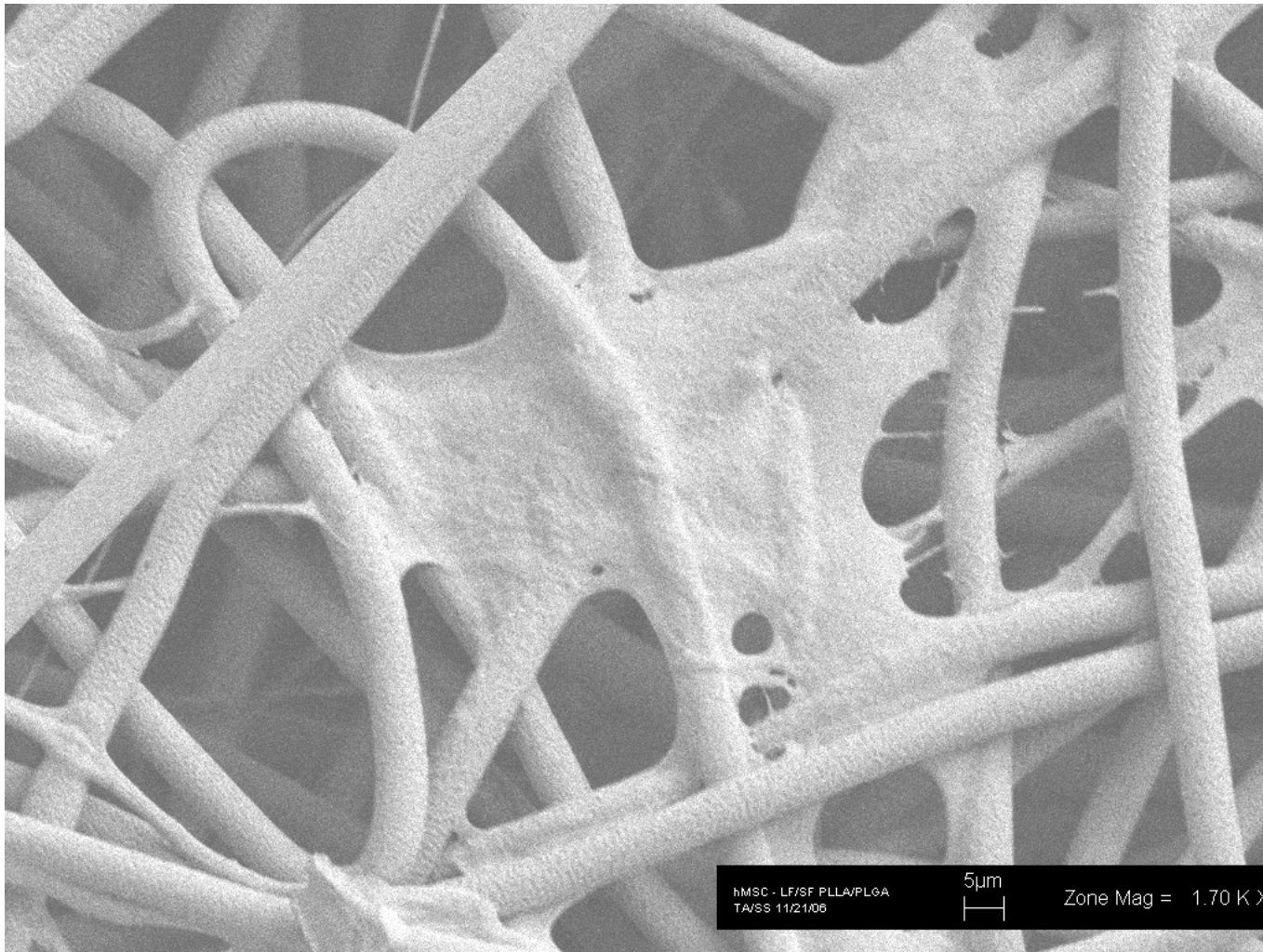
***Shanmugasundaram, S; +Mautone, A S; *Jaffe, M; **Rizio, L; *Livingston Arinzeh, T**

***Department of Biomedical Engineering, New Jersey Institute of Technology, NJ**

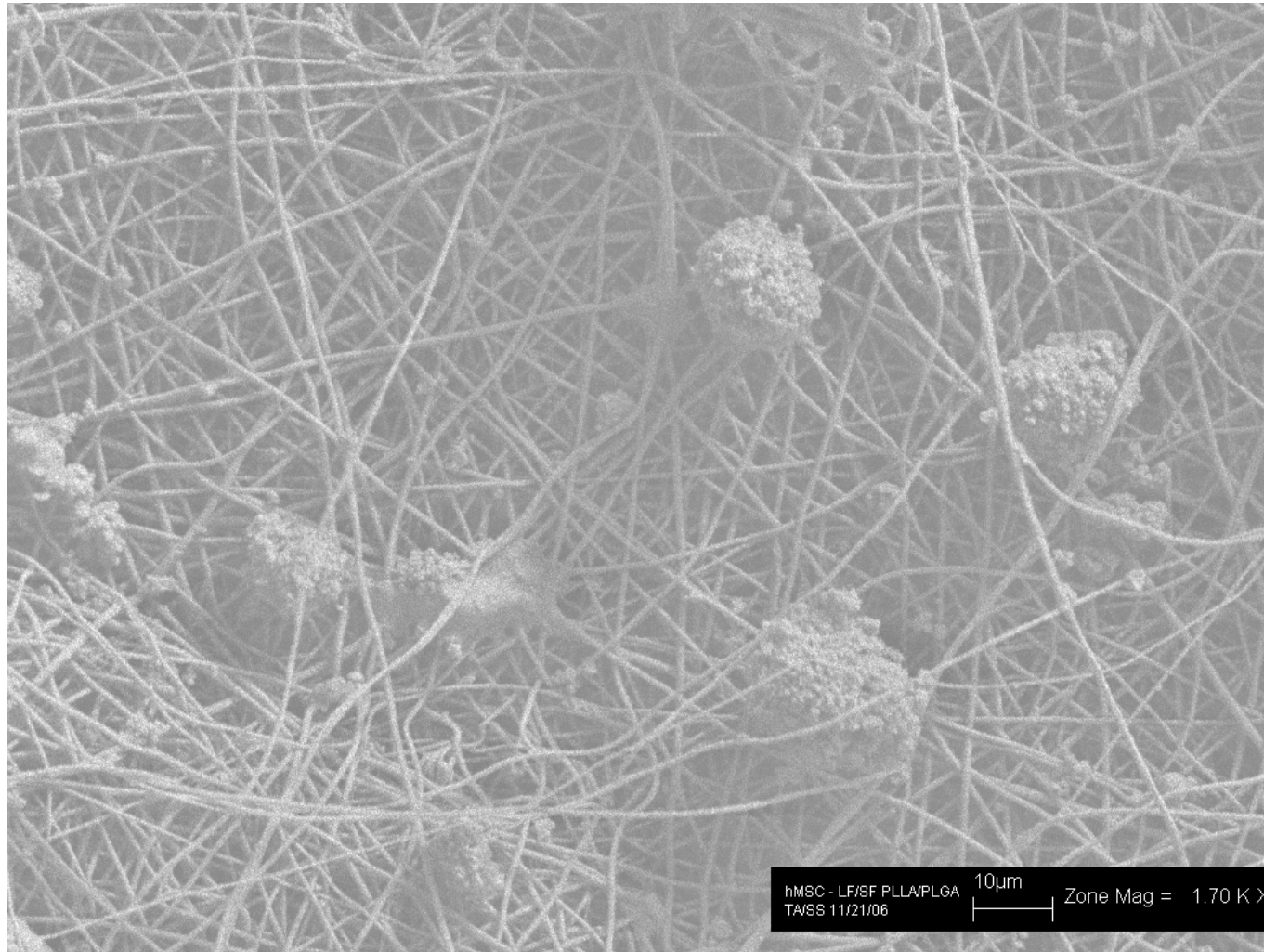
**** New Jersey Sports Medicine Institute, NJ**

+Department of Biomedical Engineering, University of Virginia, VA

“We propose to investigate mesenchymal stem cells (MSCs) in combination with fibrous scaffolds as a potential tissue engineering therapy for bone and cartilage regeneration.”



PLLA electrospun scaffold with average fiber diameter about 5 μ m. The cell morphology is flat. Cartilage cell produces Type II collagen and glycoaminoglycans. Flat cell production is low.



PLLA electrospun scaffold with average fiber diameter about 300 nm. The cell morphology is round. Cartilage cell produces Type II collagen and glycoaminoglycans. Flat cell production is high.

THE EFFECT OF VARYING THE ARCHITECTURE OF SCAFFOLDS ON MESENCHYMAL STEM CELL OSTEOGENESIS AND CHONDROGENESIS

Conclusions

1. TCPS plate culture used as a control.
2. The osteogenic differentiation studies demonstrated the higher levels of mineralization occurred on both PLLA micro- and nano-fibers compared to TCPS.
3. The chondrogenic differentiation data currently suggests that nano-fiber scaffolds support Type II collagen synthesis better than micro-fiber.

Clarification of Terms

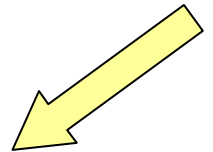
There are four terms that are often used to describe the degradation of a tissue scaffold/implant device. The European Society of Biomaterials has provided these definitions.

1. *Biodegradation*: degradation of physical structure caused by a biological agent (enzyme, microbe or cell).
2. *Bioerosion*: a water-insoluble polymer broken into smaller fragments under physiological conditions.
3. *Bioresorption, Bioadsorption*: a polymer or its degradation products removed by cellular activity.

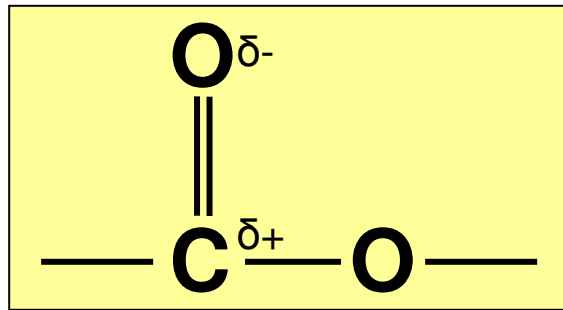
Basic Considerations

The ultimate fate of an implanted device is very important.

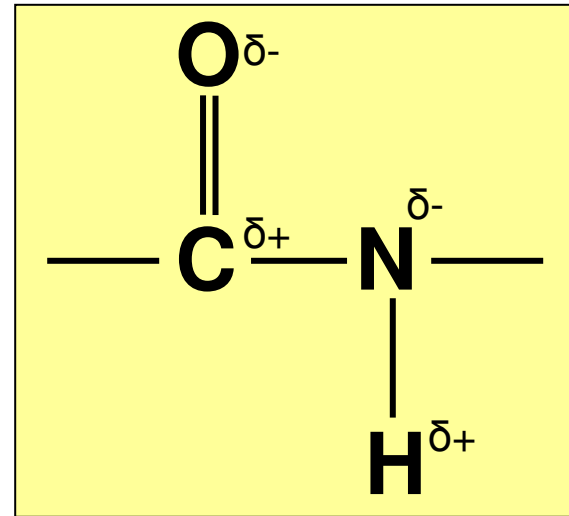
1. A device that is biodegradable will break down into progressively smaller fragments that will eventually be metabolized. This is a desirable outcome.
2. Material that is bioeliminable will dissolve into low molecular weight compounds that can be excreted by natural pathways. This is a desirable outcome.
3. A device may have to be surgically removed. This is a much less attractive alternative.
4. A very small number of materials have been FDA approved (homo- and copolymers of glycolic acid, lactic acid, caprolactone, p-dioxanone and trimethylene carbonate)



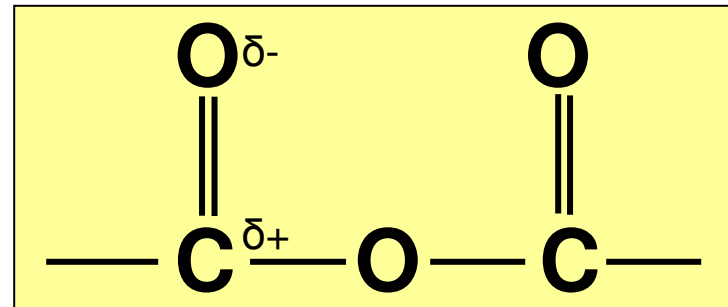
Typical Biodegradable Polymers



Ester bond

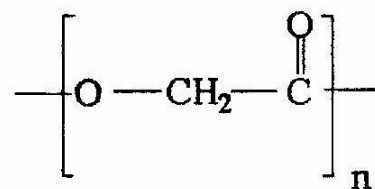


Amide bond

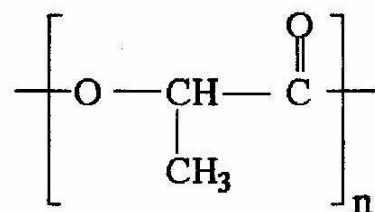


Anhydride bond

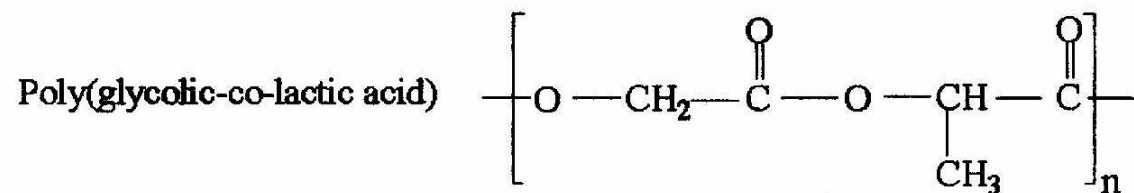
Poly(glycolic acid)



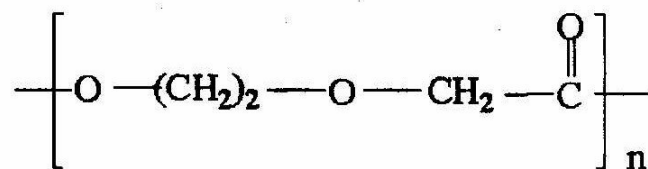
Poly(lactic acid)



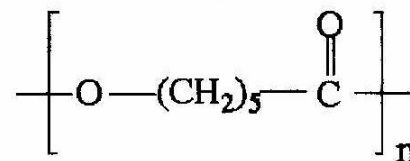
Poly(glycolic-co-lactic acid)



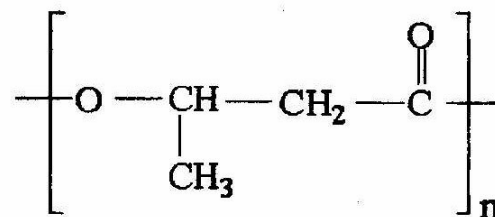
Poly(dioxanone)



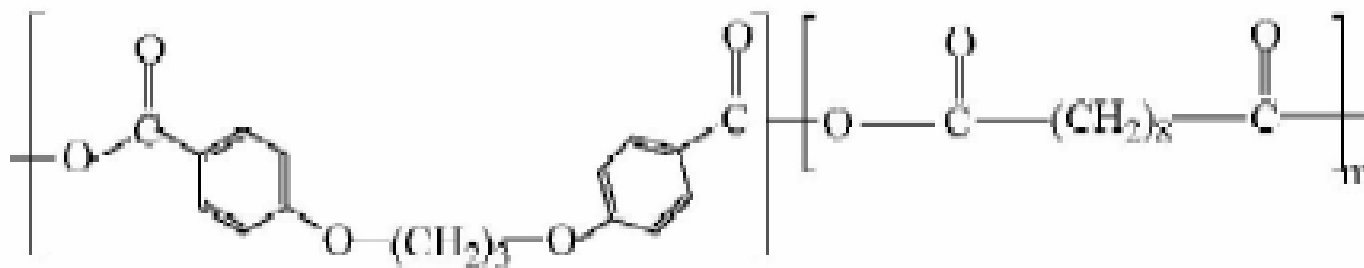
Poly(caprolactone)



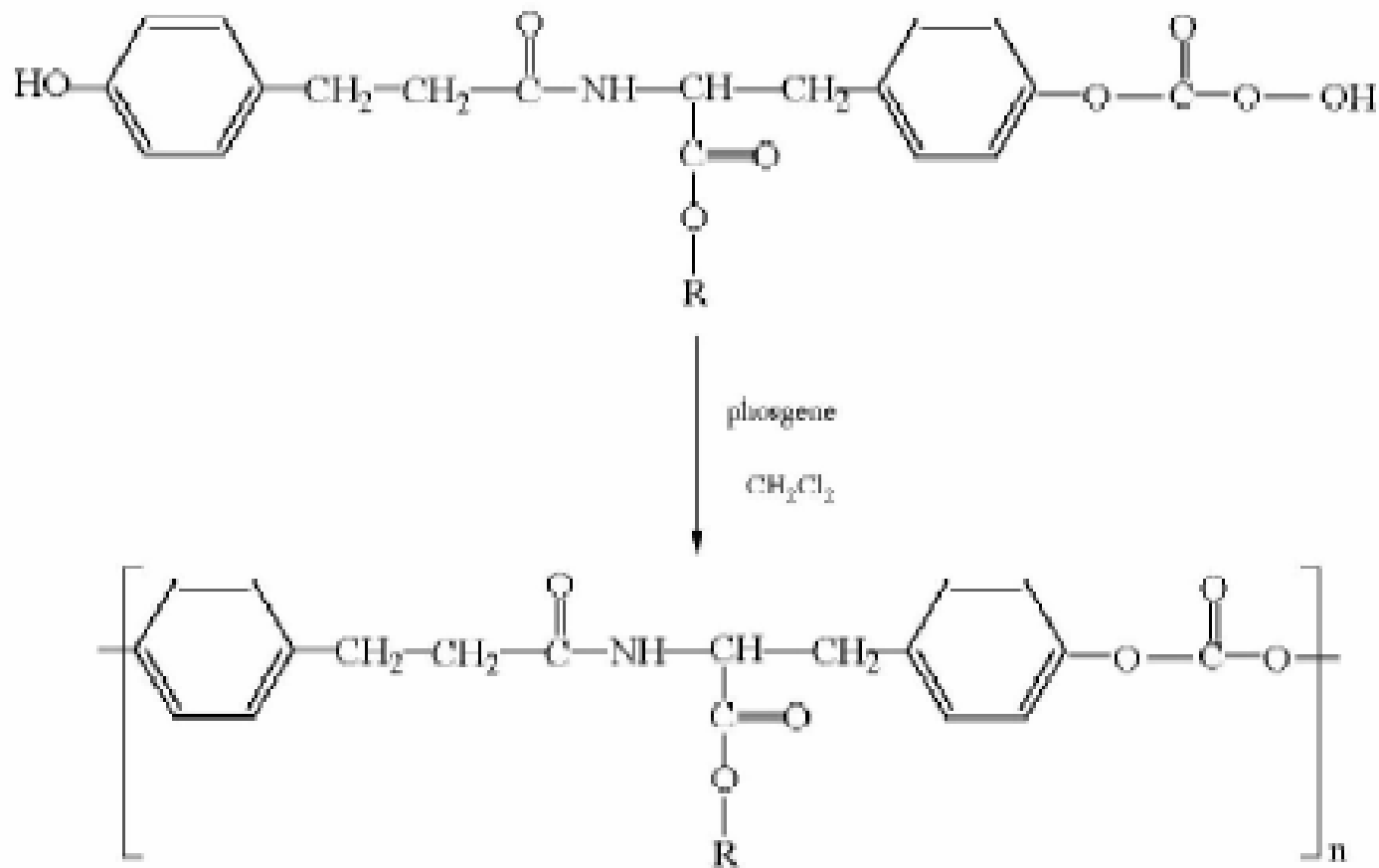
Poly(3-hydroxybutyrate)



poly[1,6-bis(carboxyphenoxy) sebacic acid]



Polyanhydride is used to deliver carmustine, an anticancer drug, to sites in the brain where a tumor has been removed. The degradation products are non-toxic and have controlled surface erosion degradation mechanism that allows delivery of drugs at a known rate. (*Langer and coworkers, Brem, et al., 1995; Burkoth and Anseth, 2000*)



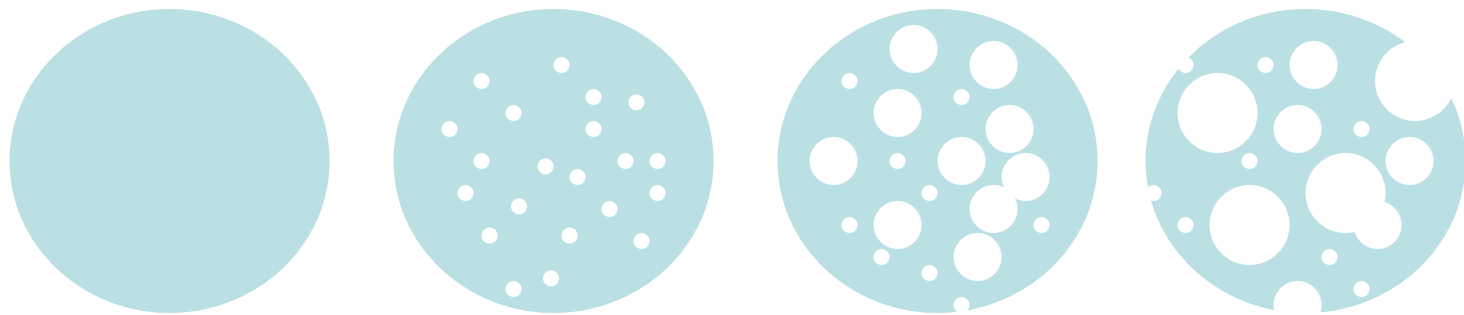
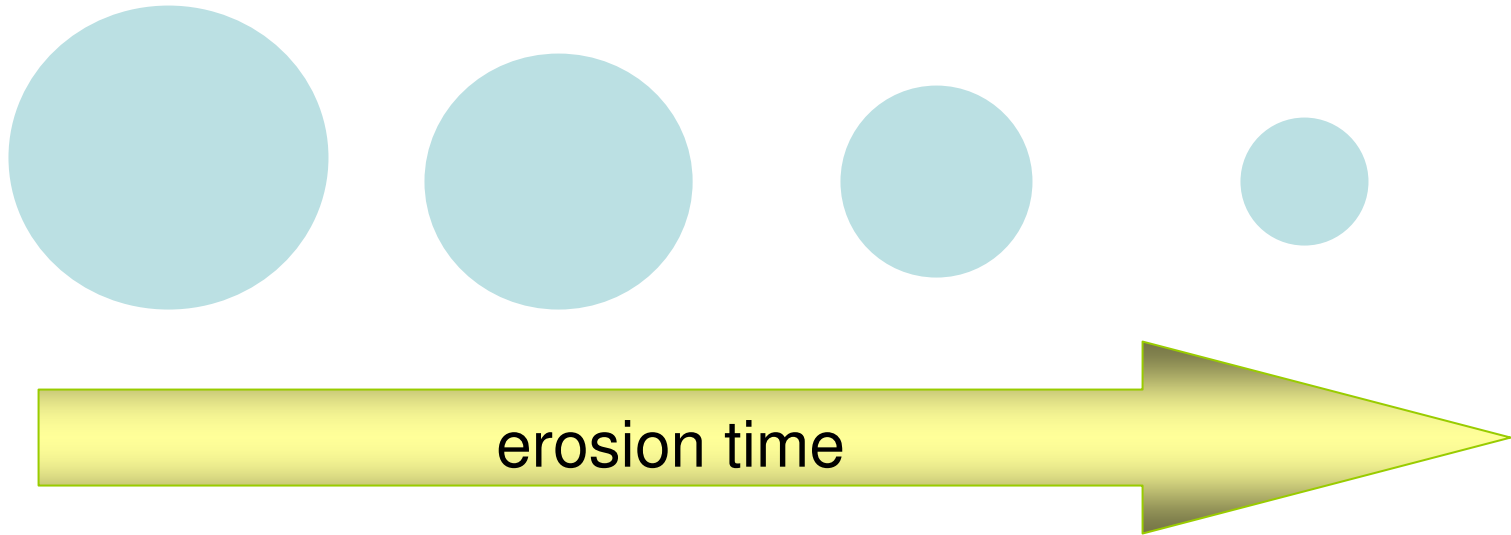
Tyrosine-based polycarbonates have been reported as promising degradable polymers for use in orthopaedic applications (Muggli *et al.*, 1998; Tangpasuthadol *et al.*, 2000a,b). These polymers possess three potentially hydrolysable bonds: amide, carbonate and ester.

Polymer Degradation and Erosion

The chemical degradation that occurs as a consequence of hydrolysis or enzymatic reaction will result in the physical erosion of the polymer device. The manner in which that erosion takes place is important to the performance of the device. Two distinct modes of erosion have been identified.

1. Surface (or heterogeneous) erosion
2. Bulk (or homogeneous) erosion

Surface Erosion



Bulk Erosion

Surface versus Bulk Erosion

The advantage of the surface eroding polymers is the predictability of the erosion process. The size of the device will decrease, but the shape will be retained. This is desirable for drug delivery applications, where the release of the drug can be related directly to the rate of erosion of the polymer.

For bulk eroding polymers, degradation is not confined to the surface of the device. The size of the device will remain nominally constant for a substantial portion of the erosion time. This is more desirable for tissue engineering applications.

Polymer Device Erosion

Although chemical degradation is the fundamental causal process that results in erosion, polymer erosion is more complex than degradation. The physical erosion process depends on many other processes, such as chemical kinetics, swelling, monomer/oligomer dissolution, monomer/oligomer diffusion, morphological changes (e.g. oligomer crystallization).

Characterization of erosion can involve monitoring molecular weight, weight loss and changing geometry. The complex interaction between these parameters, however, can be confounding. Some poly(anhydrides) can show a substantial molecular weight loss, while there is no loss of mass and no change in geometry. Because of this, erosion must be evaluated for each polymer and each fabricated device.

A Quantitative Distinction Between Surface and Bulk Erosion

Surface erosion proceeds by the hydrolysis and removal of fragments from the surface. This limits mass loss to occur only from the surface.

For bulk erosion to occur the fluid must diffuse into the polymer. The time, t_{diff} , for water to travel a mean distance can be calculated from the diffusion constant of water in the polymer.

The average time to degrade several polymer bonds, $E(t_n)$, can be calculated from hydrolysis kinetics.

The time scales of water diffusion into the polymer and the degradation of polymer bonds can be compared.

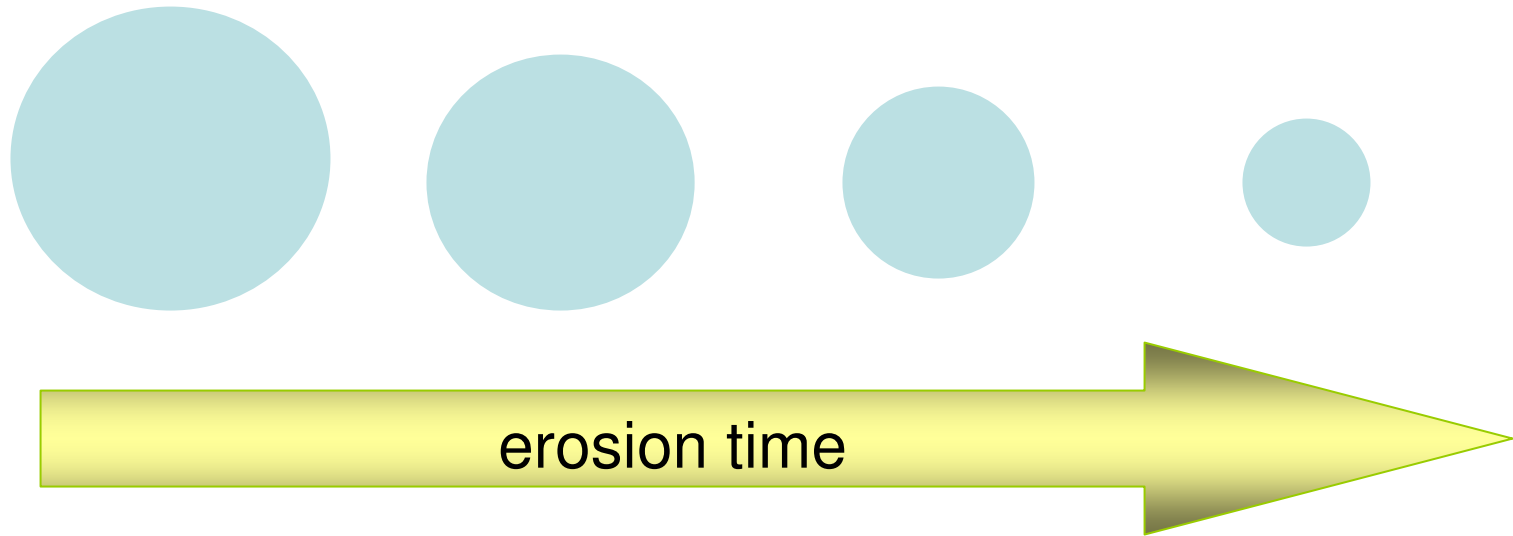
Water Diffusion and Polymer Degradation

A dimensionless erosion number can be defined as the ratio of the water diffusion time and the polymer degradation time,

$$\varepsilon = \frac{t_{diff}}{E(t_n)} = \frac{\text{water diffusion time}}{\text{hydrolysis time}}$$

- If the hydrolysis is fast compared to water diffusion, $E(t_n) \ll t_{diff}$, then surface erosion will occur
- If the diffusion of water is fast compared to hydrolysis, $E(t_n) \gg t_{diff}$, then bulk erosion will occur.

Surface Erosion: $E(t_n) \ll t_{\text{diff}}$, hydrolysis faster than diffusion



Bulk Erosion: $E(t_n) \gg t_{\text{diff}}$, diffusion faster than hydrolysis

Length Scale of Diffusion and Hydrolysis

The time for diffusion of water is a function of the distance that the water has to travel. The time to degrade n polymer bonds is related to the length scale of those bonds.

$$t_{diff} = f_1(L)$$

$$E(t_n) = f_2(L)$$

For $\epsilon > 1$ surface erosion occurs, and for $\epsilon < 1$ bulk erosion. For large devices where L is small relative to device size, surface erosion will dominate. However, since both t_{diff} and $E(t_n)$ depend on L , as the device erodes there is an $L_{critical}$ where $\epsilon = 1$, and there is a change from surface to bulk erosion mechanism.

Chemical structure	Polymer	λ (s ⁻¹)	ϵ^a	L_{critical}^b
$\left[\text{R}-\overset{\text{O}}{\parallel}\text{C}-\text{O}-\overset{\text{O}}{\parallel}\text{C} \right]$	Poly(anhydrides)	1.9×10^{-3} Ref. [30]	11,515	75 μm
$\left[\text{O}-\underset{\text{R}}{\overset{\text{R}}{\text{C}}}-\text{O}-\text{R} \right]$	Poly(ketal)	6.4×10^{-5} Ref. [30]	387	0.4 mm
$\left[\text{O}-\underset{\text{R}}{\overset{\text{OR}}{\text{C}}}-\text{O}-\text{R} \right]$	Poly(ortho esters)	4.8×10^{-5} Ref. [30]	291	0.6 mm
$\left[\text{O}-\underset{\text{R}}{\overset{\text{H}}{\text{C}}}-\text{O}-\text{R} \right]$	Poly(acetal)	2.7×10^{-8} Ref. [30]	0.16	2.4 cm
$\left[\text{O}-(\text{CH}_2)_5-\overset{\text{O}}{\parallel}\text{C} \right]$	Poly(ϵ -caprolactone)	9.7×10^{-8} Ref. [31]	0.1	1.3 cm
$\left[\text{O}-\underset{\text{CH}_3}{\overset{\text{H}}{\text{C}}}-\overset{\text{O}}{\parallel}\text{C} \right]$	Poly(α -hydroxy-esters)	6.6×10^{-9} Ref. [30]	4.0×10^{-2}	7.4 cm
$\left[\text{N}-\underset{\text{R}}{\overset{\text{H}}{\text{C}}}-\overset{\text{O}}{\parallel}\text{C} \right]$	Poly(amides)	2.6×10^{-13} Ref. [30]	1.5×10^{-6}	13.4 m

Summary

1. The physics of the macromolecular chain allow a uniquely wide range of physical behavior for polymer materials.
2. Physical behavior of polymer material is strongly influenced by internal morphology, chain flexibility and molecular weight.
3. Polymer molecular weight must be described statistically as the number average or weight average molecular weight.
4. In terms of forming technologies, there are two types of polymer materials; thermoplastics and thermosets
5. Degradable medical devices are typically fabricated from polymers with chemically hydrolysable bonds. Polymers of this type include poly(esters), poly(amides) and poly(anhydrides).
6. There are two physical mechanisms of erosion; surface erosion and bulk erosion. Depending on device application, one mechanism will be preferred over the other.