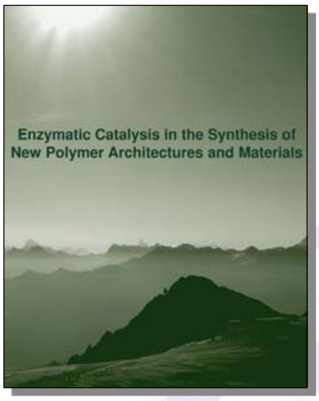
Enzymatic Catalysis in the Synthesis of New Polymer Architectures and Materials



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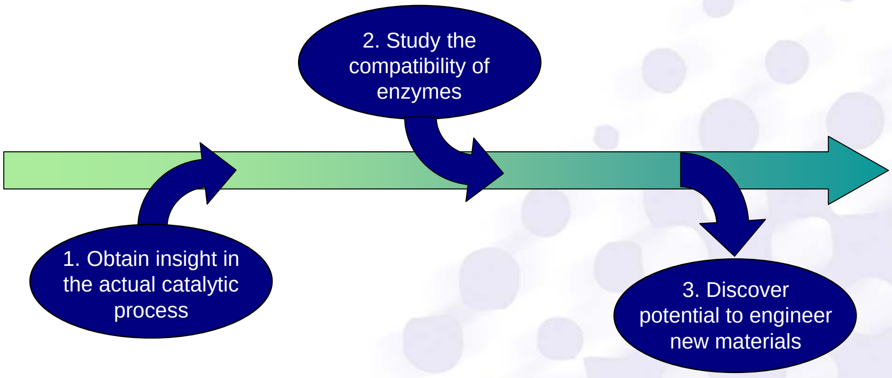
Laboratory of Polymer Chemistry
Technische Universiteit Eindhoven

DPI interest in biocatalysis

Website Dutch Polymer Institute - 20/11/07

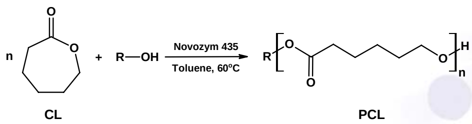
Objective Thesis

"Can enzymes offer new perspectives in polymer chemistry?"



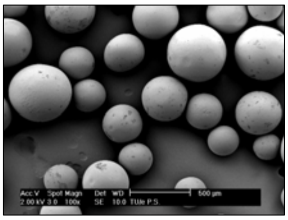
Concepts

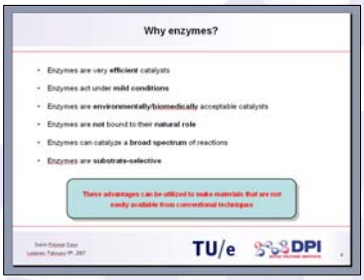
eROP: Enzymatic ring-opening polymerization



1993: Knani et al. *J. Pol. Sci. A*, 31, **5**, 1221-1232

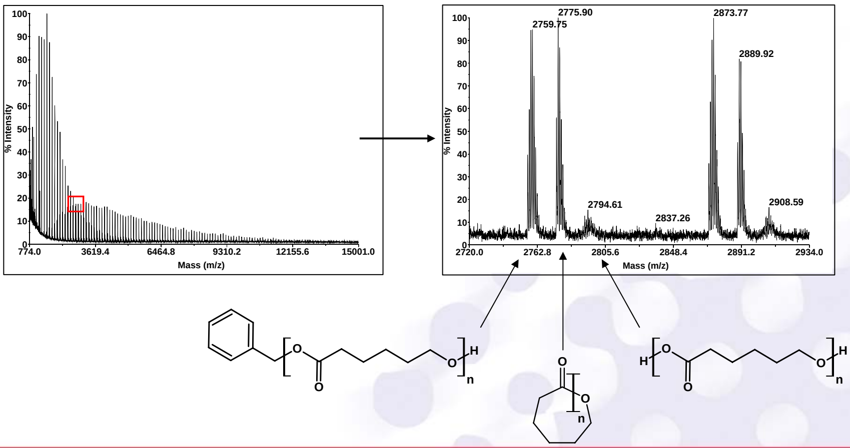
Novozym 435





1. Insight in Catalytic Process

MALDI-TOF-MS



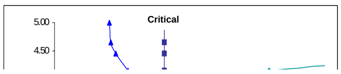
LCCC

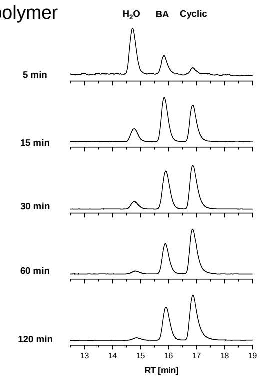
Liquid Chromatography under Critical Conditions (LCCC)

- Separation based on difference in end-functionality
- Only technique to distinguish between different polymer species in a quantitative manner!

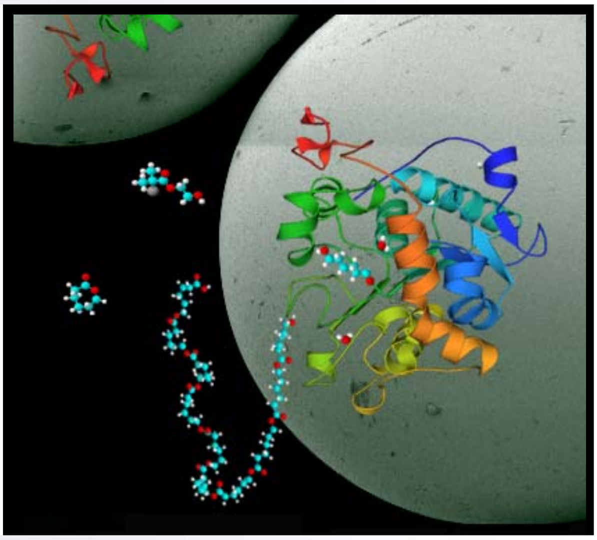
Observations:

- Large amounts of polymeric side-products
- Initial nucleophile is water





	Presence [w/w-%]	
H_2O	BA	Cyclic
62	31	7
23	51	26
16	49	35
12	56	32
9	50	41



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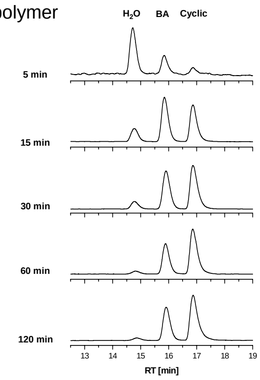
Therefore:

- Minimize water concentration
- Optimize initiator performance
- Reduce cycle formation



Presence [w/w-%]

H_2O	BA	Cyclic
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De Geus et al. *manuscript accepted in Biomacromolecules* **2007**

Reduce polymer side-products

Minimize water concentration

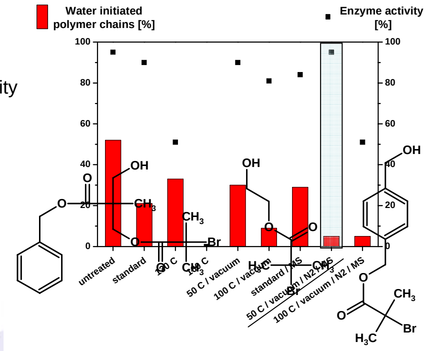
- Enzyme needs water to function
- Develop drying technique that allows enzyme activity with minimal water initiation

Optimize initiator performance

- Determine criteria for an initiator to compete with other nucleophiles (size, chirality, polarity)

Reduce cycle formation

- Define appropriate reaction conditions to minimize the formation of cyclic polymer structures
  → work in bulk

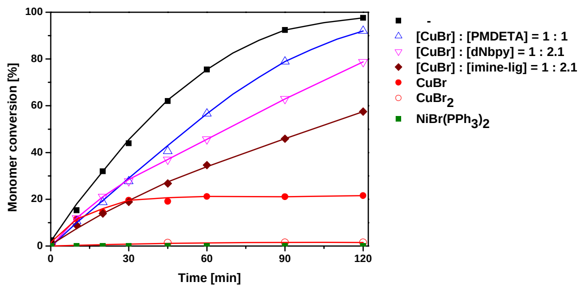


De Geus et al. *Macromolecules* **2005**, 38, 4220

2. Compatibility of Enzymes

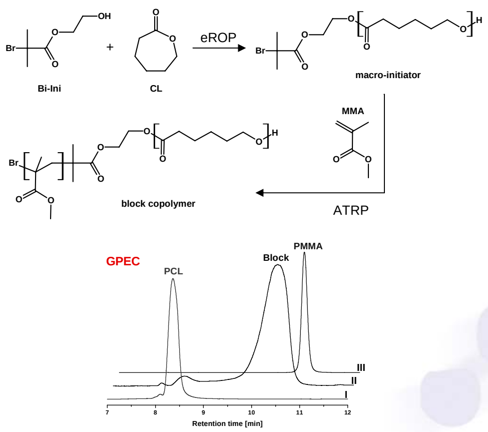
Model system

- Combination of controlled radical polymerization and eROP
- Check mutual influence:
  - ATRP-system on eROP
  - eROP-system on ATRP

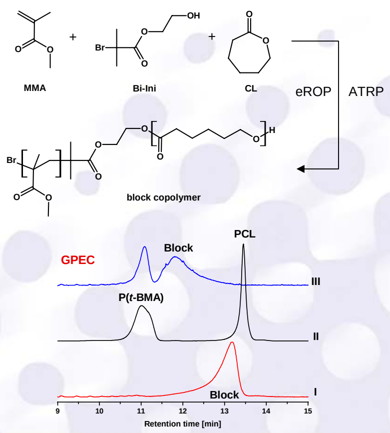


Chemoenzymatic Cascade Approach

Traditional approach



Cascade approach



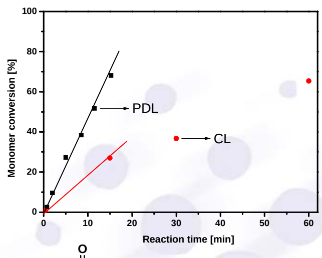
Duxbury et al. *J. Am. Chem. Soc.* **2005**, 127, 2384

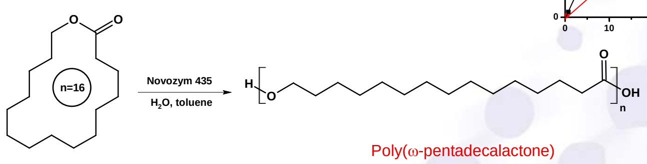
De Geus et al. *J. Pol. Sci. A* **2006**, 44, 4290

3. Engineer New Materials

Advantages of enzymes:

- Stereo-, regio- and enantioselectivity
- Different behavior towards large lactones (n>12)





Poly(ω-pentadecalactone)

- Aliphatic polyester → biocompatibility/biodegradability
- Structural resemblance with linear polyethylene → push M_w to its limit
- High molecular weight PPDL only accessible with enzymes

Fiber applications!

Polypentadecalactone

High molecular weight PPDL

- Decrease amount of nucleophiles
- Overcome diffusional problems during polymerization (heterogeneous catalyst)
- Molecular analysis at elevated temperature (high crystallinity)

M_w [kg/mol]	M_w/M_n [-]	T_m [ºC]	T_g [ºC]	ΔH_m [J/g]	χ_c [-]
190	3.2	95	-25	138	59

Polymer	T_g [ºC]	T_m [ºC]	E [MPa]	σ_{break} [MPa]	σ_{yield} [MPa]	ε_{yield} [%]	ε_{break} [%]
PLLA	57	170-180	1000-3000	n.d.	50	<4	<7
PCL	-60	55-60	400	n.d.	16	7.0	800-1000
PPDL	**-25**	**95**	**420**	**38**	**17.5**	**15**	**1200**
LLDPE	-60	122-130	250-500	13-27	9-19	-	100-965
LDPE	-25	100-120	200-300	8-30	9-14	-	100-650
HDPE	-125	130-140	1100	21-32	n.d.	-	1200

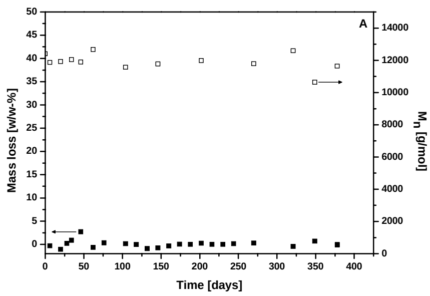
Future application of PPDL

Biomedical fiber applications

- Hydrophobic and crystalline polymer material
- Metal-free synthesis
- Can be chemically incorporated with other (hydrophilic) segments:
  - PEG
  - lactones
  - lactide/glycolide

Material could be used as fiber or tape for:

- Suturing
- Bone repair
- Tissue engineering
- Stents



- Continuation of this work in DPI #608

Highlights

Enzymatic polymerization

1. Obtain insight in actual catalytic process
   - ✓ Development of LCCC to quantify different polymer species
   - ✓ Water is initially most active nucleophile in eROP
   - ✓ Optimize reaction conditions to minimize side-products

2. Study the compatibility of enzymes towards other polymerization techniques
   - ✓ Investigation of mutual influence
   - ✓ Combination of eROP and controlled radical polymerization in one pot (cascade)

3. Discover its potential to engineer new materials
   - ✓ Development of high molecular weight PPDL only accessible with enzymes!
   - ✓ Material assessment to position its possible application (biomedical fibers)

Acknowledgements

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Laboratory of Polymer Technology

Laboratory of Macromolecular and Organic Chemistry

Laboratory of Process Design

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Hogeschool Nijmegen, HAN

DSM Research

KU Leuven

University of Nottingham

CIDETEC, San Sebastian

Number of publications generated from this project: 8