

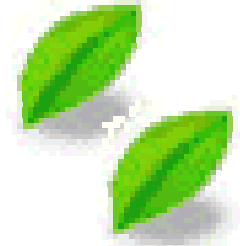


Biodegradable Polymers in Drug Delivery

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Outline



Introduction

Types of biodegradable polymers and their applications

Degradable mechanism

Surface characterizations (XPS, SIMS, AFM)

Summary and Future prospects

Introduction

Idealized drug delivery: Required amount of active agents at desired time and at desired site of action in body

Methods:

Mixed with polymer

Encapsulated in nano- and microparticles

Attached to polymer chains

- Using biodegradable polymers drug release
- **Advantages:** disappear over time



Biodegradable Polymer from natural, synthetic or semi-synthetic sources

- Natural Polymers

 - Polysaccharides

 - Protein-based polymers

 - Others: collagen, Hyaluronate, Chitosan, Fibrin, Alginate, Agarose,

- Synthetic Polymers

 - Polyesters: Poly (glycolic acid) PGA, Poly (lactic acid) PLA, and copolymer PLGA, polycaprolactone PCL

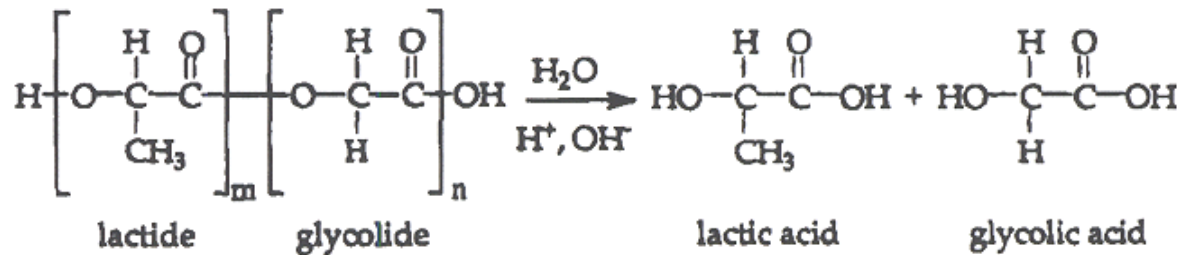
 - Polyanhydrides

 - Poly (ethylene glycol) PEG and its derivatives and copolymers

 - Polyamides, Poly (vinyl alcohol) PVA , Polypeptides

Poly (lactic acid-co-glycolic acid) (PLGA)

-----the “**gold standard**” of biodegradable polymers

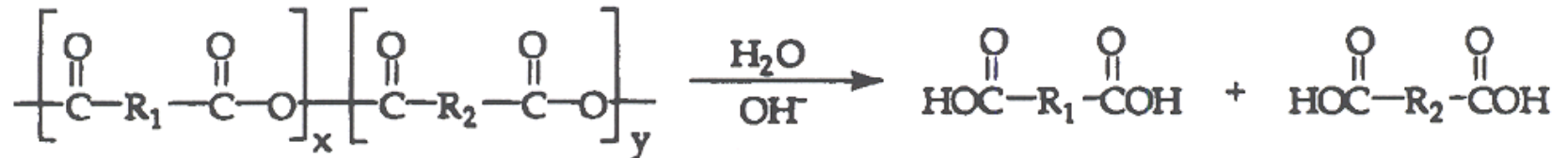


- Used as a resorbable suture material for decades
- Biocompatibility and FDA approval
- Commercial availability
- Controllable degradation rate (from a few weeks to many months)
 - dependent on MW
 - ratio of the copolymer components

Polyanhydrides

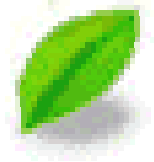


- Introduced to the field of controlled drug delivery more than 20 years



- Undergo hydrolytic bond cleavage to form water-soluble degradation products
- Extensive research: study chemistry, toxicity and medical applications

Critical **design parameters** of biodegradable polymers



- Classical physical properties
 1. Mechanical property
 2. Degradation: controlled degradation due to hydrolysis, the action of enzymes or dissolution.
- Biocompatibility: no damage in adjacent cells

Degradation

The process of polymer chain scission by the cleavage of bonds between the monomers in polymer backbone

Biodegradation

The chemical breakdown of materials by the action of living organisms which leads to changes in physical properties.

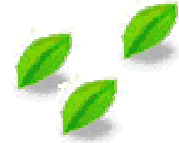
Erosion

The mass loss of a polymer matrix due to the loss of monomers, oligomers or even pieces of non-degraded polymer.

Erosion can be the result of biological, chemical or physical effects.

Degradation is the most important part of erosion.

Degradable mechanism



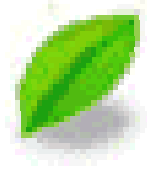
- Degradation is characterized by a loss of molecular weight and initiates polymer erosion.
- Four major modes of polymers degradations:
 - Photo-degradation
 - Mechanical-degradation
 - Thermal-degradation
 - Chemical-degradation
- **Chemical degradation** is the most important for biodegradable polymers

- **Hydrolysis** is the most important mode of chemical degradation.
- Hydrolysis-----breakdown of organic materials through the use of water

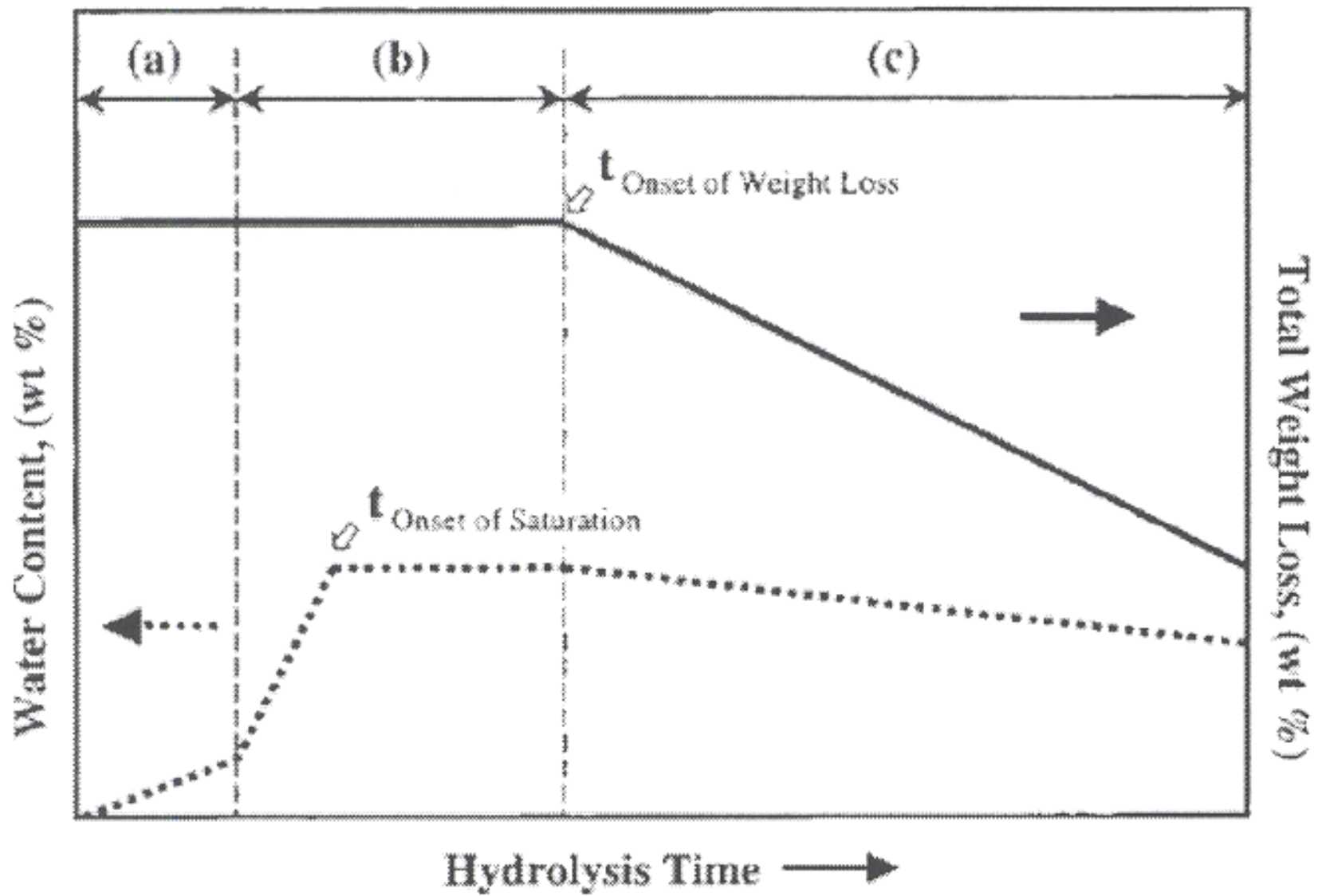
Catalyzed by acids, bases, salts, or enzymes.

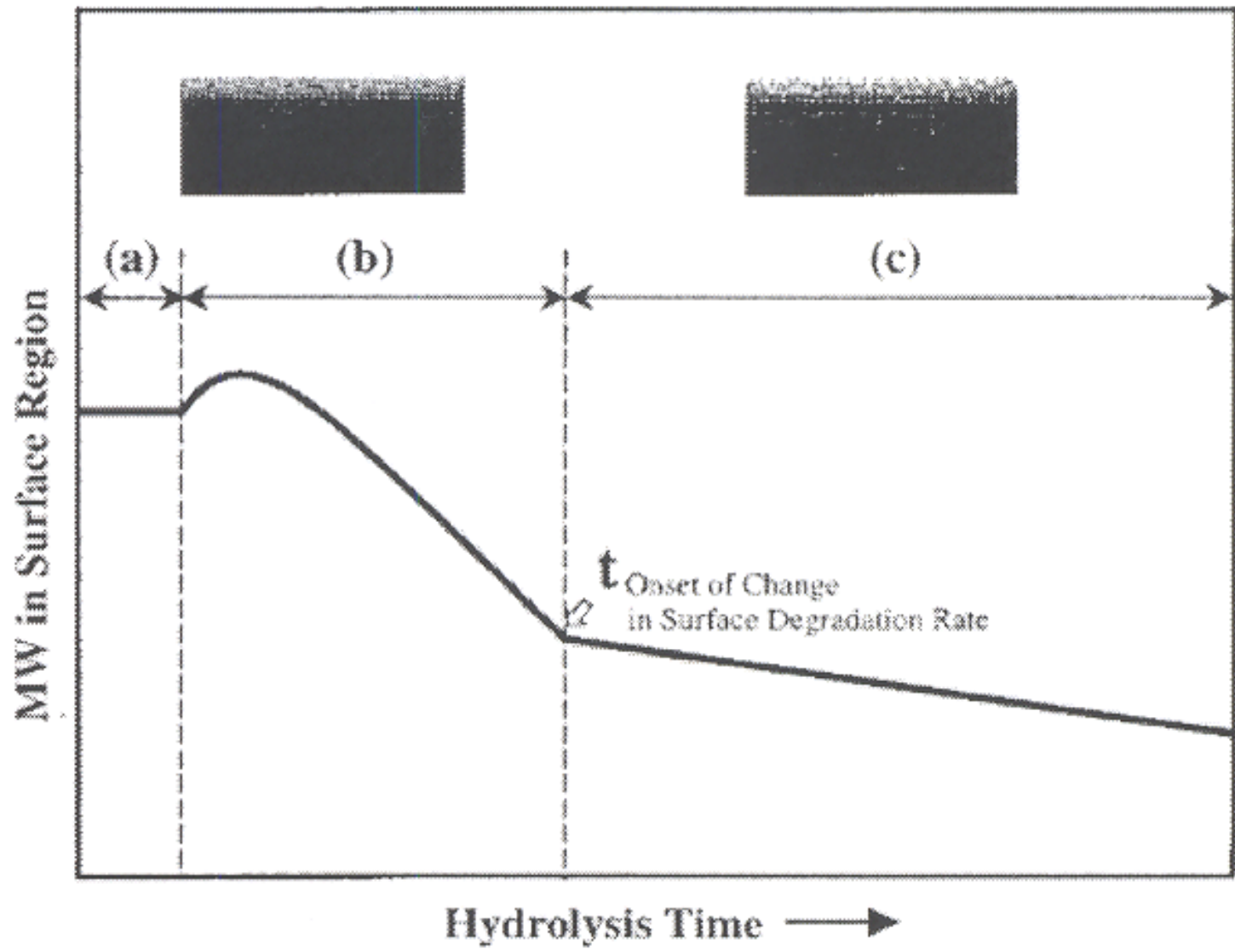
The result of its chemical structure, its morphology, its dimensions and the body's environment.

General stages of hydrolysis



- A Starts with water penetrates deeply into the interior areas
- B The functional groups in polymer chains hydrolyze and absorb the water.
Water reacts with the polymer resulting in cleavage of covalent chemical bonds
- C Polymer is broken down to oligomers and monomers (transported from the polymer bulk controlled by diffusion)
The release of degradation products leads to the mass loss which is characteristic for erosion.

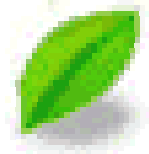




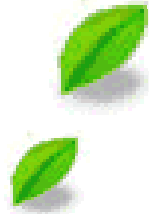
Factors affecting the velocity of degradation



- Chemical bond nature: functional groups
- Water uptake: degradation rates increase when raising the content of the hydrophilic components
- PH: change degradation rates of polyesters by orders of magnitude
- Crystalline and molecular weight
- Copolymer composition



Enzymatic degradation

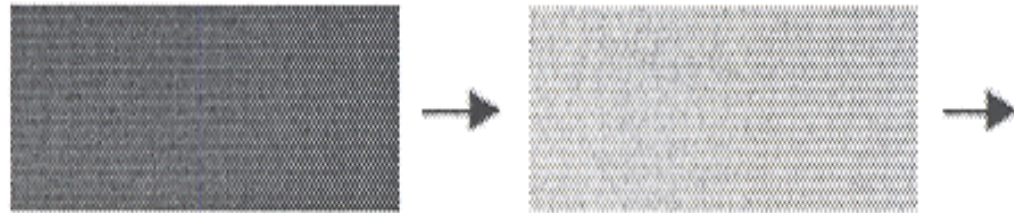


- Mainly effective for naturally polymers (polysaccharides and polypeptides)
- Serve a classic catalytic function, altering reaction rate (via ion or charge transfer) by modifying activation energy
- **Mechanism:**
 - Develop conformation allows “**recognition**” of chain sequences (**receptor**) on biopolymers.
 - Complexes form between segments of the enzyme and the biopolymer substrate which result in enhanced bond cleavage rates.

Bulk erosion



Bulk erosion



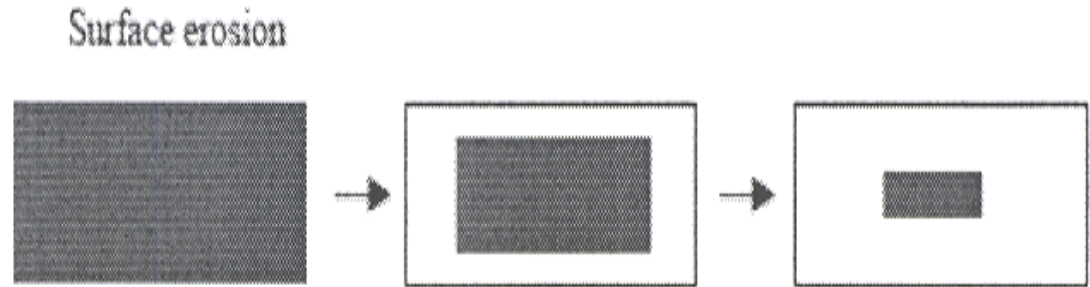
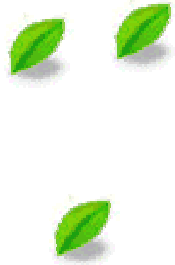
Water molecules permeate into the bulk of the matrix at a faster rate than erosion

Exhibit complex degradation/erosion kinetics

Most of the biodegradable polymers (PLGA)



Surface erosion



The rate of erosion exceeds the rate of water permeation into the bulk of the polymer

Desirable:



the kinetics of erosion

rate of drug release (zero order)

Examples: polyanhydrides

Surface characterizations

Biodegradable polymers' performance depends on

-  bulk properties (molecular weight, adhesion, solubility)
-  **surface microstructure and interfacial behavior**

Study of surface interactions between the polymer materials and the biological system

Understanding the degradation and controlled drug release mechanisms

Surface characterizations tools

- X-ray photoelectron spectroscopy (XPS)
 - Secondary ion mass spectrometry (SIMS)
 - Atomic force microscope (AFM)
 - Others (FT-IR, ISS, AES and et al)
-
- Studies of the surface of biodegradable polymers provide:
 - Chemical composition (XPS)
 - Structural information (XPS, SIMS)
 - Image of the morphological changes during degradation (AFM)

XPS

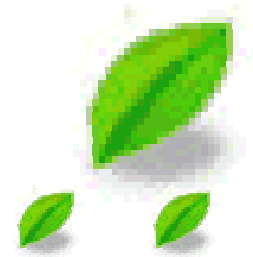
- $E_K = h\nu - E_B - \Phi$

E_K ----the kinetic energy

E_B ----the binding energy

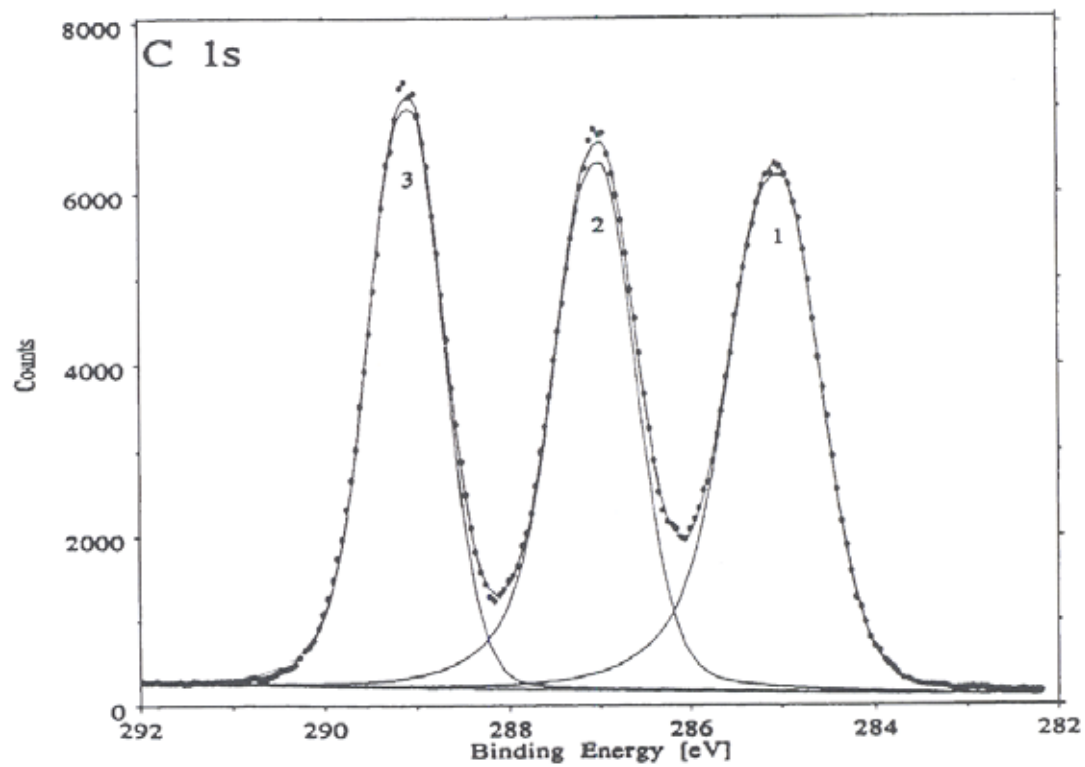
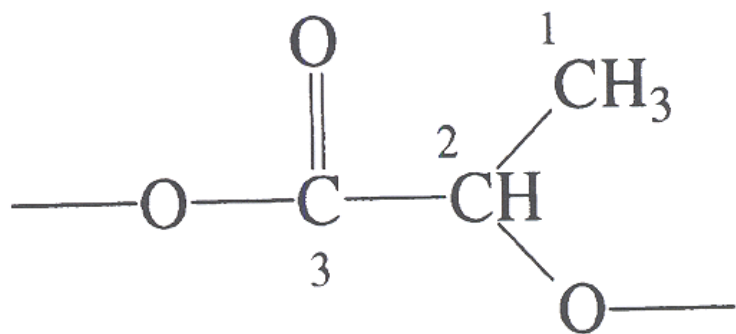
h ----the energy of the X-ray photon

----the work function

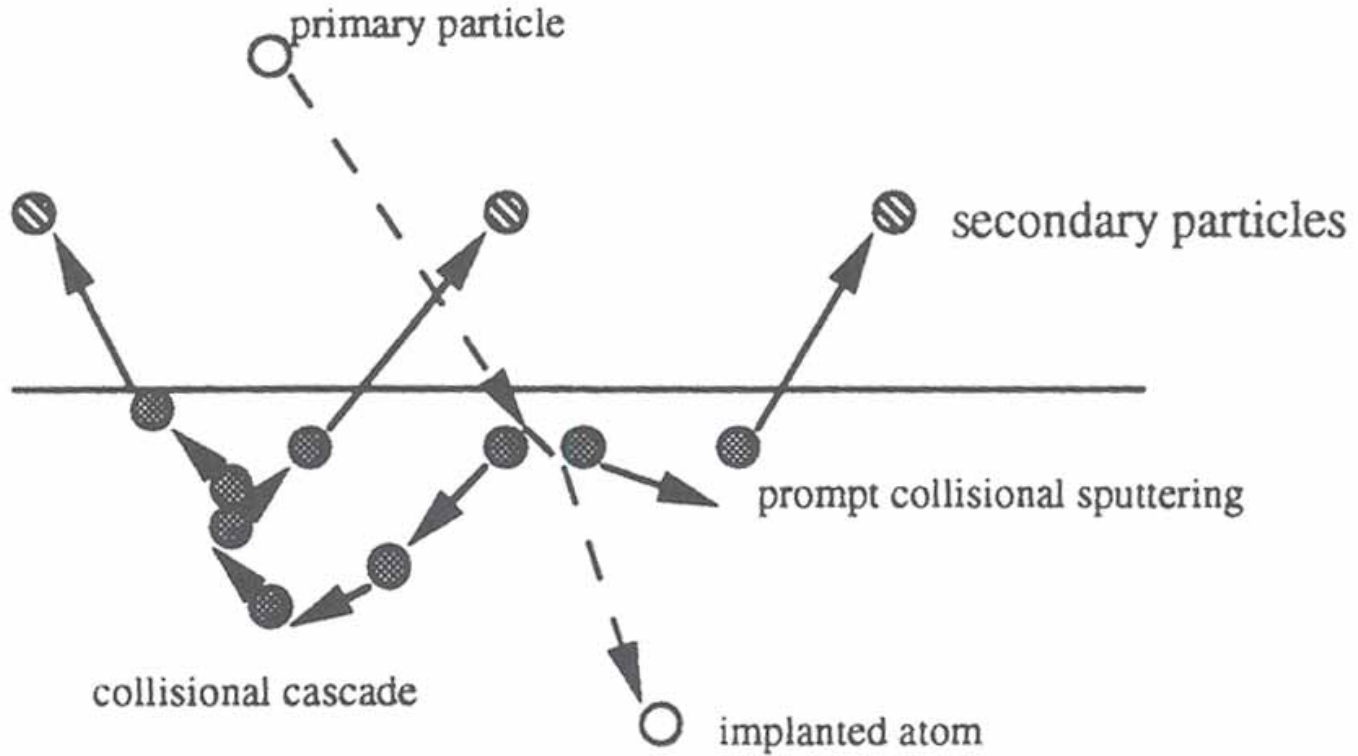


Each elemental core level orbital has a distinctive binding energy

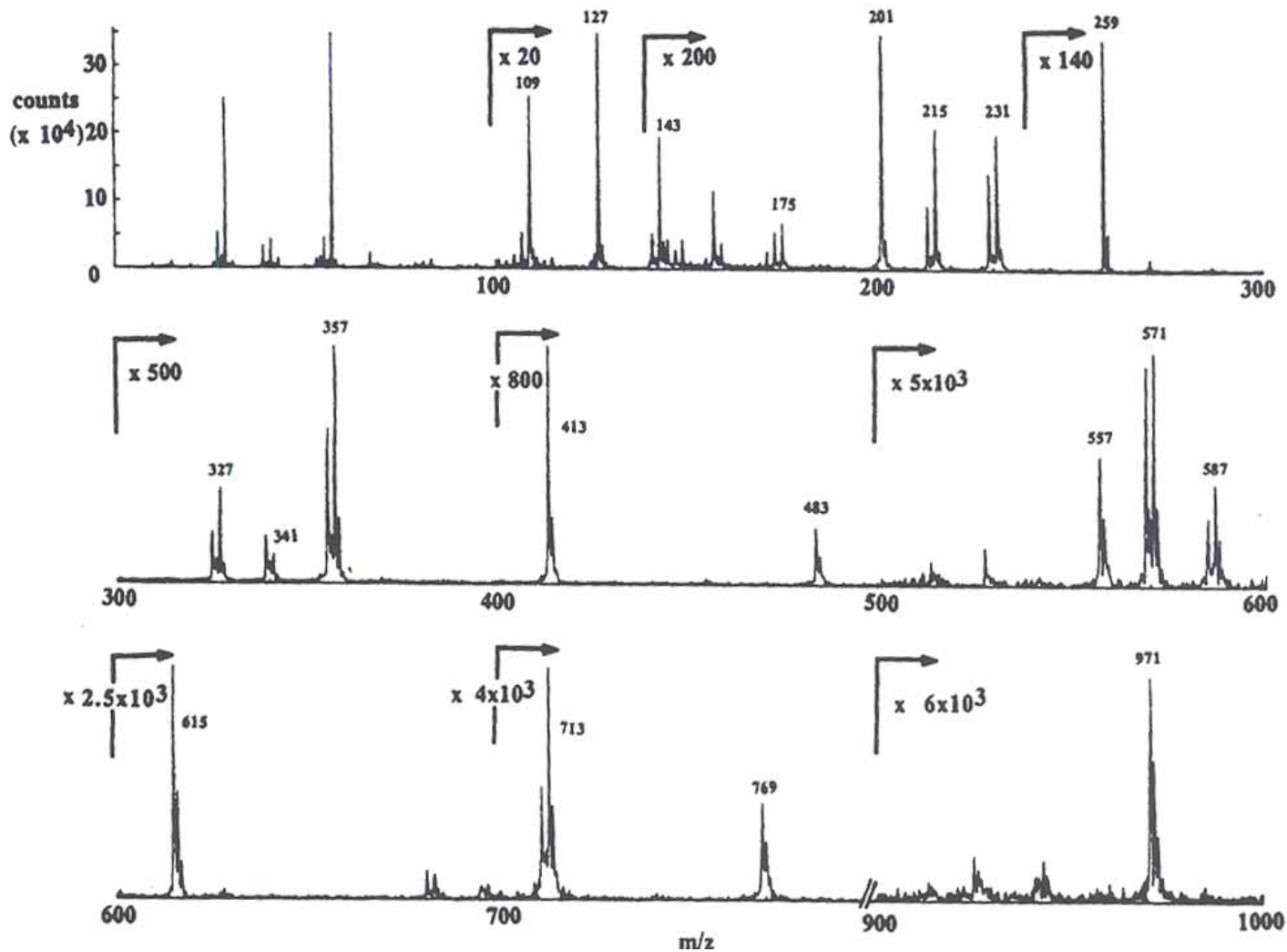
Chemical environment influences the binding energy of elemental core level



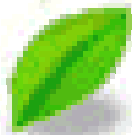
SIMS



TOF-SIMS of DETOSU poly (ortho esters)



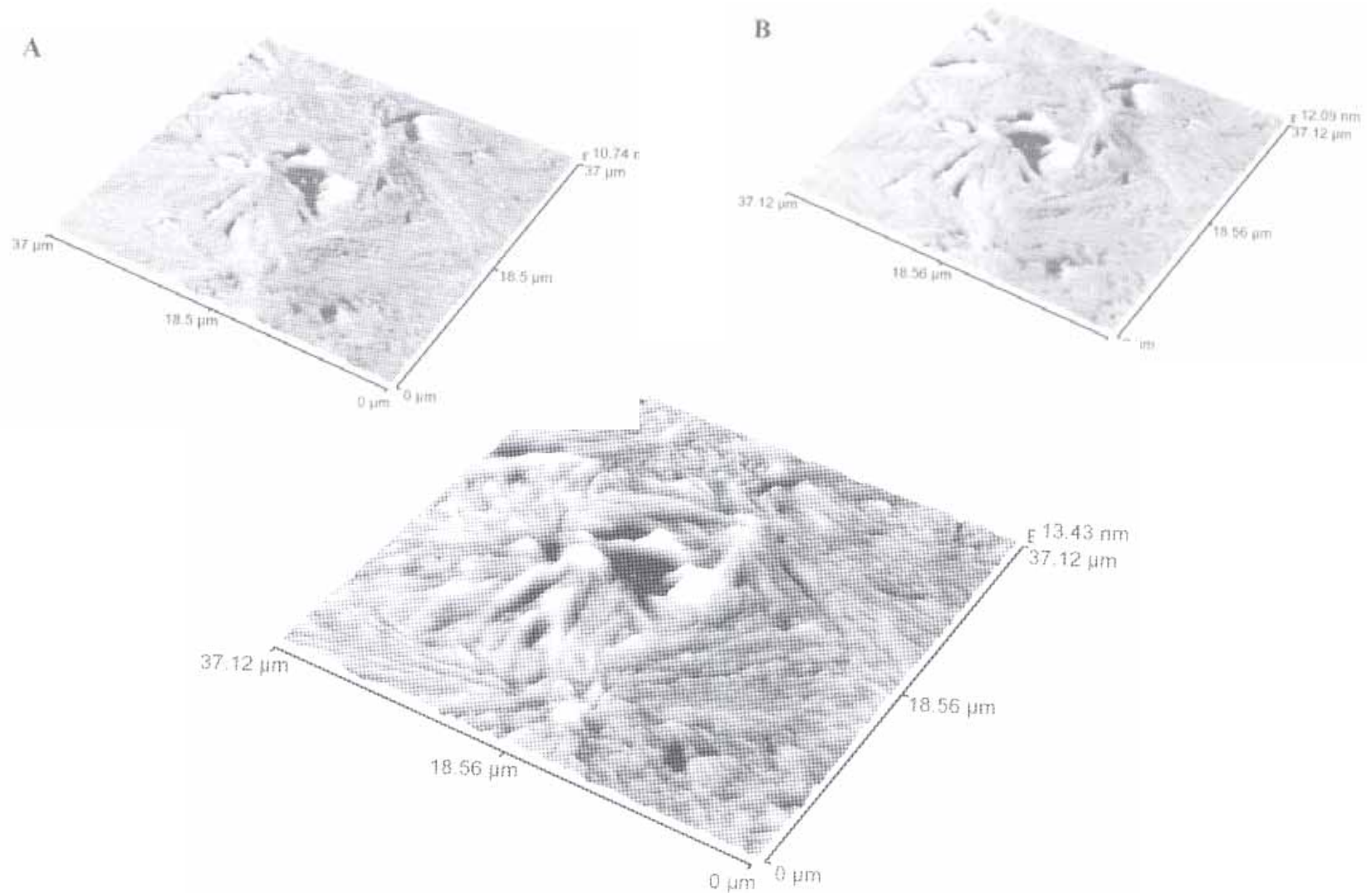
AFM



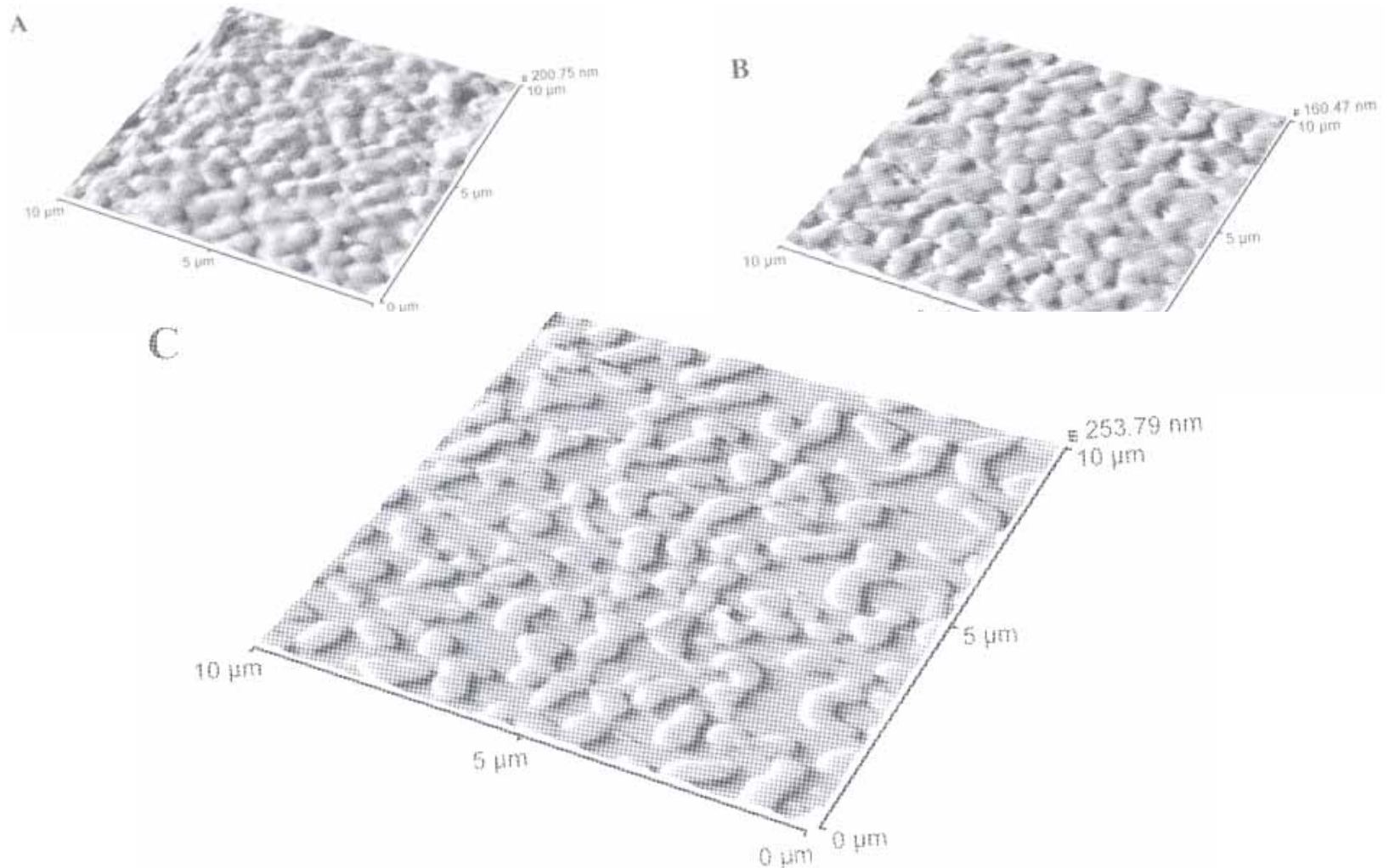
- Study the influence of surface morphology on degradation
- Advantages:
 - Applied in aqueous environments
 - Obtain very high resolution images
 - Possible to image dynamic processes like surface erosion and protein absorption



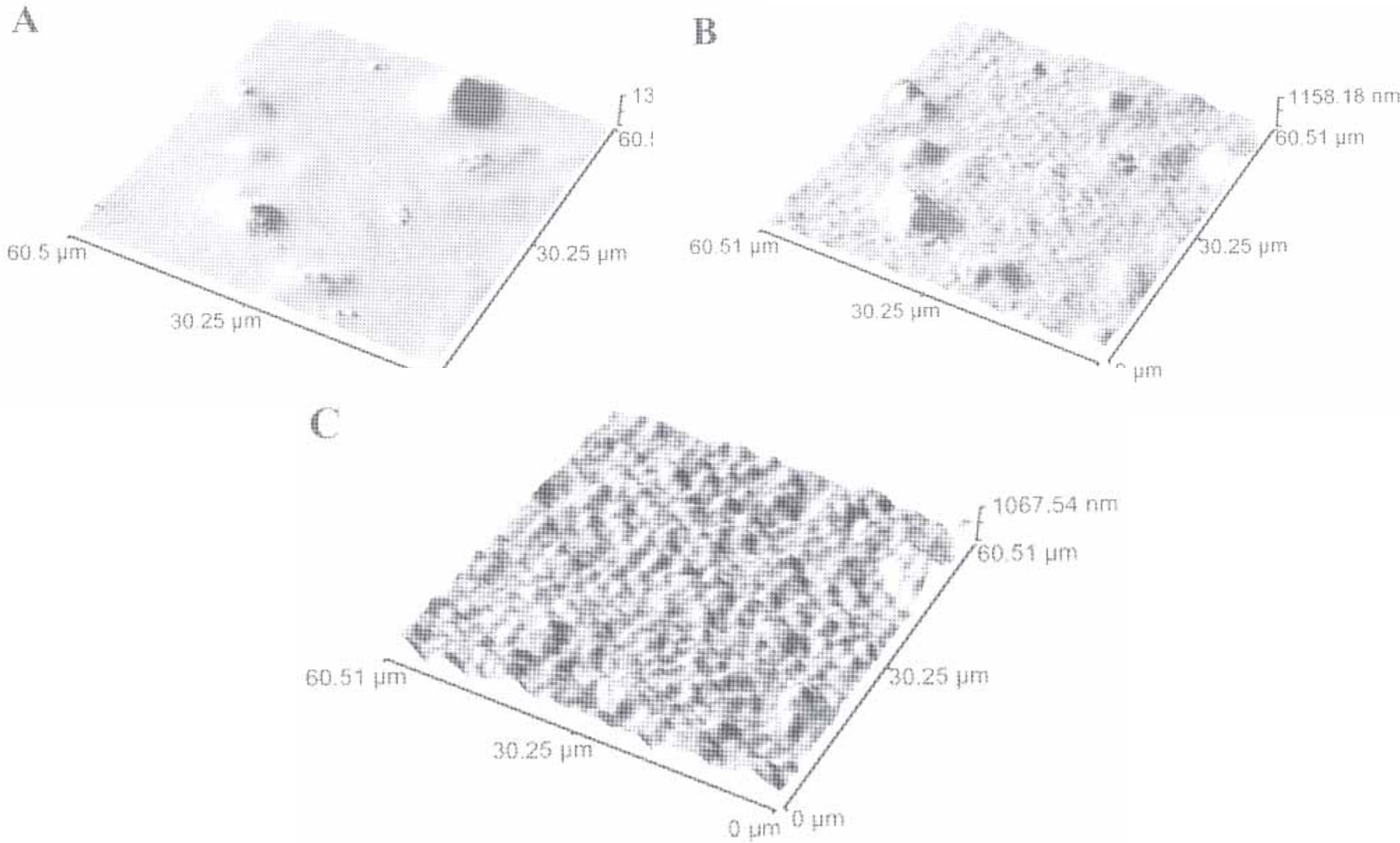
AFM imaged erosion of a poly (sebacic anhydride) (PSA) film



AFM visualisation of the erosion of an immiscible biodegradable blend containing (50% PSA and 50% PLA)



The release of bovine serum albumin from a poly (ortho-ester) film



Summary and Future prospects

- Increasing applications in pharmaceutical, medical areas.
- A variety of therapeutic agents (small molecule drugs, proteins or even DNA encoding a protein) use biodegradable polymer release systems
- Improve the processing of biodegradable polymers (nanocomposites)
- Required for complete understanding of the interfacial chemistry and physics of degradation.

References



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