Reactive and hybrid separations of chemicals and bioactive substances: modelling and optimisation

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Palaeontology

study of prehistoric life forms on Earth through the examination of plant and animal fossils

Introduction

Palaeontologist

researcher working on...

Distillation

Absorption

Extraction

Adaptive Palaeontologist

researcher working on...

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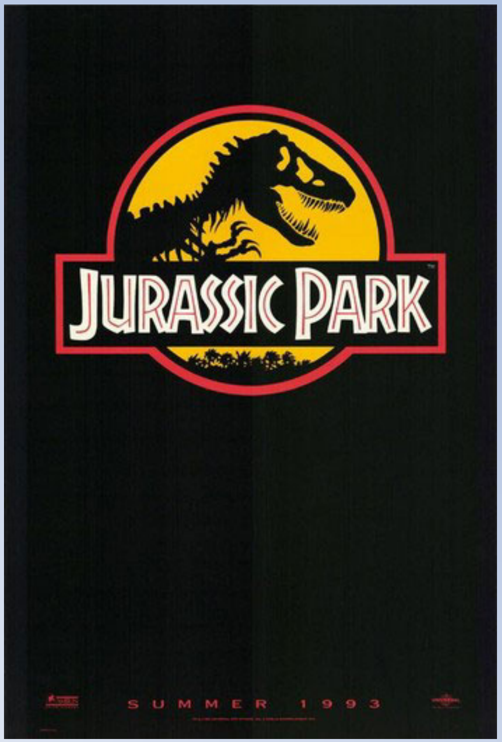
Palaeontologist

researcher working on...

Distillation
Absorption
Extraction



Adaptive Palaeontologist

researcher working on...

(Bio)reactive and Hybrid Separations

Bioseparations

- Bioextraction
- Membrane adsorption
- Downstream Processing

Hybrid Bioseparations

- Distillation & membranes
- …
- …

Distillation
Absorption
Extraction
Membranes

Reactive Separations

- Reactive distillation
- Reactive absorption
- Reactive extraction
- Membrane reactor

Hybrid Separations

- Distillation & membranes
- Extraction & crystallization
- Distillation & crystallization

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  - …
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Distillation
Absorption
Extraction
Membranes

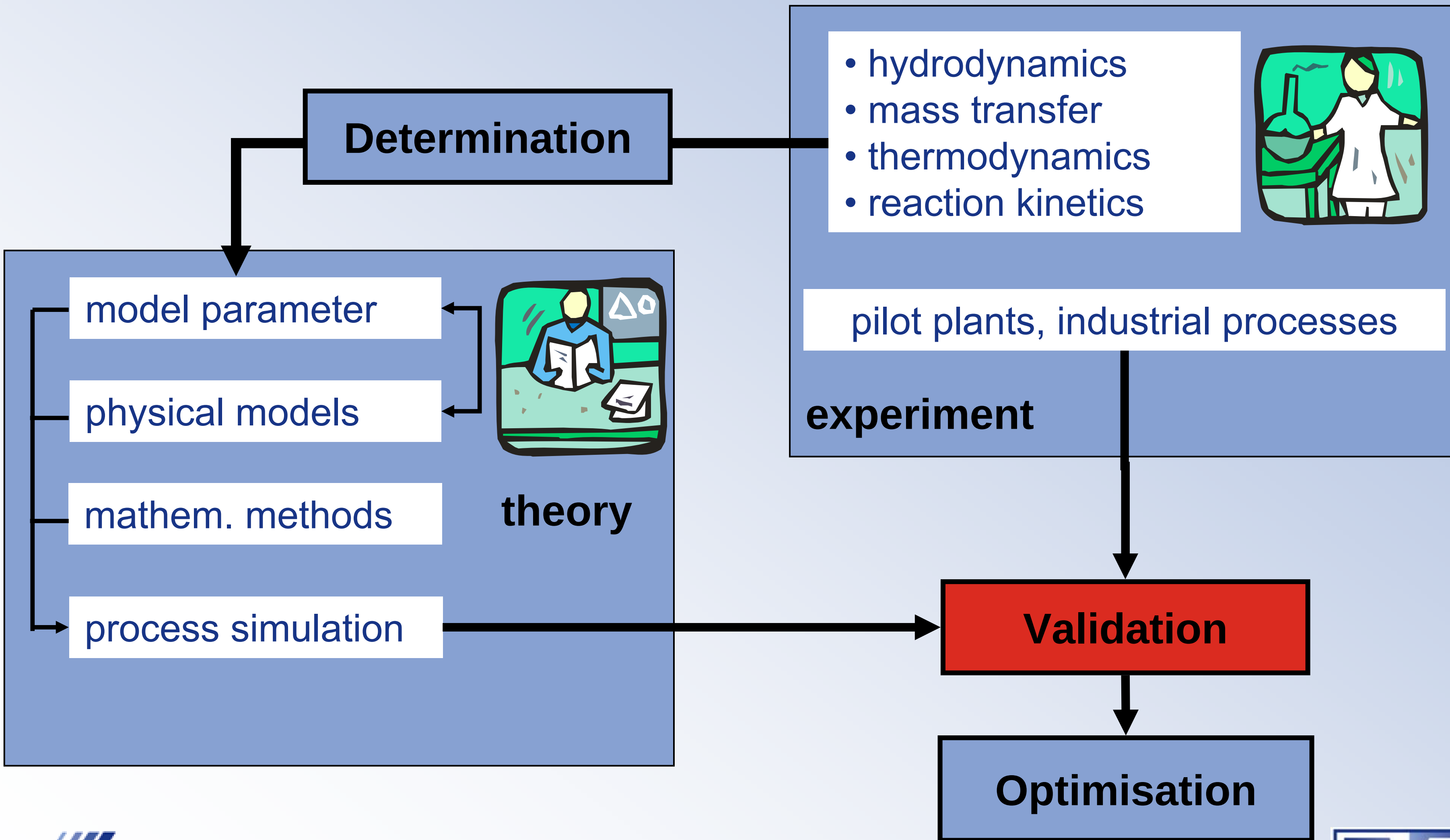
- ***Reactive distillation***
- ***Reactive absorption***
- Reactive extraction
- ***Membrane reactor***

Reactive Separations

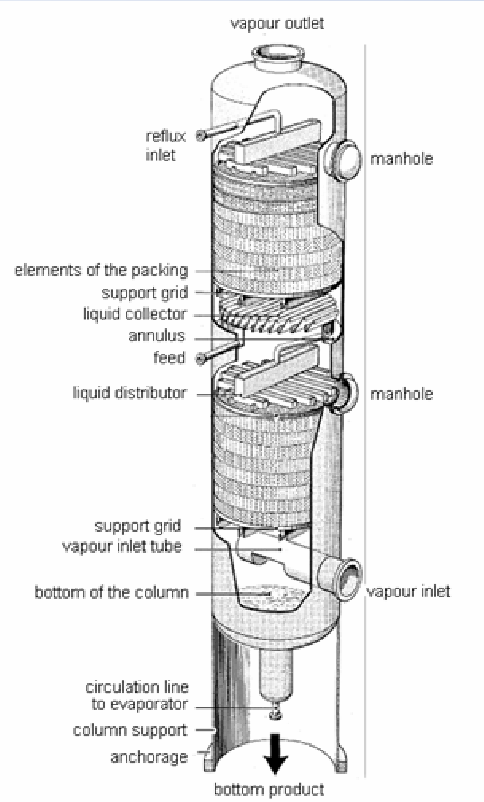
- Distillation & membranes
- Extraction & crystallization
- Distillation & crystallization

Hybrid Separations

Interaction of Experiment and Theory

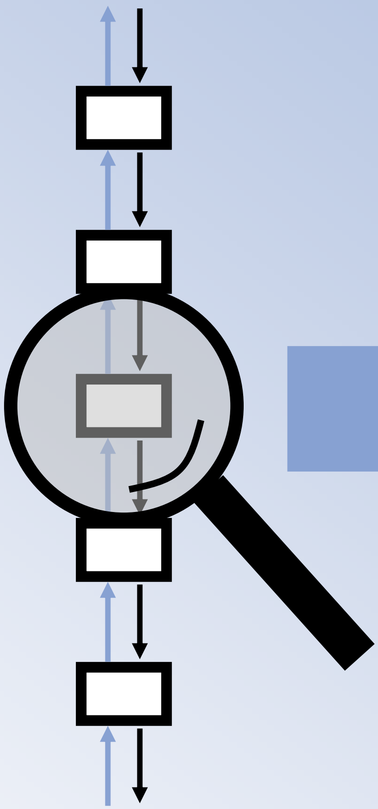


Reactive Separations: Modelling Concept



Assembly of a packed column

Apparatus



Segmented column

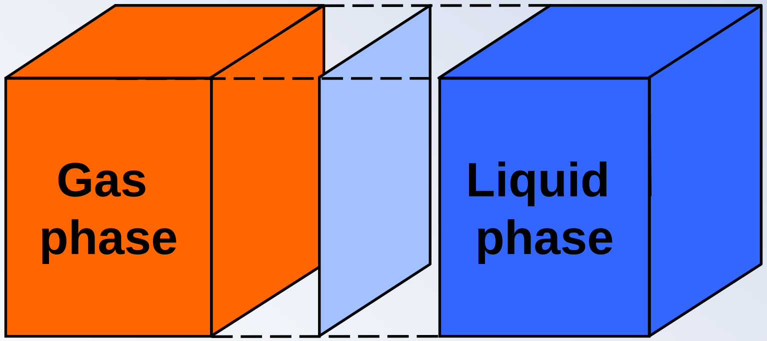
- black-box
- short-cut
- equilibrium stage model
- rate-based approach
- CFD

Stage model

Reactive Separations: Modelling Concept

Equilibrium Stage Model

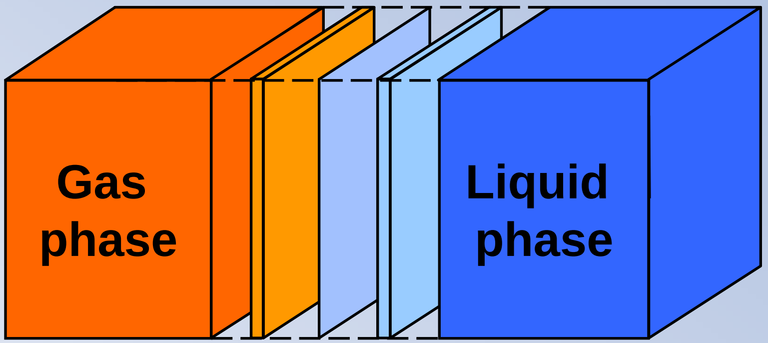
Sorel E.,
Rectification de l'Alcool (1893)



- gas and liquid phase in equilibrium
- efficiency factor to consider the influence of column internals
  Packing: HETP
  Tray: η (Tray efficiency)
- Reaction in bulk phase

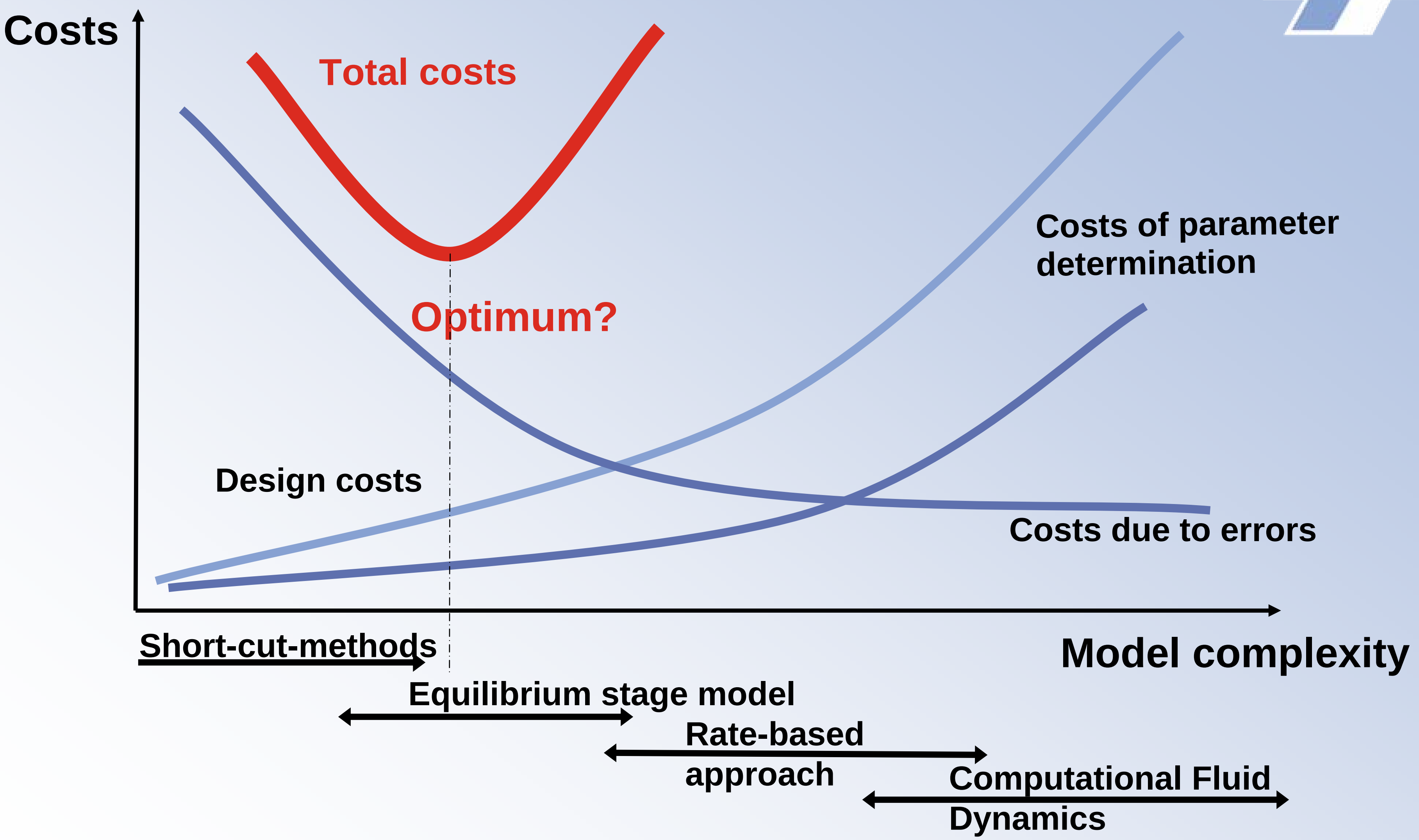
Rate-Based Model

Taylor R., Krishna R.,
Chem. Eng. Sci. 55 (2000)



- only interface in equilibrium
- interfacial area and mass transfer coefficient for different column internals
- reaction in film and bulk phase
- influence of reaction on mass transfer rate

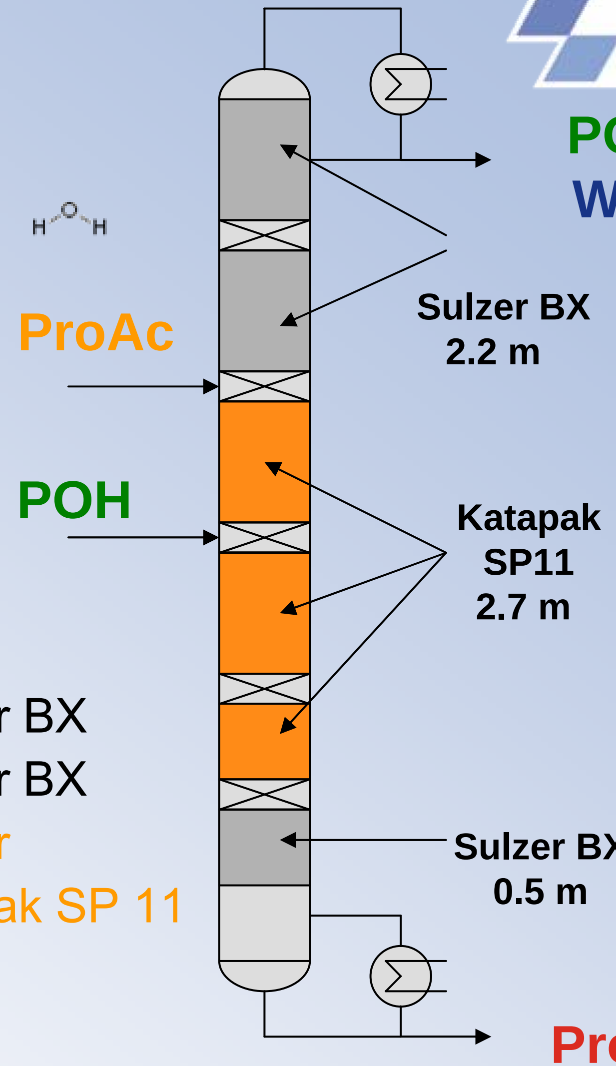
Costs of Computer Aided Process Design

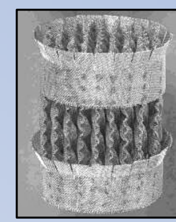


Catalytic Distillation

Synthesis of propyl propionate

Esterification





Column diameter:	50 mm
Height of packing:	5.4 m
Rectifying section:	2.2 m Sulzer BX
Stripping section:	0.5 m Sulzer BX
Catalytic section:	2.7 m Sulzer Katapak SP 11

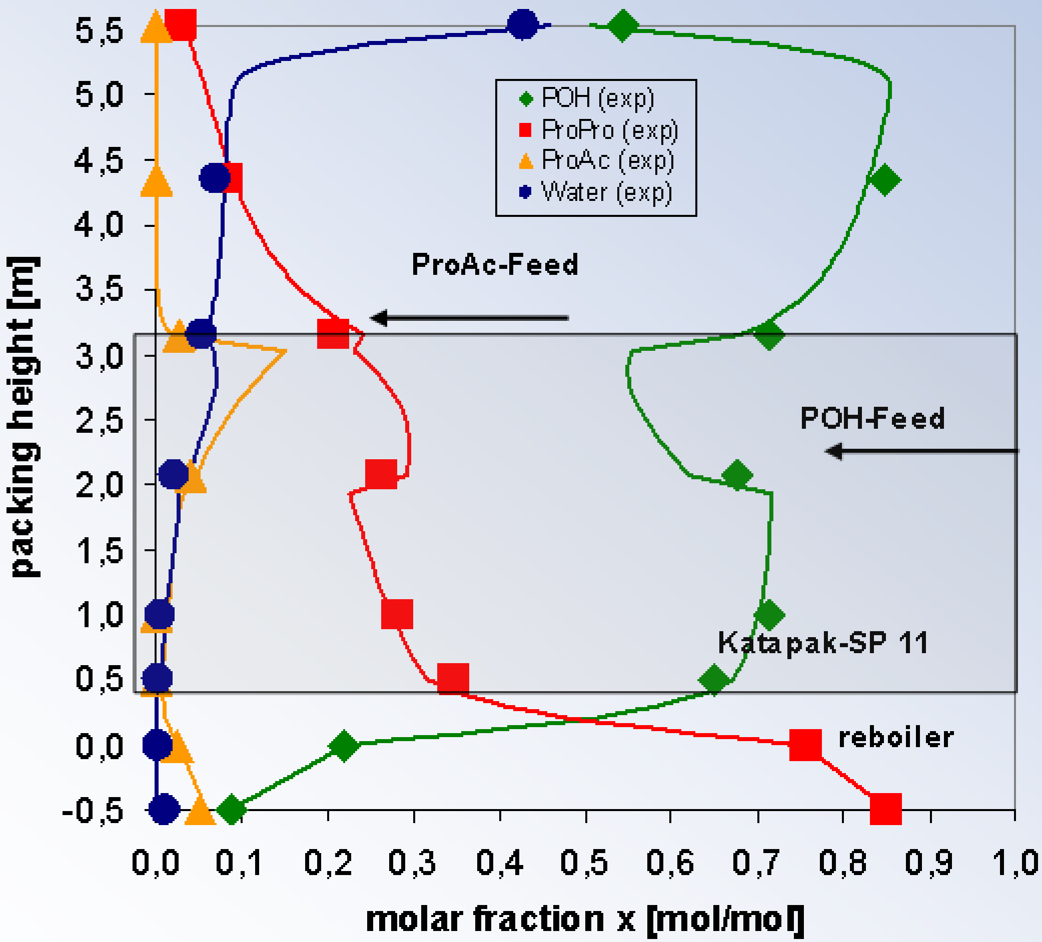
Buchaly C., Kreis P., Górak, A.,
Chemical Engineering and Processing
Sep (2007) accepted

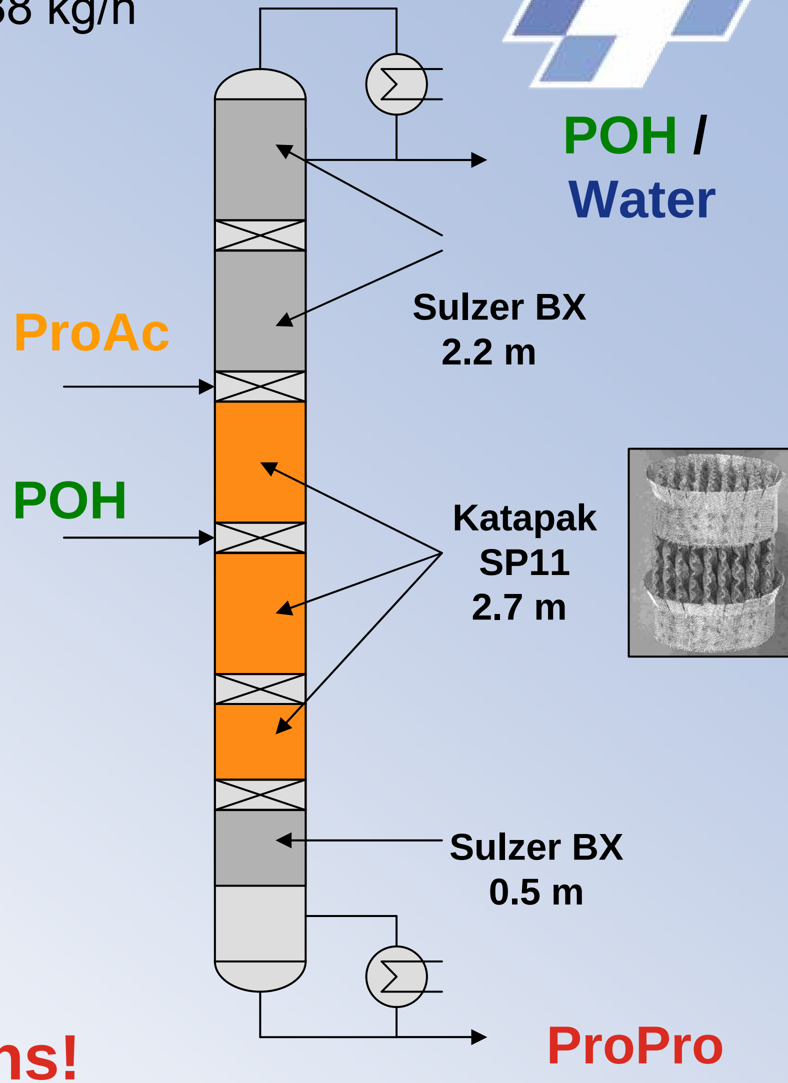
INSERT

TVT

Catalytic Distillation

$\chi_{POH/ProAc}$ 2.0; RR 2.5; feed: 2.0 kg/h; distillate 0.88 kg/h

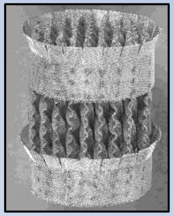




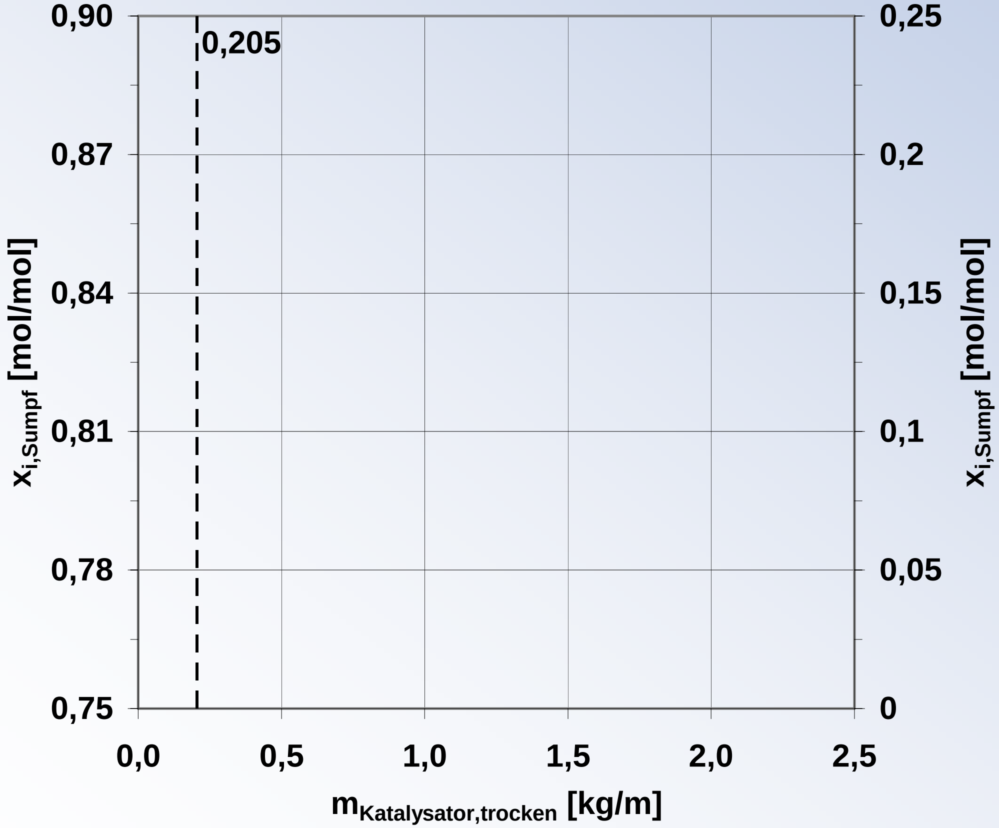
Results from rate-based simulations!

Catalytic Distillation

- Katapak SP-11 (DN50)



⇨ $m_{catalyst,dry}$ = 0,205 kg/m



Catalytic Distillation

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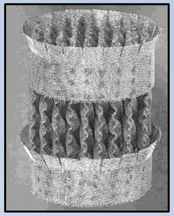

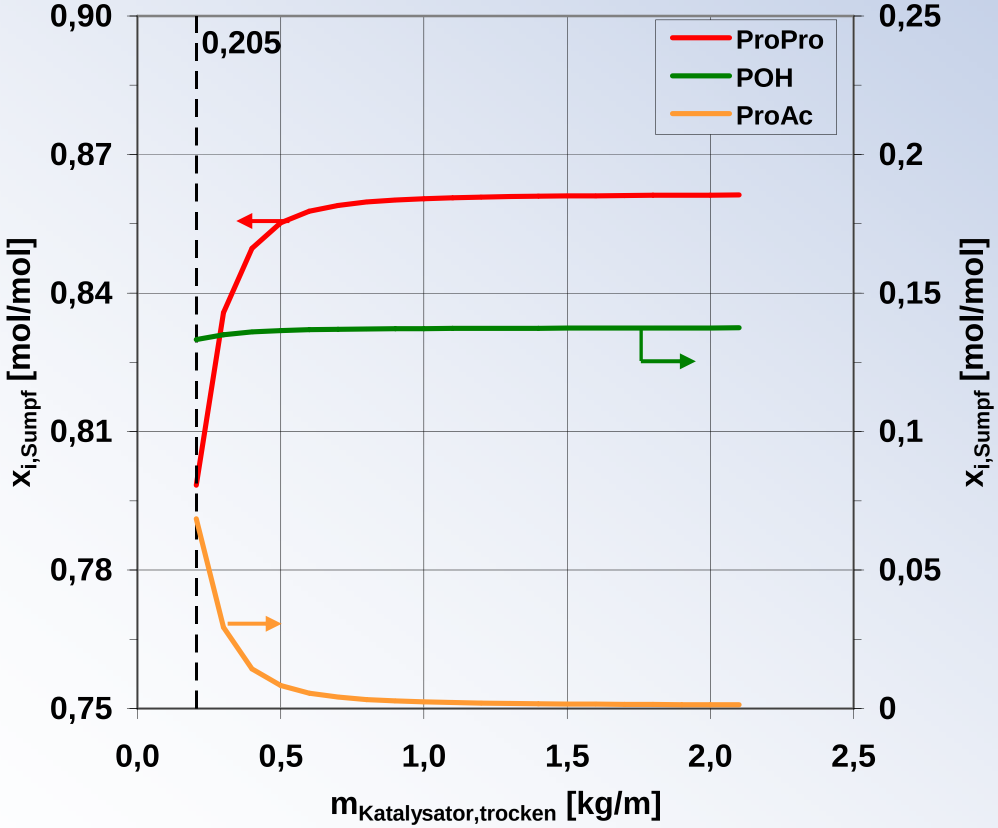

- rate based model
  - validated reference model
  - mass transport limitation & reaction kinetic

Catalytic Distillation

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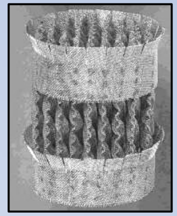
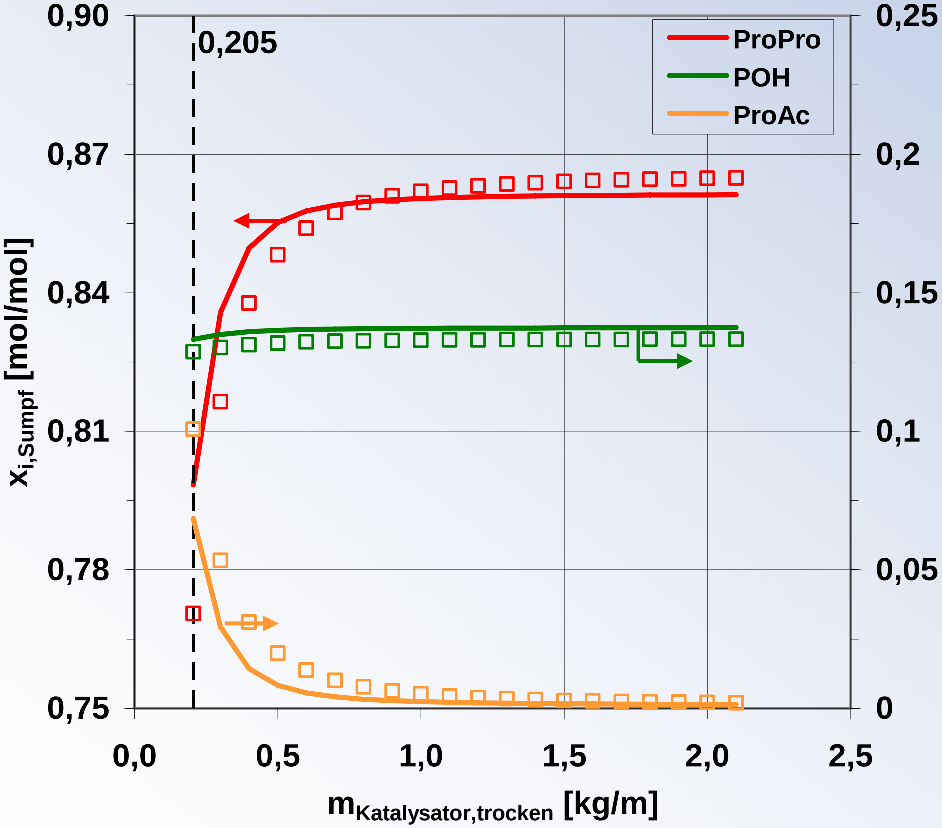




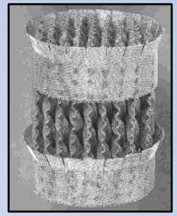
- rate based model
  - validated reference model
  - mass transport limitation & reaction kinetic

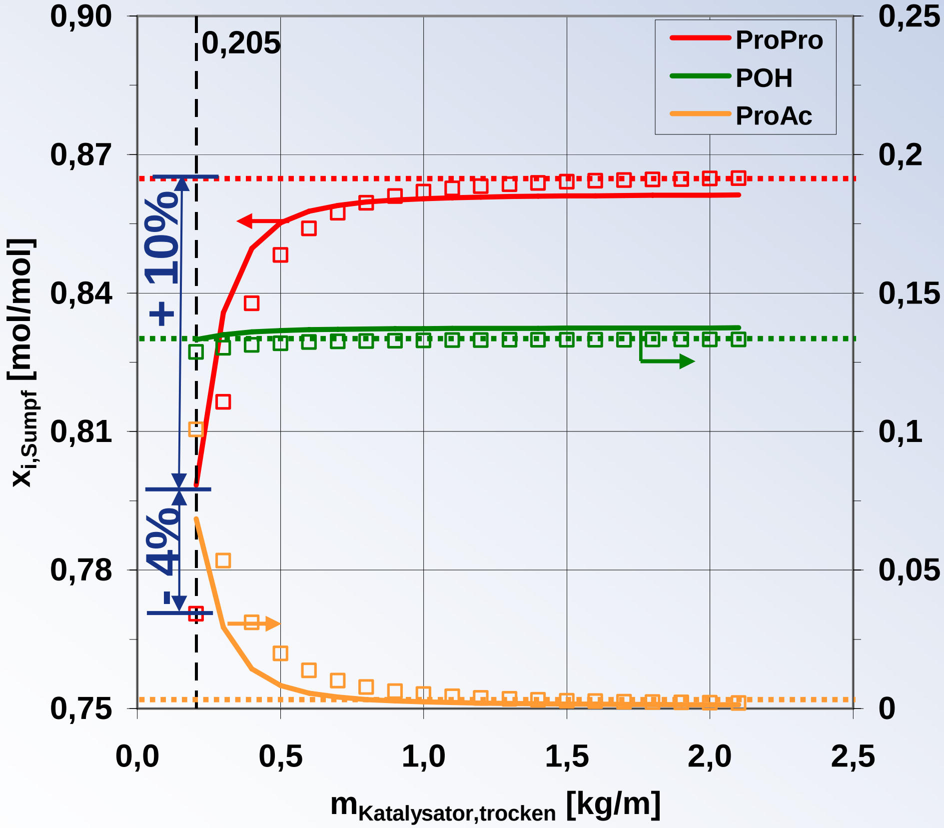
- EQ model with reaction kinetic
  - no mass transport limitation
  - reaction rate << mass transport rate

Catalytic Distillation

- Katapak SP-11 (DN50)

  ⇒ $m_{catalyst,dry}$ = 0,205 kg/m

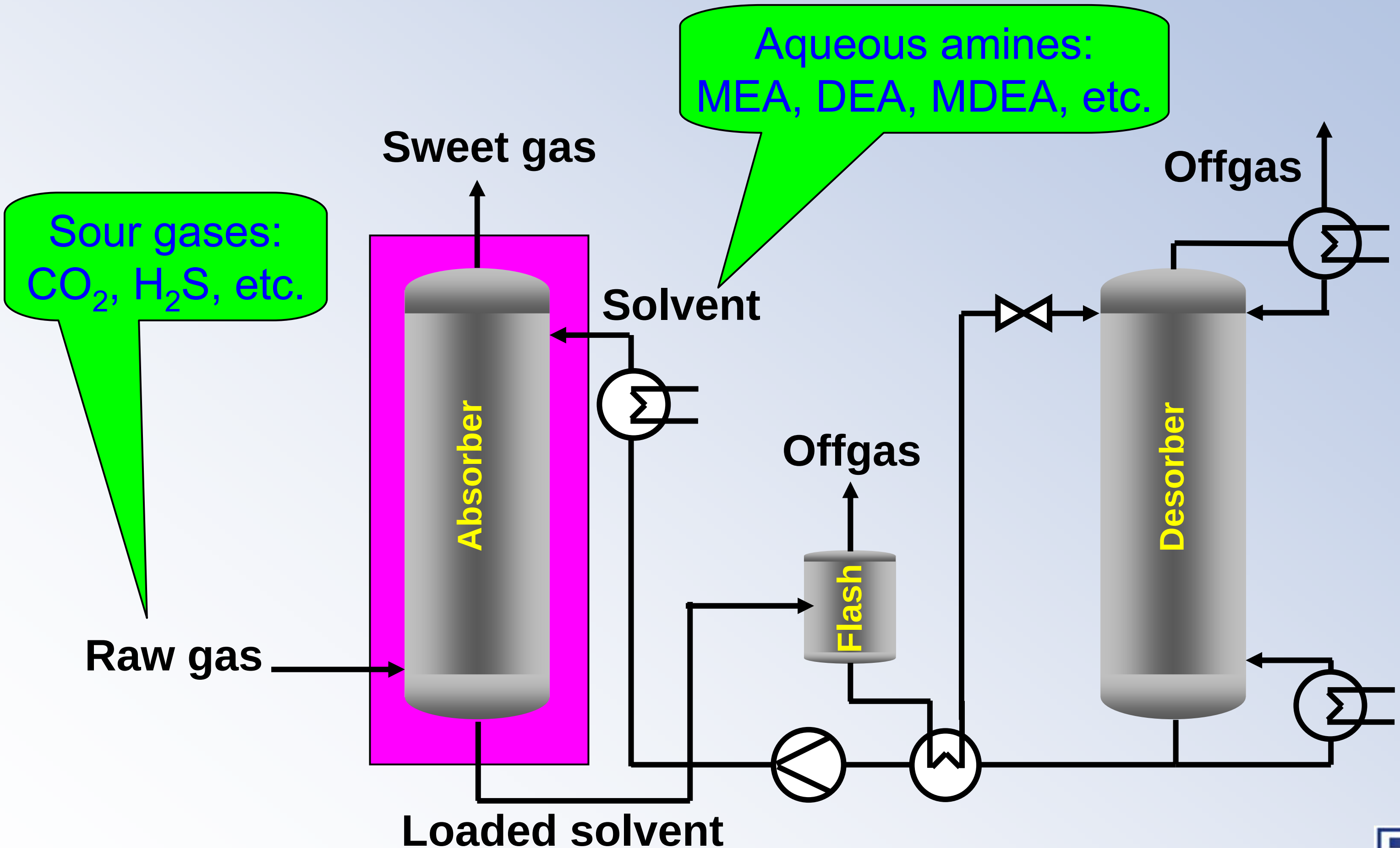




- rate based model
  - validated reference model
  - mass transport limitation & reaction kinetic
- EQ model with reaction kinetics
  - no mass transfer limitation
  - reaction rate << mass transport rate
- EQ model with reaction equilibrium
  - most simple model (VLE, K_{eq})

Equilibrium stage model is a good first approximation

Rate based modelling of sour gas absorption with aqueous amine solutions



Kucka L., Müller, I, Kenig E.Y., Górak A.,
Chem. Eng. Sci. 58 (2003)

Reactive Absorption

Studied system: MEAH-H_2O and CO_2

Kinetically controlled reactions:

$$CO_2 + MEAH + H_2O \rightleftarrows MEACOO^- + H_3O^+$$

$$CO_2 + OH^- \rightleftarrows HCO_3^-$$

Instantaneous reactions:

$$HCO_3^- + H_2O \leftrightarrow H_3O^+ + CO_3^{2-}$$

$$MEAH + HCO_3^- \leftrightarrow MEACOO^- + H_2O$$

$$MEAH + H_3O^+ \leftrightarrow MEAH_2^+ + H_2O$$

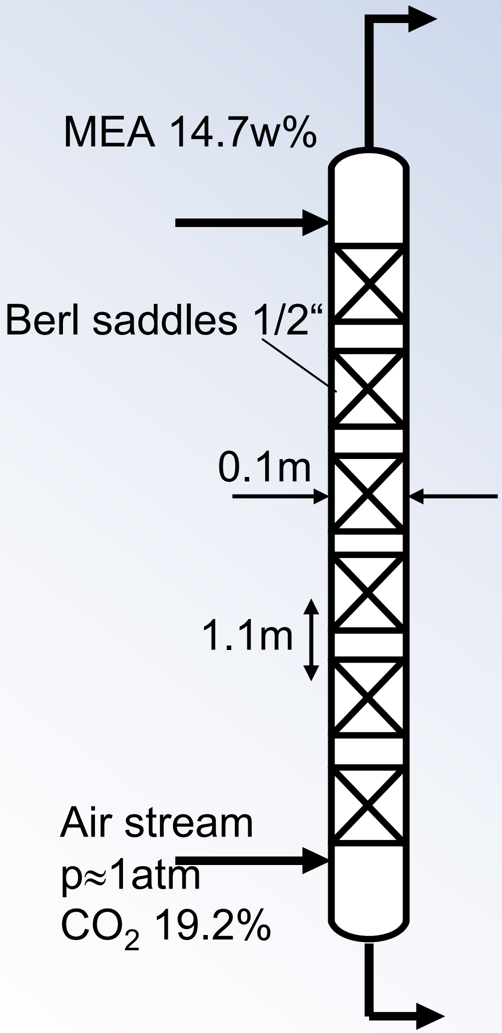
$$2\,H_2O \leftrightarrow H_3O^+ + OH^-$$

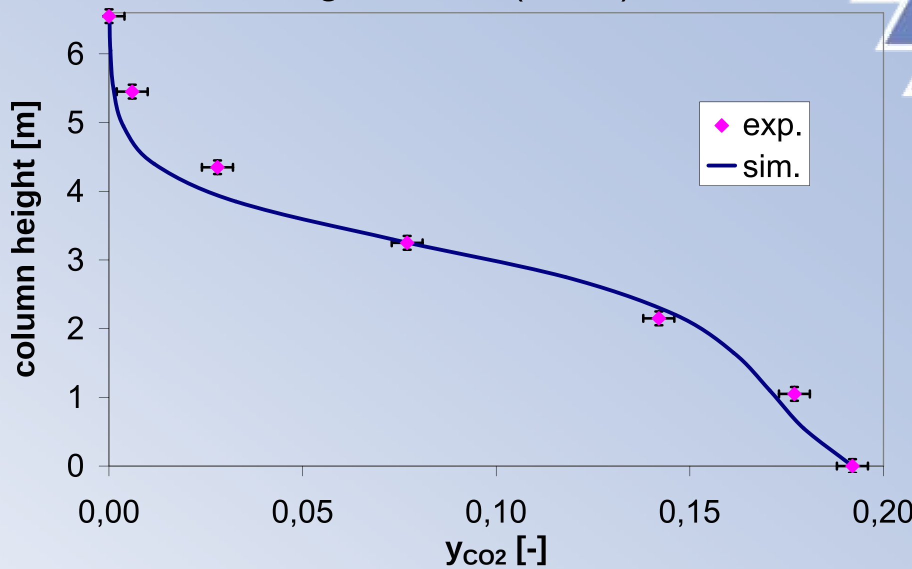
➡ **Complex system:**

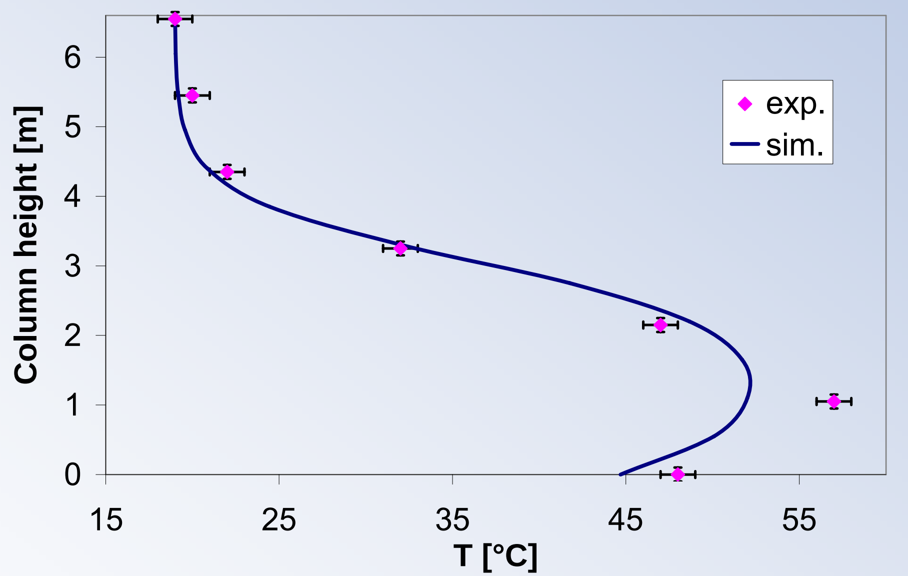
- **Parallel reactions**
- **Consecutive reactions**
- **Electrolytes**

Reactive Absorption

Experiments: Tontiwachwuthikul et al., *Chem. Eng. Sci. 47* (1992)







Rate-based approach is a MUST!

aspentech
process. to the power of e.

Modeling Gas Absorption Processes

- Based on Aspen Custom Modeler, Kucka et al. (2003) developed one of the most rigorous rate-based models to simulate acid gas absorption by aqueous amine solutions.
- Kucka et al. (2003) summarized that rigorous, first principles based mathematical models for amine acid gas treating processes should consider :
  - Electrolyte thermodynamics,
  - Reaction kinetics,
  - Heat and mass transfer resistance,
  - Column configuration and hydrodynamics.

Kucka, L., Müller, I., Kenig, E.Y., Górak, A., “On the Modeling and Simulation of Sour Gas Absorption by Aqueous Amine Solutions,” *Chem. Eng. Sci.*, ***58***, 3571-3578 (2003)

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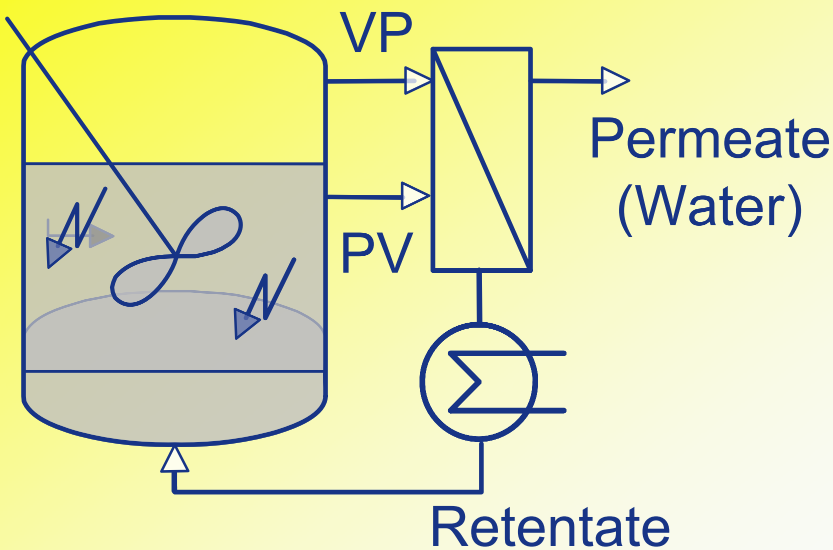
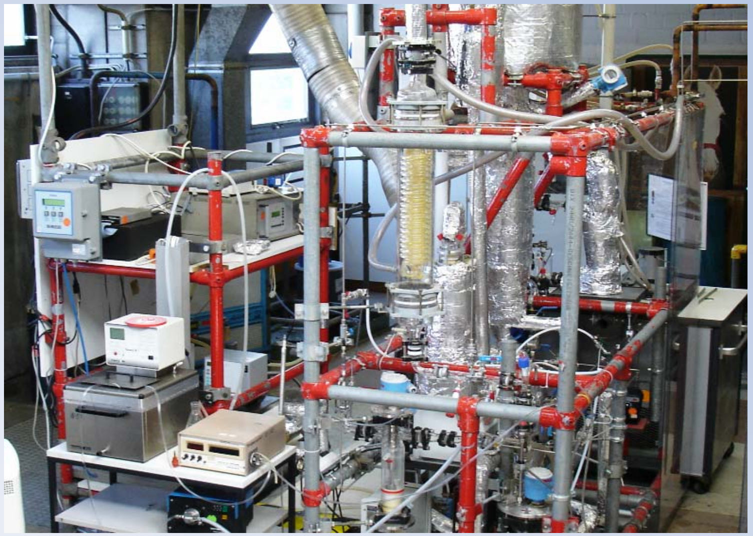
From: Chau-Chyun C. et al., Annual AIChE Meeting, San Francisco (2006)

Membrane Reactor

- Dewatering of heterogeneously catalyzed batch esterification by pervaporation to shift equilibrium
- Experimental investigation of pilot scale membrane reactor
- Process analysis of membrane reactor
- Scale up of flat membrane modules (lab scale to pilot scale)



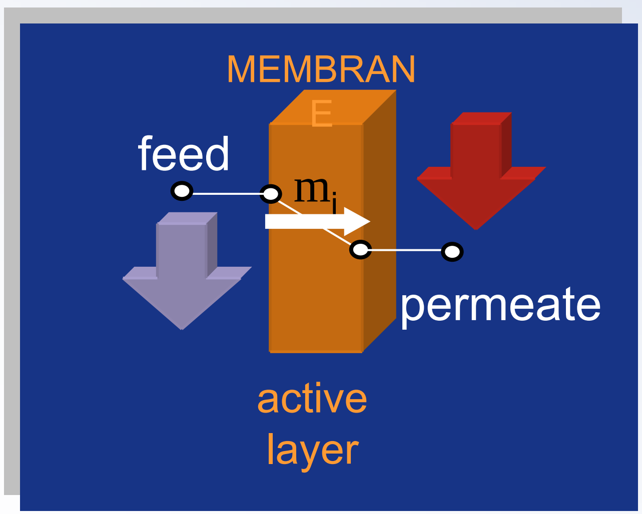
Alcohol + Acid ↔ Ester + Water

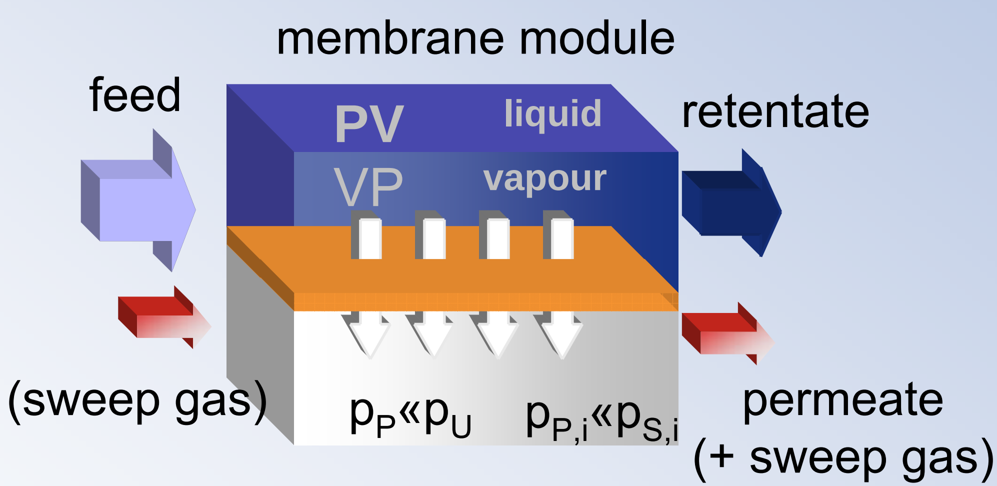


Membrane reactor equipped with 0.5 m^2 membrane area from Sulzer Chemtech

Separation of liquid (PV) / vapour (VP) mixtures

- application of „dense" polymeric membranes or inorganic membranes
- mass transport: sorption, diffusion and desorption ->SDM
- driving force: difference in chemical potential

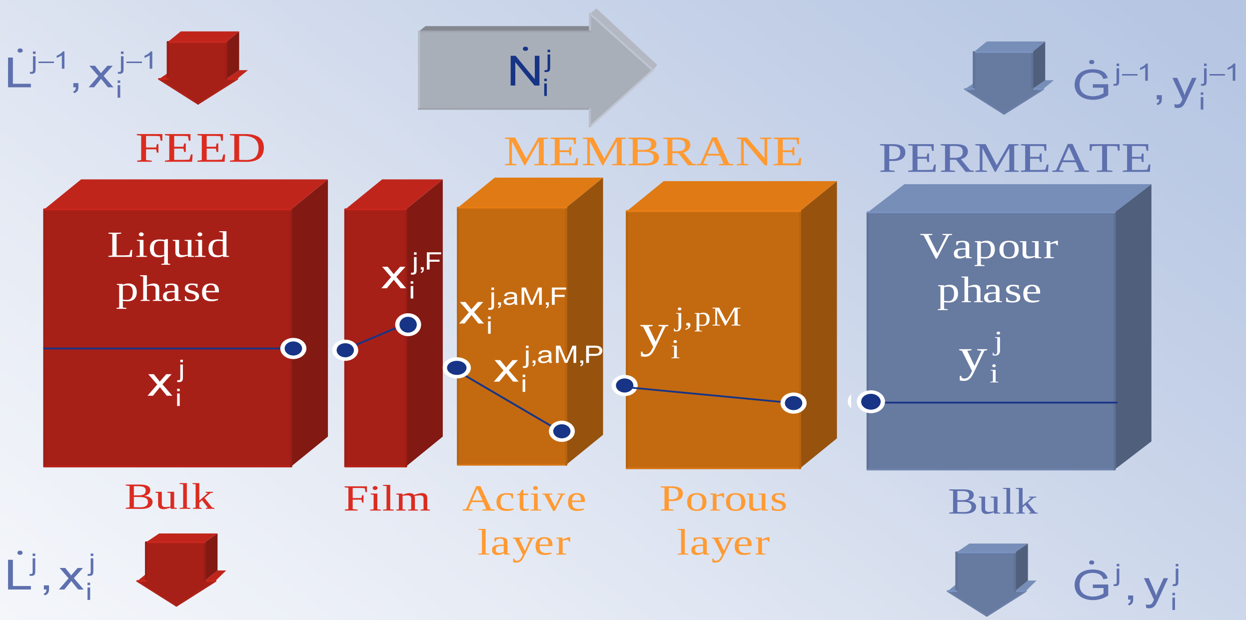




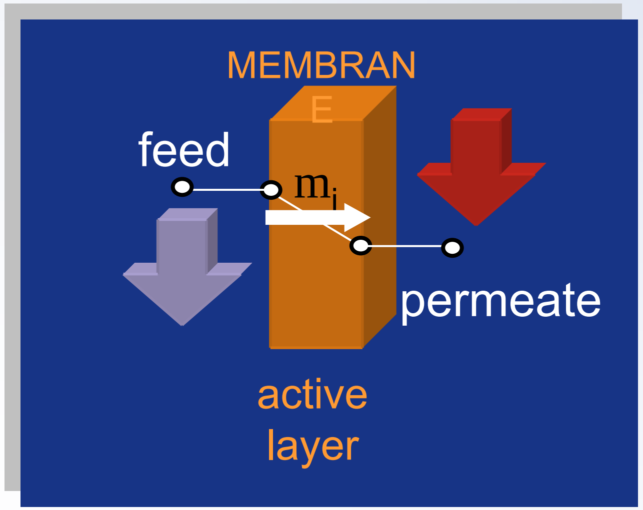
$$N_i^j = Q_i^j \cdot \Delta DF_i^j$$

flux = permeance x driving force

Membrane Reactor



Rate based modelling of membrane separation



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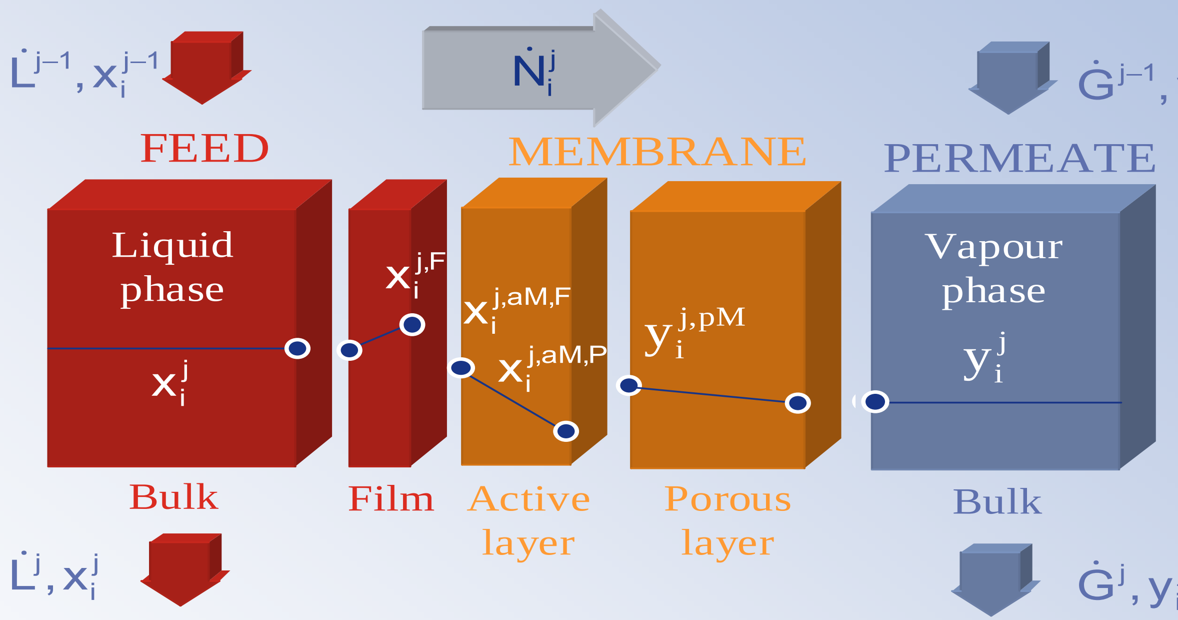
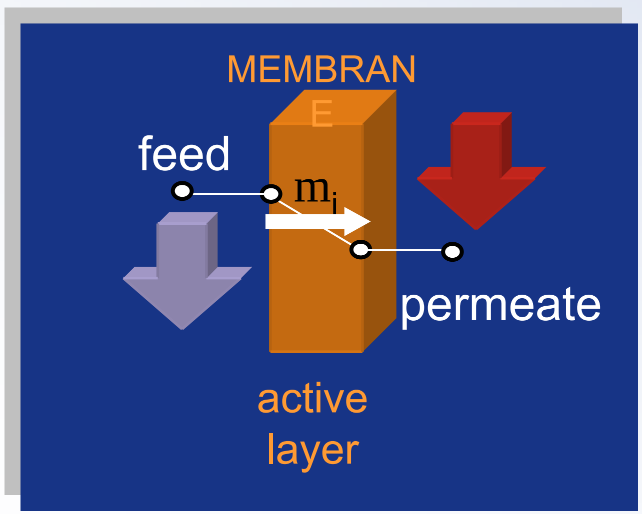


Rate based modelling of membrane separation

mass transport model	permeance Q	
short-cut model (SC)	Q_i^0	constant
Arrhenius (AR)	$Q_i^0 \cdot exp\left(-\frac{E_i}{R}\left(\frac{1}{T^0}-\frac{1}{T}\right)\right)$	T-dependent
Meyer-Blumenroth (MB)	$\frac{\bar{D}_i(T)}{\bar{\gamma}_i}$	DF: activities
Hömmerich (HÖ)	$A_i^* \frac{b_i(T) \cdot a_i^F}{1 + b_i(T) \cdot a_i^F} \cdot \frac{1}{\bar{a}_i}$	DF: activities
sorption/diffusion (SD)	$\frac{\bar{c}_i(T) \cdot \bar{D}_i(T)}{\bar{f}_i} \cdot \frac{1}{\delta_M}$	DF: fugacities



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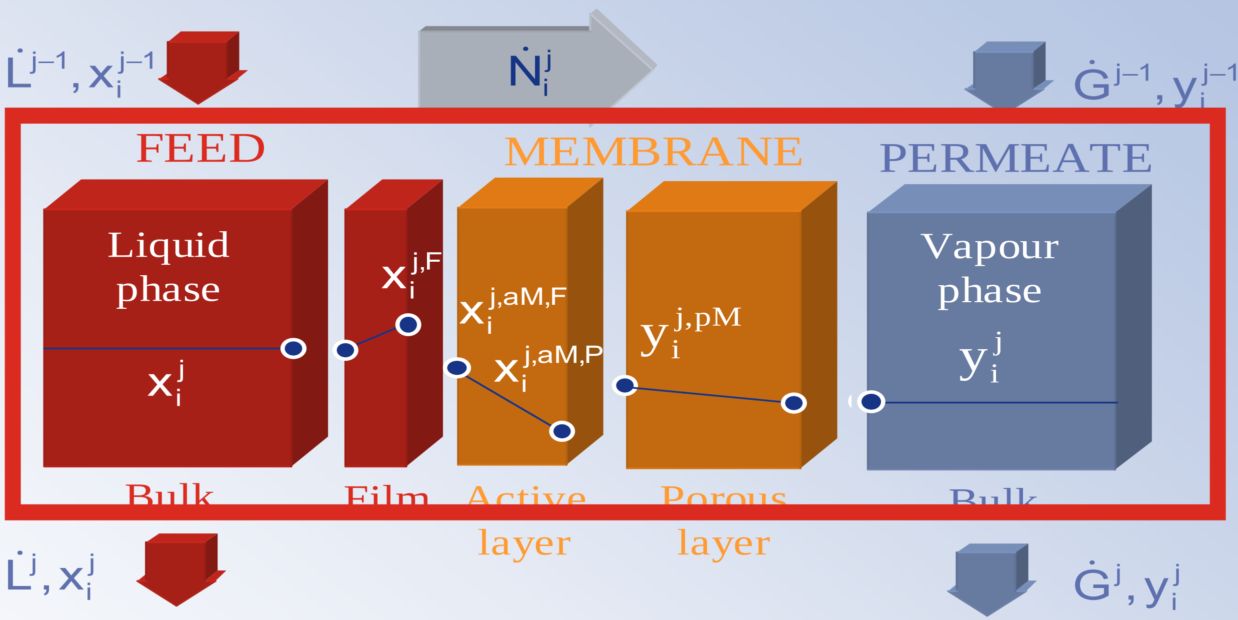
Membrane Reactor



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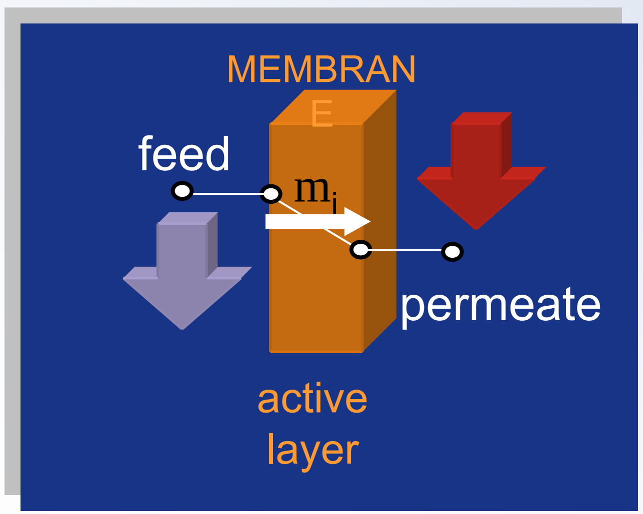

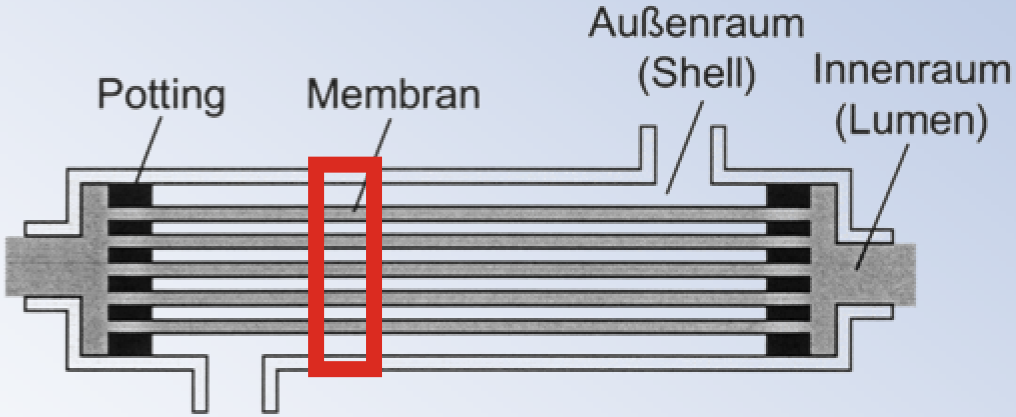

$$N_i^j = Q_i^j \cdot \Delta DF_i^j$$

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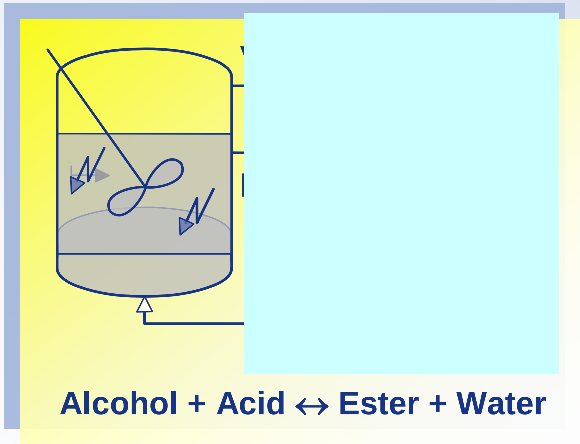
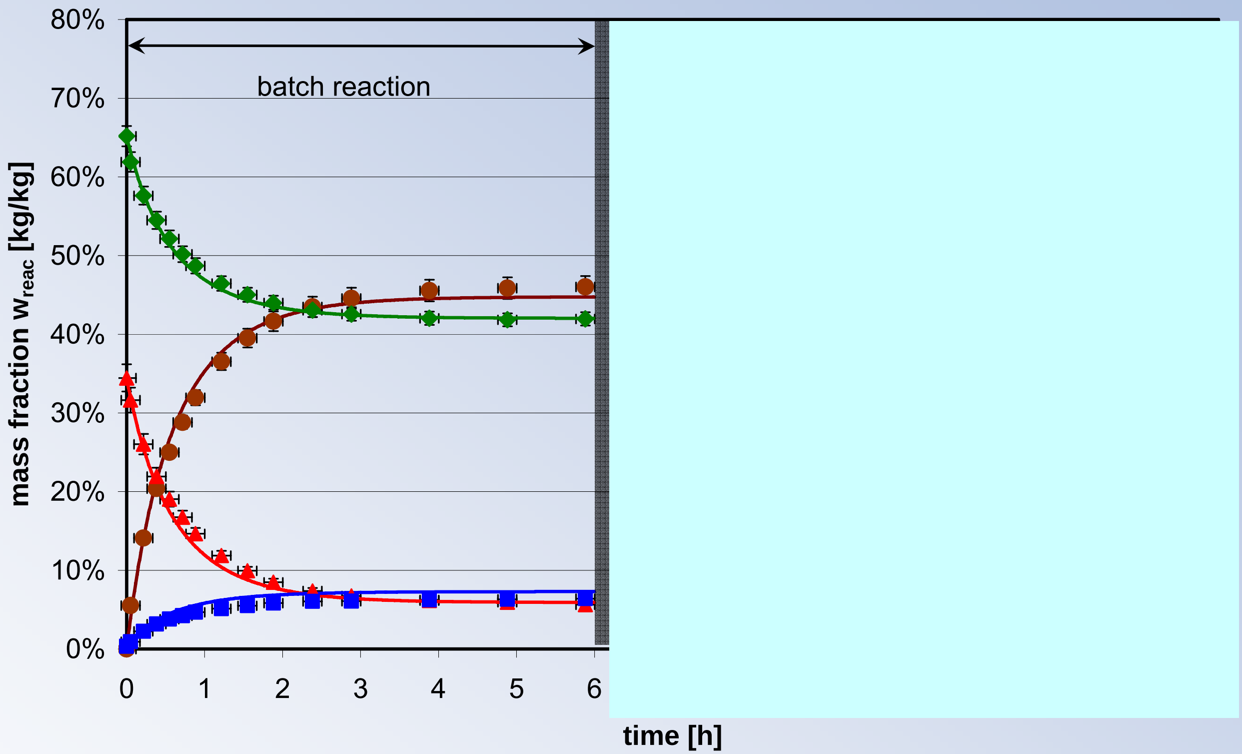
Membrane Reactor

- Initial alcohol to acid ratio: 2.3 : 1
- Batch reaction at 83°C in fixed bed side reactor with Amberlyst 46

➔ **propionic acid conversion: 83% after 6 hours**





exp. vs. sim.

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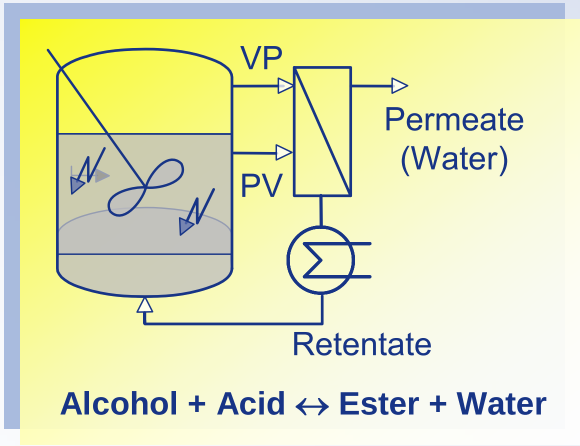

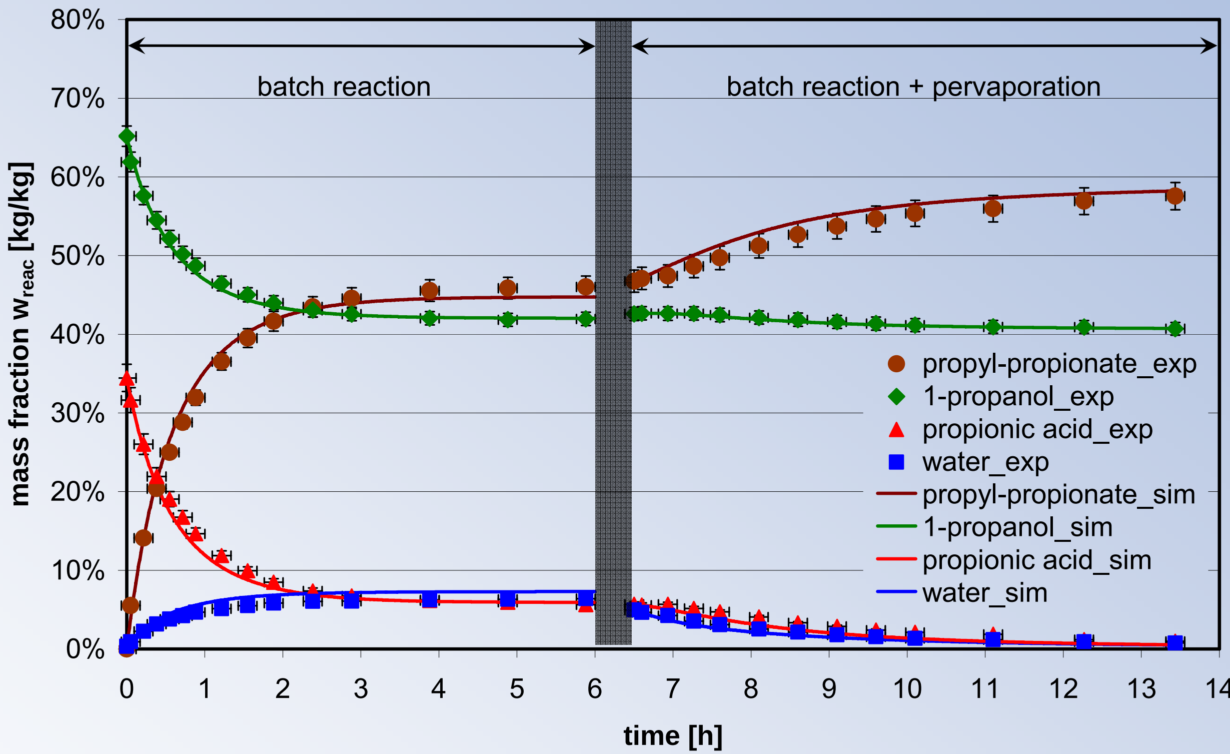

exp. vs. sim.

- Batch reaction at 83°C and pervaporation at 85°C

propionic acid conversion: 99% after 13.5 hours

(Bio)reactive and Hybrid Separations

Bioseparations

- Bioextraction
- Membrane adsorption
- Downstream Processing

Hybrid Bioseparations

- Distillation & membranes
  - …
    - …

Distillation

Absorption

Extraction

Membranes

- Reactive distillation
- Reactive absorption
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Reactive Separations

- Distillation & membranes
- Extraction & crystallization
- Distillation & crystallization

Hybrid Separations

(Bio)reactive and Hybrid Separations

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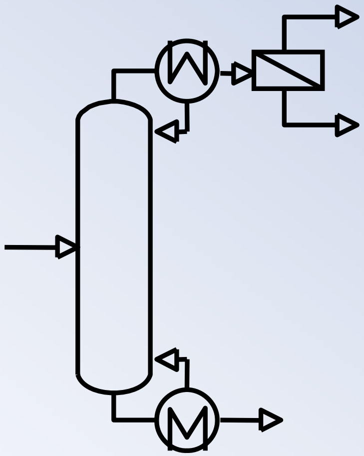
Hybrid Separations

- *Distillation & membranes*
- Extraction & crystallization
- *Distillation & crystallization*

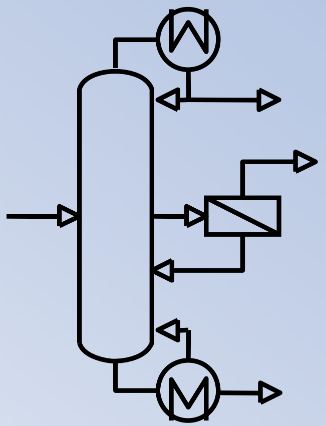
Membrane Assisted (Reactive) Distillation



- **Azeotropic binary mixtures**

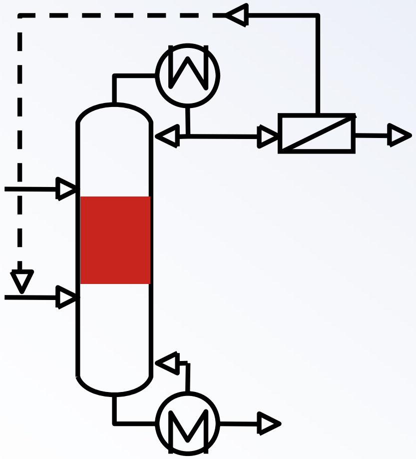
  Splitting of azeotropes with VP

  (Bio-Ethanol)



- **Non-ideal multicomponent mixtures**

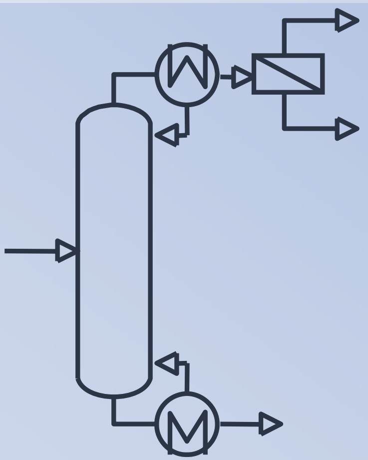
  Selective removal of one component



- **Multicomponent reacting mixtures**

  Recovering of educts with VP

Membrane Assisted (Reactive) Distillation



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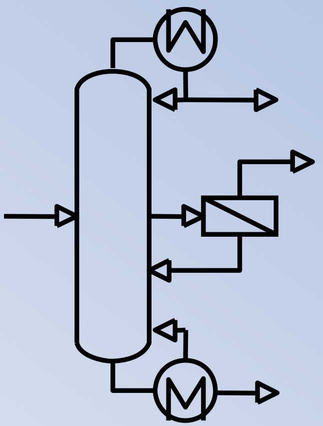
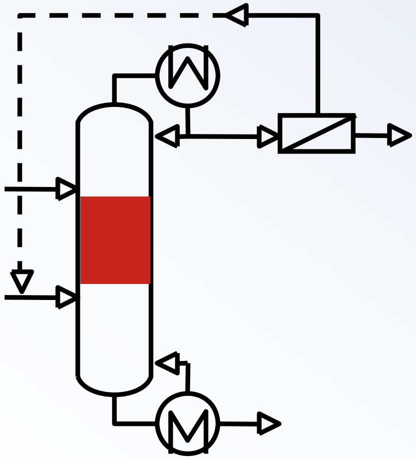
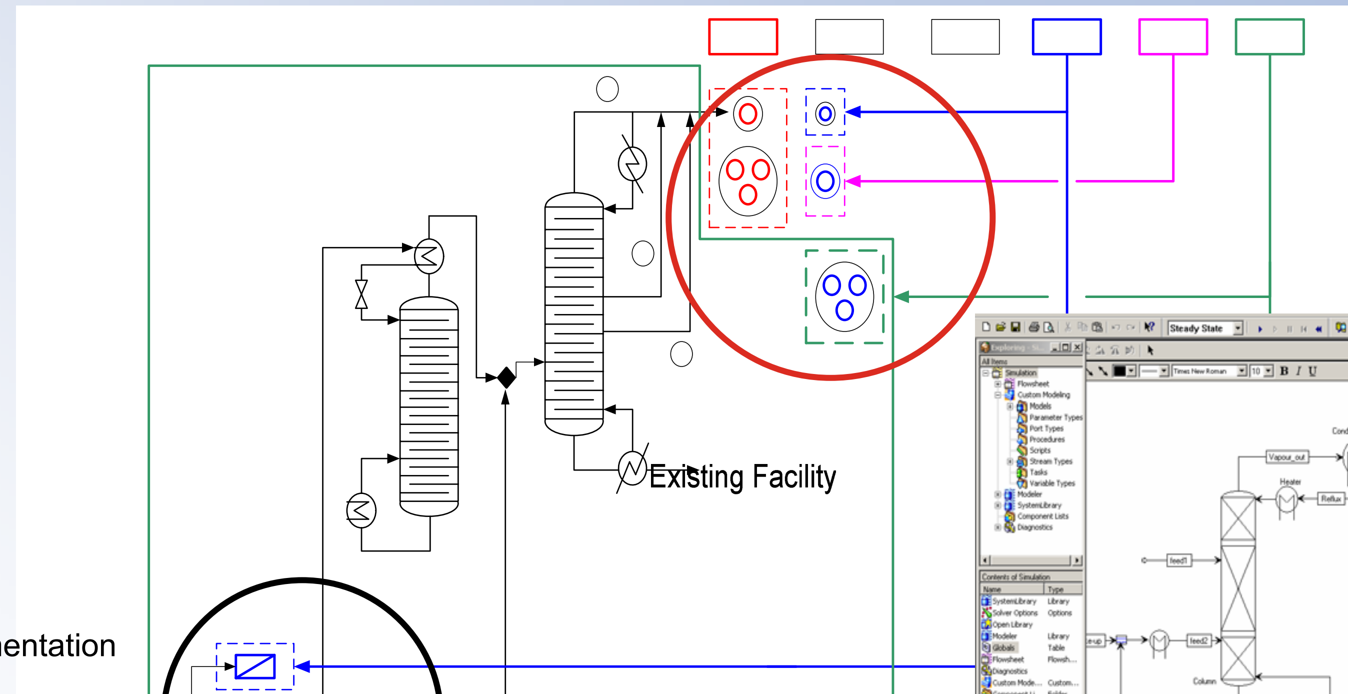




- **Multicomponent reacting mixtures**

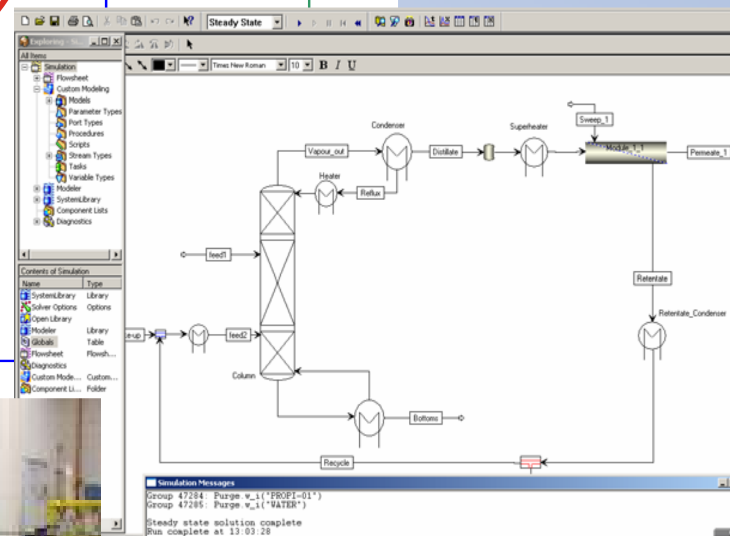
  Recovering of educts with VP

Bioethanol production

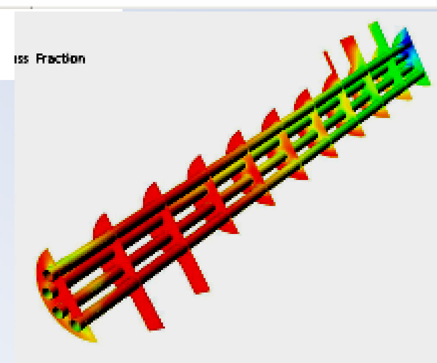


Fermentation broth

Detailed modelling, simulation & optimization



lab & pilot plant experiments for model validation



Integrated material and process development

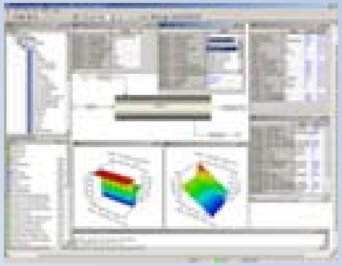
procedure

membrane development

experiments in lab scale

determination of the model parameter

simulation studies in industrial scale



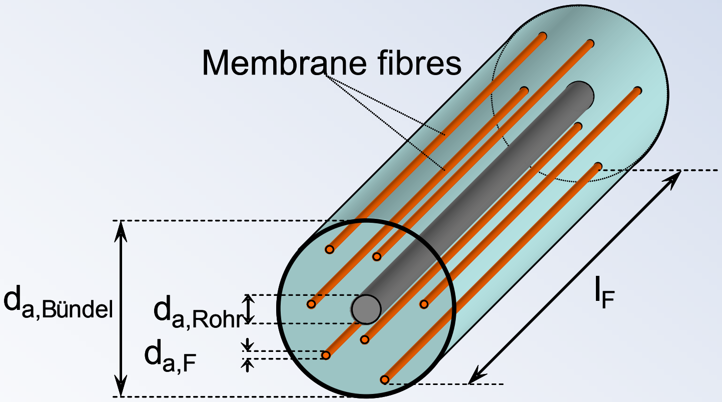
Courtesy Whitefox Techn.

optimal membrane

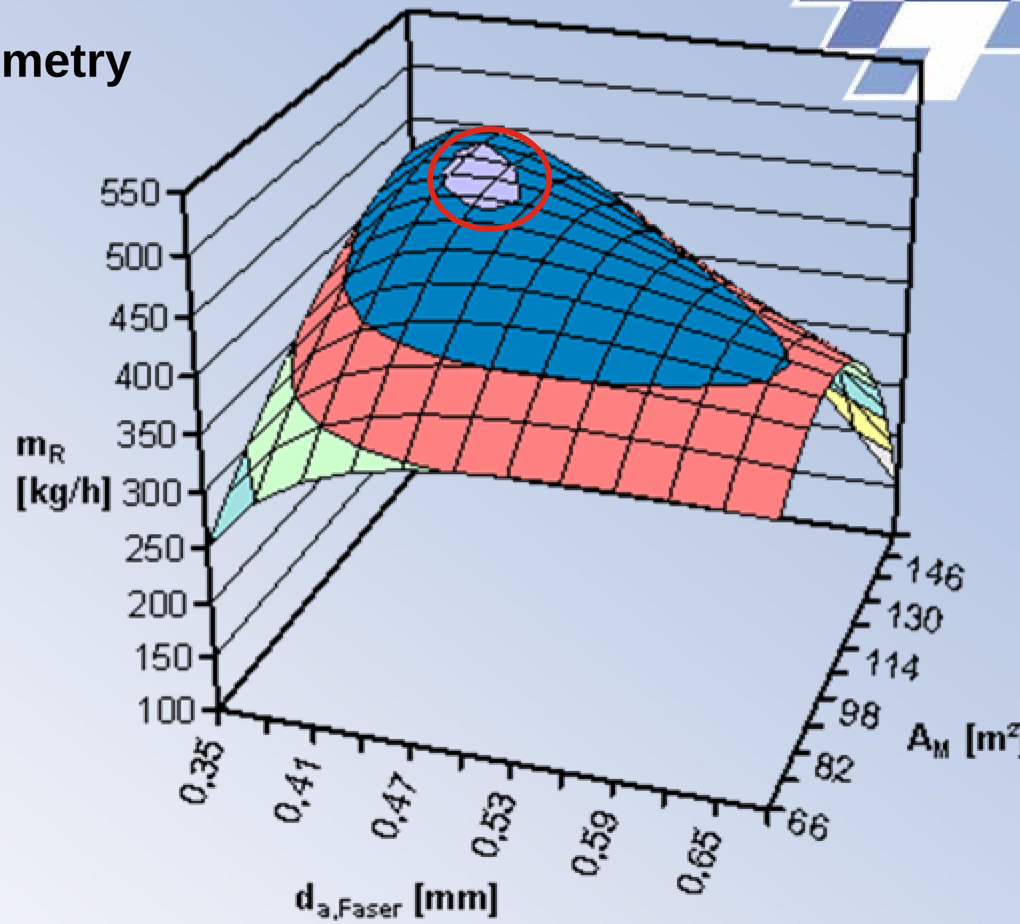
Bioethanol production

Optimization of the module geometry

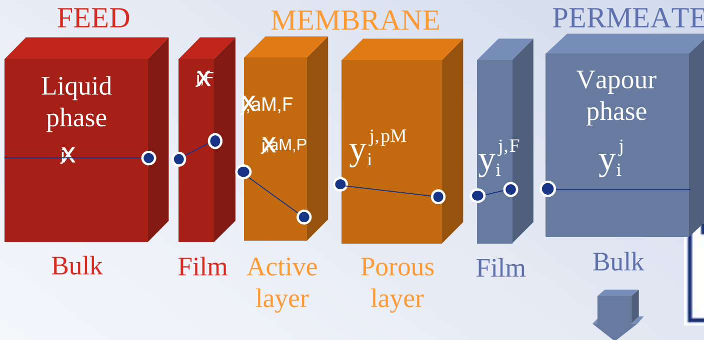
- fibre diameter
- membrane area



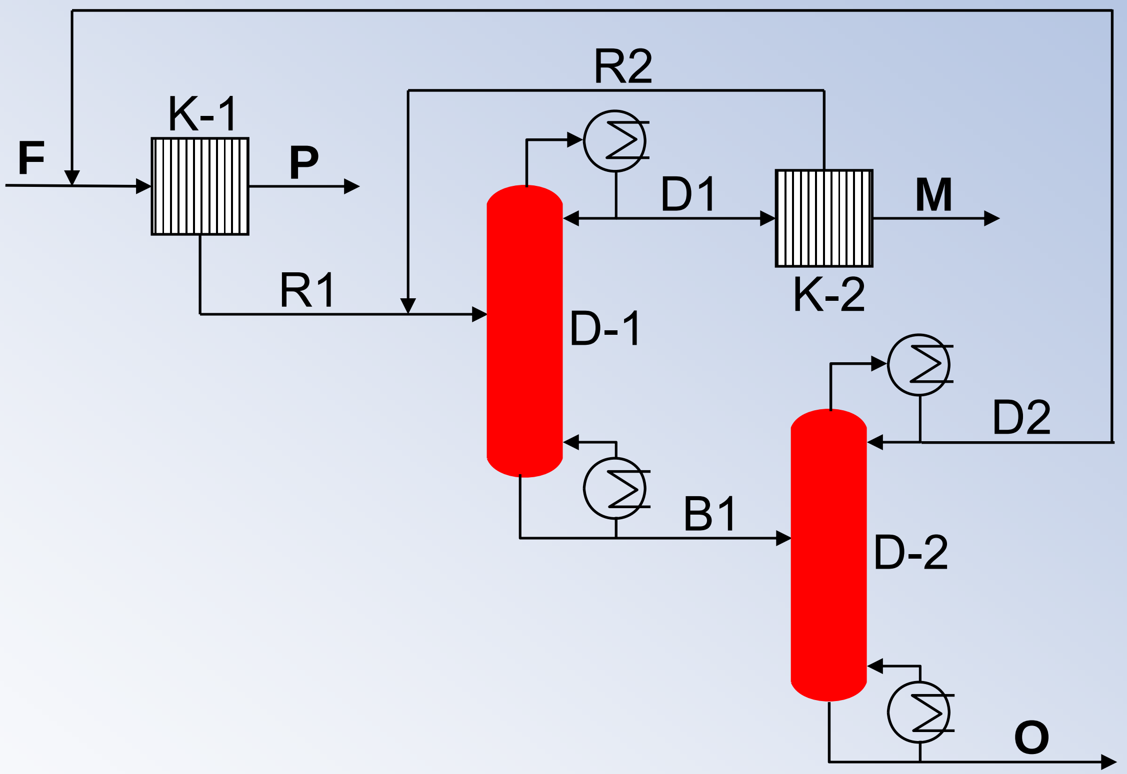
constant volume of the fibre bundle

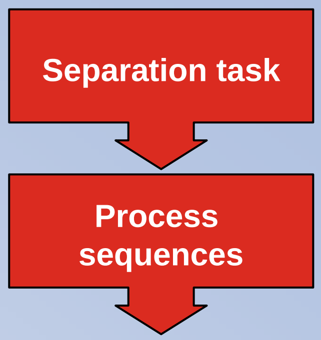


Based on rigorous modelling of membrane separation (VP)



Distillation and Crystallization

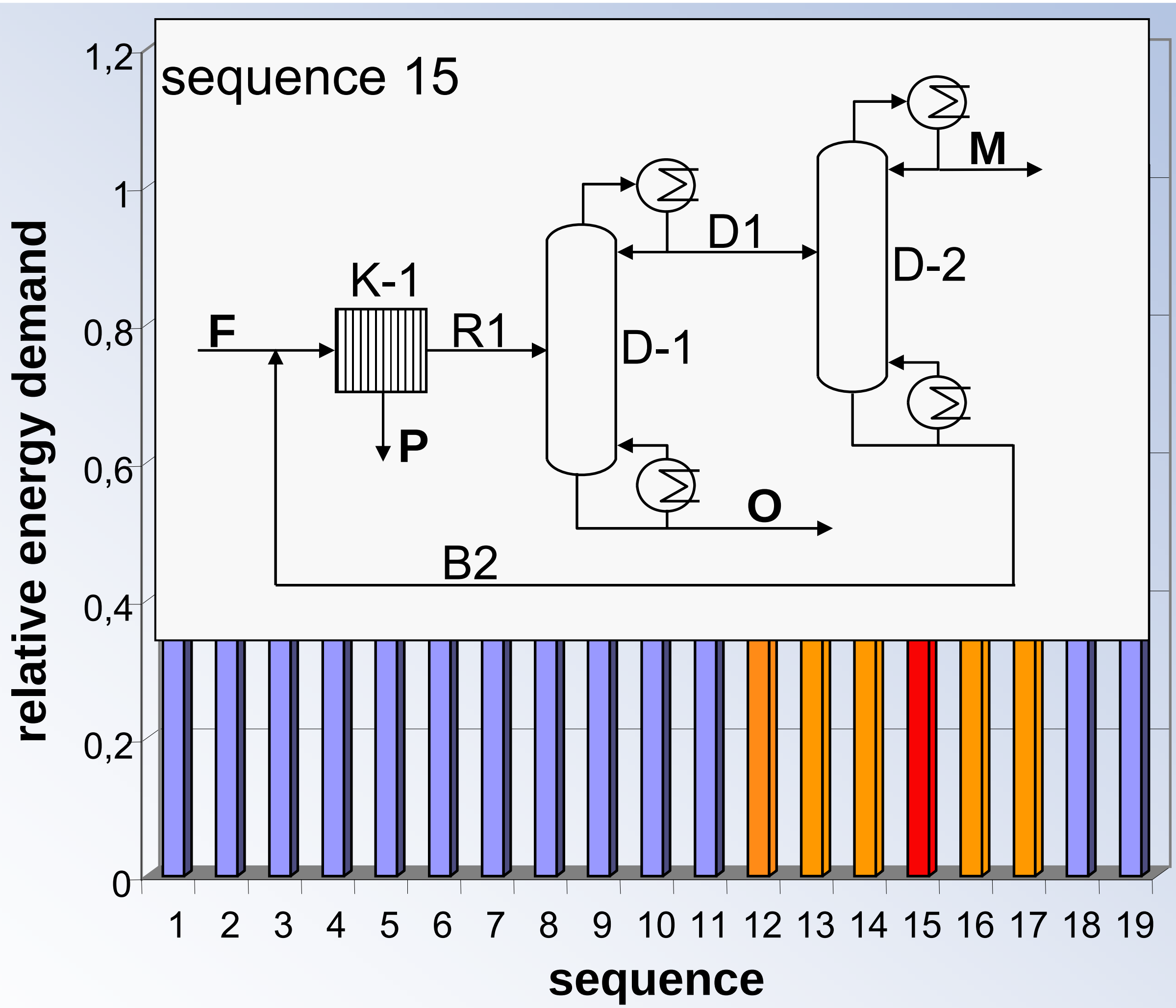


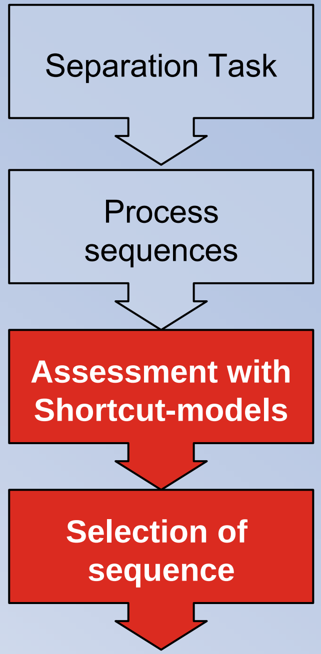


Is that the optimal structure?

- Separation of a ternary isomeric mixture
- Structural and operational degrees of freedom

Distillation and Crystallization





- Separation of a ternary isomeric mixture
- Structural and operational degrees of freedom

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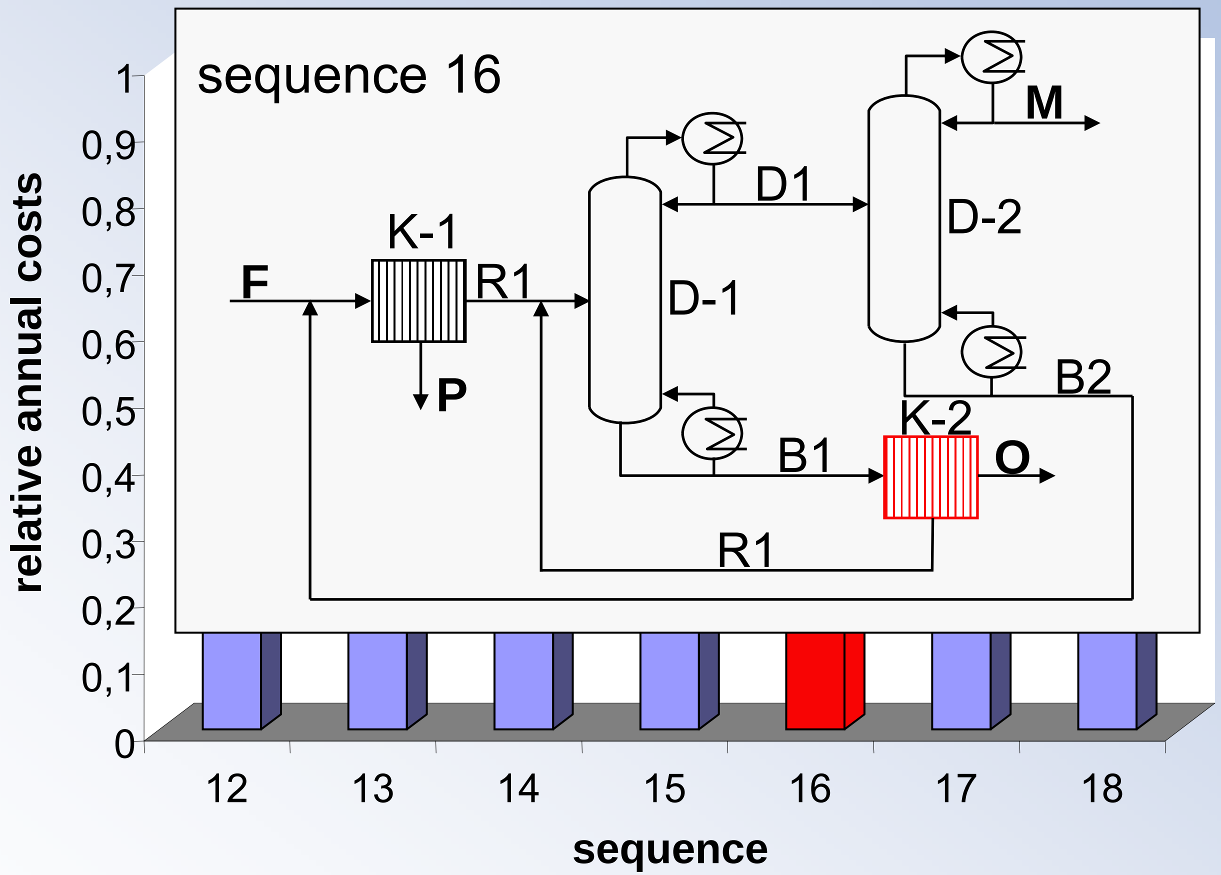
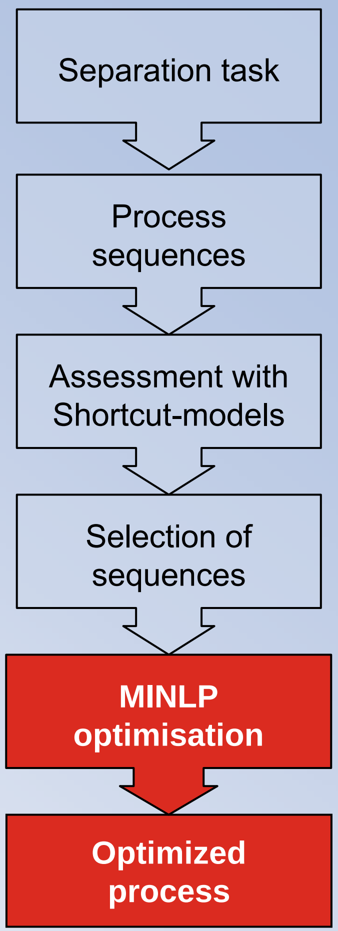
Distillation and Crystallization





- Sequence 16 with lowest total costs
- 65 % costs savings by hybrid process design

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(Bio)reactive and Hybrid Separations

Bioseparations

- Bioextraction
- Membrane adsorption
- Downstream Processing

Hybrid Bioseparations

- Distillation & membranes
  - …
    - …

Distillation

Absorption

Extraction

Membranes

Reactive Separations

- Reactive distillation
- Reactive absorption
- Reactive extraction
- Membrane reactor

Hybrid Separations

- Distillation & membranes
- Extraction & crystallization
- Distillation & crystallization

(Bio)reactive and Hybrid Separations

Bioseparations

- Bioextraction
- *Membrane adsorption*
- *Downstream Processing*

Hybrid Bioseparations

- Distillation & membranes
- ...
- ...

Distillation

Absorption

Extraction

Membranes

Reactive Separations

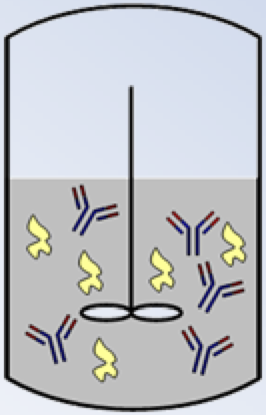
- Reactive distillation
- Reactive absorption
- Reactive extraction
- Membrane reactor

Hybrid Separations

- Distillation & membranes
- Extraction & crystallization
- Distillation & crystallization

TVT

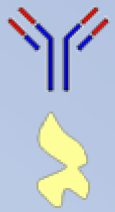
Approach for Selective Purification of Antibodies



Purification problem:

How to separate the target protein

from impurities



Technologies for separation of bioactive substances

Samatou J., Wentink A.E., Rosa P., Azevedo A., Aires-Barros R., Bäcker W., Górak A., ESCAPE-17 (2007)

Chromatography

© Merck KgaA

Membrane Adsorption

© Sartorius AG

Extraction

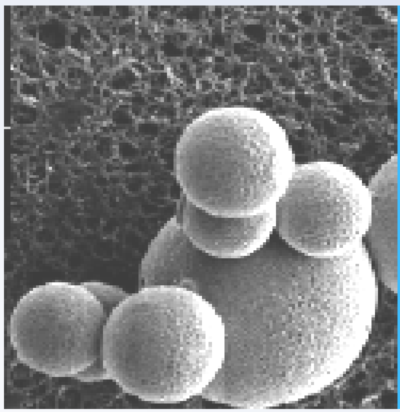
© Twente University

Approach for Selective Purification of Antibodies

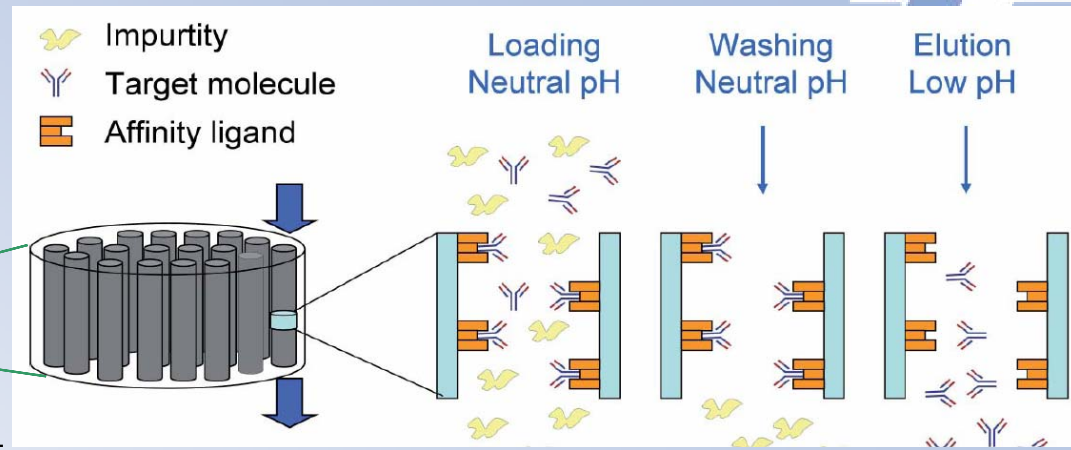
Integrated material and process development

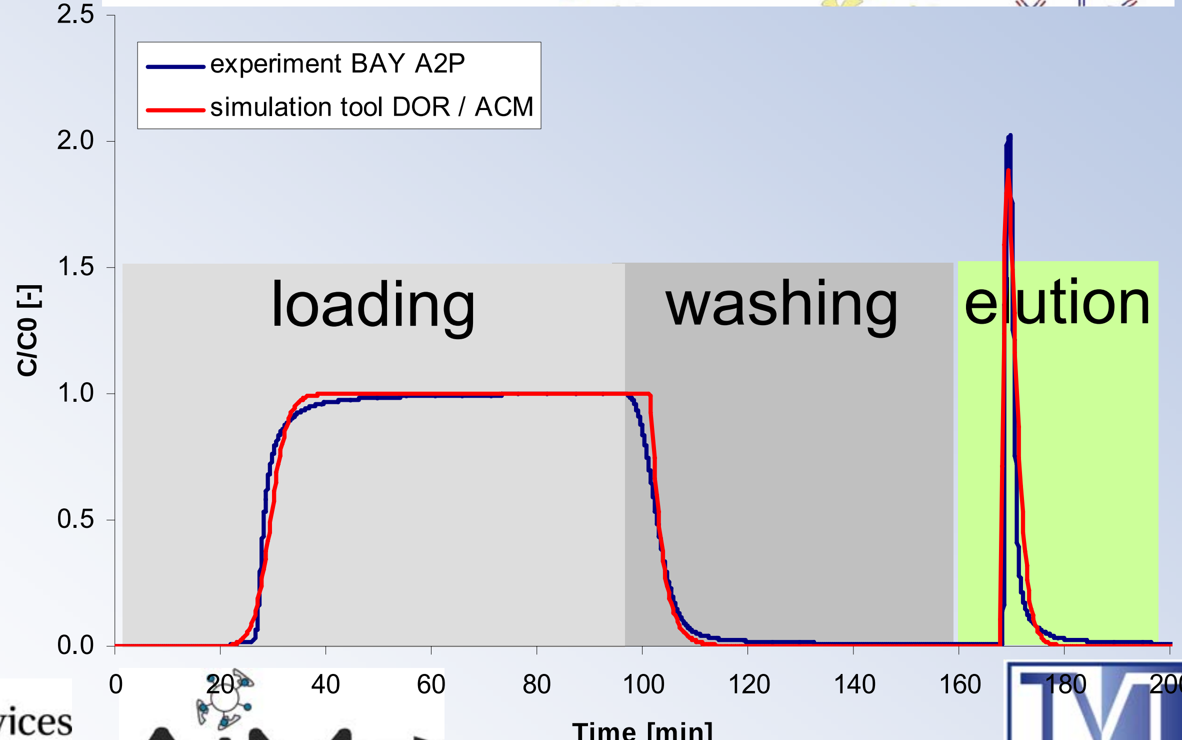
Membrane adsorbers

- Affinity membranes
- Ion-exchange membranes



Courtesy Sartorius AG





Development of detailed mathematical models for process design and reliable scale up for different geometries

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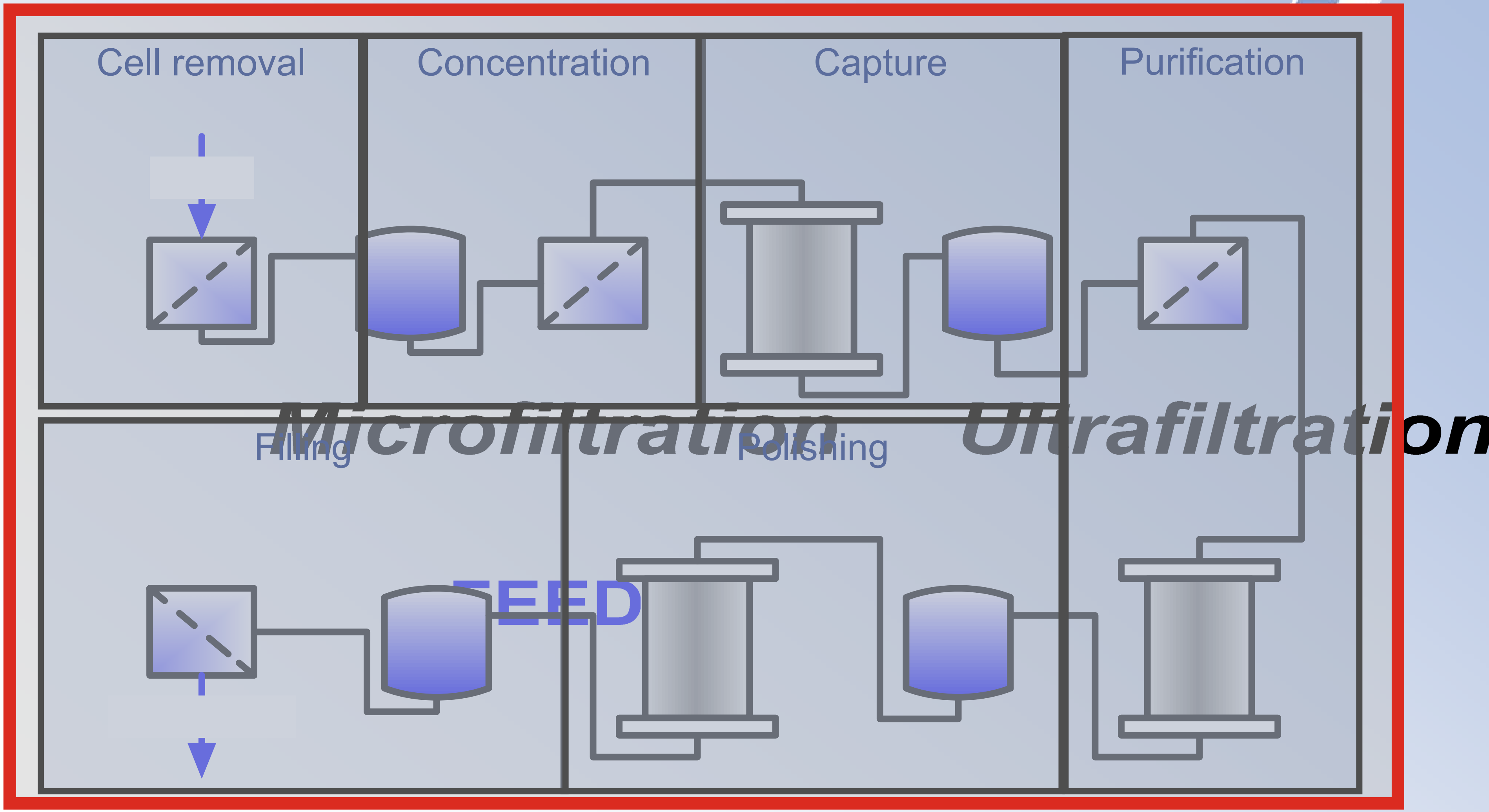
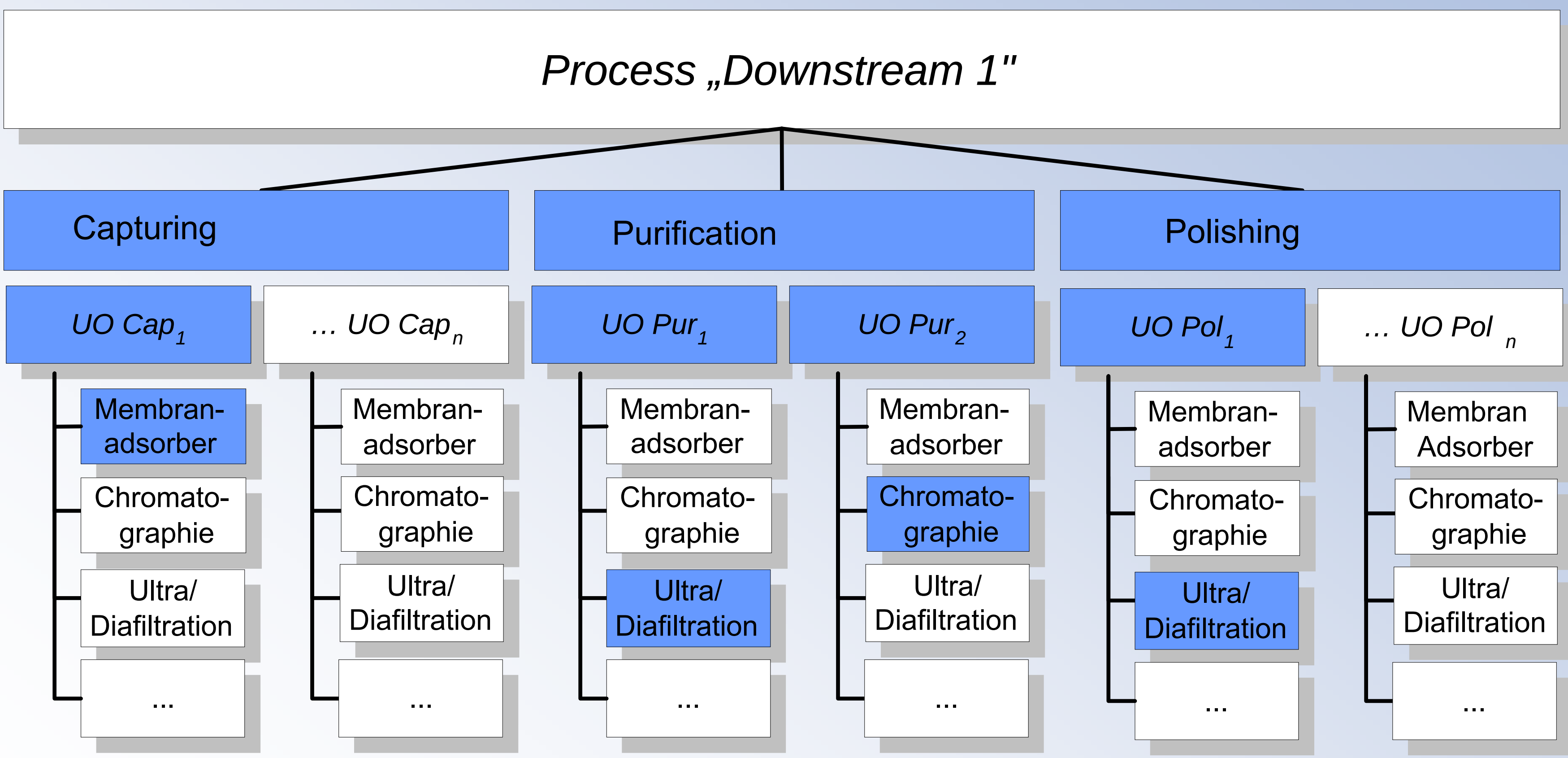
Generic modelling approach

Generic process for purification of bioactive substances



Model structure in process model



Downstream process

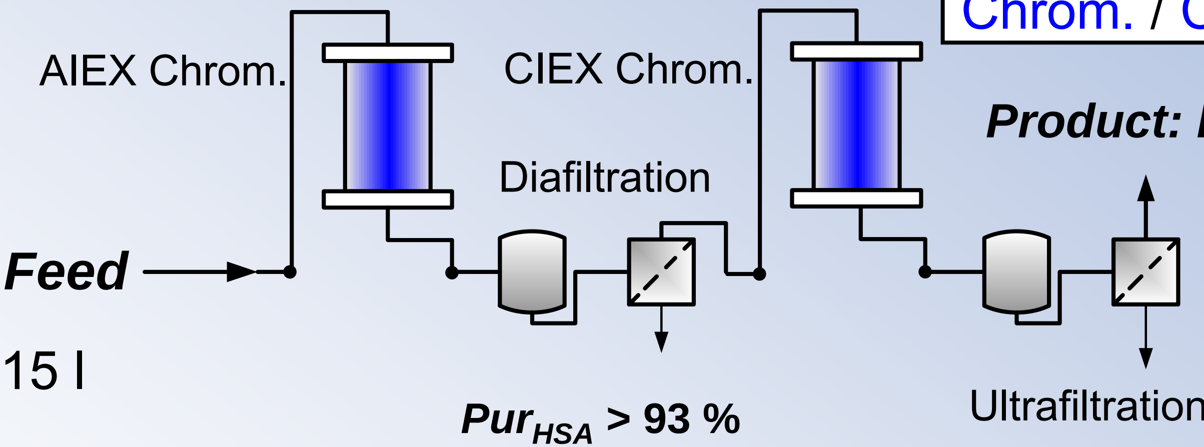
C. Frerick , P. Kreis, A. Górak, A. Tappe, D. Melzner, CEP (2007), *accepted*

Implemented models

Model complexity (increasing towards the top)

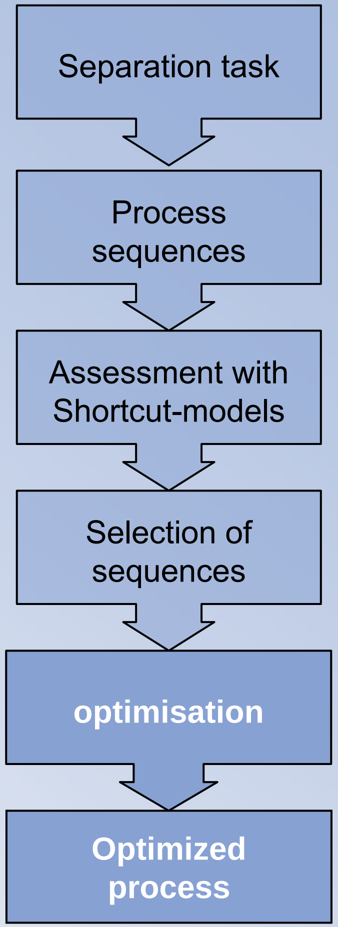
Chromatography (IEX, SEC)	Membrane adsorber (IEX)	Filtration (UF, DF, NF)
General rate model Convection, dispersion, film & pore diffusion		
Transport dispersive model Convection, dispersion, effective mass transfer	***Transport dispersive model*** Convection, dispersion, radial diffusion	
Ideal stage model Convection, solid & liquid equilibrium	***Ideal stage model*** Convection, solid & liquid equilibrium	***Resistance model*** Membrane & gel resistance
Short Cut Yields	***Short Cut*** Yields	***Short Cut*** Yields

Case study



15 l

Pur_{HSA} > 93 %
Y_{HSA} > 75 %
c_{HSA} = 50 g/l

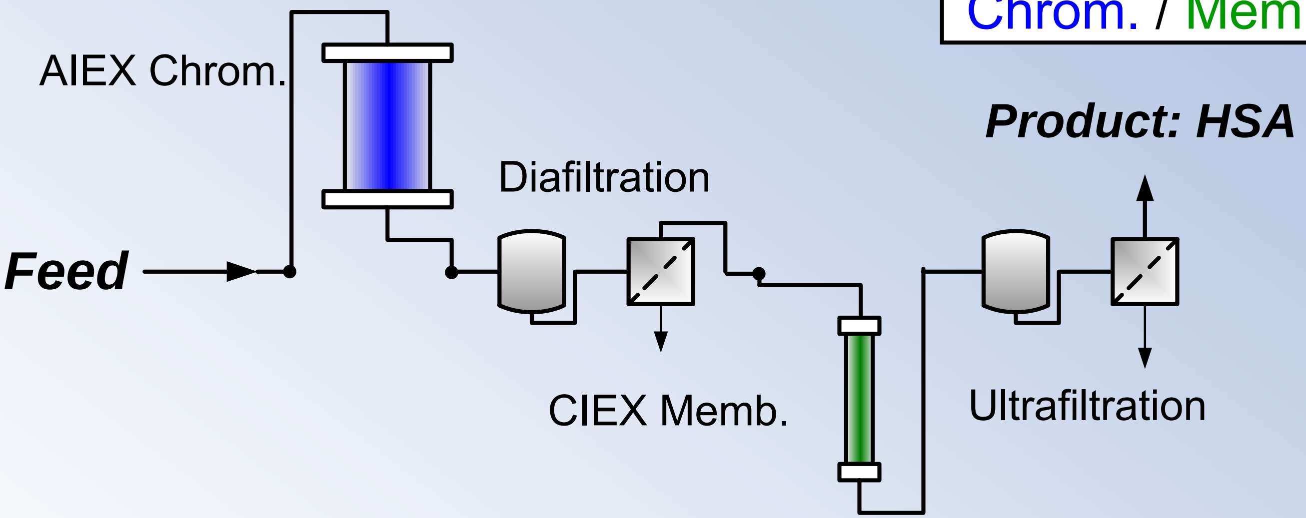


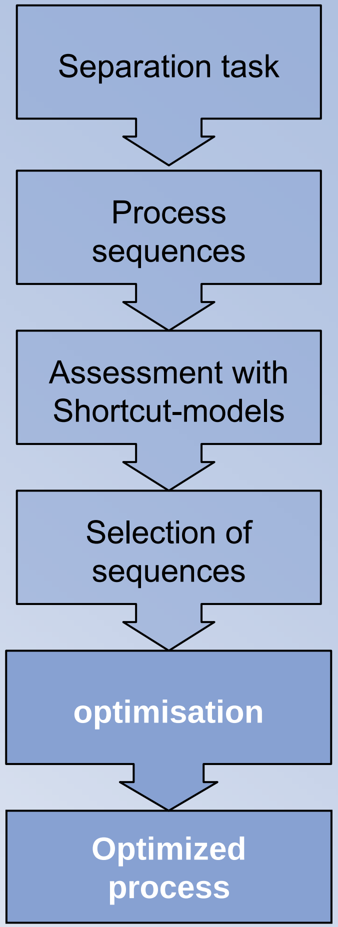
model parameters

- mass transfer models
- adsorption isotherms (membrane adsorber / chromatography)

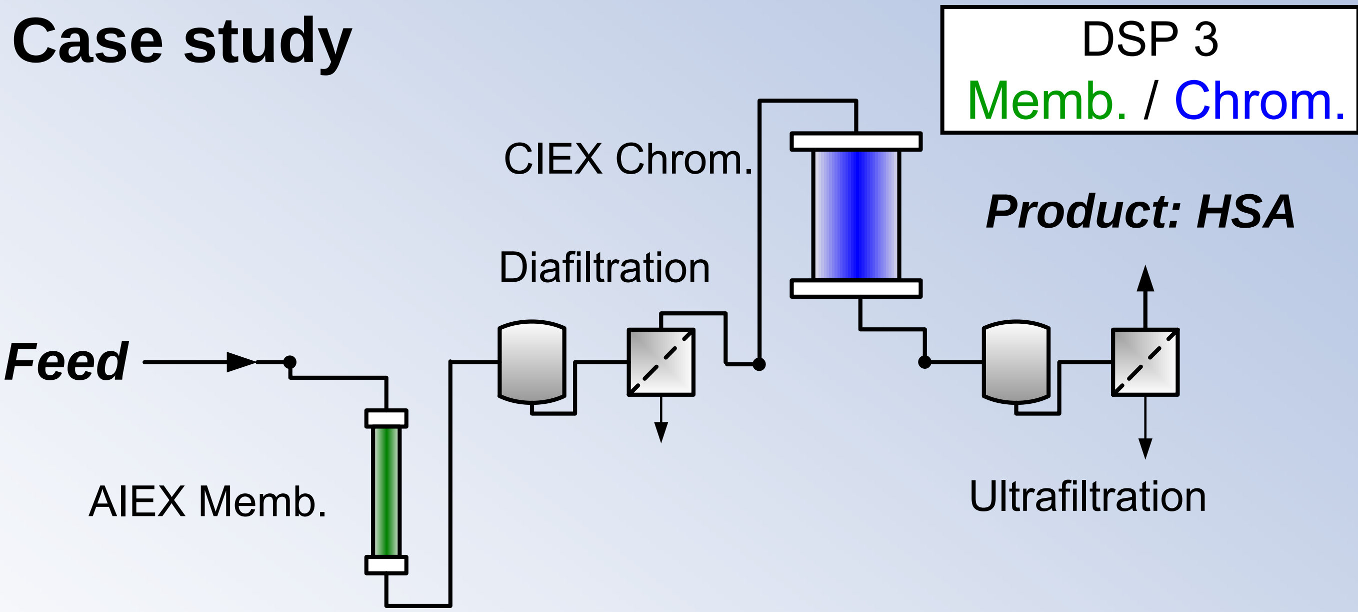
Case study

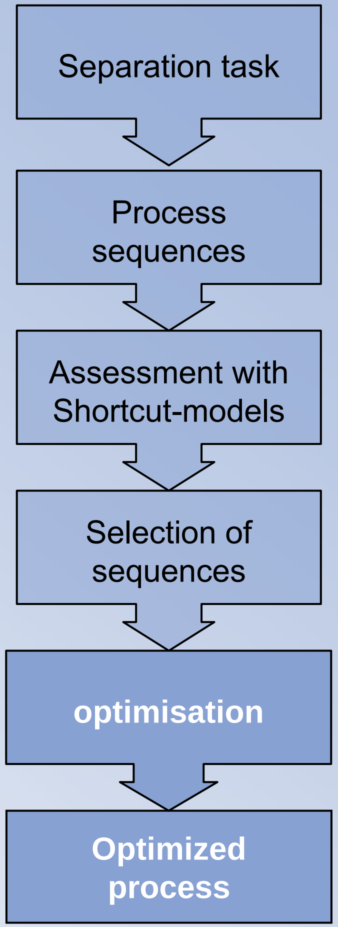
DSP 2
Chrom. / Memb.





Case study

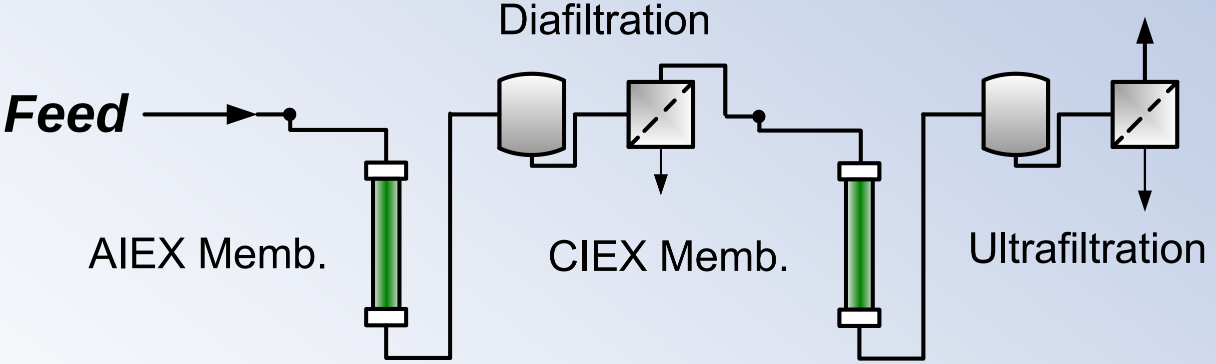

DSP 3
Memb. / Chrom.
Product: HSA
Feed
AIEX Memb.
Diafiltration
CIEX Chrom.
Ultrafiltration

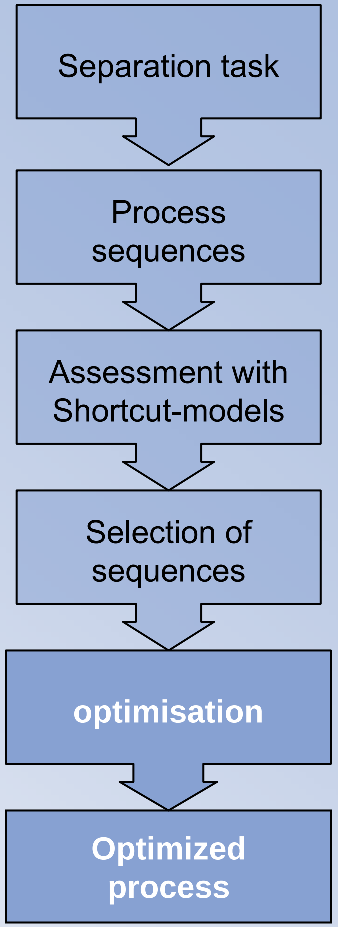

Separation task
Process sequences
Assessment with Shortcut-models
Selection of sequences
optimisation
Optimized process

Case study

DSP 4
Memb. / Memb.

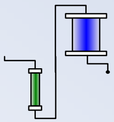
Product: HSA

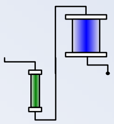


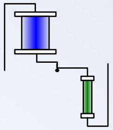


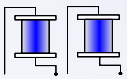
Results

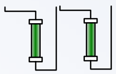
Starting population

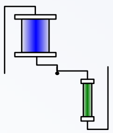
Parent 1 

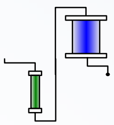
Parent 2 

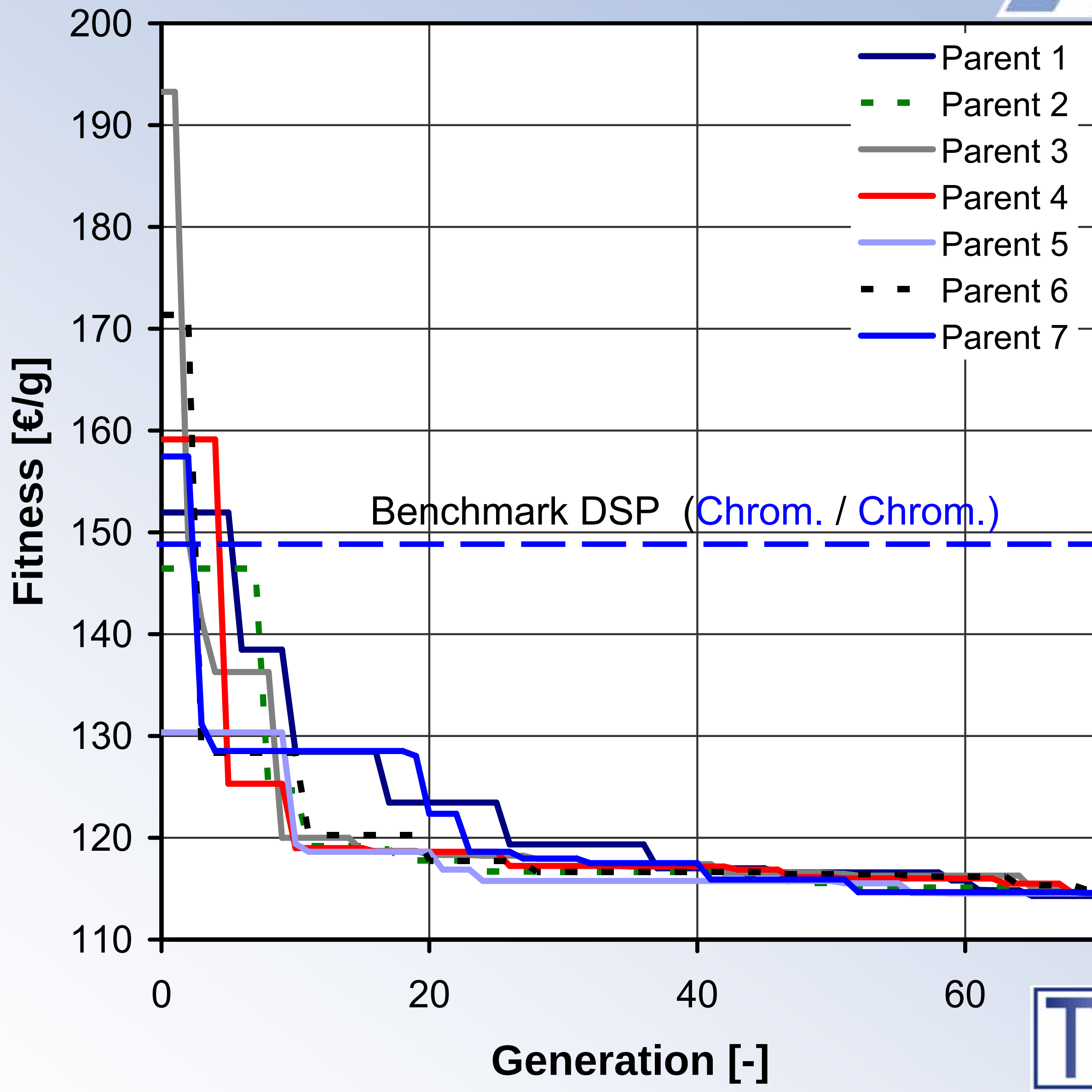
Parent 3 

Parent 4 

Parent 5 

Parent 6 

Parent 7 

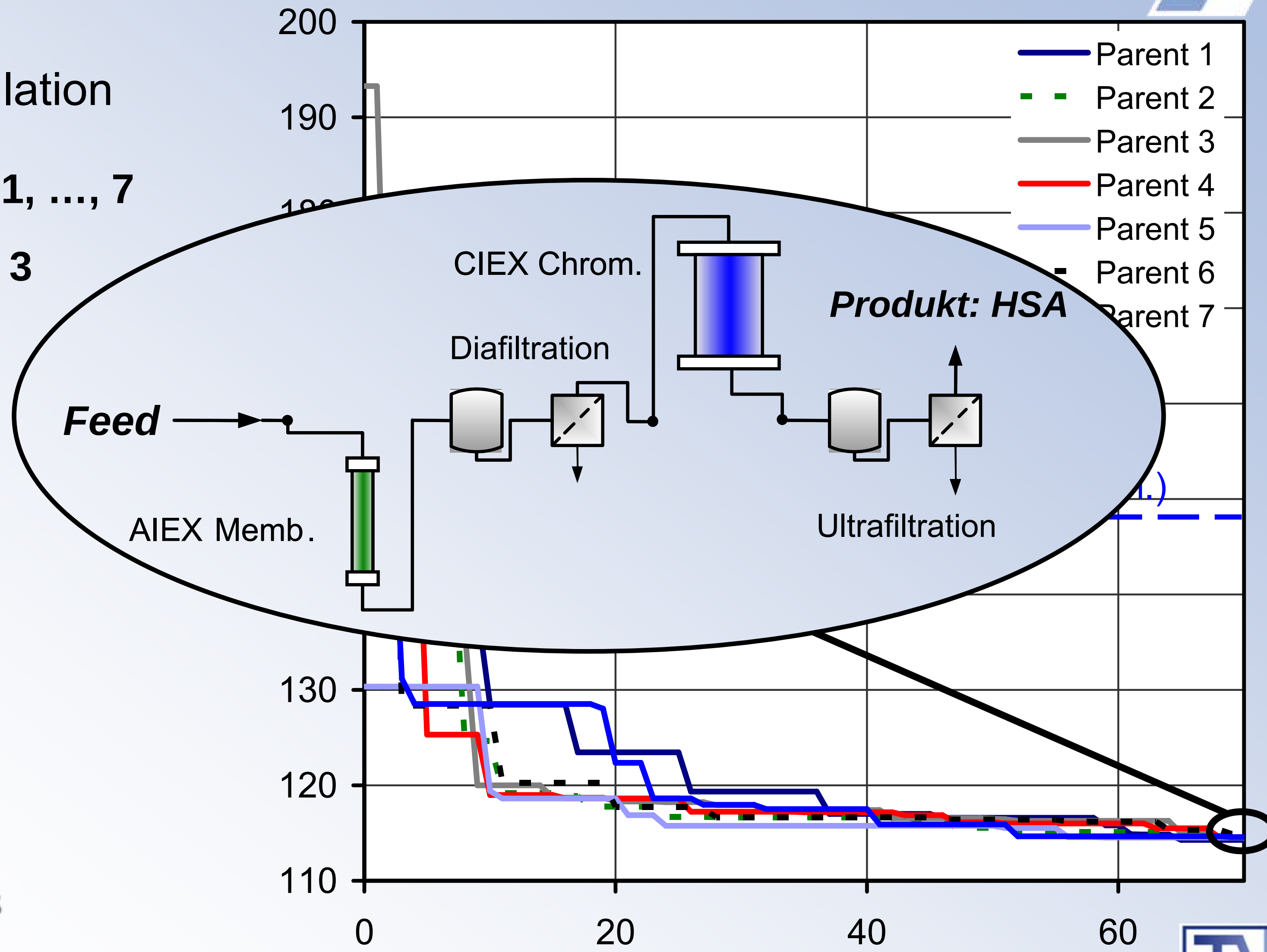


Results

End population

Parent 1, …, 7

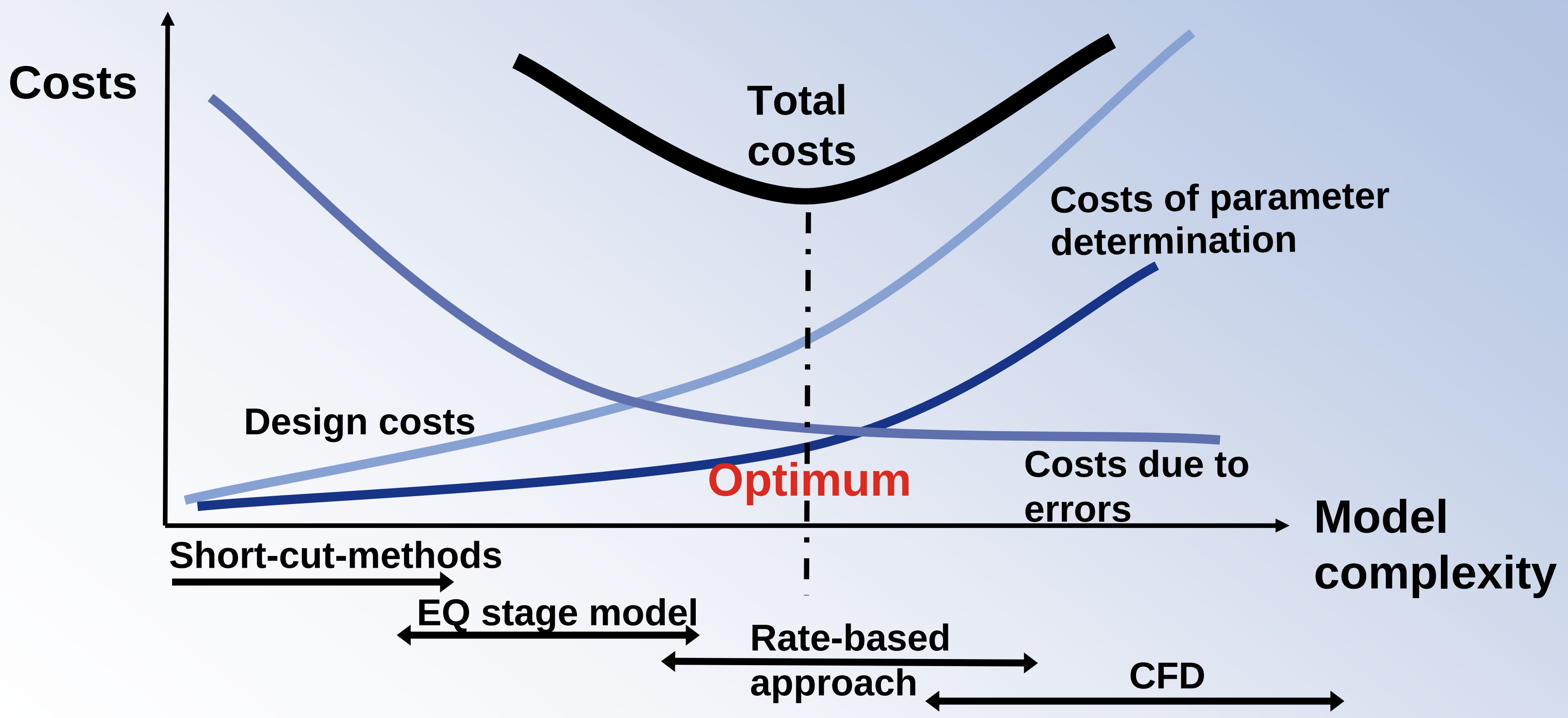
→ DSP 3



> 20% cost reduction

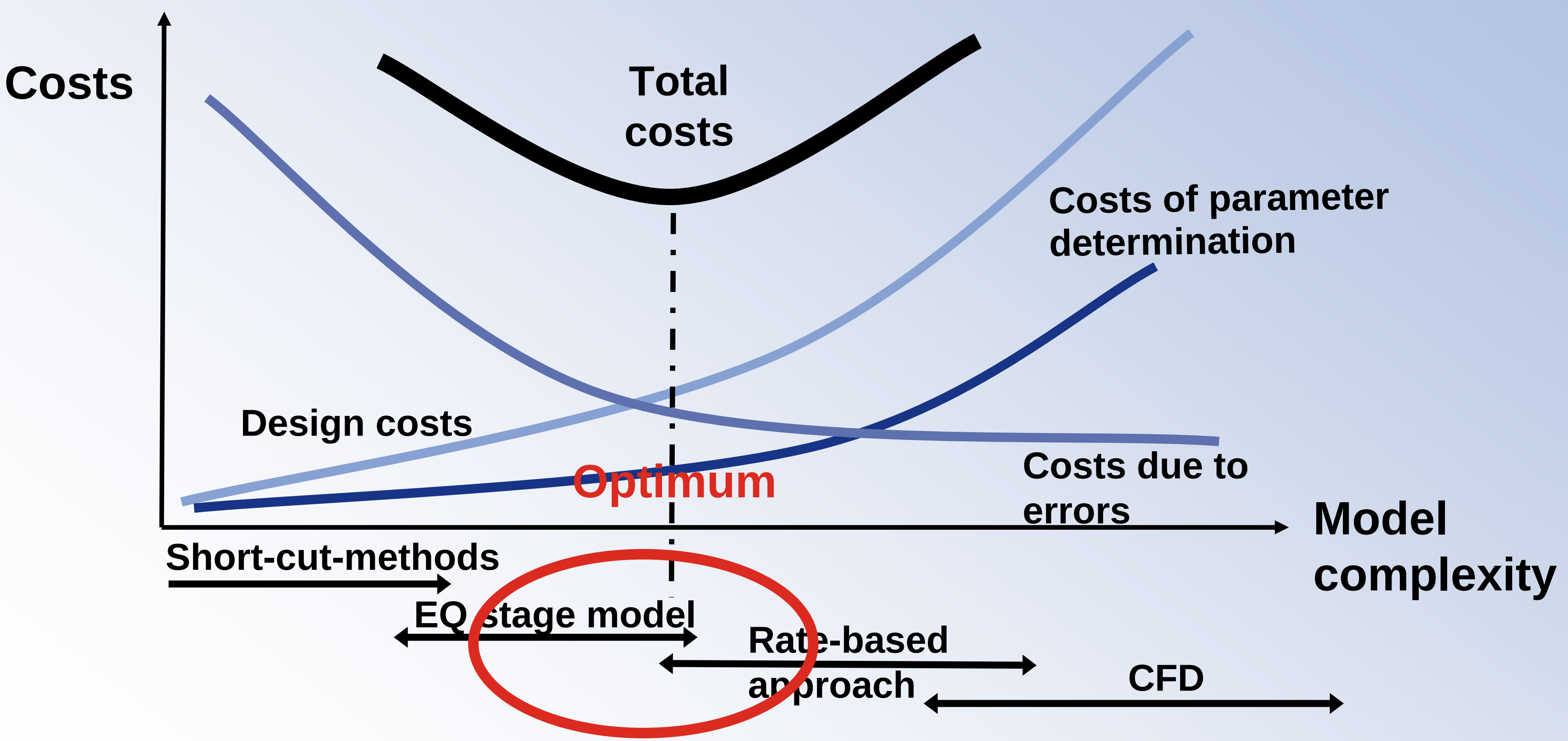
Recommendations: Reactive absorption

- **Rate-based** approach is a MUST!
- **Stefan-Maxwell** equations are usually not necessary
- **Film reaction** has to be included in the model



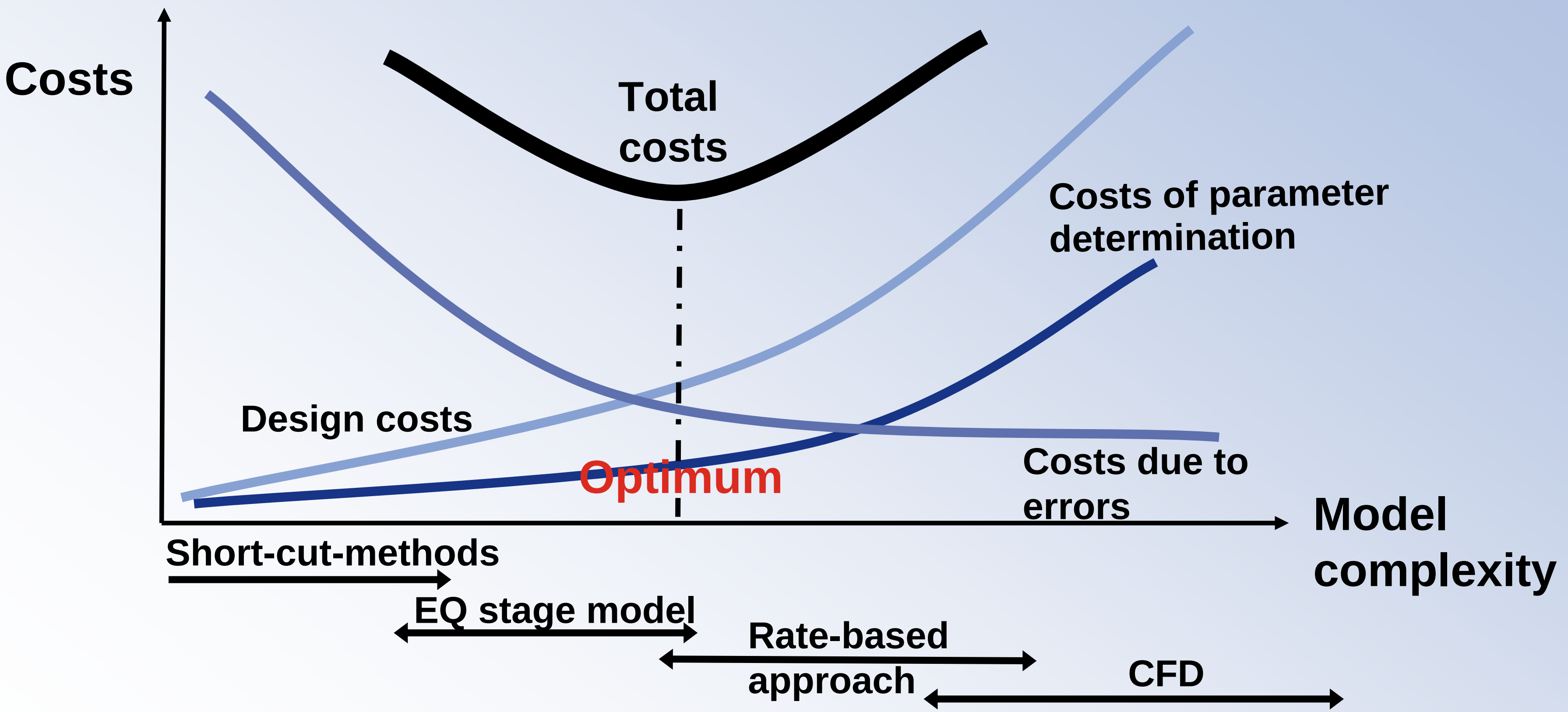
Recommendations: Reactive distillation

- **Rate-based** approach recommended but sometimes not necessary
- **Equilibrium reaction** is NOT sufficient

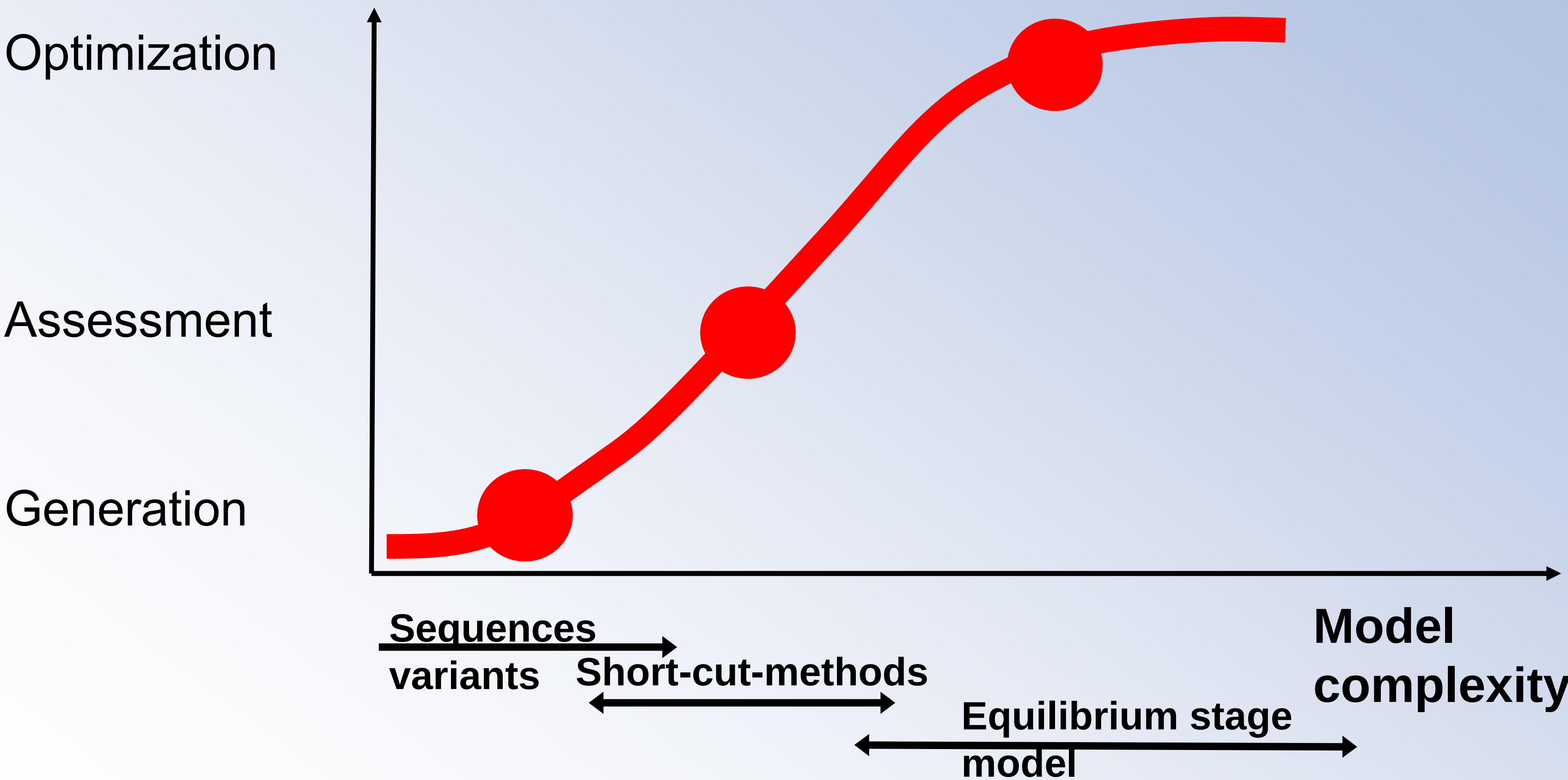


Recommendations: Hybrid processes

• optimal modelling depths strongly depends on investigated **unit operations and chemical system**

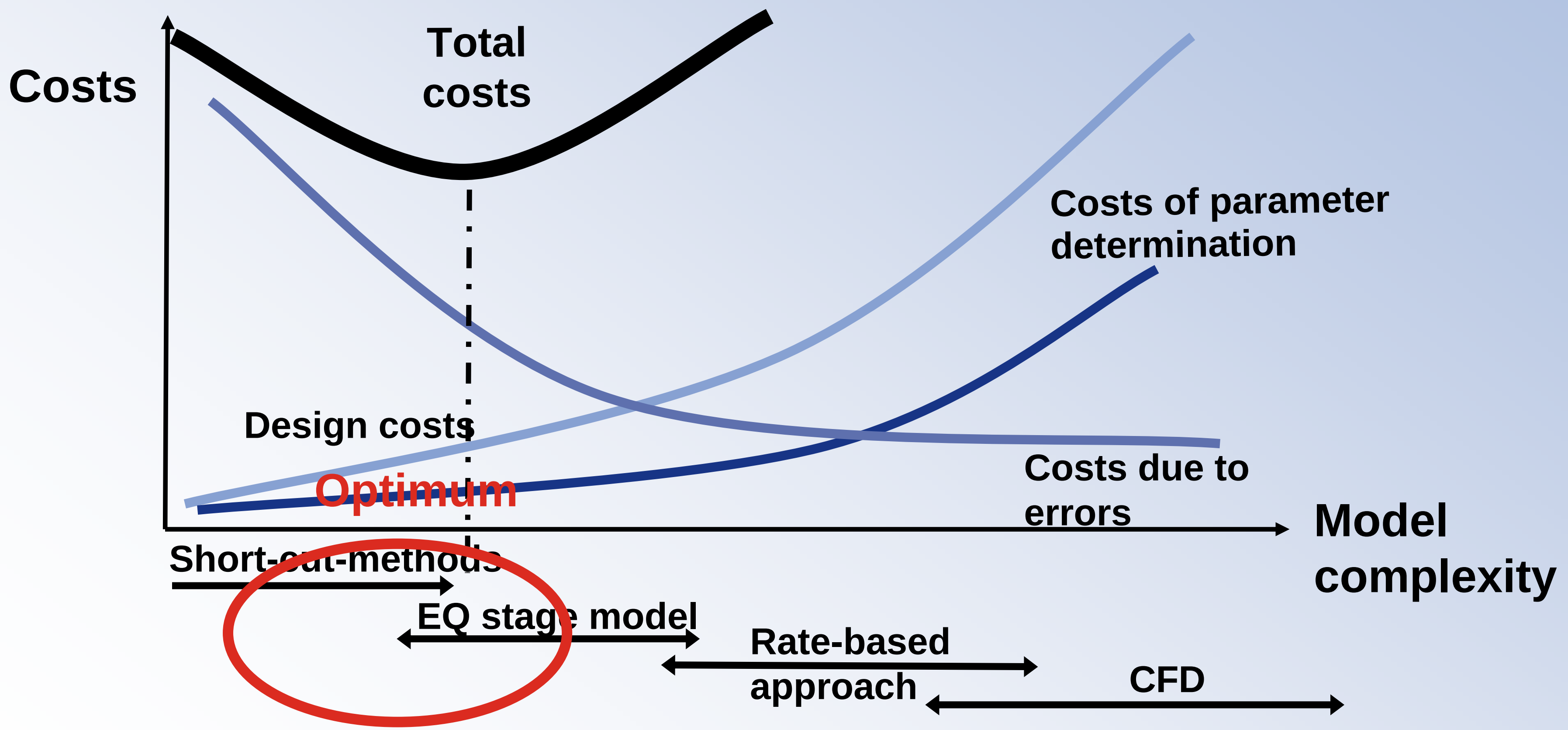


Recommendations: Hybrid processes



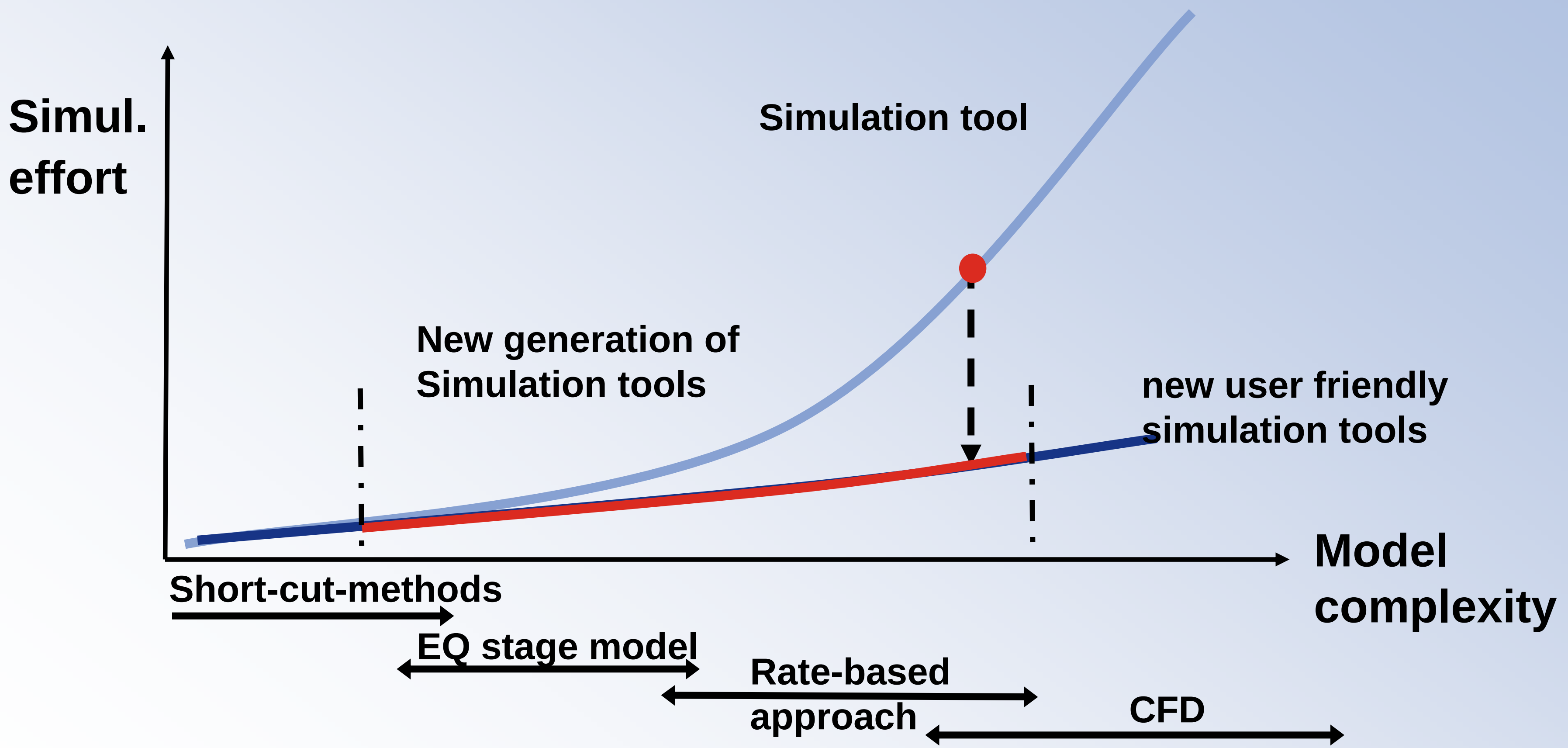
Recommendations: Bio(reactive)separations

- rather **simple models** should be used since the knowledge on biothermodynamics and hydrodynamics is limited



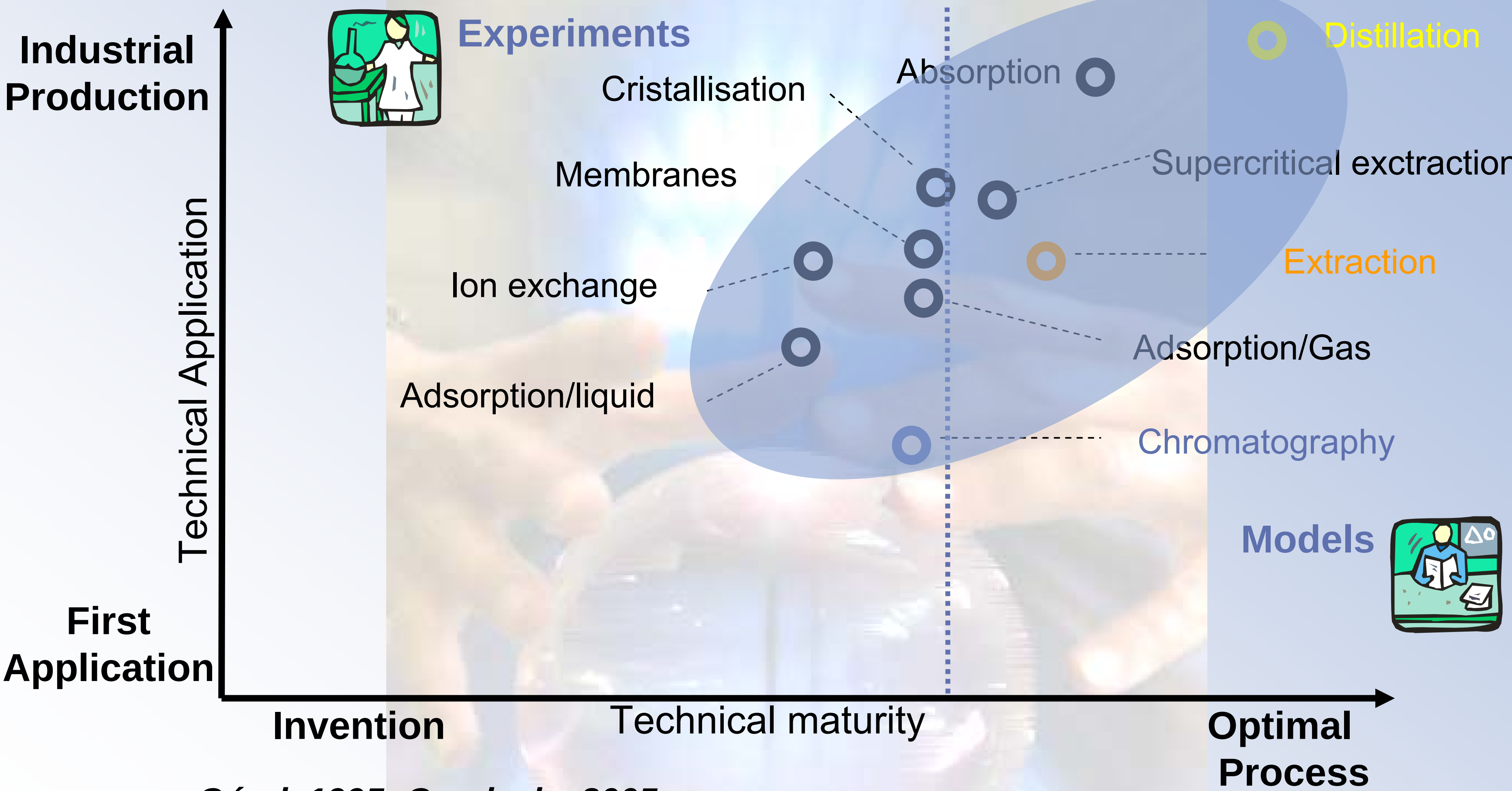
Recommendations: Modelling & Simulation

New generation of **simulation tools** enable user to chose the **optimal modelling depth** for each special separation task



Outlook

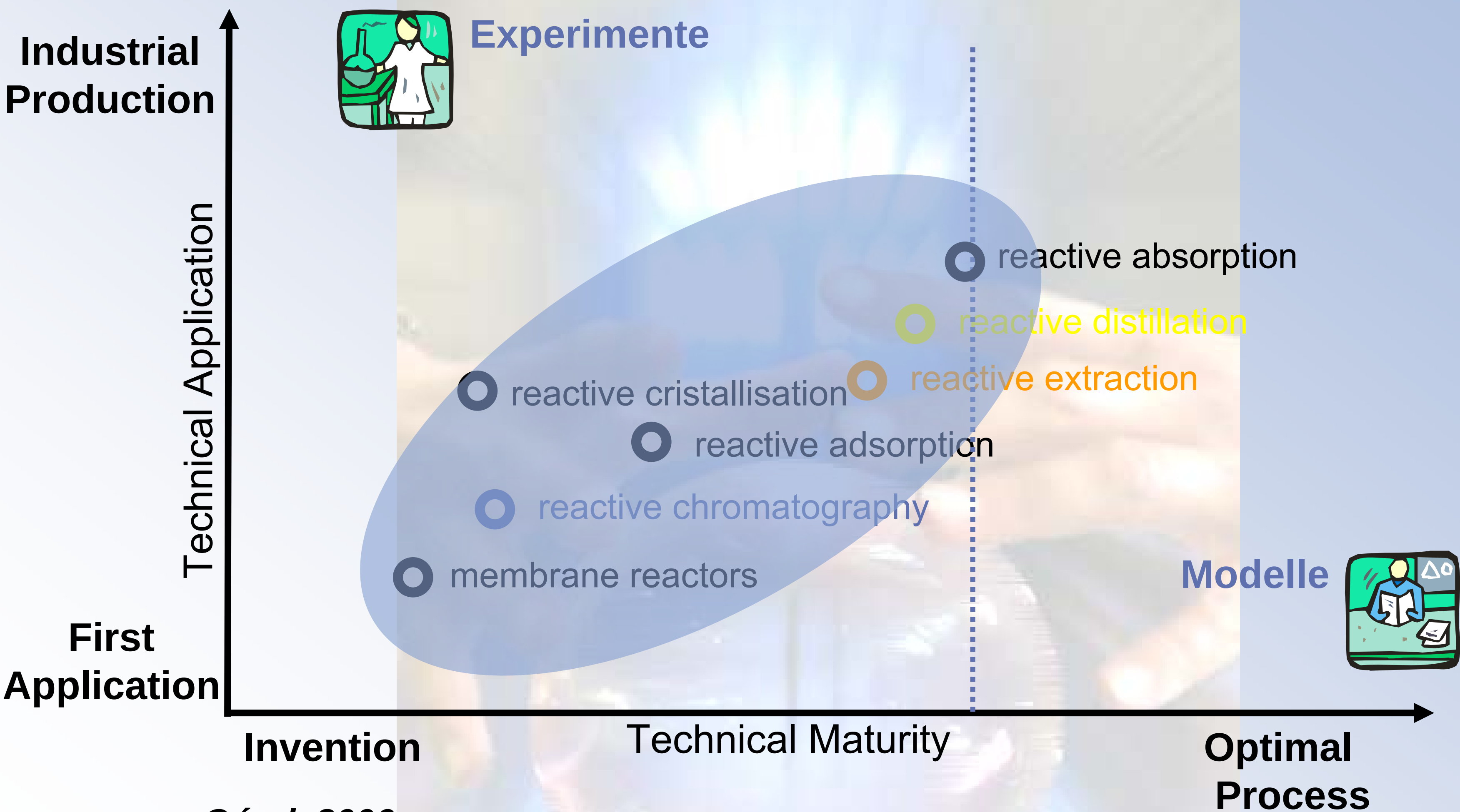
Outlook



Górak 1995; Goedecke 2005

Classical separation processes

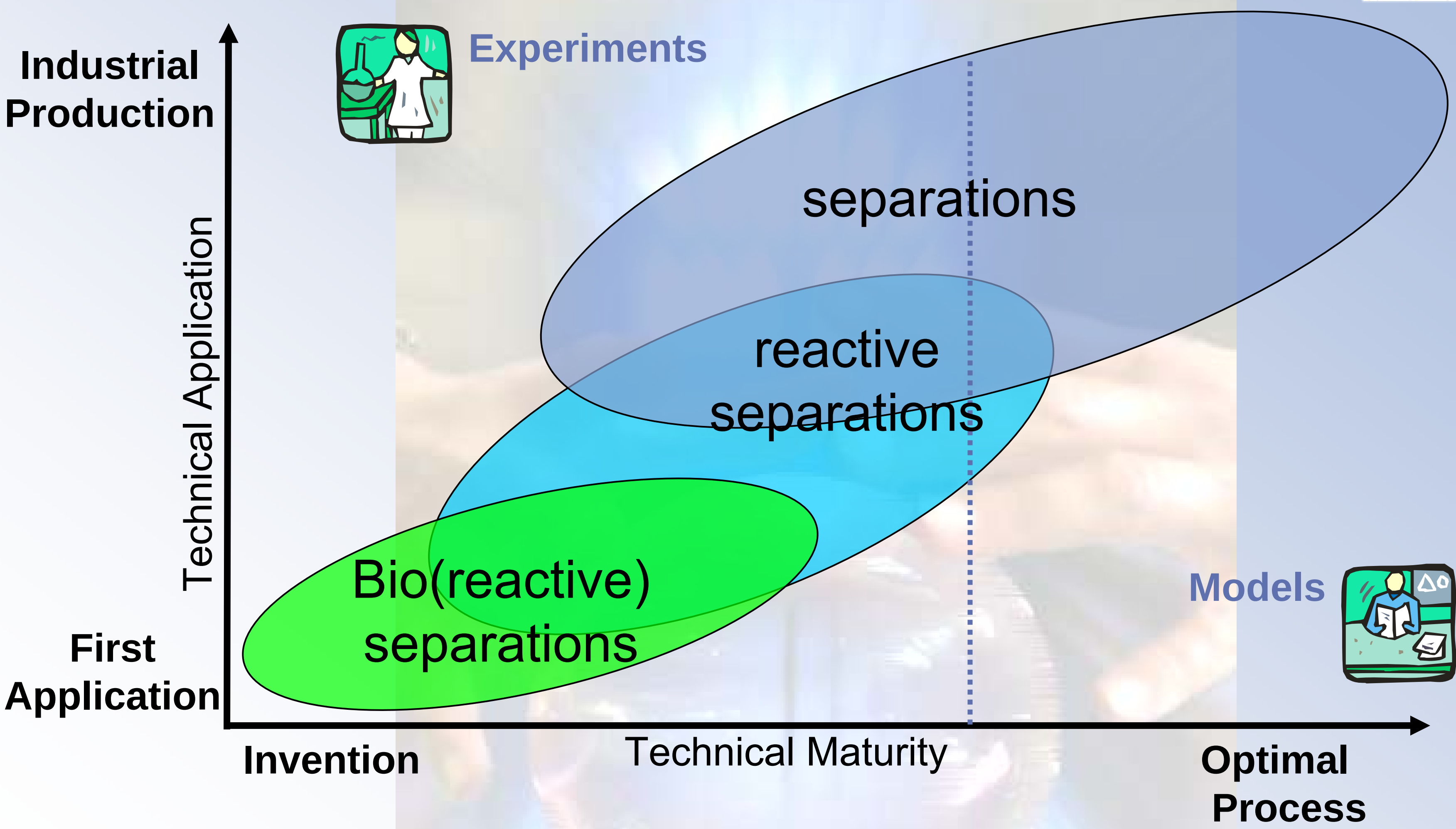
Outlook



Górak 2006

Reactive separation processes

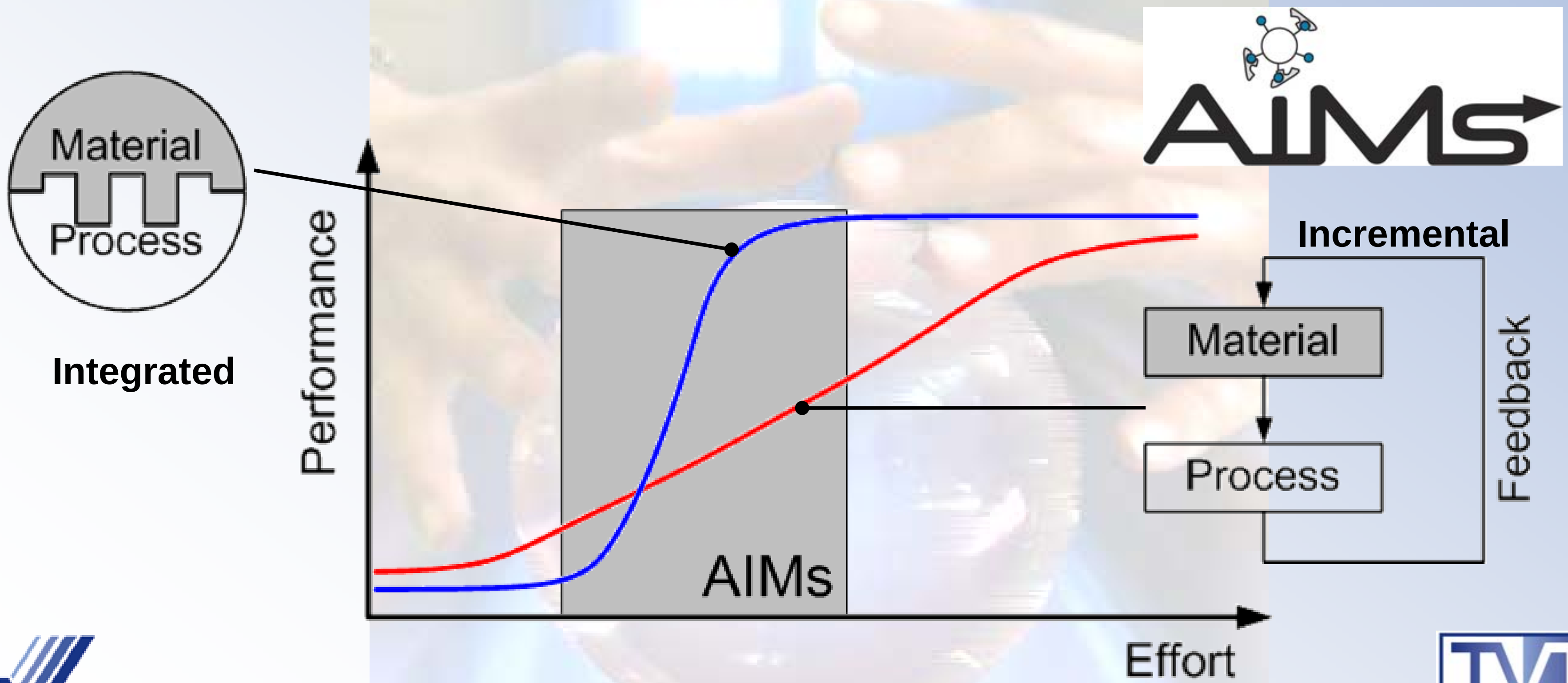
Outlook


Industrial Production
Experiments
Technical Application
separations
reactive separations
Bio(reactive) separations
Models
First Application
Invention
Technical Maturity
Optimal Process

Outlook

Integrated material und process development for

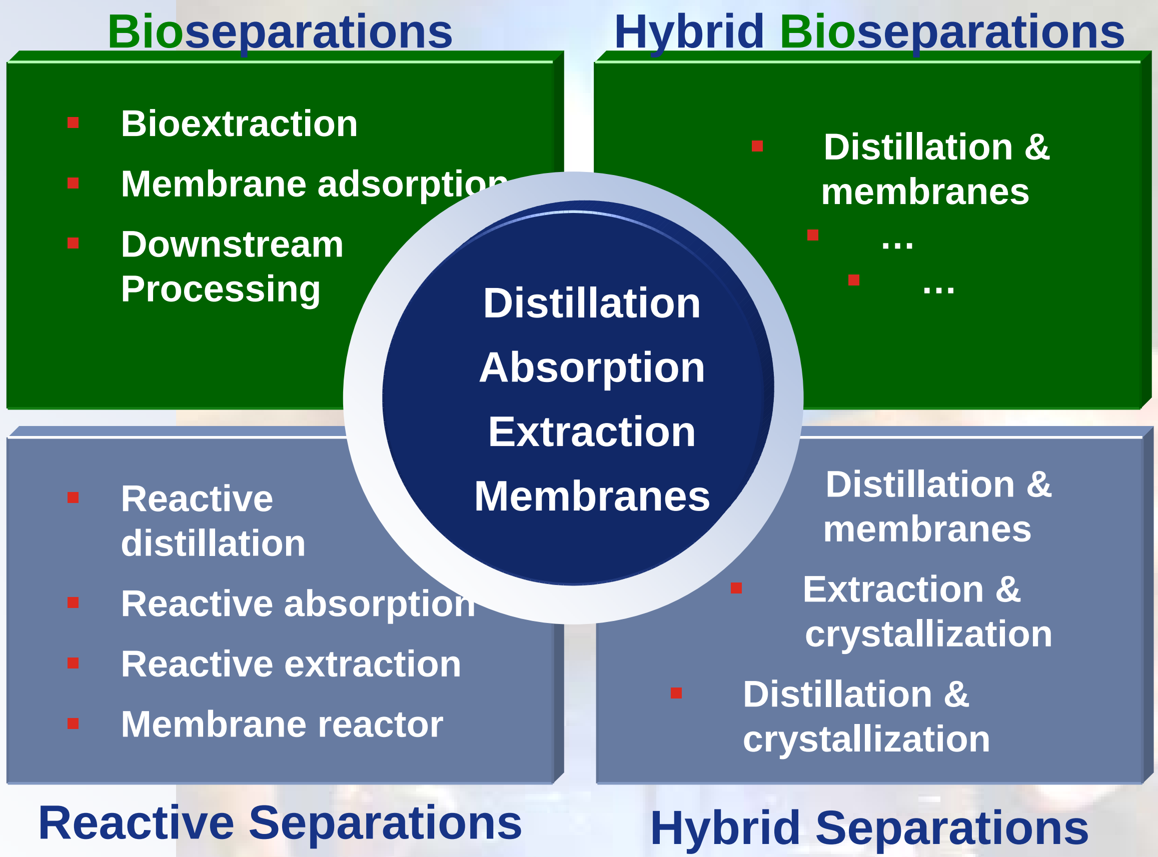
- **monoclonal antibody purification (adsorbens/membrane adsorbers, solvents/bioextraction)**
- **bioethanol production (membranes/distillation)**



Design of a new class of interactive materials

Outlook

Reactive and hybrid (bio)separations belong to the emerging area of Process Intensification
Charpentier, Ind.Eng.Chem.Res., (2007), 46, 4365



"The innovative character of Process Intensification is in nice harmony with the objectives of Process Systems Engineering: a symbiosis between them has high potential"
Moulijn, Stankiewicz,Grievink,Górak: ESCAPE 16 (2006)

Outlook

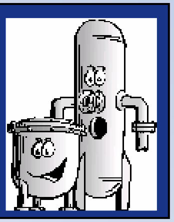
Reactive and hybrid (bio)separations belong to the emerging area of Process Intensification
Charpentier, Ind.Eng.Chem.Res., (2007), 46, 4365

The devil is in the details

- **Reaction kinetics**
- **Thermodynamics of electrolytes**
- **Charged biomolecules**
- **Aggregates and emulsions**
- **Hydrodynamics of viscous system**
- **Many more….**

„No more of the old formula: Let's make it a foot bigger in diameter and 5 ft. higher just for good luck"

- Walter G. Whitman (1924)



"The innovative character of Process Intensification is in nice harmony with the objectives of Process Systems Engineering: a symbiosis between them has high potential"
Moulijn, Stankiewicz,Grievink,Górak: ESCAPE 16 (2006)

Acknowledgements

BASF The Chemical Company

bp

Bayer Technology Services

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DECHEMA

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ÅBO AKADEMI

ETH Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

CIOP PIB

Budapest University of Technology and Economics

SIEMENS

SULZER
Sulzer Chemtech

Eni

degussa. creating essentials

XEPTAGEN LIFE BIOTECHNOLOGY

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