MACBETH
Membranes And Catalysts Beyond Economic and Technological Hurdles

Winterschool

-

Membrane reactors for BOC

30.01.2024

The project has received funding from the European Union's Horizon 2020 research and innovation program under Grant Agreement N°869896.

MACBETH

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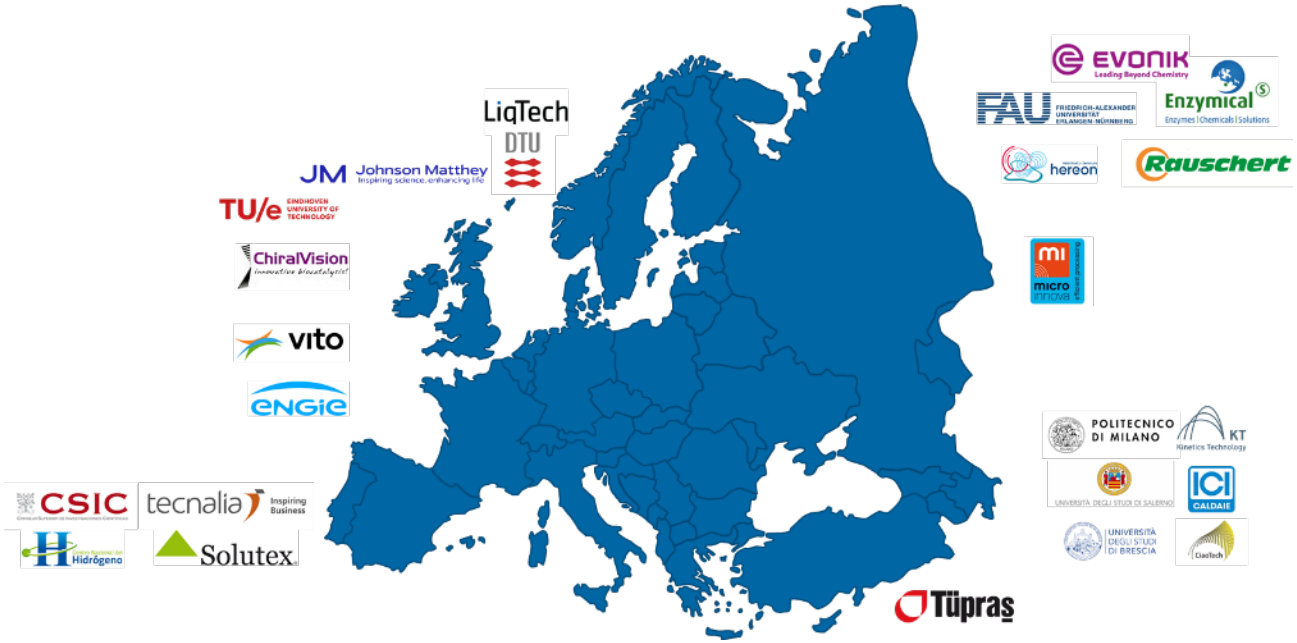

PROJECT BUDGET: 20,7 M€

PROJECT DURATION: 11/2019 – 10/2024

CONSORTIUM: 24 partners

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MACBETH

H2 – Hydrogen Production

Conversion of from biogas or natural gas

For production of pure hydrogen

HYFO – Hydroformylation

Conversion of olefins and syngas to aldehydes

To produce specialty chemicals.

PDH – Propane Dehydrogenation

Conversion of propane to propylene

For the production of petrochemicals

BOC – Bio Catalytical Oil Cleavage

Conversion of edible oils to fatty acids or their alkyl ester derivatives

For the food industry and biofuels

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BOC Case – Who we are …

- Case Leader
- Process Development

- Enzyme Immobilization

- Membrane Separation

- Engineering

- Modelling

- Consulting
- Possible End-User

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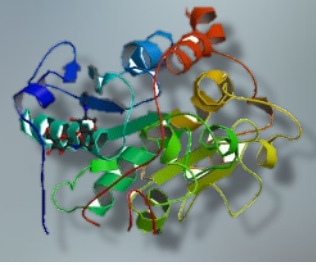
ChiralVision introduction:



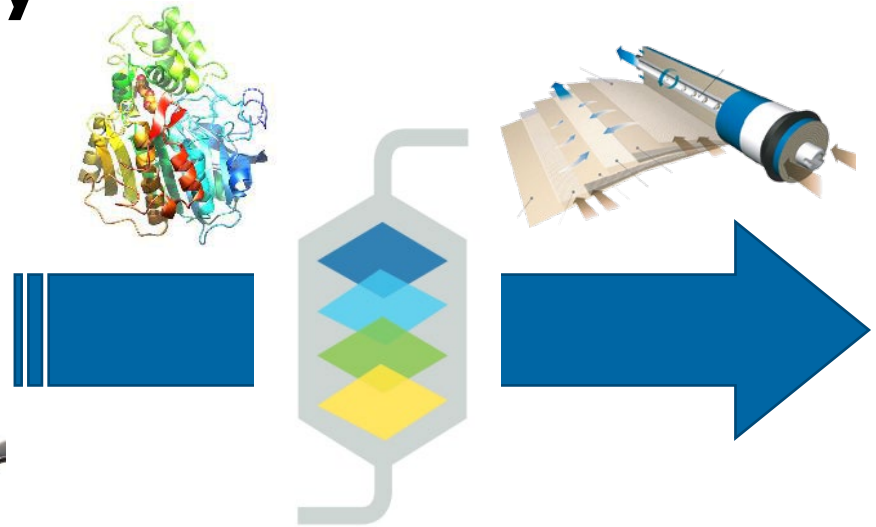
- Dedicated to the application of biocatalysis
- Founded in 2006
- Headquarters in Den Hoorn, The Netherlands

Business model / Market:

- Technology platform: Immobeads™ & Immozymes™
- Immobeads: special porous polymeric beads
- Immozymes: enzymes immobilized on Immobeads
- Enzymatic Process Development
- Chiral compounds with high purity (>99% ee)

BOC Case

Bio Technology



- **Fish Oil**
- **Biocatalysis**
- **Membrane Separation**
- **Omega 3 Concentrate**

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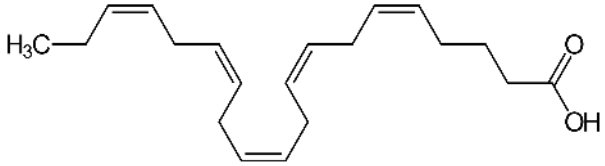
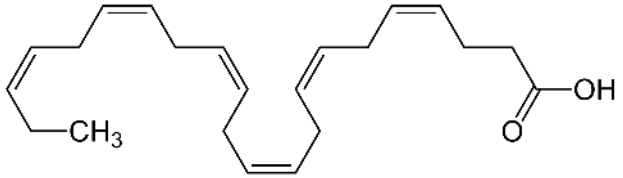
BOC Case - **B**iocatalytical **O**il **C**leavage

- Enzymatic Enrichment of Omega-3-Fatty Acids

  EPA and **DHA** in Fish Oil



eicosapentaenoic acid (**EPA**)



docosahexaenoic acid (**DHA**)

✓ Health benefits:

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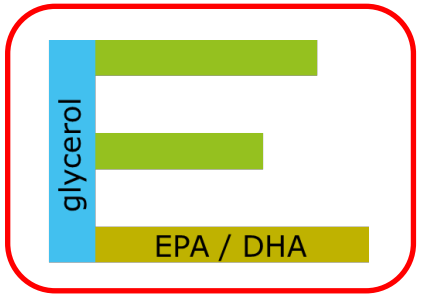
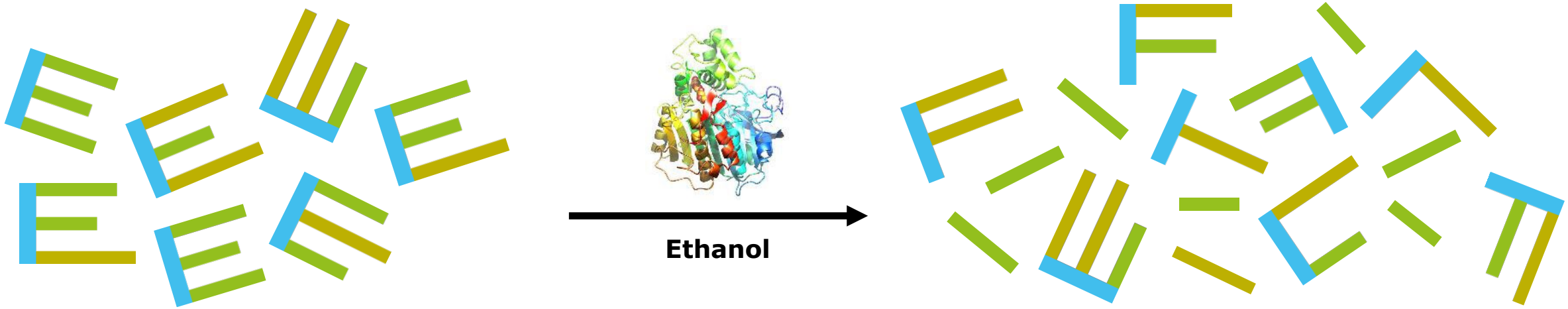
Enzymatic Reaction



- Selective Cleavage of "Short and Medium" Chained Fatty Acids



Triglycerides

Monoglycerides, Diglycerides, Fatty Acid Ethyl Ester

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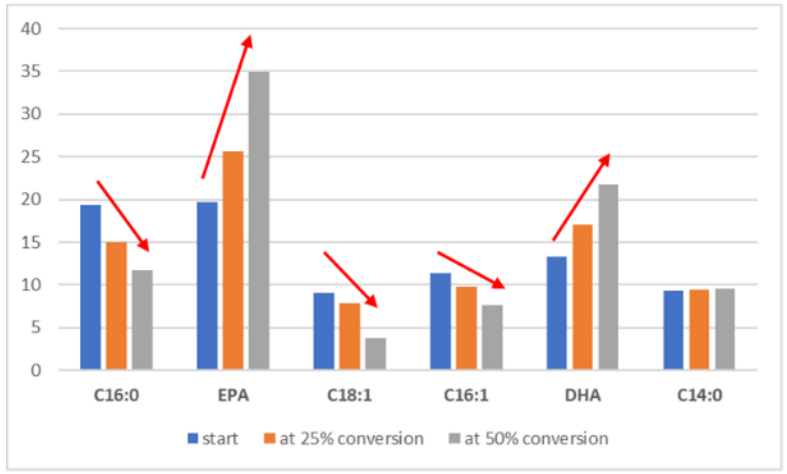
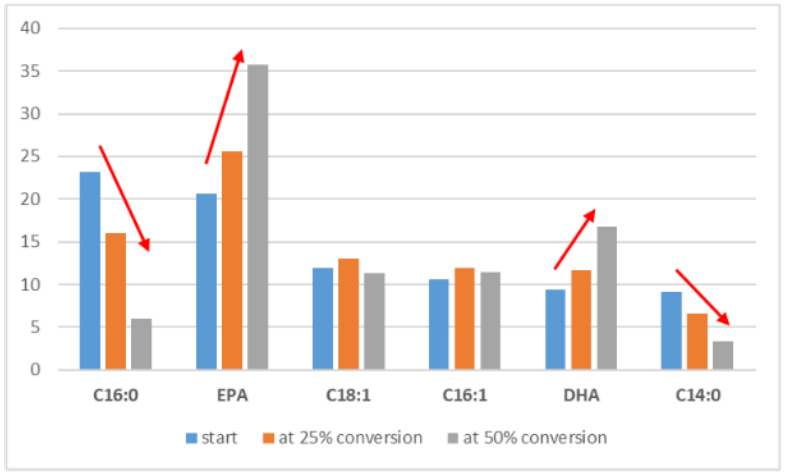
Enzyme Selection

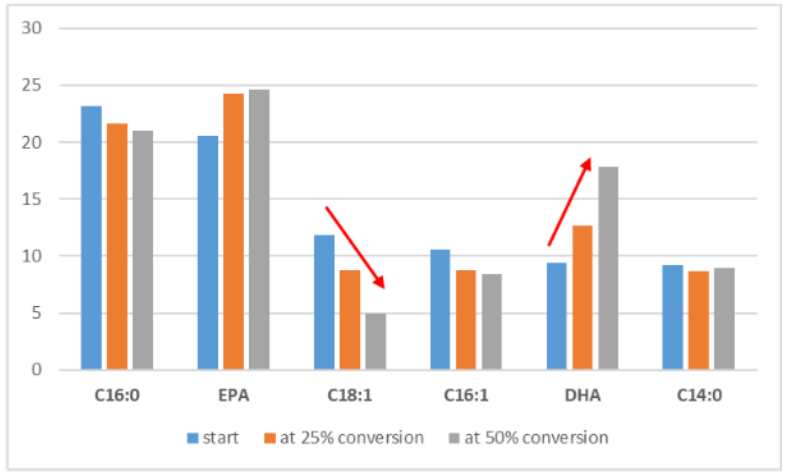
Lipase A



Lipase B



Lipase C



- ✓ **Various enzymes were screened**
- ✓ **Selectivity towards specific fatty acids is different for each enzyme**

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Enzyme immobilization technology

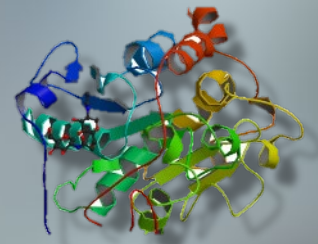
Enzyme application requires various process conditions:

- batch use
- continueous use
- aqueous / biphasic / organic media
- solvent change
- temperature changes
- filtration
- recycling up to 1000 cycles

Immobilization conditions can be stressfull:

- covalent, adsorbed and ionic interaction with carrier surface
- narrow pores
- drying, rewetting
- high or low enzyme loading

A historic overview



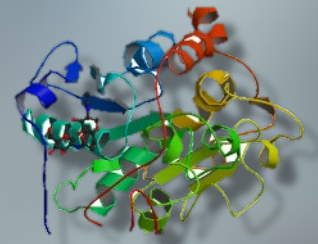
The early days: 1916-1940s
- Isolation of proteins by immunologist
- Glass, alumina, charcoal

The underdeveloped phase (1950s)
- amylase, deaminase, chymotrypsin, Dnase, lipase, catalase, ribonuclease
- bentonite, cellulose, Amberlite XE-97, Dowex-2, Dowex-50, polyaminostyrene, sol-gel

The developing phase (1960s)
- Whole cells, invertase, trypsin, urease, subtilisin, chemotrypsin, LDH, amino acylase, peroxidase, amylase, pen G acylase, galactosidase
- CLEC, PVA, polyacrylamide, x-linked dextran, agarose, Diaion

The developed phase (1970s)
- Industrial scale α-amylase, (pen G) acylase, invertase
- reversible covalent, affinity, spacers, dozens other techniques

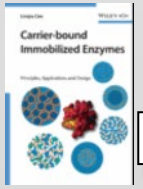
A historic overview



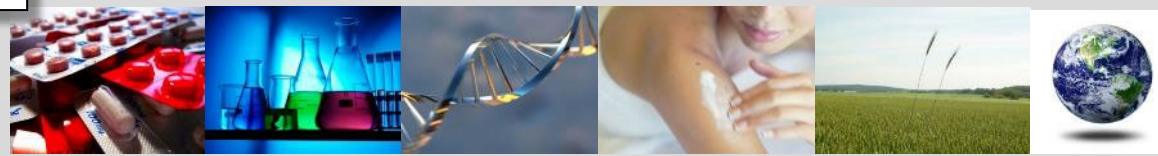
The post developed phase (1980s)
- manufacturing of pharma and agrochemicals (mild conditions, low energy, short routes). Klibanov: enzymes in organic solvents. Site specific immobilization
- Eupergit C

Rational design of immobilized enzymes (1990s)
- CLEC, CLEA, carrier free
- robust improved enzymes that are highly active and stable under process conditions

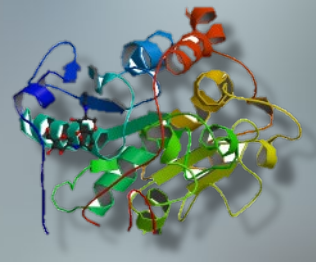
A new era (2000s to date)
- directed evolution of enzymes provide maximized performance. Multi enzyme immobilization
- Highly porous carriers, renewable, bio based, biodegradable



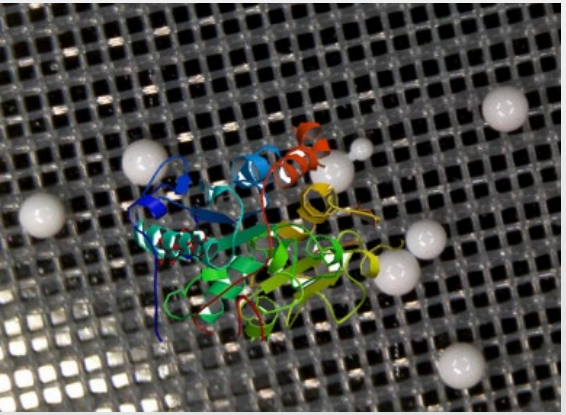
Dr. Linqiu Cao, Carrier-bound Immobilized Enzymes: Principles, Application and Design

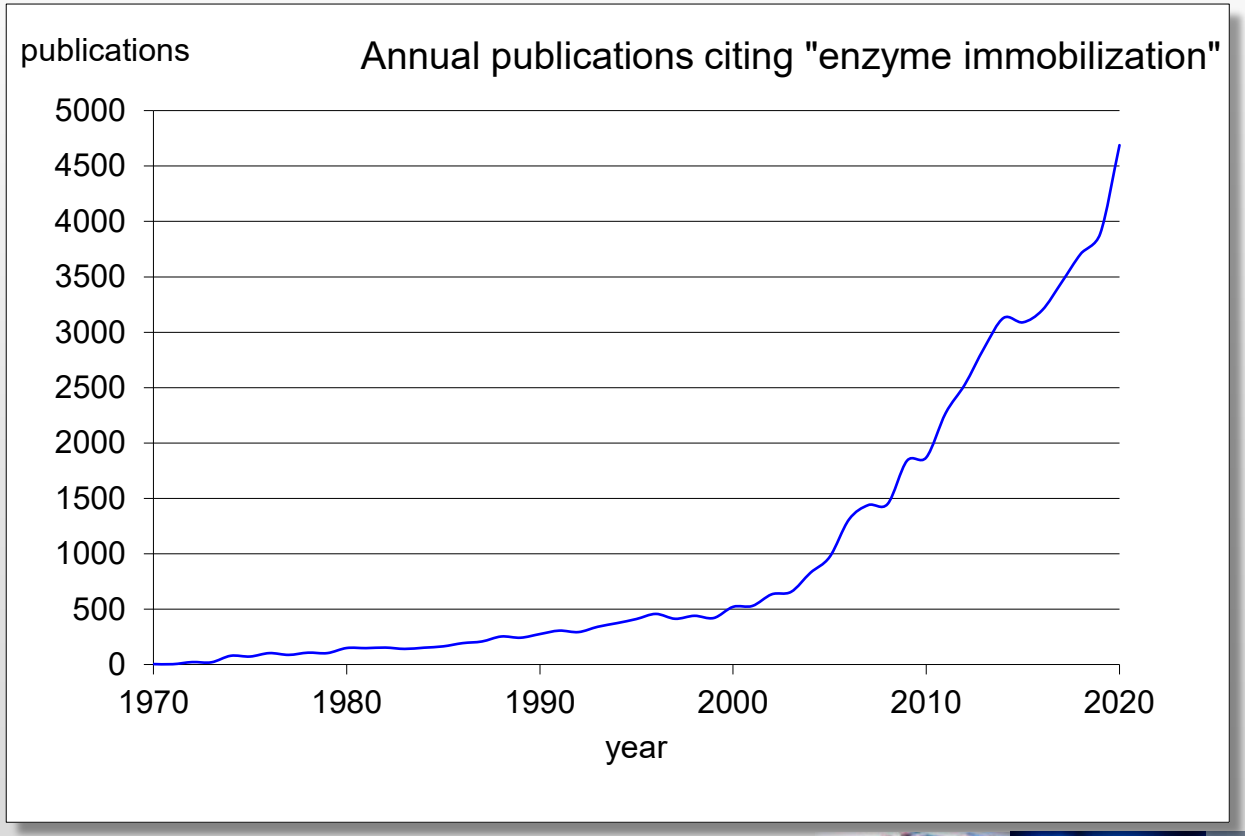


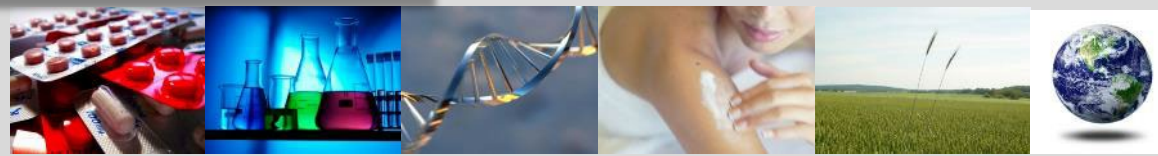
Immobilized enzyme R&D over the years



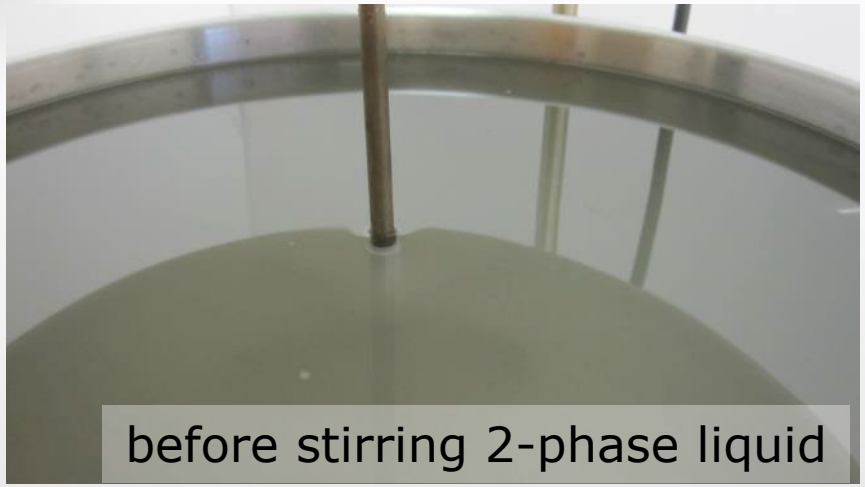
- The market interest in immobilized enzymes is growing
- Biotechnology gave a firm boost to applicability







Polyacrylic resin production


before stirring 2-phase liquid

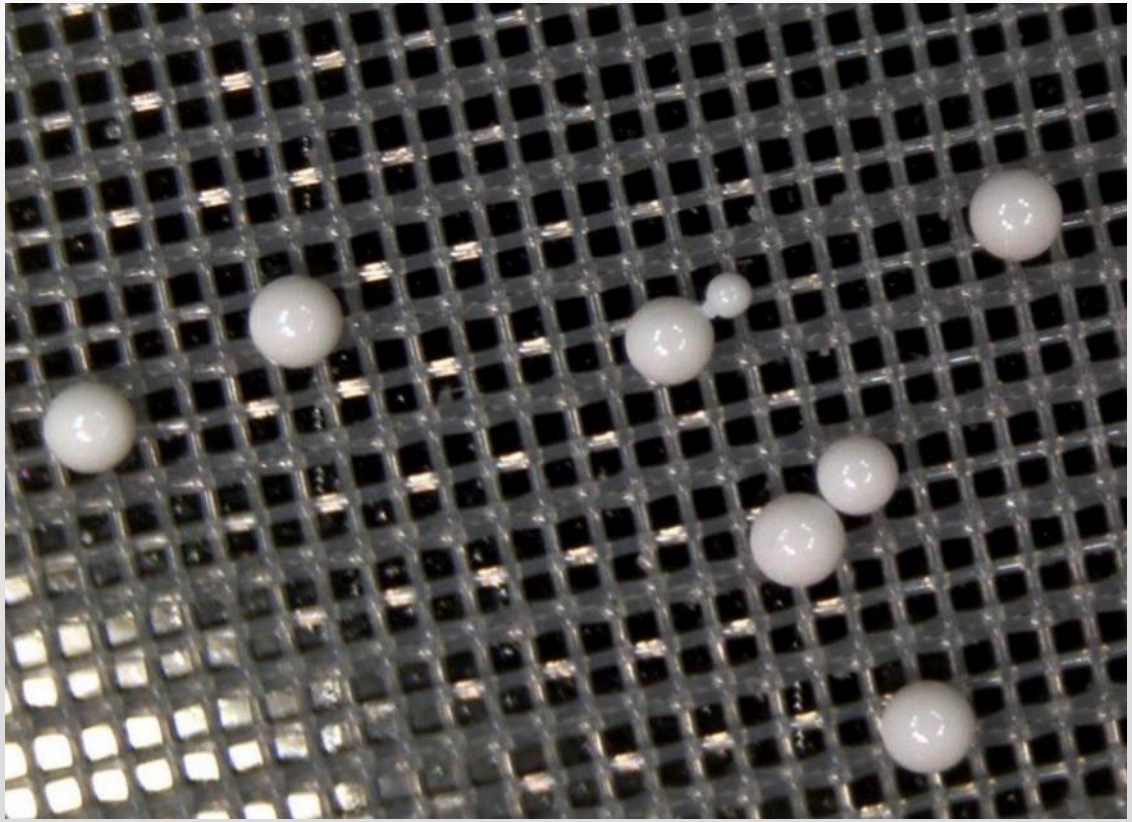

stirring produces droplets

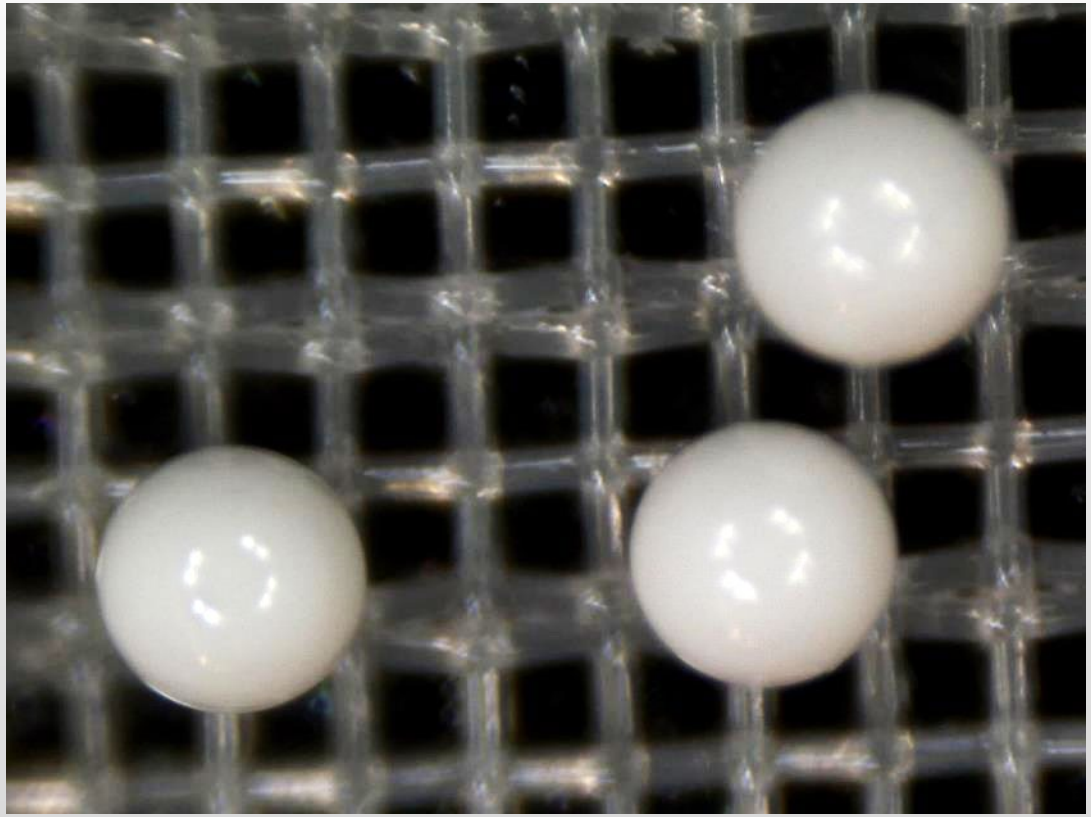

droplets polymerizes into beads


beads filtered and collected

Immobeads: magnification 100x

IB-COV-1 on a 100 µm sieve

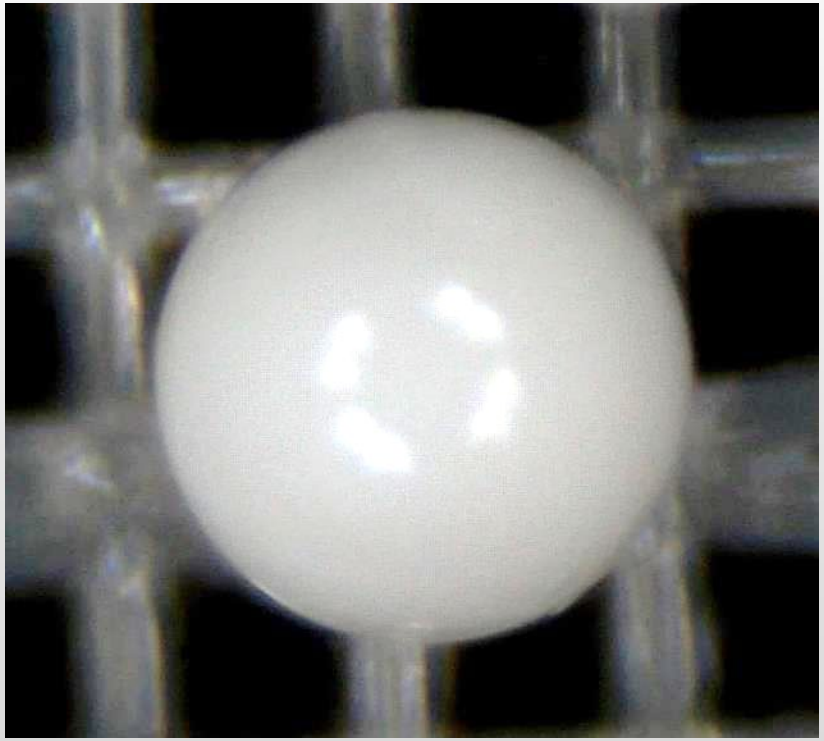




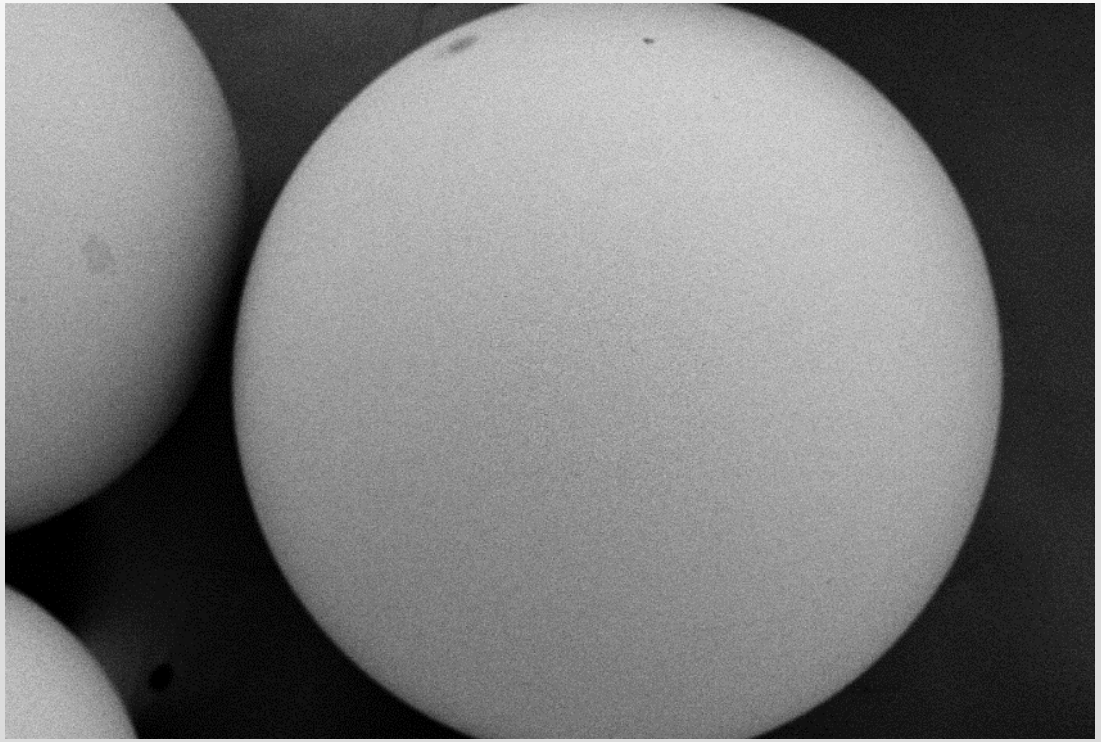
Magnification 1000x

Switching to electron microscopy

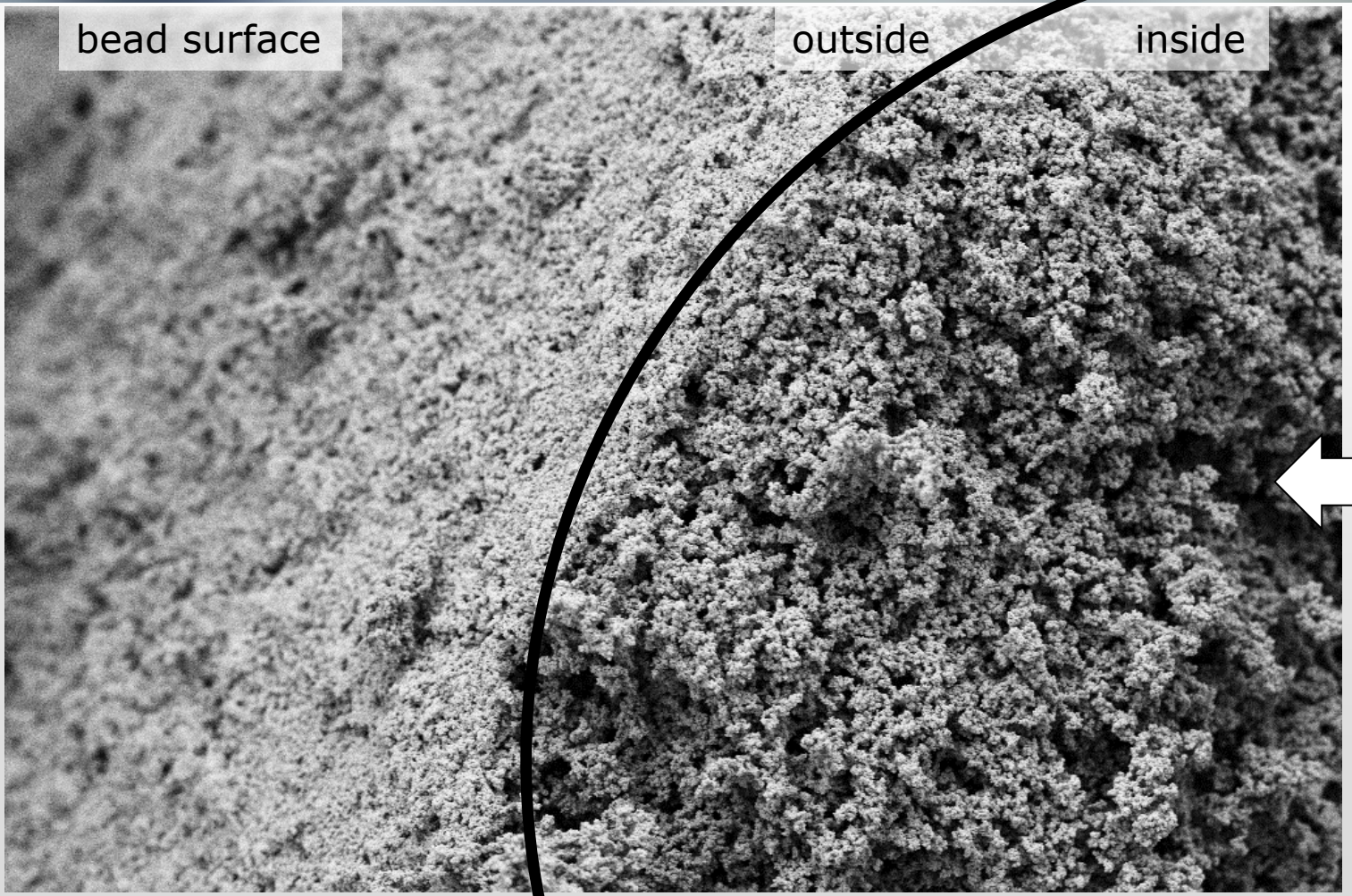
light microscopy



scanning electron microscopy (SEM)



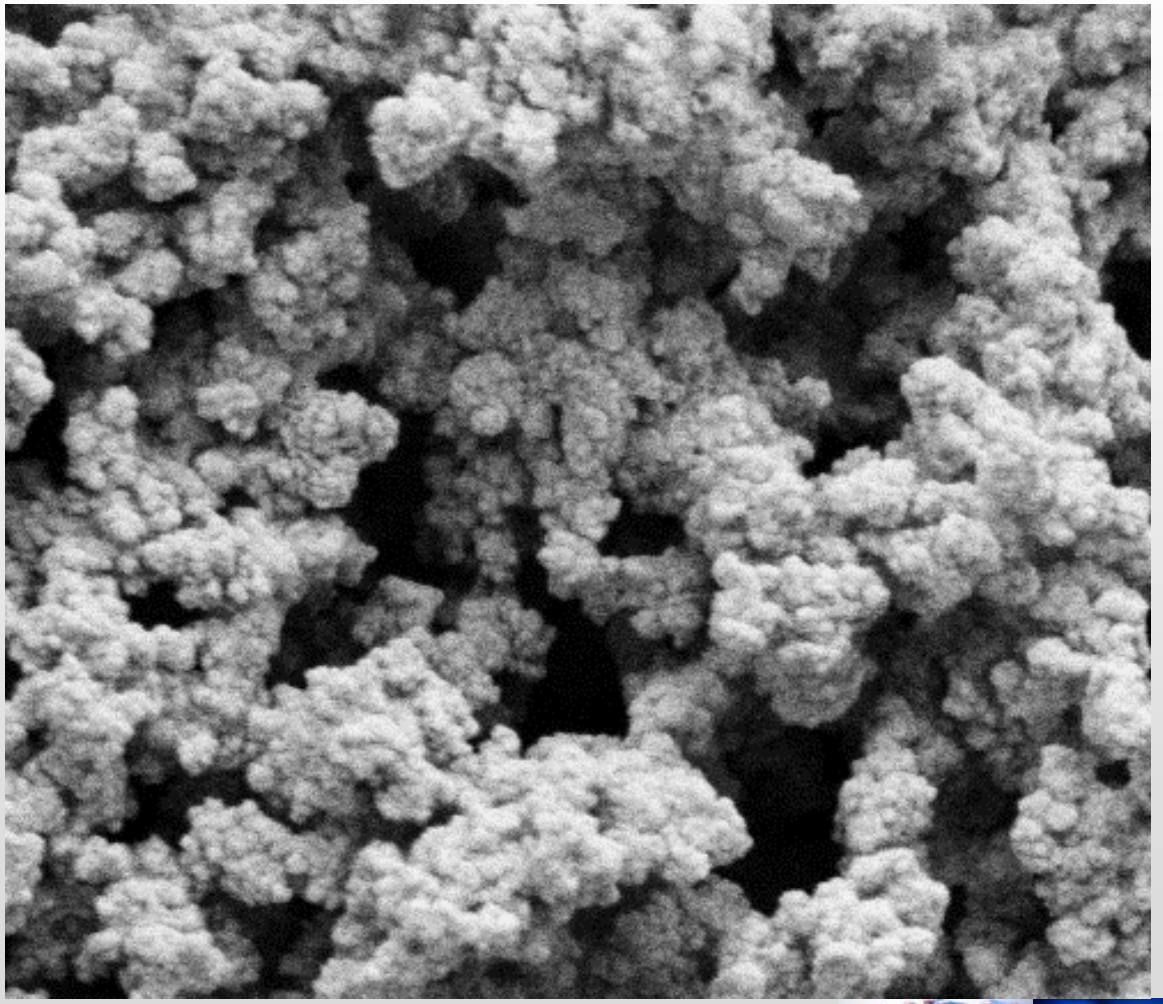
Magnification 10.000x, cross-section



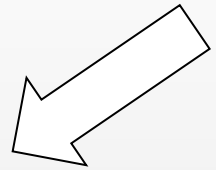
internal pore structure becomes visible

Magnification 100.000x

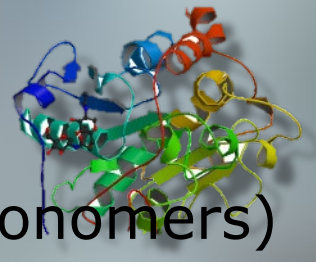
Pores are visible



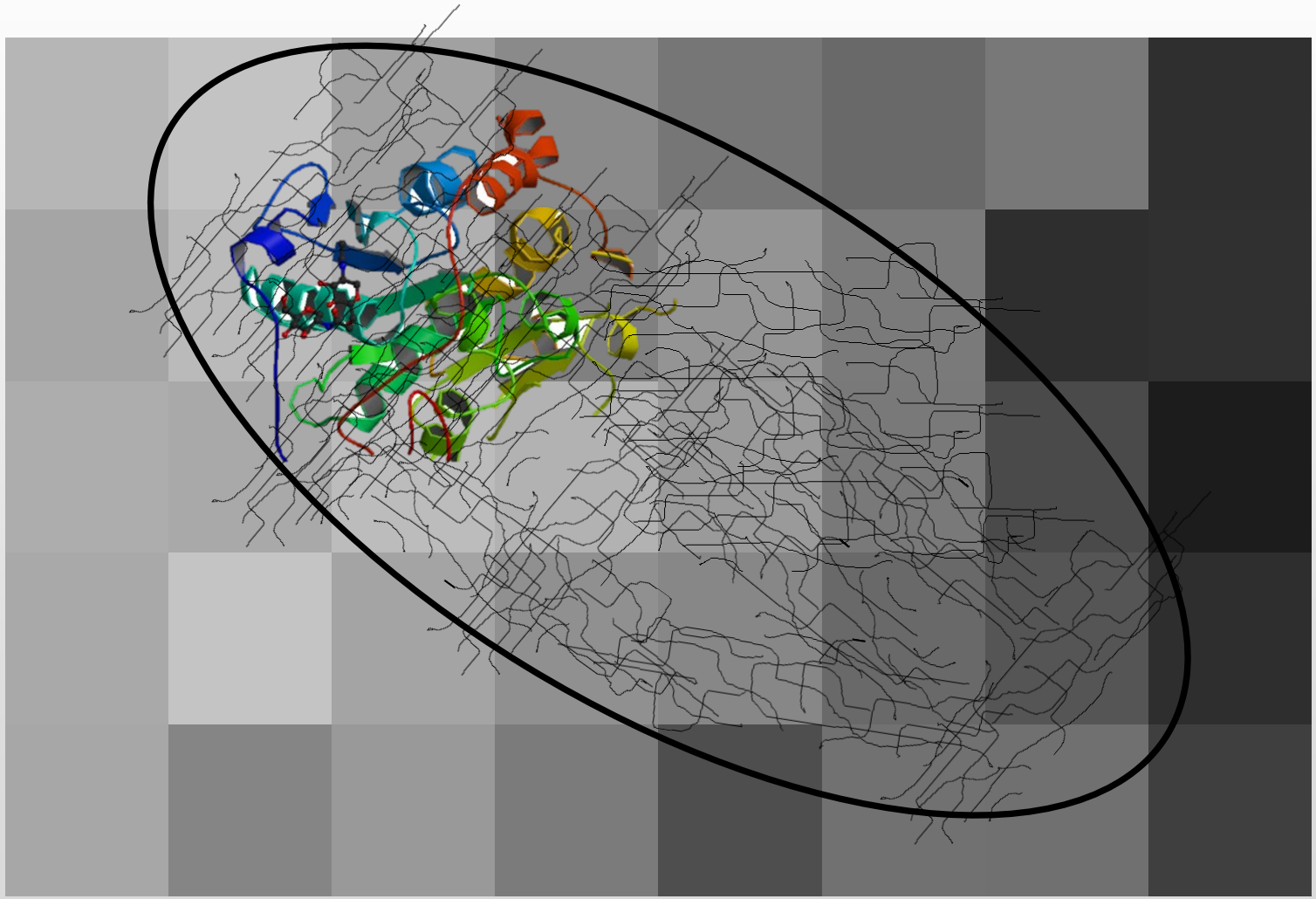
enzyme, to scale



Magnification 10.000.000x



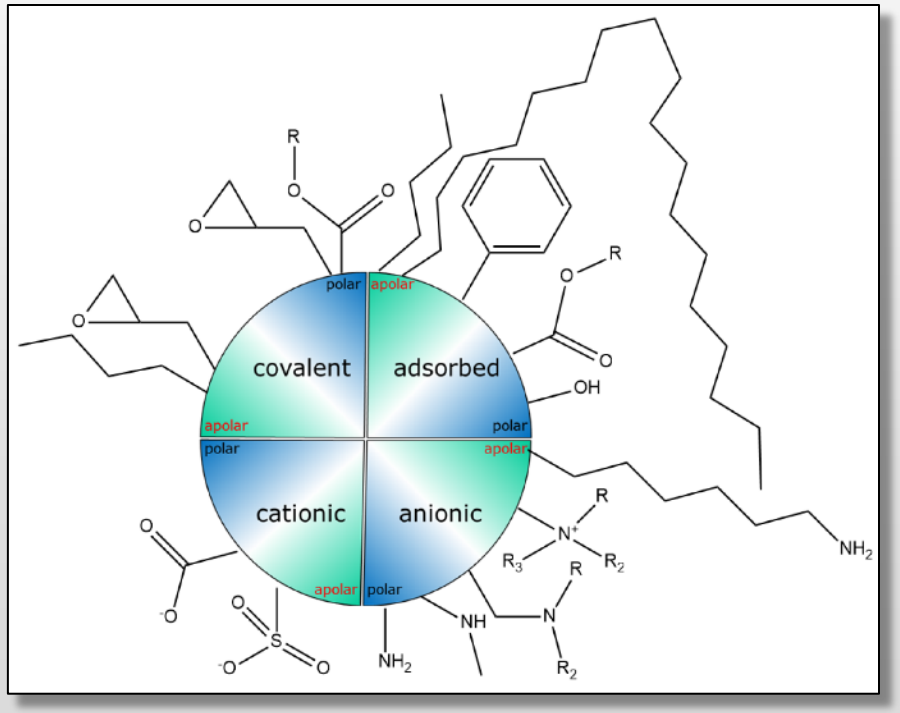
10-20 nm cross-linked polymer substructure (~1 million monomers)



enzyme is CalB

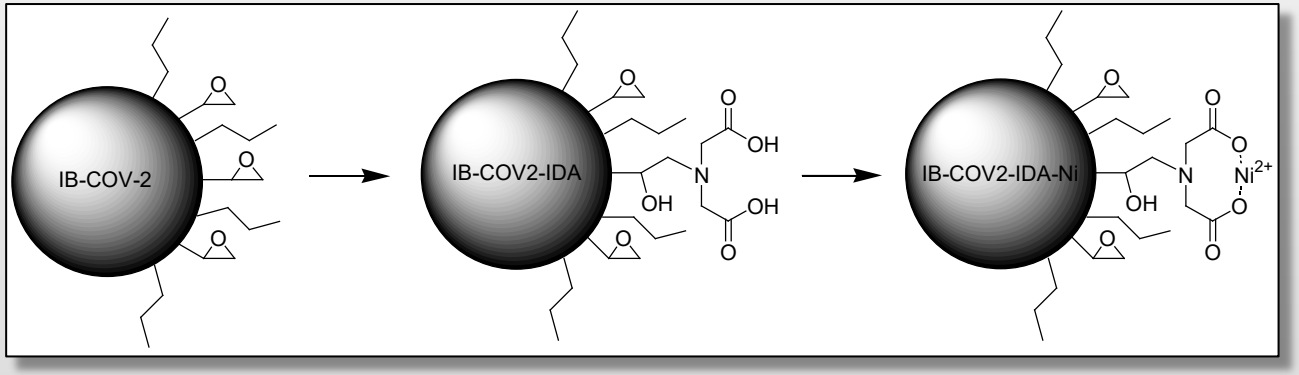
Immobead binding chemistry

Classic binding:
- Covalent
- Hydrophobic / hydrophilic
- Cationic
- Anionic

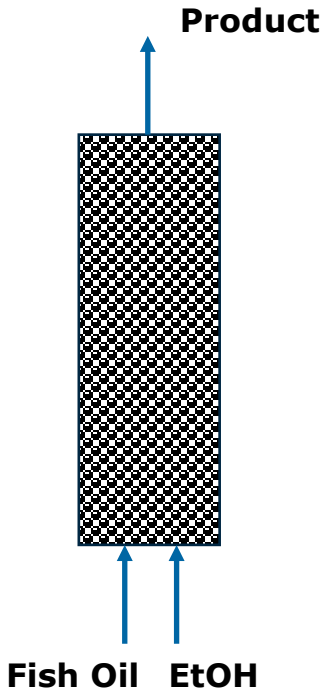


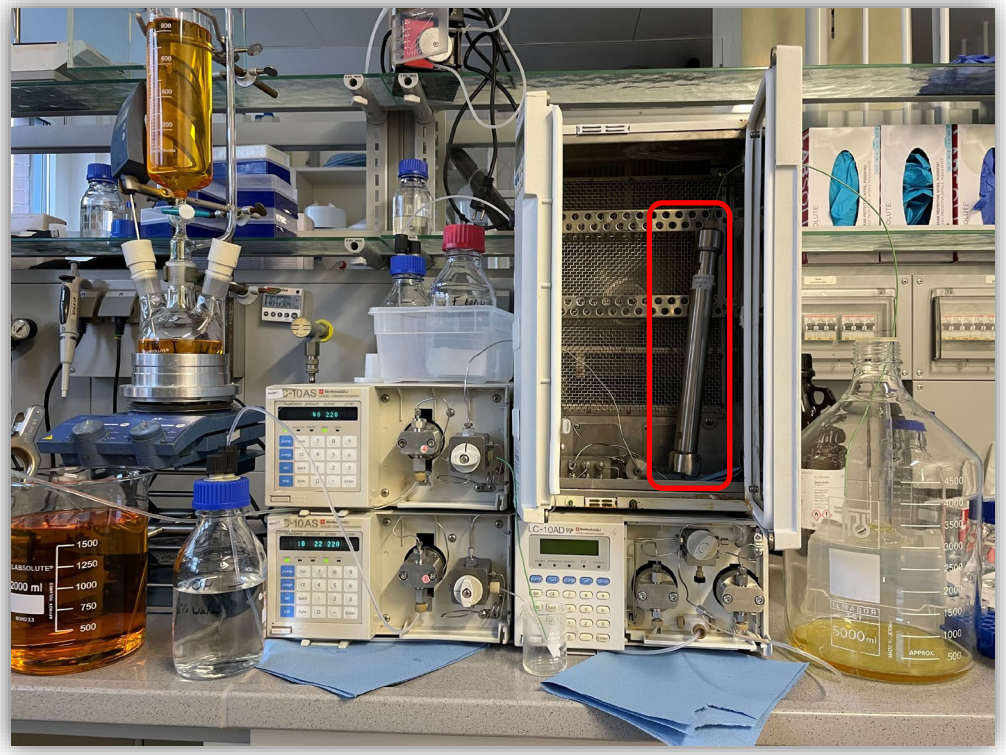
Selective affinity binding:

- His tag binding provides more conformational freedom for enzymes
- Typical activity recoveries: 25 – 100%



BOC Case – Flow Reactor Development





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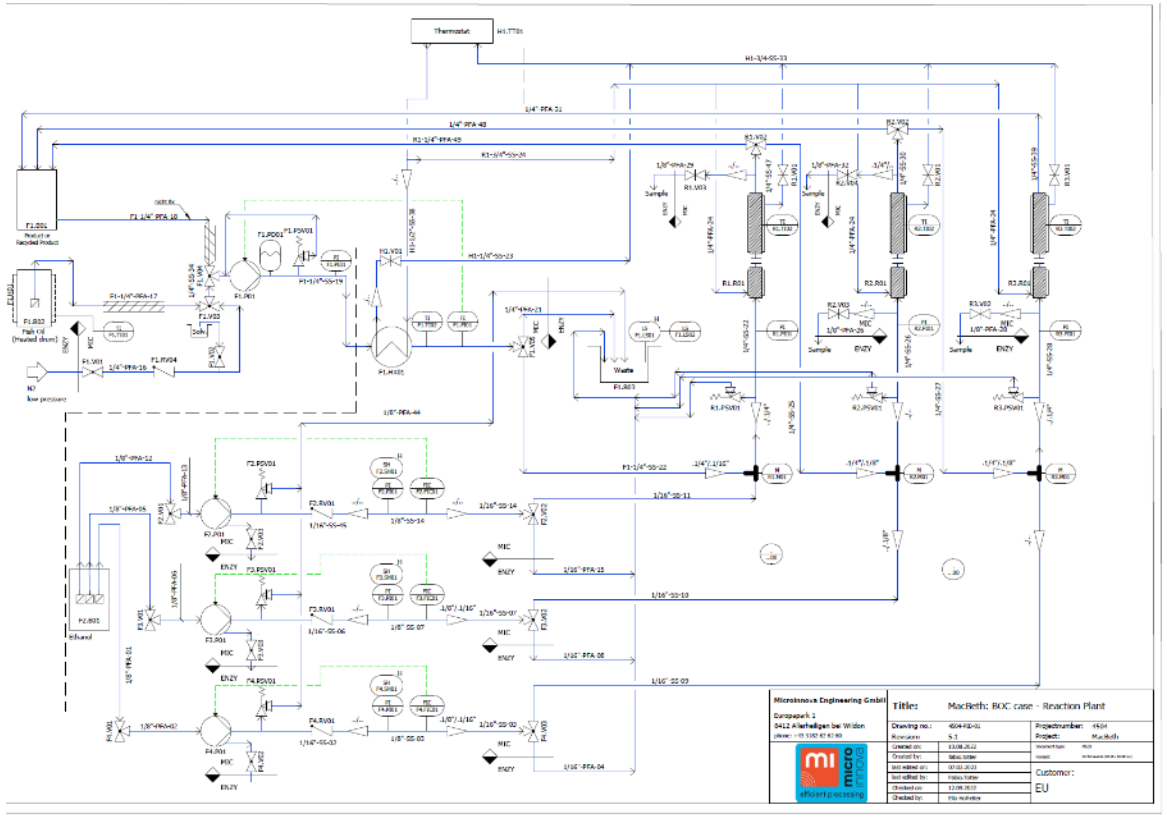
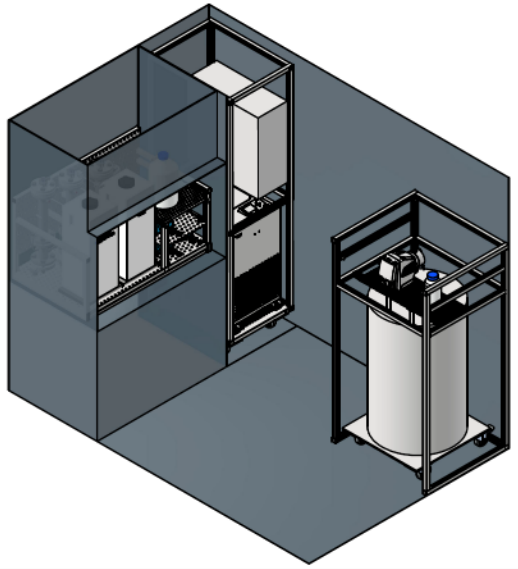
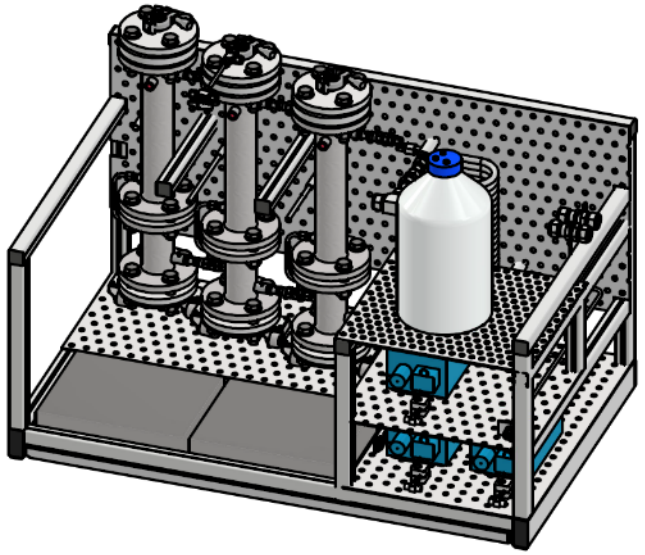
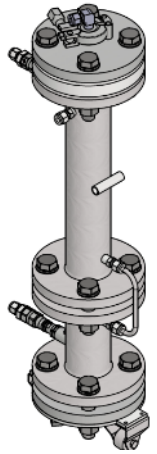
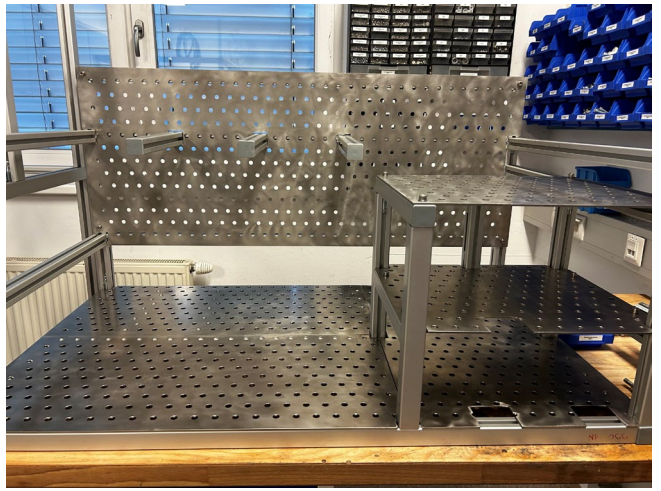
BOC Case – Engineering of Pilot Plant











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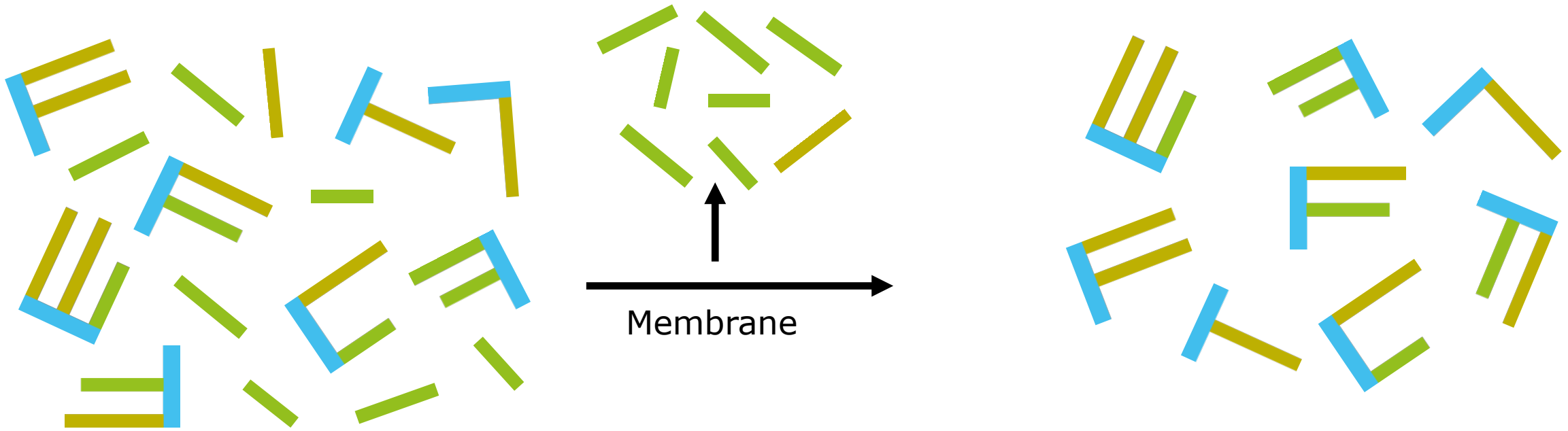
Membrane Separation

- Remove Fatty Acid Ethyl Ester from the **EPA**/**DHA** Enriched Fish Oil



~ 30% EPA/DHA

~ 50% EPA/DHA

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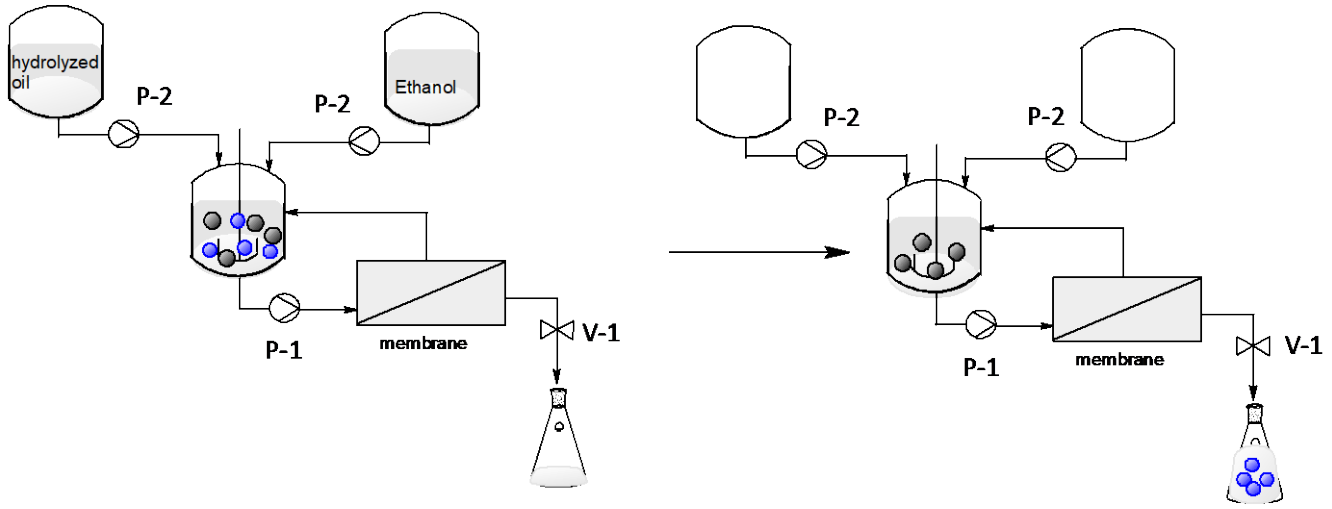
Process simulation

Input: 750 g oil hydrolysis mixture +250 g ethanol – oil **Ex-Microinnova V24/25**

Oil purification → Permeate rework (concentration) → Retentate ethanol wash → 497 g enriched oil (± 80% Tg/DG)

	Solutex Area % (30 bar) T034			
	TG	DG	MG	FAEE
Feed	32,66	31,26	8,61	27,3
End retentate	41,02	43,42	11,1	3,99



Input: 4500 g oil hydrolysis mixture – oil Ex-Microinnova V28

Output: 1138,4 g enriched oil – (in analysis)

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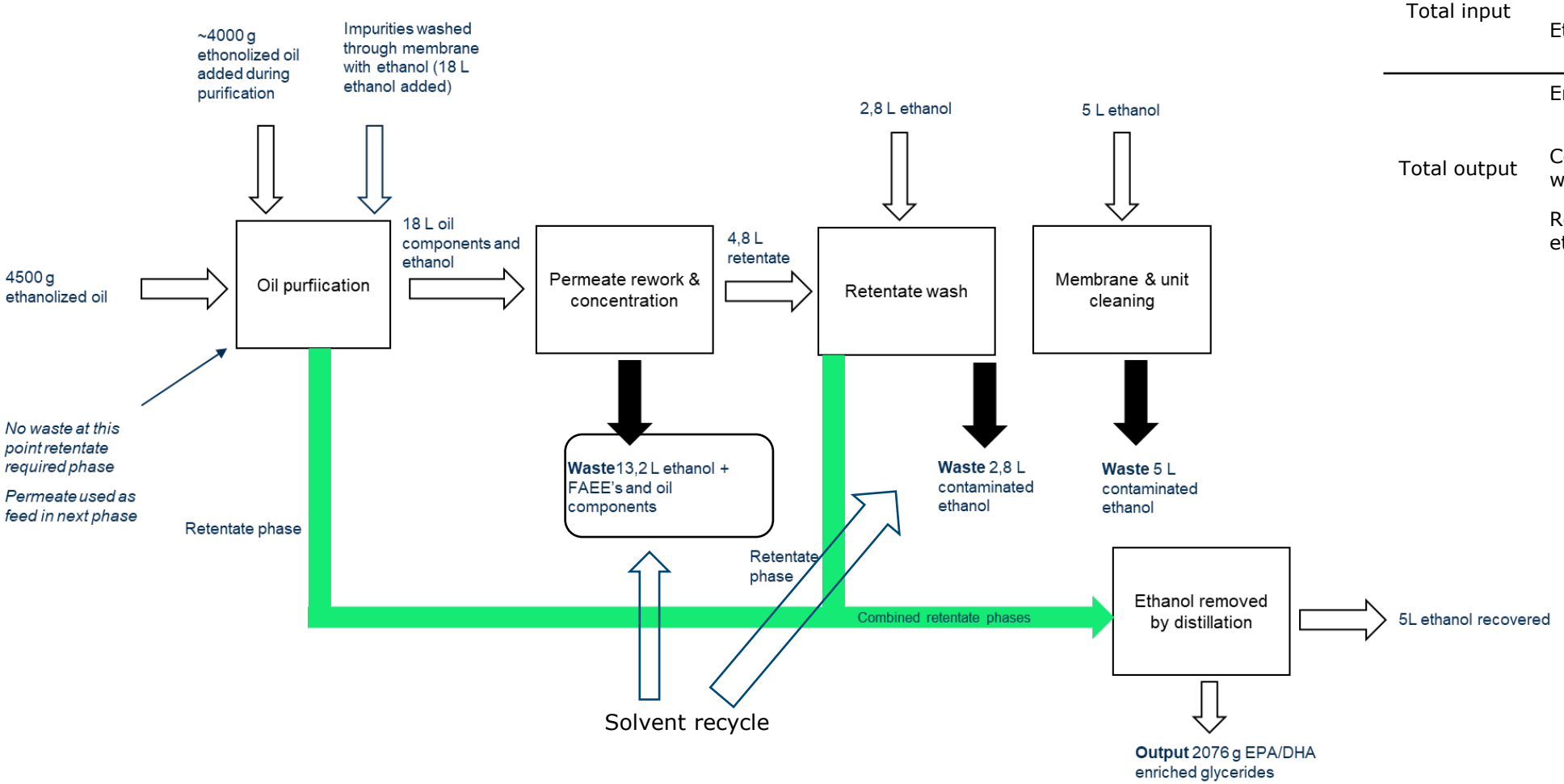
Overview scaled up process



Total input	Ethanolized oil	8500 g	
	Ethanol	25,8 L	
	Enriched oil	2076 g	product
Total output	Contaminated waste ethanol	21 L	waste
	Recovered ethanol	5 L	Ex-distillation (reusable)

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BOC Case – First demonstrator ready!

- ✓ **Successful Implementation of Enzymatic Flow Reactor**
- ✓ **Throughput: 2 – 5 L/h**
- ✓ **Results of first trials are very promising and encouraging**

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Successful Proof of Concept

enzymatic reaction

membrane separation

Omega-3 **34%** **45%** **50%**

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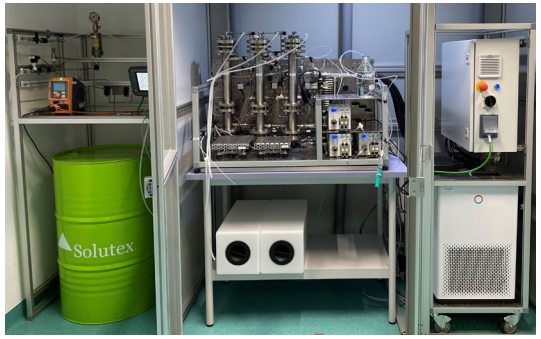
BOC Case: From **TRL0** to **TRL6** in 4 years



Start	6 Months	18 Months	30 Months	42 Months	48 Months
TRL0	**TRL1-2**	**TRL3**	**TRL4**	**TRL5**	**TRL6**
	Basic Concept	**Concept Validation**	**Experimental Pilot**	**Demonstration Pilot**	**Industrial Pilot**

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MACBETH - BOC Case

Thank you for your attention!

https://www.macbeth-project.eu/

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