



生醫材料導論

合成生醫高分子

Synthetic biopolymer

曾靖嬪

Ching-Li Tseng

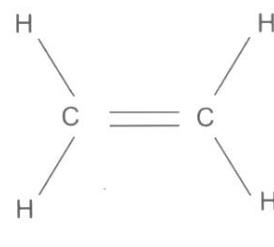
Graduate Institute of Biomedical Materials & Tissue Engineering
Taipei Medical University

Repeat Units

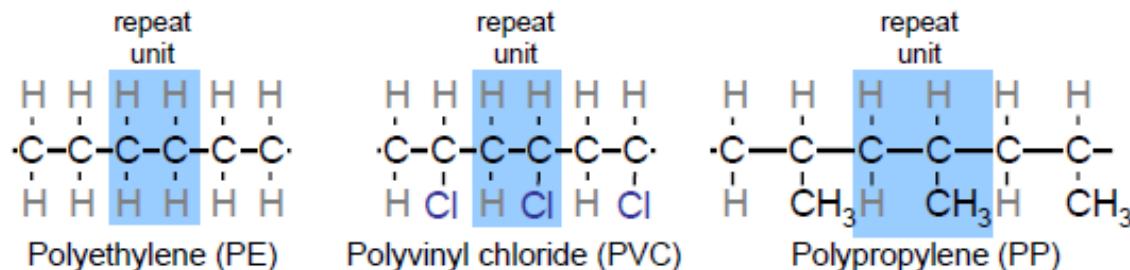
Polymer

Poly + mer

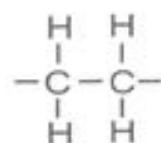
- A “mer” is a structural entity composed of a fixed number of atoms in a given structure that is repeated over and over to form the polymer.
- Through covalent bonding in the main molecular chain backbone with C, N, O, Si, etc.
- Repeating unit (n) > 1,000.
- Also called macromolecules because of their size, which can be on the order of 10^5 - 10^6 g/mol.
- Hydrogen-carbon covalent bonds as a main constituent.



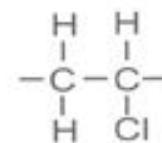
ethylene



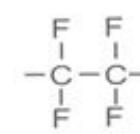
Adapted from Fig. 14.2, Callister 7e.



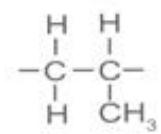
Polyethylene (PE)



Polyvinyl chloride (PVC)

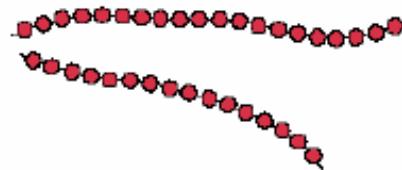


Polytetrafluoroethylene (PTFE)

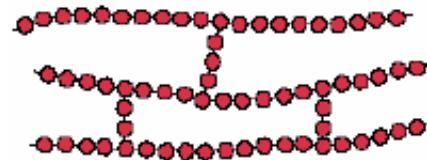


Polypropylene (PP)

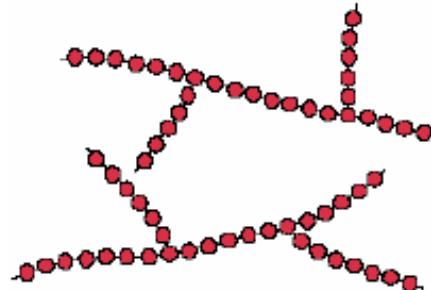
Repeat Units



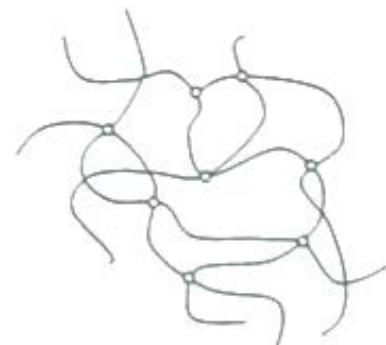
Linear



Cross-linking



Branch



Net-work



Graft copolymer

.....AAAAAAA.....

Homopolymer

.....ABABABAB.....

Alternating-copolymer

.....AABABBAABABBABBB.....

Random-copolymer

.....AAABBBAAA.....

Block copolymer

TABLE 2.5

Structure of Common Polymers

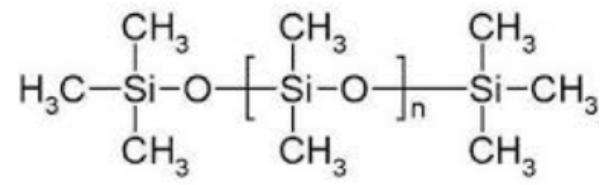
Polymer	Structure
Poly(ethylene)(PE)	$\text{---CH}_2\text{---CH}_2\text{---}$ n
Poly(ethylene glycol) (PEG) 聚乙二醇	$\text{---CH}_2\text{---CH}_2\text{---O---}$ n
Poly(styrene) (PS) 聚苯乙烯	$\left[\text{---CH}_2\text{---CH}(\text{C}_6\text{H}_5)\text{---} \right]_n$
Poly(methyl methacrylate) (PMMA)	$\left[\text{---CH}_2\text{---C}(\text{CH}_3)(\text{COOCH}_3)\text{---} \right]_n$
Poly(glycolic acid) (PGA) 聚乙醇酸	$\left[\text{---O---CH}_2\text{---C}(=\text{O})\text{---} \right]_n$
Poly(lactic acid) (PLA) 聚乳酸	$\left[\text{---O---CH}(\text{CH}_3)\text{---C}(=\text{O})\text{---} \right]_n$
Poly(tetrafluoroethylene) (PTFE) 聚四氟乙烯	$\text{---CF}_2\text{---CF}_2\text{---}$ n

Repeat Units

Table 7-1. History of Some Commercially Important Polymers

Date	Polymer	Date	Polymer
1930	Styrene-butadiene rubber	1944	Polyethylene terephthalate
1936	Polyvinyl chloride	1947	Epoxies
1936	Polychloroprene (Neoprene)	1955	Polyethylene, linear
1936	Polymethylmethacrylate	1956	Polyoxymethylene
1937	Polystyrene	1957	Polypropylene
1939	Nylon 66	1957	Polycarbonates
1941	Polytetrafluoroethylene	1964	Ionomer resins
1942	Unsaturated polyesters	1965	Polyimides
1943	Polyethylene, branched	1970	Thermoplastic elastomers
1943	Nylon 6	1974	Aromatic polyamides
1943	Silicones	1980s	Ultrahigh-molecular-weight polyethylene

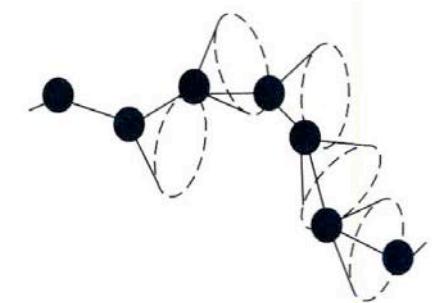
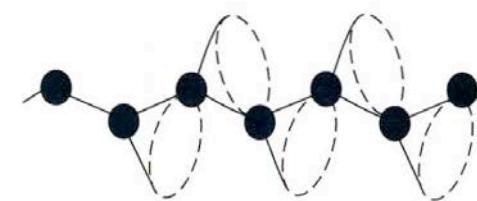
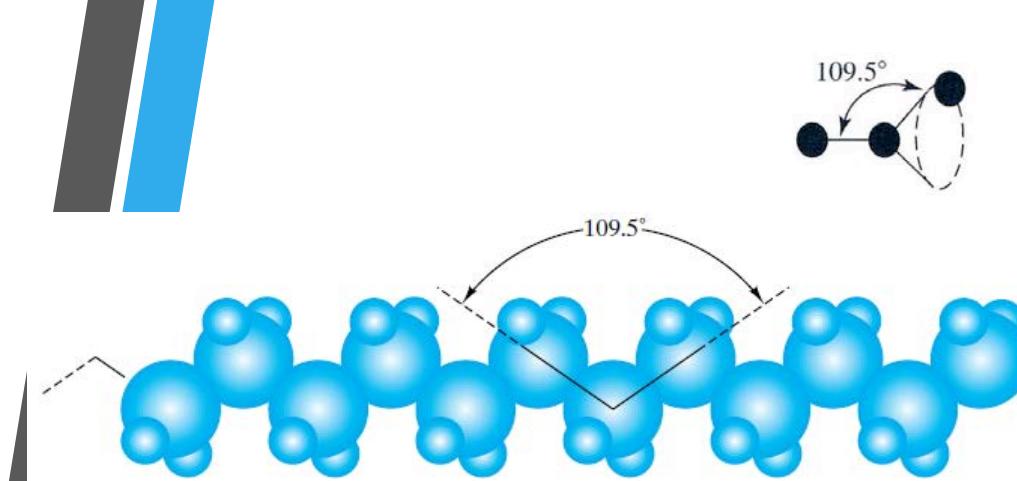
Modified with permission from Billmeyer (1984). Copyright © 1984, Wiley.

Polydimethylsiloxane
(PDMS)

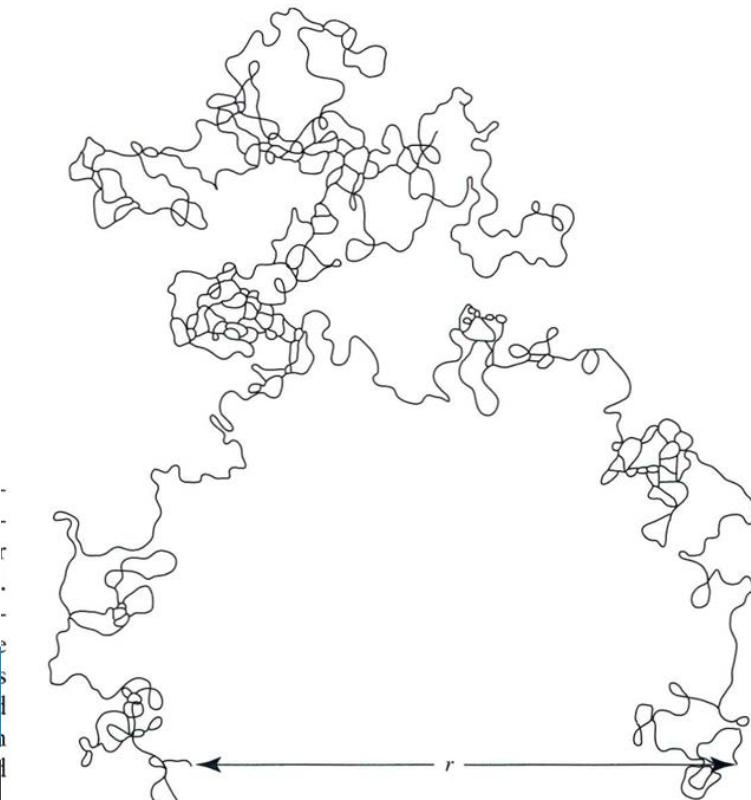
商標名Teflon®

聚二甲基矽氧烷

Configuration



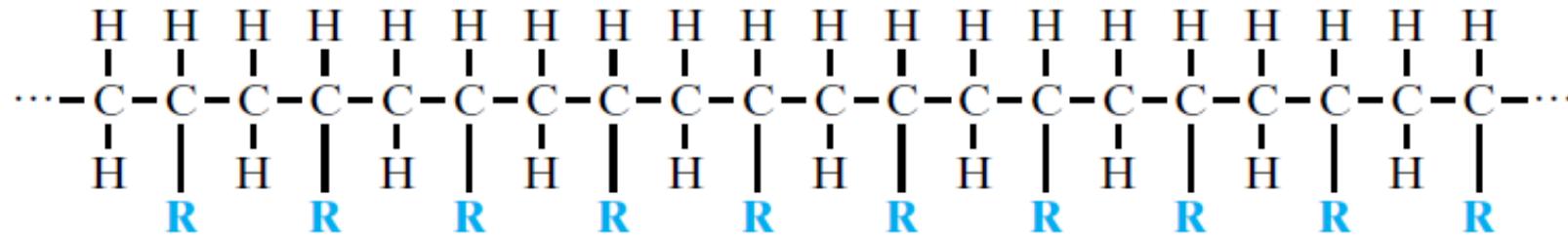
Single macromolecules can take a **variety of shapes**, primarily due to the **rotation of the carbon atoms in the backbone**



□ Isotactic configuration (等規)

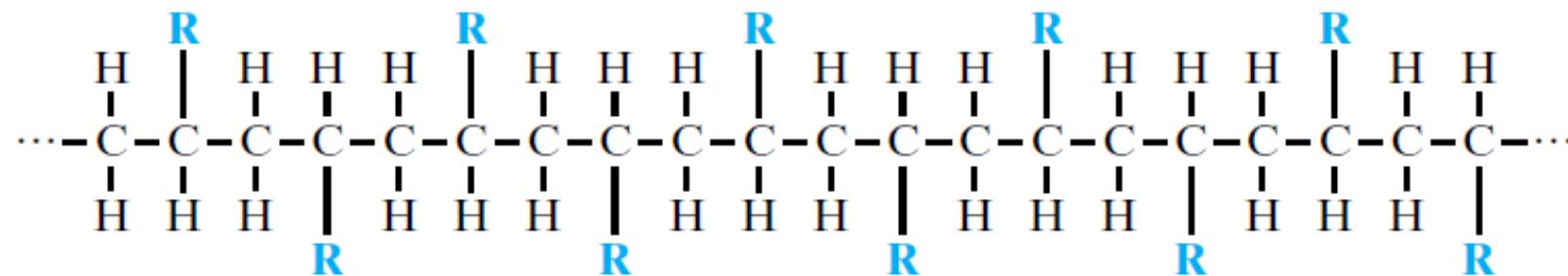
Configuration

R groups are arranged on **the same** side of the chain.



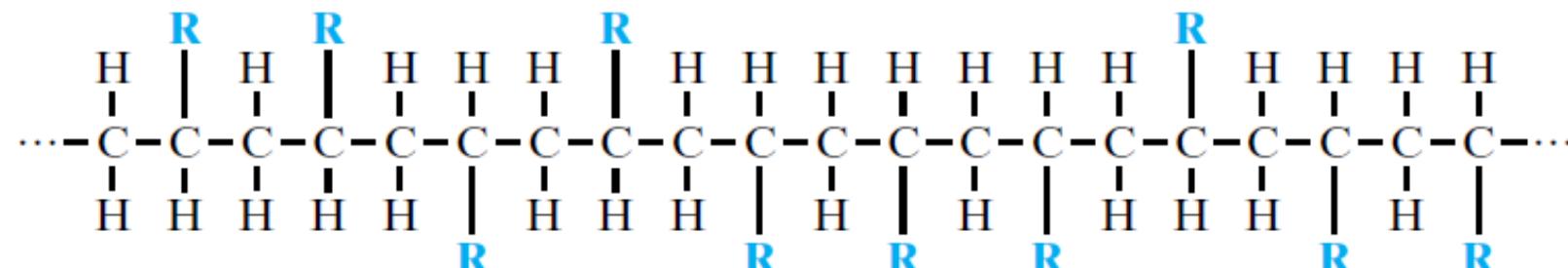
□ Syndiotactic configuration (間規)

R groups **alternate positions** on either side of the chain, **regularly**.



□ Atactic configuration (無規)

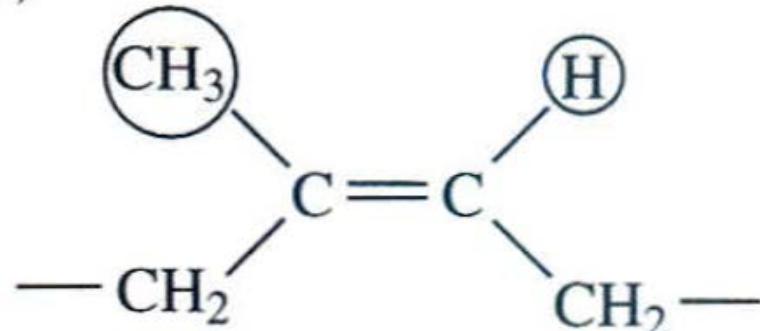
R groups are situated **randomly**.



Configuration

Polymer with C=C

(a)

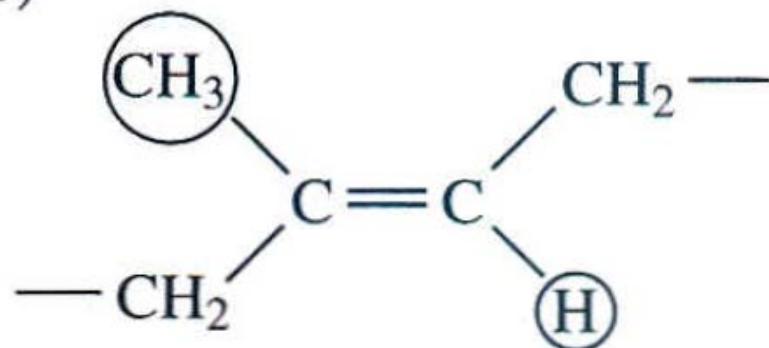


Cis- form

CH_3 and H constituents are found on the **same side** of the $\text{C}=\text{C}$.

cis-polyisoprene (natural rubber)

(b)



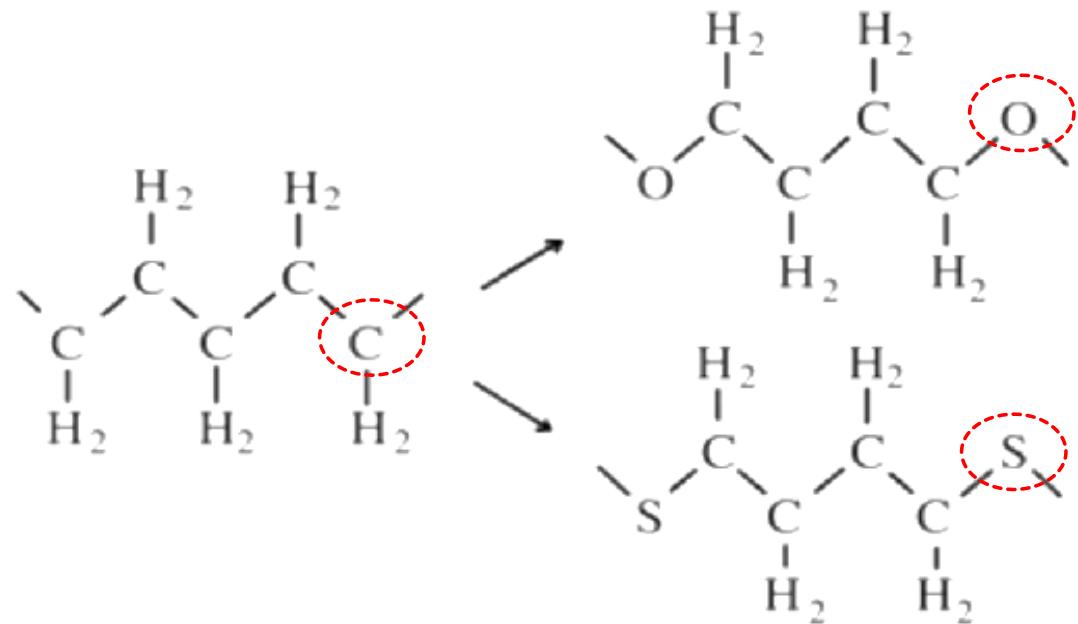
Trans-form

CH_3 and H constituents are found on **opposite side** of the $\text{C}=\text{C}$.

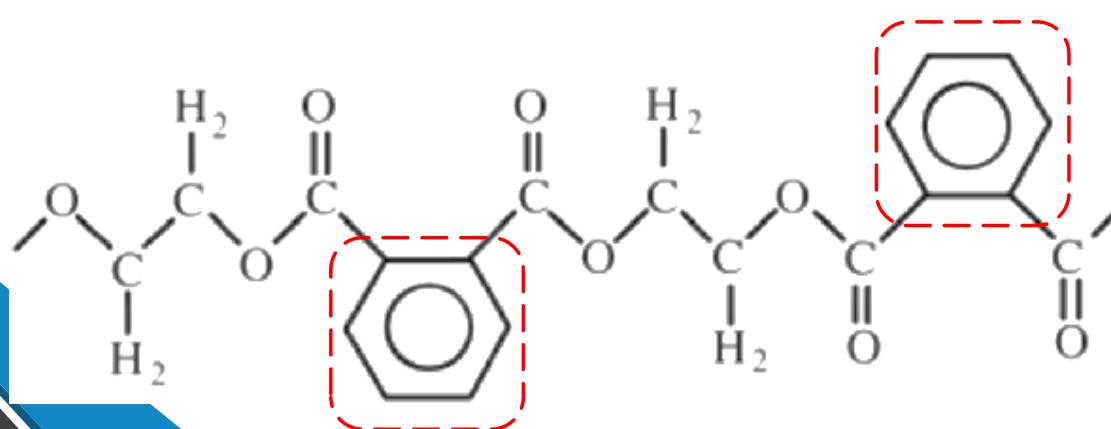
trans-polyisoprene (gutta percha)

Effect of Composition

Chemical composition of the backbone
(the main molecular chain) or of side chains)



Flexible



polyethylene terephthalate

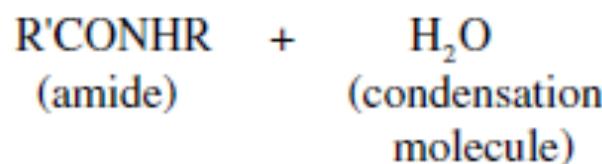
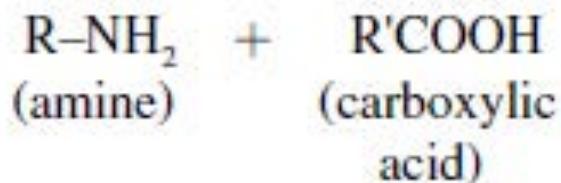
(polyester, Dacron®)

stiffer

Polymerization

- Condensation
- Additional polymerization

Condensation



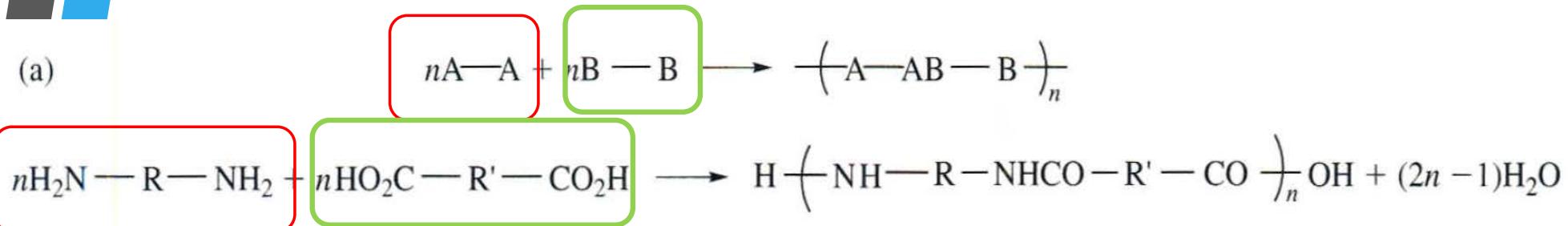
The condensing molecule is always water (H_2O).

TABLE 1.2.2.3 Examples of Common Organic Reactions

Reactants	Product
$R-OH + \text{C}_3\text{H}_5O-$ Alcohol epoxide	$R-O-CH_2-CH_2-OH$ Ether bond
$R-OH + HO-C(=O)-R'$ Alcohol carboxylic acid	$R-O-C(=O)-R'$ Ester bond
$R-C(=O)-OH + \begin{array}{c} H \\ \\ N-R' \\ \\ H \end{array}$ Carboxylic acid amine	$R-C(=O)-N(H)-R'$ Amide bond
$\begin{array}{c} H \\ \\ R-N(H)- \\ \\ H \end{array} + O=C=N-R'$ Amine isocyanate	$R-N(H)-C(=O)-N(H)-R'$ Urea bond
$R-OH + O=C=N-R'$ Alcohol isocyanate	$R-O-C(=O)-N(H)-R'$ Urethane bond

Condensation

(a)



(b)

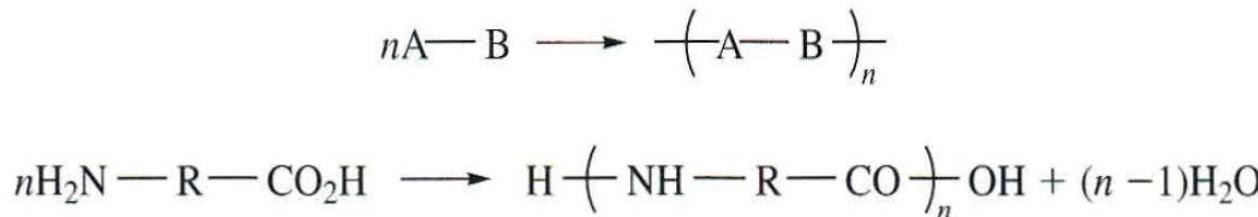
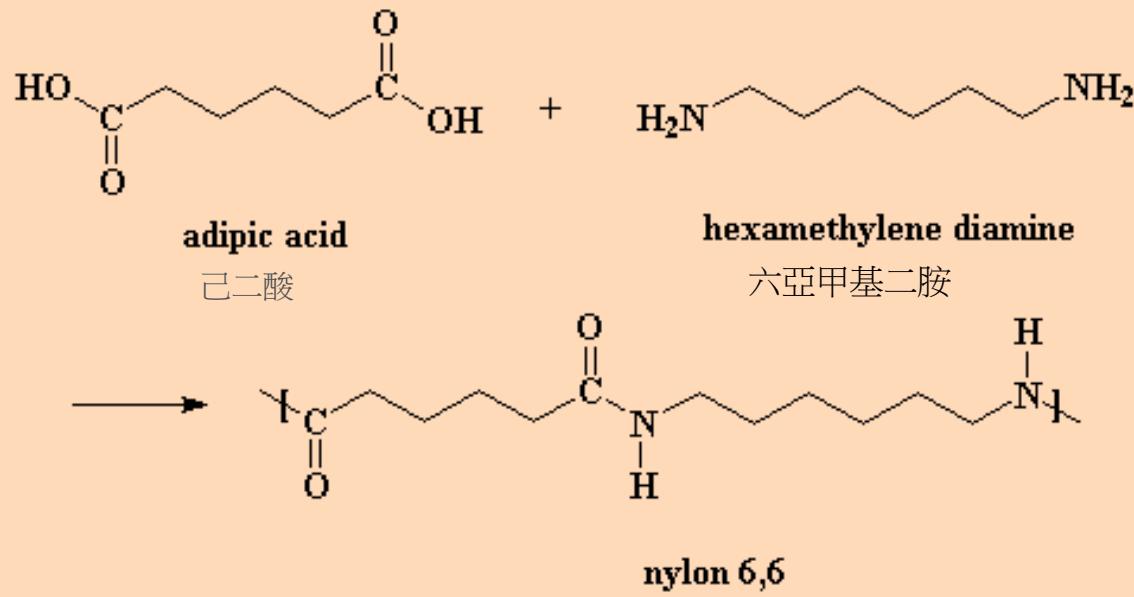


Figure 2.29

Condensation, or step reaction, polymerization mechanisms can be classified into two general groups, depending upon the types of monomers involved in the reaction. (a) The first group involves bifunctional or polyfunctional monomers, with each monomer possessing only one type of functional group. (b) The second group involves a single monomer species having both types of functional groups. In this figure, the general equation for each reaction mechanism (A and B are two different types of functional groups) is followed by an example reaction. (Adapted with permission from [10].)

Condensation



Condensation reaction of adipic acid and hexamethylenediamine to produce a repeat unit of Nylon 6.6.

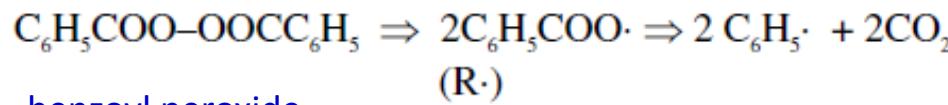
Table 7-2. Typical Condensation Polymers

Type	Interunit linkage
Polyester	O -C-O-
Polyamide	O H I -C-N-
Polyurea	H O H -N-C-N-
Polyurethane	O H I -O-C-N-
Polysiloxane	R -Si-O- R
Protein	O H I -C-N-
Cellulose	-C-O-C-

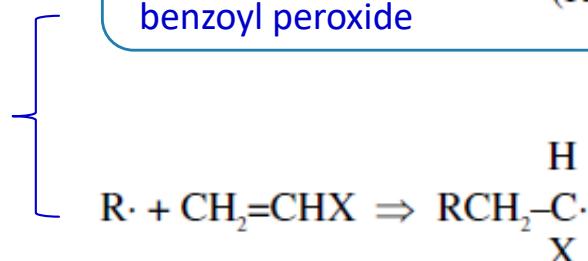
Addition or Free Radical Polymerization

(1) Initiation

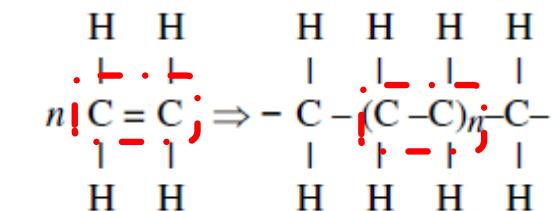
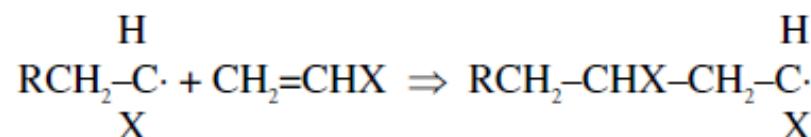
Free radical as initiator



benzoyl peroxide

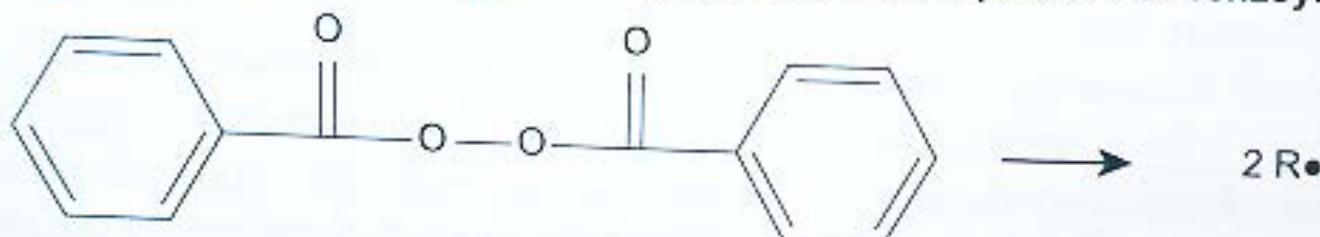


The breaking of a double bond can be made with an initiator



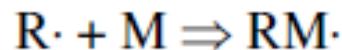
The free radicals (initiators) can react with monomers

Initiation - free radicals are generated through the decomposition of benzoyl peroxide.

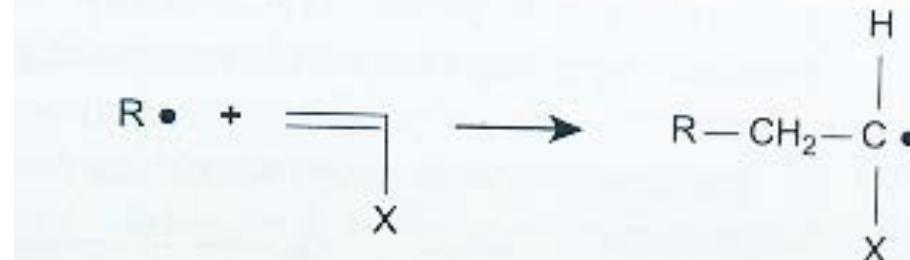


Addition or Free Radical Polymerization

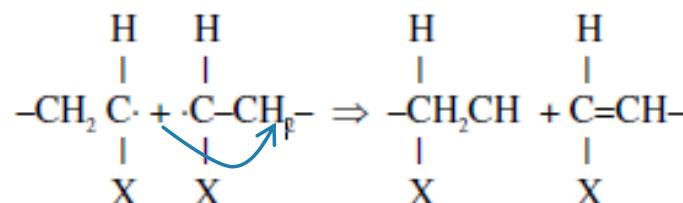
(2) Propagation



Propagation - free radicals produce polymer chains through addition across carbon-carbon double bonds. X denotes a generic side group.

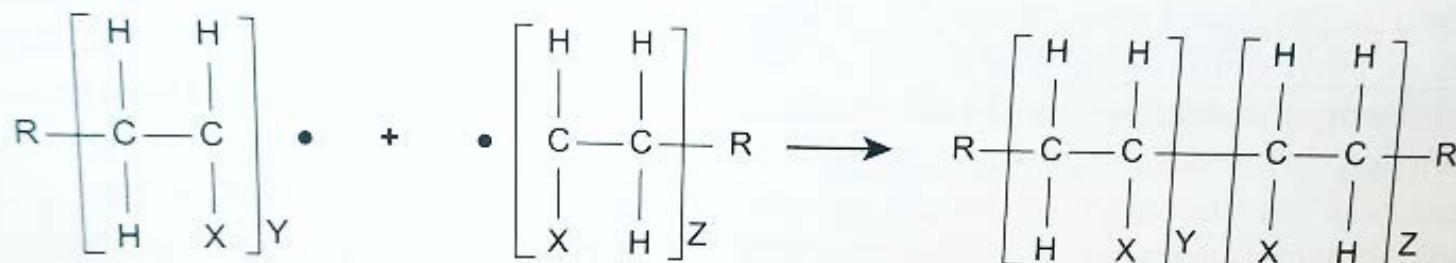


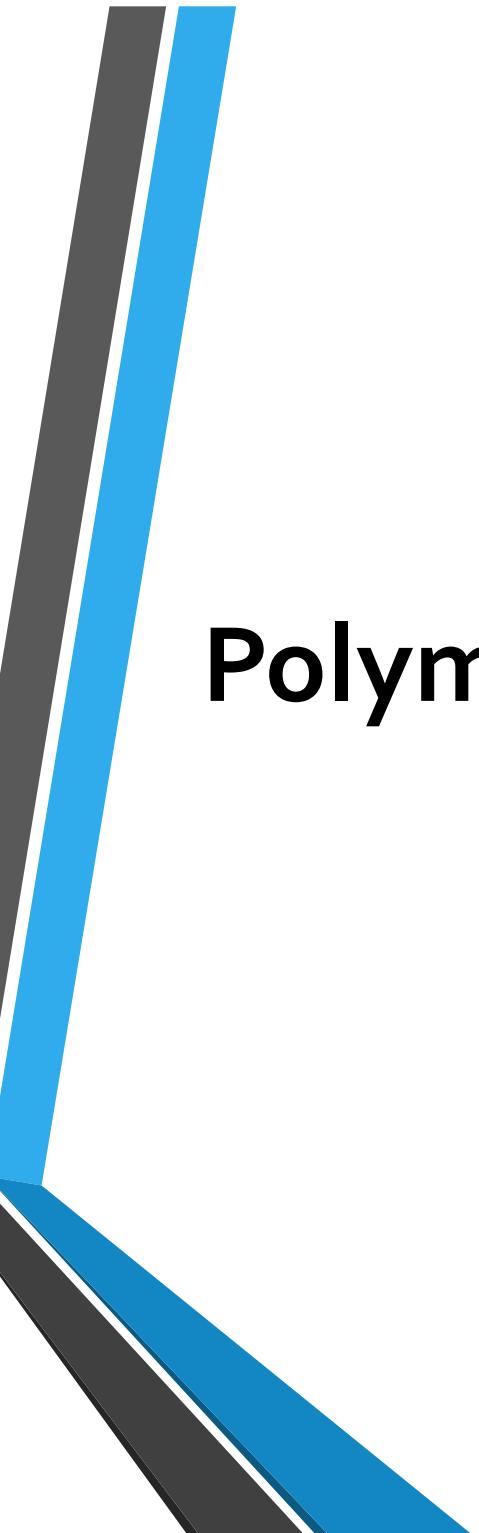
(3) Termination



Disproportionate termination

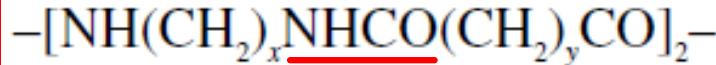
Termination - two free radicals react to form a single bond through coupling to form one polymer chain.





Polymeric Implant Materials

Polyamides (聚醯胺)

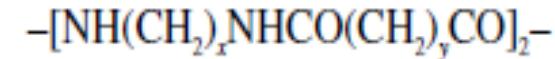


diamines and diacids

Polyamides

Nylon 6 ($x = 5$)

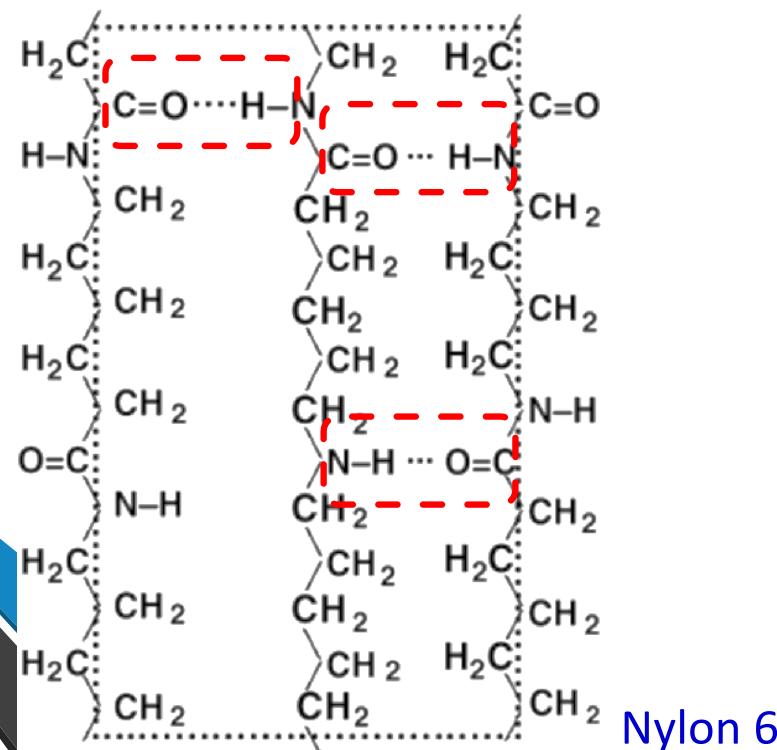
Nylon 11 ($x = 10$)



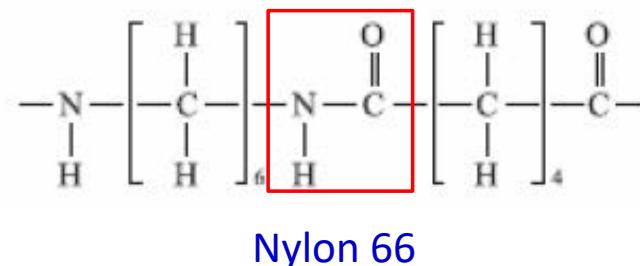
Nylon 66 ($x = 6, y = 4$)

Nylon 610 ($x = 6, y = 8$)

- Designated by the number of carbon atoms in the repeating units.
- Nylons can be polymerized by step-reaction (or condensation) and ring-scission polymerization.

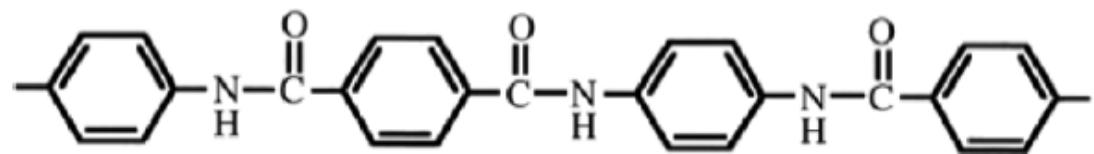


- Excellent fiber-forming ability due to **interchain hydrogen bonding** and a high degree of crystallinity, which increases strength in the fiber direction
- Proteolytic enzymes aid to hydrolyze** by attacking the amide group.



Polyamides (Nylons)

- The number and distribution of –CONH– groups are important factors.
- They have excellent fiber-forming ability due to interchain hydrogen bonding.
- A high degree of crystallinity, which increases strength in the fiber direction.
- The nylons are hygroscopic (吸濕) and lose their strength *in vivo* when implanted. The water molecules serve as plasticizers, which attack the amorphous region.



Kevlar[®] poly (p-phenylene terephthalate)

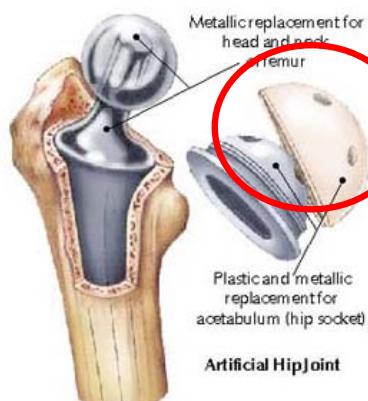
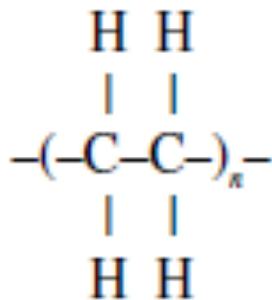
Table 7-5. Properties of Polyamides

Properties	66	610	6	11	Aramid ^a	Kevlar ^b
Density (g/cm ³)	1.14	1.09	1.13	1.05	1.30	1.45
Tensile strength (MPa)	76	55	83	59	120	2700
Elongation (%)	90	100	300	120	<80	2.8
Modulus of elasticity (GPa)	2.8	1.8	2.1	1.2	>2.8	130
Softening temperature (°C)	265	220	215	185	275	–

^a Molded parts, unfilled.

^b Kevlar[®] 49 (duPont) fibers.

Polyethylene (PE) 聚乙烯



acetabular cup of a hip joint prosthesis

- Linear crystallized thermoplastics
- High-density polyethylene **does not contain branches**. The result is better packing of chains, which increases density and crystallinity.
- The crystallinity is usually **50 to 70%** and **70 to 80%** for the **low-** and **high-**density polyethylenes, respectively.
- **UHMWPE (ultrahigh-molecular-weight polyethylene)** have a longer chain fold length than the conventional PE with **increasing crystallinity**, often used for such load-bearing surfaces as total hip and knee joints.

Properties	Low density	High density	UHMWPE*	Enhanced UHMWPE ^b
Molecular weight (g/mol)	$3\sim4 \times 10^3$	5×10^3	2×10^6	same
Density (g/cm ³)	0.90–0.92	0.92–0.96	0.93–0.94	same
Tensile strength (MPa)	7.6	23–40	27 min.	higher
Elongation (%)	150	400–500	200–250	same
Modulus of elasticity (MPa)	96–260	410–1,240	c	2,200
Crystallinity (%)	50–70	70–80	d	e

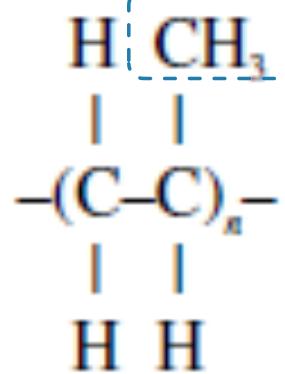
* Data from ASTM F648: also, 2% deformation after 90 minutes recovery subjected to 7 MPa for 24 hours (D621).

^c Close to 2,200 MPa.

^d Higher than high-density polyethylene

^e Equal or slightly higher than d.

Polypropylene (PP) 聚丙烯



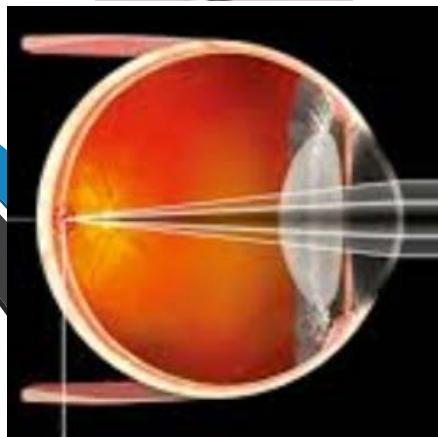
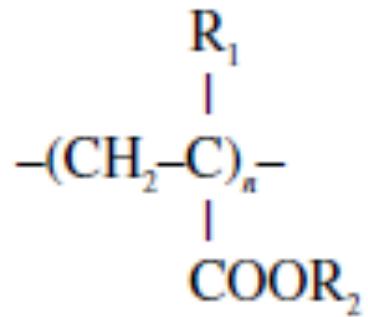
- They usually crystallize.
- Polypropylene has an **exceptionally high flexural fatigue life**; hence it has been used to make integrally molded hinges for finger joint prostheses.
- It also has **excellent environmental stress-cracking resistance**. The permeability of polypropylene to **gases** and **water vapor** is between that of low- and high-density polyethylene.



Table 7-7. Properties of Polypropylene

Properties	Values
Density (g/cm ³)	0.90–0.91
Tensile strength (MPa)	28–36
Elongation (%)	400–900
Modulus of elasticity (GPa)	1.1–1.55
Softening temperature (°C)	150

Polyacrylates (聚丙烯酸酯)



polymethyl-acrylate (**PMA**):

$\text{R}_1: \text{H}$ $\text{R}_2: \text{CH}_3$

polymethyl-methacrylate (**PMMA**) $\text{R}_1=\text{R}_2=\text{CH}_3$

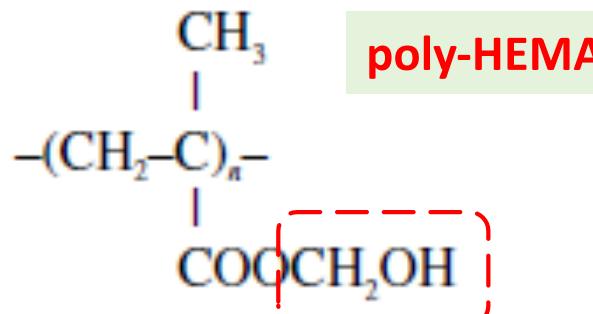
- Used extensively in medical applications as (hard) **contact lenses**, **implantable ocular lenses**, and as **bone cement** for joint prosthesis fixation.
- The bulky side groups inhibit crystallization; therefore, these polymers are **usually amorphous**, and lacking heterogeneities to scatter light, are **transparent**.
- Hard and brittle in comparison with other polymers.

	PMA	PMMA
Tensile strength	7 Mpa	60 MPa
Softening Temp.	33°C	125°C
Light transparency		92% transmission
Refraction		1.49

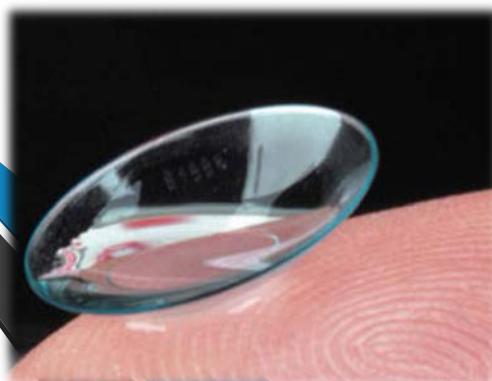
Poly-acrylates

First hydrogel polymer

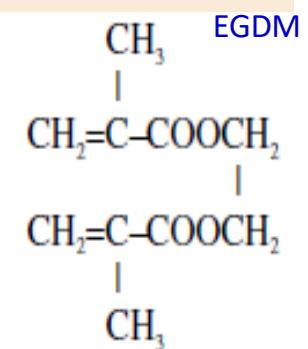
poly(hydroxyethyl-methacrylate)



HEMA unit



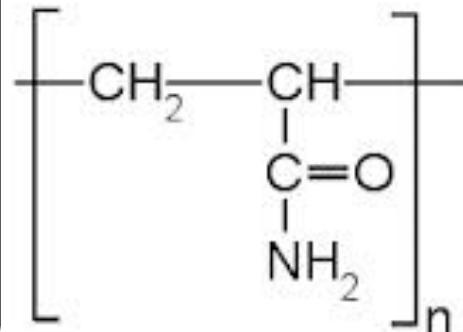
- The **OH group** is the **hydrophilic group** responsible for hydration of the polymer. (Absorb water more than 30% of its weight)
- Transparent
- Crosslinking agent such as ethylene glycol dimethacrylate (EGDM), a hydrophilic monomer.



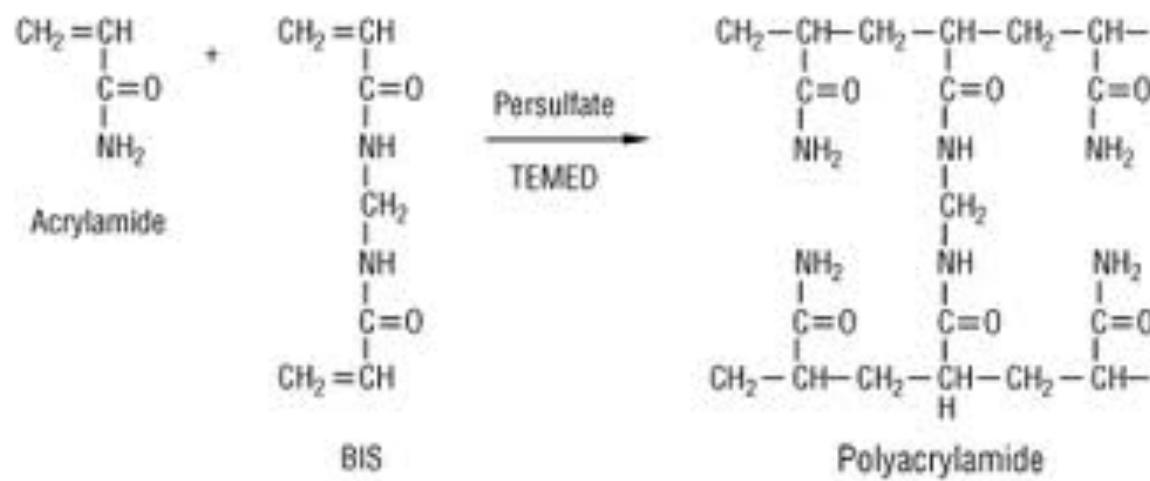
Material	Tensile Modulus (GPa)	Tensile Strength (MPa)	Elongation at Break (%)	Water Absorption (%)
Polyethylene (PE)	0.8–2.2	30–40	130–500	0.001–0.02
Poly(methyl methacrylate) (PMMA)	3–4.8	38–80	2.5–6	0.1–0.4
Polytetrafluoroethylene (PTFE)	1–2	15–40	250–550	0.1–0.5
Polylactide (PLA)	3.4	53	4.1	<0.5
Poly(hydroxyethyl 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

Polyacrylates (聚丙烯酸酯)

polyacrylamide hydrogel



- Water content of the copolymer can be increased to over 60%.
- Have a relatively low oxygen permeability in comparison with silicone rubber.
- The oxygen permeability can be increased with increased hydration (water content) or decreased (lens) thickness.



骨水
泥

Bone Cement (PMMA)

Bone cement has been used for clinical applications to secure **firm fixation** of joint prostheses for hip and knee joints

- Primarily made of **poly(methylmethacrylate) powder** and monomer **methylmethacrylate liquid**,

<https://www.youtube.com/watch?v=7BCPpMHbfIQ>

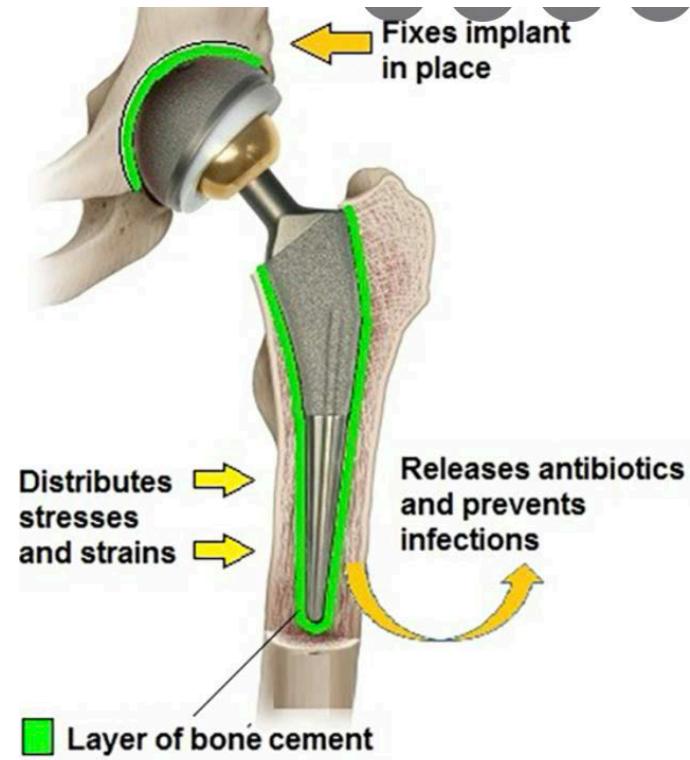


Table 7-9. Composition of Bone Cement*

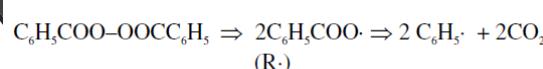
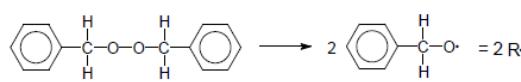
▲ Liquid component (20 ml)

Methyl methacrylate (monomer)	97.4 v/o (volume %)
N,N-dimethyl-p-toluidine <small>promote curing of the finished compound</small>	2.6 v/o
Hydroquinone <small>prevent premature polymerization</small>	75 ± 15 ppm

▲ Solid powder component (40 g)

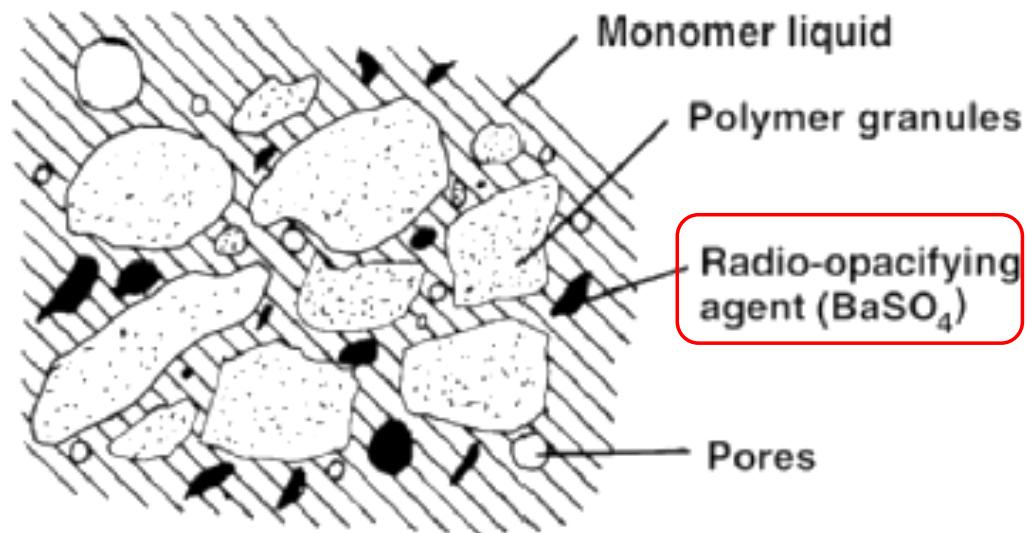
Polymethyl methacrylate	15.0 w/o (weight %)
Methyl methacrylate-styrene-copolymer	73.5 w/o
Barium sulfate (BaSO_4), USP	10.0 w/o
Dibenzoyl peroxide <small>activator</small>	1.5 w/o

Initiator: example - benzoyl peroxide



*Surgical Simplex® P Radiopaque Bone Cement (Howmedica Inc. Rutherford, NJ) (1977).

Bone Cement (PMMA)



Large pores are detrimental to the mechanical properties



Table 7-12. Molecular Weight of Bone Cement

Types of m.w. (g/mol)	Monomer	Powder	Cured
M_n (number average)	100	44,000	51,000
M_w (weight average)	100	198,000	242,000

Table 7-10. Requirements for Powder Liquid Mixture

Maximum dough time (min)	Setting time range (min)	Maximum exotherm ($^{\circ}\text{C}$)	Minimum intrusion (mm)
5.0	5-15	90	2.0

From ASTM F451.

Bone Cement (PMMA)

Factors affecting bone cement properties

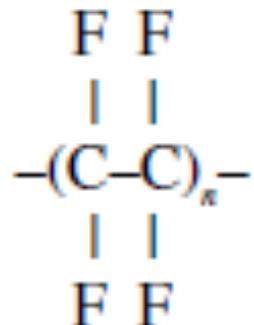
➤ Intrinsic Factors

- Composition of monomer and powder.
- Powder particle size, shape, and distribution; degree of polymerization.
- Liquid/ powder ratio.

➤ Extrinsic Factors

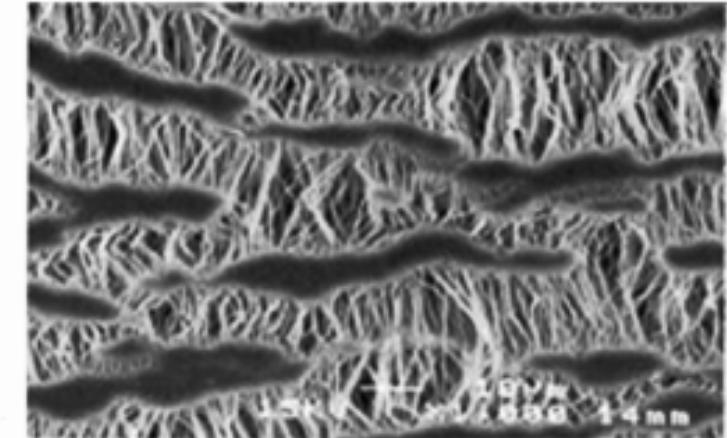
- Mixing environment; **temperature, humidity, type of container.**
- Mixing technique; rate and number of beating with spatula.
- Curing environment; temperature, humidity, pressure, contacting surface (tissue, air, water, etc.)

Fluorocarbon Polymers



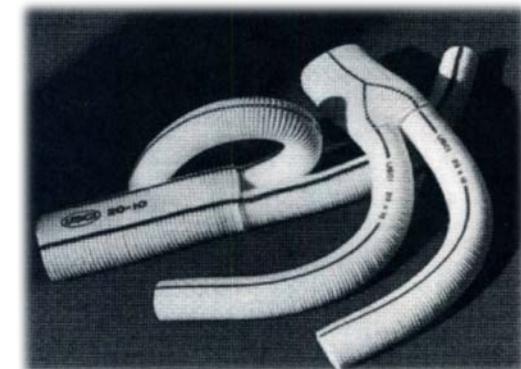
polytetrafluoroethylene (PTFE)
Teflon^R (DuPont)

Abbreviation	Generic polymer name	Structure
PTFE	Poly(tetrafluoroethylene)	$\begin{array}{c} \text{F} \quad \text{F} \\ \quad \\ +\text{---C---C---+}_n \\ \quad \\ \text{F} \quad \text{F} \end{array}$
PVDF	Poly(vinylidene fluoride)	$\begin{array}{c} \text{F} \quad \text{H} \\ \quad \\ +\text{---C---C---+}_n \\ \quad \\ \text{F} \quad \text{H} \end{array}$
FEP	Fluorinated ethylene-propylene	$\begin{array}{c} \text{F} \quad \text{F} \quad \text{F} \quad \text{F} \\ \quad \quad \quad \\ +\text{---C---C---C---C---+}_n \\ \quad \quad \quad \\ \text{F} \quad \text{F} \quad \text{CF}_3 \quad \text{F} \end{array}$



(b)

Microstructure of PTFE after being expanded.

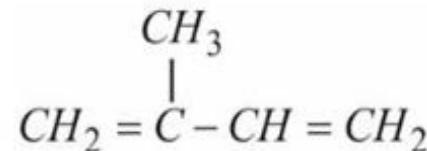


- Highly crystalline (over 94% crystallinity), with an average molecular weight of $0.5 \sim 5 \times 10^6$ g/mol.
- Has a very high density ($2.15 \sim 2.2$ g/cm³), and a low modulus of elasticity (0.5 GPa) and tensile strength (14 MPa).
- Has a very low surface tension (18.5 erg/cm²) and friction coefficient (0.1).
- Inert material

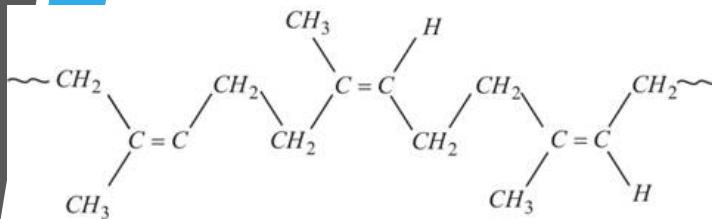
Rubbers

橡膠

cis-1,4 polyisoprene
(聚異戊二烯)



Structure of Isoprene: Monomer of Natural Rubber



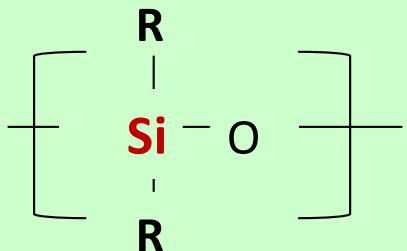
Natural rubber is made mostly from the **latex** of the *Hevea brasiliensis* tree

- Natural, and synthetic rubbers
- A material that at room temperature can be stretched repeatedly at least twice its original length and upon release of the stress, returns immediately with force to its approximate original length **by ASTM**
- Addition of **sulfur (5%)**, increase its tensile strength (*300 psi to 3000 psi*)



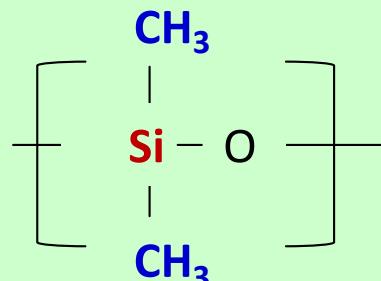
Rubber - Silicone

- General category of synthetic polymer whose back bone is made of repeating **silicone** to oxygen bonds.
- The silicone atoms are also bonded to organic groups, typically **methyl group**.
- The simultaneous presence of “**organic**” groups attached to an “**inorganic**” **backbone** gives silicones a combination of unique properties, making possible their use as fluids, emulsions, compounds, resins and elastomers in numerous application.
- Their **excellent biocompatibility** makes silicones well suited for use in numerous personal care, pharmaceutical, and medical device applications



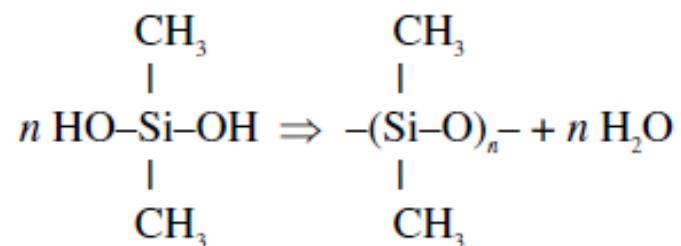
siloxane

矽氧烷



Polydimethylsiloxane

PDMS



Rubbers

Oxygen permeability of contact lenses made of various materials versus thickness.

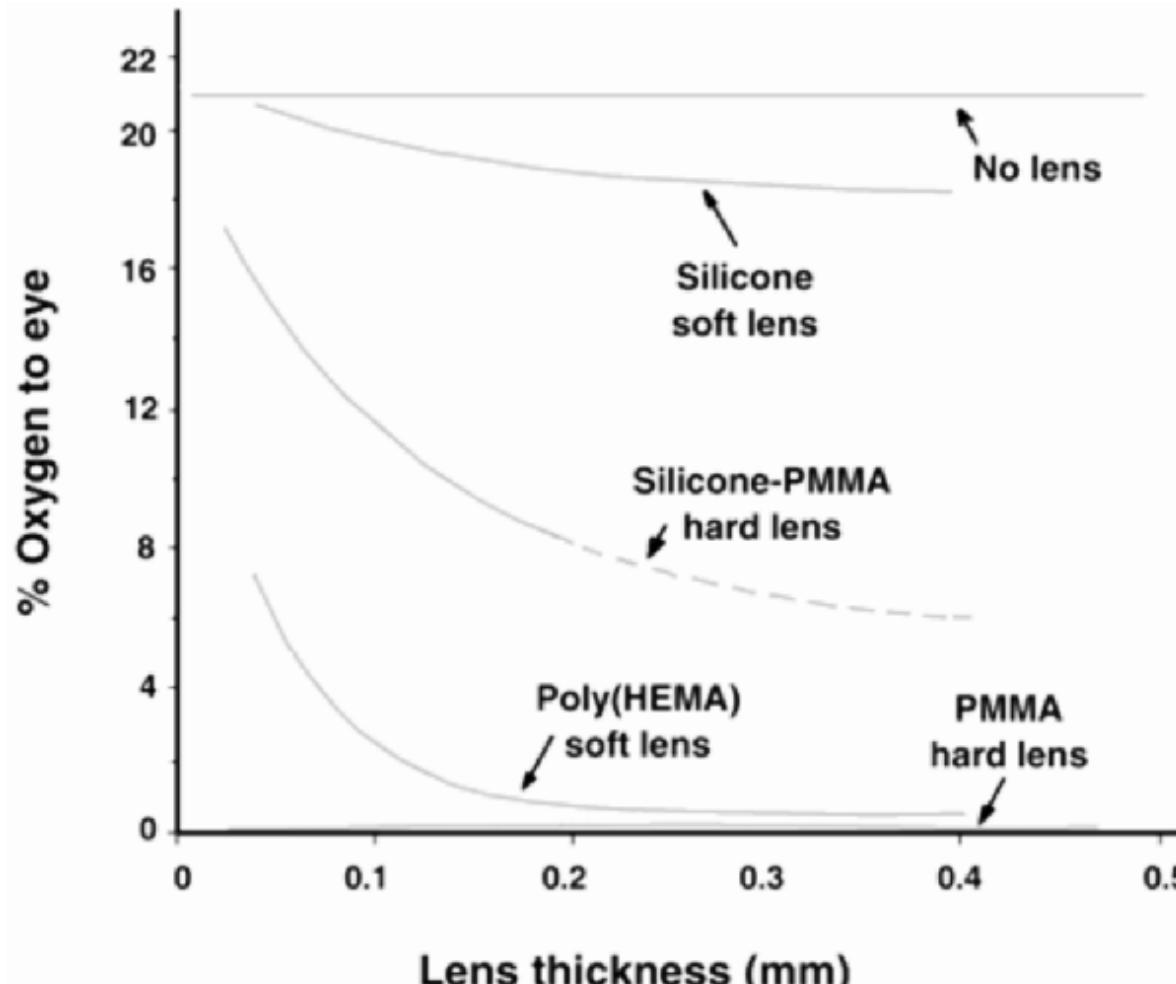


Figure 7-8. Ultimate tensile strength versus time for polymethylmethacrylate in saline solution at 37°C.

Polyurethanes (PU)

聚氨酯

- Developed in 1930 s
- Block copolymer –alternating

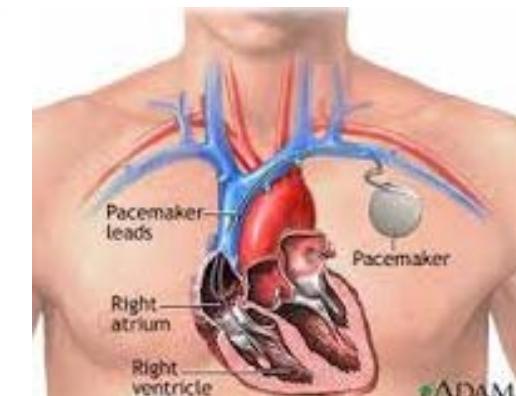
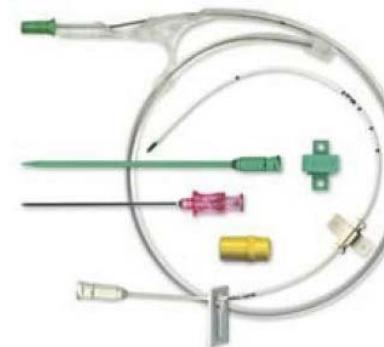
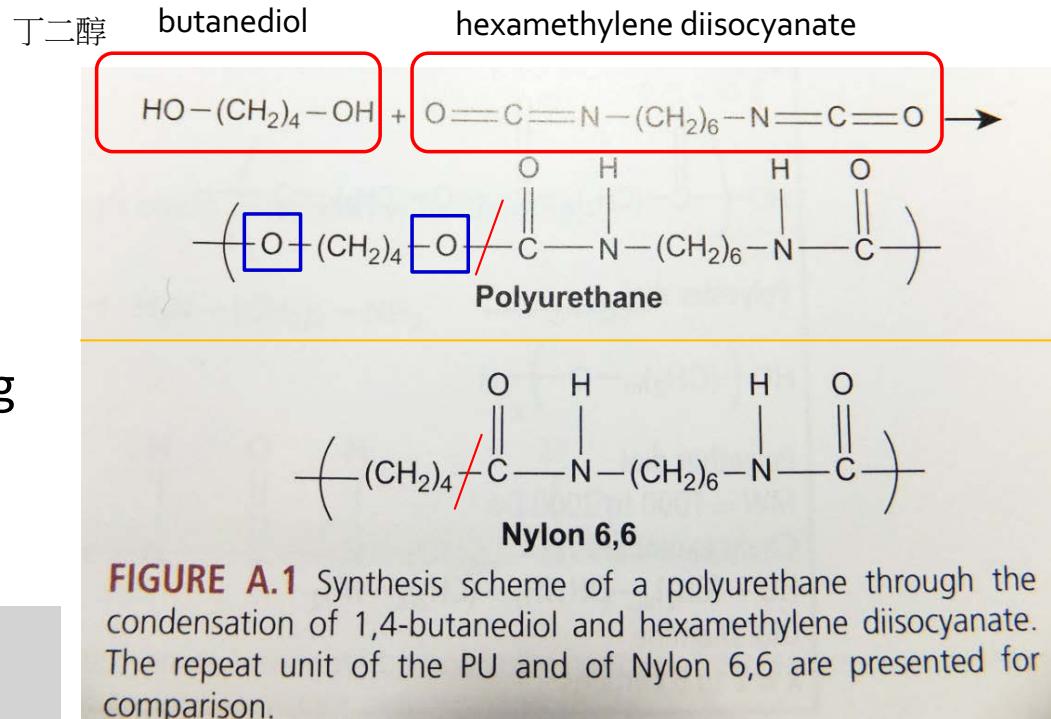
-----**ABABABABABABA**-----
Alternating copolymer

- Excellent mechanical properties
- Stability
- Good biocompatibility

Hard segment :

1. glassy or crystalline at the use temperature
2. providing highly efficient reinforcing microdomains (strength, toughness)

Soft segment: rubbery

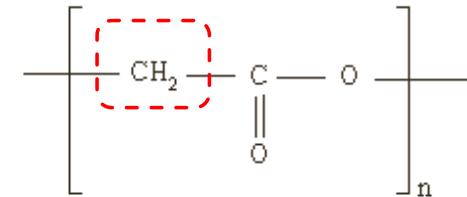


Poly(α -esters)

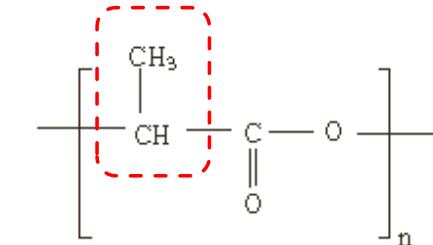
聚酯

R-CO-O-R

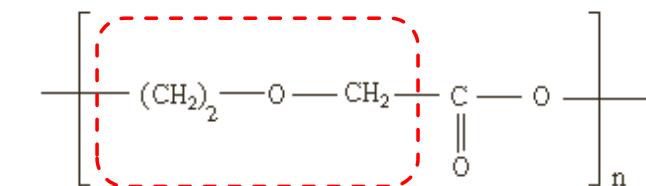
- Poly(α -ester)s are thermoplastic polymers with hydrolytically labile aliphatic ester linkages in their backbone.
- Although all **polyesters** are theoretically degradable only aliphatic polyesters with reasonably short aliphatic chains between ester bonds can degrade over the time frame required for most of the biomedical applications.
- Poly(α -ester)s comprise the earliest and most extensively investigated class of biodegradable polymers.
- Among the class of poly(α -esters), the most extensively investigated polymers are **poly(glycolic acid)** and **poly(lactic acid)**.



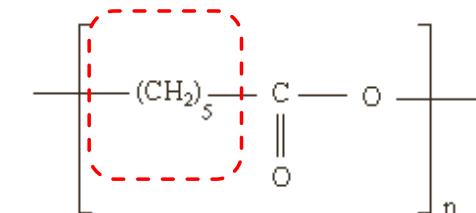
Poly(glycolide) 聚乙醇酸



Poly(lactide) 聚乳酸



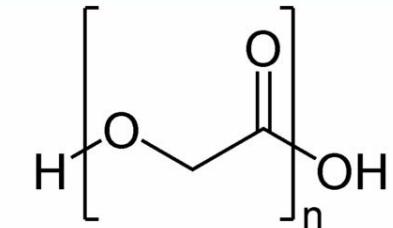
Poly(dioxanone) 聚對二惡烷酮



Poly(caprolactone) 聚己内酯

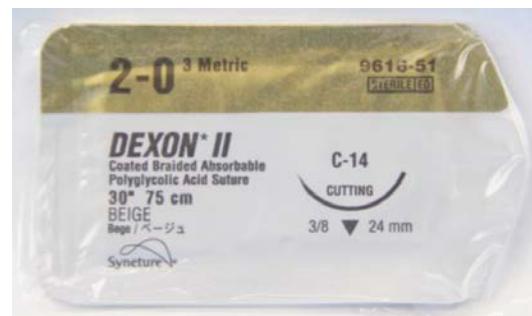
Polyglycolide (PGA) polyglycolic acid

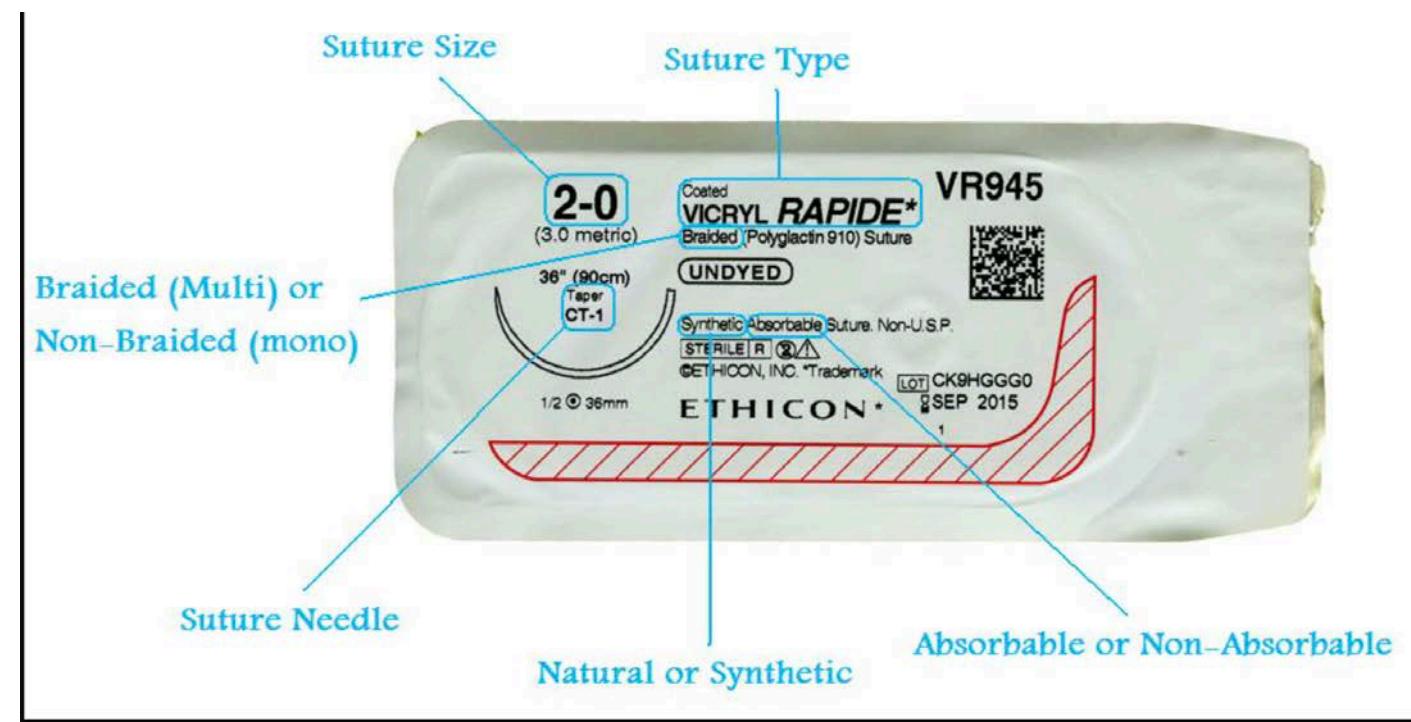
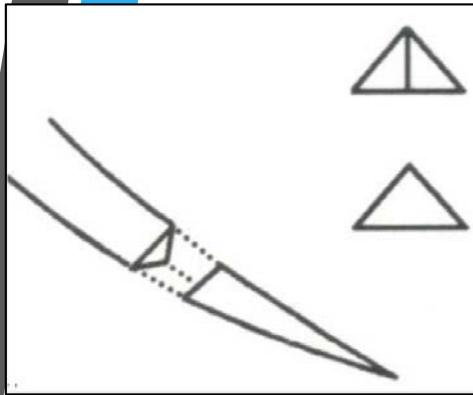
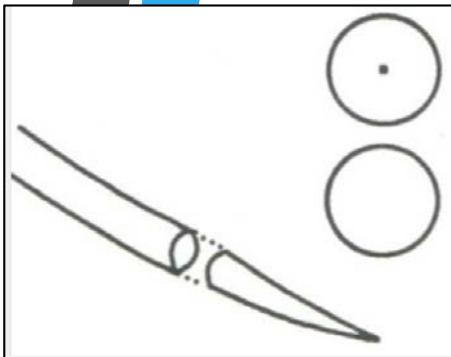
聚乙醇酸



- Polyglycolide is a highly crystalline polymer (45–55% crystallinity) and therefore exhibits a high tensile modulus with very low solubility in organic solvents (exhibit a modulus of approximately 12.5 Gpa).
- PGA shows excellent mechanical properties due to its **high crystallinity**, therefore polyglycolides (PGA) have been investigated as **bone internal fixation devices** (Biofixs).
- Due to its excellent fiber forming ability, polyglycolide (PGA) was initially investigated for developing resorbable sutures. The first biodegradable synthetic suture called **DEXONs** that was approved by the United States (US) Food and Drug Administration (FDA) in 1969 was based on polyglycolide.

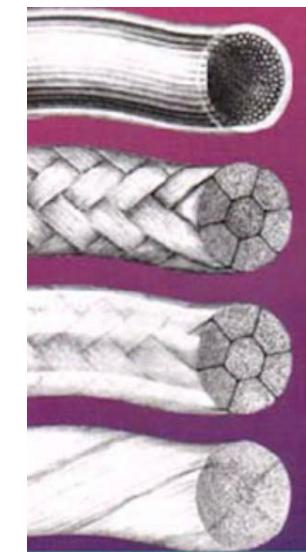
DEXONs





Time of complete breakdown of sutures:

- Vicryl Rapide – 2 weeks
- Undyed Monocryl – 3 weeks
- Dyed Monocryl – 4 weeks
- Coated Vicryl – 4 ½ weeks
- PDS – 9 weeks
- Panacryl – 70 weeks



Polyglycolide (PGA)

聚乙醇酸

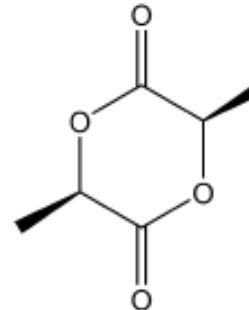
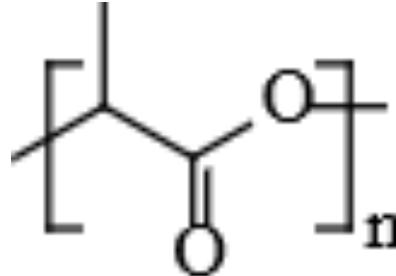
Get your NEW SKIN
Dr.PGA
Hydrating Gel Mask!



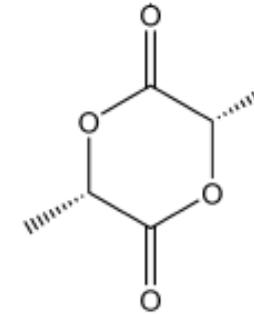
- Non-woven polyglycolide fabrics have been extensively used as scaffolding matrices for tissue regeneration due to its excellent degradability, good initial mechanical properties and cell viability on the matrices.
- The polymer is known to **lose its strength in 1–2 months** when **hydrolyzed** and **loses mass within 6 – 12 months**.
- In the body, PGAs are broken down into **glycine** which can be excreted in the **urine** or converted into **carbon dioxide** and **water** via the **citric acid cycle** .
- The high rate of degradation, **acidic degradation products** and **low solubility** however, **limit the biomedical applications for polyglycolide (PGA)**. Therefore, several copolymers containing glycolide units are being developed to overcome the inherent disadvantages of polyglycolide.

Polylactide (PLA)

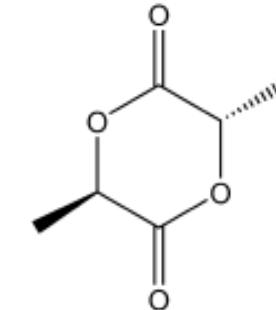
聚乳酸



D,D-lactide



L,L-lactide



D,L-lactide

- poly(L-lactide) (PLLA) is also a crystalline polymer (37% crystallinity).
- It has a glass transition temperature of 60–65 °C and a melting temperature of approximately 175 °C.
- **Poly(L-lactide) is a slow-degrading polymer** compared to polyglycolide (PGA), has **good tensile strength** and a high modulus (approximately **4.8 GPa**) and hence, has been considered **an ideal biomaterial for load bearing applications**, such as orthopaedic fixation devices. (BioScrews, Bio-Anchors, etc.)
- PLLA can also form high strength fibers and was FDA approved in 1971 for the development of an **improved suture** over DEXONs.

Polylactide (PLA)

Sculptra

BEFORE



AFTER



BEFORE



AFTER



- An injectable form of PLLA (Sculptras) has recently been approved by the FDA for the **restoration or correction of facial fat loss**.
- Sculptra is an injectable product that restores and corrects the signs of facial fat loss by replacing lost volume.
- Poly-L-lactic acid (PLLA) is a **biocompatible , biodegradable material** that has been widely used for many years in surgical products. The effects are long-lasting; they were shown in a **clinical study to last for up to 2 years** after the first treatment session.

Polylactide (PLA)

- However, being **more hydrophobic** than polyglycolide, the degradation rate of PLLA is **very low**.
- High molecular weight PLLA can take **between 2 and 5.6 years** for total resorption in vivo. *The rate of degradation however, depends on the degree of polymer crystallinity as well as the porosity of the matrix.*
- Even though the polymer is known to **lose its strength in approximately 6 months** when **hydrolyzed**, no significant changes in mass will occur for a very long time.
- Polylactides undergo hydrolytic degradation via the random scission of the ester backbone. It **degrades into lactic acid** a normal human metabolic by-product, which is broken down into **water** and **carbon dioxide** via the citric acid cycle.



Poly(lactide-co-glycolide), PLGA

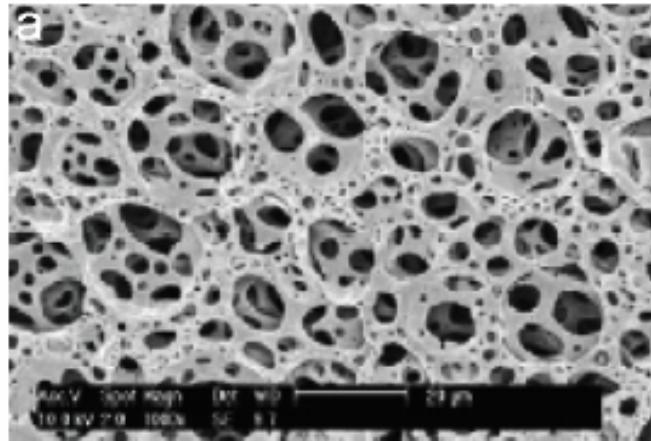
乳酸-甘醇酸共聚合物

- Different ratios of poly(lactide-co-glycolides) have been commercially developed and are being investigated for a wide range of biomedical applications.
- **PANACRYL** is commercially developed **suture** from the co-polymer with a higher LA/GA ratio in order to decrease the rate of degradation. (Also, PuraSorbs 80L:20G, Vicryls 90G:10L etc.)
- Other applications of PLGA are in the form of meshes (Vicryl Meshs). The tissue engineered **skin graft** (Dermagrafts) use a Vicryl Meshs as the scaffolding structure. PLGA demonstrates good cell adhesion and proliferation making it a potential candidate for tissue engineering applications.
- PLGA-collagen matrix is currently in the market (CYTOPLAST Resorbs) as a guided tissue regeneration membrane.

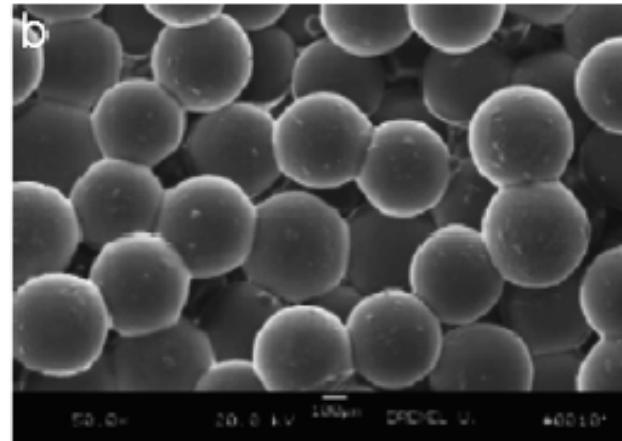




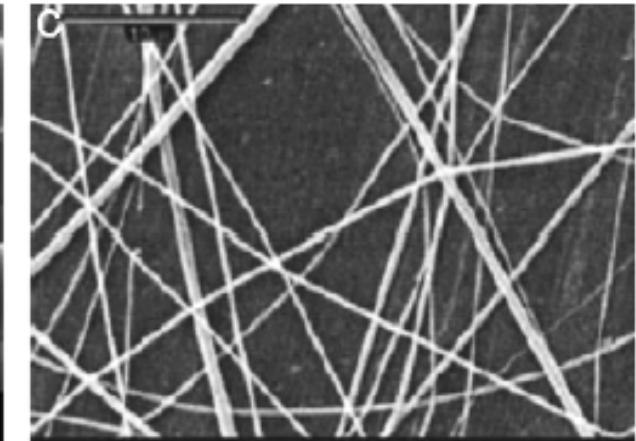
Porous three-dimensional structures developed from PLGA



gas foaming



microsphere sintering



electrospinning

SmartScrew-Bionx



- Self-reinforced PLLA
- 2.0, 2.7, 3.5, 4.5 mm
- 4.5 mm cannulated
- 36-60 moisture absorb.
- 90% at 24 weeks
- \$120-\$190

TABLE 1.4**Synthetic and Naturally Derived Polymers Commonly Used in Biomedical Applications**

Polymer	Applications
Synthetic	
Poly(2-hydroxyethyl methacrylate)	Contact lenses
Poly(dimethyl siloxane)	Breast implants, contact lenses, knuckle replacements
Poly(ethylene)	Orthopedic joint implants
Poly(ethylene glycol)	Pharmaceutical fillers, wound dressings
Poly(ethylene terephthalate)	Vascular grafts, sutures
Poly(ϵ -caprolactone)	Drug delivery devices, sutures
Poly(lactic-co-glycolic acid)	Resorbable meshes and sutures
Poly(methyl methacrylate)	Bone cements, diagnostic contact lenses
Poly(tetrafluoroethylene)	Vascular grafts, sutures
Poly(isoprene)	Gloves
Poly(propylene)	Sutures
Naturally derived	
Alginate	Wound dressings
Chitosan	Wound dressings
Collagen	Orthopedic repair matrices, nerve repair matrices, tissue engineering matrices
Elastin	Skin repair matrices
Fibrin	Hemostatic products, tissue sealants
Glycosaminoglycan	Orthopedic repair matrices
Hyaluronic acid	Orthopedic repair matrices

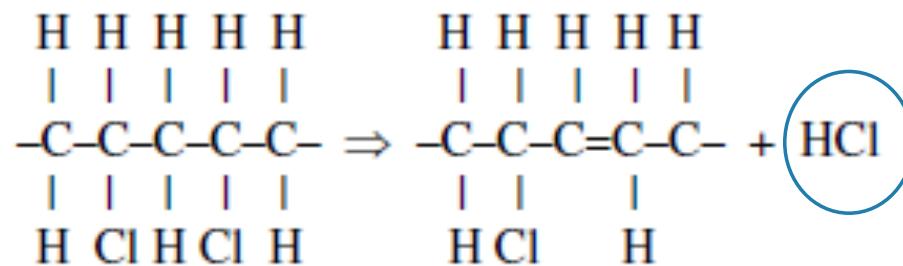


Deterioration of Polymers

Chemical Effects

- If a linear polymer is undergoing deterioration, the **main chain** will usually be **randomly scissored** (cut).
- Sometimes **de-polymerization occurs**, which differs from random chain scission.
- Crosslinking of a linear polymer may result in deterioration

polyvinylchloride



Sterilization Effects

	Temp	Non-suitable	Suitable
Dry heat	160 to 190°C	<ul style="list-style-type: none">PolyethylenePolymethylmethacrylatePolyamide (nylon)	<ul style="list-style-type: none">Polytetrafluoroethylene (Teflon®)Silicone rubber
Steam (autoclaving)	120–135°C at high steam pressure	<ul style="list-style-type: none">PolyvinylchloridePolyacetalsPolyethylenes (<i>low-density variety</i>)Polyamides (nylons)	<ul style="list-style-type: none">Polypropylene
Chemical agents	<ul style="list-style-type: none">Room temp (Ethylene, propylene oxide gas)Sodium hydrochloride solution		<ul style="list-style-type: none">Most polymers can be sterilized with this method
Radiation (Co ⁶⁰)		<ul style="list-style-type: none">Polyethylene	

Mechano-chemical Effects

- Cyclic or constant loading deteriorates polymers.
- When the polymer is stored in water or in saline solution, its strength will decrease. (at higher temp)
- Cyclic or constant loading deteriorates polymers.

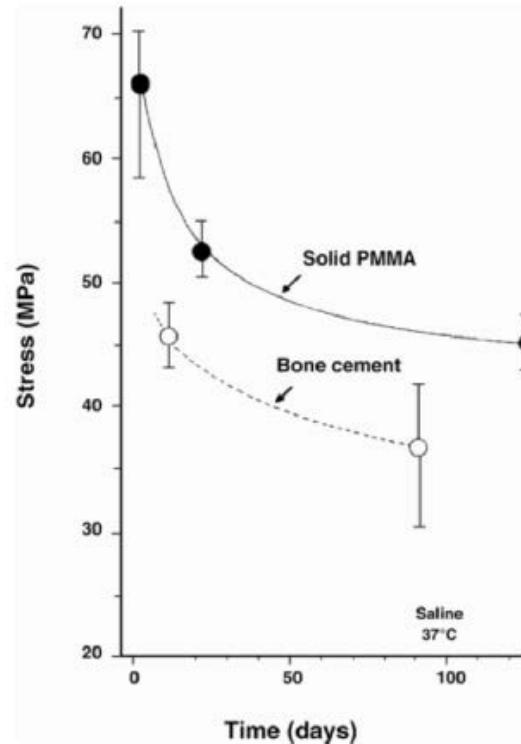


Figure 7-8. Ultimate tensile strength versus time for polymethylmethacrylate in saline solution at 37°C. Note the large decrease in tensile strengths for both solid and porous bone cement. Unpublished data from T. Parchinski, G. Cipoletti, and F.W. Cooke, Clemson University, 1977.

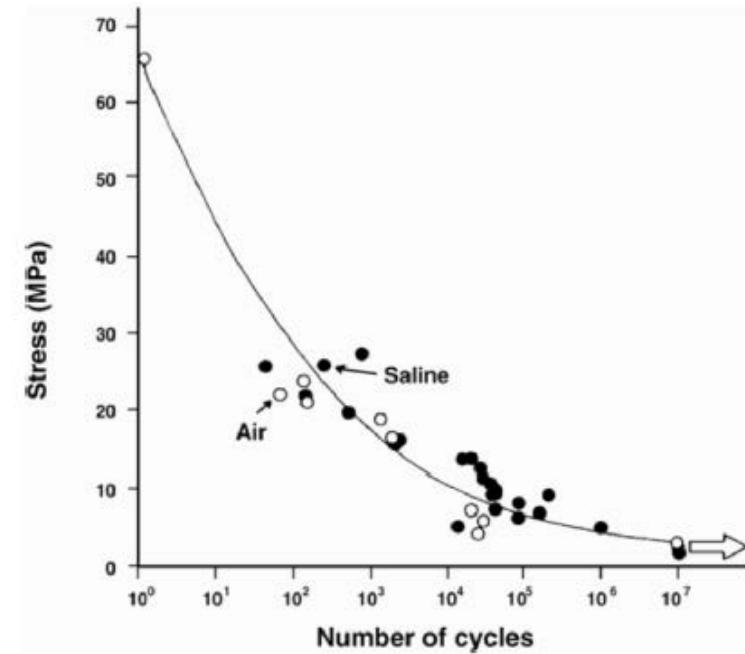
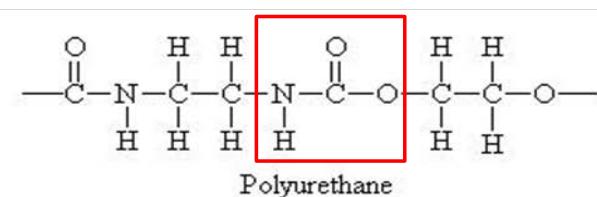
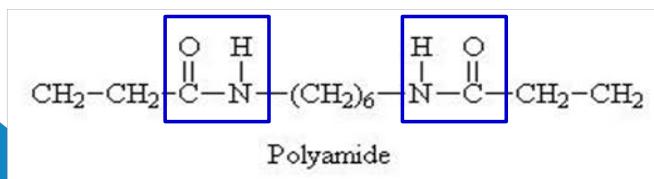
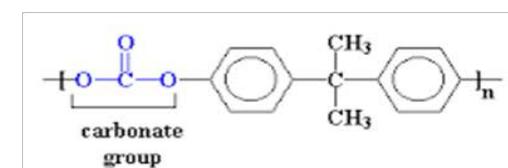
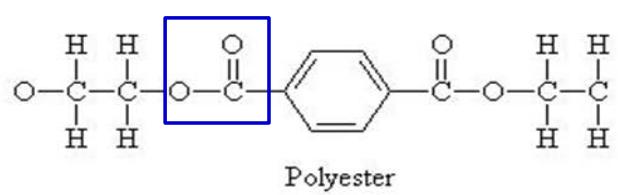
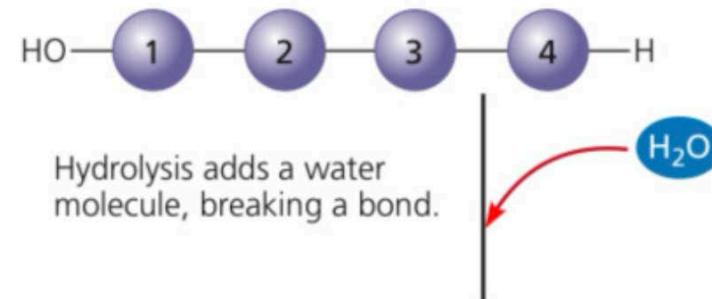


Figure 7-9. Fatigue test of solid polymethylmethacrylate. Note the S-N curve is the same for both samples, non-treated and soaked, in saline solution at 37°C. Unpublished data from T. Parchinski and F.W. Cooke, Clemson University, 1977.

Hydrolytically degradable polymers

- Hydrolytically degradable polymers are polymers that have hydrolytically labile chemical bonds in their back bone. The functional groups susceptible to **hydrolysis** include **esters, carbonates, amides, urethanes** etc.
- Hydrolytically degradable polymers are generally **preferred as implants** due to their minimal site-to-site and patient-to-patient variations compared to enzymatically degradable polymers .



In-Vivo Environmental Effects

- The body environment is very hostile, and all polymers begin to deteriorate as soon as they are implanted.
 - Ionic attack (especially hydroxyl ion, OH)
 - Dissolved oxygen.
 - Enzymatic degradation
- Most hydrophilic polymers such as polyamides and polyvinyl alcohol will react with body water and undergo rapid deterioration.
- The hydrophobic polymers like polytetrafluoroethylene (Teflon®) and polypropylene are less prone to deteriorate in vivo.

Table 7-17. Effect of Implantation on Polymers

Polymers	Effects of implantation
Polyethylene	Low-density ones absorb some lipids and lose tensile strength. High-density ones are inert and no deterioration occurs.
Polypropylene	Generally no deterioration.
Polyvinylchloride (rigid)	Tissue reaction, plasticizers may leach out and material becomes brittle.
Polyethyleneterephthalate	Susceptible to hydrolysis and loss of tensile strength (in polyester).
Polyamides (nylon)	Absorb water and irritate tissue, lose tensile strength rapidly.
Silicone rubber	No tissue reaction, very little deterioration.
Polytetrafluoroethylene	Solid specimens are inert. If fragmented into pieces, irritation will occur.
Polymethylmethacrylate	Rigid form: crazing, abrasion, and loss of strength by heat sterilization. Cement form: high heat generation, unreacted monomers during and after polymerization may damage tissues.

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Reference:

- J. S. Temenoff & A.G. Mikos (2008) Chap 2 Chemical structure of biomaterials, “Biomaterials - The Intersection of Biology and Materials Science”. Pearson Prentice Hall.
- Joon Park & R.S. Lakes (2007) Chap 7 , Polymeric implant materials. “Biomaterials -An Introduction” 3rd edition . Springer.
- 王盈錦 、林峰輝 、胡孝光、 黃玲惠、 黃義侑 、蔡瑞瑩 、闞山璋 (2007) 第10章高分子生醫材料. “生物醫學材料” ，合記圖書出版社.