Lecture 4
Biomaterials Surfaces: Chemistry

Like metallic implants, some polymers used in biomaterials applications are susceptible to chemical reactions that lead to degradation through hydrolysis. In many cases, a polymer is specifically chosen for its ability to degrade in vivo.

Polymer Hydrolysis

Polymer hydrolysis involves the scission of susceptible molecular groups by reaction with H_2O.

- May be acid, base or enzyme catalyzed
- Not surface-limited if water penetrates bulk

a) Molecular & Structural Factors Influencing Hydrolysis

- Bond Stability
- Hydrophobicity: $\uparrow$ hydrophobicity $\Rightarrow \downarrow$ hydrolysis
- MW & architecture: higher MW $\Rightarrow \downarrow$ hydrolysis
- Morphology
  - crystallinity $\downarrow$ hydrolysis
  - porosity $\uparrow$ hydrolysis
- T_g: less mobility $\Rightarrow \downarrow$ hydrolysis

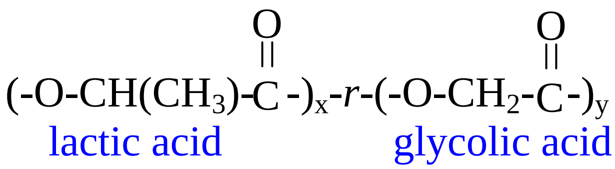
Bond Stability

Susceptible linkages at bonds where resonance stabilized intermediates are possible…

- Esters: $\text{R-}\overset{\overset{\text{O}}{||}}{\text{C}}\text{-O-R'} + H_2O \rightarrow \text{R-}\overset{\overset{\text{O}}{||}}{\text{C}}\text{-OH} + \text{HO-R'}$

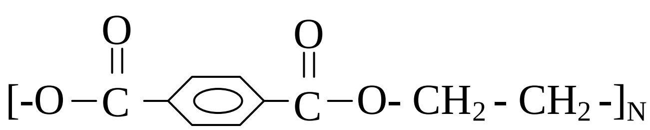
Example 1: poly(lactide-co-glycolide)

Properties: rapid degradation, amorphous, $T_g \sim$ 45-55°C
Uses: bioresorbable sutures, controlled release matrices, tissue engineering scaffolds

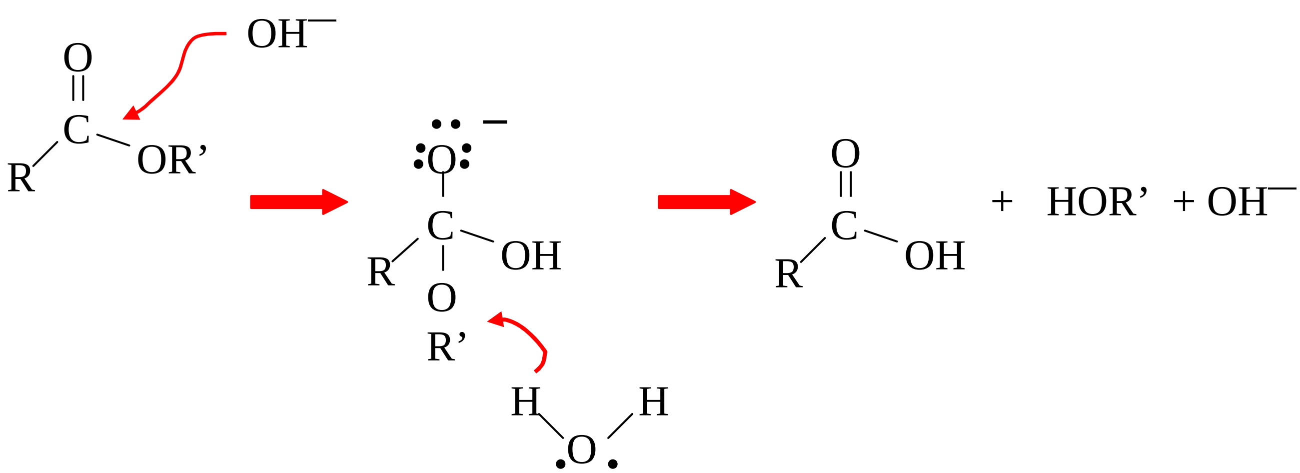


Example 2: polyethylene terephthalate (Dacron)

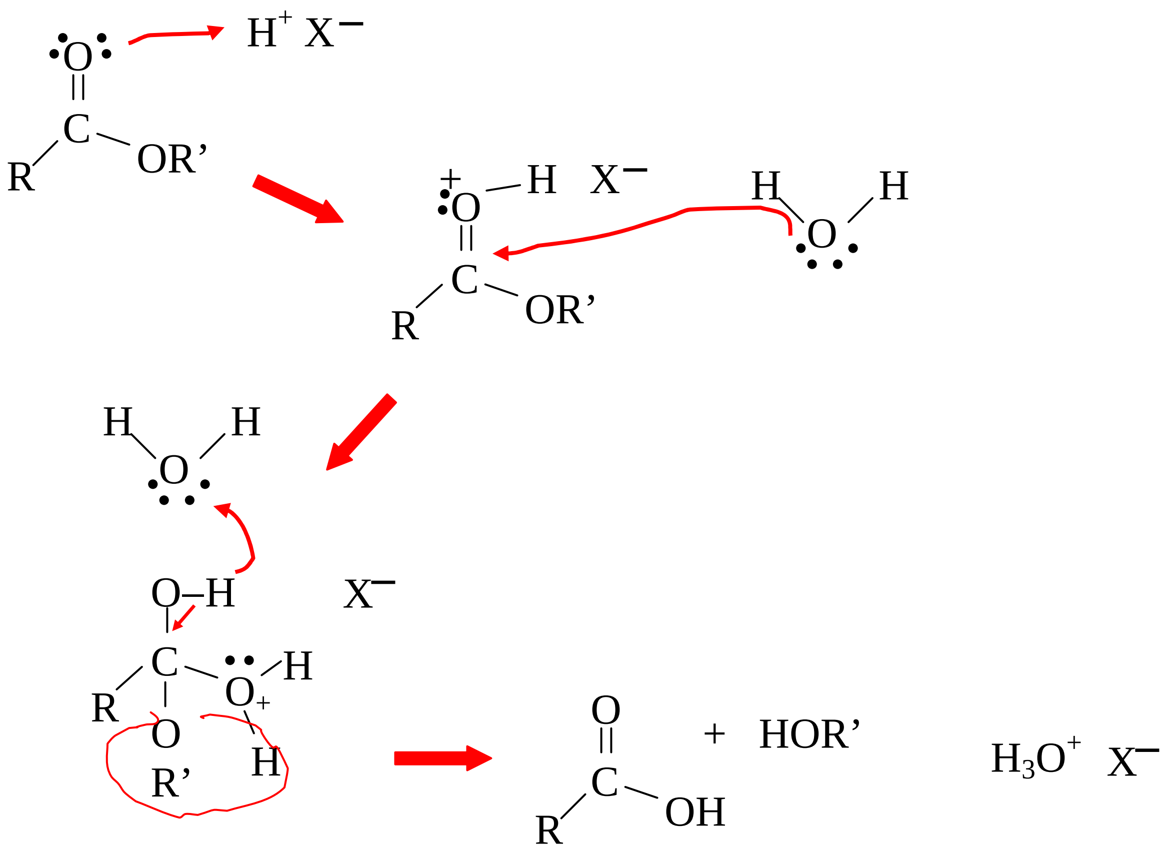
Properties: very slow hydrolysis, semicrystalline, $T_g \sim$ 69°C
Uses: vascular grafts, arterial patches, heart pumps



base-catalyzed polyester hydrolysis:



acid-catalyzed polyester hydrolysis:



- Amides: $R\text{-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-NH-R'} + H_2O \rightarrow R\text{-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-OH} + H_2N\text{-R'}$

  amide or peptide linkage,
  also found in proteins!

Example: Nylon 6,6
poly(hexamethylene adipamide)

$$(\text{-NH-}(CH_2)_6\text{-NH-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-}(CH_2)_4\text{-}\overset{\displaystyle O}{\overset{\|}{C}}\text{-})_N$$

Properties: ~9% H_2O uptake, semicrystalline, T_g~50°C

Uses: removable sutures, prosthetic joints

- Anhydrides: $R\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-}R' + H_2O \rightarrow R\text{-}\overset{O}{\overset{\|}{C}}\text{-}OH + HO\text{-}\overset{O}{\overset{\|}{C}}\text{-}R'$

Example: poly(sebacic acid anyhydride) $(\text{-}(CH_2)_8\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}\overset{O}{\overset{\|}{C}}\text{-})_N$

Properties: rapid degradation (surface-based)
Uses: drug delivery matrices

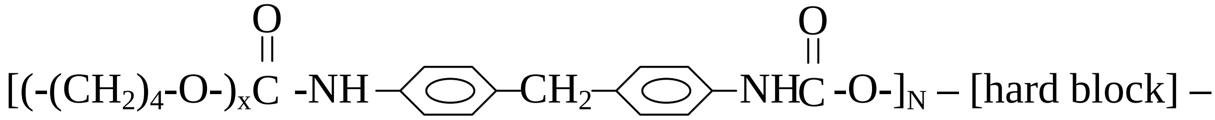
- Ethers: $R\text{-}O\text{-}R' + H_2O \rightarrow R\text{-}CH_2\text{-}OH + HO\text{-}CH_2\text{-}R'$

Example: polyethylene oxide (PEO) $(\text{-}CH_2\text{-}O\text{-}CH_2\text{-})_N$

Properties: water soluble, semicrystalline, $T_g \sim -60°C$
Uses: hydrogels, protein-resistant coatings

- Urethanes: $R\text{-}NH\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}R' + H_2O \rightarrow R\text{-}NH\text{-}\overset{O}{\overset{\|}{C}}\text{-}OH + HO\text{-}R'$

Example: polyether urethane



Properties: "soft" block of SPU "Biomer", slow hydrolysis
Uses: pacemaker lead sheaths & connectors

- Ureas: $\text{R-NH-}\overset{\overset{\displaystyle O}{||}}{C}\text{-NH-R'} + H_2O \rightarrow \text{R-NH-}\overset{\overset{\displaystyle O}{||}}{C}\text{-OH} + H_2N\text{-R'}$

- Carbonates: $\text{R-O-}\overset{\overset{\displaystyle O}{||}}{C}\text{-O-R'} + H_2O \rightarrow \text{R-O-}\overset{\overset{\displaystyle O}{||}}{C}\text{-OH} + \text{HO-R'}$

Rates of Hydrolysis: anhydride > ester > amide > ether

Stable Polymer Chemistries:

- Olefins
  e.g., UHMWPE: joint cup liners
- Halogenated hydrocarbons
  e.g., PVC: catheters; PTFE: vascular grafts
- Siloxanes
  e.g., PDMS: soft tissue prostheses
- Sulfones
  e.g., PSf: renal dialysis membranes

b) Biological Factors Influencing Hydrolysis

- pH variations
  inflammation/infection ⇒ ↓pH, catalyzes hydrolysis

- Hydrolases—enzymes that catalyze hydrolytic reactions

  - Proteolases: catalyze hydrolysis of peptide bonds
  - Esterases: catalyze hydrolysis of ester bonds
  - Produced by phagocytic cells

c) Influence of Hydrolysis on *In Vivo* Performance

- Loss of structural integrity
  e.g., i) polyester urethanes: rapid degradation in orthopedic reconstructions (no longer used)

  ii) PET fibers: deterioration after long periods in cardiovascular applications

- Toxicity/mutagenicity
  e.g., i) segmented polyurethanes (SPUs): suspected tumorigenicity of degradation products

  ii) cyanoacrylates (soft tissue adhesive): hydrolysis generates formaldehyde