Development of Biomedical Technologies and Products for Tissue Engineering

materials that
belong to the body

Prepared by
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Staff Scientist
DSM PTG

Advances in Tissue Engineering 2010
18th Annual Short Course
August 11 through 14, 2010
Rice University, Houston, Texas

Focusing on advances in the science and technology of tissue engineering and featuring leading scientists from Rice University, the Texas Medical Center, industry, and other institutions.

RICE
Unconventional Wisdom

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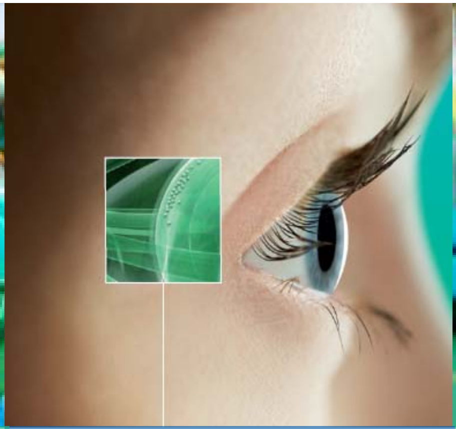
SAFETY FIRST

- **Chemical Synthesis Laboratory**
  - PPE (personal protective equipment)
  - -isocyanates: moisture sensitive, inert atmosphere handling
  - Toxic: hood or respirator; butyl gloves
  - Solvents: DMAc, THF, etc.(residuals),
- **Biological Interactions**
  - Double gloves;
  - Solvents/ buffer solutions carrying biologics: cell culture media (blood agar, calf serum albumin, etc)
- **Additional requirements**

DSM Biomedical
A world class Biomedical Portfolio



Medical Coatings

- Lubricious
- Anti-Microbial
- Anti-Fouling

ComfortCoat™ medical coatings

VitroStealth™ non-fouling coating

Drug Delivery

- Resorbable Polymer Platform for local delivery

Trancerta™ Drug Delivery

Biomedical Materials

- Ophthalmic Materials
- UHMwPE
- UHMwPE Fibers
- Polyurethanes
- TPE Medical
- Rigid Polymer

Dyneema Purity® fiber

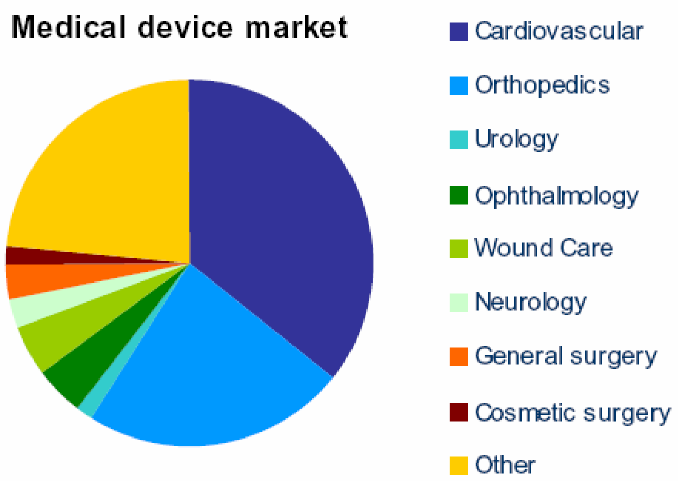
Bionate® PCU
BioSpan® SPU
CarboSil® TSPCU
Elasthane™ TPU
PurSil® TSPU

Solutions

- Design Support
- Prototyping
- Component Fabrication
- Device Assembly

Protocol

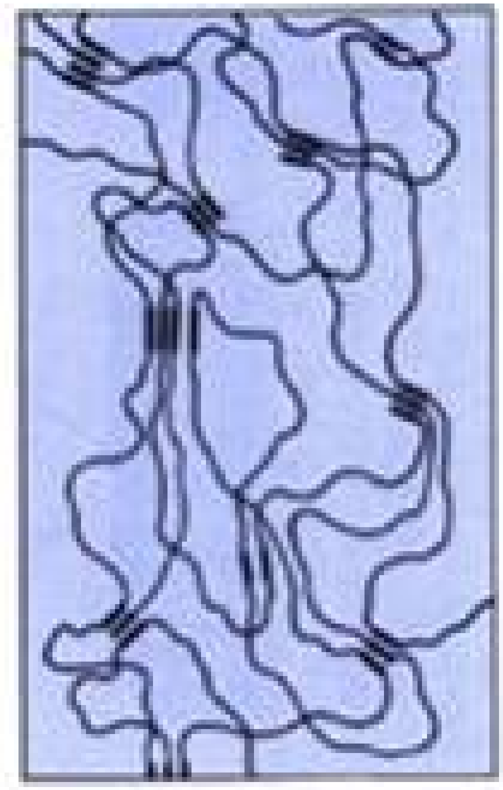
- **DSM Biomedical**
- **Polyurethanes for Biomedical Application**
  - Overview
  - Raw materials, synthesis
  - properties
- **Polyurethane End Group Modifications**
  - Surface characteristics/ methods
  - Antimicrobial alternatives
- **Polyurethanes for Tissue Engineering**
  - Specific examples



"Materials that belong to the body"

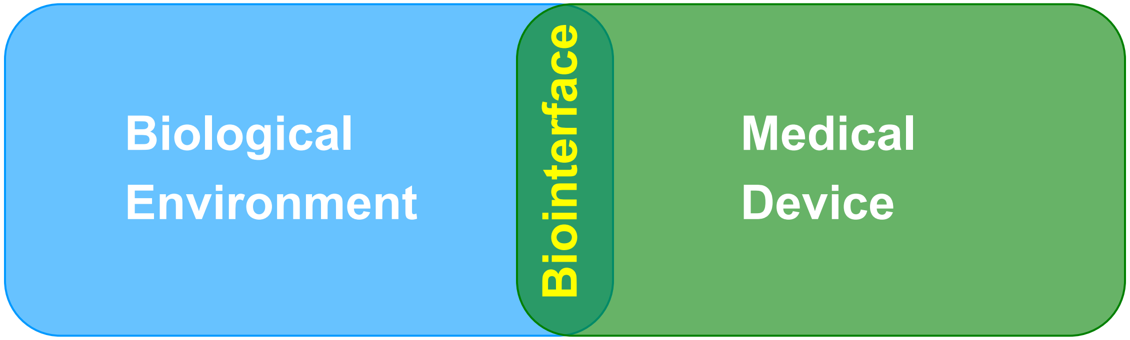
Typical Polymeric Biomaterials Today

- Industrial base polymers
  - Not designed for biomedical applications
  - Little or no consideration of surface properties or biostability
  - Used as biomaterials because they are:
    - Easily Processed
    - Cheap
    - Available
  - May be contraindicated for long-term implants
- Coatings are extensively used
  - Disguise base polymer
  - Change surface properties for device use
    - Often required for safety and efficacy



Medical Device Requirements

Biointerface: Where the device-biological interactions take place



A medical device has to satisfy both structural and functional requirement in a biological environment (Form-Fit-Function).

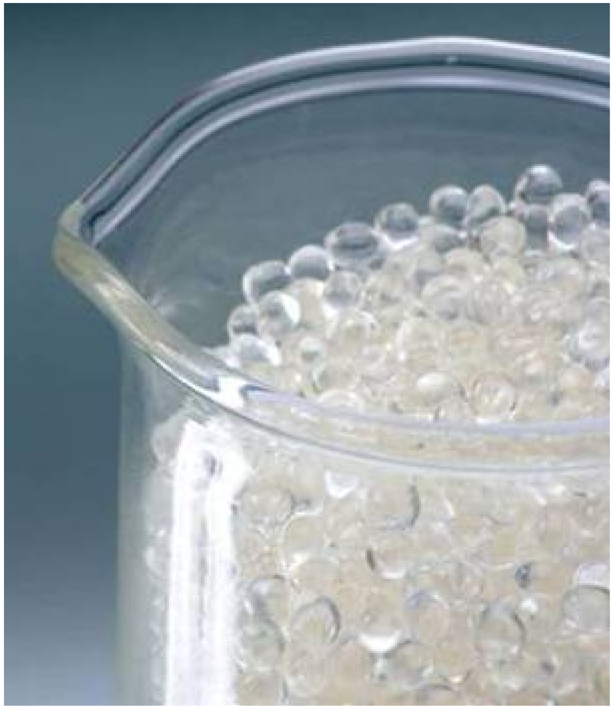
The device-biological interface is where many critical interactions take place and thus plays an important role in determining compatibility and efficacy.

New Possibilities with Polyurethanes

Widest range of possible bulk and surface properties:

- Large number of possible reactants
  - **Hard segments**
    - Diisocyanates
    - Diols » urethane and/or diamines » urea
  - **Soft segments**
    - Polyols and polyamines
    - Single or mixed
  - **End groups**
  - **Pendant groups**
- Many possible structures
  - **Linear**
  - **Linear with pendant groups or end groups**
  - **Branched or dendtritic**
  - **Crosslinked**
- Easily synthesized by batch or <u>continuous</u> polymerization
- May be designed for biostability <u>or</u> bio-resorption!

Very Flexible



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DSM Biomedical Polyurethane Family

Bionate® thermoplastic polycarbonate-urethane

- Best mechanical strength, Good oxidative stability, Good abrasion resistance

CarboSil® thermoplastic silicone-polycarbonate-urethane

- Excellent flexibility, Thromboresistant, Good oxidative stability

Elasthane™ thermoplastic polyether-urethane

- Excellent Strength, Good abrasion resistance, Thromboresistant

PurSil® thermoplastic silicone-polyether-urethane

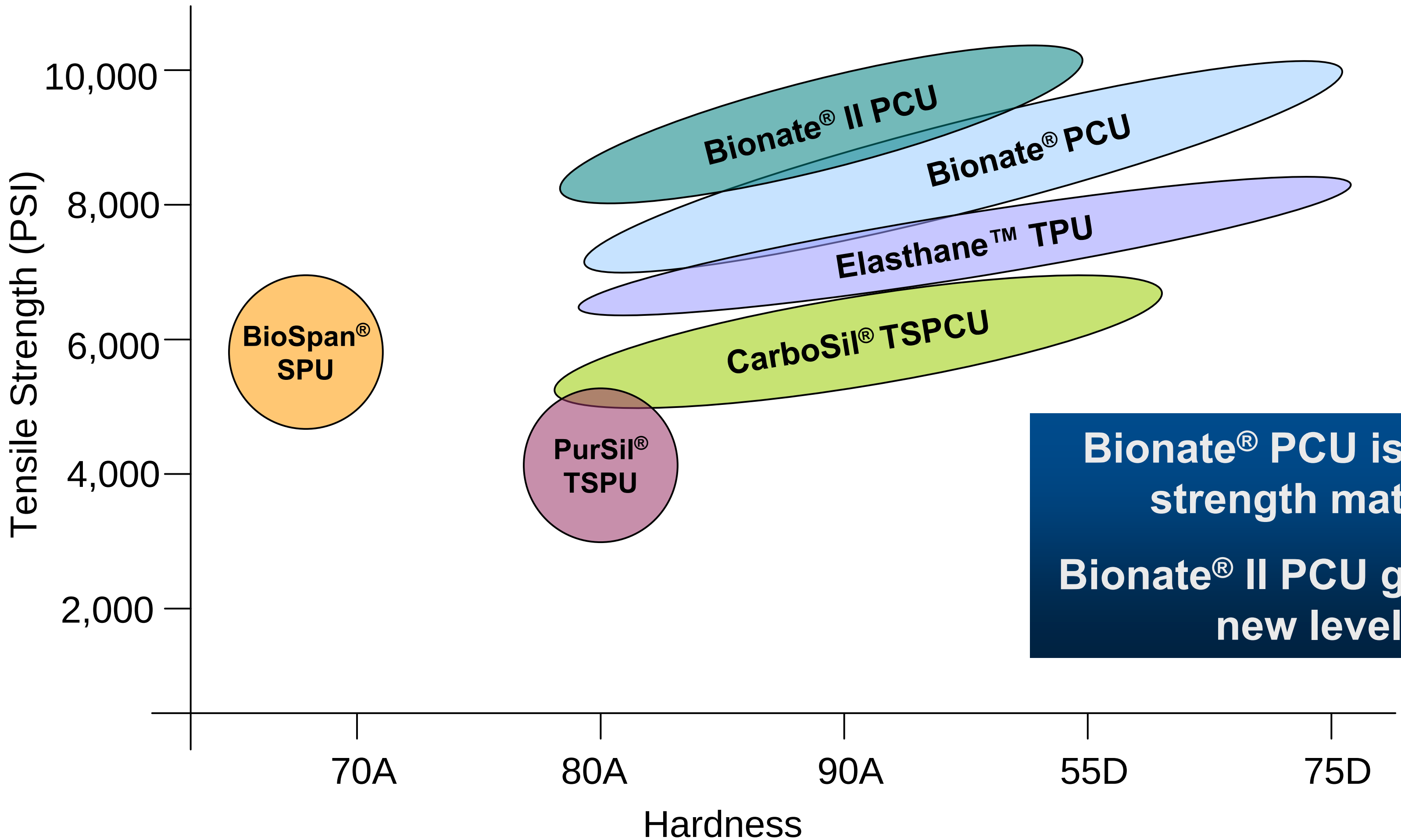
- Outstanding elasticity, Thromboresistant, Aromatic or aliphatic versions

BioSpan® segmented polyurethane

- Best flex life, Thromboresistant, Solution based

All polymer families have extensive FDA Master Files

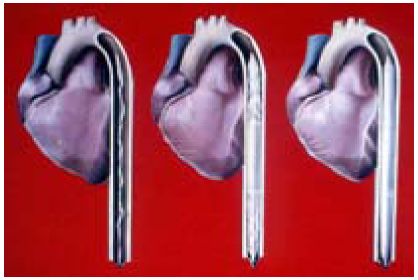
Polyurethane Family Strength Comparison



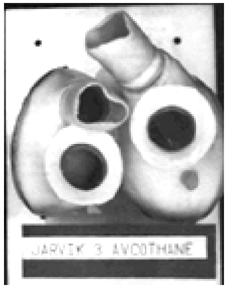
Bionate® PCU is high strength material

Bionate® II PCU goes to new levels

Polyurethanes in Cardiovascular Applications



AVCO IAB 1971: First Clinical Cardiac Assist Device



Jarvik III TAH

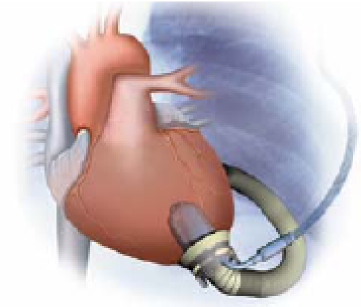
Abiocor TAH

Abiomed BVS

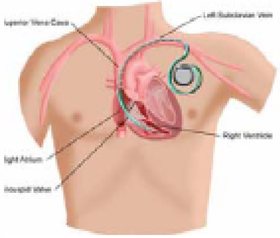
Thoratec PVAD and IVAD

TCS HeartMate® LVAD

Thoratec HeartMate II



Jarvik 2000



Pacemakers (Various)

Sunshine Heart C-Pulse™ 2009

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Polyurethanes in Orthopedics

Zimmer Dynesis Dynamic Spinal Stabilization

- Over 14 years global experience

Medtronic Bryan Sofamor Danek Prosthetic Cervical Disc

- 15,000 cases implanted without fracture
- 3 to 6 year explants showed no trend of degradation

Axiomed Freedom Lumbar Disc

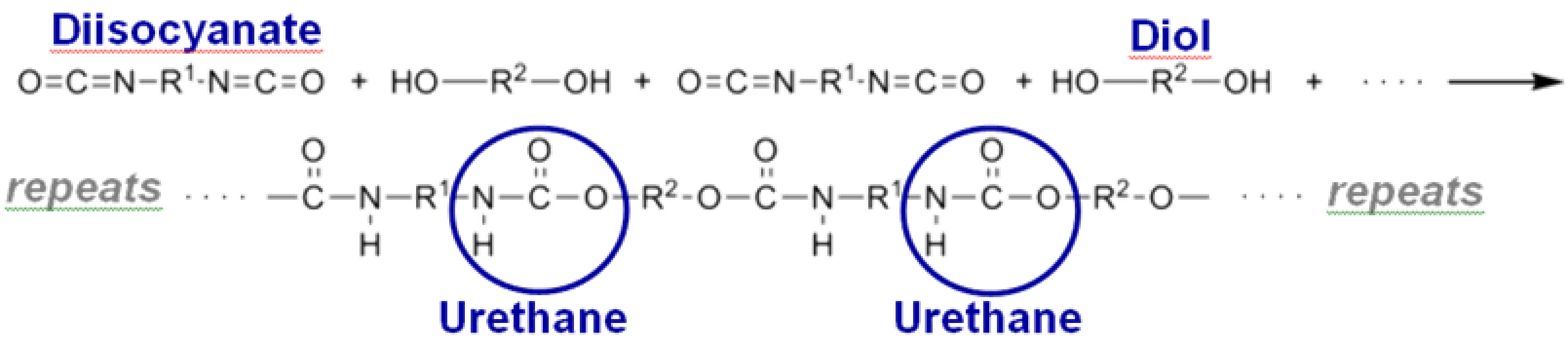
- CE Mark received

Active Implants Tribofit Hip System

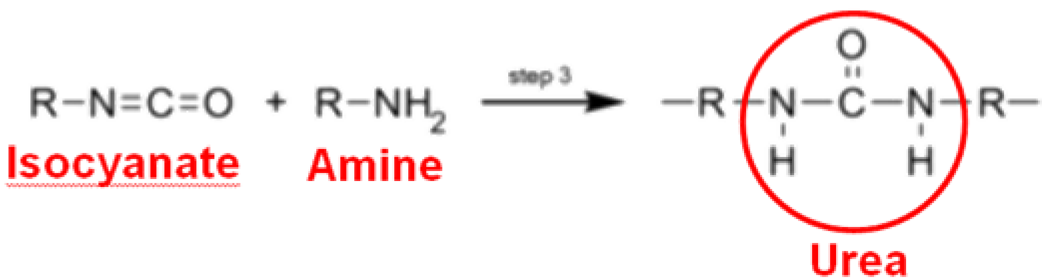
- CE Mark received
- Several hundred implantations

Polyurethane Chemistry

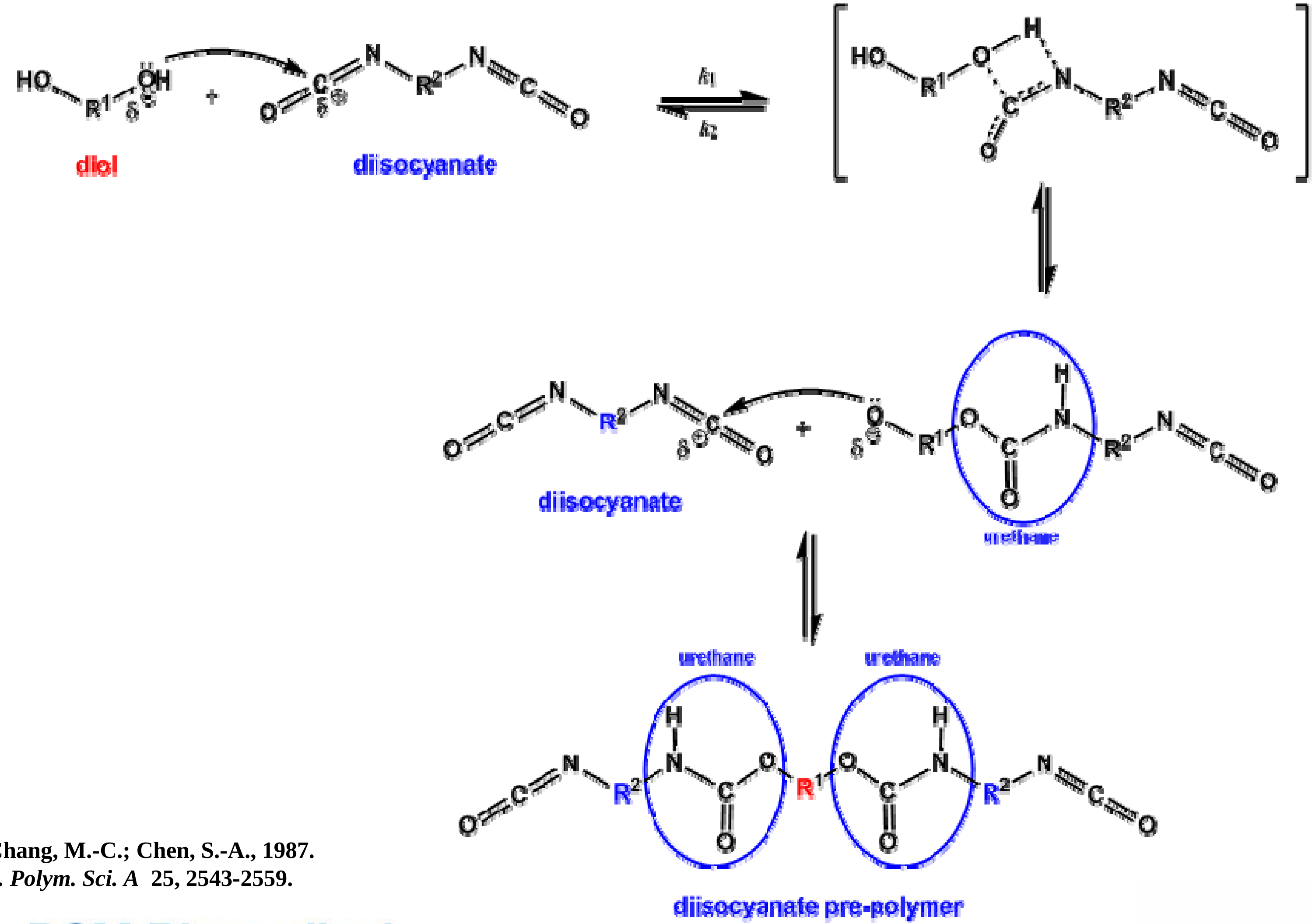
Polyurethane hard segment formed by reacting diisocyanates with low-MW diols (R^1 may be 'aromatic' or 'aliphatic'):



Urea formed by reacting a diisocyanate with an amine:



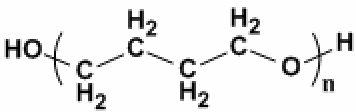
Polyurethane Synthesis



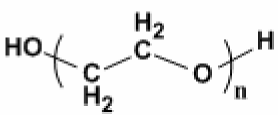
Chang, M.-C.; Chen, S.-A., 1987.
J. Polym. Sci. A 25, 2543-2559.

Polyurethane Soft Segment Candidates

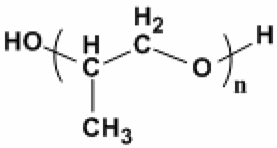
polyethers



poly(tetramethylene oxide)
PTMO

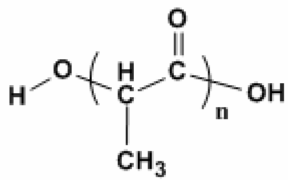


poly(ethylene oxide)
PEO

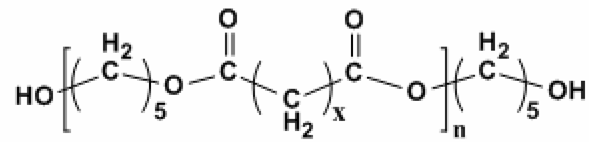


poly(propylene oxide)
PPO

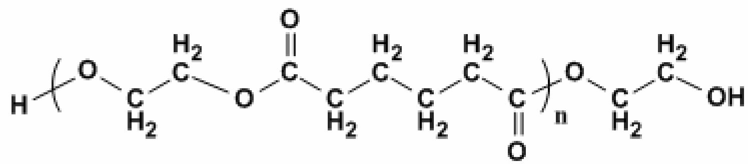
polyesters



poly(lactide)
PLA

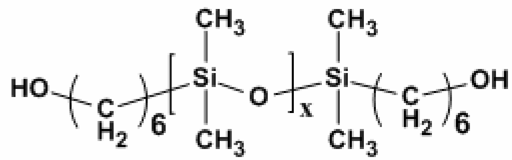


poly(caprolactone)
PCL



Poly(ethylene glycol)adipate
PEGA

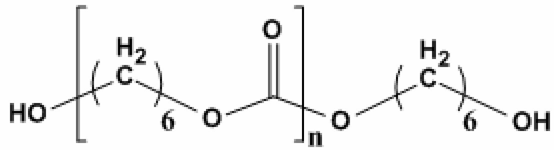
polysiloxane



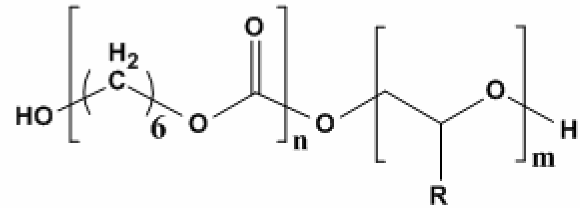
poly(dimethylsiloxane) diol
PDMS

Biostable Soft Segments:

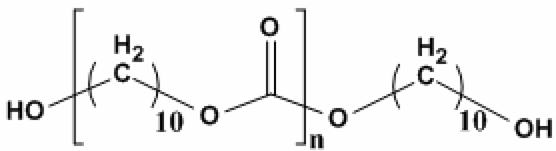
Polycarbonate diols



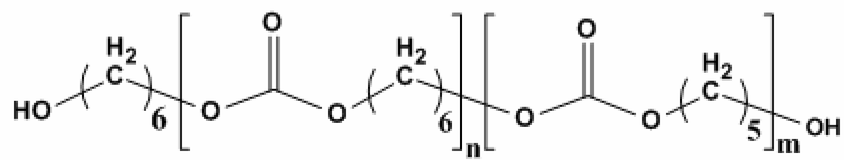
poly(1,6-hexamethylene carbonate) diol
HMCD



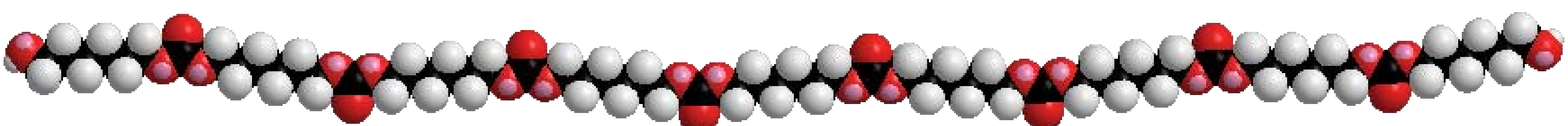
oligocarbonate diol
containing oxyethylene fragments



poly(decamethylene carbonate) diol
HMCD



polyhexamethylene–pentamethylene carbonate diol
PHMPMCD



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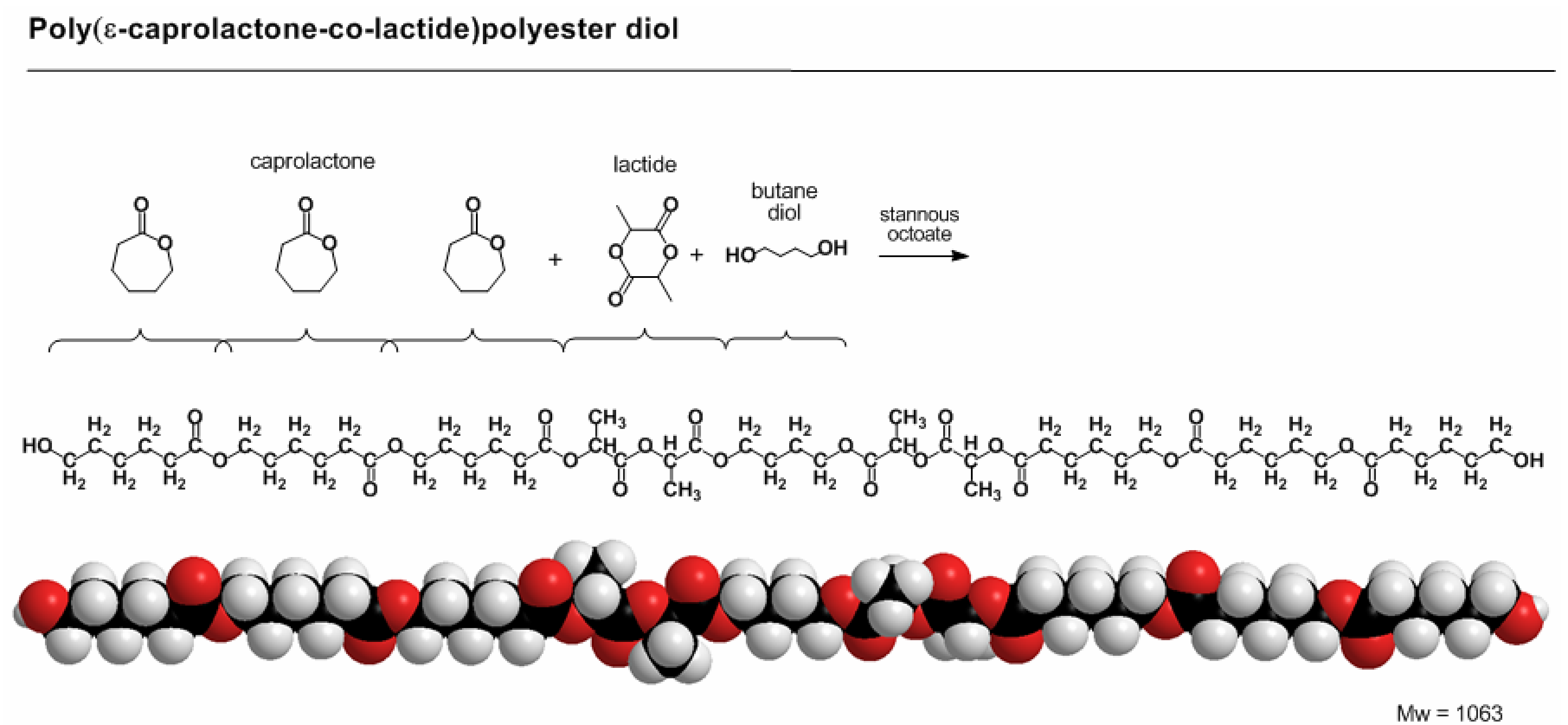
Biodegradable Soft Segments:



Wang, W.; Ping, P.; Yu, H.; Chen, X.; Jing, X., "Synthesis and characterization of a novel biodegradable, thermoplastic polyurethane elastomer", *Journal of Polymer Science Part A: Polymer Chemistry* 2006, *44*(19), 5505-5512.)

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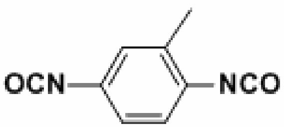
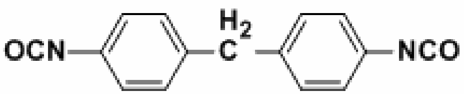
Hard Segment Components

Diisocyanates

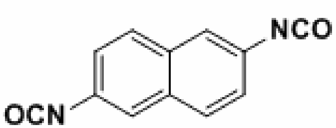
Aromatic



toluene diisocyanate
(i.e., mixed isomers)
TDI



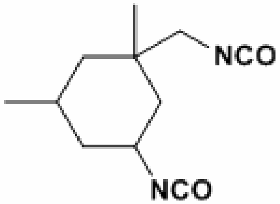
methylene diphenyldiisocyanate
MDI



napthalene diisocyanate
NDI

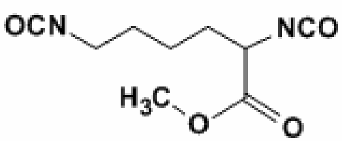
Aliphatic

(hexane diisocyanate)
HDI

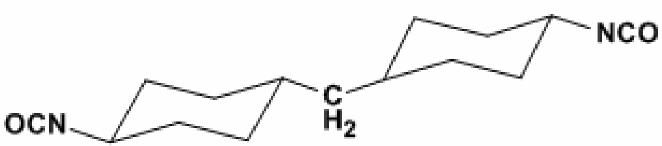


isophorone
diisocyanate
IPDI

1,4-diisocyanatocyclohexane
(cyclohexyl-diisocyanate)
CHDI



lysine-diisocyanate
LDI



cyclohexylmethylene-diisocyanate
CHMDI

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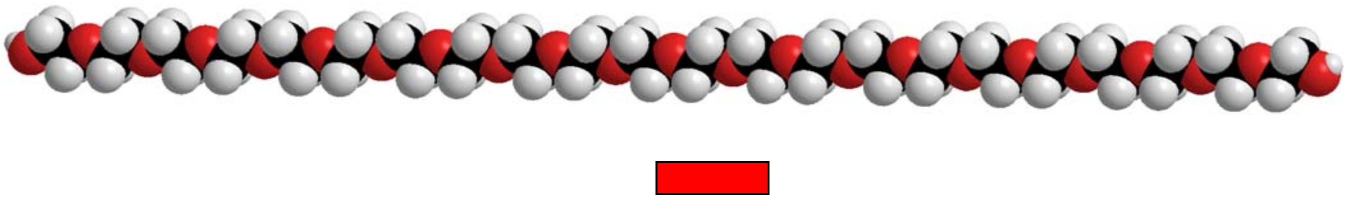
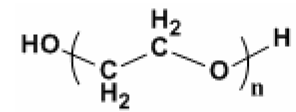
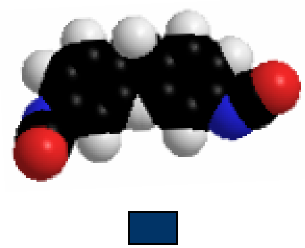
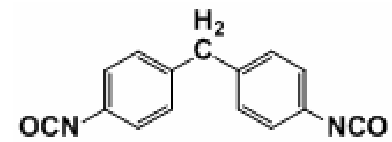
PU synthesis example: PEG soft segment w/ MDI



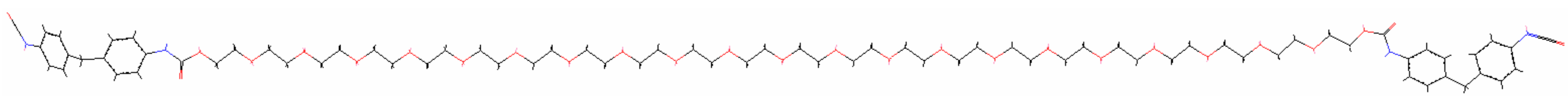


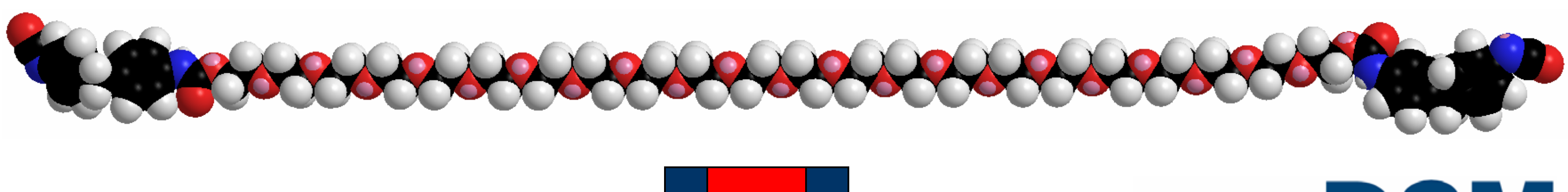
poly(ethylene oxide)
PEO





Methylene diisocyanate
MDI
Mw: 250.25





Chain Extenders

Chain Extenders

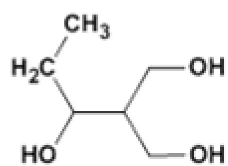
Polyols

ethylene glycol
EG

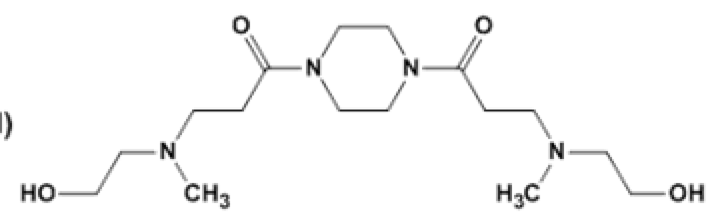
1,4-butane diol
BDI

glycerine
(1,2,3-propanetriol)

2-methyl-1,3-propanediol
MPD



trimethylolpropane
TMP

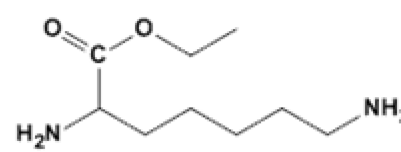


1,4-Bis{β-[n-methyl-N-(2-hydroxyethyl) amino]propionyl}piperazine
PIME

Diamines

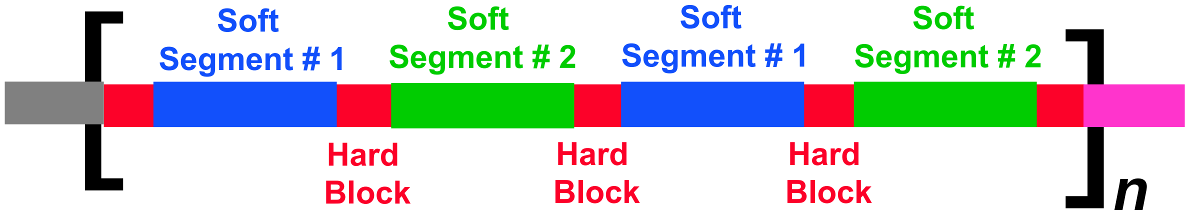
ethylene diamine
ED

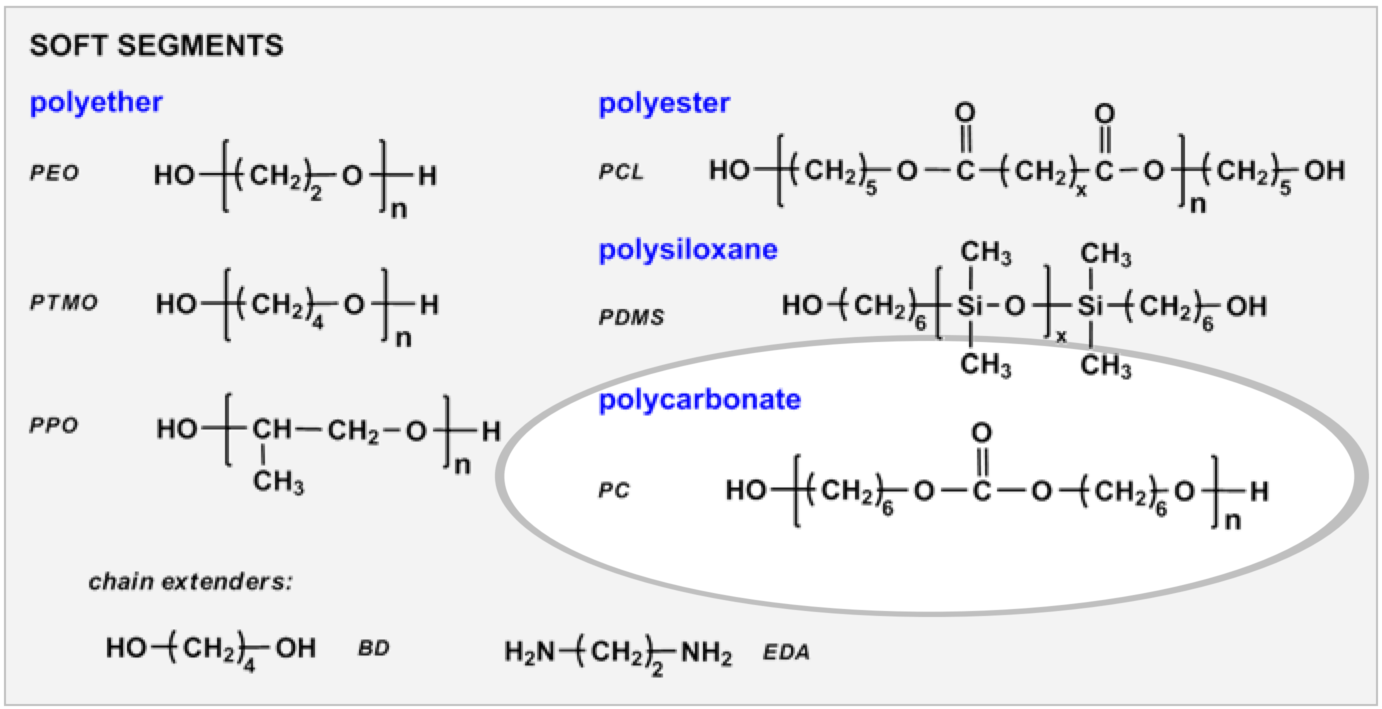
putrescine
PUT

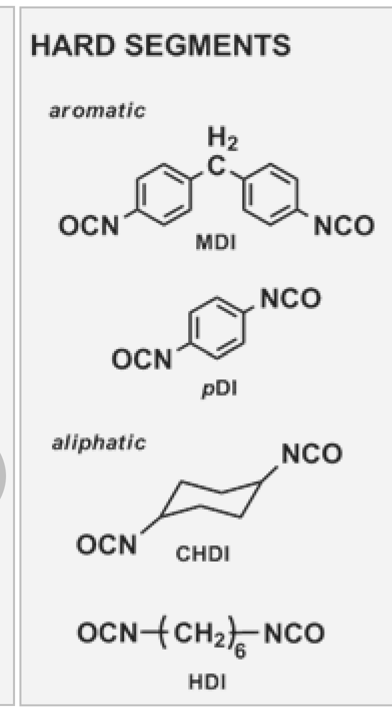


lysine ethyl ester
LEE

Segmented Polyurethane







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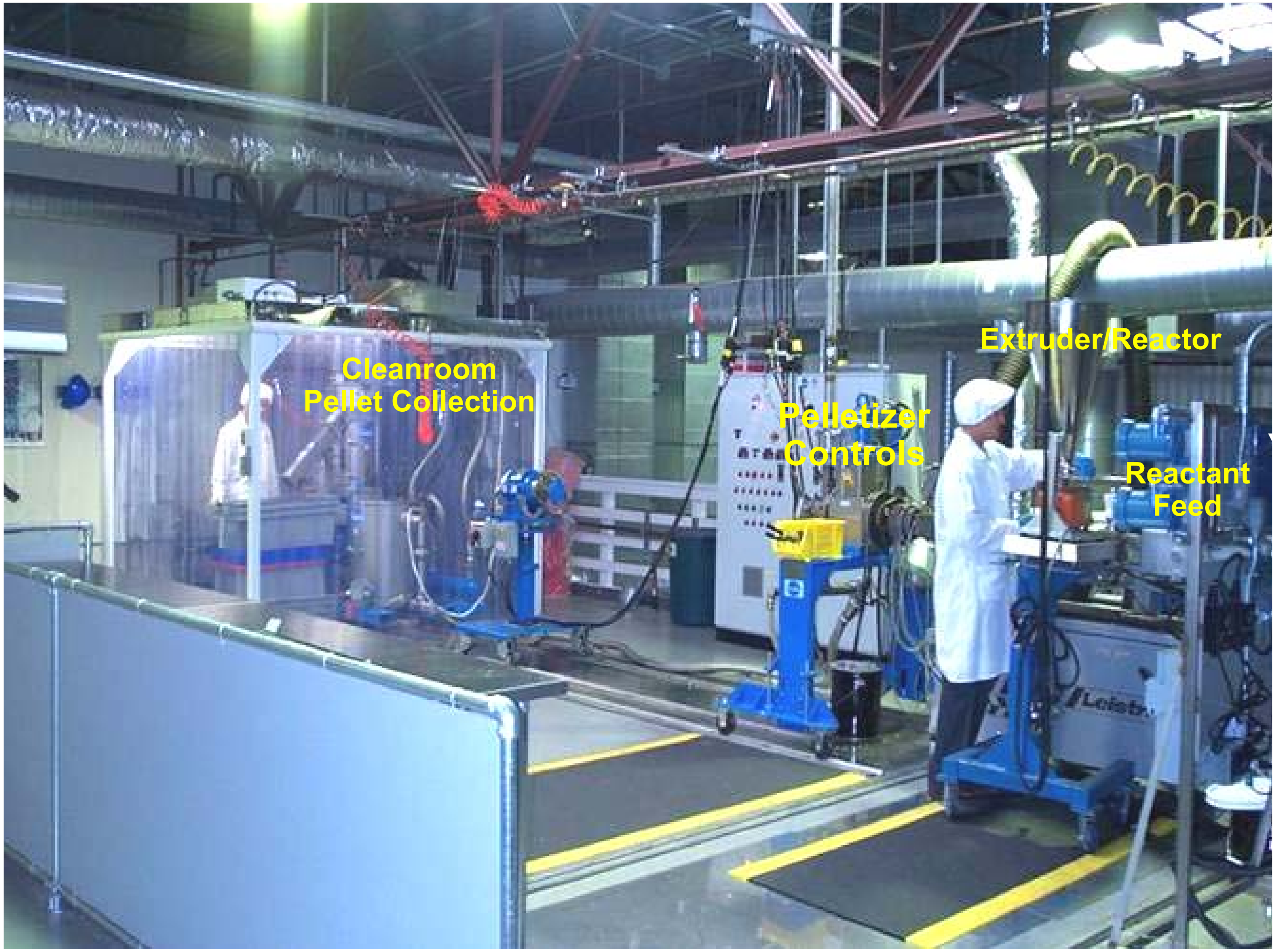
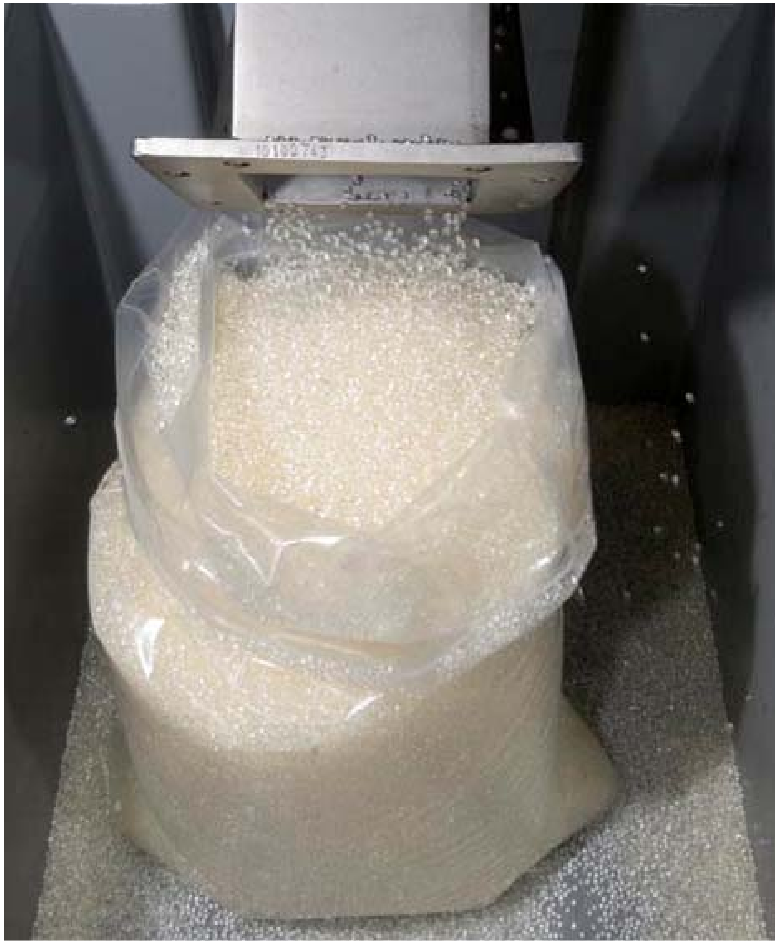
Continuous Reactor:



*Thermoplastic Pellets: The main raw material for fabrication of device components**



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Structure

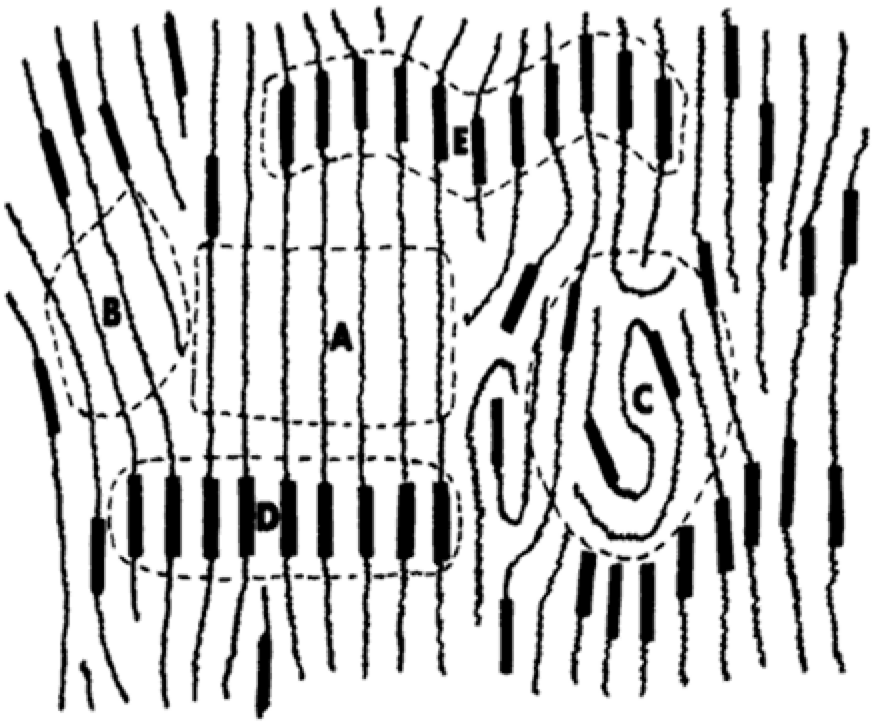
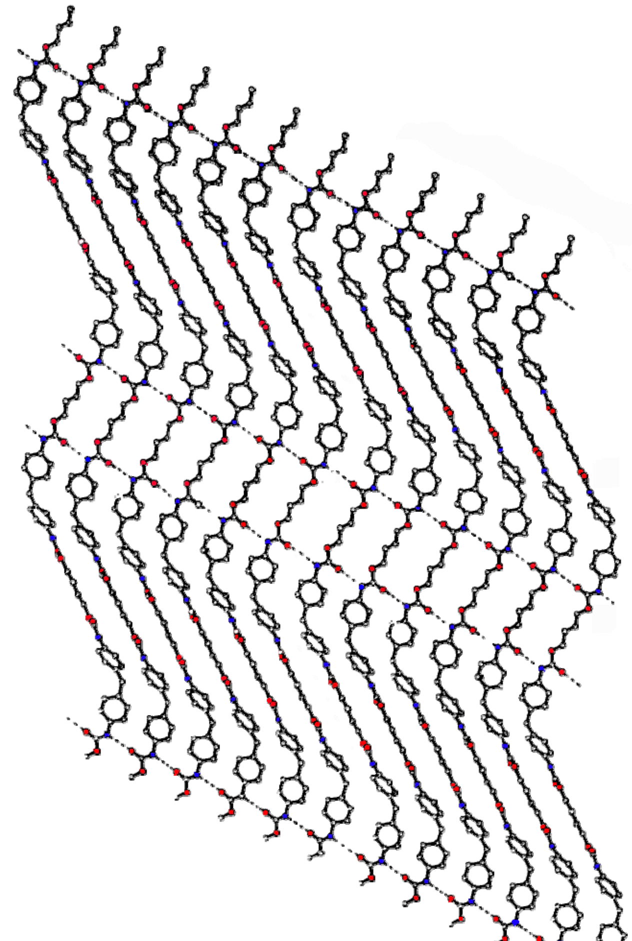


FIGURE 12 Morphological model of segmented polyurethane. (A) Stress-crystallized soft segment; (B) paracrystalline soft segment; (C) amorphous "solution" of hard and soft segments; (D) crystalline hard segment domains; (E) paracrystalline hard segment domains. From Wilkes, C.E. and Yusek, C.S. *J. Macromol. Sci. — Phys. B*, B7:157, 1973.



Blackwell, J.; Gardner, K. H., "Structure of the hard segments in polyurethane elastomers", *Polymer* 1979, *20*(1), 13-17

General trends: Structure – Property - Biodegradation

- **Polyesterurethanes:** rapidly undergo hydrolytic degradation rendering them unacceptable for long-term implantation;
- **Polyetherurethanes:** hydrolytically stable but subject to oxidative degradation:
  - metal ion oxidation (MIO), auto-oxidation (AO)
  - environmental stress cracking (ESC),
  - Bio-degradation:
    - Reactive oxygen intermediates released by adhering macrophages and foreign body giant cells can initiate biodegradation.
- General principles, biostability:
  - *Higher Mw and crosslinked polyurethanes degrade slower than the low Mw polyurethanes*

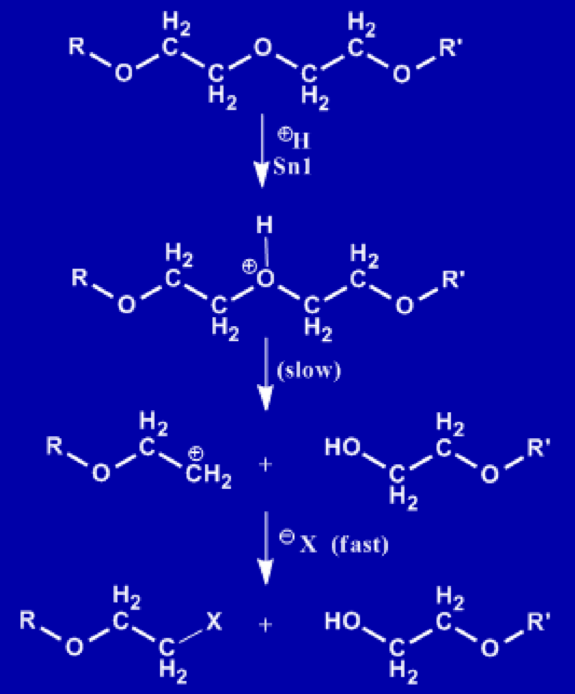
Polyether urea urethanes>> polyether urethanes > polyester urethanes

biostability ranking based on comparisons of chain scission and surface pitting [1]:

PEU < PEU-S ≤ PCU < PCU-S

- An increase in hard segment size leads to restrictions in polymer chain mobility, increased modulus and increased biostability;
- Surface composition varies with segment composition and concentration
- Polyurethane surface chemistry controls biodegradation/ biostability that can lead to ultimate failure/success of these materials in clinical applications:

Cleavage of a polyether urethane by Sn1 type acid hydrolysis [2]



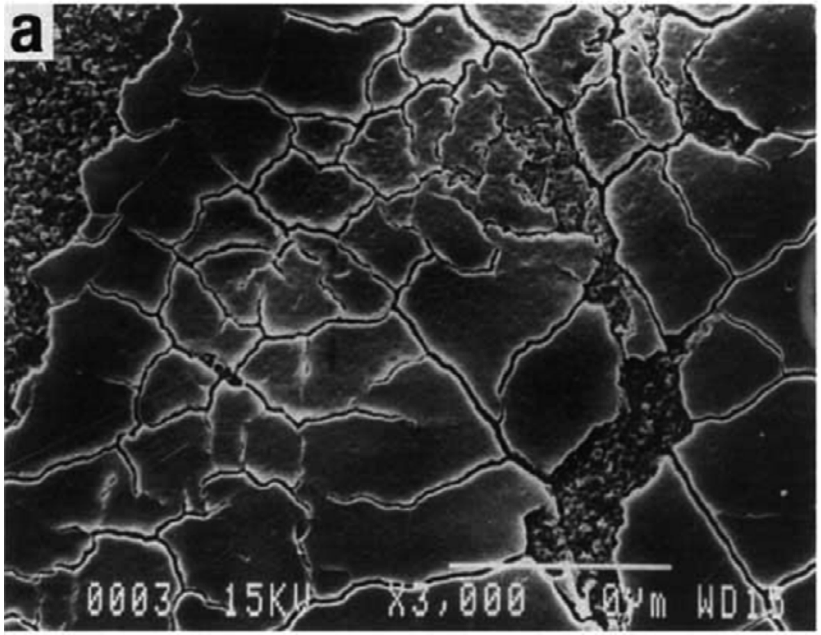
[1] Christenson, E. M.; Wiggins, M. J.; Anderson, J. M.; Hiltner, A., "Surface modification of poly(ether urethane urea) with modified dehydroepiandrosterone for improved *in vivo* biostability", *Journal of Biomedical Materials Research Part A* **2005**, *73A(1), 108-115.*

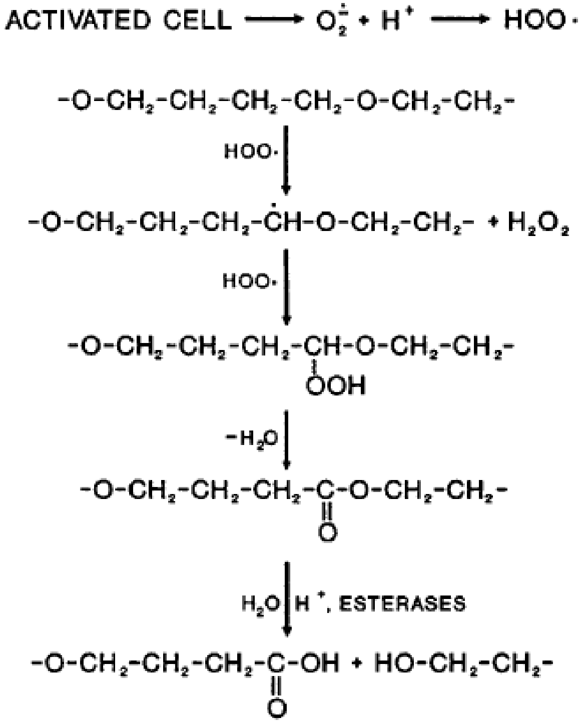
[2] Pinchuk, L., "A review of the biostability and carcinogenicity of polyurethanes in medicine and the new generation of 'biostable' polyurethanes", J Biomater Sci Polym Ed. 1994, 6(3), 225-267.

Degradation Mechanism:

…on the carbon α to the ether linkage on the polyether soft segment……

"abstraction of a hydrogen atom from the α-methylene position followed by chain scission and/or chemical crosslinking of the PEU soft segment…"[1]



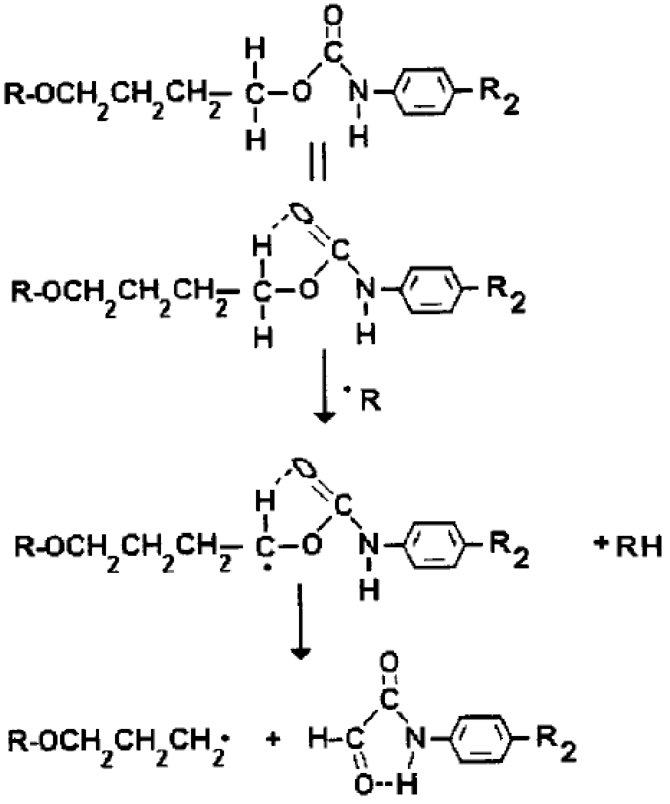


Wu, Y.; Sellitti, C.; Anderson, J. M.; Hiltner, A.; Lodoen, G. A.; Payet, C. R., "An FTIR-ATR investigation of *in vivo* poly(ether urethane) degradation", *Journal of Applied Polymer Science* 1992, *46*(2), 201-211.

Degradation Mechanism:

……,on the carbon α to the to the urethane group ……

The degradation mechanism of a polyurethane urea at the carbon alpha to the urethane group:



From: Pinchuk, L., "A review of the biostability and carcinogenicity of polyurethanes in medicine and the new generation of 'biostable' polyurethanes", *J Biomater Sci Polym Ed.* 1994*, 6*(3), 225-267, after Tyler and Ratner..

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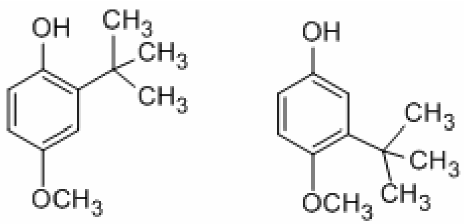
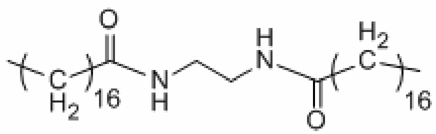
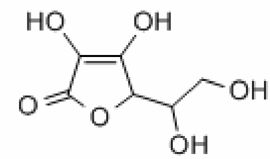
Additives, Stabilizers, Catalysts



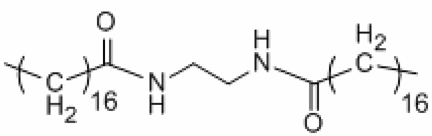
2-tert-butyl-4-hydroxyanisole
and
3-tert-butyl-4-hydroxyanisole (mixture)



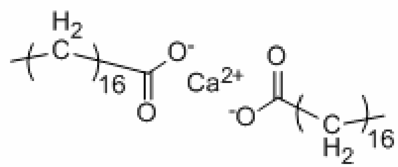
N-[2-(octadecanoylamino)ethyl]
octadecanamide



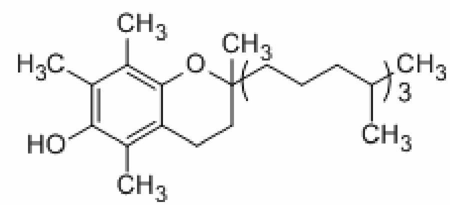
ascorbic acid



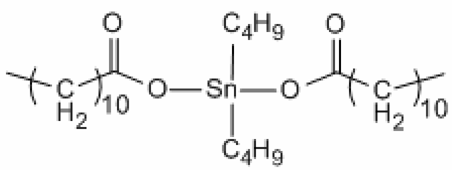
N-[2-(octadecanoylamino)ethyl]
octadecanamide



Calcium octadecanoate



a-tocopoherol



[dibutyl(dodecanoyloxy)stannyl]
dodecanoate

Surface Engineering

- Surfaces and surface properties are important across a wide range of values: surfaces largely determine how materials interact with each other and with their environment.

- Most surface properties are determined by atoms located within the top few atomic layers, i.e., within a few nanometers from the surface

- Specifying Biomaterials for Devices:

Satisfying Bulk <u>and</u> Surface Property Requirements

Surface also influence bulk properties:
(stability, absorption, drug release, degradation, etc.)

Environment Response

Dynamic Surfaces:

All surfaces or interfaces will respond to environmental change to reduce the interfacial free energy

Conformational rearrangement

- **Functional groups on polymers can rearrange**
- **Self Assembling Monolayer End Groups (SAME^{TM})**
- **Adsorption (Contamination → Surfaces adsorb molecules)**

Optimum Bulk ≠ Optimum Surface!

Solutions: ***After Device Fabrication ($$$):***

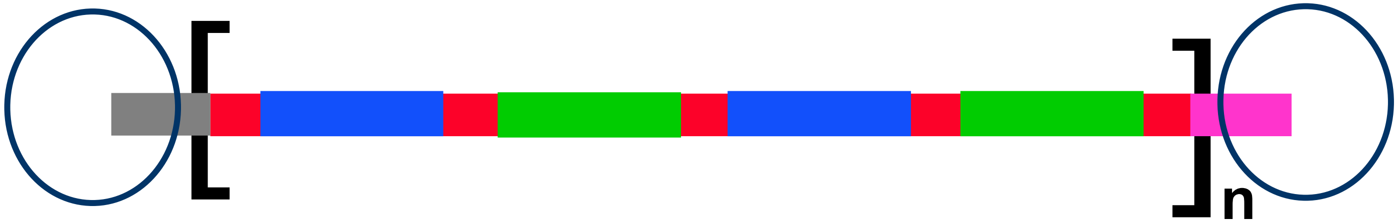
Apply topical treatments or coatings

Before Device Fabrication ($):

Modify polymers during synthesis to harness '*Surface Activity*' + '*Self Assembly*

Surface Modification with SAME® Technology

SAME® —[Multi-block polymer]$_n$— SAME®

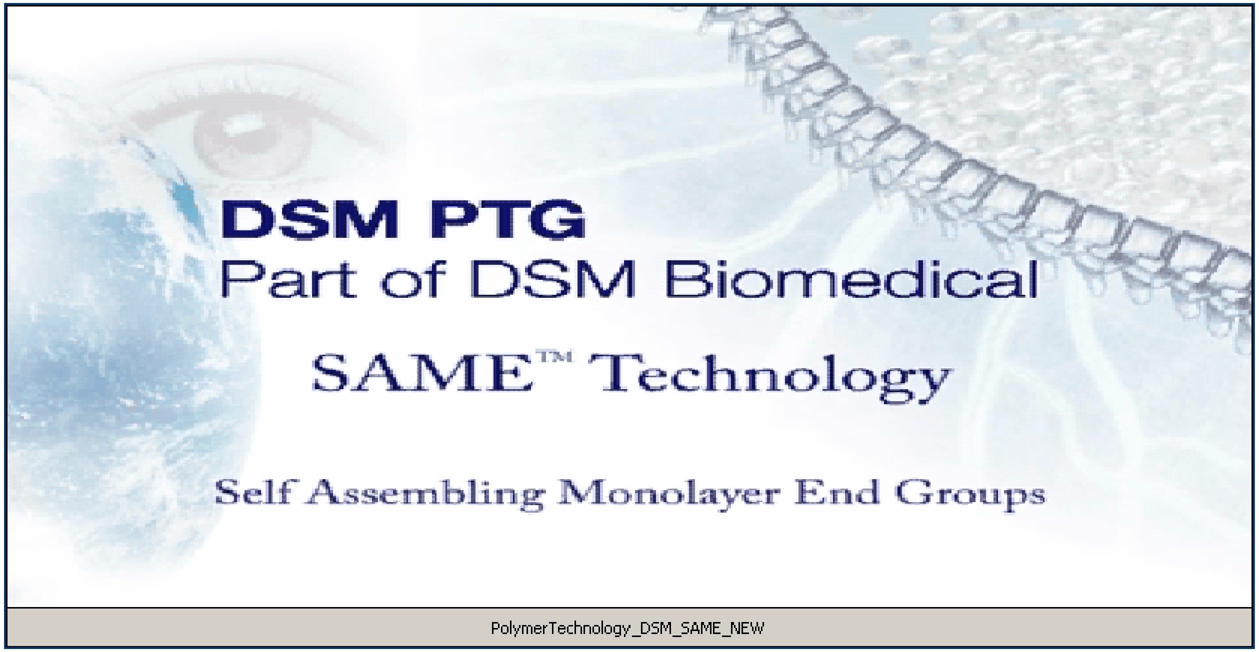


Surface Properties
- ■ = SAME® # 1
- ■ = SAME® # 2

Bulk Properties
- ■ = Soft Segment # 1
- ■ = Soft Segment # 2
- ■ = Hard Block

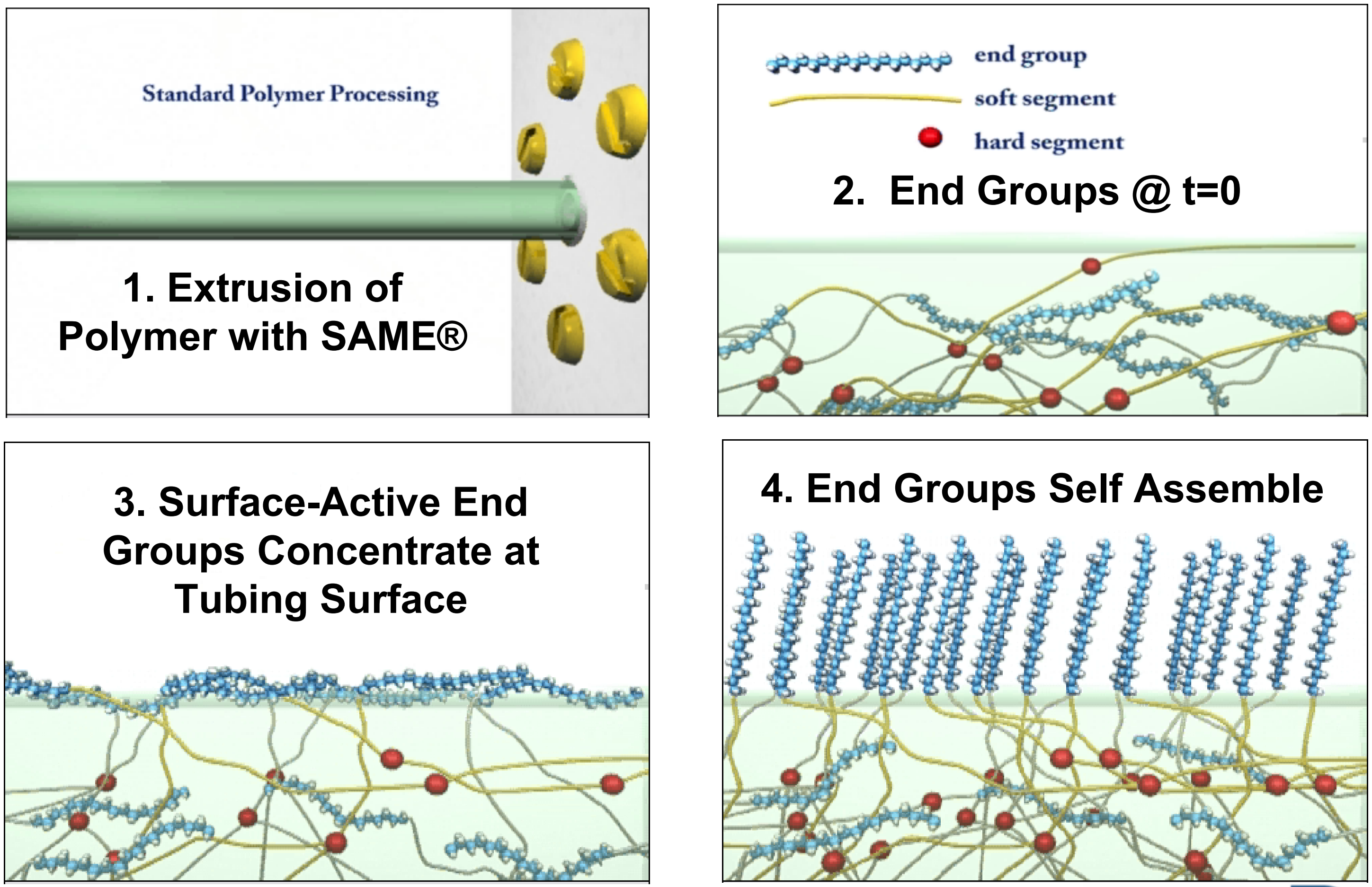
SAME® = *Self Assembling Monolayer End Group*

Self Assembly Video



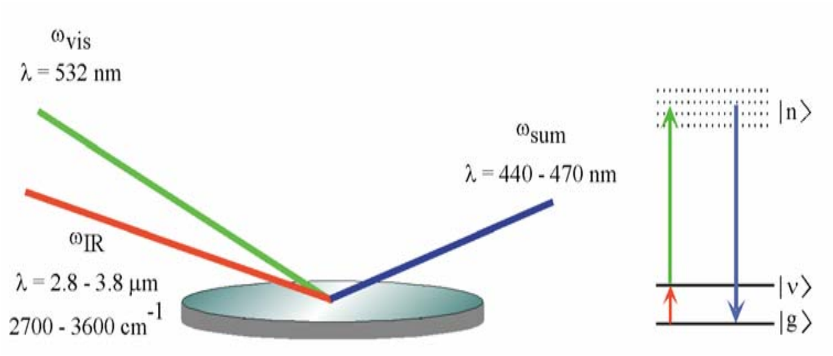
Not to scale

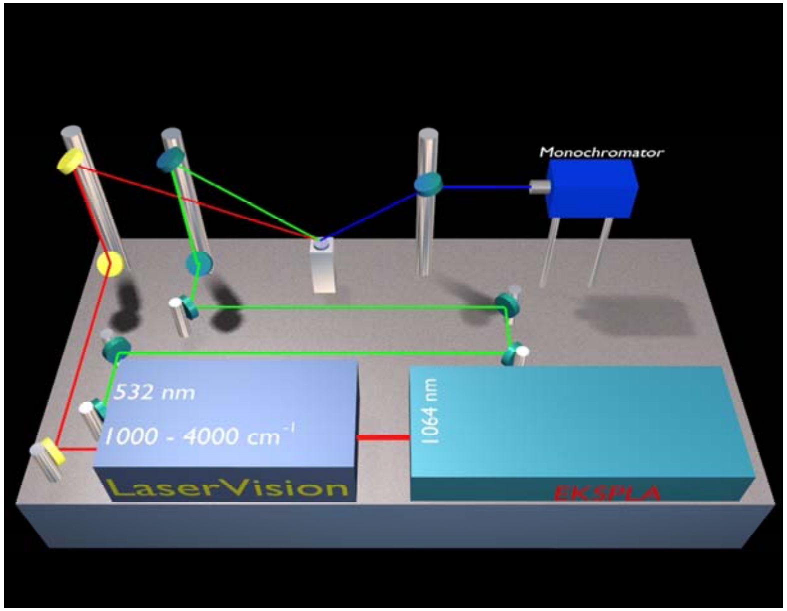
Self Assembly on Extruded Polyurethane Tubing

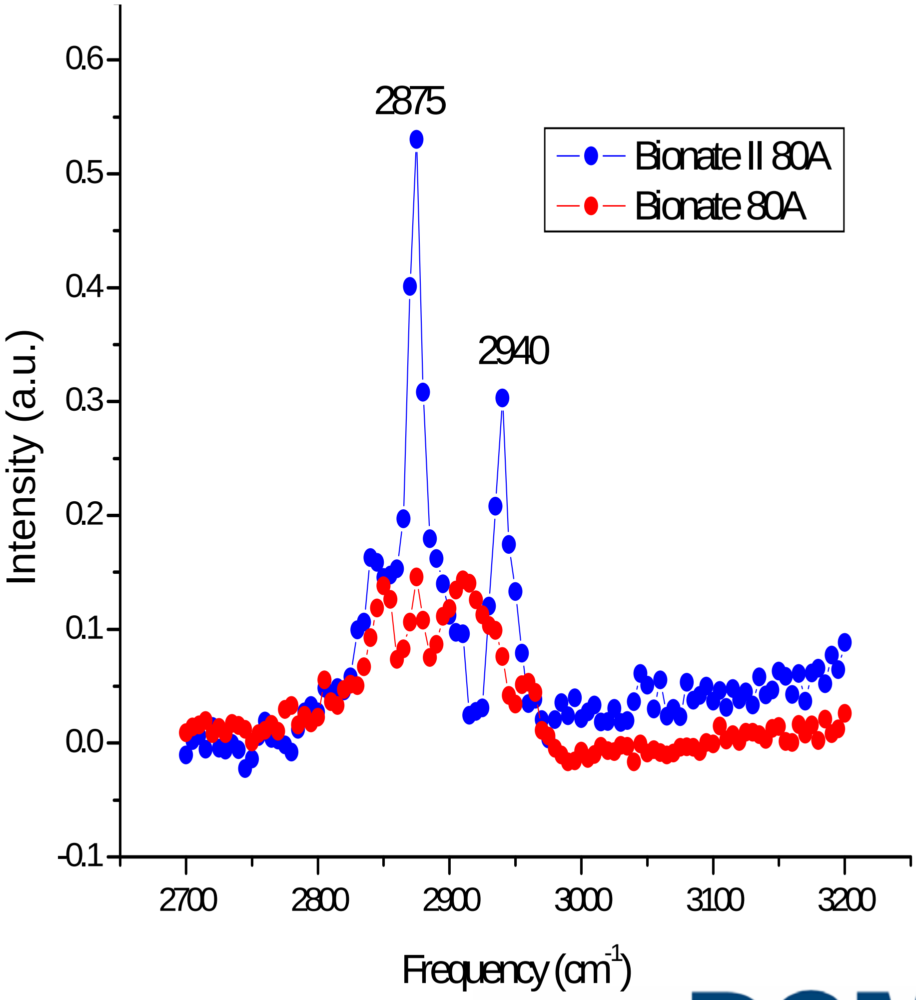


Schematic only. Not to scale

Sum Frequency Generation







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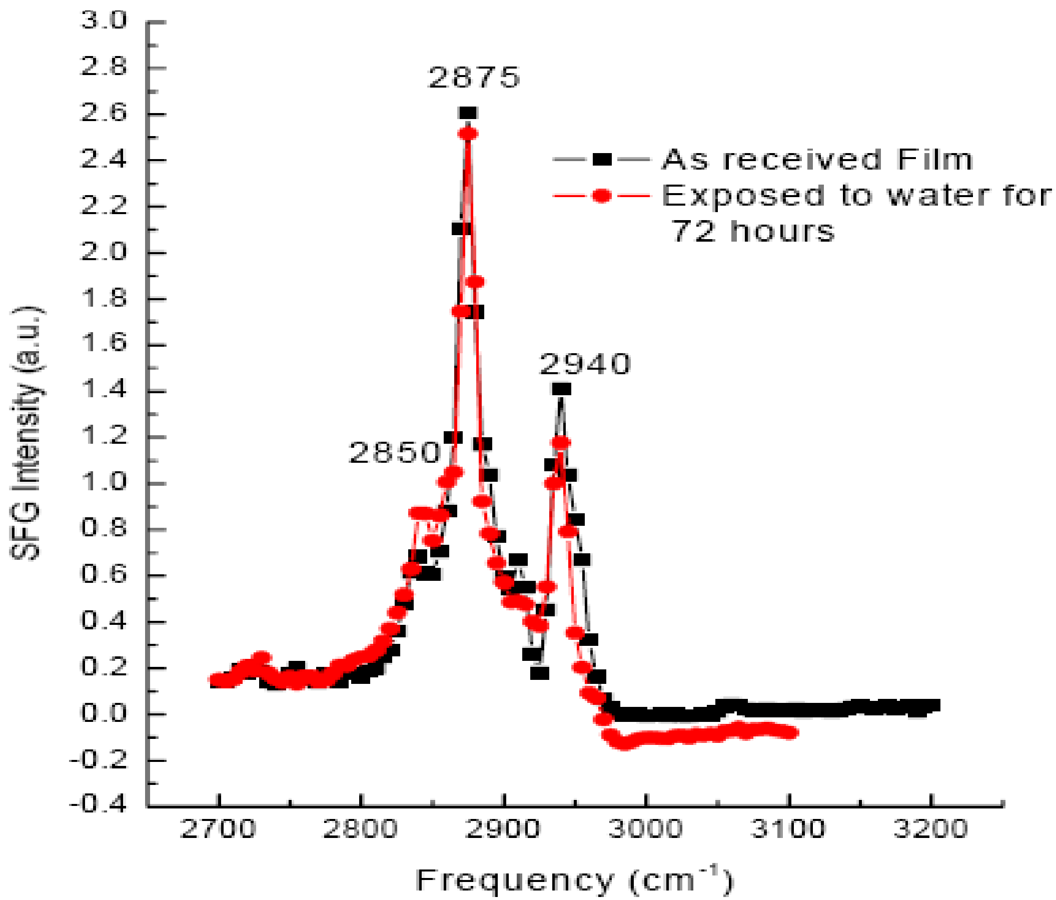
SAME® Technology Stability



- Bionate 55D with SAME® technology is shown before and after exposure to DI H2O in Water at 37 ºC for 72 hours.

SFG confirms SAME® technology stability

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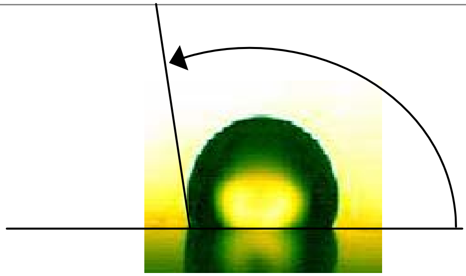
Contact Angle

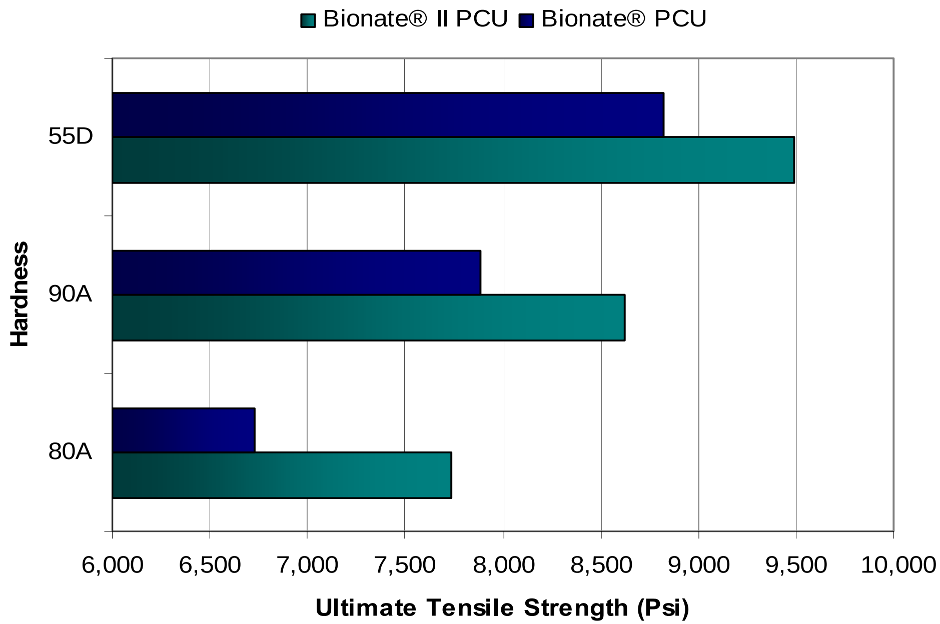


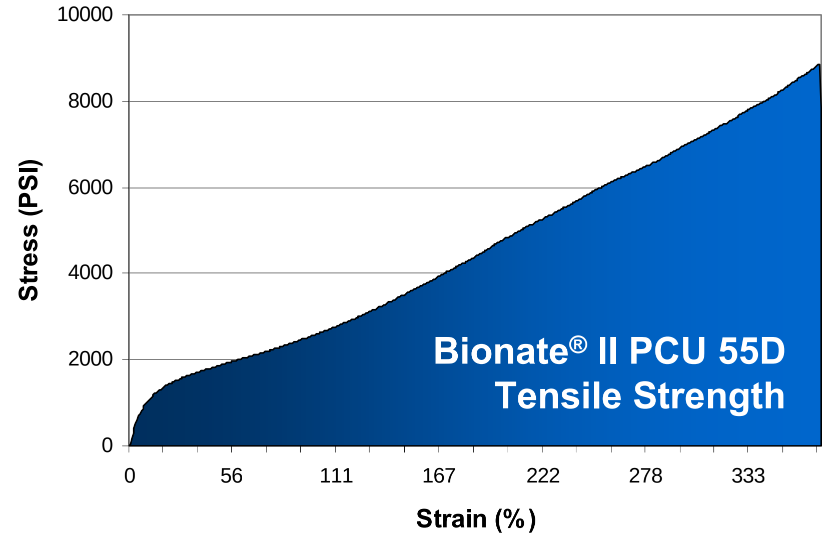
	Average	Std. Dev.
Bionate® 55D PCU	78.3	1.6
Bionate® 90A PCU	78.2	.8
Bionate® 80A PCU	76.5	0.5
Bionate® II 55D PCU	97.5	1.5
Bionate® II 90A PCU	98.8	2.3
Bionate® II 80A PCU	97.2	1.3
UHMWPE	104	2.6

PCU Material More Hydrophilic

All done with distilled water.

Bionate® II PCU Property Summary



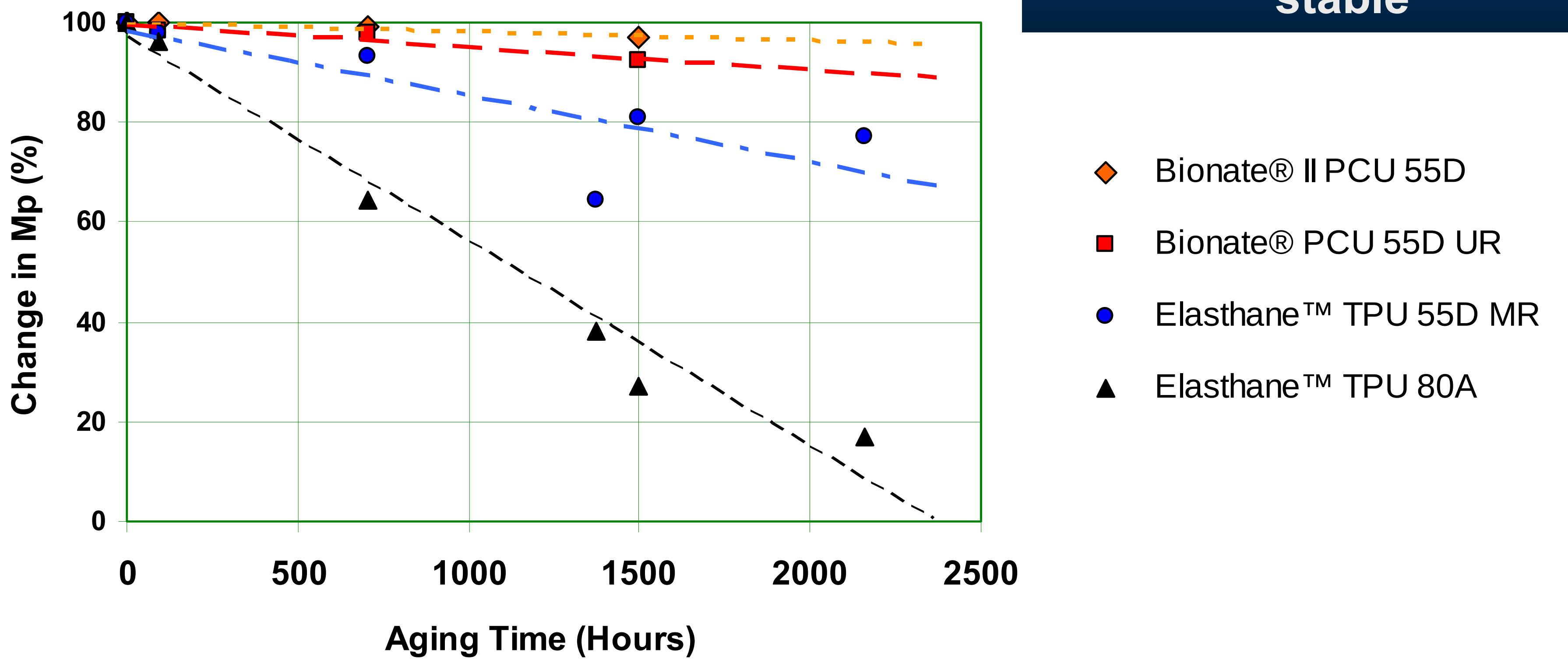


	80A	90A	55D
MW (kg/mole)	243	253	231
MFR (g/10min) 224 °C, 2160g	25	18	36
Tensile (PSI)	8231	8499	8960
Elongation (%)	518	385	372

In Vitro Oxidative Stability of Elastomers

Bionate® II PCU is the most oxidatively stable

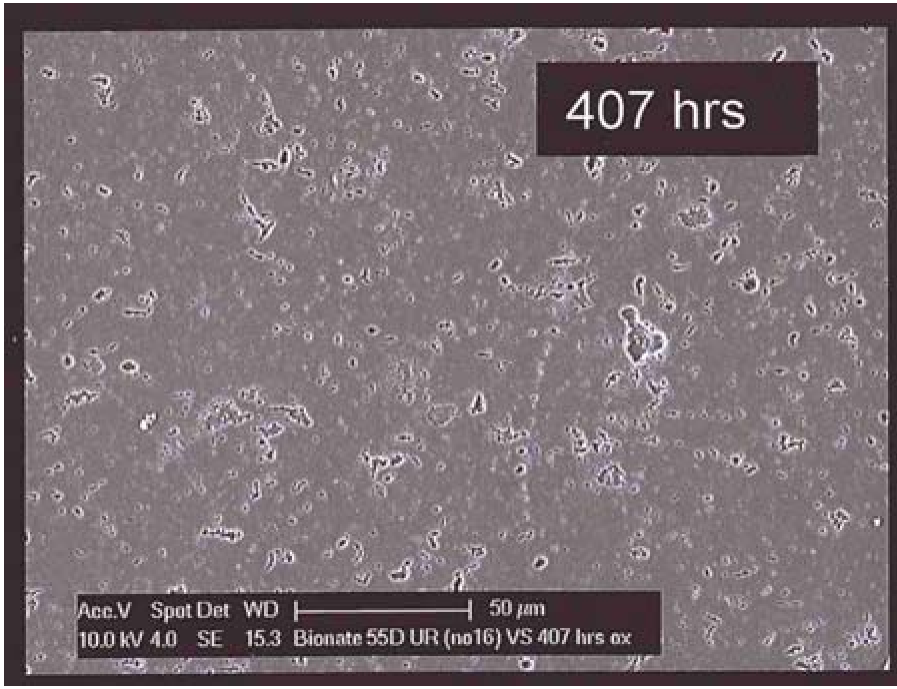
In Vitro Oxidative Stability Results



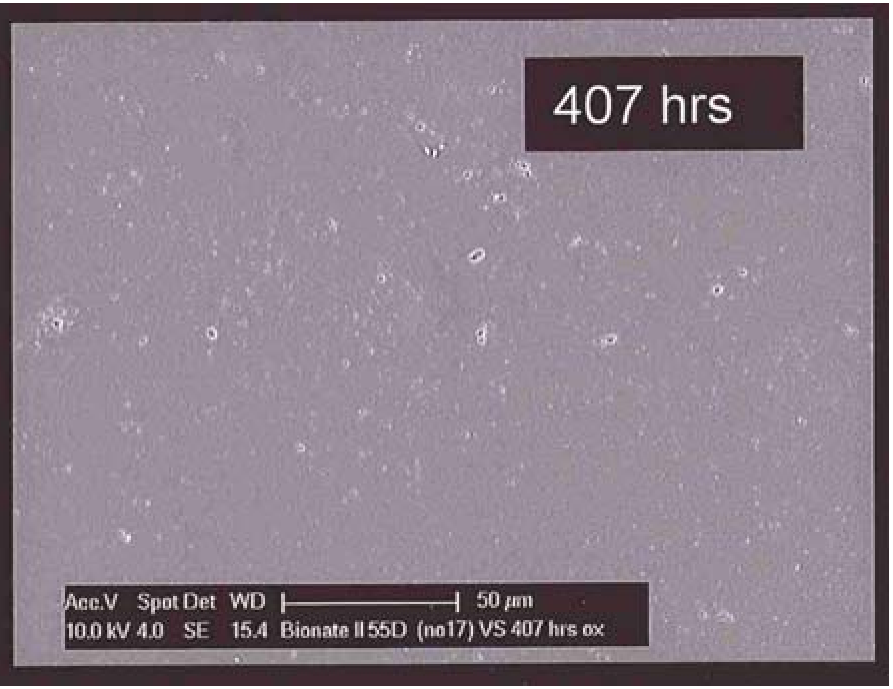
Peak Molecular Weight with exposure to hydrogen peroxide over time:
***conditions*: 37°C, (20% H_2O_2 +0.1 M $CoCl_2$).**

In Vitro Oxidative Stability SEM Comparison

Bionate® II PCU better than Bionate® PCU



Bionate® PCU 55D



Bionate® II PCU 55D

SEM Graphic showing exposure to hydrogen peroxide over time;
***conditions*: 37°C, (20% H_2O_2 +0.1 M $CoCl_2$)**

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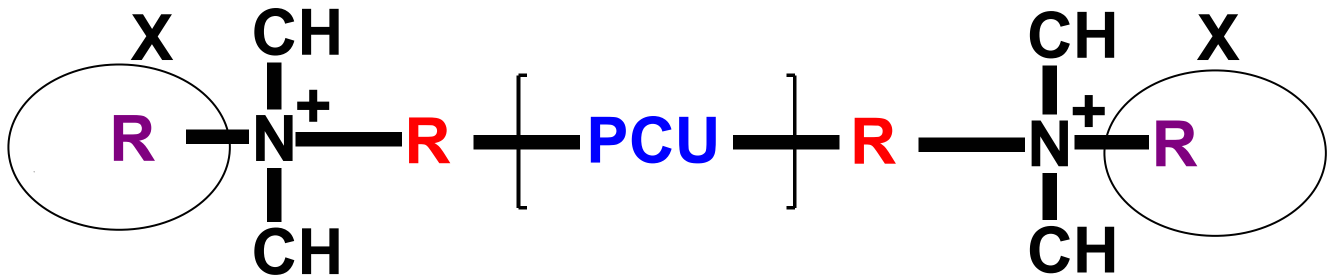
Polyurethane With Antimicrobial SAME® Technology



R_1: $-\left(CH_2CH_2O\right)_m-$ spacer

R_2: $-\left(CH_2\right)_n-CH_3$ end group

PCU: Polycarbonate urethane

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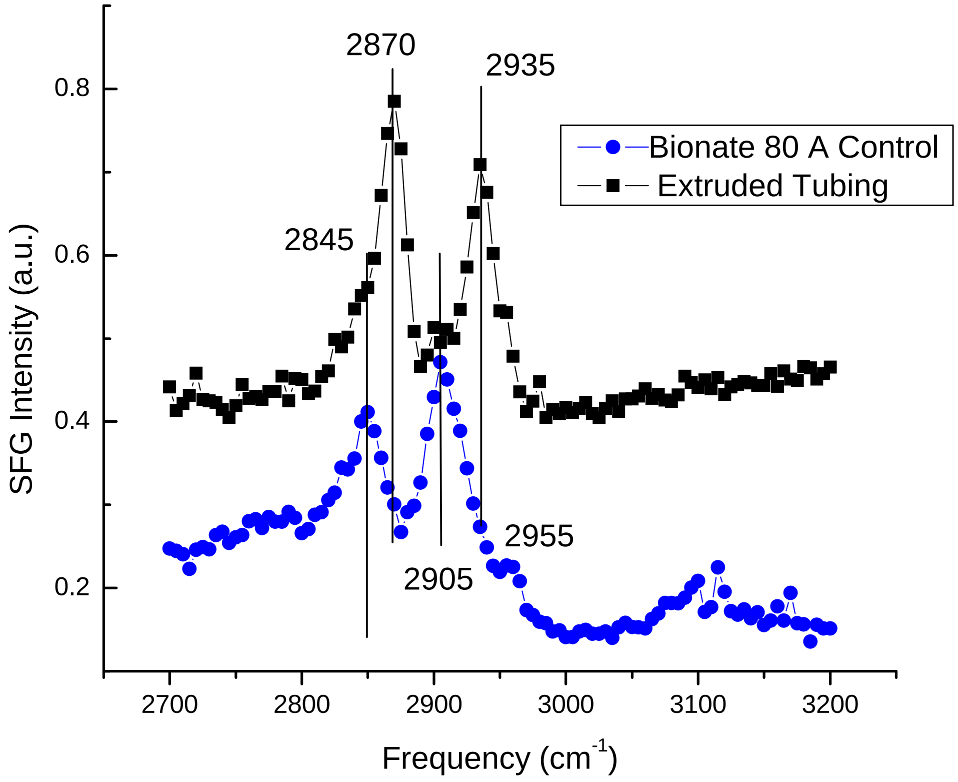
Surface Assembly of SAME® Quaternary Amines

Sum Frequency Generation Spectroscopy (SFG) analysis



Tubing with SAME® Quat:

2870 cm^{-1} = CH_3 Symmetric Stretch

2935 cm^{-1} = CH_3 Fermi Resonance

Bionate® PCU 80A Control

2845 cm^{-1} = CH_2 Symmetric Stretch

2905 cm^{-1} = CH_2 Asymmetric Stretch

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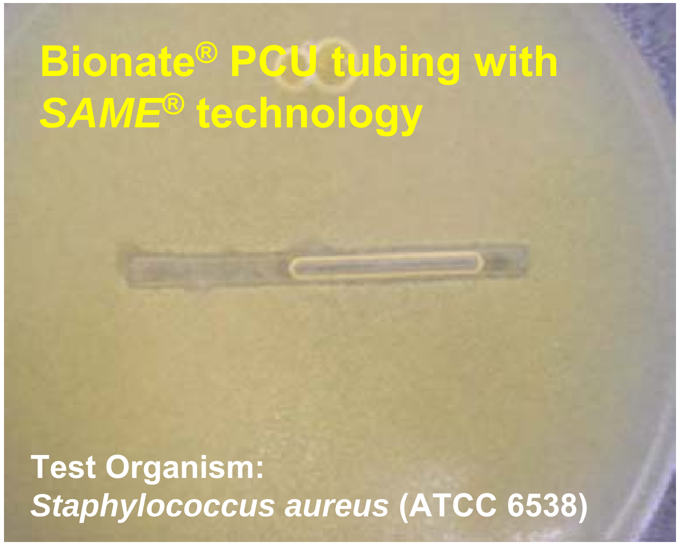
Antimicrobial Properties on Extruded Films/ Tubing

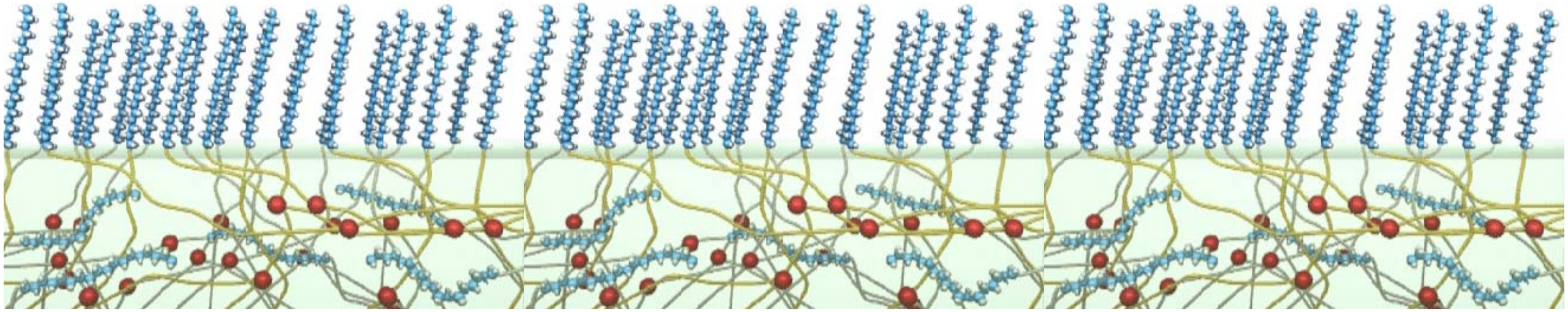
Bionate® PCU80A with quaternary amines Incorporated as End Groups	24 Hour % Cell Reduction Relative to Control	
	Staphylococcus aureus (+)	*Pseudomonas aeruginosa (-)*
$C_{18}H_{37}N^{+}(Me)_2(EtO)_3HCl^{-}$	>99.999	94.7



Application of SAME® Technology

- Passive thrombo-resistance
- Enhanced biostability
- Improved abrasion resistance
- Reduced self adhesion of device surfaces
- Enhanced lubricity
- Antimicrobial activity
- Covalently-bound, non-leaching processing aids

Integrated functional surface characteristics



Bionate® II PCU is an innovative, medical polymer with built-in surface technology. It is designed for chronic implants, enhanced for processing and backed by an established FDA master file.

Innovative SAME® Surface Technology

Optimum surface properties without impacting bulk properties

Key Benefits

- Surface activity and self assembly enable tailored surface properties
- Customized surface chemistries enable unique designs

Block Copolymers with SME® & SAME® Technology

- SME® (Surface Modifying End Groups)
  - surface-active end groups are covalently bound to a base polymer during synthesis
- SAME® (Self Assembling Monolayer End Groups)
  - surface-active end groups are covalently bound to a base polymer during synthesis and spontaneously self assemble on the surface

This technology is patented and a key differentiator for DSM PTG

Bionate® II PCU Key Benefits

Innovative Surface

- Patented built-in surface technology, Self Assembling Monolayer End group (SAME®)
- End groups covalently bound to the polymer structure for durability
- More consistent surface properties than surface modifying additives
- Wide range of potential surface modifications
- Eliminates the need for additional surface processing

Enhanced Performance

- Improved oxidative stability
- 10% stronger than 1st generation Bionate® PCU
- Outstanding abrasion resistance when compared to silicone elastomers

Bionate® II PCU Key Benefits (cont.)

Improved Processing

- Reduced polymer self adhesion and improved mold release capabilities without processing additives

Established Family

- Line extension of the Bionate® polymer family
- Backed by an established Master File
- Track record of success with implantable devices
- One of the most extensively tested polymer families

Applications in Tissue Engineering

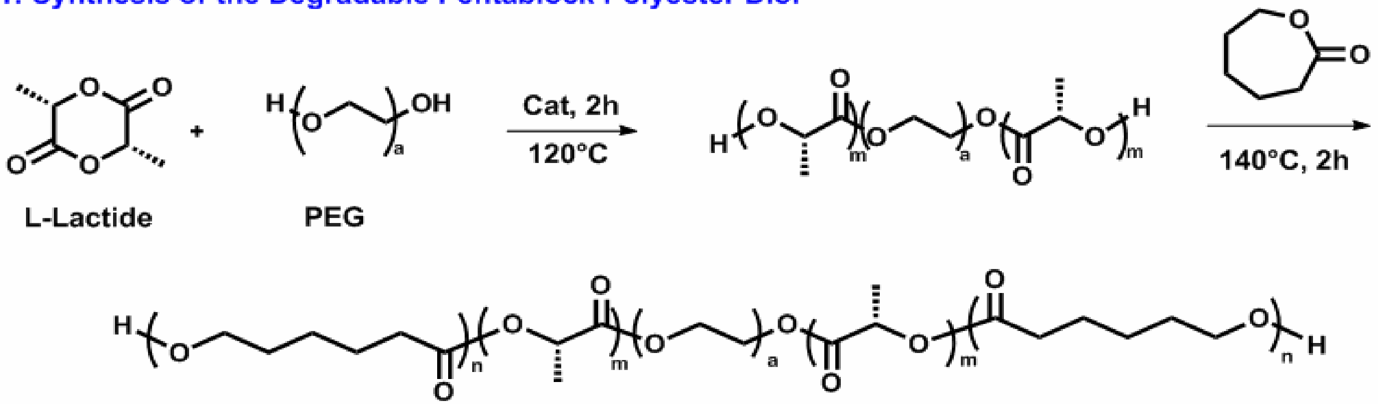
Application: biostable or bioresorbable?

- **surface characteristics/ surface modification requirements?**
    - **physical properties:**
        - **hydrophilicity**
        - **cell adhesion/ integration**
        - **modulus: softening temp (Tg)**

- **scaffold engineering:**
    - **porosity, dynamic mechanical properties, degradation rate, and release of growth factors…….**

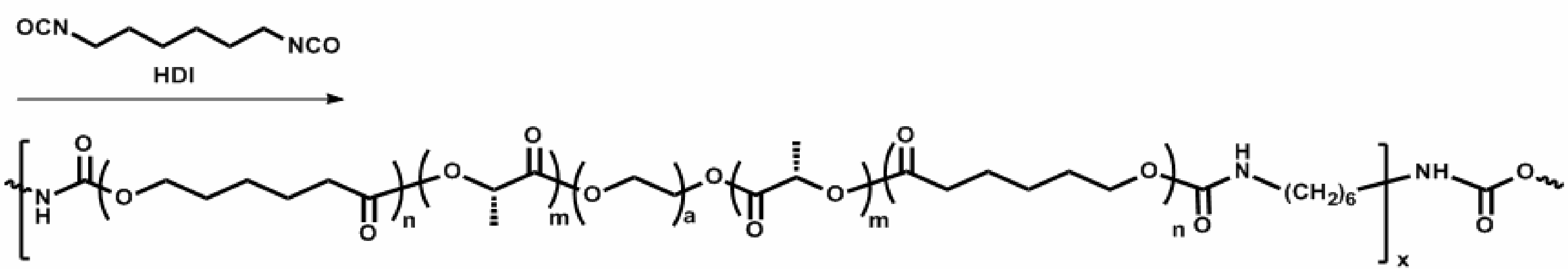
Bioresorbable multiblock polyesterurethane

Step 1: Synthesis of the Degradable Pentablock Polyester Diol



Penta-block polyester diol

Step 2: Chain Extension of the Degradable Pentablock Polyester Diol with 1,6 hexamethylene diisocyanate to yield the Multiblock polyester-urethane



EO/(LA+CL) – ethylene oxide : (lactide + caprolactone) ratio in polymer enables tunability of strength and degradation properties

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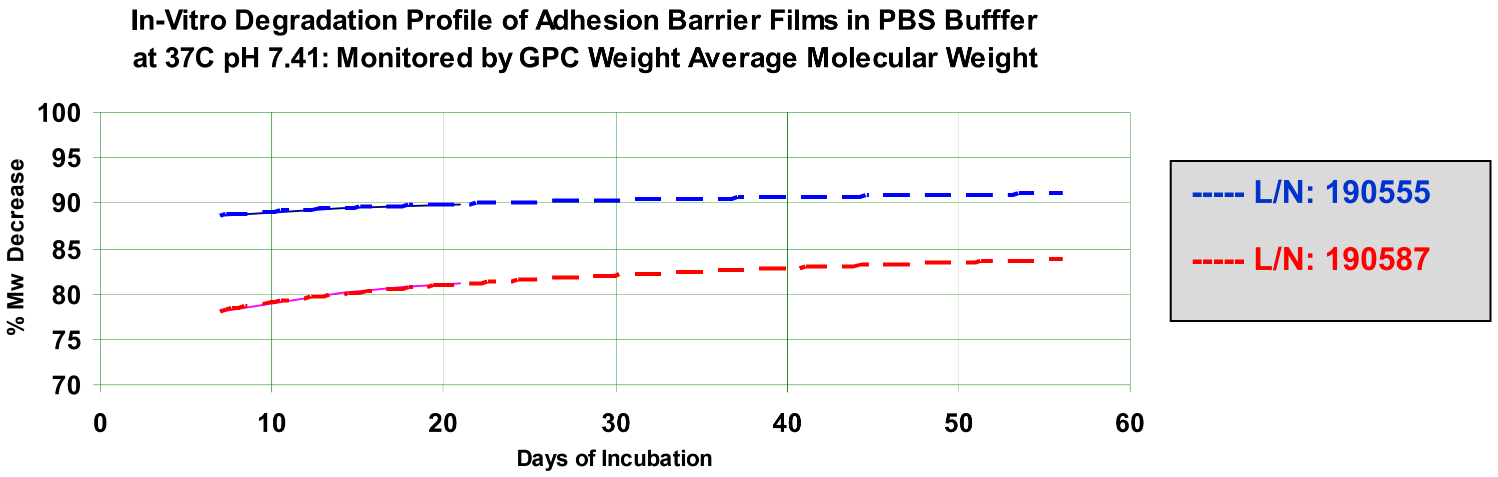
Bioresorbable polymer development:

Tensile Properties of Adhesive Barrier Films

Lot	EO/(LA+CL)	Thickness mil	Load at break N	Elongation at break %
190555	4	3.5	6.88	804
190587	2	6.0	17.41	817

Two fast degrading adhesion barrier films with different tensile properties and degradation rates were provided to customer for animal testing.

Tissue adhesion barrier testing in progress



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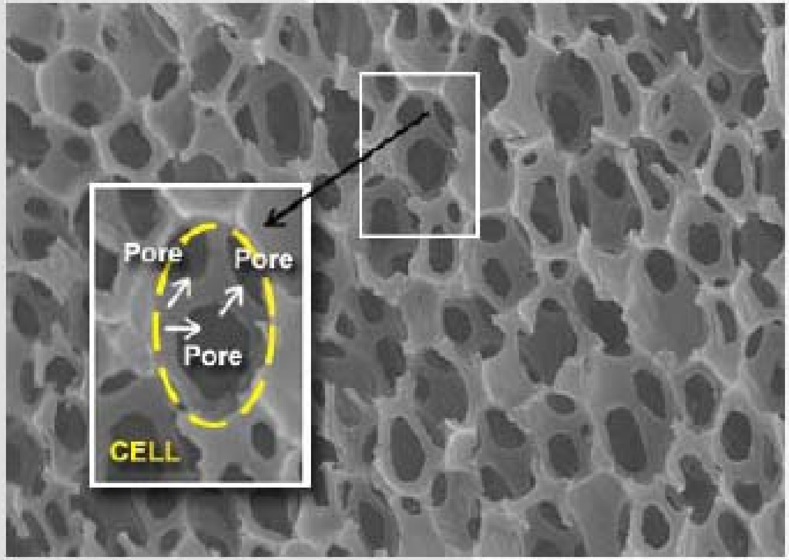
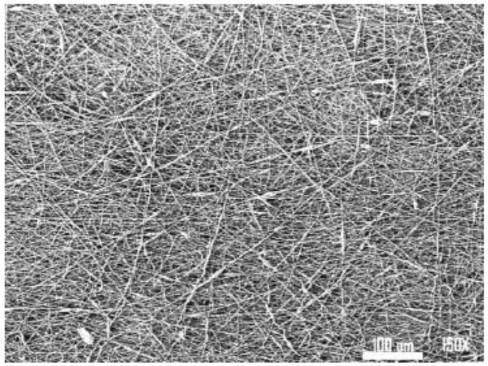
Biomerix Biomaterial™:
Biostable polycarbonate polyurethane urea scaffolds



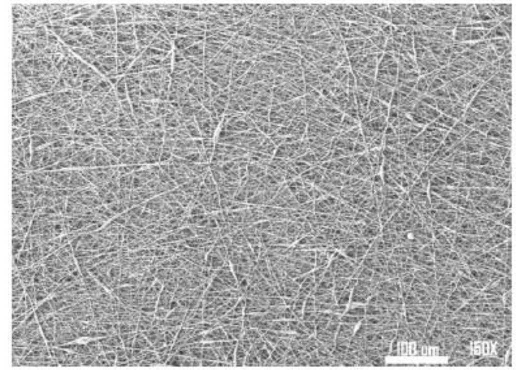
23x Magnified View of Biomerix Biomaterial™

The Biomerix Biomaterial™ is a three-dimensional scaffold specifically designed to support tissue ingrowth and biointegration. This proprietary, medical grade biomaterial is a cross-linked, reticulated polycarbonate polyurethane-urea. The scaffold embodies a unique microarchitecture consisting of an interconnected three-dimensional network of cells and pores.

Micropatterning of Electrospun Polyurethane Fibers ….



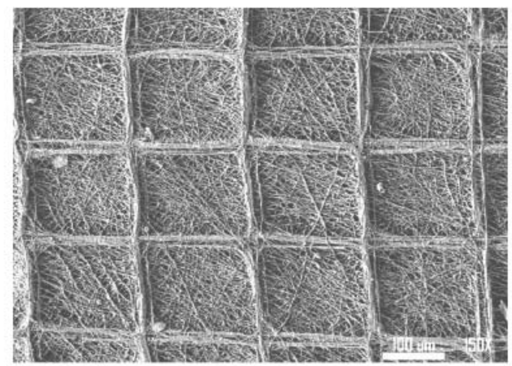
PEUU Fibers Flat PDMS



PEUU Fibers Patterned PDMS

- No PEUU fiber patterning was observed on patterned substrates
- No fiber fusion was observed

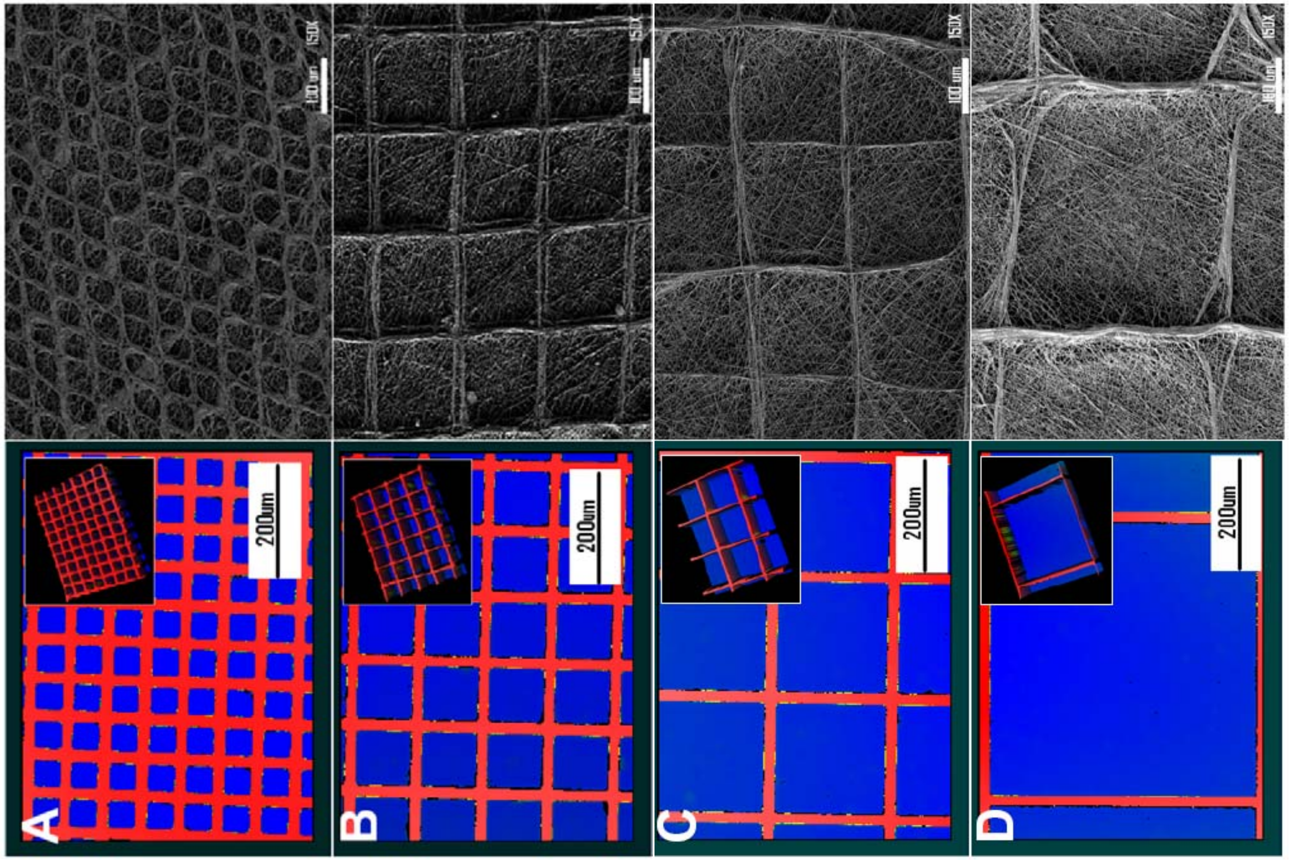
Electrospinning parameters were kept constant → differences were attributed to material specific effects



PEsU Fibers Patterned PDMS

Micropatterning of Electrospun Polyurethane Fibers through use of Soft Lithography Molding
D. K. Dempsey[1], C. Schwartz[1], R. S. Ward[2], A. V. Iyer[2], J. P. Parakka[2], E. Cosgriff-Hernandez[1]; Texas A&M Univ., College Station, TX, 2) DSM-PTG, Berkeley, CA. Poster Number 257
35th Annual Meeting of the Society for Biomaterials, Friday, April 23, 2010, 4:45-5:30pm,

Micropatterning of Electrospun Polyurethane Fibers through Control of Surface Topography



Micropatterning of Electrospun Polyurethane Fibers through Control of Surface Topography, "*David K. Dempsey[1], Christian J. Schwartz[2], Robert S. Ward[3], Ananth V. Iyer[3], James P.Parakka[3], Elizabeth M. Cosgriff-Hernandez[1]** 1)Department of Biomedical Engineering, Texas A&M University, College Station, Texas, 77843-3120, 2) Department of Mechanical Engineering, Texas A&M University, College Station, Texas, 77843-3123 3DSM-PTG, Berkeley, California, 94710: *in press.*

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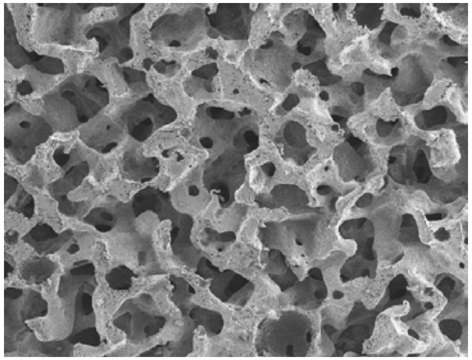
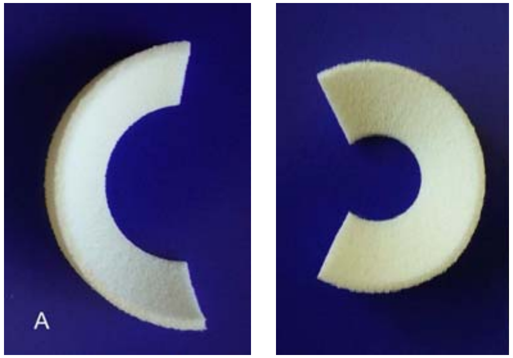
Commercial degradable polyurethanes

Trade name	Supplier	Chemistry	Applications
Degrapol™	AB Medica Spa (Italy)	Porous foam	Nerve and bone regeneration
Lacthane™	Polyganics (Netherlands)	Foams; BDI based	Wound and nasal dressing; (CE marked and FDA approved) Surgical sealant;
Epidel™	Interface Biologics (Canada)	PU-co-drug; PCL based polyol	Catheter cuffs; Antimicrobial
Novosorb™	PolyNovo Biomaterials (Australia)	Injectable gel; X-linked polymer; NCO prepolymers	Porous non porous monoliths orthopaedic
Actifit™	Orteq (Netherlands)	BDI, PCL, BD; Porous patch	Meniscal repair (CE Marked Clinical July 2008)
SynBioSys™	Octoplus BDI, PLGA, PEG, PCL (Netherlands)	BDI, PLGA, PEG, PCL	Stent coatings (Clinical trials) Drug eluting microspheres
Artelon™	Artimplant (Sweden)	Polyurethane urea Fibres, scaffolds, films and granules	ACL (ligament fixation) Bone scaffolds (odontology)

- Scaffold that supports healing of the meniscus
- Porous aliphatic polyurethane based on 1,4-butanediisocyanate and poly(e-caprolactone); ~20% of the polymer and consist of urethanes made from1-4-butanediisocyanate (BDI) and 1-4-butanediol (BDO) moieties;
- **CE mark since July 2008**

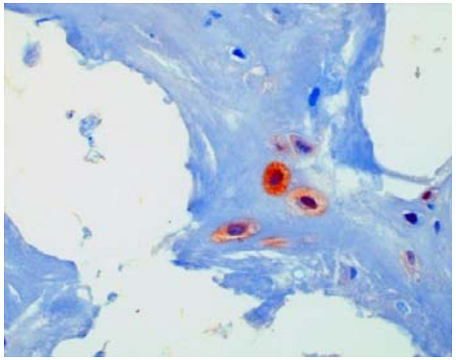


Porous structure of Actifit



Medial and lateral Actifit

Arthroscopic look of sutured Actifit



Tissue after 12 months with fibrochondrocytes

http://www.orteq.com/

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Polyganics

- **Lacthane® biodegradable polyurethanes**
  - **Based on 1,4-butanediisocyanate(BDI).**
  - **Excellent mechanical properties due to uniform block length.**
  - **Contain soft segments are based on poly (ether) esters.**

    By varying the soft segment composition degradation speed can be accurately controlled between 1 hour and ½ year.
  - **Proven biocompatibility**

- Nasopore® Nasal dressing
  - High blood absorption capacity
  - Fragments within 5 days
  - CE and FDA approved
- C-Seal® colorectal drain
  - Prevents anastomic leakage following low anterior resection of the rectum.
  - Fragments after 2 weeks
  - Product is currently clinically evaluated
- Otopore® wound dressing for middle and outer ear surgery.
  - Wound compressing for a few days
  - Fragments within several weeks
  - CE and FDA approved
- Oroantral communication plug
  - Novel closure method for oroantral communications
  - Compression strength for 2 – 3 weeks
  - Simple alternative for clinical procedure
  - Product is currently clinically evaluated

Conclusion

- **Polyurethanes are an extremely versatile material in terms of physical properties biostability and biodegradability;**

- **As Biomaterials, polyurethanes satisfy bulk and surface property requirements:**
  - Bionate® II PCU with SAME® technology allows for independent optimization of bulk and surface properties
  - SAME® technology provides a simple and effective method for manufacturing polymers with functional surfaces without negative impacting polymer bulk properties

- **Processability of these materials is being applied and developed.**

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