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Improving productivities in fermentation processes

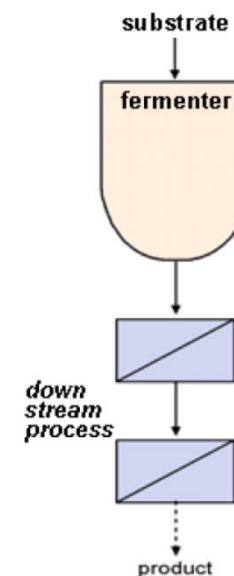
Heleen De Wever

Köln, 23-25 April 2013



Bio-based production chemicals

Aspect	Current practice
Substrate	Single
Microorganisms	Pure culture
Operation mode	Batch
Sterilization equipment	Yes
Product titre	High
Product recovery	Separate/downstream
Product separation	Low amount of impurities



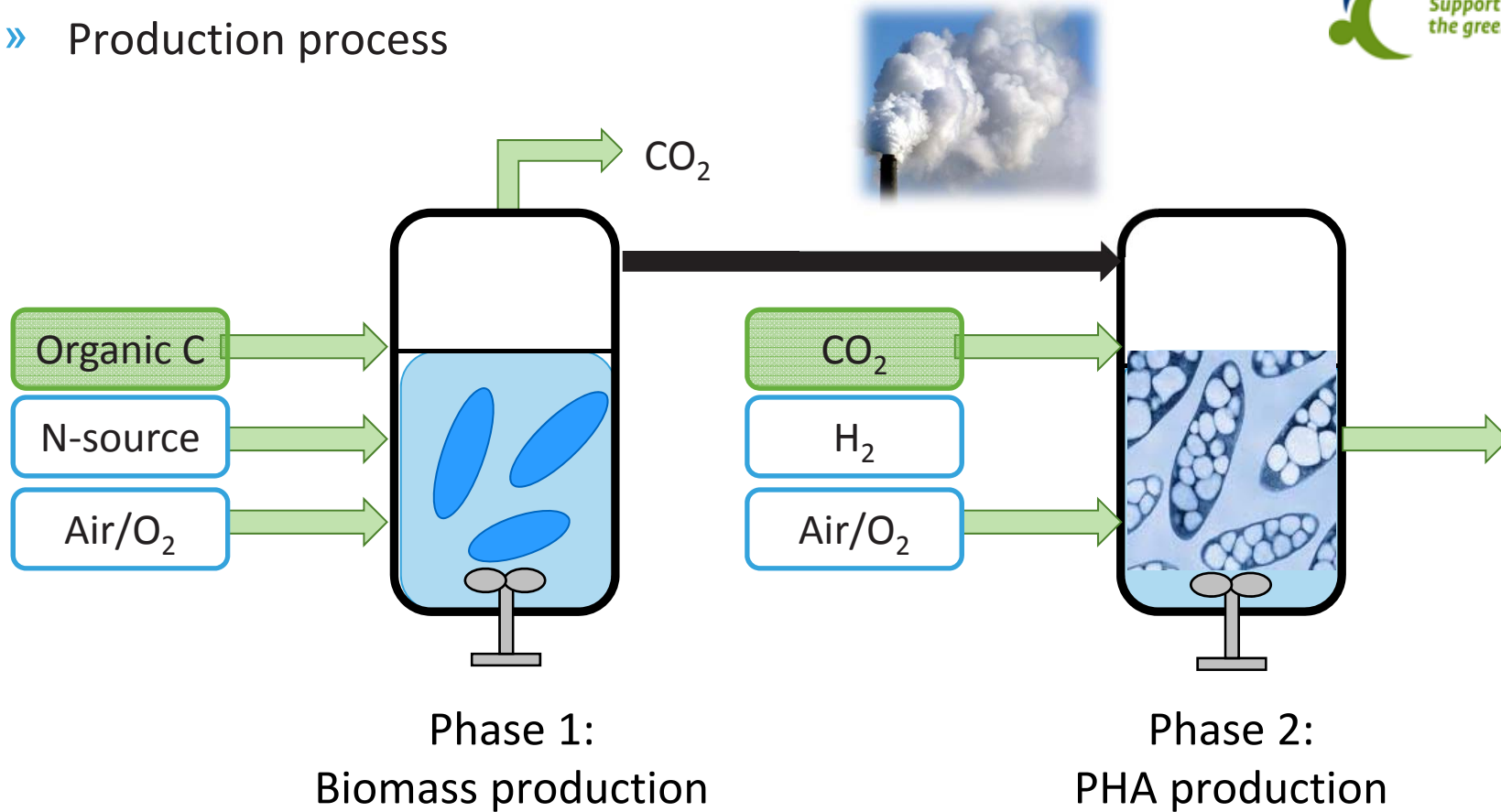
Conventional

Case: Bioplastics from waste streams

- » Renewable resource:
 - » Organic waste stream
 - » Offgases
- » Target compound:
 - » Fully biobased biodegradable group of bioplastics selected
 - » Polyhydroxyalkanoates (PHA) - general
 - » Polyhydroxybutyrate (PHB)
- » Biocatalyst: pure bacterial culture
- » Concept: fed-batch process

Case: Bioplastics from waste streams

» Production process

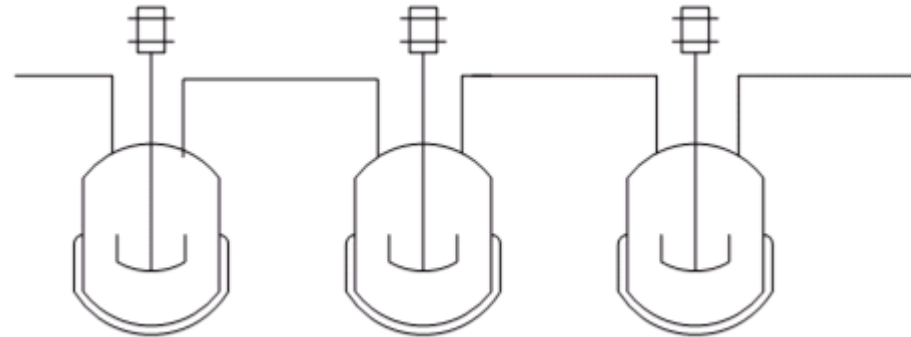
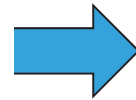
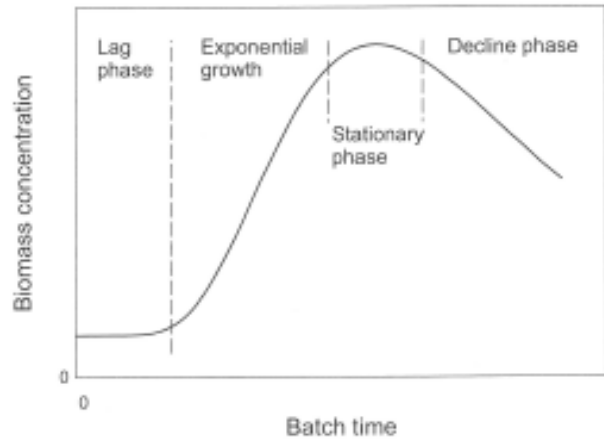


Bio-based production chemicals

Aspect	Current practice	Future
Substrate	Single	2nd generation feedstocks Organic waste
Microorganisms	Pure culture	Undefined mixed culture
Operation mode	Batch	Continuous
Sterilization equipment	Yes	No
Product titre	High	Low
Product recovery	Separate/downstream	Integrated
Product separation	Low amount of impurities	Dilute product stream High amount of impurities Different technologies

Our approach: high conversion efficiencies and product concentrations through process intensification

From batch to continuous processes ...



High titer and productivity by using several stirred tanks in series

Advantages

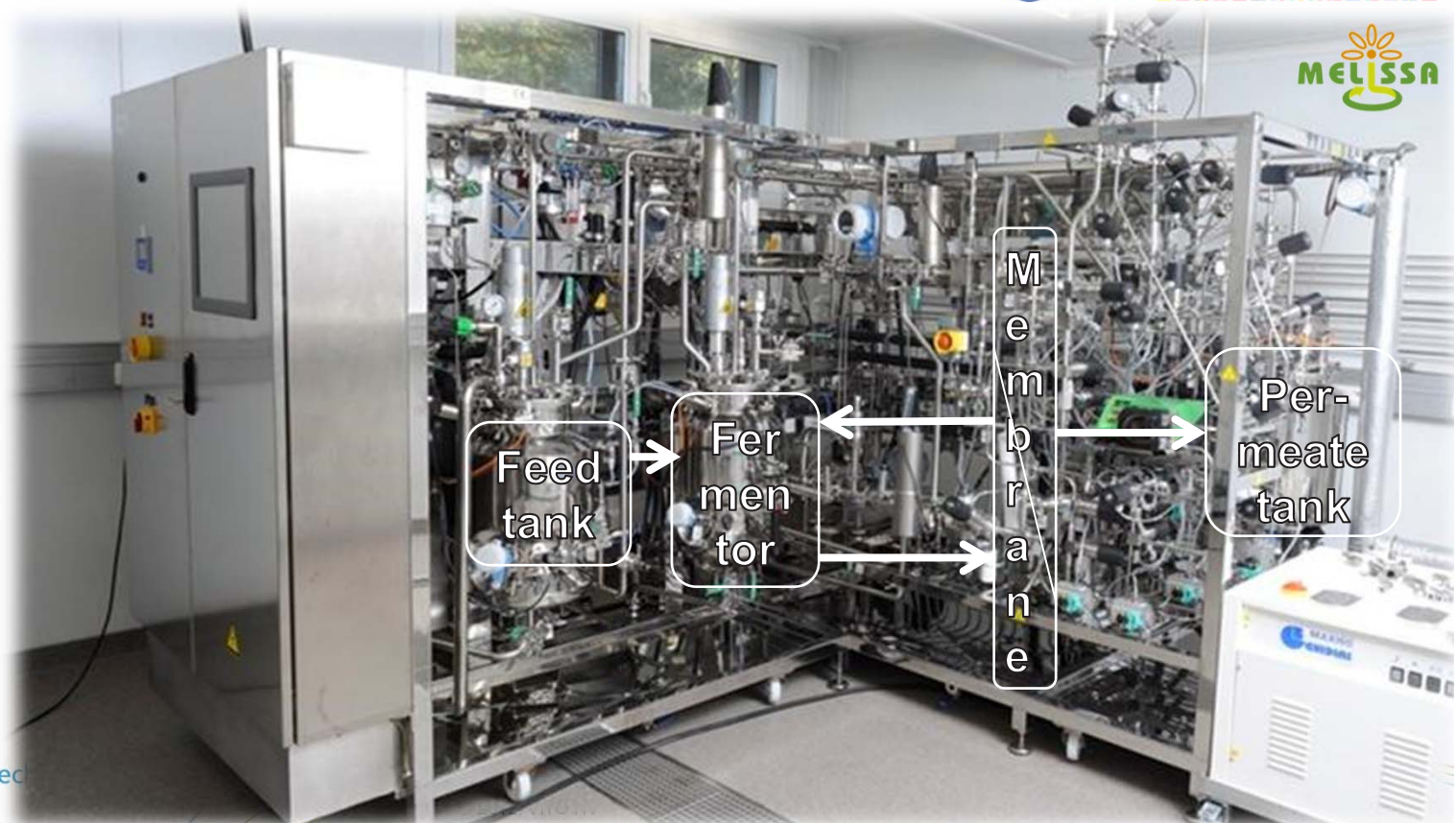
- » Increase throughput
- » Reduce cleanup time
- » Reduce required footprint
- » Often only feasible alternative for high volume, low value products

Challenges

- » Advanced process control
- » Maintain sterility
- » On-line quality measurements

... to high cell density fermentation ...

- » Membrane bioreactors (MBRs): cell retention by membranes
 - » **Advantage:** increased throughput and productivity
 - » **Challenge:** membrane fouling control



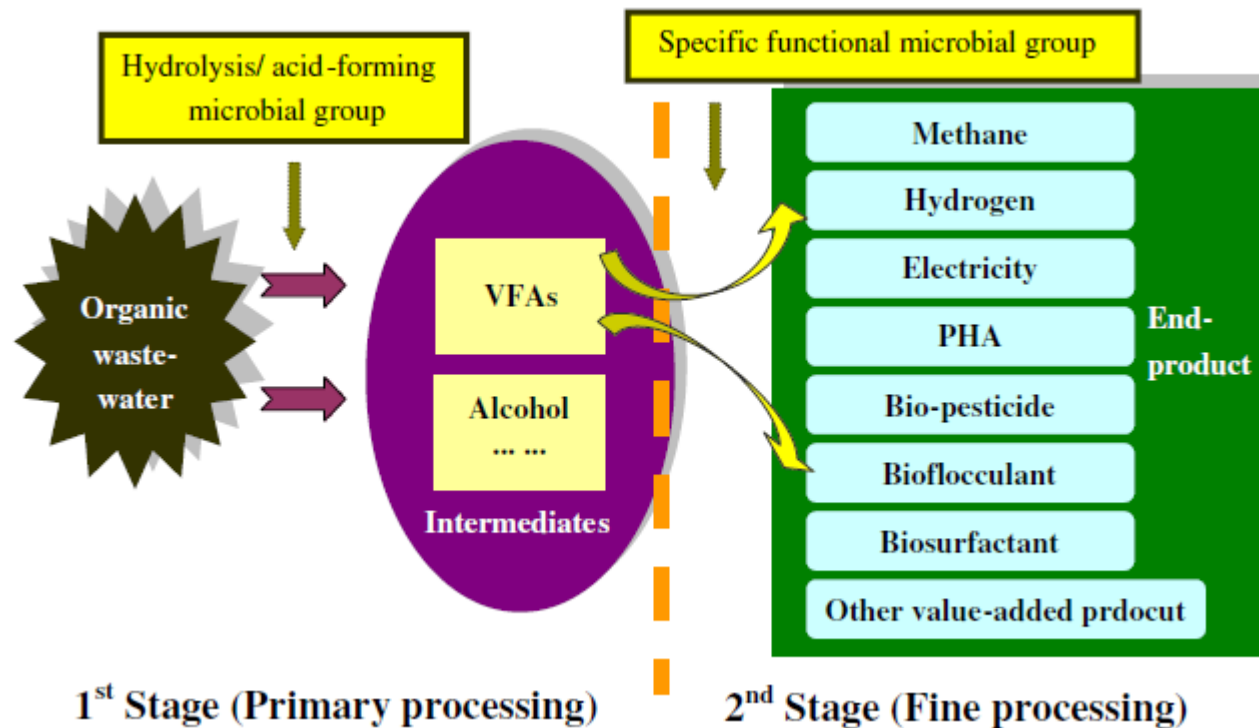
Case: Organic acids from waste

- » Renewable resource:
 - » Organic waste stream consisting of
 - » Non-edible residues of plants
 - » Fecal material
 - » Toilet paper
- » Target compound:
 - » Volatile Fatty Acids (VFA, acetate – propionate – butyrate)
 - » Part of closed loop system for Advanced Life Support in space
- » Biocatalyst: undefined mixed bacterial culture
- » Concept: continuous fermentation at increased cell density (MBR)



Towards integrated biorefinery concepts

- » Two-stage bioconversion processes based on organic acids from waste



(Source: Li and Yu, 2011)

... to inclusion of product removal techniques

» *In-situ* product recovery or removal (ISPR)

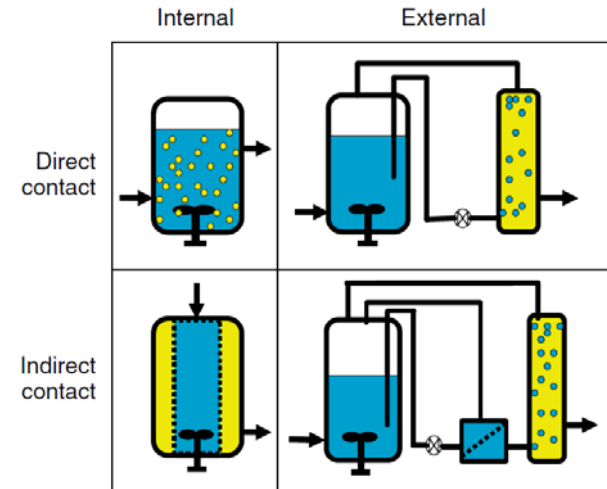
» **Advantages:**

- » Integration of fermentation with first step of downstream process
- » Higher productivity by removal of product inhibition

» Concentrated feedstocks can be fermented

» **Challenges:**

- » Match mode of operation of bioreactor/separation units
- » Optimize integrated set-up for maximum productivity gain



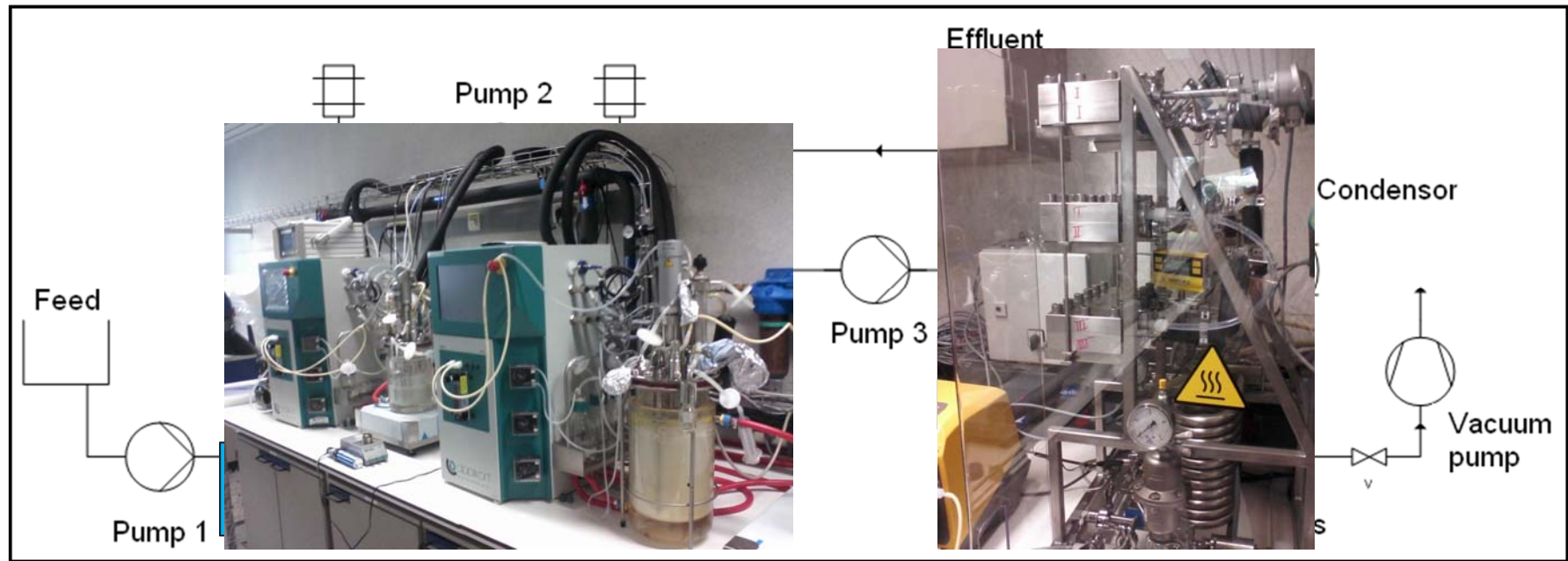
Source: Woodley et al. (2008)

Case: Biobutanol from sugars

- » Acetone-Butanol-Ethanol (ABE) fermentation one of the largest biotechnological processes ever developed
- » Process challenges
 - » Product inhibition, low product concentrations and low productivity
 - » Cost of substrates
- » Renewable resource: sugars
- » Target compound: butanol
- » Biocatalyst: pure bacterial culture
- » Concept: continuous fermentation with *in-situ* butanol removal

Case: Biobutanol from sugars

- » *In-situ* butanol removal by organophilic pervaporation
 - » Proof-of-concept: continuous conversion in two-stage fermentation using commercial composite membrane with PDMS top layer



Case: Biobutanol from sugars

- » Our own optimization studies in long-term continuous experiments

Result	Gain
Increased productivity from 0.35 to 1.15 g.L ⁻¹ .h ⁻¹	Decreased fermentor cost
Increased flux from 375 to 620 g.m ⁻² .h ⁻¹	Decreased capital costs for pervaporation
Increased permeate concentration from 120 to >200 g.L ⁻¹	Decreased energy consumption in distillation section

- » Next step: switch to high cell-density fermentation (MBR concept)

Conclusions

- » Bioconversions on organic waste streams present challenges in terms of product separation and purification
- » Combination of bioconversion and separation technology results in improved productivities
 - » Current efforts are mainly at laboratory scale
 - » Need for upscaling, demonstration of robustness

VITO experience

- » Feedstocks:
 - » Synthetic media and organic waste streams
 - » Synthetic gas mixtures and waste gases
- » Target compounds:
 - » Intracellular: bioplastics
 - » Extracellular: organic acids, alcohols, biosurfactants, ...
- » Biocatalysts:
 - » Pure bacterial cultures and mixed cultures
 - » Enzymes
- » Concepts:
 - » Batch, fed-batch and continuous operation
 - » Single and multistage fermentations, stand-alone or integrated with separation technology

