Lecture 4:

Biomaterials Surfaces: Chemistry

Hydrolysis

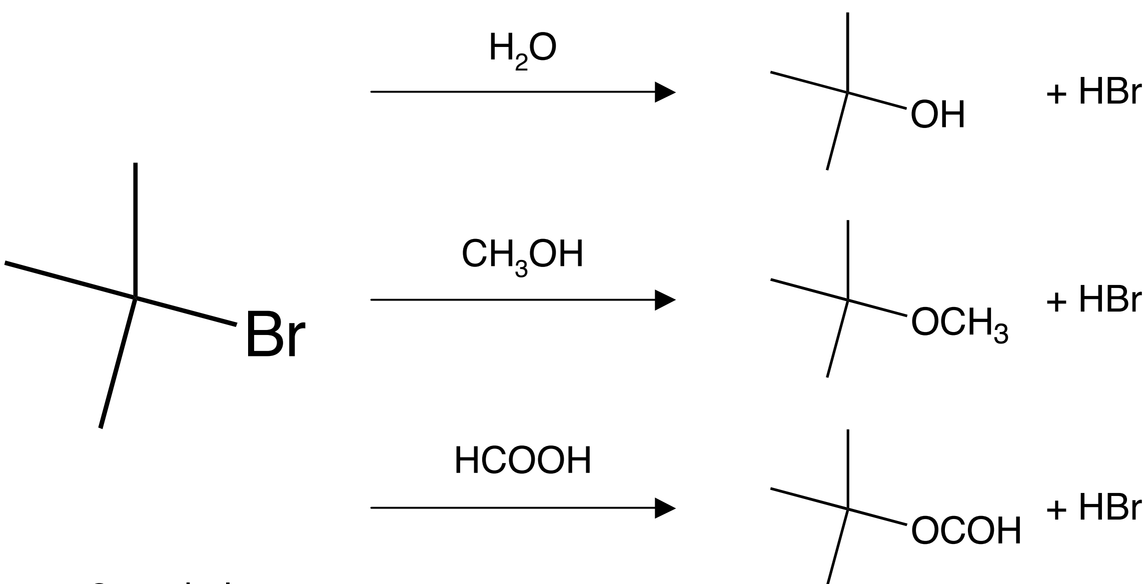
Supporting notes

3.051J/20.340J Materials for Biomedical Applications,
Spring 2006

Hydrolysis

- Hydrolysis is a kind of "Solvolysis",

  solvent + lysis: cleavage by the solvent.



Hydoloysis

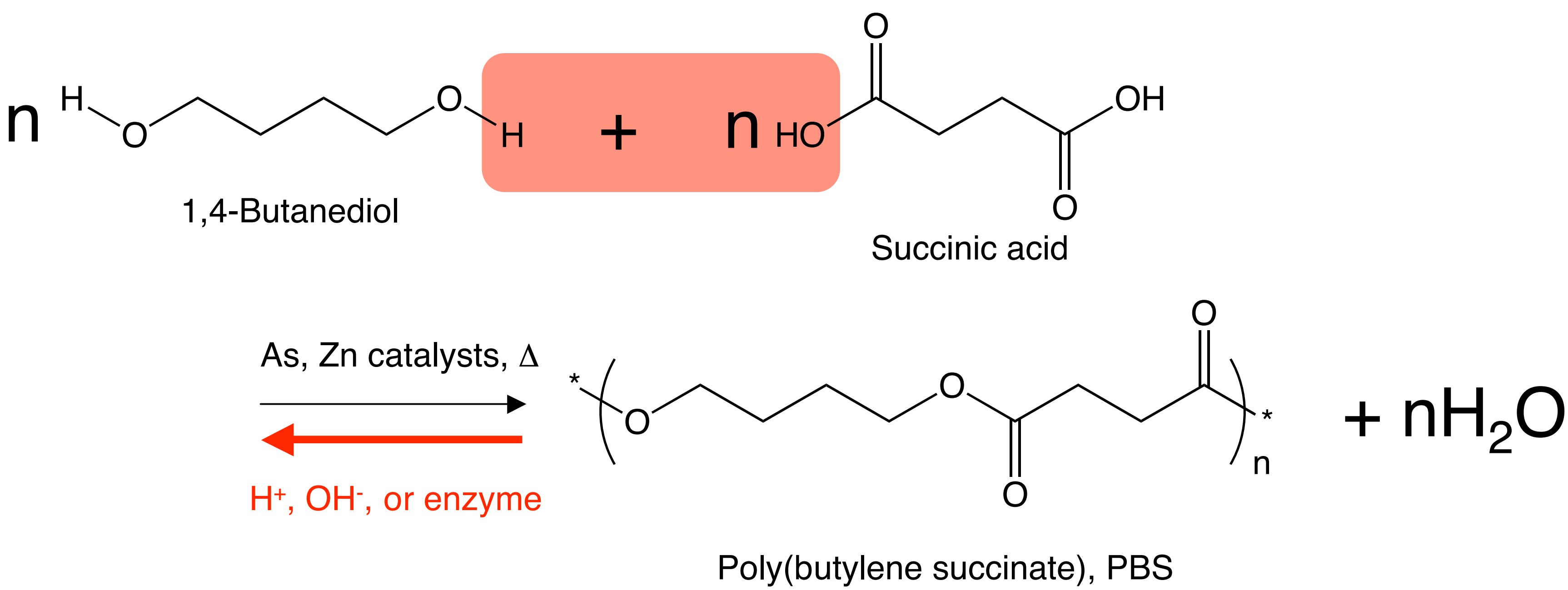
Methanolysis

Formic acidolysis

2-Bromo-2-methyl propane

Polymer Hydrolysis

- Polymers prepared by polycondensation can be susceptible to hydrolysis.



Hydrolysable is “degradable”.

Synthetic polymers

- Polyesters
- Polyamides
- Polyanhydrides
- Polyethers
- Polyurethanes
- Polycarbonates
- Polyureas

Material properties can be tuned readily. Cheaper!

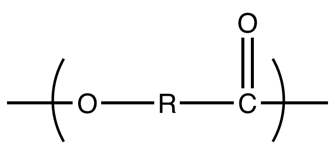
Naturally-occurring polymers

- Proteins and polyamides
  - Collagen
  - Fibrinogen and fibrin
  - Gelatin
  - Casein
- Polysaccharides
  - Cellulose
  - Starch and amylose
  - Chitin and chitosan
  - Dextran
- Polynucleotides
  - DNA and RNA

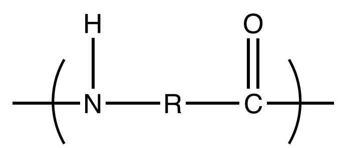
Biodegradation:

An event which takes place through the action of enzymes and/or chemical decomposition associated with living organisms (bacteria, fungi, etc.) or their secretion products.

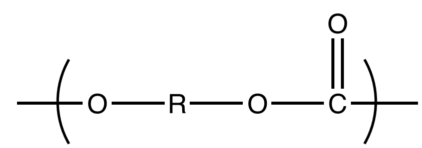
Albertsson and Karlsson, in Chemistry and Technology of Biodegradable Polymers 1994



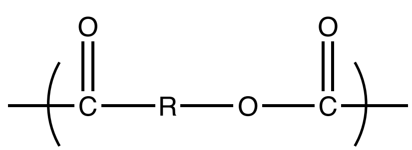
Polyester



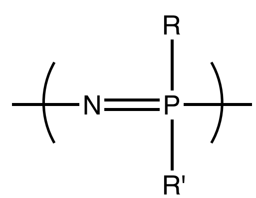
Polyamide



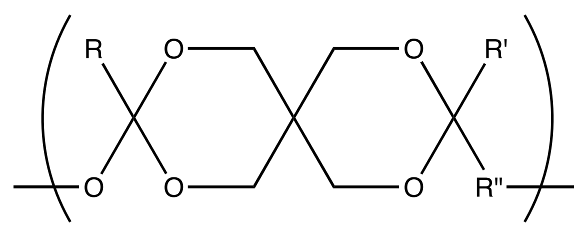
Polycarbonate



Polyanhydride



Polyphosphazene



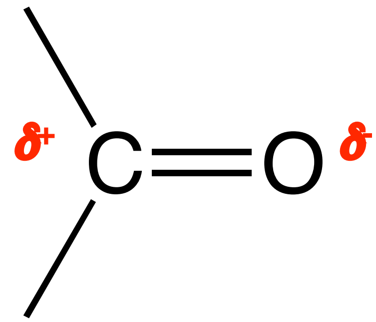
Poly(ortho ester)

Typical examples of synthetic biodegradable polymers

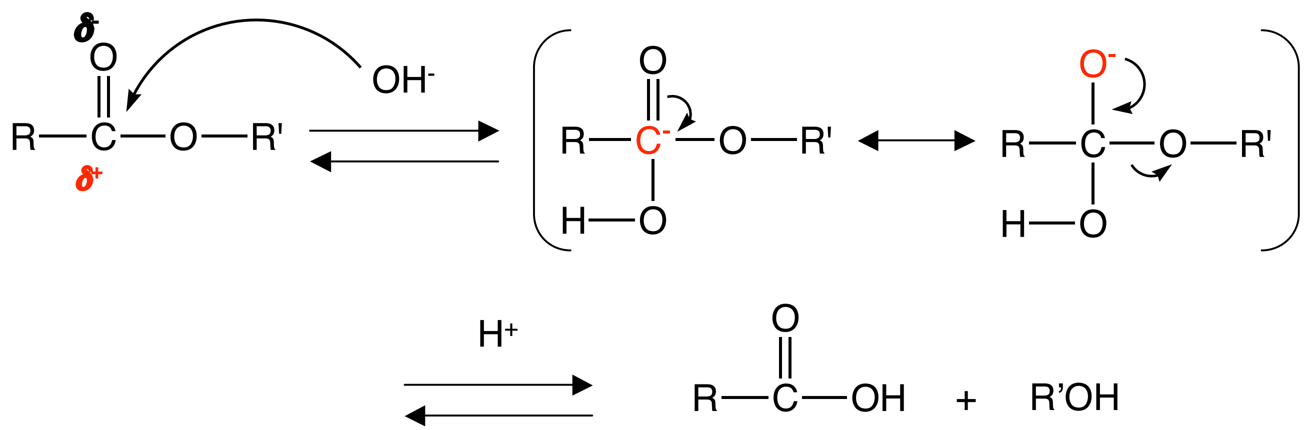
Key factors in hydrolysis

1. Bond stability

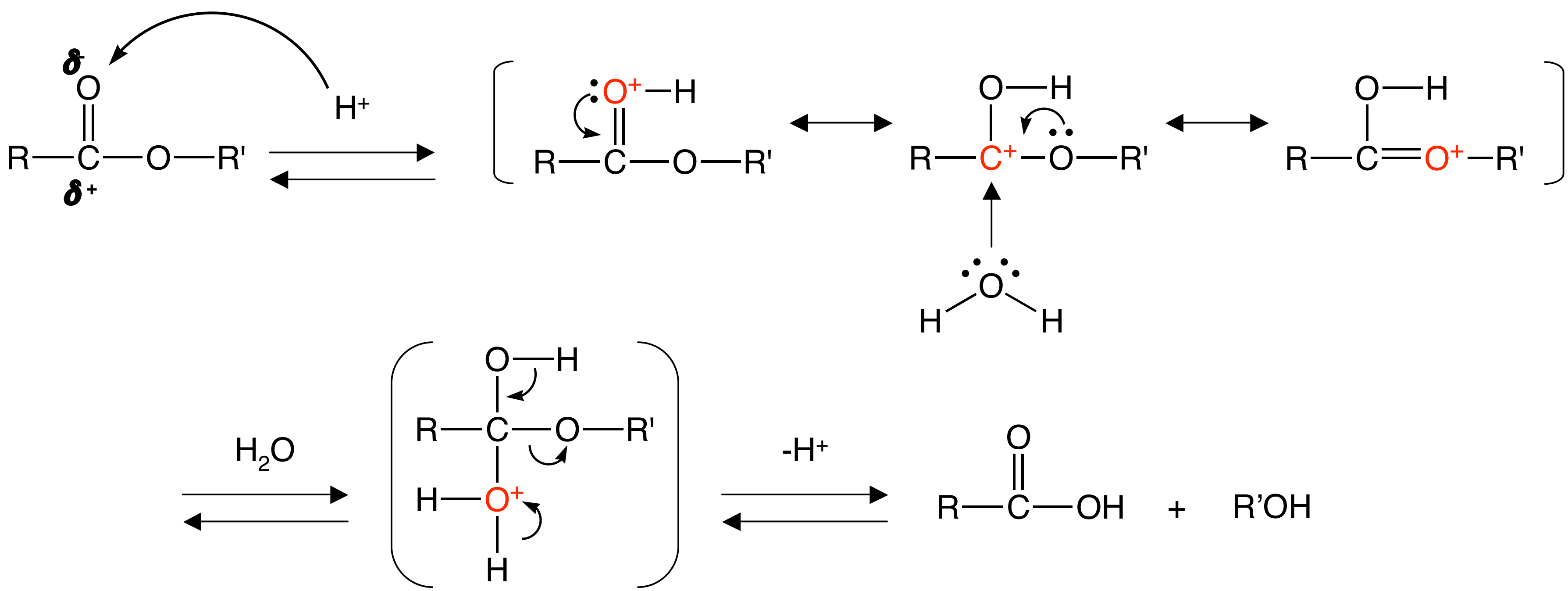
Example: Hydrolysis of polyester



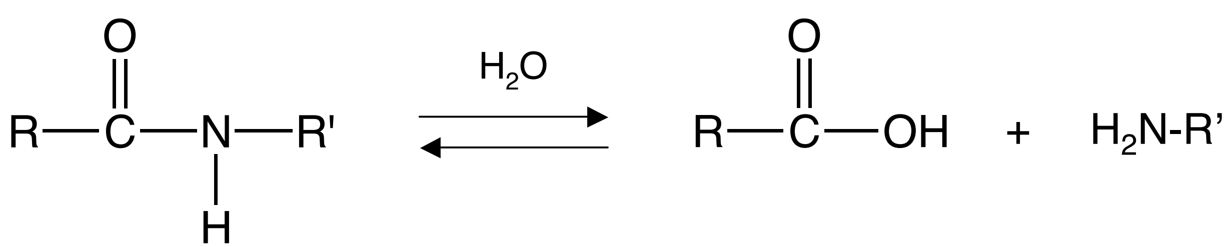
Base-catalyzed polyester hydrolysis



Acid-catalyzed polyester hydrolysis



Polyamide hydrolysis



Key factors in hydrolysis

2. Hydrophobicity

3. Molecular weight & architecture

4. Morphology Crystallinity, porosity

5. $\boldsymbol{T_g}$ Mobility of polymer chain

Chance to contact with H_2O

Example: Hydrolysis of amorphous and crystalline poly(*L*-lactide) (PLLA)

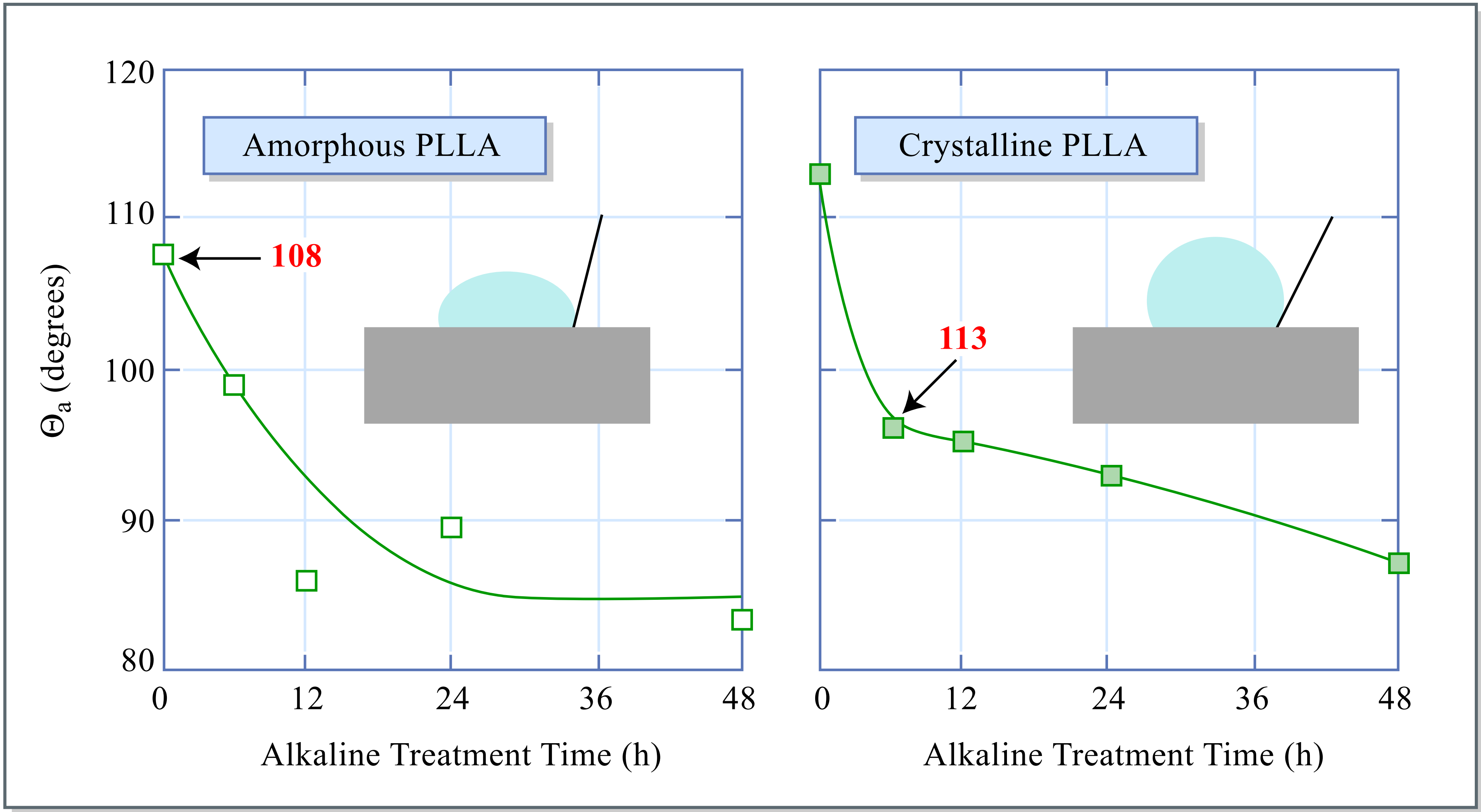
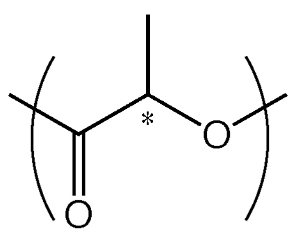


Figure. Advancing contact angle (Θ_a) of amorphous PLLA and crystalline PLLA films treated in 0.01 N NaOH solution as a function of alkaline treatment time



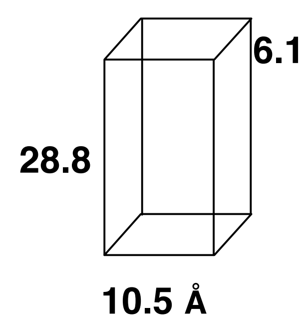
PLLA

Tsuji et al. *Polym. Int.*, **52**, 843, 2003

Orthorhombic crystal structure of α-PLLA

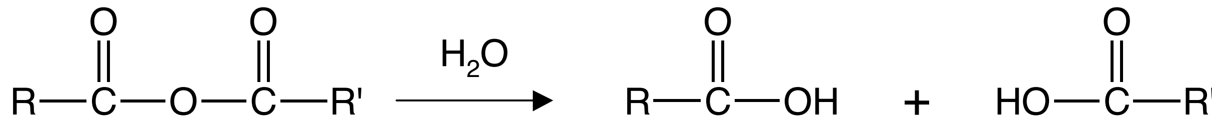
Figures removed for copyright reasons.

$d_{crystal}$: 1.290 g/cm^3
$d_{amorphous}$: 1.248 g/cm^3

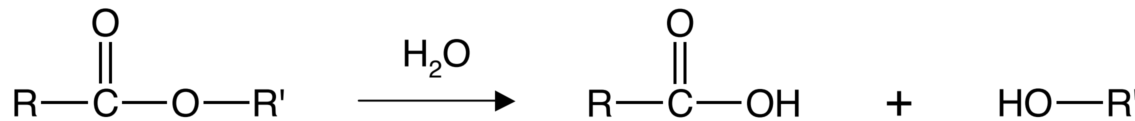


Hydrolysable polymers

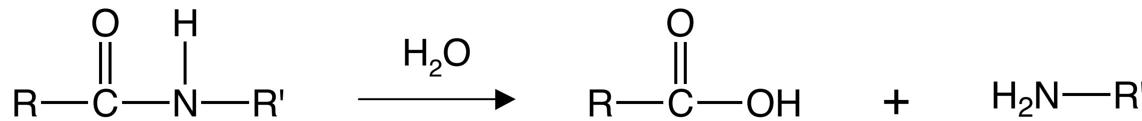
Polyanhydride



Polyester



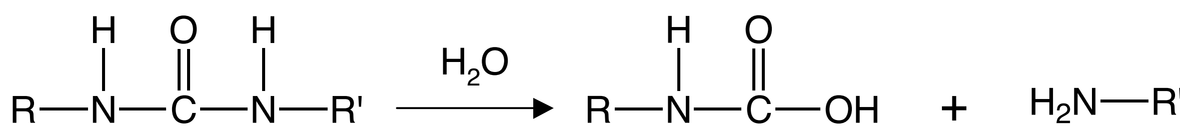
Polyamide



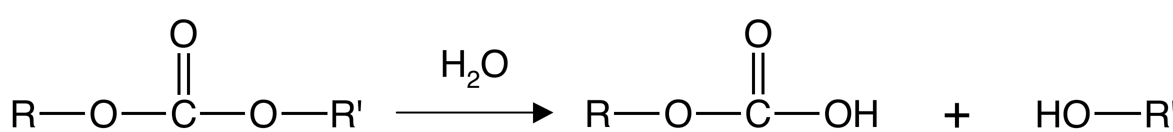
Polyether

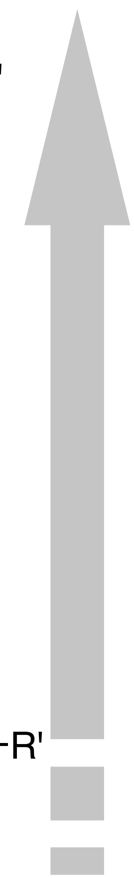
Polyether urethane

Polyurea



Polycarbonate





Poly(sebacic anhydride)

Properties: rapid degradation, T_g: 50 °C, T_m : 80 °C

Uses: drug delivery matrices

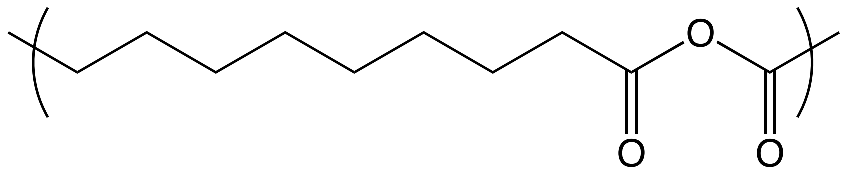
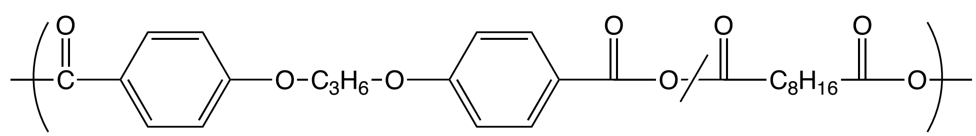


Table. Half-lives of hydrolyzable polymers

Polymer class	Half-life
Polyanhydrides	0.1 h
PLLA	3.3 years
Polyamides	83,000 years

Göpferich, *Biomater.*, **17**, 103, 1996

Incorporation of hydrophobic segment



Poly(bis-(*p*-carboxyphenoxy)propane-*co*-sebacic anhydride)

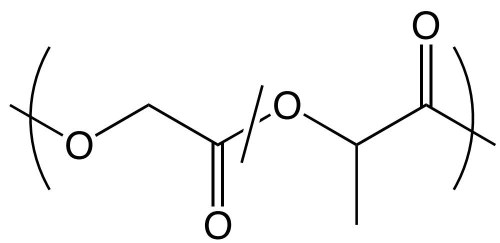
Tabata et al., *Pharm. Res.*, **10**, 391, 1993

Poly(glycolide-*co*-lactide) (polyglactide)

Properties: rapid degradation, amorphous*, T_g: 45-55 °C

Uses: bioresorbable sutures, controlled release matrices, tissue engineering scaffolds

*Depending on composition



Glycolate (GA)   Lactate (DL-LA)

Dexon®: the first synthetic bioresorbable suture in 1960s.

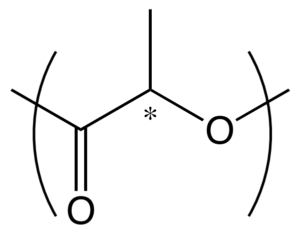
(PGA) Histological response can be predictable in comparison to non-synthetic materials.

High-crystalline nature limits processability.

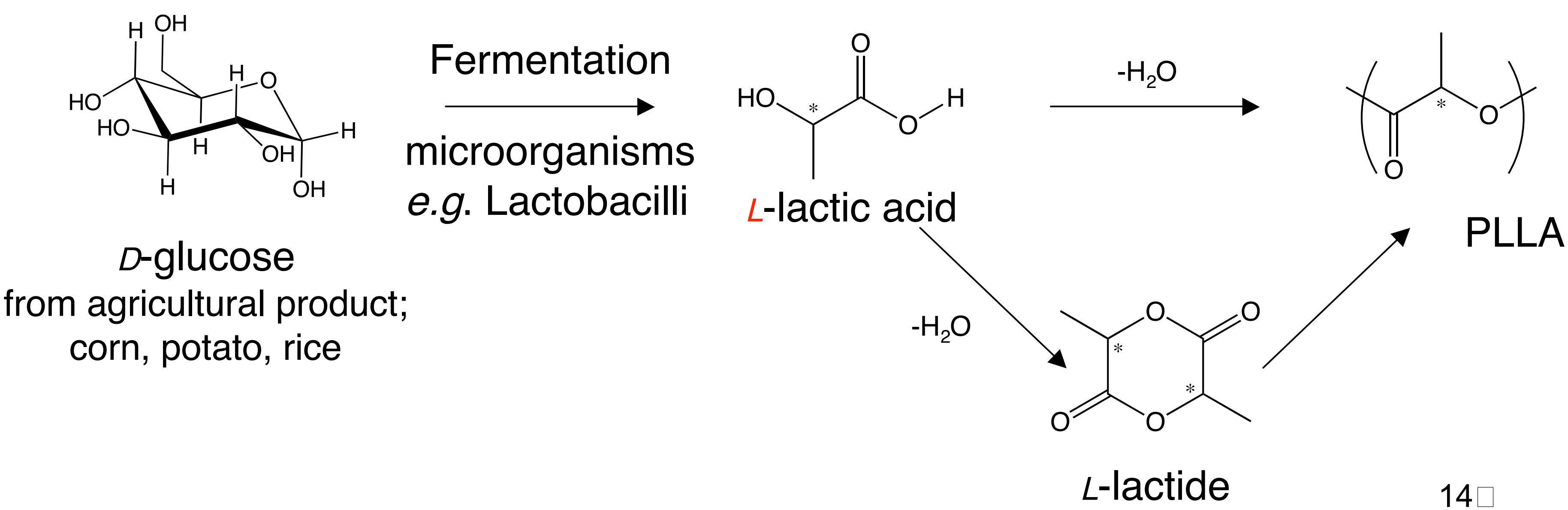
Poly(*L*-lactide), poly(*L*-lactic acid) (PLLA)

Properties: rapid degradation, semicrystalline, T_g: 60 °C, T_m: 180 °C

Uses: fracture fixation, ligament augmentation



PLLA



Physical properties of various plastics

	PLLA	PET	PS	PP
Density/g/cm^3	**1.27**	1.34	1.04	0.90
Tensile strength/MPa	**66.7**	55.9	43.1	37.3
Yong's modulus/MPa	**3300**	2600	3300	2100
Elongation@break/%	**4**	300	2	700
Cost/$/lb	**1-5**	0.75	0.55	-

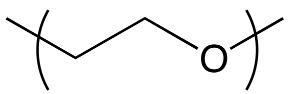
*Polymeric materials were non-oriented (as prepared).

Tsuji, *Polylactic acid*, JPS press, Kyoto, 1997,
Ikada, *Macromol. Rapid Commun.*, **21**, 117, 2000

Polyethylene oxide (PEO)

Properties: water soluble, semicrystalline, T_g: -60 °C, T_m: 60 °C

Uses: hydrogel, protein-resistant coatings



PEO

Two photos removed for copyright reasons.

Figure 6 in Irvine, D., et al. "Nanoscale Clustering of RGD Peptides at Surfaces Using Comb Polymers. 1. Synthesis and Characterization of Comb Thin Films." *Biomacromolecules* 2, no. 1 (2001): 85 -94.

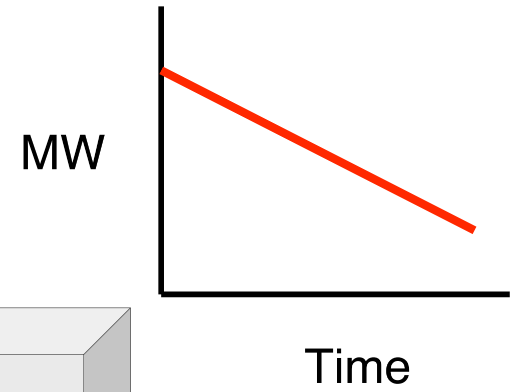
Rate of hydrolysis:

anhydride > ester >> amide >>>> ether etc.

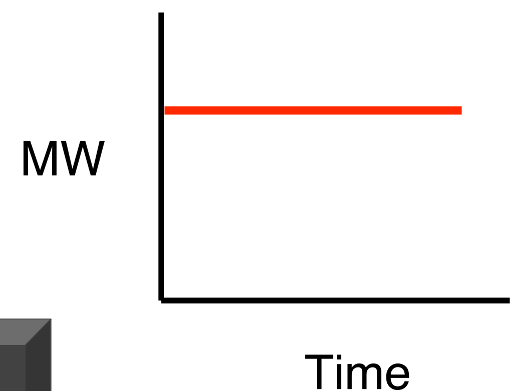
Matrices for drug delivery (anhydride > ester)

Hydrolysis of polymeric materials

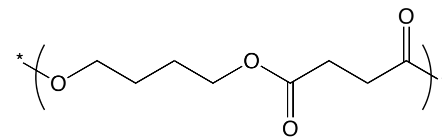
Acid- or base-catalyzed hydrolysis



Enzymatic hydrolysis -surface erosion-



Hydrolysis of Bionole® (PBS)



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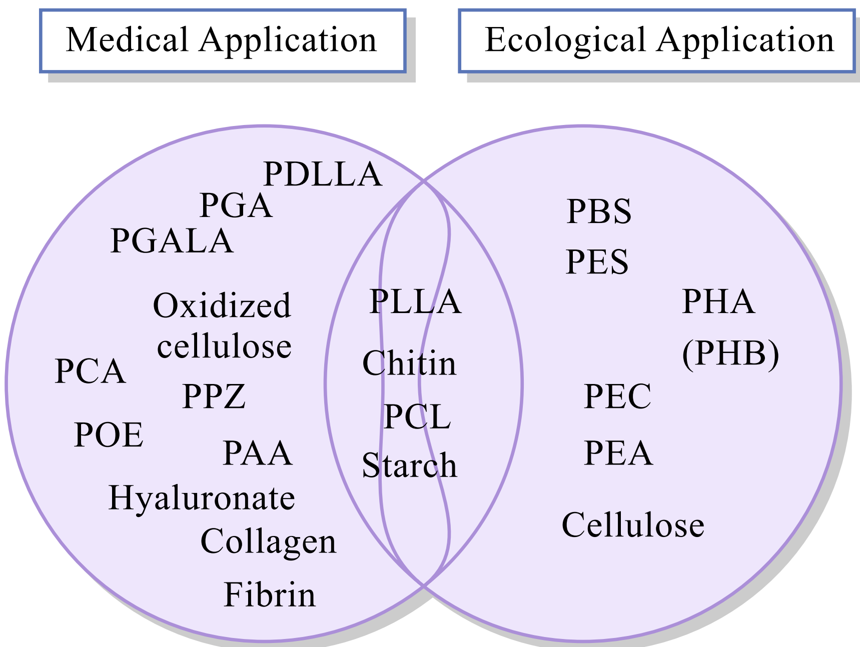
Alkaline treated

Lipase PS treated

Taniguchi I., unpublished results

Application of biodegradable polymers and minimal requirements of biomaterials



PAA: Poly(acid anhydride)
PBS: Poly(butylene succinate)
PCA: Poly(α-cyanoacrylate)
PCL: Poly(ε-caprolactone)
PEA: Poly(ester amide)
PGA: Poly(glycolide), Poly(glycolic acid)
PGALA: Poly(glycolide-co-lactide), Poly(glycolic acid-co-lactic acid)
PDLLA: Poly(DL-lactide), Poly(DL-lactic acid)
PHA: Poly(hydroxyalkanoate
PHB: Poly(3-hydroxybutyrate)
PLLA: Poly(L-lactide), Poly(L-lactic acid)
POE: Poly(orthoester)
PEC: Poly(ester carbonate)
PES: Poly(ethylene succinate)

Application of Biodegradable Polymers

Minimal Requirements of Biomaterials

A) Non-toxic (biosafe)
Non-pyrogenic, Non-hemolytic, Chronically non-inflammative, Non-allergenic, Non-carcinogenic, Non-teratogenic, etc.

B) Effective
Functionality, Performance, Durability, etc.

C) Sterilizable
Ethylene oxide, γ-Irradiation, Electron beams, Autoclave, Dry heating, etc.

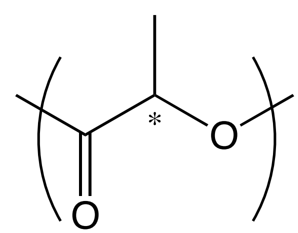
D) Biocompatible
Interfacially, Mechanically, and Biologically

Figure by MIT OCW.

Figure by MIT OCW.

Microbial degradation of PLLA (rare case)

Photos removed for copyright reasons.



PLLA

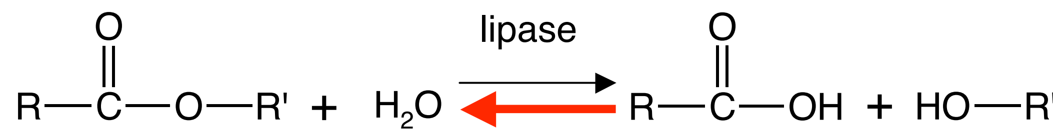
Hydrolysable polymer
Esterases do not degrade
except proteinase K.

Figure. SEM images of PLLA film treated with microbe
Jarerat et al., *Macromol. Biosci.,* **2**, 420, 2002

Enzymatic degradation -Lipase-

Lipase: an esterase (EC3.1.1.3)

stable in organic solvents @ high temp.



In toluene at 90 °C

Two figures removed for copyright reasons.

MW of the polyester is usually low (< 10 k).

Poor mechanical properties.

Brzozowski, et al., *Nature* **1991**, *351*, 491