# Biodegradable Solid Polymeric Materials
(continued)

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<td>Supplementary Reading:</td>
<td>R.J. Young and P.A. Lovell, “Introduction to Polymers,” ch. 4 <em>Polymer Structure</em> pp. 241-309 (crystallization of polymers, Tm, glass transition, etc.)</td>
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Last time

MATERIALS FOR IMPLANT APPLICATIONS:

(1) PERMANENT/IMPLANTS

(2) BIOELIMINABLE
  - WATER-SOLUBLE, SUITABLE FOR KIDNEY CLEARANCE

(3) BIODEGRADABLE
  - BREAKDOWN BY HYDROLYSIS
  - O ESTERS
  - O O
  - CO-C-
  - O-C-O
  - ANHYDRIDES
  - CARBONATES
  - N-C-
  - AMIDES
  - HYDROLYSIS
Last time

3 Pathways of Polymer Breakdown:

* Crosslink Degradation:

* Side Chain Degradation:

* Backbone Degradation:

H₂O → Insoluble

H₂O → Soluble
Physical chemistry of hydrolysis: structure influences mechanism of erosion as well as overall rate

- Mechanisms of dissolution:

  - Bulk erosion
  - Surface erosion

  - Matrix dimensions constant until failure
  - Linear loss of mass at surfaces

  MW decays w/time
Factors controlling solid polymer degradation rates

5 FACTORS:

- Bond Stability: Amides > Esters > Orthoesters > Anhydrides

- Hydrophobicity

- Steric Effects

- Production of Autocatalytic Breakdown Fragments

- Microstructure
  - Crystallinity
  - Phase Separation
  - Porosity

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(2) Effect of polymer hydrophobicity on solid polymer erosion rate

![Diagram showing the effect of polymer hydrophobicity on solid polymer erosion rate.](image)

- **Polyanhydride Sample Degradation Rate Constant**: $k$ (mm/hr)
- **Percent Mass Loss**
- **Time (hr)**

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**Polyanhydride Sample Degradation Rate Constant $k$ (mm/hr)**

- $1.00 \times 10^{-6}$
- $1.00 \times 10^{-5}$
- $1.00 \times 10^{-4}$
- $1.00 \times 10^{-3}$
- $1.00 \times 10^{-2}$
- $1.00 \times 10^{-1}$
- $1.00 \times 10^{0}$

**Percent Mass Loss vs. Time (hr)**

- Poly(MSA)
- Poly(MCPh)
- 72/25 Poly(MSA-co-CPH)
- 50/50 Poly(MSA-co-CPH)
- 75/25 Poly(MSA-co-MSA)
- Poly(MSA-co-MC)

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**Figure by MIT OCW.**
(3) Steric effects controlling polymer hydrolysis rates

• Local structure

• Glass transition (Tg)

\[ \text{POLYGLYCOLIDE} \]

\[ \text{POLYLACTIDE} \]

\[ (\text{H-C-O-C-C-O})_n \]

\[ (\text{H-C-C-O-C-C-O})_n \]

\[ \text{H}_2\text{O} \text{ INTRUSION} \]

\[ \text{PLASTICIZERS} \]

\[ \text{POLYMER} \]

\[ \text{BULK ERODING} \]

\[ \text{POLYMERS TYPICALLY} \]

\[ \text{HAVE 1-2 WT% H}_2\text{O} \]
(4) Production of autocatalytic products

- Polyesters:

Oligomer solubility in H₂O:
Critical MW for solubility:
- Polycapro lactone: ~5 kDa
- PLA: ~1.2 kDa

\[ \text{PH} \downarrow \text{...catalyzes} \quad \text{degradation?} \]
Hydrolysis rate theory

No acid catalysis:

\[
\text{H}_2\text{O} + \overset{\text{O}}{\text{C}}\overset{\text{O}}{-} \xrightarrow{\text{k}'} \overset{\text{O}}{-}\text{C}\overset{\text{O}}{\text{H}} + \text{H}_2\text{O} - \\
\overset{\text{E}}{-} \\
\overset{\text{E}}{-}
\]

\[
\frac{d[\text{cooh}]}{dt} = k' [\text{H}_2\text{O}][\text{E}] \leq k_{\text{eff}} \quad \therefore [\text{cooh}] = [\text{cooh}]_0 + k_{\text{eff}} t
\]

\(= \text{constant} \quad \text{if} \ k' \text{ is small} \)

Relationship to molecular weight (M):

\[
\overset{\text{H}_2\text{O}}{-}\text{COOH} + \overset{\text{H}_2\text{O}}{-}\overset{\text{OH}}{-}\text{COOH} \quad \frac{[\text{cooh}]}{\text{MW}} = \frac{\rho}{\text{MOL. WEIGHT}} \\
(\rho = 1 \text{ for many polymers})
\]

\[
\frac{1}{\text{MW}} \leq \frac{1}{\text{MW}_0} \quad \frac{\rho}{\text{cm}^3}
\]

\[
\text{INITIAL MOL. WT.}
\]
Mechanisms of hydrolysis: polyesters

*Esters can be both acid and base catalyzed during hydrolysis*

- **acid-catalyzed hydrolysis:**

  \[
  \text{ester} + \text{H}_2\text{O} \rightarrow \text{carboxylic acid} + \text{alcohol}
  \]
Mechanisms of hydrolysis: polyesters

• Base-catalyzed hydrolysis: (saponification)

Nucleophilic substitution at acyl carbon
Rate of chain cleavage

Autocatalysis of chain degradation:

\[
\frac{d[\text{COOH}]}{dt} = k'' [\text{COOH}] [\text{H}_2\text{O}] [\text{E}] \leq k_{\text{eff}} [\text{COOH}]
\]

\[
[\text{COOH}] = [\text{COOH}]_0 e^{-k_{\text{eff}} t}
\]

\[
\ln \frac{\text{MW}}{\text{MW}_0} = e^{-k_{\text{eff}} t}
\]

(transition states)

Observed for many degradable polymers

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(Pitt 1987)
(5) Phase separation

Semicrystalline polymers:

2 (or more) immiscible components:
Crystallinity and Phase Separation Effects.

• Zong, 1999
Crystalline regions resist hydrolysis

Figure 4. Selected WAXD profiles for the crystalline (a) PGA and (b) PGA-co-PLA samples during in vitro degradation.

Changes of degree of crystallinity of crystalline PGA and PGA-co-PLA samples during in vitro degradation.
Crystalline regions resist hydrolysis

Figure 10. Schematic diagram of in vitro degradation mechanism in the dual lamellar stacks model of semicrystalline samples.

(Zong 1999)

Figure removed for copyright reasons.

Please see:

(5) Phase separation: Hydrolysis in polymer blends

Blends of hydrophilic and hydrophobic polymers

Amorphous state - miscible

Incompatible crystal lattices

e.g. poly(lactide)/poly(ethylene oxide)

\[
\text{e.g. PEO (CH}_2\text{-CH}_2\text{-O)}_n
\]

INCREASED H\text{}_2\text{O UPTAKE}

HYDROPHILIC COMPONENT

LEACH OUT HYDROPHILIC COMPONENT

INCREASED H\text{}_2\text{O UPTAKE, BUT PEO NOT LEACHED AWAY}

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Blends of poly(L-lactide) with poly(ethylene oxide)

Mass loss of several PLLA/PEO blends during hydrolytic degradation.

Figure by MIT OCW.
Constrained mass loss: PLLA-b-PEO-b-PLLA triblock copolymers
Summary of factors controlling solid polymer degradation rates:

- Bonds with short 1/2 life: $\frac{dmw}{dt}$ → ↑
- Increasing hydrophobicity: ↓
- Bulky pendant groups: ↓
- Autocatalysis: ↑
- Crystallinity: ↓
- Phase separation: Usually ↑
Bulk vs. surface erosion: how do we predict it?

**Bulk erosion**

**Surface erosion**

Figures removed for copyright reasons.
Please see:


Images of Surface Erosion removed due to copyright restrictions.
Göpferich theory of polymer erosion

- If polymer is initially water-insoluble, and hydrolysis is the only mechanism of degradation, then two rates dominate erosion behavior:

1) Rate of \( H_2O \) diffusion into matrix
\[ \Rightarrow t_{\text{diff}} \]

2) Rate of chain cleavage by \( H_2O \)
\[ \Rightarrow t_c \]

\( t_{\text{diff}} \ll t_c \rightarrow \text{bulk erosion} \)

\( t_{\text{diff}} \gg t_c \rightarrow \text{surface erosion} \)
Rate of water diffusion into polymer matrix

\[ \langle x \rangle = 2 \left( \frac{D_{\text{H}_2\text{O}} t}{\ell} \right)^{1/2} \]

\[ t_{\text{DIFF}} = \frac{\langle x \rangle^2 \pi}{4 D_{\text{H}_2\text{O}}} \]

Figure by MIT OCW.

(Atkins 1997)
Rate of chain cleavage

Consider bonds breaking within some volume of the sample.
- Bond breaks are independent stochastic events w/ mean

\[ t = 0 \]
\[ 1 \quad 2 \quad 3 \quad 4 \quad \ldots \]

\[ \Delta t \quad \Delta t \quad \Delta t \quad \Delta t \]

DISTRIBUTION OF TIMES BETWEEN BREAKS IS EXPONENTIAL:

\[ p(t) = k e^{-kt} \]

\[ = \text{probability that time between breaks is } t \]

Poisson kinetics

INCREASING \[ k \]

INCREASING \[ t \]
Further Reading