Techno-economic analysis of new fermentation processes

EuroBioRef Summer School

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novozymes
Rethink Tomorrow

Agenda

- **Short introduction to Novozymes**
- **Case study – going behind the scenes**
  - A realistic case on typical work done at Novozymes to assess new market opportunities
  - Bridging fermentation technology and process economics – similar approach for all enzymatic/fermentation processes
  - Production of 1-butanol by fermentation
- **Key concepts**
  - The difference between fuel and chemical production
  - Importance of feedstock and byproducts (“biorefinery”)
  - Competitiveness and the indifference curve
- **Questions and Answers... but don’t wait until last minute!**

Novozymes in brief

GLOBAL PRESENCE

- Global leader in industrial enzymes & microorganisms
- More than 700 products used in 130 countries within >30 different industries
- More than 5,400 employees worldwide

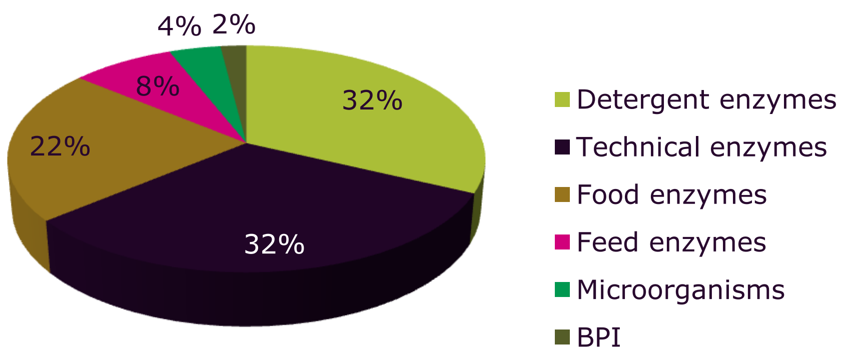
R&D

- Market leader in all main industries
- 47% global market share within industrial enzymes
- ~ 14% of sales invested in R&D
- > 6,000 patents in place

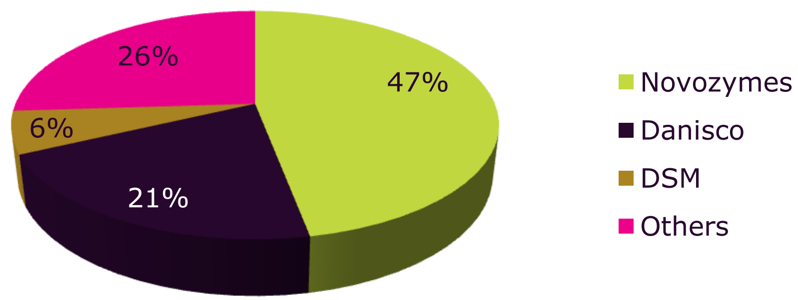
PERFORMANCE

- Global sales USD 1.7bn (FY 2010)
- Operating profit margin 21,8% (FY2010)
- ROIC 22.2% (FY2010)

Novozymes sales by industry FY2010



Market share of enzymes FY2010 (industrial use)



novozymes® Rethink Tomorrow

Uniquely diversified to create synergies and new opportunities

- Unique biotech-focused business with a strong legacy of delivering growth, earnings, and cash flows
- Development and production of enzymes since 1941
- Leveraging competencies across segments accelerates pace of innovation

Enzyme Business

Detergent enzymes

- Laundry & dishwasher detergents

Technical enzymes

- Corn ethanol
- Starch conversion to syrups
- Textiles

Food enzymes

- Baking
- Brewing
- Oil & fats
- Wine & juice

Feed enzymes

- Monogastric animals
- Substituting phosphate
- Enhancing protein uptake

BioBusiness

BioAg

- Biofertility
- Biopesticides
- Bioyield enhancements

Microorganisms

- Cleaning Solutions
- Wastewater Solutions
- Aquaculture

Biopharma

- Medical devices
- Drug delivery and formulation
- Cell culture

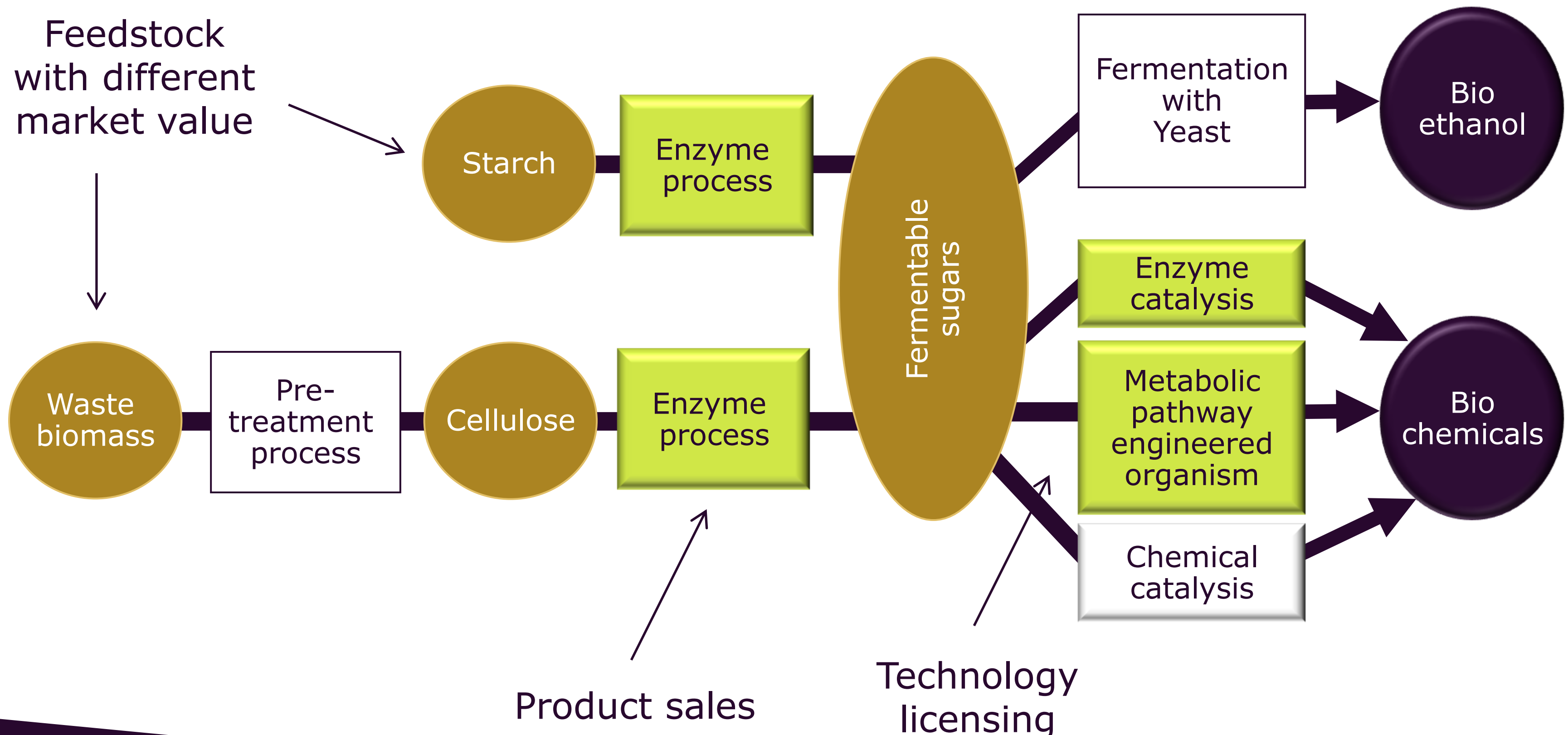
Business development

- **Biochemicals**
- Biogas
- Acquisitions

BioBusiness - Biochemicals

Bio-based chemicals fit well with Novozymes

- Leverages Novozymes technology, competences and business development expertise
- Leverages partnerships with grain processors and chemical companies



Case study: Butanol (1-butanol)

- **What can butanol be used for – and how is butanol produced**
  - Chemical intermediate
  - Biofuel

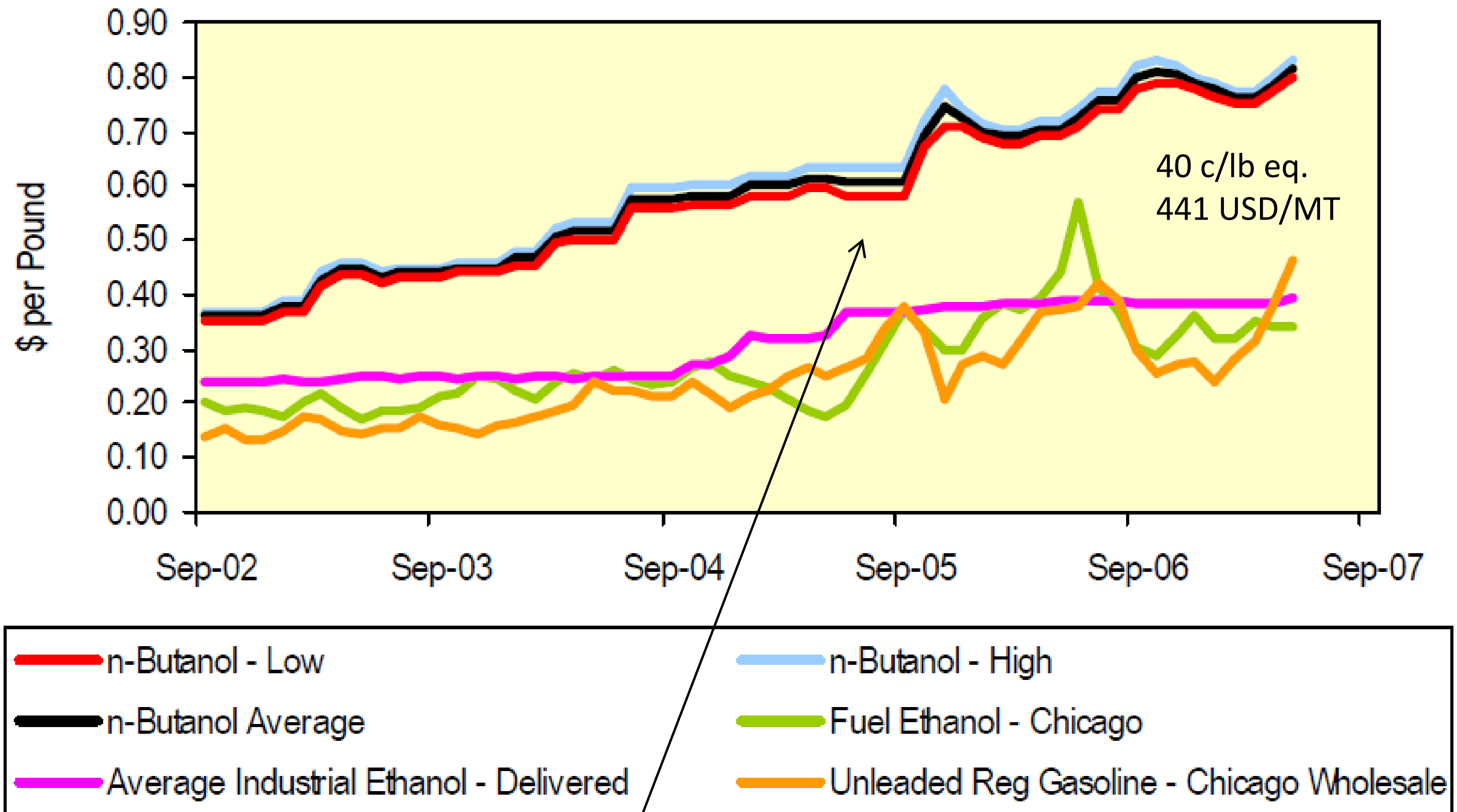
- **Are all 4 isomers of commercial interest?**
  - Can they be produced by fermentation?
  - Do they have similar production costs?
  - Focus on 1-butanol (n-butanol)

- **How is physiology and fermentation performance linked to cost of production?**
  - What is required from our feedstock (raw materials)?
  - What is required from our microorganism in terms of butanol yield on raw material, titre and productivity?

Butanol… we are talking about 4 chemicals, not 1. Any preference?

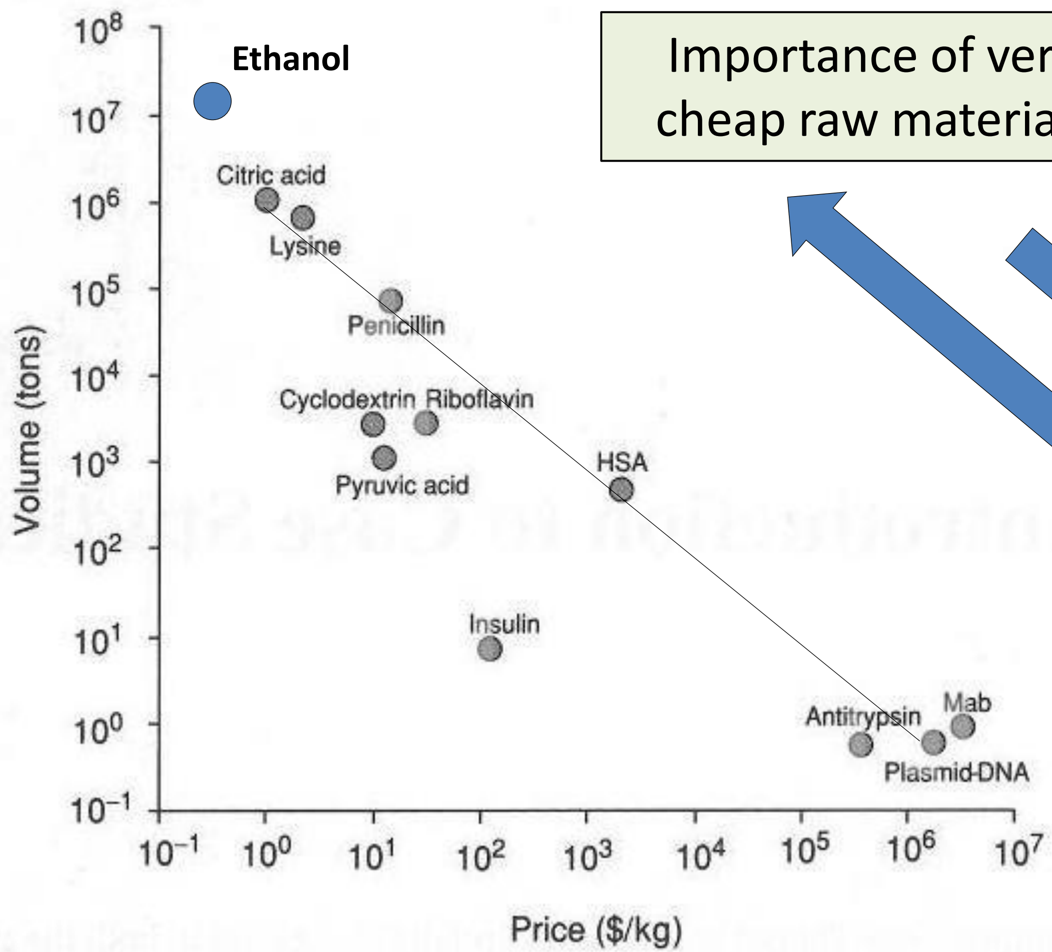
- **1-butanol**
  - Produced for app. 100 years by (Acetone, Butanol, Ethanol) ABE fermentation
  - Fermentation plants in South Africa and the Soviet Union were shut down 2-3 decades ago... They were not competitive ☹
  - Recent decision to start commercial production in China, not for fuel purposes but for chemical production ☺
- **2-butanol and isobutanol**
  - Never produced in commercial scale
  - Relatively small chemical market
  - Large interest as new biofuel by companies like DuPont/BP (ButaMax joint venture) and GEVO
- **Tert-butanol**
  - Very difficult to find attractive metabolic pathways from glucose
  - Never produced in commercial scale by fermentation... and it is hard to see who has a real interest

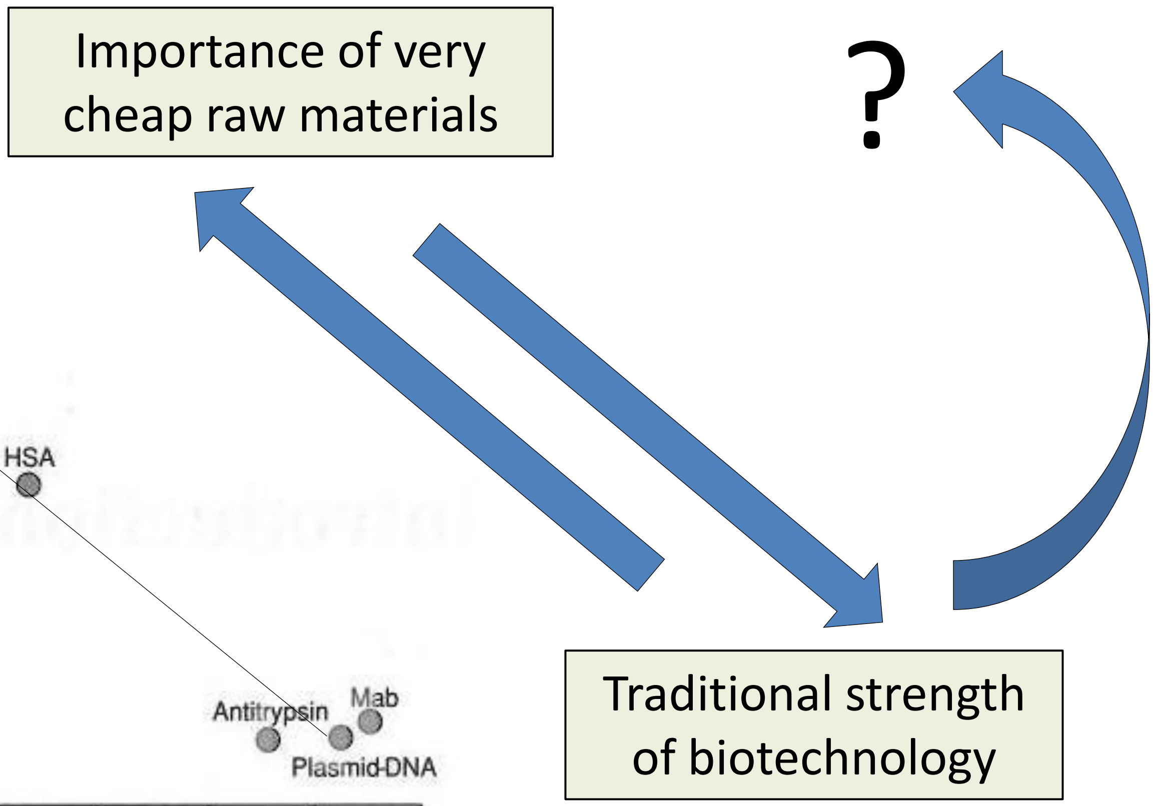
Chemicals (here 1-butanol) are normally priced much higher than fuel



Is this difference significant?

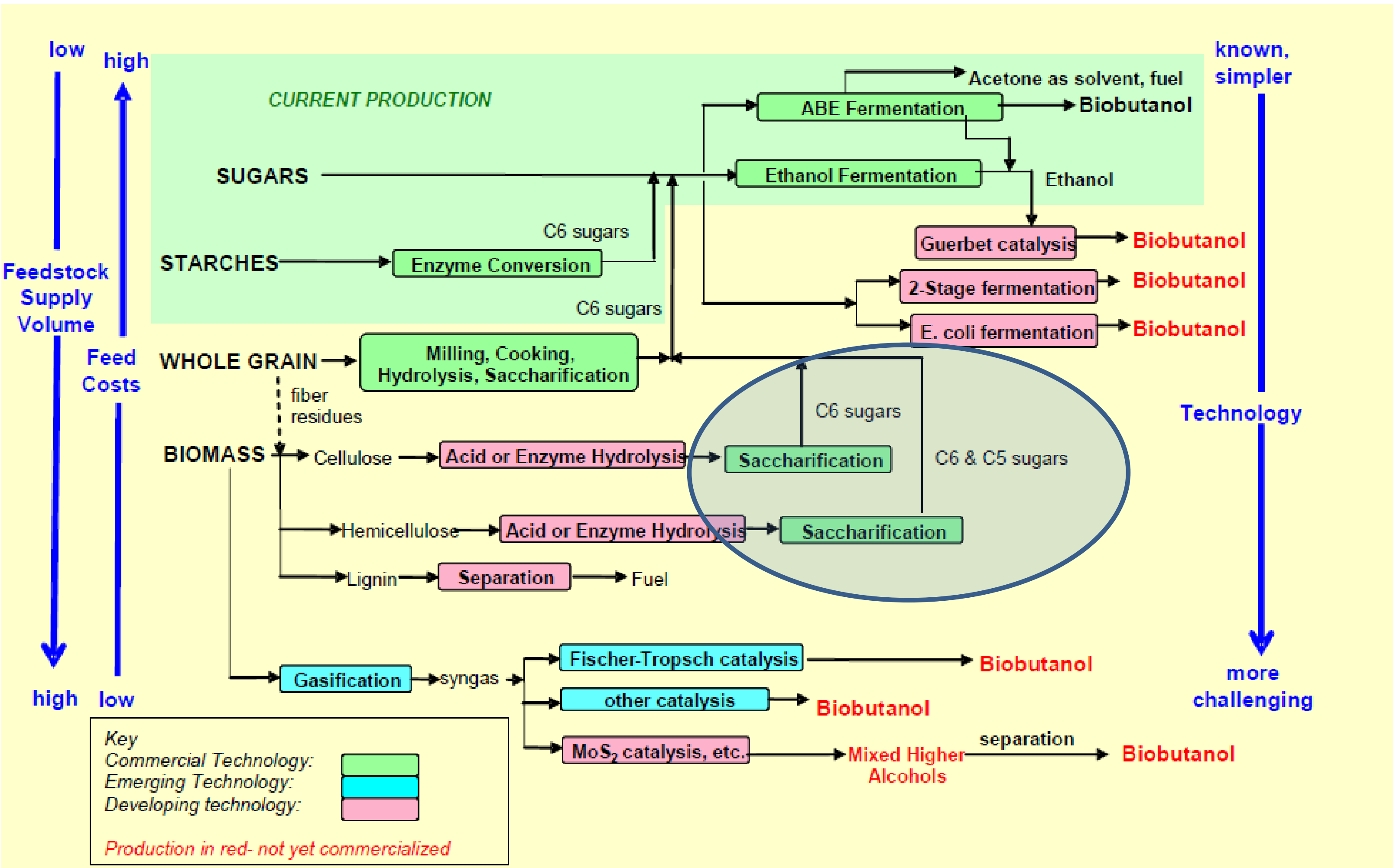
Commodity chemicals are cheap
- otherwise they would not be commodities



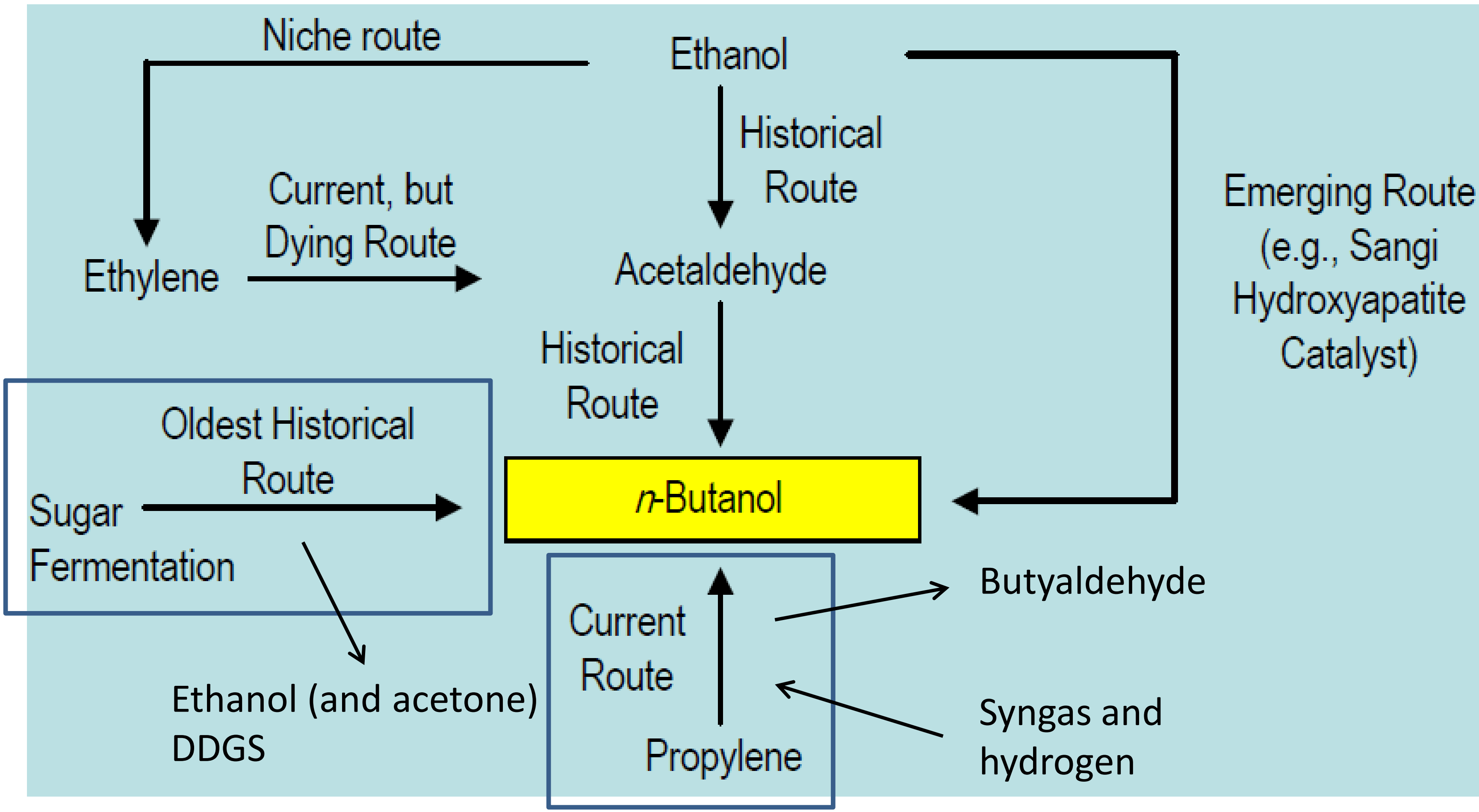


Source: Heinzle et al.: Development of sustaniable bioprocesses

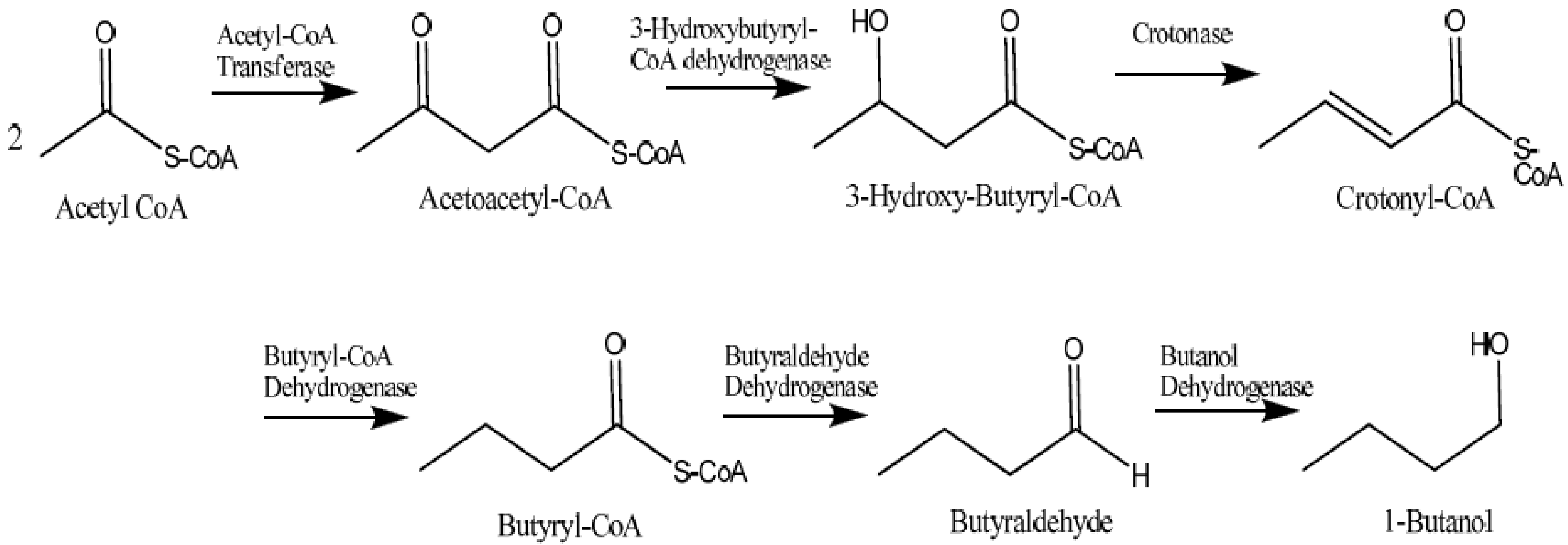
Overview of production routes, the production route competitive analysis is important



Competitive production analysis: Sugar (fermentation) vs. propylene oxo-route

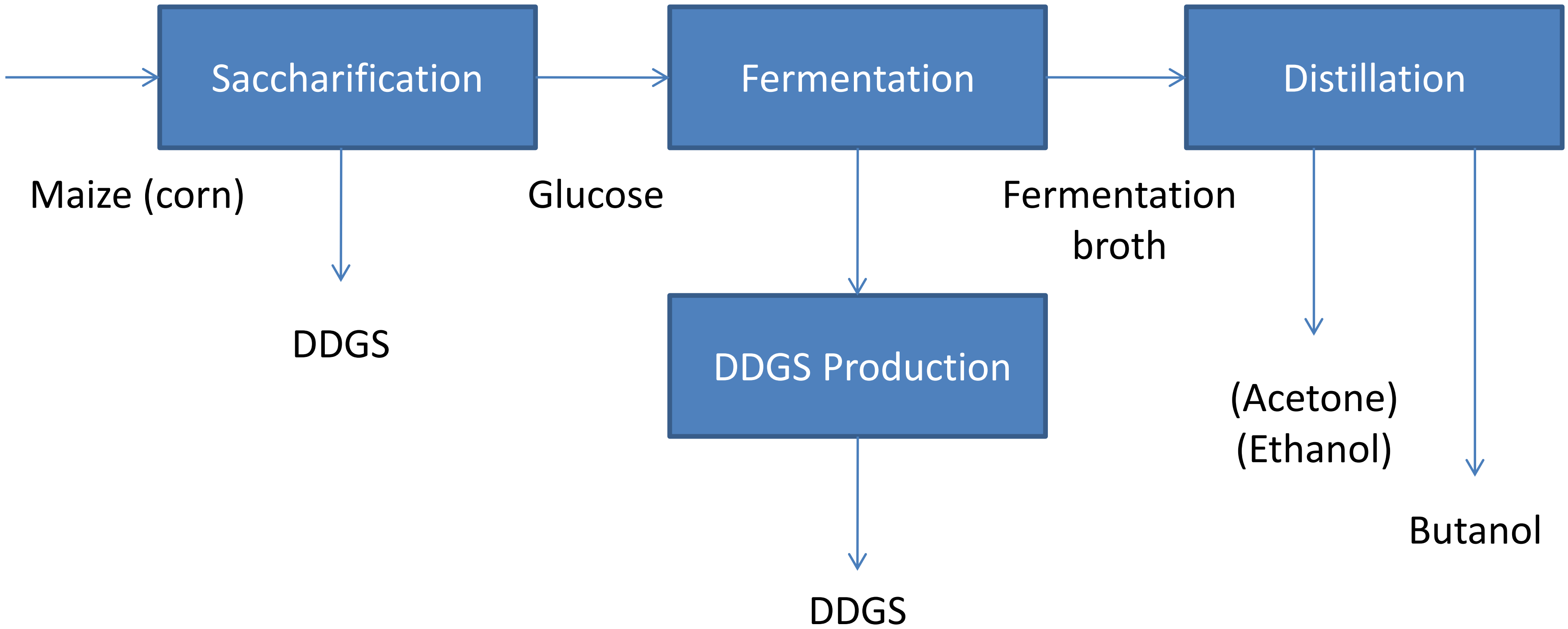


Metabolic engineering strategy



- Express “ABE pathway” to 1-butanol in selected host
- Always look for the maximum theoretical yield when producing commodity chemicals!!!
- Maximum theoretical yield is 1 mol of 1-butanol (as well as 2-butanol and isobutanol) per mol of glucose, i.e. 74.12/180.16 = **0.41 g/g**

Schematic overview of possible 1-butanol fermentation production process



Distillers Dry Grain Solubles (DDGS) is an **important co-product** and feed additive

The principles of "cost of production" (Illustrative numbers)

	UNIT COSTS	Yields	Cost
PETRO			
Propylene	926	0.850	787
Syngas	309	0.443	137
Hydrogen	794	0.030	24
Butyraldehyde	419	-0.330	-138
BIO			
US Corn	158	3.900	614
DDGS	182	-1.560	-284

	PETRO	BIO
Total Investment (MUSD)	136.1	139.4
Raw materials	948	614
By-Product Credits	-138	-284
Utilities	75	124
Variable Costs	884	455
Labor costs	22	28
Maintenance materials	16	13
Operating supplies	1	2
Total Direct Costs	923	497
Plant overhead	18	22
Taxes and insurance	18	15
Plant Cash Cost	959	535
Depreciation (12 yr life)	76	78
Plant Gate Cost	994	617
G&A, sales, research	65	45
Net Production Cost	1059	661
ROI Before taxes	227	233
Product Value	1286	894

Product value indicates an expected market price before the technology is competitive

All numbers are in USD/MT

Process economics of butanol production by fermentation

- **Purpose**: Build a process economic model that simulates cost of production based on given microbial performance
  - Process economic model based on "industry data" and slightly modified
  - Data not easily accessible… nobody wants to disclose costs!

- **Key parameters of the fermentation process**
  - Yield of (co)products (g/g)
  - Titre (or concentration) of product (g/L)
  - Fermentation time (h) or productivity (g/L/h)
  - Robustness, the strain must work all the time!

- **Assumption on sensitivity analysis**
  - Keep it simple: Treat all unit operations as "independent units", i.e. no real process optimisation
  - Saccharification must be scaled to deal with total amount of feedstock (maize)
  - Recovery must be scaled to deal with volume of fermentation broth

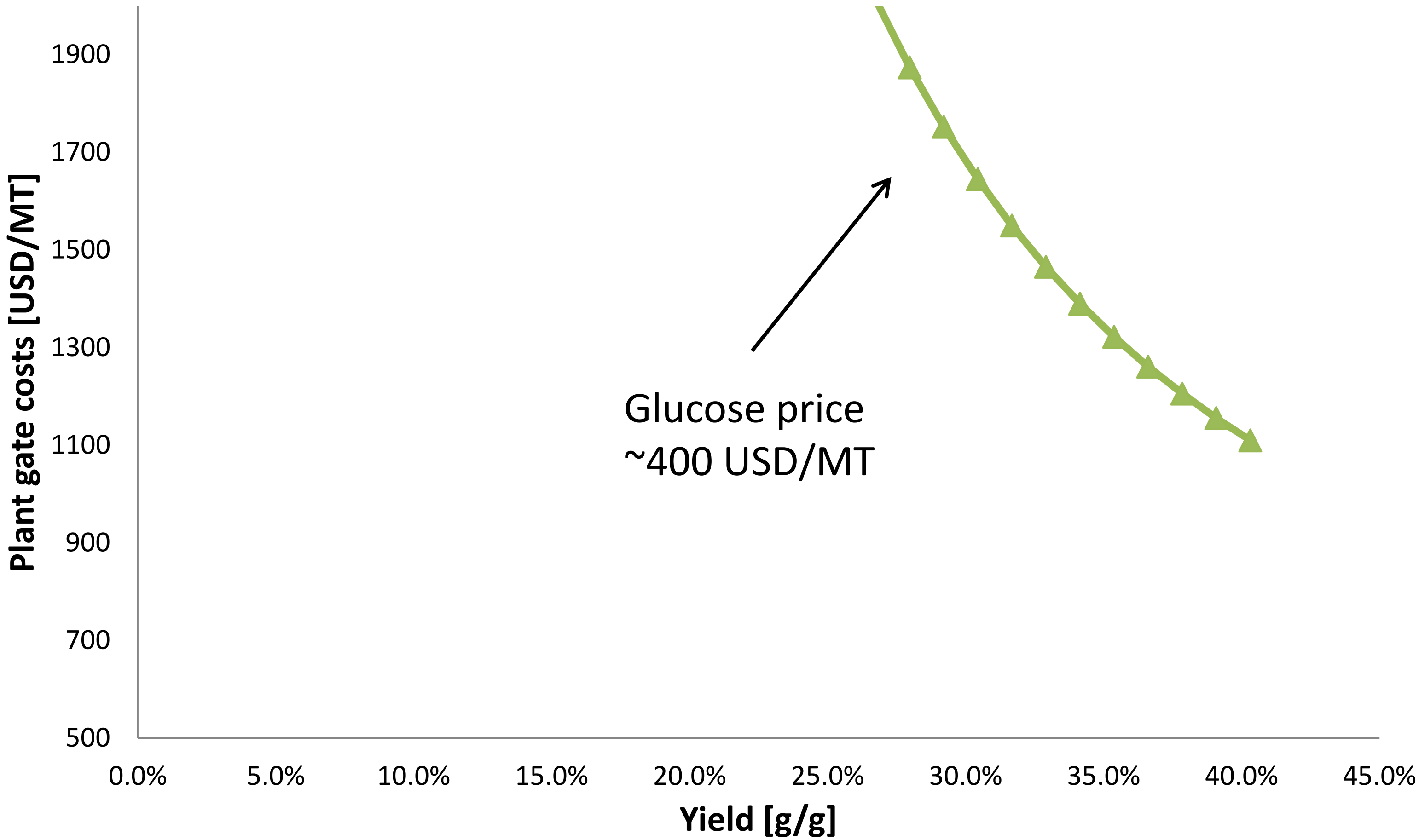
Simulation of fermentation performance

- **Assumption on plant**
  - Scale: 150 metric ton of 1-butanol per year
  - On-stream operating factor: 0.90
  - Location: US Midwest (typical benchmark)

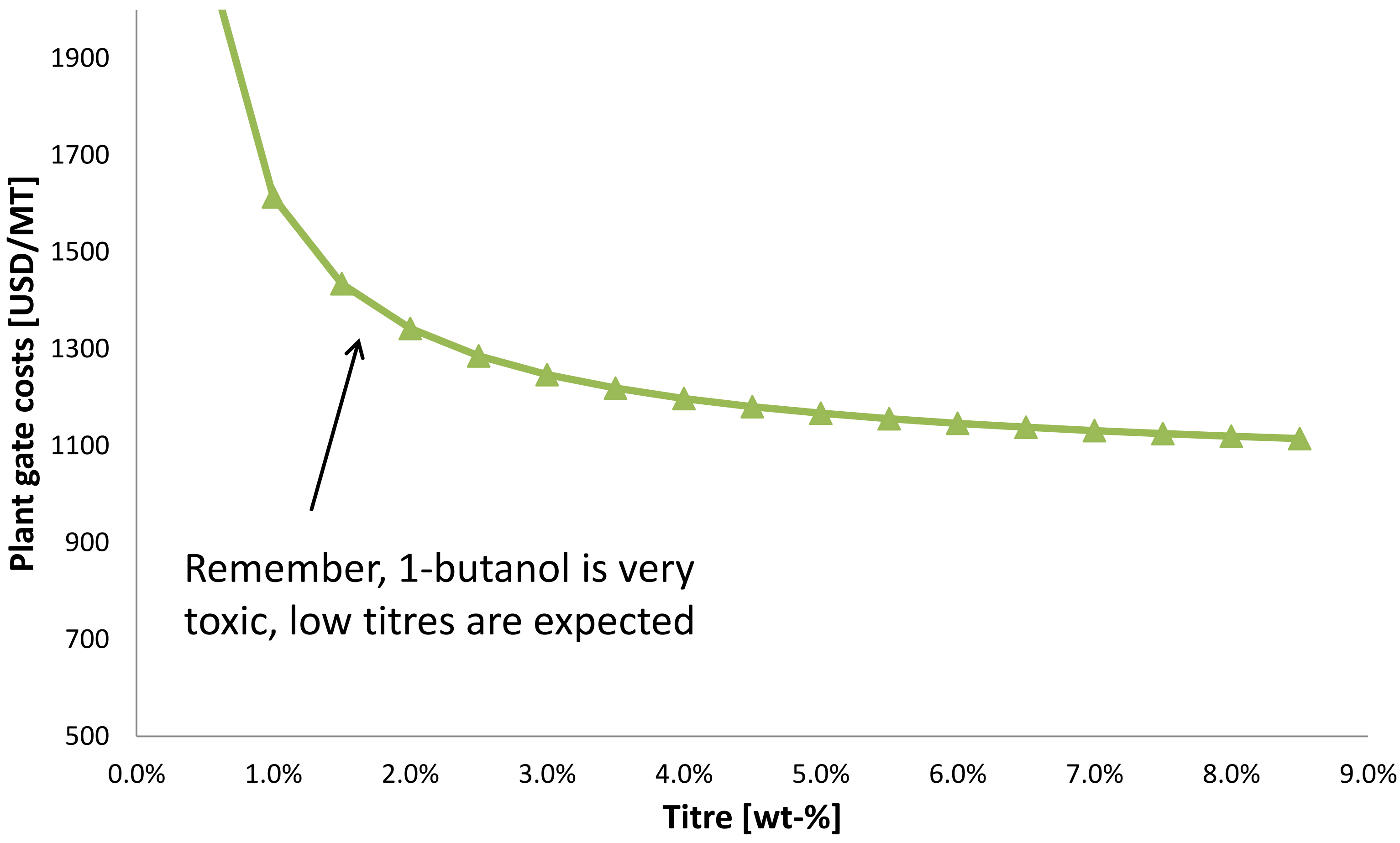
- **Key parameters of fermentation process**
  - Corn (maize): 6 USD/bushel
  - Yield of 1-butanol: 0.381 g/g (or 92.6% of theoretical yield)
  - Titre: 2.0 wt-%
  - Fermentation time: 72 h

- **Realistic or optimistic fermentation process? Remember, we benchmark against an established process!**

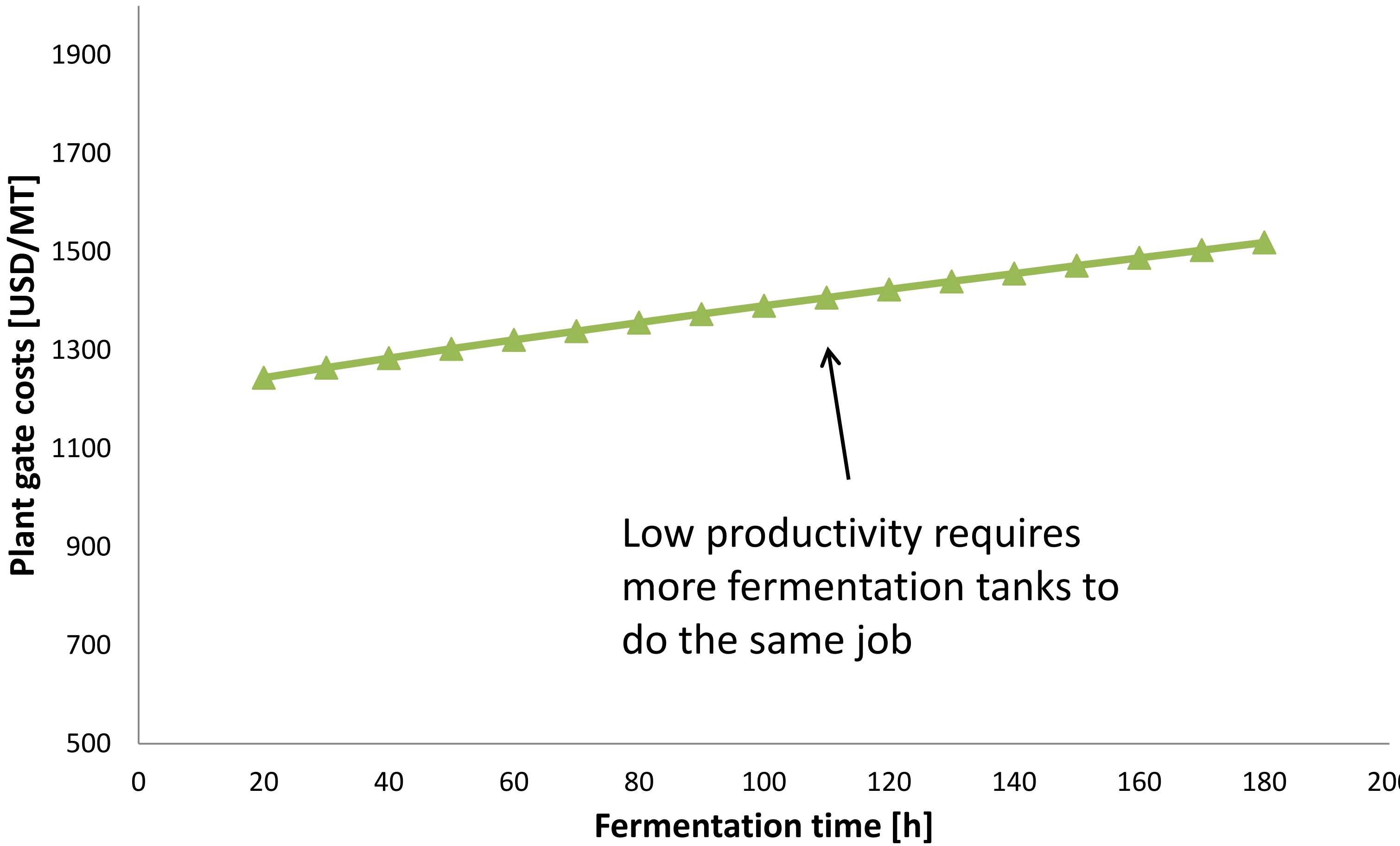
Yield losses should be avoided!



Titre must be high for economic feasibility: It is expensive to operate with dilute systems



Fermentation time is the least important parameter but critical for capacity utilisation



The indifference curve: How does competitiveness change with feedstock prices?

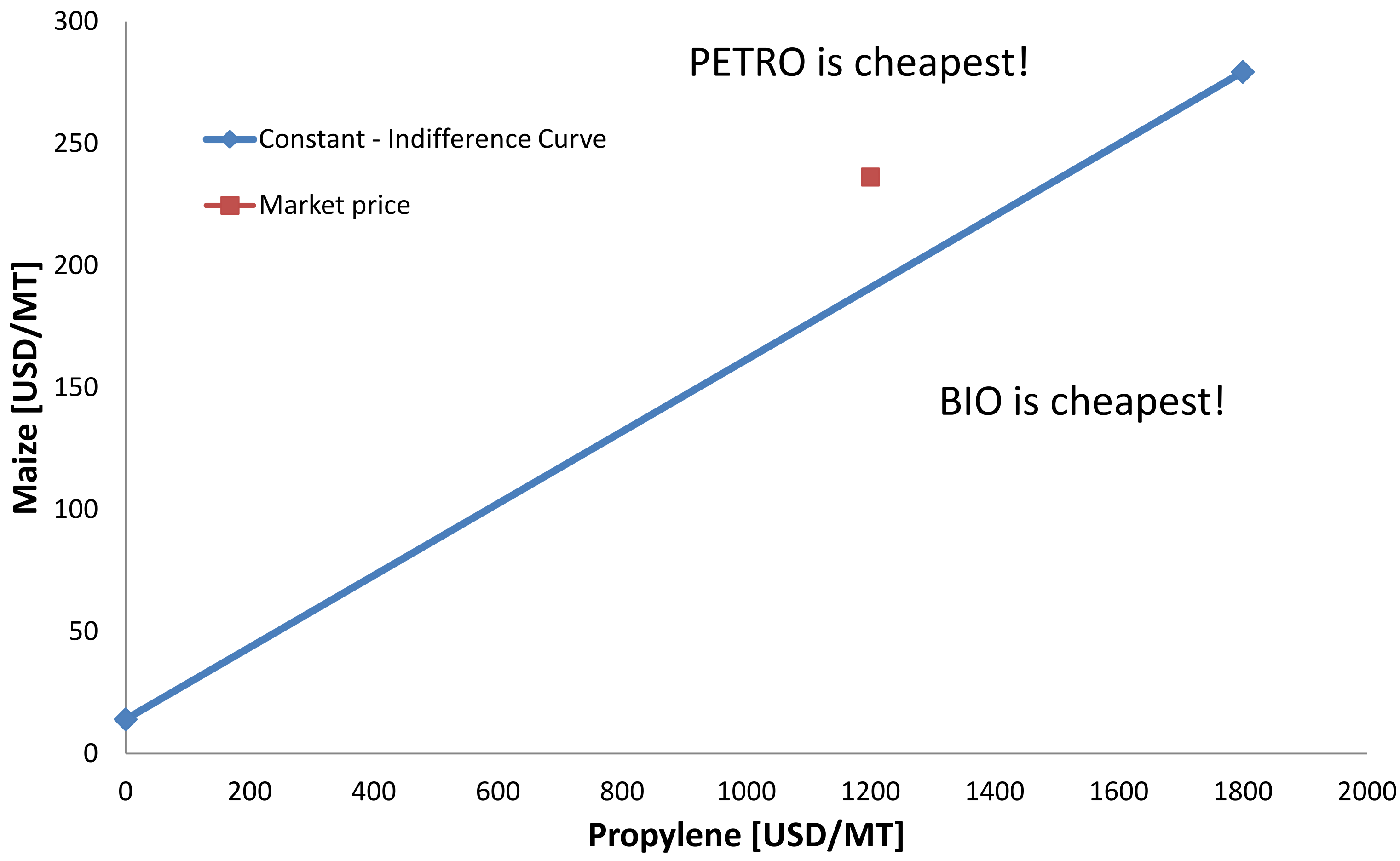
- Fermentation optimisation is great but we heavily dependent on cheap feedstock!
- When are we indifferent between feedstock?
- Assume: Cost of maize (corn) and propylene are variable, everything else is unchanged

Cost of production

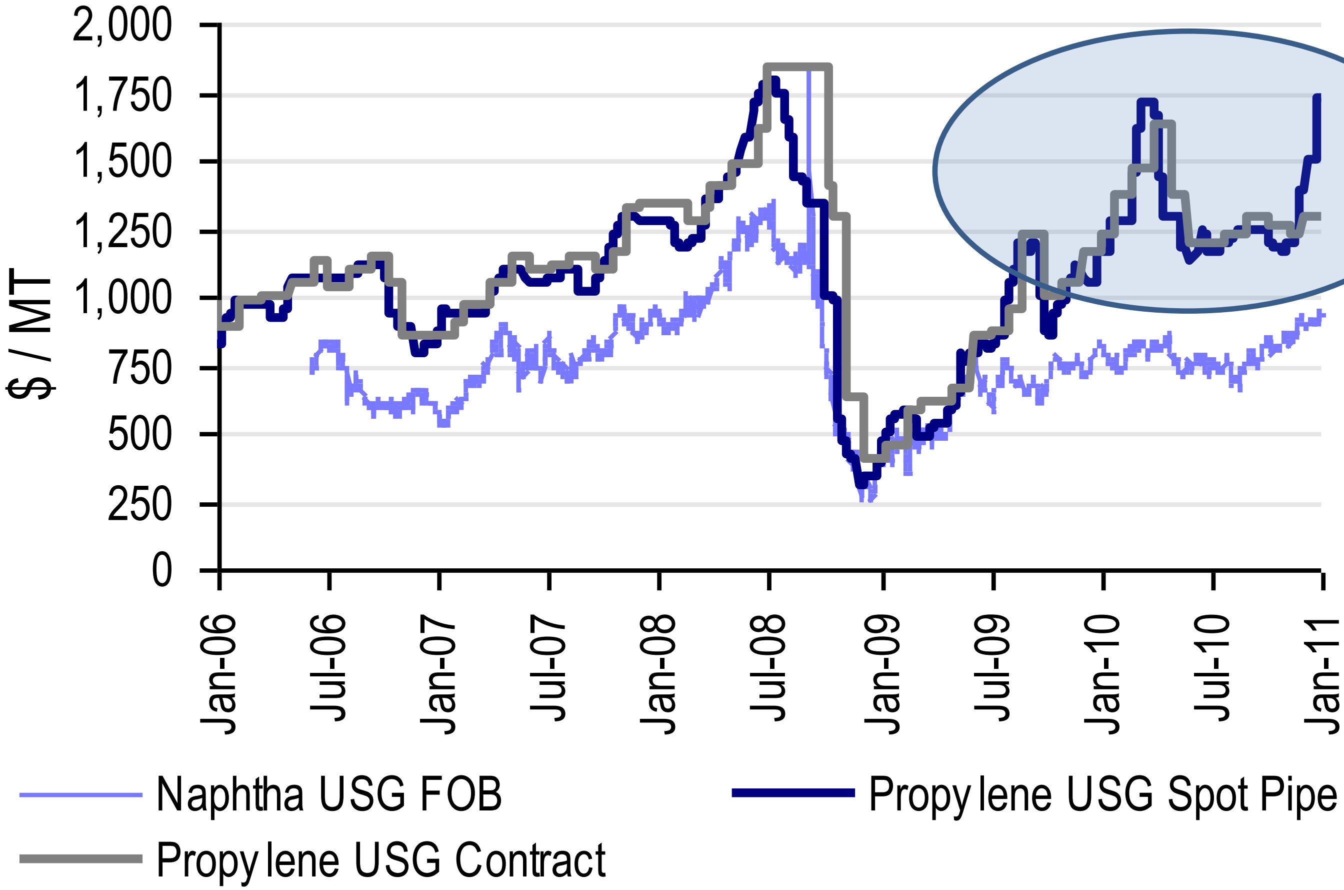
	Intercept	Slope
PETRO	374	0.642
BIO	313	4.355

Note the slope of the curve, below and above 1

The 1-butanol indifference curve



Propylene and C3 chain pulling away from naphtha: A beginning of a new normal?



Source: Thomson Financial

Conclusions on biochemicals

- **Production of commodity biochemicals by fermentation is a new and exciting but also challenging task**

- **Market and technical analysis go hand-in-hand**
  - Availability of <u>cheap feedstock</u> is crucial for economic feasibility
  - Do not "forget" co-product(s) in your analysis
    - "Carbon and Joule" counts in the production process
    - The biorefinery is not a choice – it is a necesity!
  - Process economics is important… so do it at some stage!
  - Your process is not alone, you have to look at competitiveness in a dynamic environment... today and tomorrow!

- **The 1-butanol case is a good example of how the initial market analysis and economic analysis support business development**
  - Further work requires an analysis of R&D resources to develop process
  - Market potential of technology (revenue potential) etc. etc.

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