FuturEnzyme
Technologies of the FUTURe for low-cost ENZYMEs for environment-friendly products

Webinar: Fantastic enzymes: Where and how to find them

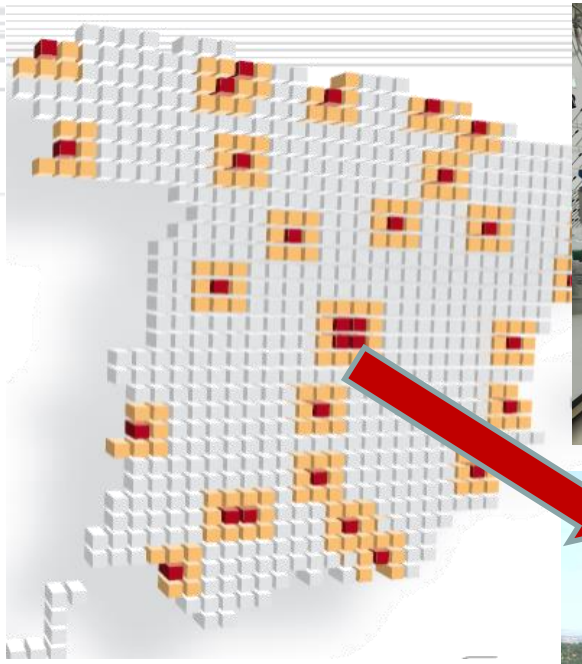
Presentation: Enzymes wanted, reason: the bioeconomy, the climate change and the consumer demands

By: Manuel Ferrer

6 september 2022

Project funded by the European Union's Horizon 2020
Research and Innovation Programme under grant agreement No [101000327]

The ICP, CSIC



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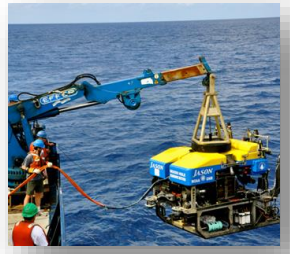
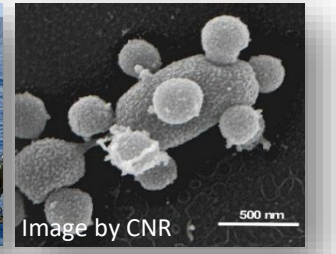
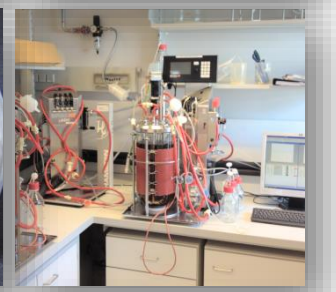






The planet we want

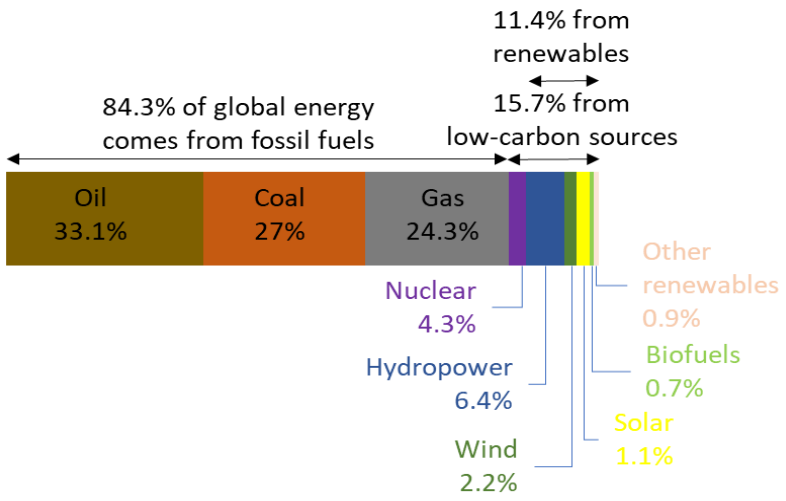
- You get up in the morning, you dress yourself into your nice high-tech clothes, perfectly clean after laundry, and apply some cosmetics to your glowing skin. Then you are ready to go outside to eat the world! But, what world?



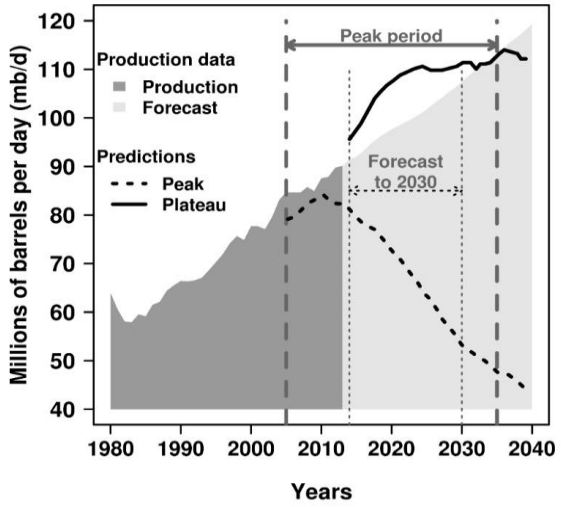
Image by Ainhoa Draws for the for the FuturEnzyme H2020 project

The problem dimension in a fossil-fueled scenario

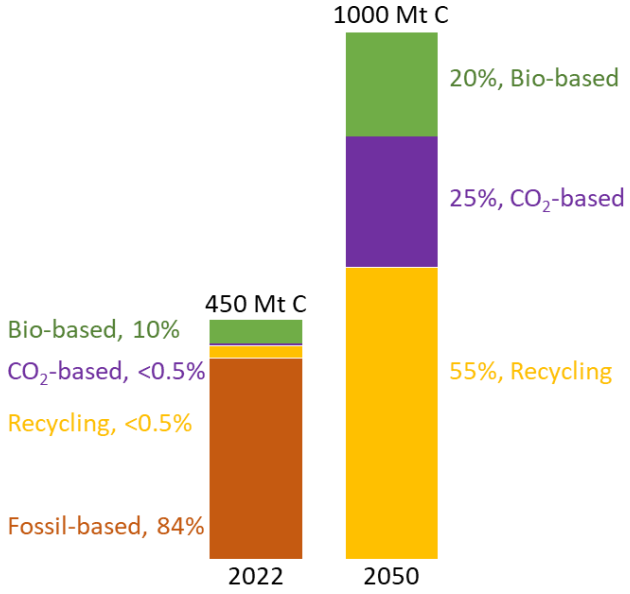
- The chemistry of the planet is changing faster than hundreds of thousands of years ago
  - CHEMICAL LEVEL
    - GREENHOUSE GASES: emission reached averages of 410 ppm for CO_2
    - CONTAMINATION: 400 Mt of hazardous waste and 20 Mt chemicals produced and disposed each year
    - GLOBAL CARBON DEMAND FOR CHEMICALS AND DERIVED MATERIALS: will increase at a CAGR 2.7%
    - GLOBAL WARMING will exceed 2.2°C by 2100



A. Global primary energy consumption by source



B. Oil production projections

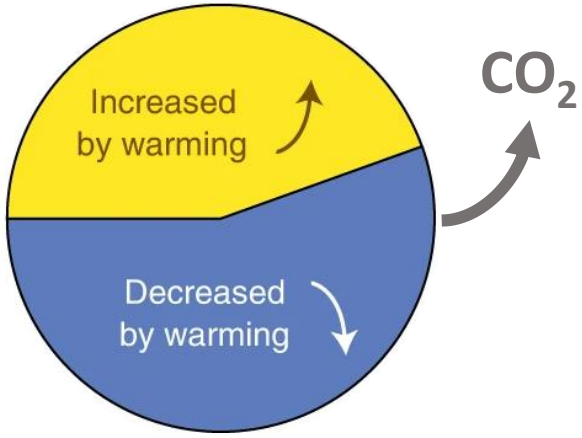


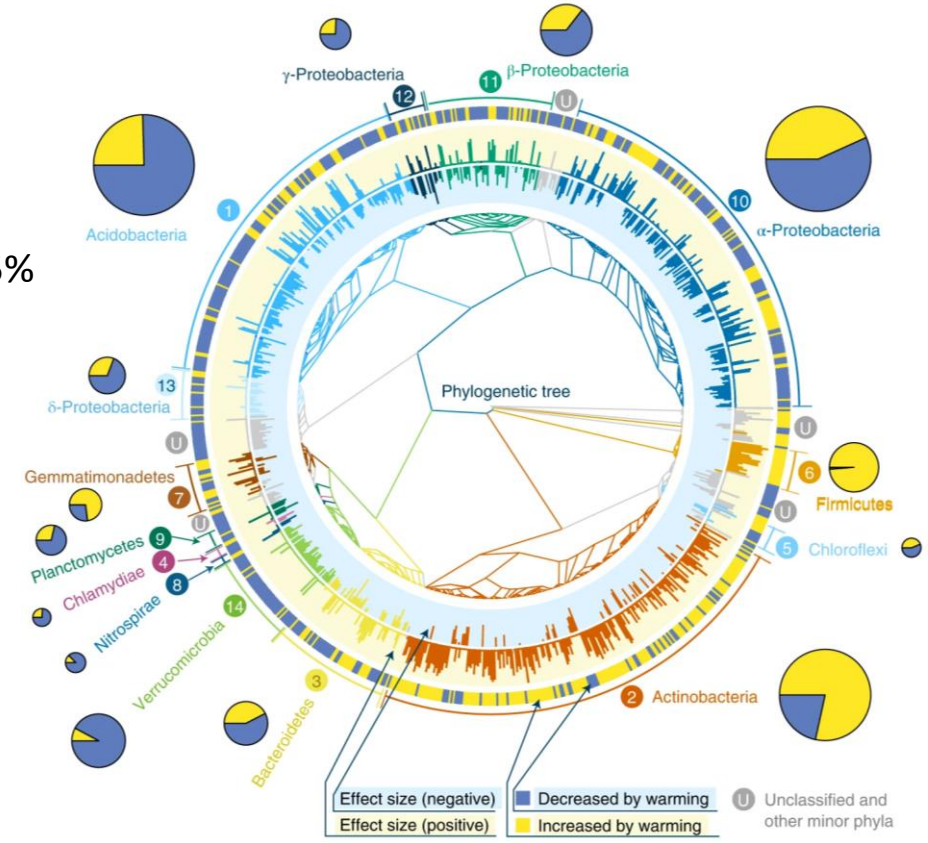
C. Global carbon demand for chemicals

Coscolín, C. et al. (2019). https://doi.org/10.1007/978-3-030-14796-9_13; OurWorldinData.org; https://renewable-carbon.eu; *Compound Annual Growth Rate

The problem dimension in a fossil-fueled scenario

- The biology of the planet is also changing faster than hundreds of thousands of years ago
  - BIOLOGICAL LEVEL
    - ECOSYSTEMS: 85% will be affected
    - PLANT AND ANIMAL DIVERSITY: 16-30% species might go extinct
    - MICROBIAL DIVERSITY: 16% will be lost and new redistribution will occur
      - METABLIC ACTIVITY: Prokaryotic CO_2 production will rise by 0.05-0.15%



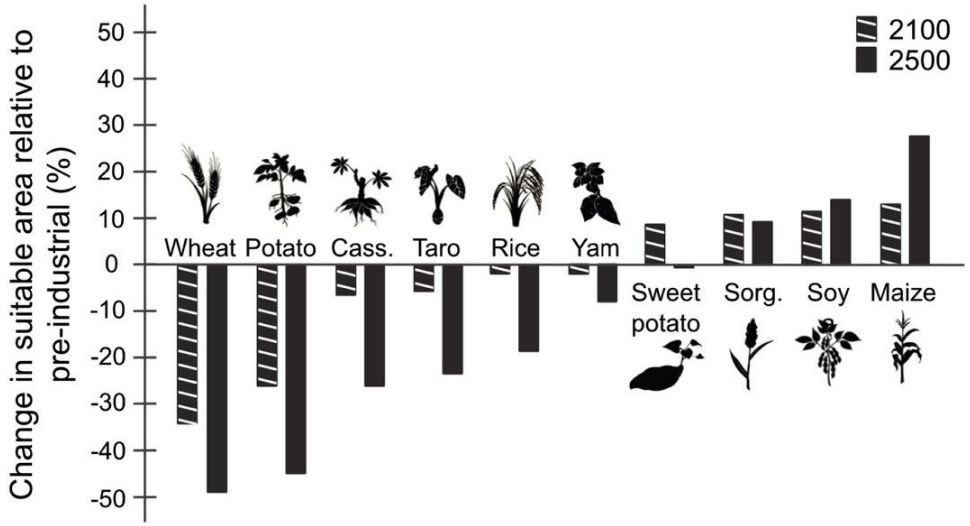


A. Detrimental effects of anthropogenic climate change in microbial biodiversity and functional processes

Nature Reviews Microbiology 17, 569–586 (2019); Global Ecology and Biogeography 30, 987–999 (2021); Nature Microbiology 7, 1054–1062 (2022); Oxford Open Climate Change 1, kgab007 (2021); Global Change Biology 28, 349-361 (2022)

The problem dimension in a fossil-fueled scenario

- The economy and socio-economy is also changing
  - ECONOMIC LEVEL
    - The GLOBAL ECONOMY could lose 2.6-10% of its total economic value by 2100
    - Agriculture will be the sector most affected by heat stress (in 108 countries)
  - SOCIOECONOMIC consequences can be also substantial
    - Conflict risk will increase by 11%
    - Agricultural productivity will decrease −2% to −15%
    - Food price will increase between 1.3% and 56%
    - Food-demand gap will reach 1.26 billion tons



A. Changes in cultivable area for different crops

Let’s talk about solutions

- SOLUTIONS DRIVEN BY GEO-POLITICAL ACTIONS FOLLOWED BY RESEARCH AND APPLICATIONS
  - BIOECONOMY provides “green growth” solutions for European Green Deal ambition and geopolitical challenges
  - The EU’s BIOECONOMY strategy needs regional and local strategies in support of the green transition
  - Support from EU instruments for global/local BIOECONOMY strategies

2015

2016

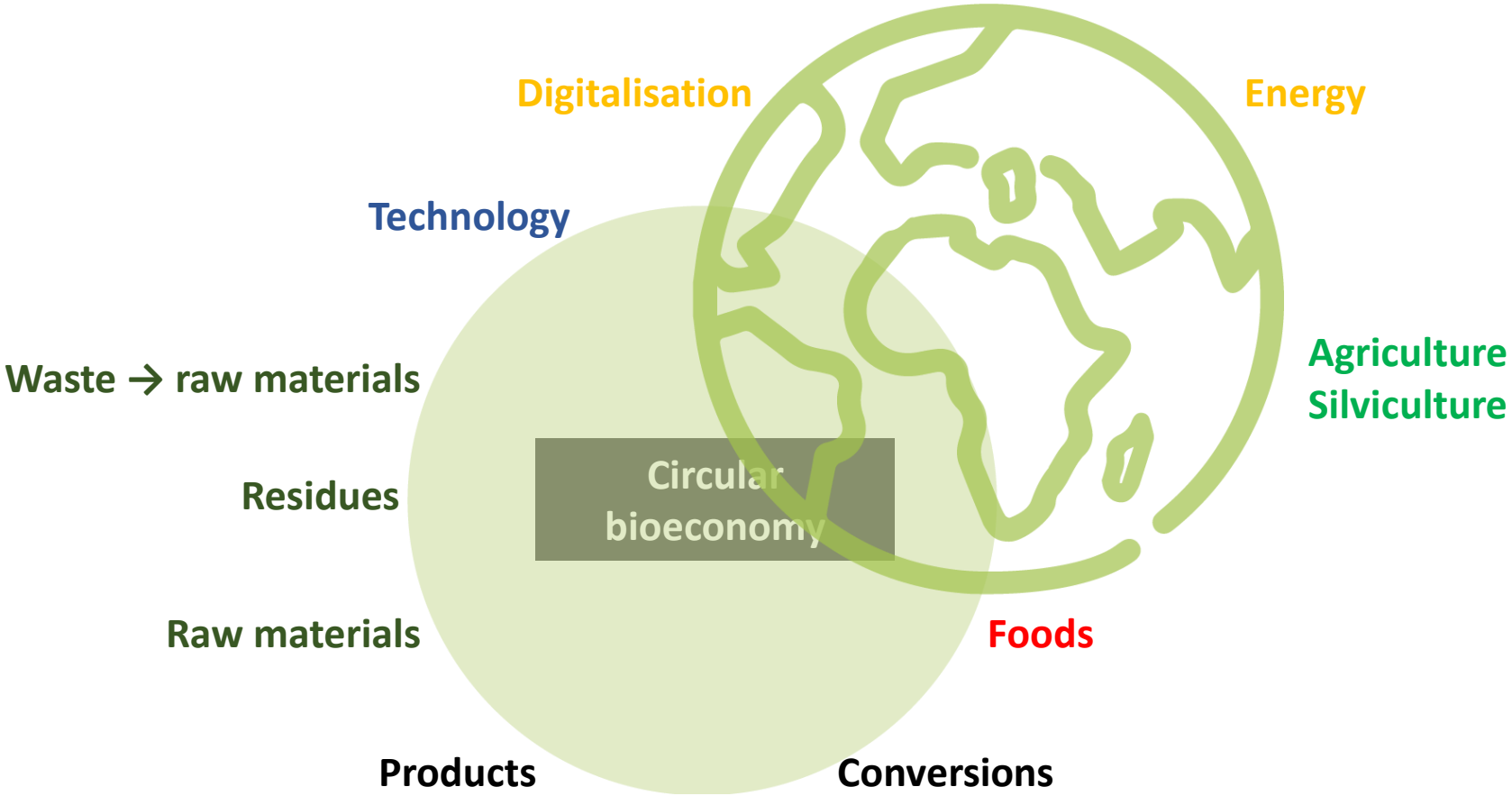
2020

Funded by the European Union

NextGenerationEU

2021

Let’s talk about solutions: CIRCULAR BIOECONOMY

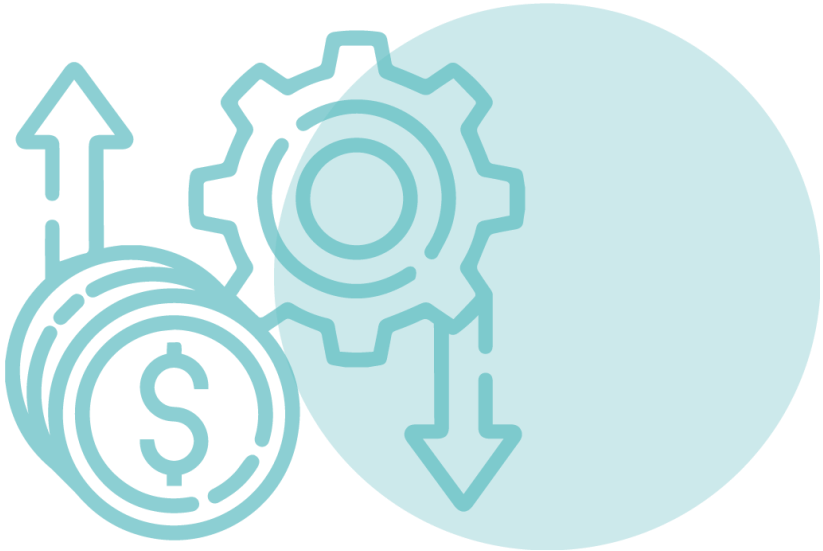


https://research-and-innovation.ec.europa.eu/research-area/environment/bioeconomy/bioeconomy-strategy_en; https://biooekonomie.de/; https://www.journals.elsevier.com/efb-bioeconomy-journal/call-for-papers/biocatalysis-key-to-a-circular-bioeconomy

Let’s talk about solutions

- SOLUTIONS DRIVEN BY ECO-CONSUMERS' DEMANDS
  - 61% consumers are concerned about the state of the environment and, in particular, their carbon emissions
  - 50% of consumers are however willing to pay a higher price for environment-friendly consumer products

A. Consumers are becoming increasingly eco-conscious



B. Consumers are willing to pay for greener alternatives

https://www.fashionrevolution.org/resources/consumer-survey/; Sustainable Production and Consumption 28, 1232-1248 (2021); Oxford Open Climate Change 1, kgab003 82021)

Nature can provide solutions, the ENZYMES

- ENZYMES: Simplified scheme of main molecules of life today

DNA

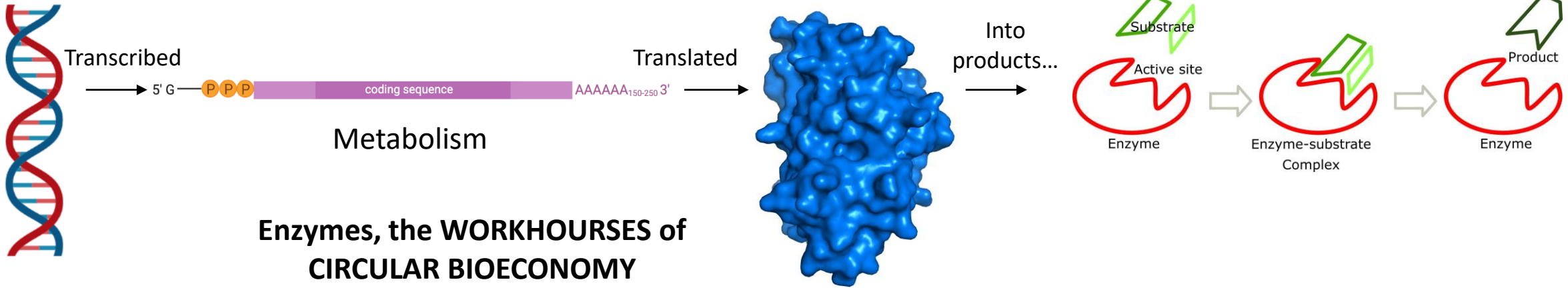
Stores information

RNA

Carries information

Enzyme

Main metabolic machinery



Metabolism

Enzymes, the WORKHOURSES of CIRCULAR BIOECONOMY

New ENZYMES = New PRODUCTS

- ENZYMES: a biological macromolecule with multiple applications in the CIRCULAR BIOECONOMY

Into products…

AUTOMOTIVE SECTOR
17 | 756,000 | €36 billion

Examples of bioeconomy:
Car-body parts reinforced by natural fibres, car-interior lining and seats based on bioplastics, tyres based on dandelion

BUILDING INDUSTRY
317,300 | 1,900,000 | €172 billion

Examples of bioeconomy:
Wooden structures, composite materials reinforced by natural fibres, insulation materials, bio-based screw anchors, bio-based concrete admixtures

CHEMICAL INDUSTRY
2,121 | 434,312 | €186 billion

Examples of bioeconomy:
Bioplastics, bio-based platform chemicals.

ENERGY
923 | 220,157 | €466 billion

Examples of bioeconomy:
Pellet stoves, biogas, biodiesel fuel, bioethanol, synthetic fuels, algae, kerosene, enzymes for better oil extraction

AGRICULTURE AND FORESTRY
285,000 | 1,000,000 | €32 billion

Examples of bioeconomy:
Precision agriculture, plant and animal breeding, short-rotation forestry, aquaculture

MECHANICAL ENGINEERING
6,227 | 978,000 | €207 billion

Examples of bioeconomy:
Bioreactors, bioprocess engineering, agricultural technology and equipment, greenhouse technology, biolubricants

PHARMACEUTICAL INDUSTRY
923 | 135,773 | €36 billion

Examples of bioeconomy:
Biopharmaceuticals, medicinal plants and herbs.

FOOD & BEVERAGE INDUSTRY
6,000 | 555,000 | €41,4 billion

Examples of bioeconomy:
Enzymes, fragrances, amino acids, natural food additives, probiotics, food from lupin protein

CONSUMER GOODS
- | - | €203 billion

Examples of bioeconomy:
Bio-based tensides, bio-active constituents in cosmetics, enzyme-based additives for cleaning agent

TEXTILES AND CLOTHING
1,300 | 111,313 | €11.33 billion

Examples of bioeconomy:
Natural raw materials for synthetic fibres, high-tech fibres made of spider web, plant tannins

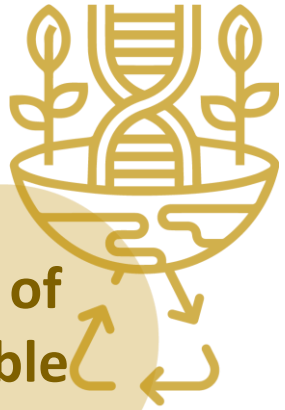
Number of companies
Number of employees
Total sales in billion euros

New ENZYMES = New PRODUCTS

Lower energy Footprint
(100 M barrels of oil)

Reduced waste production and chemicals' consumption
(up to 990 kg CO_2/kg product)

Safer process conditions

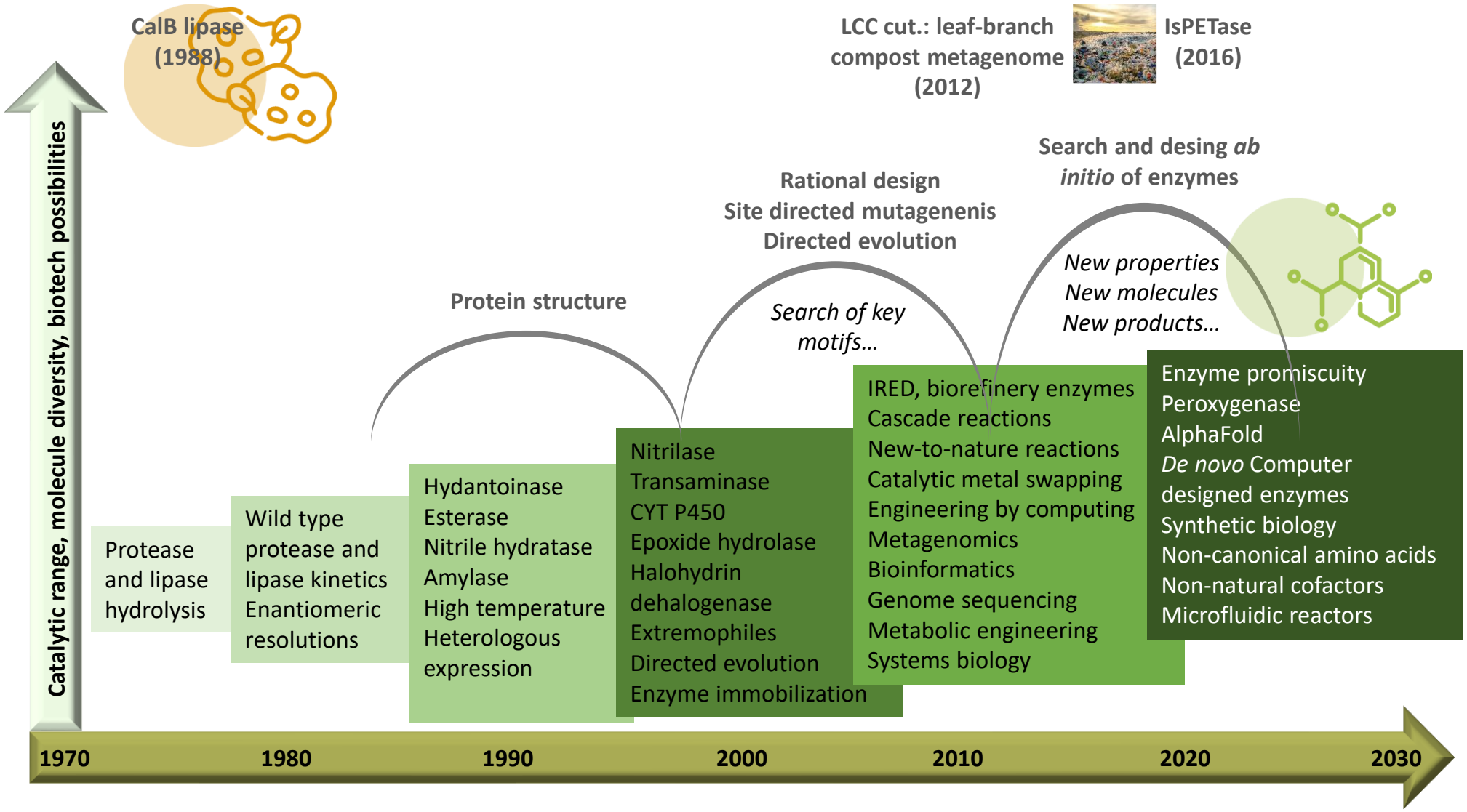


The use of renewable feedstocks
(biomass)

Contribute 0.04% ($14,508 million) of world trade
Reduce economic losses, derived from global warming, by 0.5%

Contribute job creation: 3.8 million job-years of employment

Interconnection between technologies, enzymes and products



Chemical Reviews 118, 801−838 (2018)

Developments in lines of research and funding

KBBE: Knowledge-Based Bio-Economy

Bio-refinery

indox industrial oxidoreductases

mamba

Mine for and use of new microbial activities (enzymes)

MaCuMBA

Marine Microorganisms: Cultivation Methods for Improving the microbial biotechnology

micro3

Marine Microbial Biodiversity, Bioinformatics, Biotechnology

KILL SPILL

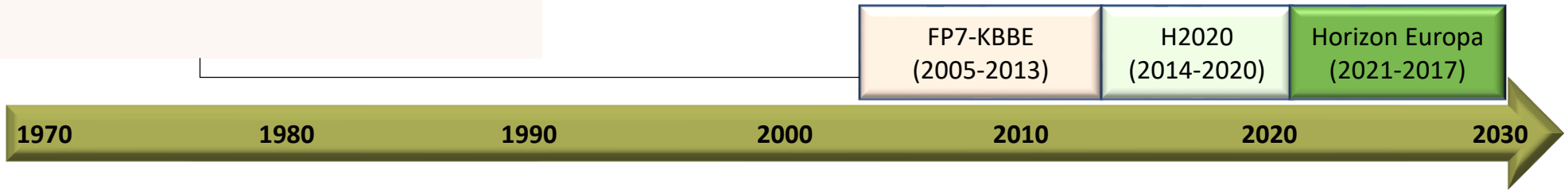
Develop efficient, economically and environmentally viable bioremediation solutions

MICROBE KNOWLEDGE

- C. 30 M microbial species
- 420000 described species (1.4% total)
- 30000 formally described species (1000 per annum)

ENZYME KNOWLEDGE

- C. 200 million proteins exist
- 287000 enzymes identified (0.1% total; or 2300 per annum)
- 170000 protein structures solved
- <500 enzymes used commercially



https://cordis.europa.eu/projects/es; https://www.bbi.europa.eu/projects/

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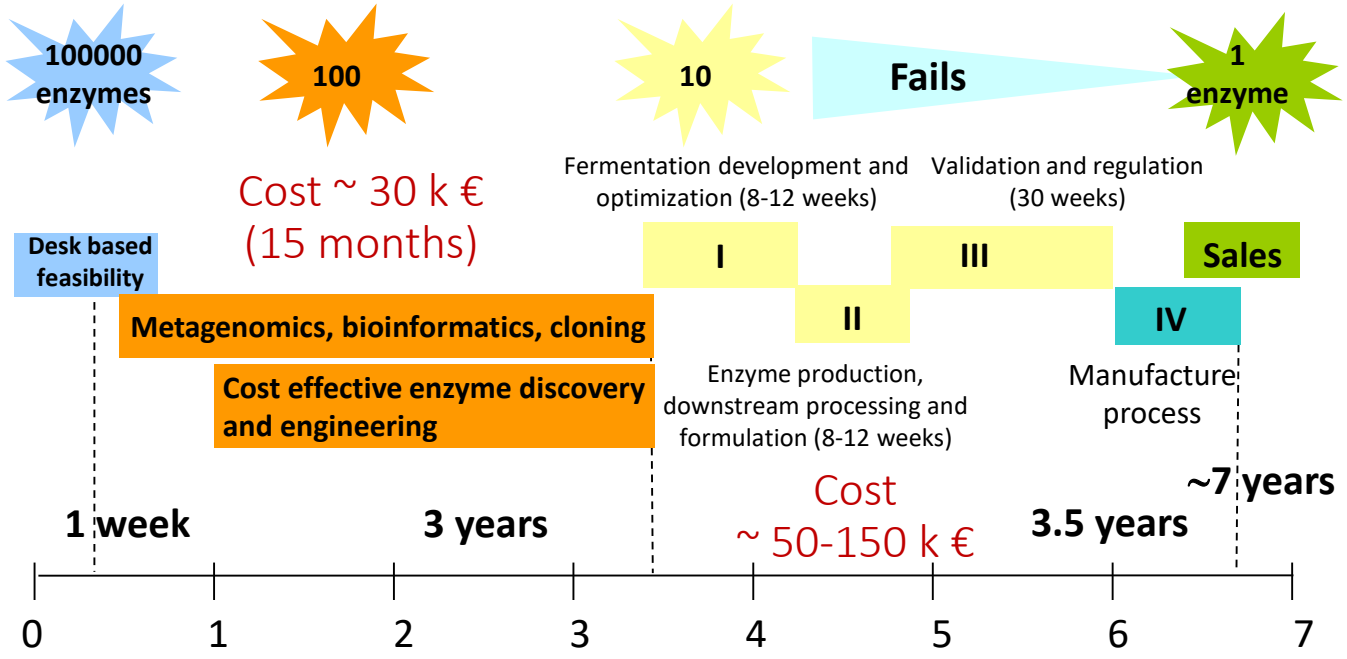

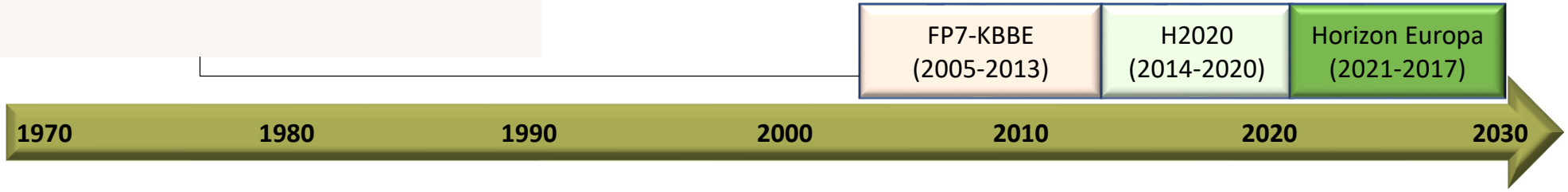

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H2020: Innovation, delivering economic solutions (processes and products) to end users

INMARE

Overcome technological bottlenecks to better explore biodiversity for enzymes potentially transferable to the market

WOODZYMES WOOD TRANSFORMING ENZYMES

SUSBIND

Enzymes = wood based building blocks and wood panels

SMARTBOX

Enz x2 Enzymatic oxidation/oxyfunctionalization

Enzymes = oxy-functionalization for bio-based products

PERCAL

Enzymes = chemical building blocks

Enzymes for more environment-friendly consumer products (detergents, cosmetics, textiles, nutraceuticals)

Horizon Europe: Actions encompassing climate-neutrality, circularity and zero pollution

- Broadening the spectrum of robust extremophiles, enzymes, drugs, metabolites and chemicals and microbial hosts in industrial biotechnology
- Optimization
- Testing and demonstrations

FP7-KBBE (2005-2013) | H2020 (2014-2020) | Horizon Europe (2021-2017)

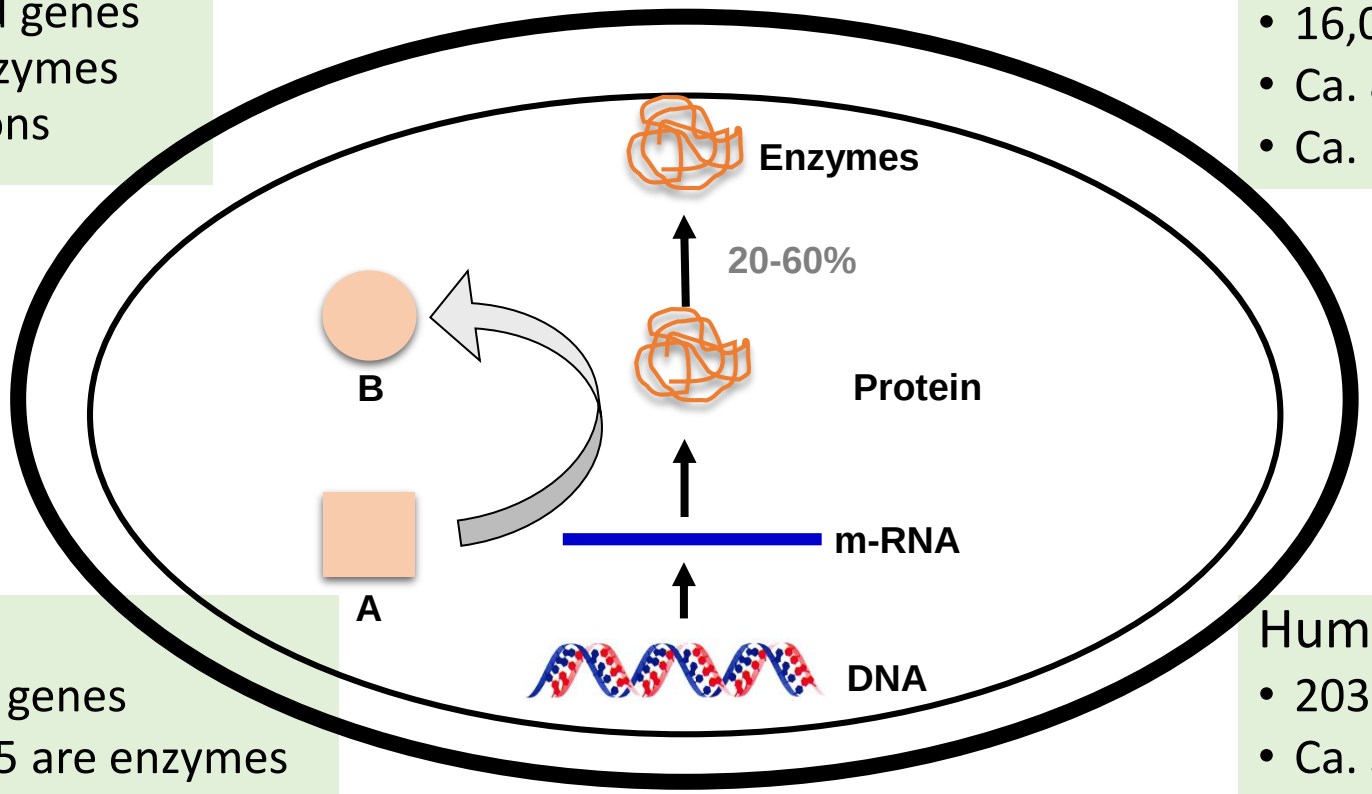
1970 1980 1990 2000 2010 2020 2030

https://cordis.europa.eu/projects/es; https://www.bbi.europa.eu/projects/

Looking for a needle (ENZYME) in a haystack (ENVIRONMENT)

Bacterium
- 4391 predicted genes
- Ca. 607 are enzymes
- Ca. 700 reactions

Fungus
- 16,000 genes
- Ca. 800 are enzymes
- Ca. 1069 reactions



Plant
- 22000-125000 genes
- Ca. 3235-15295 are enzymes
- Ca. 2597 to 3635 reactions

Human
- 20365 proteins
- Ca. 3428 are enzymes
- Ca. 4000 reactions

SwissProt (release 01_2022); PLOS Computational Biology 2, 786–793 (2006); FEMS Microbiology Letters 366, fny285 (2019)

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1 gram:
- 10^3-10^5 microbial species
- 1 billion bacteria
- 1000 billion enzymes

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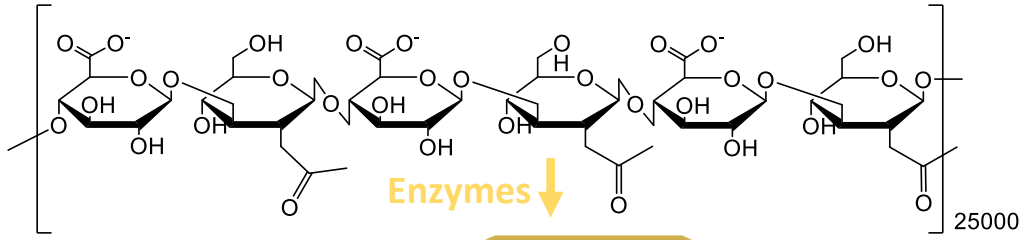
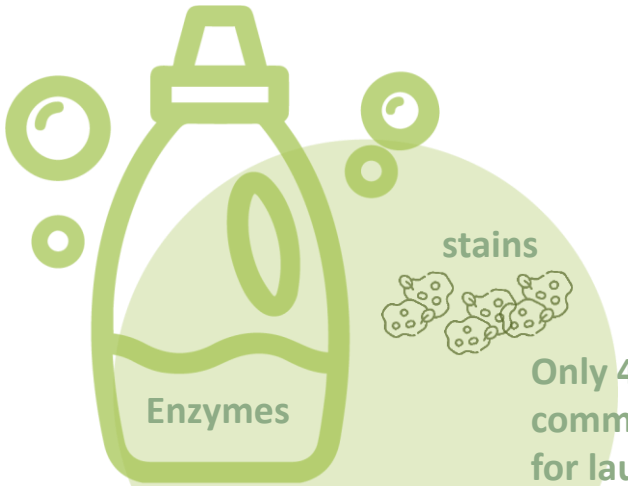
Enzymes: Where to find them

- SOURCES
  - Culture collections
  - Public databases
  - Environment: new microbes, new enzymes
  - Design enzymes from scratch

Enzymes envisioning consumer products of 2030

- By 2030 this consumption will grow at an annual rate of 4.8-6.3%
  - Manufacturer partners are continuously working to bring more efficient, greener daily used products to consumers



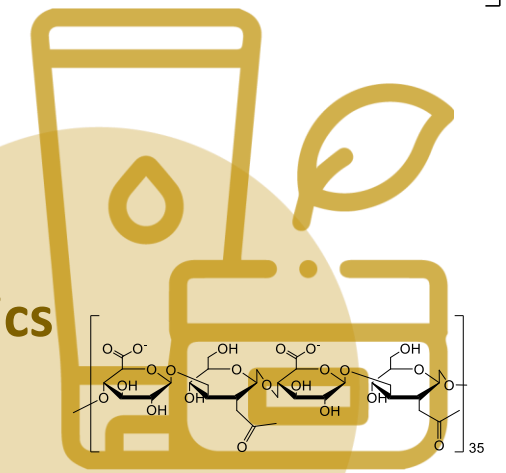


16-20 kg of detergent

Only 4-7 types commercially available for laundry detergent

Only 1-2 types commercially available

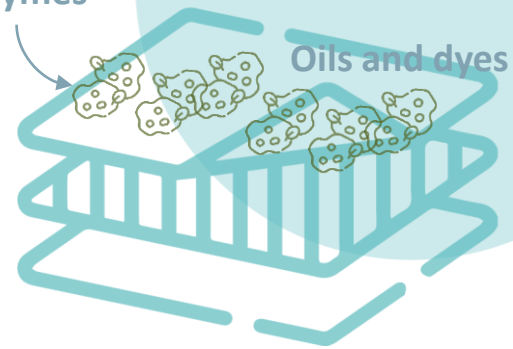
1 kg of cosmetics



Only 1-2 types commercially available

30 kg of textiles

Enzymes



Each enzyme should work under different conditions, and is subjected to different economic constraints

Enzymes envisioning consumer products of 2030

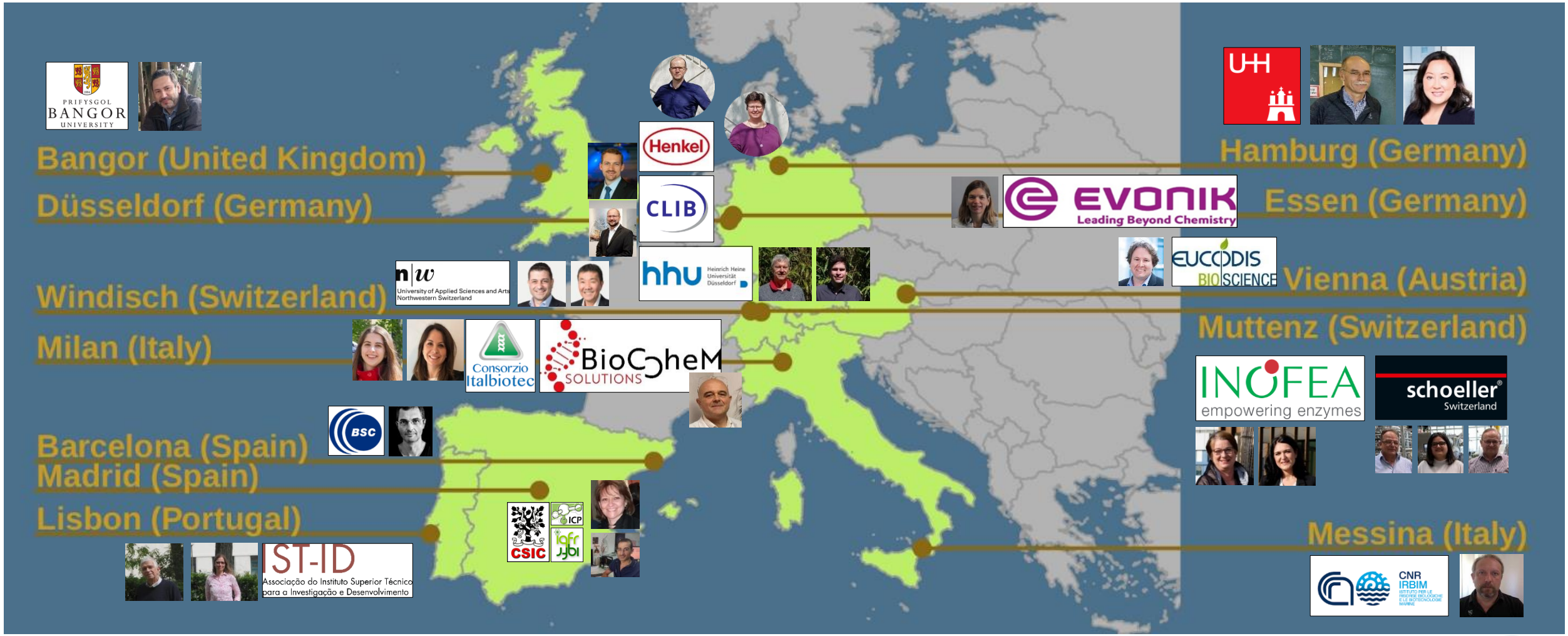
- Economic factors determines the incorporation of enzymes to consumer products

	Pharmaceutical sector	Specialty chemicals	Bulk chemicals
Product costs	> 100€ per kg	5€ per kg	<5€ per kg
Productivity (kg product/kg enzyme)	100-250 kg/kg	1000 - 4000 kg/kg	5000-20000 kg/kg
Enzyme cost	10 k€ per kg	100 k€ per kg	0.1-10 € per kg

400-3000 € per kg

The FuturEnzyme Consortium

Large industries/manufacturers (3), SMEs (3), Clusters (2), academia (7) (countries, 7)



Enzymes: how to find – what partners can offer?

Sequence

Artificial intelligence (predictive tool)

Smart enzyme with industrial specifications

Consumer and Market Feedback
Life Cycle Assessment

www.futurenzyme.eu

Genetic resources → **Selection of "smart" enzymes** → **Enzyme improvement** → **Production strains** → **Manufacturing process (yield, safety)** → **Preindustrial validations**

Set-up sophisticated screens:
- Functional
- Bioinformatics filters
- Machine learning filters

HTP (heterologous, cell-free, green chemistry-based-) production methods

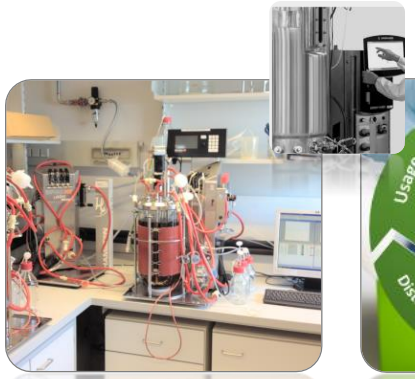
HTP analytics (real-substrates)

Manufacturers' requests and specifications

Disruptive engineering:
- Machine learning
- Supramolecular

Selection

Decision



Sustainable production

Optimal formulation

Yield and performance
Life Cycle Assessments
Policy, consumers…

Yield
Yield
Yield

Conclusions

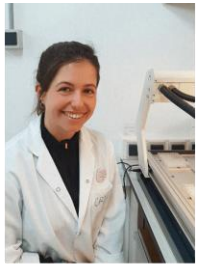
- Improved products or new products NEED cost and performance efficient enzymes
  - It is important to develop enzymes for specific markets and sectors
  - Also, to identify specific sectors in which developments would be beneficial
- Crucial to understand the biggest hurdles to bring enzymes into industrial processes
  - How could these hurdles be overcome in the future? Artificial intelligence and machine learning seem crucial
- Holistic experimentation and digitalization to develop new enzymes and products
  - Combine screens based on experimental evidences and machine learning prediction
  - Disruptive enzyme engineering approaches at genetic and supramolecular level approaches
  - Beyond state-of-the-art multiple expression technologies
  - Bioprocessing of products
  - Life cycle assessment of the products
  - Safety, risk and environmental impacts assessment of enzyme supply

Conclusions

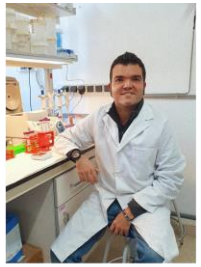
- What framework conditions are required (on EU, national or regional level) to increase the contribution of biotechnology or enzyme applications to transforming a linear fossil-based into a circular bio-economy*
  - Imagine a global problem, e.g. related to energy, pollution, water, …
  - Imagine a region issue where, for example, alternatives to coal mining have to be found.
  - Similarly, imagine a product of global importance (detergent, cosmetic, textile)
  - Also, imagine a product of local importance, biomass-related or fish-related, etc.
- If you had one 100 million euro to invest in future technology relevant to CIRCULAR BIOECONOMY, what would you look for?*

*Questions raised by Markus Müller (CLIB) during the CLIB forum event "Catalysing Alliances for Greener Products“ (https://www.clib-cluster.de/)

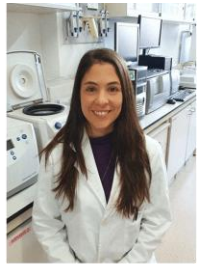
Acknowledgements

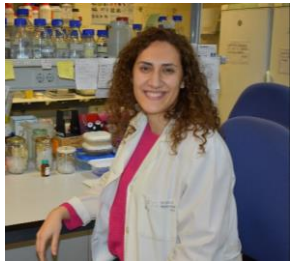

Dr. Cristina Coscolín


Laura Fernández López


David Almendral


Paula Vidal


Dr. Patricia Molina Espeja


Dr. Isabel Cea Rama


Dr. Julia Sanz Aparicio

Systems Biotechnology Group

Crystallography and Structural Biology

Plan de Recuperación, Transformación y Resiliencia

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HORIZON 2020

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