

Enzymes for Industrial Biotechnology

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Round Table on Industrial Biotechnology in Lithuania
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Main Objectives for **Industrial Biotechnology** Research

The development and production of **novel, innovative products and processes** in a **cost- and eco-efficient** manner, using increasingly **renewable raw materials**

through

the **discovery and optimization of strains and biocatalysts.**

Industrial Biotechnology

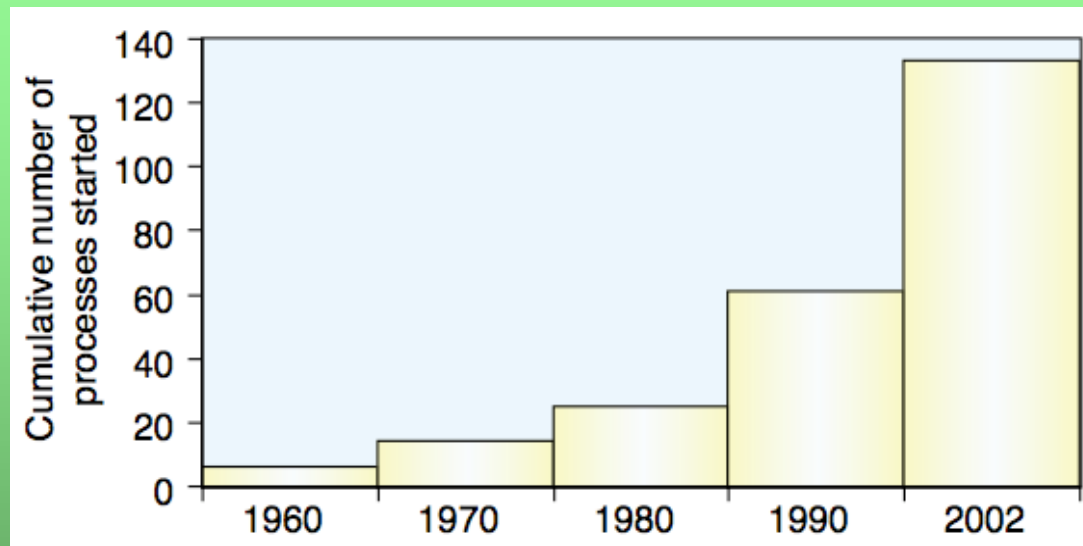
Use the same **genomic and proteomic tools**
developed for medical biotechnology
to discover new ways to make
energy, industrial raw materials, intermediates
and consumer goods

Main Tools in the Genomic and Proteomic Toolbox

- Gene Shuffling
- High Throughput Screening
- Directed Evolution
- Metabolic Engineering
- Molecular Breeding
- Protein Engineering
- Extremeophiles
- Bioinformatics

Prokaryotic biodiversity - **Industrial Biotechnology**

- Rapidly growing field
 - by **2010** biocatalysis will be used in production of **60%** of fine chemicals (McKinsey analysis)
- Applications:
 - pharmaceuticals
 - food ingredients (sweeteners, vitamins)
 - feed additives and other agrochemicals
 - organic solvents
 - polymer raw materials
 - biofuels
- Needed:
 - **novel enzymes and pathways**
 - **“Periodic table” of biochemical transformations**



Straathof et al. 2002. *Curr Opin Biotech* 13:548-56

~150 compounds are currently produced on industrial scale using biocatalysts.

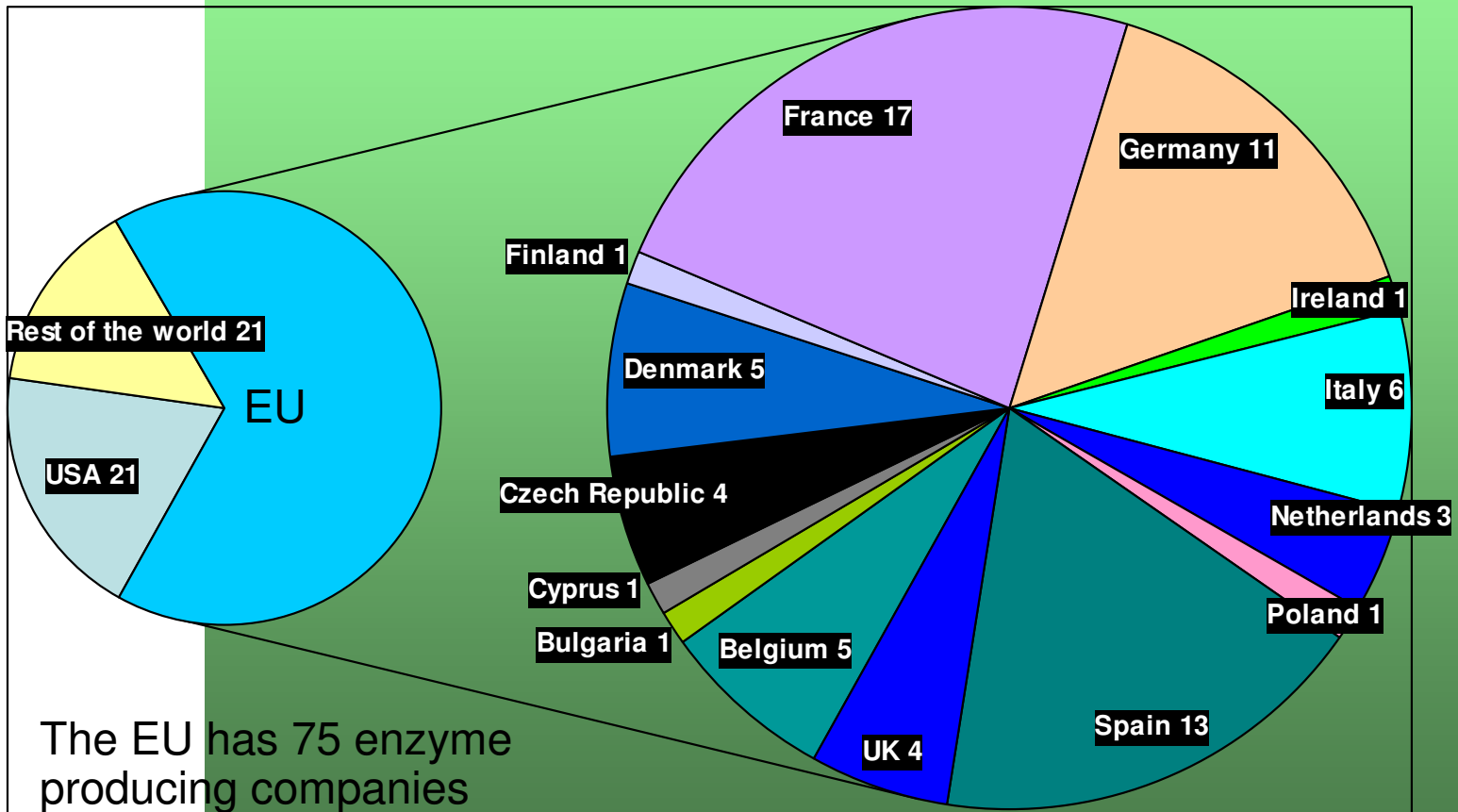
Current approaches to discovery of new enzymes

- Screening environmental samples by enrichment cultures
- Metagenome approach: cloning & expression of DNA samples in a surrogate host, then screening for desired function
- Sequence-based discovery

Still to be discovered: enzymes involved in the biosynthesis or catabolism of approximately 40 naturally occurring chemical functional groups are still not known

Industrial Biotech

Global and EU distribution of enzyme producing companies



Source: Bio4EU Draft Final Analysis report

Industrial enzymes

Currently limited to specific processes and individual steps in the manufacturing production process.

Examples of enzyme include:

- lipases;
- starch hydrolysing or modifying;
- carbohydrate oxidases/dehydrogenases

Bioelectrocatalysis

- R&D of bioelectrochemical processes in Lithuania started more than 30 years ago at Institute of Biochemistry:
- Areas of investigations:
 - Development of biosensors including ones for on-line control of biotechnological processes,
 - **Bioelectrochemical synthesis.**

- **Department of Enzyme Chemistry,
Institute of Biochemistry**
- ***Head:*** Prof. Juozas Kulys
- ***Scope:*** Investigation of oxidoreductases functioning with special emphasis to enzymes application for development of biosensors.

- **Department of Organic Chemistry**
Institute of Chemistry
- ***Head:*** Prof. Albertas Malinauskas
- ***Scope:*** Bioelectrochemistry – study on conjugation of redox enzyme catalysed reactions with electrochemical processes.

- **Department of Bioanalysis, Institute of Biochemistry**
- **Head:** Prof. Valdas Laurinavicius
- **Scopes:** Development of biosensors, immunosensors and bioanalytical systems based on redox enzymes or enzyme sequences for the medicine, food-quality-control and environment.
- • Bioelectrochemical synthesis - synthesis of mediators and mediating systems for the electrochemical wiring of redox enzymes.

- **Department of Bioelectrochemistry and Biospectroscopy, Institute of Biochemistry**
- **Head:** Prof. Valdemaras Razumas
- **Scopes:** Structure and functioning of proteins and low-molecular-weight redox-active biomolecules at **electrochemical interfaces**: acceleration of electrode processes by hydrolytic enzymes and development of biosensors based on these systems.
- Redox conversion of proteins and low-molecular-weight redox-active biomolecules on bare and modified electrodes, including electrodes modified by redox-active **self-assembling monolayers**

Enzyme screening and improvement

- R&D in Lithuania started more than 40 years ago:
- Ongoing activities:
 - Characterization of new hydrolases and oxidoreductases;
 - Genetic engineering of oxidoreductases

- **Department of Biochemistry and Biophysics, Vilnius University**
- ***Head:*** Prof. Vida Kirveliėne
- ***Scope:*** Microbial lipases: catalytic properties, stability and stabilization, immobilization, applications.

- **Department of Plant Physiology and Microbiology, Vilnius University**
- ***Head:*** Prof. Donaldas Čitavičius
- ***Scope:*** New thermophilic microorganisms (mostly thermophilic endospore-forming bacteria) and thermostable hydrolases for biotechnology.

- **Department of Molecular Microbiology and Biotechnology, Institute of Biochemistry**
- **Head:** Dr. Rolandas Meskys
- **Scopes:** Investigation of diversity of microbial metabolic pathways and enzymes by biochemical and genetic analysis of biodegradation of arenes and *N*-heterocycles.
- • Identification of new enzymatic activities and application of them for synthesis of chemicals.
- • Screening, characterization and genetic engineering of enzymes applicable for biosensors (flavin-, copper-, heme- and pyrroloquinoline quinone (PQQ)-dependent oxidoreductases).

Carriers for immobilization of biocatalysts

- Investigations of immobilization of biocatalysts in Lithuania started more than 30 years ago in Institute of Biochemistry and Institute of Biotechnology:
- Areas of investigations:
 - Immobilization for analytical applications,
 - Immobilization for organic synthesis,
 - Immobilization for medical applications.
- At the present time investigations of carriers for immobilization of biocatalysts are performed at:
 - Vilnius University - synthetic polymers (polyurethanes), modified chitosan (graft chitosan, magnetic chitosan);
 - Kaunas University of Technology – modified cellulose;
 - Institute of Biotechnology – protein based carriers (collagen, fibroin, keratin).

- **Department of Polymer Chemistry, Vilnius University**
- **Head:** Prof. Ričardas Makuška
- **Scopes:** Modified natural and synthetic polymers for biotechnology.
- • Synthesis and modification of polymer-based carriers for immobilization of enzymes,
- • Study of physico-chemical properties of native and immobilized biocatalysts, application for **organic synthesis** (in cooperation with Institute of Biotechnology).

Industrial enzymes R&D

- Lithuania is strong in terms of researchers.
- However, the capacity of Lithuania to apply this knowledge to products that lead to commercially viable businesses is lower than in the EU.

Companies involved in R&D of industrial enzymes

- ***Biocentras UAB***
- ***Beamo UAB***
- ***Malsena UAB***

The Hurdles

- Lack of appropriate political support
- Lack of investor interest

Positives

- **National Programme „Development of Industrial Biotechnology in Lithuania, Y2007-2010“ funded by Lithuanian government**
- **National Programme „Biotechnology and Biopharmacy, Y2008-2013“ is under development and will be funded by EU structural funds and Lithuanian government**

The Perspectives

- Development of the enzymatic toolbox
- Bioconversions for fine chemical synthesis
- Starch bioconversion
- Glycerol bioconversion
- **Metabolic engineering**

Ačiū už dėmesį