Biodegradable Solid Polymeric Materials (continued)

Last time: chemistry and physical chemistry of degrading polymeric solids for biomaterials

Today: Factors controlling polymer degradation rates
Theory of polymer erosion

Reading: F. von Burkersroda et al., ‘Why degradable polymers undergo surface erosion or bulk erosion,’ Biomaterials 23, 4221-4231 (2002)

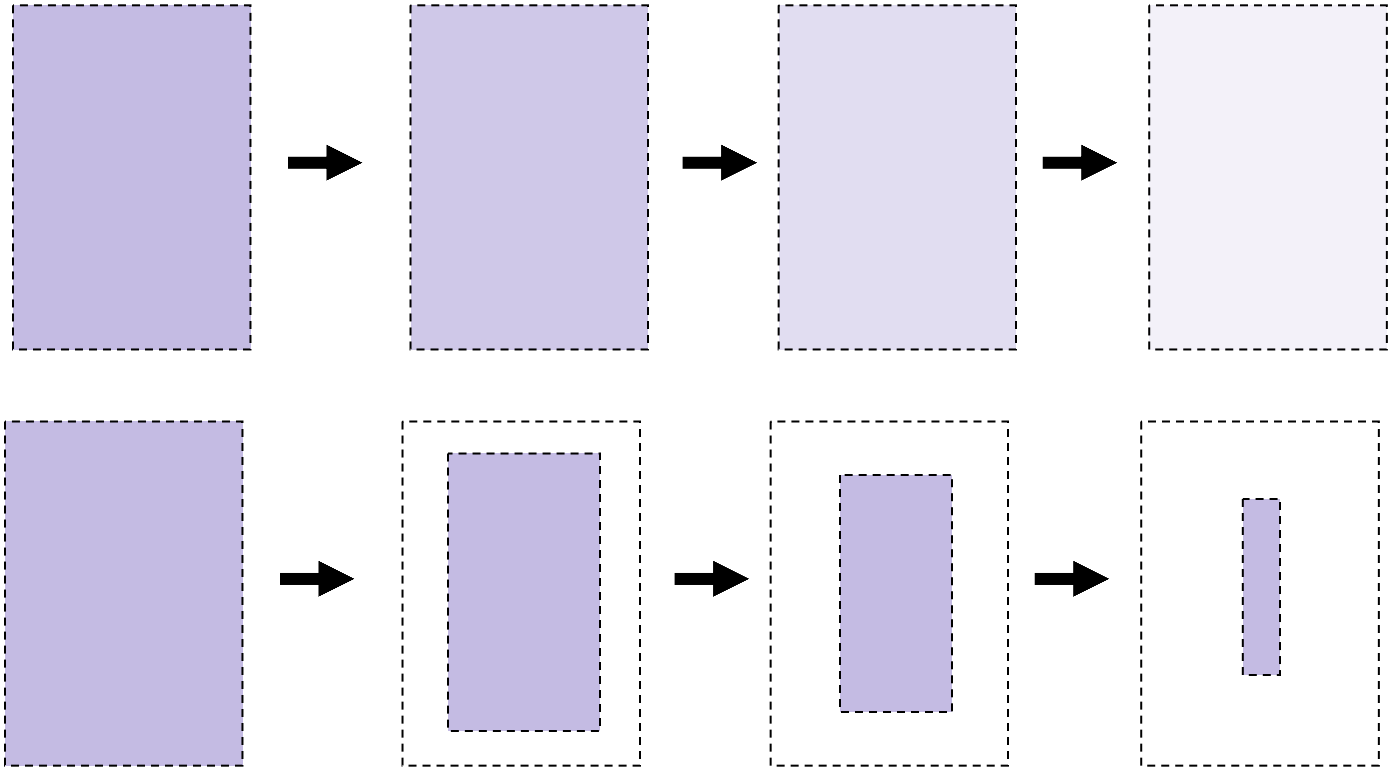
Supplementary Reading: R.J. Young and P.A. Lovell, “Introduction to Polymers,” ch. 4 *Polymer Structure* pp. 241-309 (crystallization of polymers, Tm, glass transition, etc.)

Last time

Last time

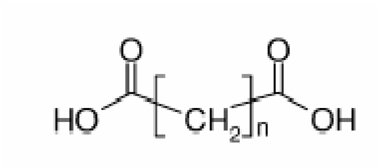
Physical chemistry of hydrolysis: structure influences mechanism of erosion as well as overall rate

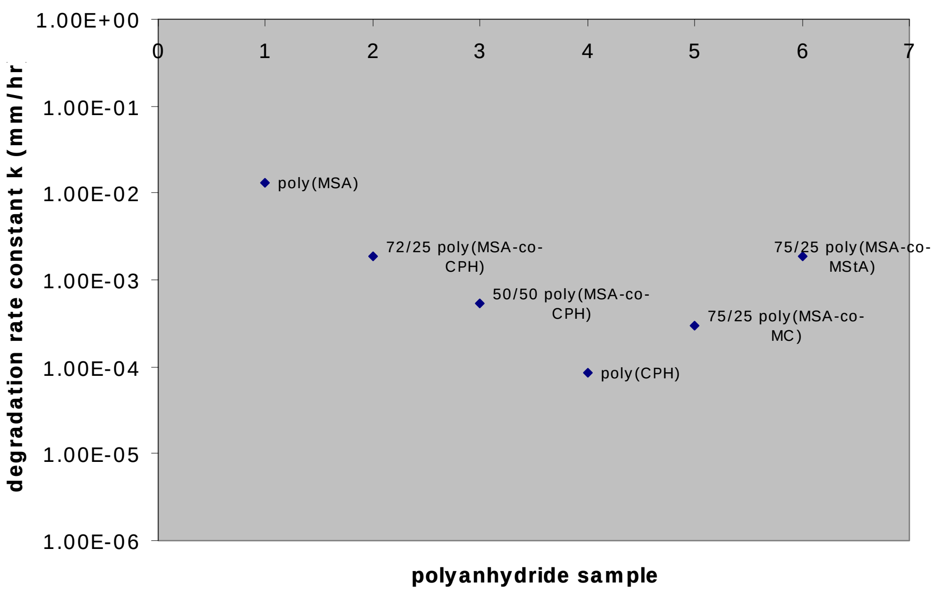
- Mechanisms of dissolution:

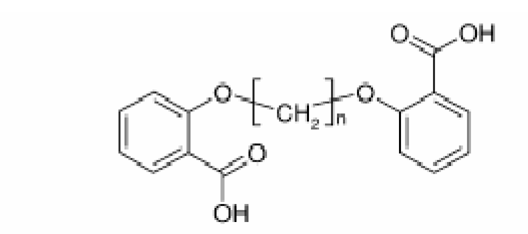


Factors controlling solid polymer degradation rates

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







n = 6 : 1,6-bis(o-carboxyphenoxy)hexane (o-CPH)

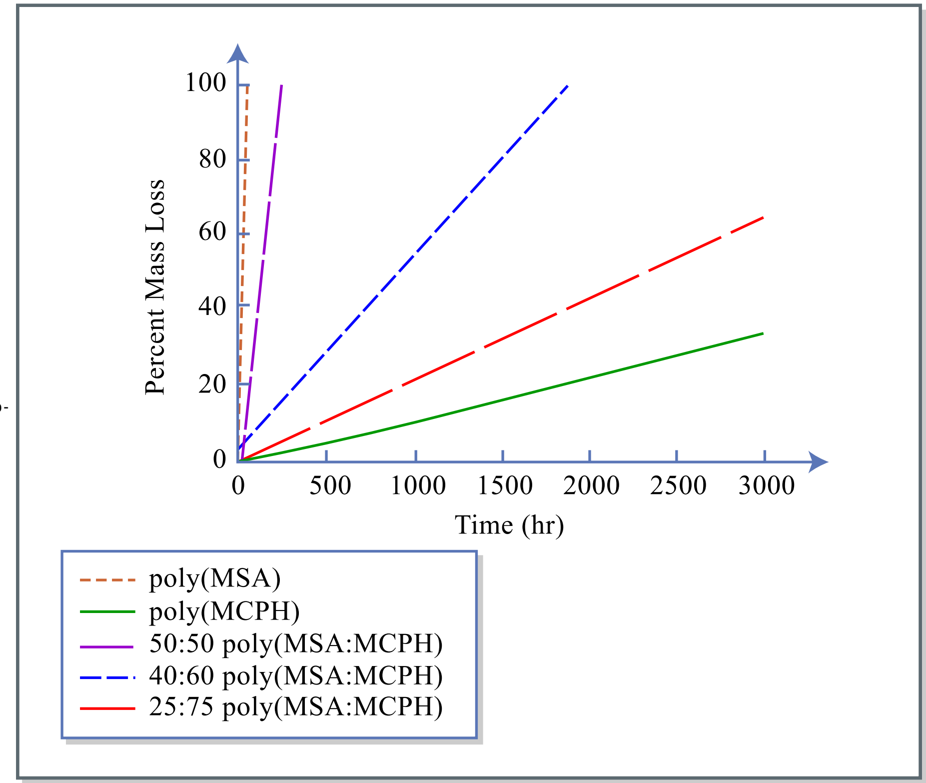


Figure by MIT OCW.

(3) Steric effects controlling polymer hydrolysis rates

- Local structure

- Glass transition (Tg)

(4) Production of autocatalytic products

- Polyesters:

Hydrolysis rate theory

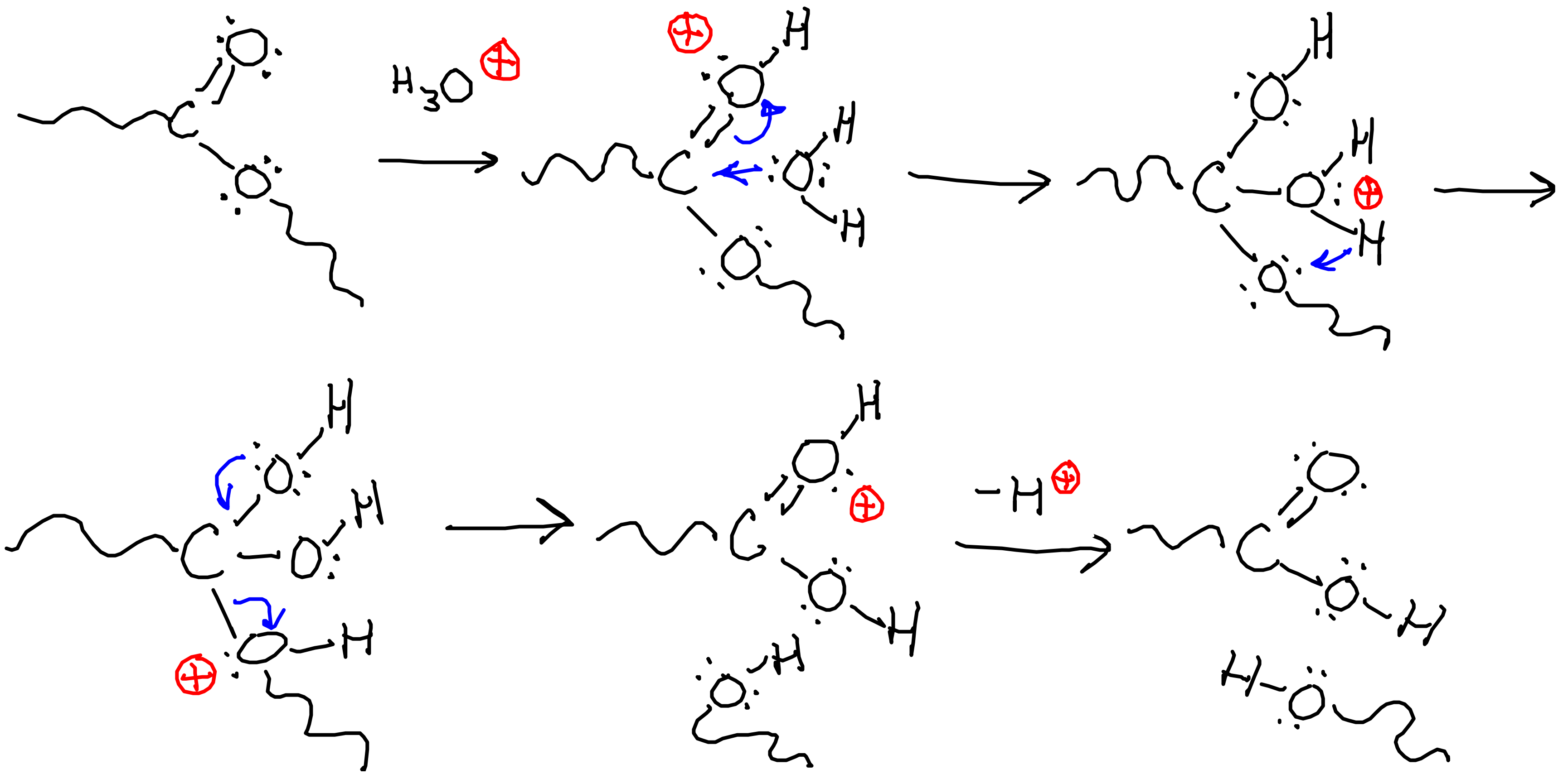
No acid catalysis:

Relationship to molecular weight (M):

(Pitt 1987)

Mechanisms of hydrolysis: polyesters

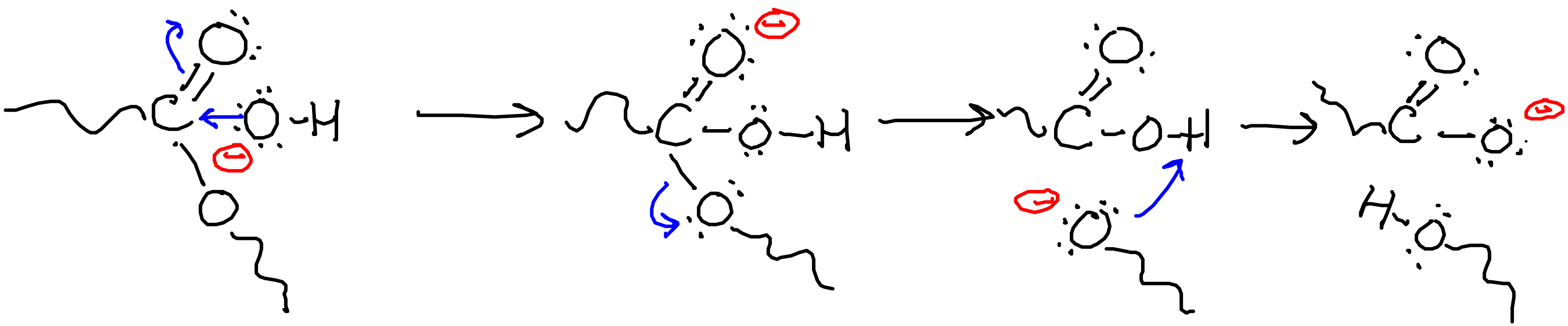
- acid-catalyzed hydrolysis:



Mechanisms of hydrolysis: polyesters

- Base-catalyzed hydrolysis:

(saponification)



Nucleophilic substitution at acyl carbon

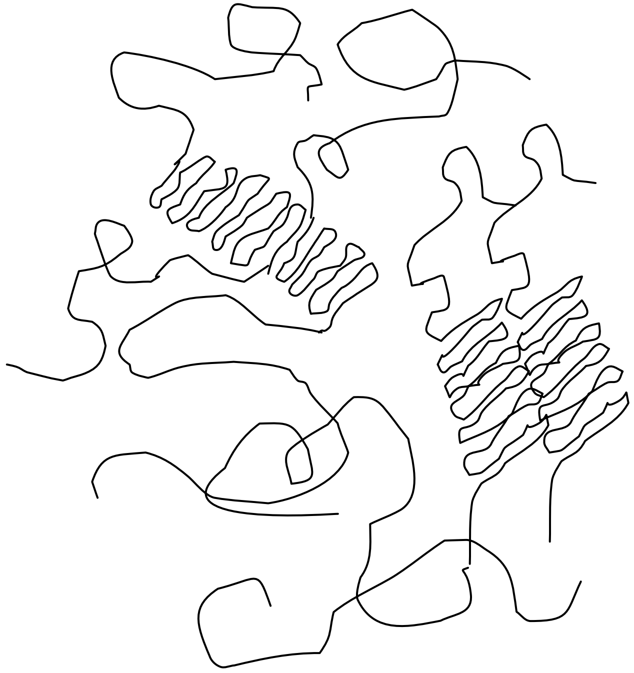
Rate of chain cleavage

Autocatalysis of chain degradation:

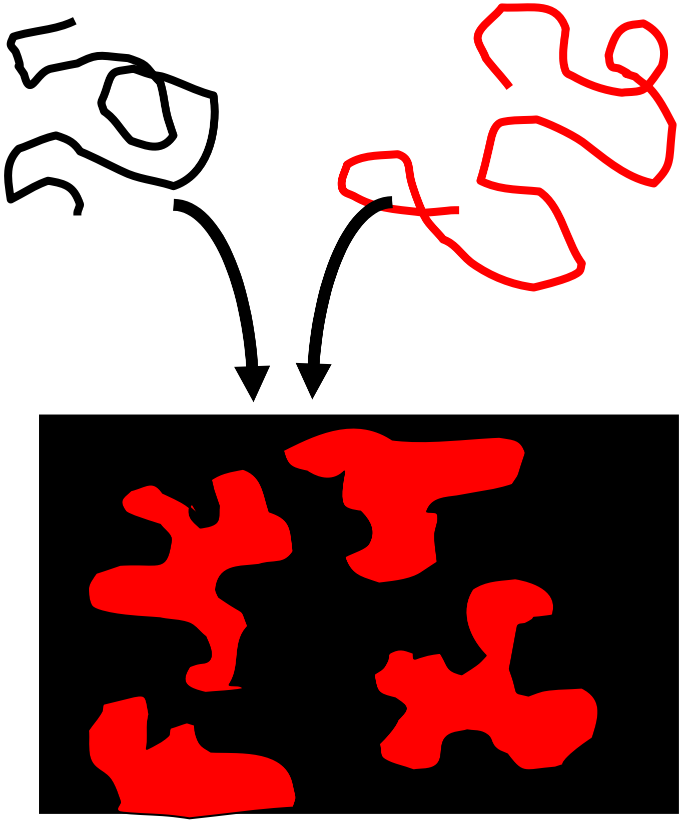
(Pitt 1987)

(5) Phase separation

Semicrystalline polymers:



2 (or more) immiscible components:



Crystallinity and Phase Separation Effects.

•Zong, 1999
•Shakesheff, K.M., M. C. Davies, C. J. Roberts, S. B. J. Tendler, A. G. Shard, and A. Domb. “In Situ Atomic Force Microscophy Imaging of Polymer Degradation in an Aqueous Environment.” *Langmuir* 10 (1994): 4417-4419.

Crystalline regions resist hydrolysis

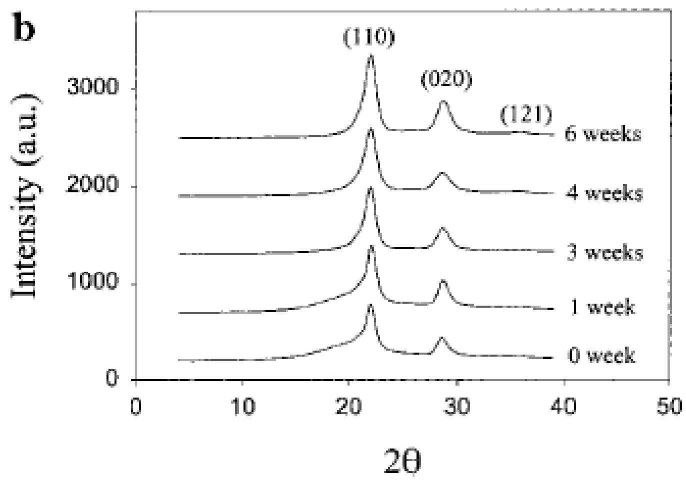
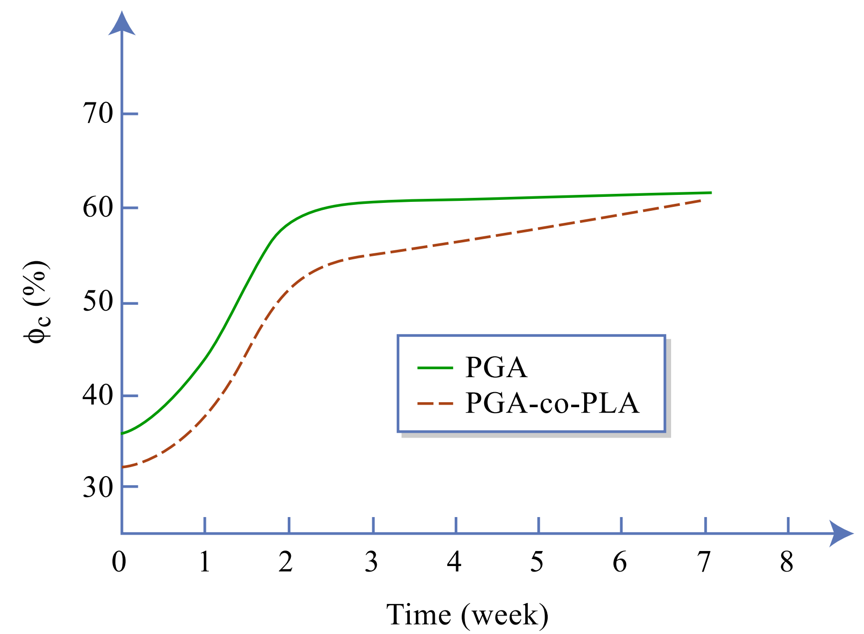


Figure 4. Selected WAXD profiles for the crystalline (a) PGA and (b) PGA-*co*-PLA samples during in vitro degradation.



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

Figure by MIT OCW.

(Zong 1999)

Crystalline regions resist hydrolysis

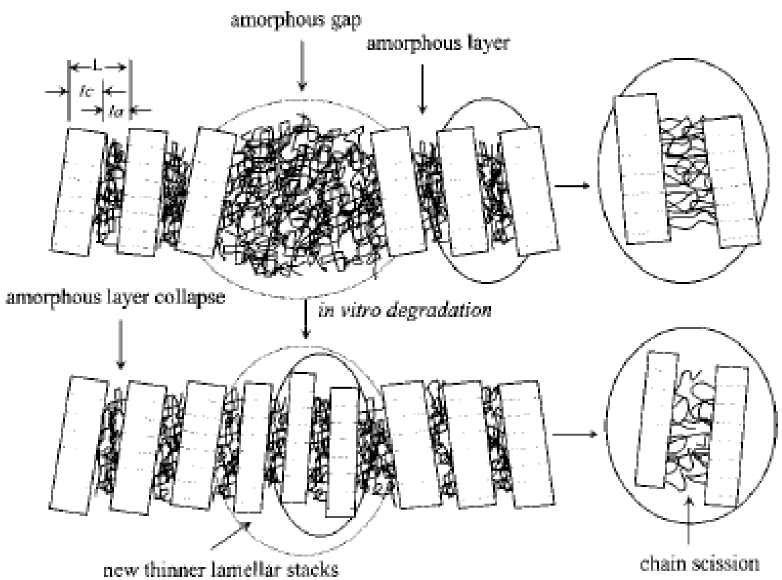


Figure 10. Schematic diagram of in vitro degradation mechanism in the dual lamellar stacks model of semicrystalline samples.

(Zong 1999)

Figure removed for copyright reasons.

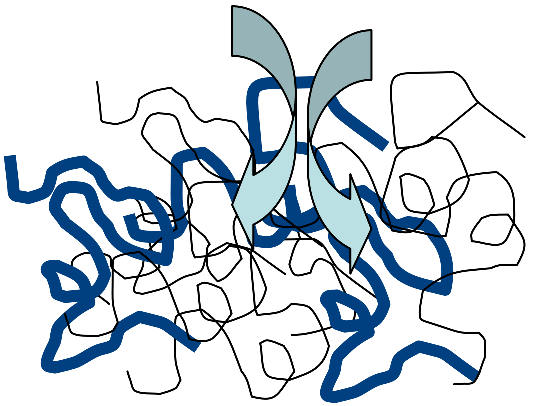
Please see:

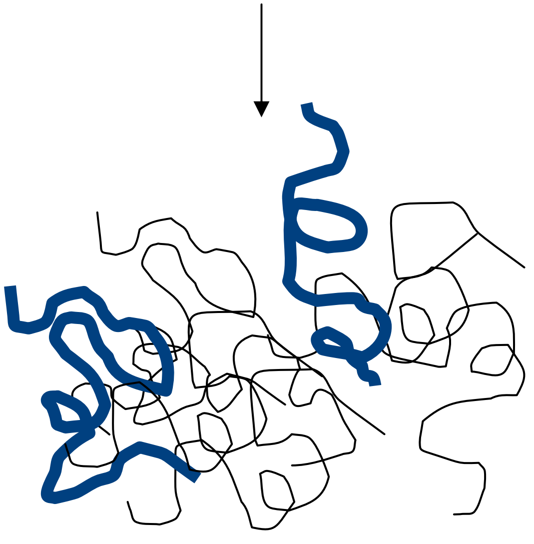
Figure 2 in Shakesheff, K. M., M. C. Davies, C. J. Roberts, S. B. J. Tendler, A. G. Shard, and A. Domb. "In Situ Atomic Force Microscopy Imaging of Polymer Degradation in an Aqueous Environment." *Langmuir* 10 (1994): 4417-4419.

(5) Phase separation: Hydrolysis in polymer blends

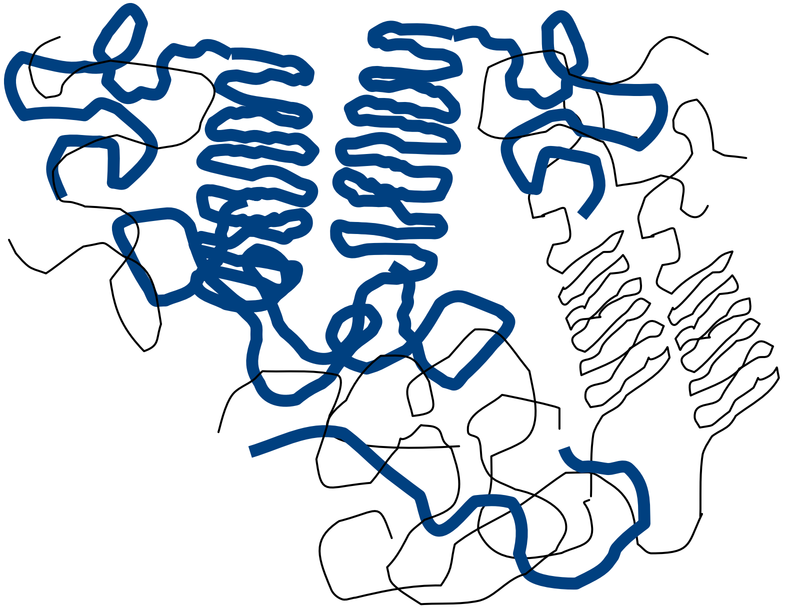
Blends of hydrophilic and hydrophobic polymers

Amorphous state - miscible



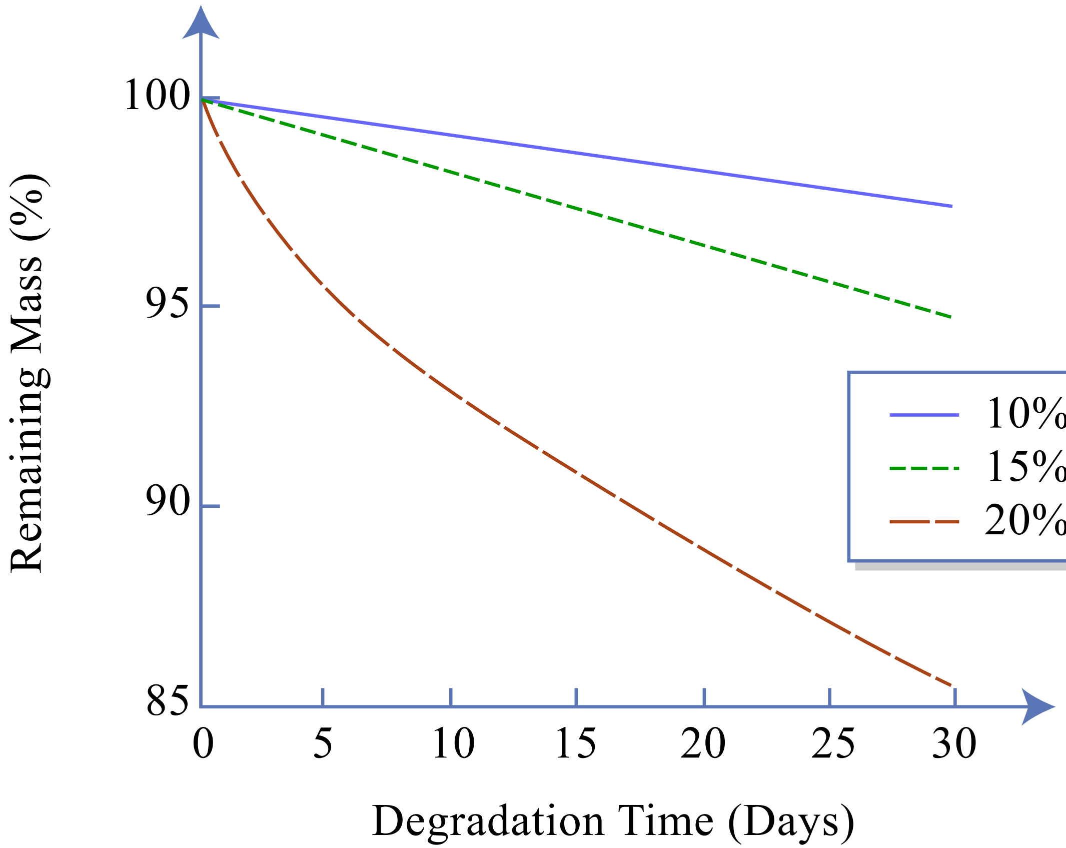


Incompatible crystal lattices



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

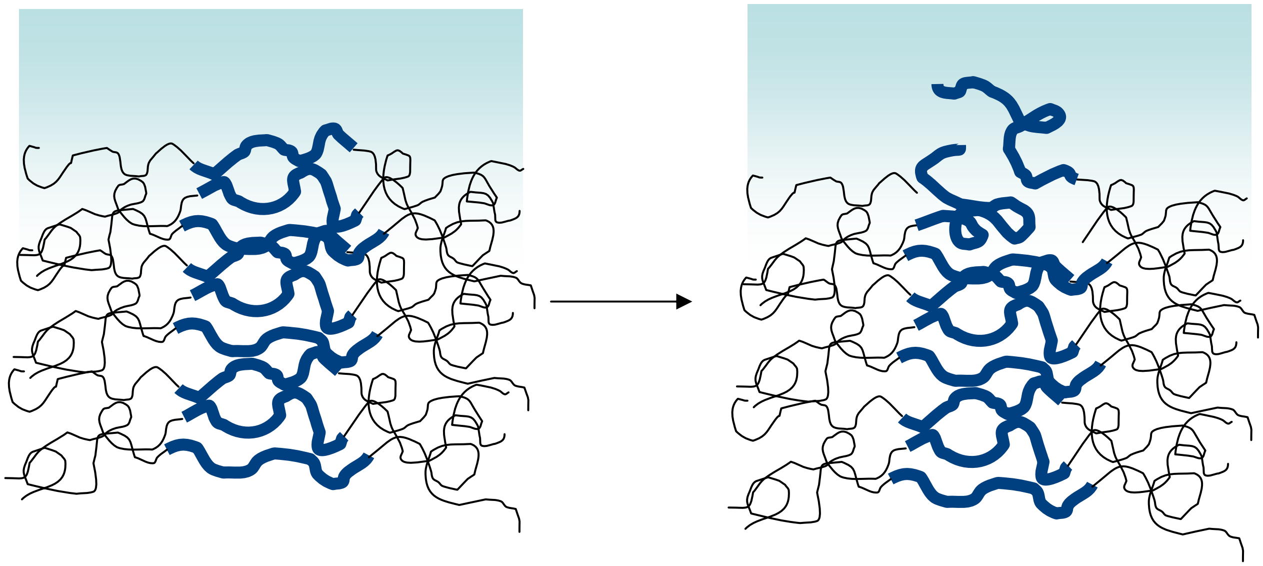
Blends of poly(L-lactide) with poly(ethylene oxide)



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:

Bulk vs. surface erosion: how do we predict it?

Bulk erosion | **Surface erosion**

Figures removed for copyright reasons.
Please see:

Fig. 8(b) in Lu, L., C. A. Garcia, and A. G. Mikos. "In Vitro Degradation of Thin Poly(DL-lactic-co-glycolic acid) Films." *J Bio Med Mater Res* 46 (1999): 236-44.

Images of Surface Erosion removed due to copyright restrictions.

Fig. 6(d) in Agrawal, C. M., and K. A. Athanasiou. "Technique to Control pH in Vicinity of Biodegrading PLA-PGA Implants." *J Biomed Mater Res* 38 (1997): 105-14.

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:

Rate of water diffusion into polymer matrix

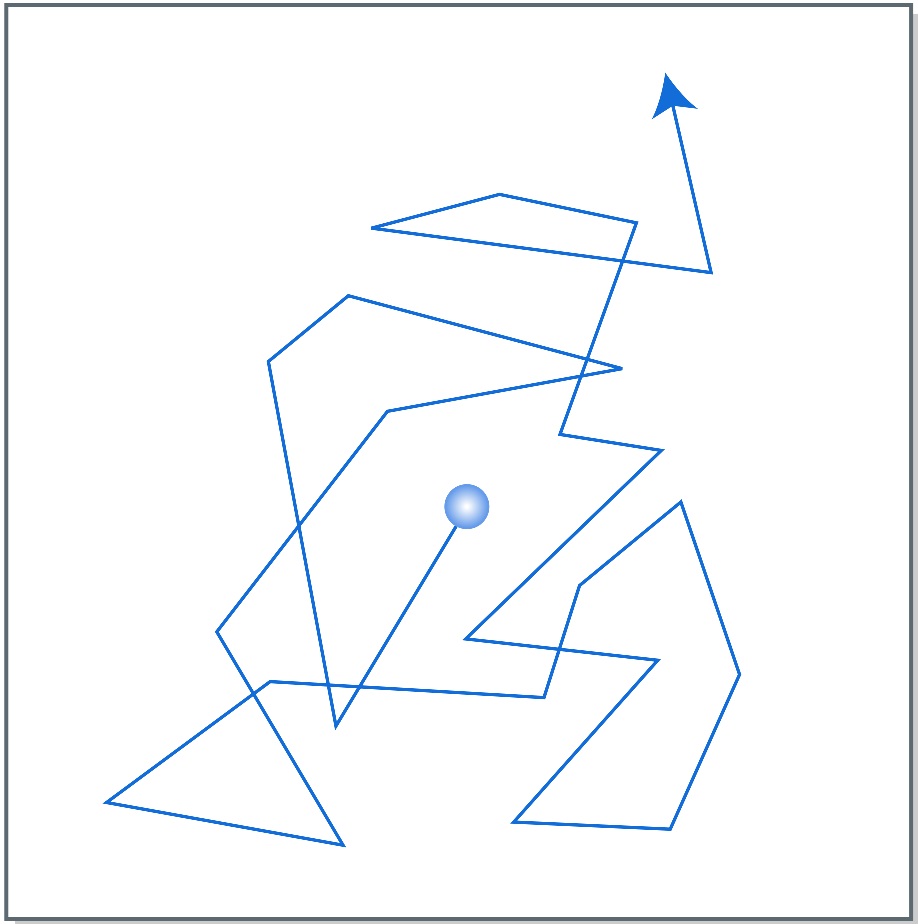
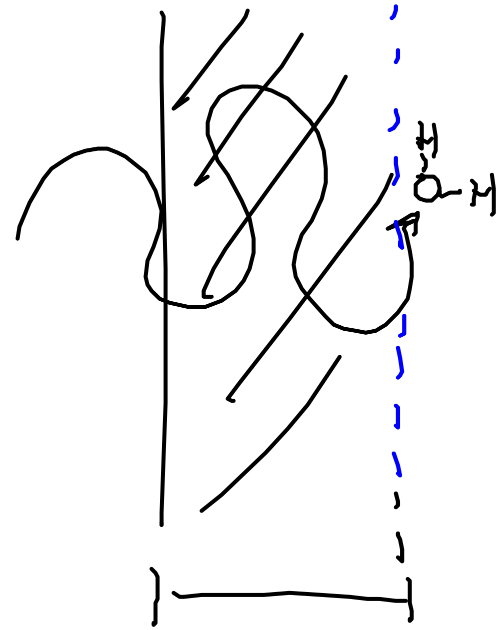
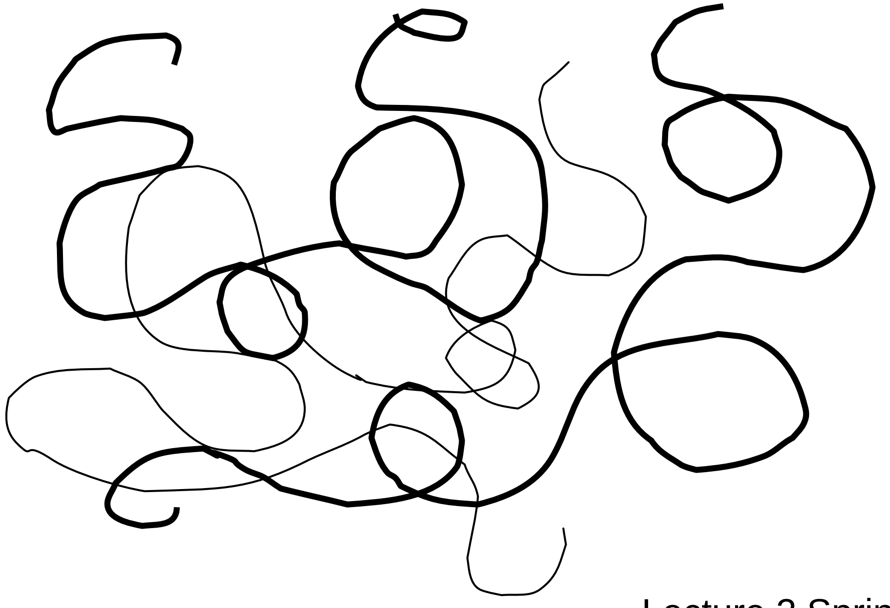


Figure by MIT OCW.



(Atkins 1997)

Rate of chain cleavage



Further Reading

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2. Gopferich, A. Polymer bulk erosion. *Macromolecules* **30**, 2598-2604 (1997).
3. Gopferich, A. Mechanisms of polymer degradation and erosion. *Biomaterials* **17**, 103-14 (1996).
4. von Burkersroda, F., Schedl, L. & Gopferich, A. Why degradable polymers undergo surface erosion or bulk erosion. *Biomaterials* **23**, 4221-31 (2002).
5. Agrawal, C. M. & Athanasiou, K. A. Technique to control pH in vicinity of biodegrading PLA-PGA implants. *J Biomed Mater Res* **38**, 105-14 (1997).
6. Lu, L., Garcia, C. A. & Mikos, A. G. In vitro degradation of thin poly(DL-lactic-co-glycolic acid) films. *J Biomed Mater Res* **46**, 236-44 (1999).
7. Tsuji, H. & Nakahara, K. Poly(L-lactide). IX. Hydrolysis in acid media. *Journal of Applied Polymer Science* **86**, 186-194 (2002).
8. Atkins, P. *The Elements of Physical Chemistry* (W.H. Freeman, New York, 1997).
9. Pitt, C. G., Marks, T. A. & Schindler, A. in *Controlled Release of Bioactive Materials* (ed. Baker, R. W.) 19-43 (Academic Press, New York, 1980).
10. Albertsson, A. C. & Varma, I. K. in *Degradable Aliphatic Polyesters* 1-40 (2002).
11. Stridsberg, K. M., Ryner, M. & Albertsson, A. C. in *Degradable Aliphatic Polyesters* 41-65 (2002).
12. Barrera, D. A., Zylstra, E., Lansbury, P. T. & Langer, R. Synthesis and RGD peptide modification of a new biodegradable copolymer: poly(lactic acid-co-lysine). *J. Am. Chem. Soc.* **115**, 11010-11011 (1993).
13. Barrera, D. A., Zylstra, E., Lansbury, P. T. & Langer, R. Copolymerization and degradation of poly(lactic acid-co-lysine). *Macromolecules* **28**, 425-432 (1995).
14. Cook, A. D. et al. Characterization and development of RGD-peptide-modified poly(lactic acid-co-lysine) as an interactive, resorbable biomaterial. *J Biomed Mater Res* **35**, 513-23 (1997).
15. Ivin, K. J. *Ring-opening polymerization* (Elsevier, London, 1984).
16. Burkoth, A. K. & Anseth, K. S. A review of photocrosslinked polyanhydrides: in situ forming degradable networks. *Biomaterials* **21**, 2395-404 (2000).
17. Burkoth, A. K., Burdick, J. & Anseth, K. S. Surface and bulk modifications to photocrosslinked polyanhydrides to control degradation behavior. *J Biomed Mater Res* **51**, 352-9 (2000).