

SFC 2010 Stockholm, September 16

**Supercritical Fluid Chromatography:
From Analytical Tool to Industrial Separation Processes**



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Preparative SFC

- reduction of organic solvents (→ **no/less solvent recovery**)
- complete separation of product from solvent by decrease in density (→ no further concentration step, high product purity)
- low operating temperature (suitable for separation of temperature sensitive substances)
- high diffusion coefficient → high number of theor. plates
- low viscosity → high flow rates → **high productivity**
- selectivity variation by change in P/ρ and T
- increase of limited solubilities by modifier adding

Chromatography: Batch versus SMB

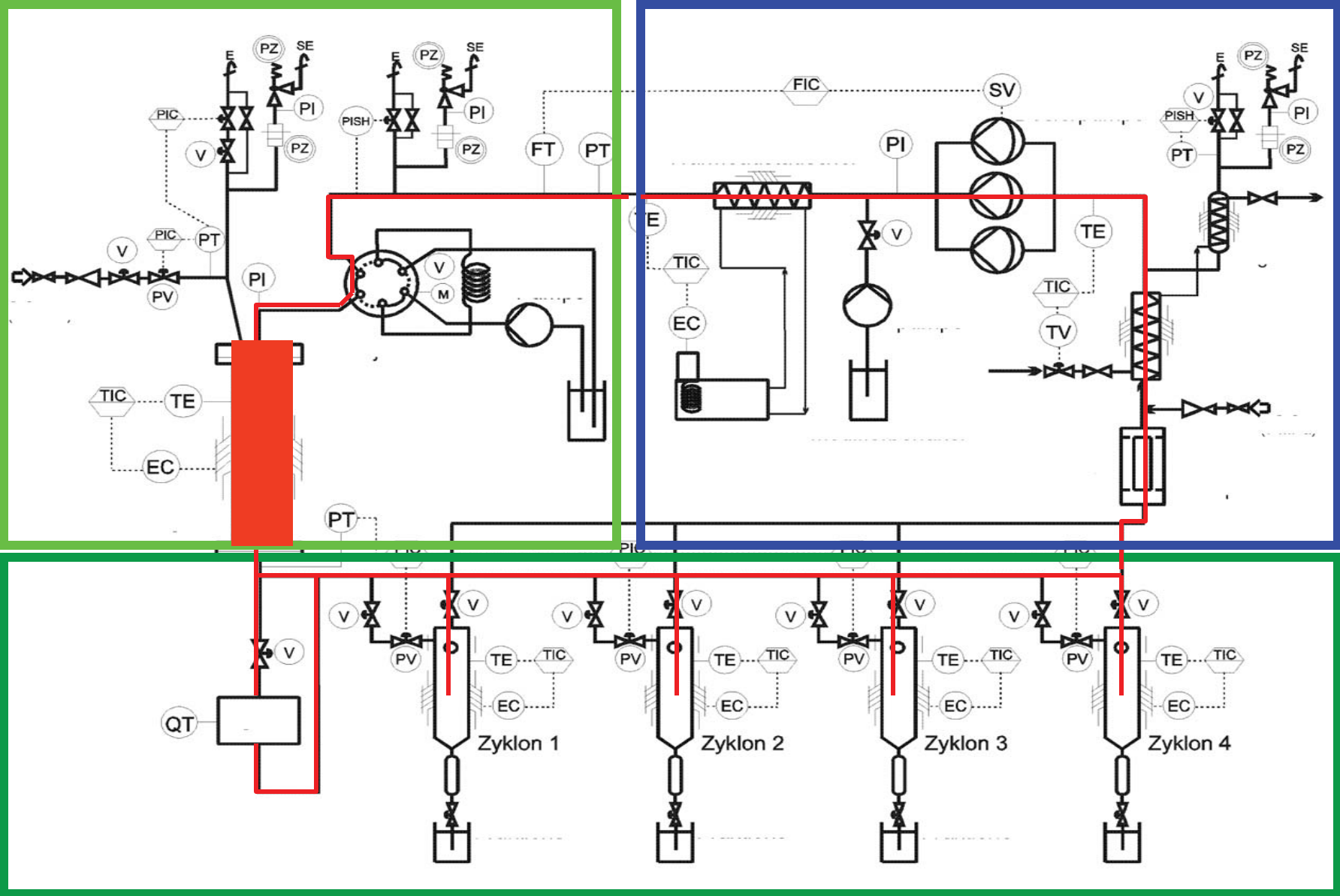
Batch-Chromatography

- ↓ discontinuity
- ↓ high solvent consumption
- ↓ dilution of products
- ↓ lost in yield due to waste fractions
- ↑ multi-component separations possible
- ↑ simple up-scaling

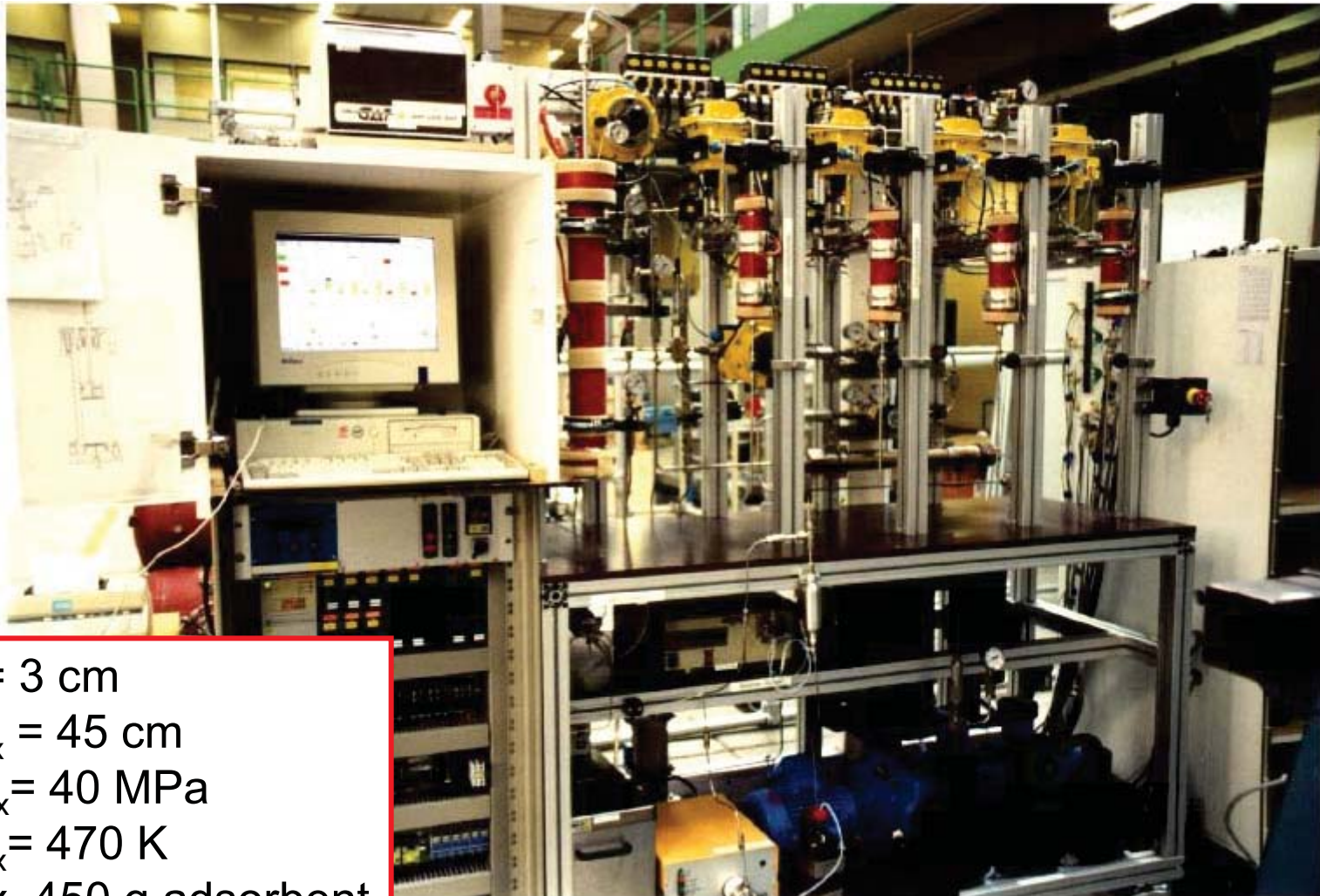
SMB-Technique

- ↑ continuous process
- ↑ lower solvent consumption
- ↑ higher concentrated products
- ↑ high yield (no waste fraction)
- ↓ especially for binary separations
- ↓ more complicated process development / technically demanding

Preparative Batch-SFC



Preparative Batch-SFC

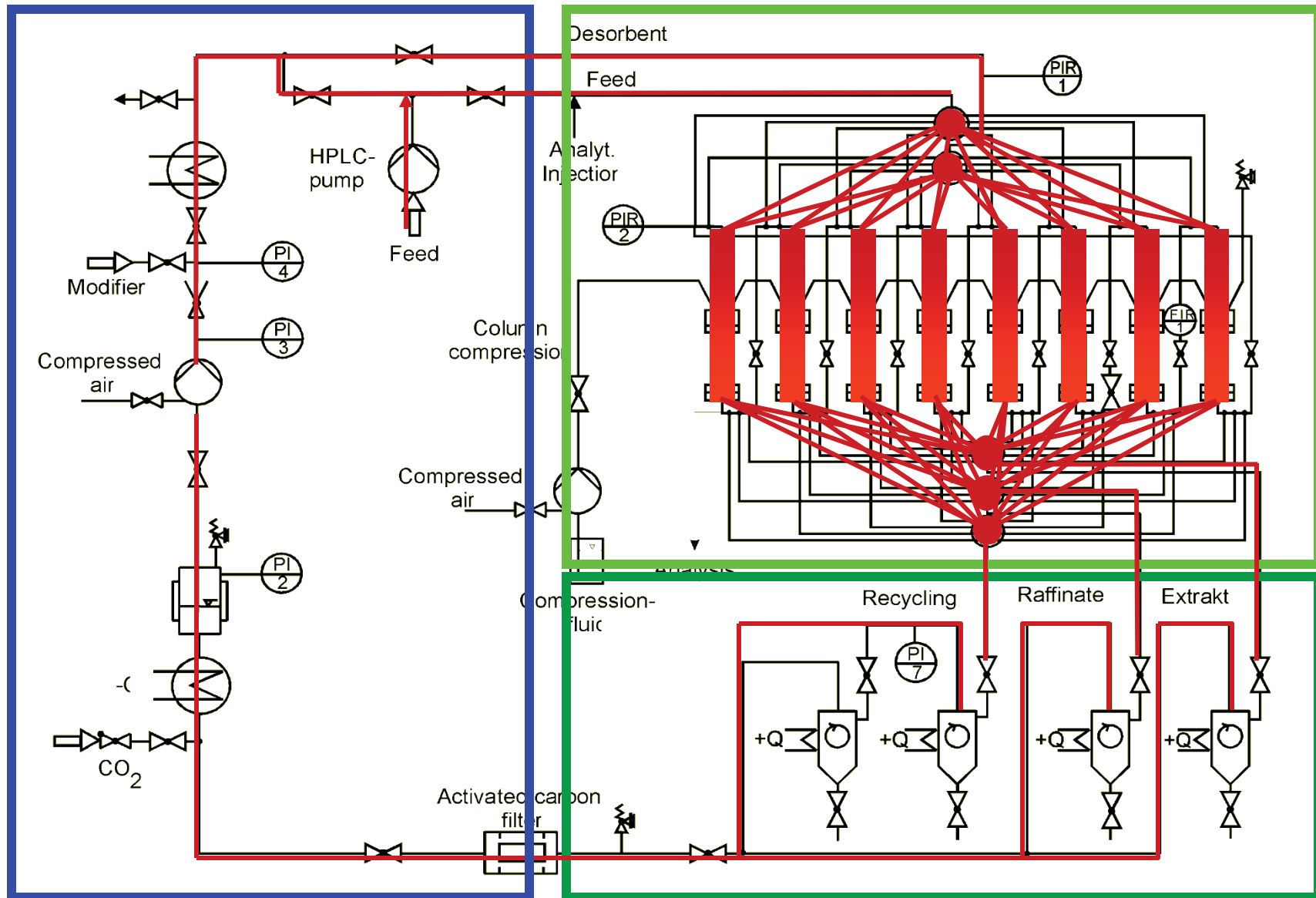


ID = 3 cm
 $L_{\max} = 45$ cm
 $P_{\max} = 40$ MPa
 $T_{\max} = 470$ K
max. 450 g adsorbent

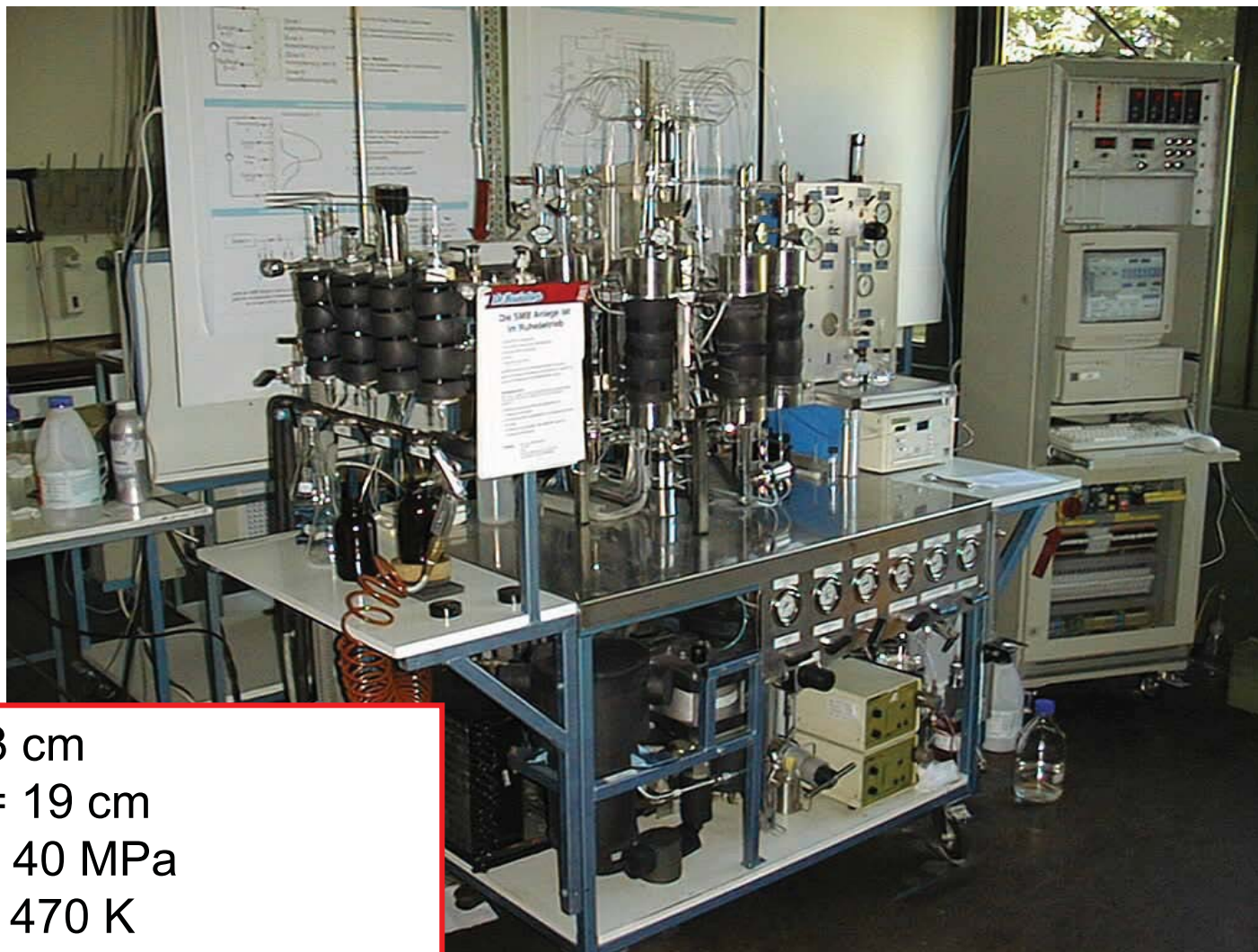
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SMB-SFC



SMB-SFC



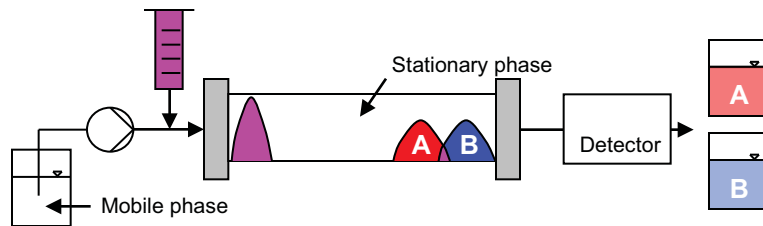
ID = 3 cm
 $L_{\max} = 19$ cm
 $P_{\max} = 40$ MPa
 $T_{\max} = 470$ K
max. 8 x 100 g adsorbent

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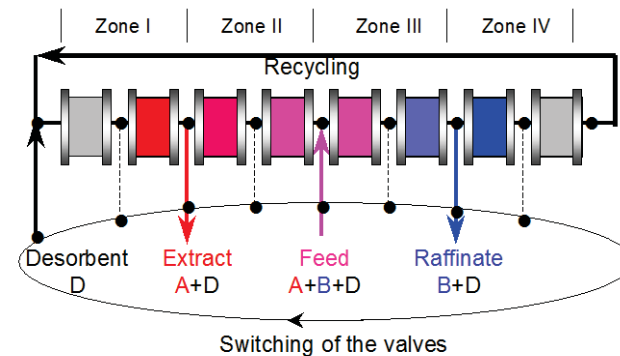
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Process development

Batch-SFC



SMB-SFC



Parameters of influence:

- Separation system (adsorbent, particle size, mobile phase composition)
- Column geometry
- Operation parameter (pressure, temperature, flow rate, injection volume, fraction period)

Additional parameters:

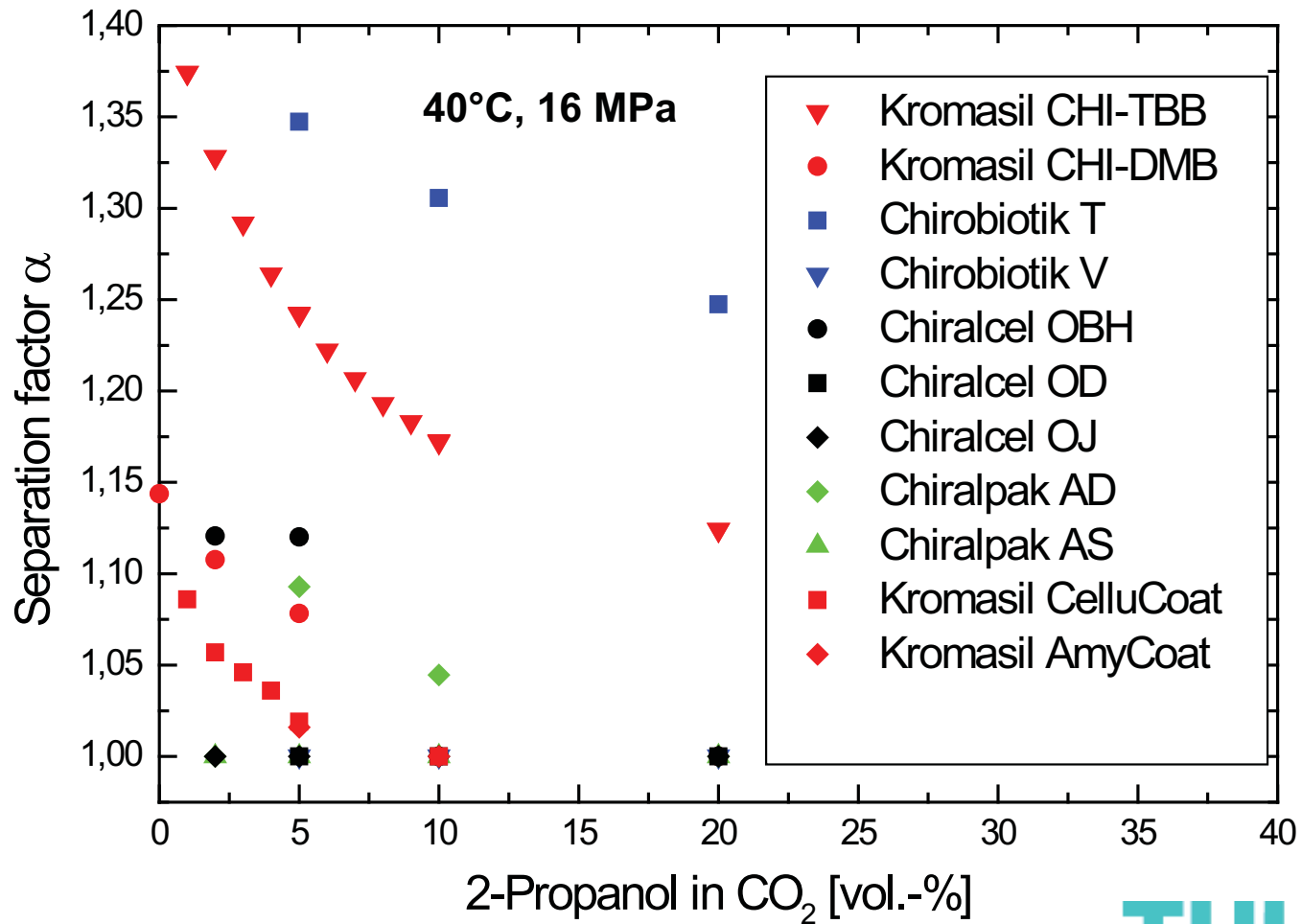
- Column configuration
- Flow rates in the different zones
- Switching time of the valves

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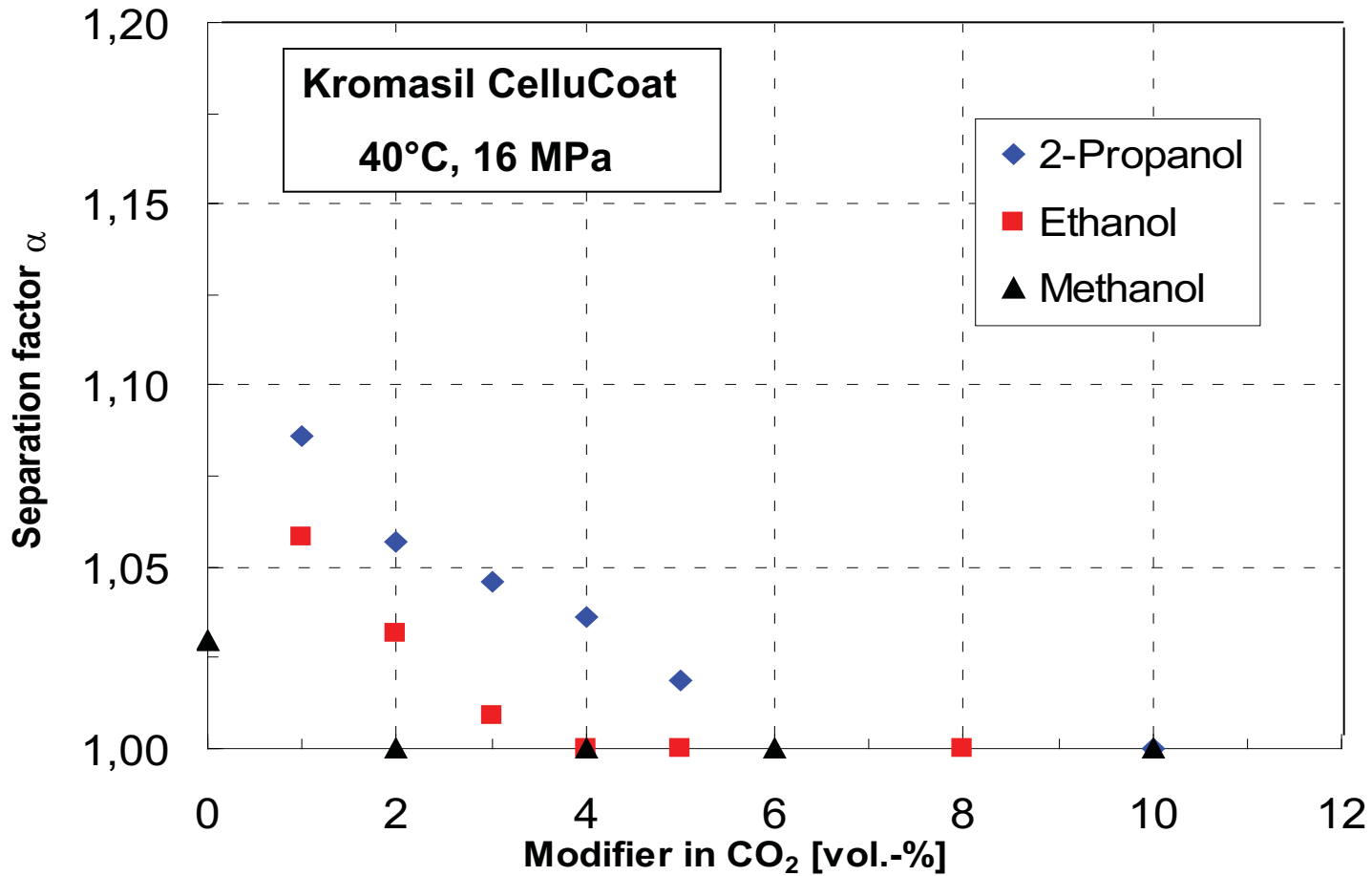
Selection of stationary phase

SFC separation of (R,S)-ibuprofen



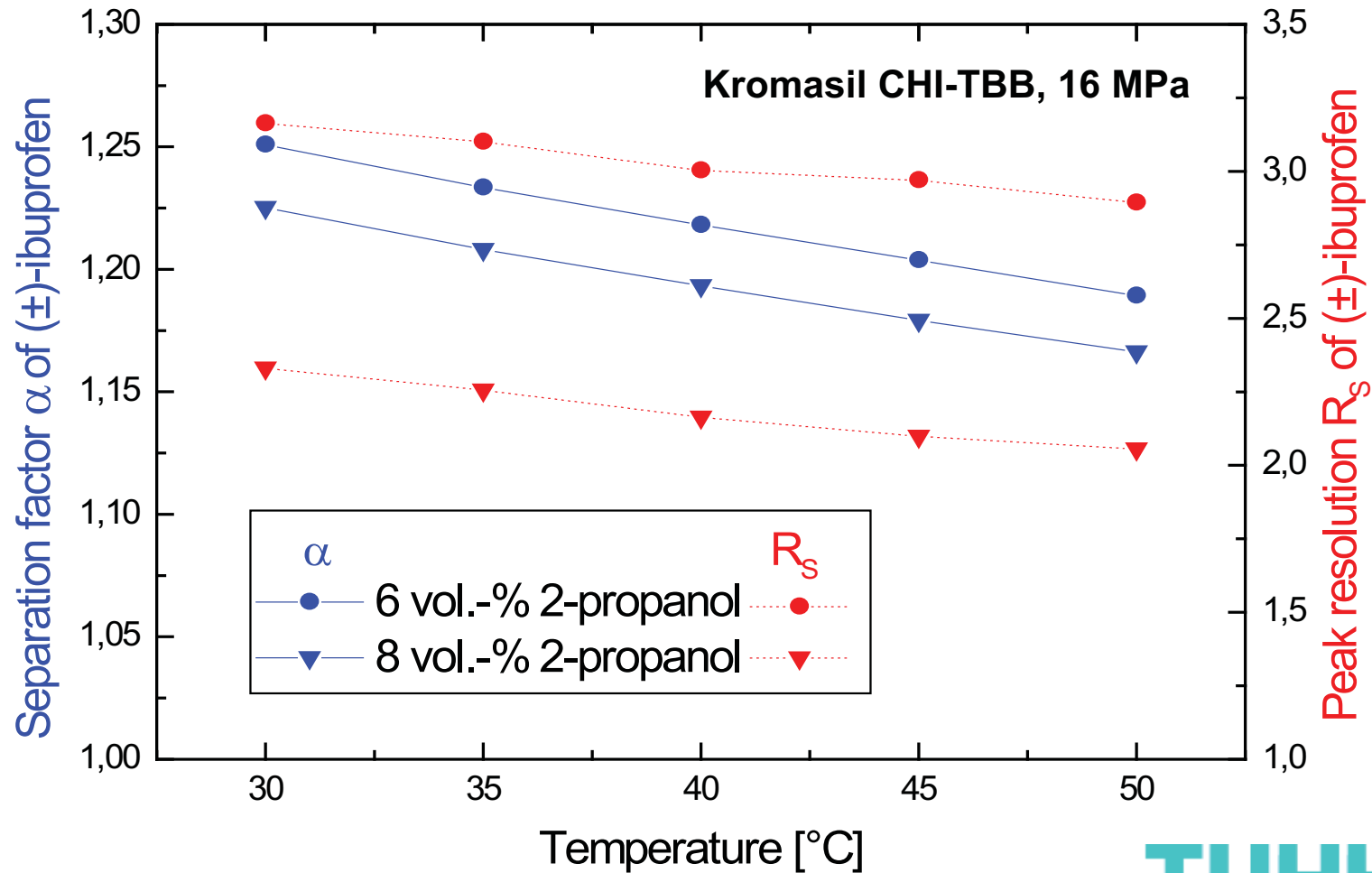
Selection of mobile phase

SFC separation of (R,S)-ibuprofen



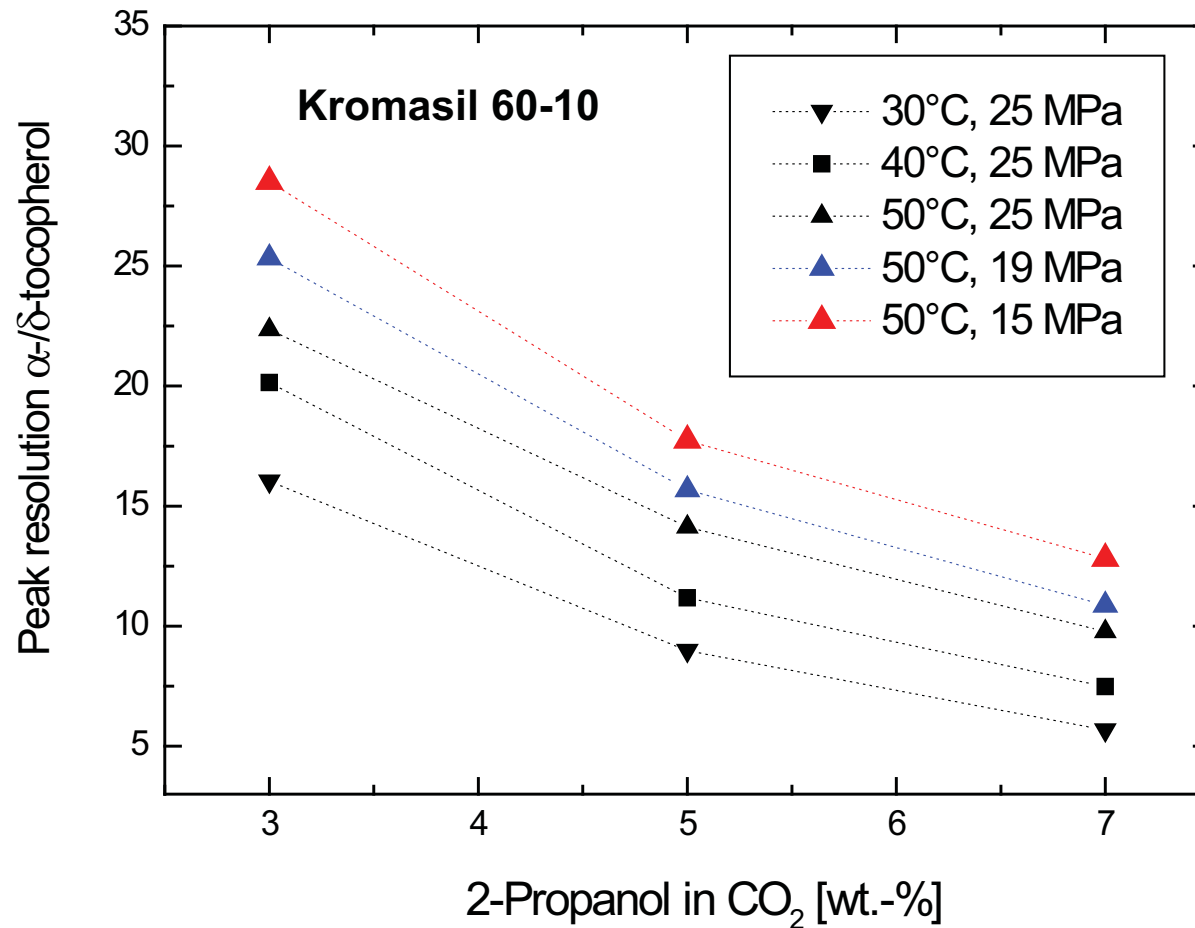
Influence of temperature

SFC separation of (R,S)-ibuprofen

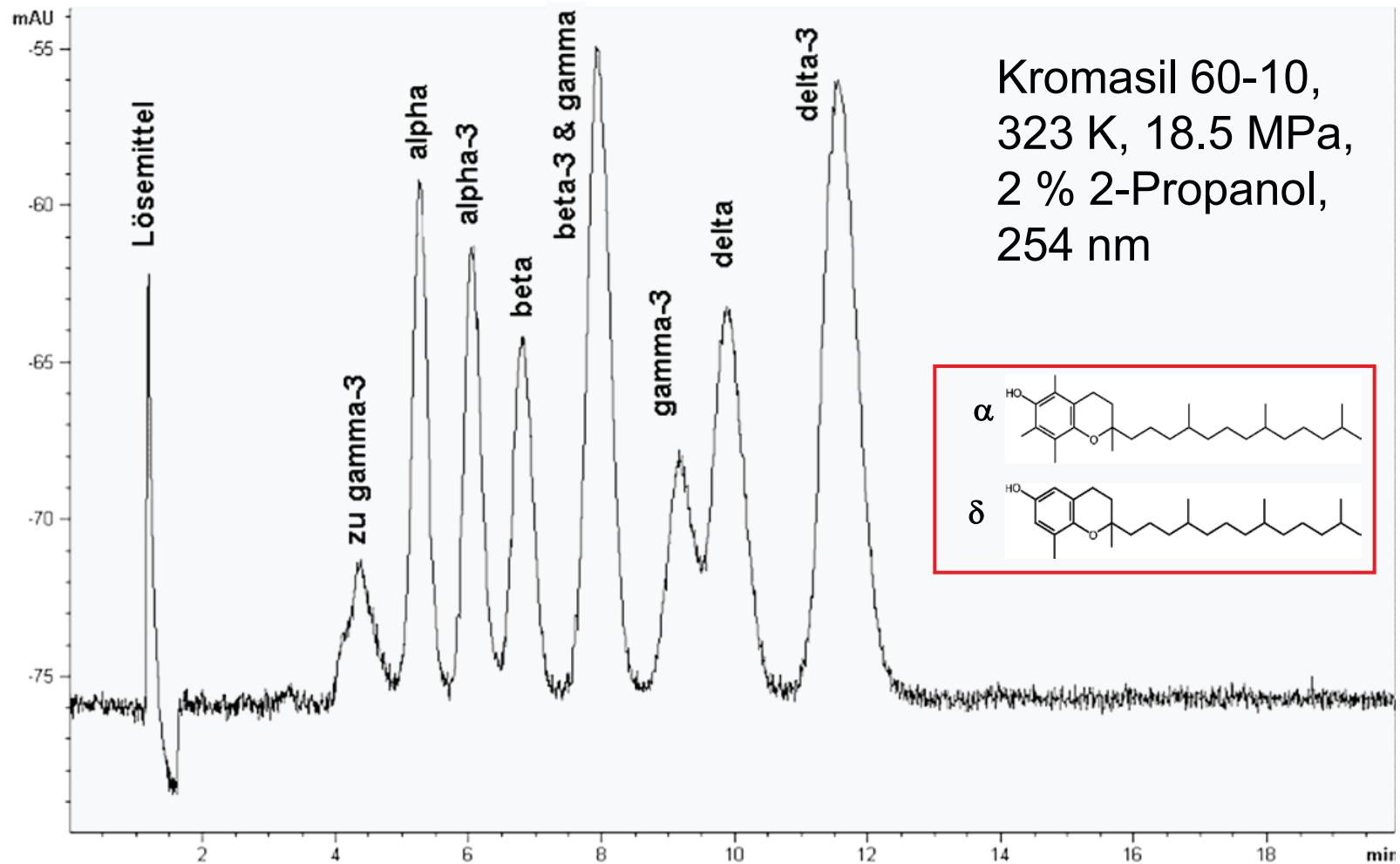


Influence of temperature and pressure

SFC separation of α -/ δ - tocopherol

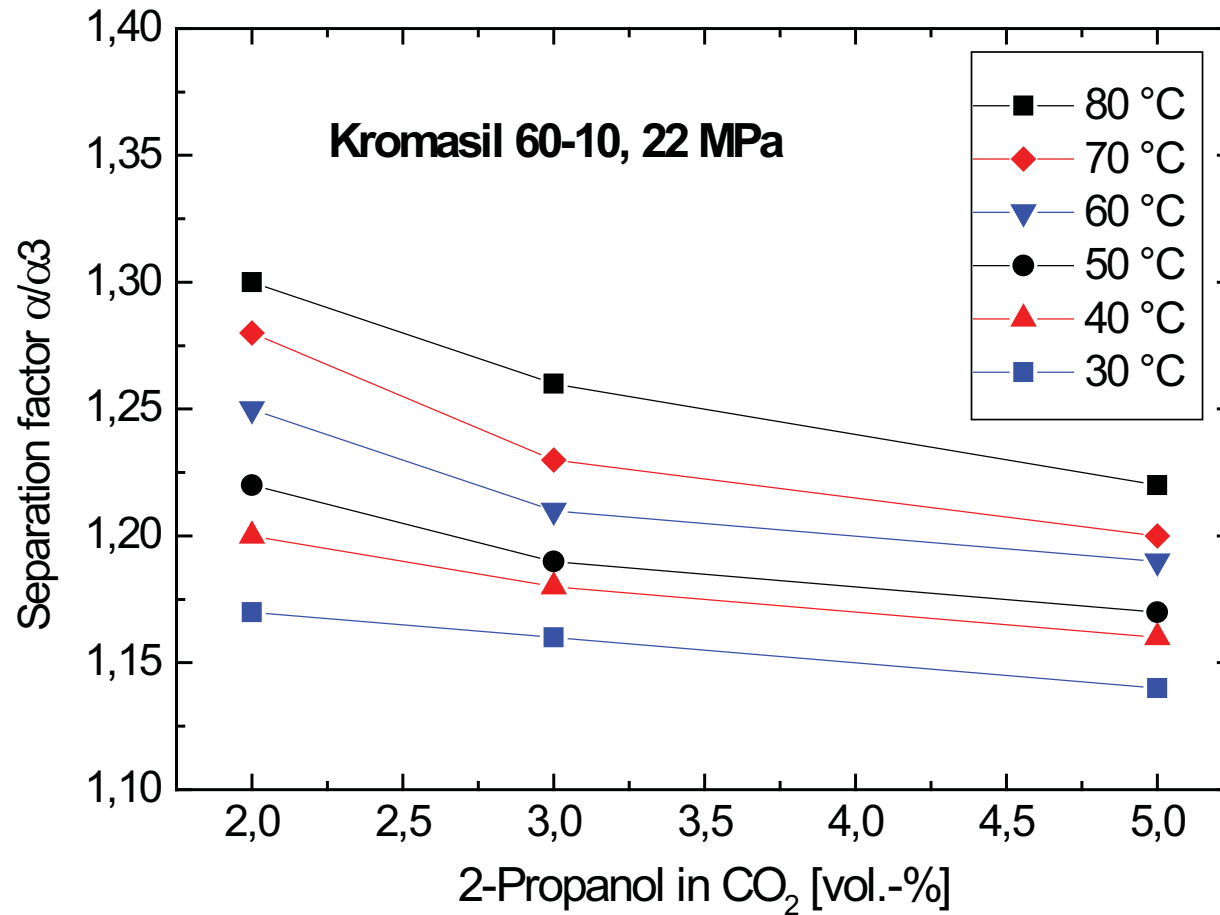


Chromatogramm of tocochromanols

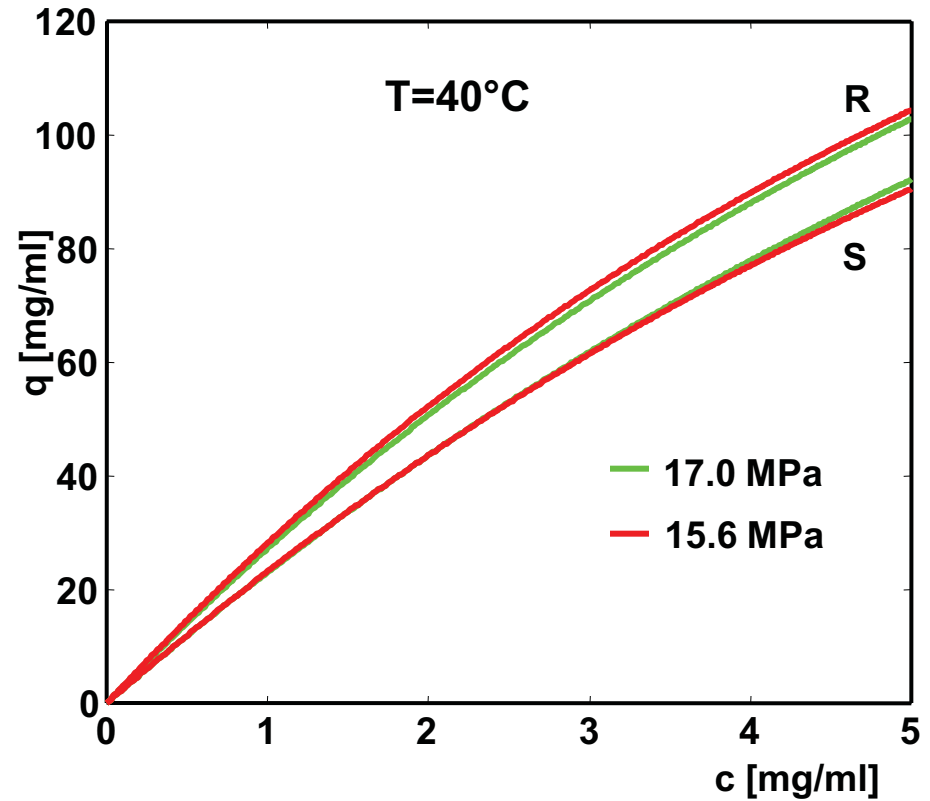
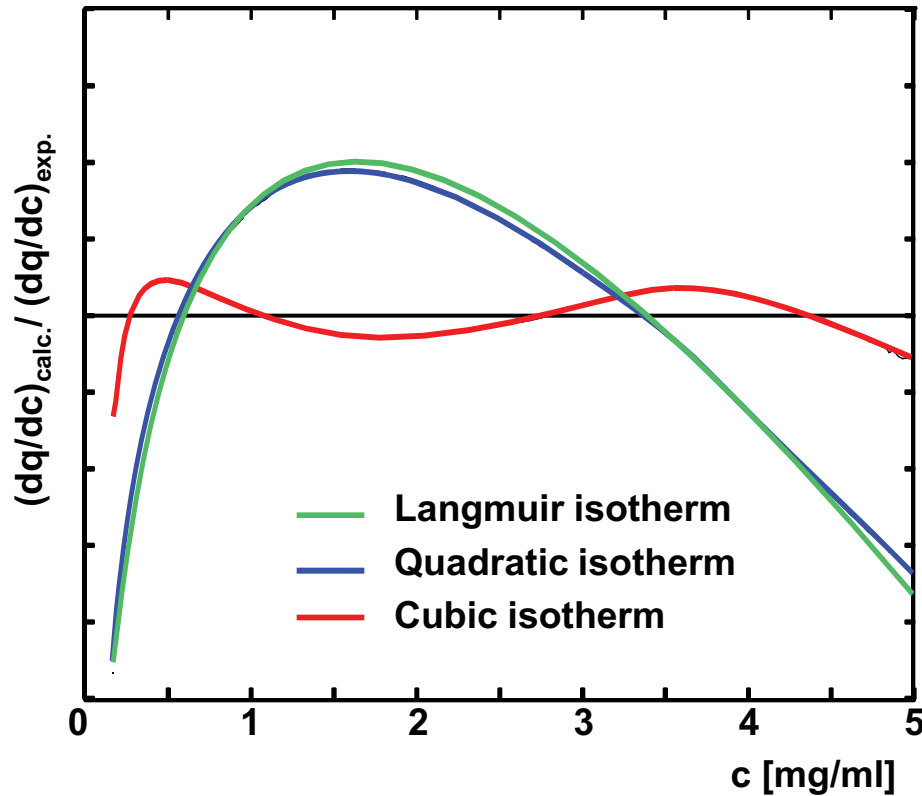


Influence of temperature

SFC separation of α -tocopherol/ α -tocotrienol



Measurement of adsorption isotherms



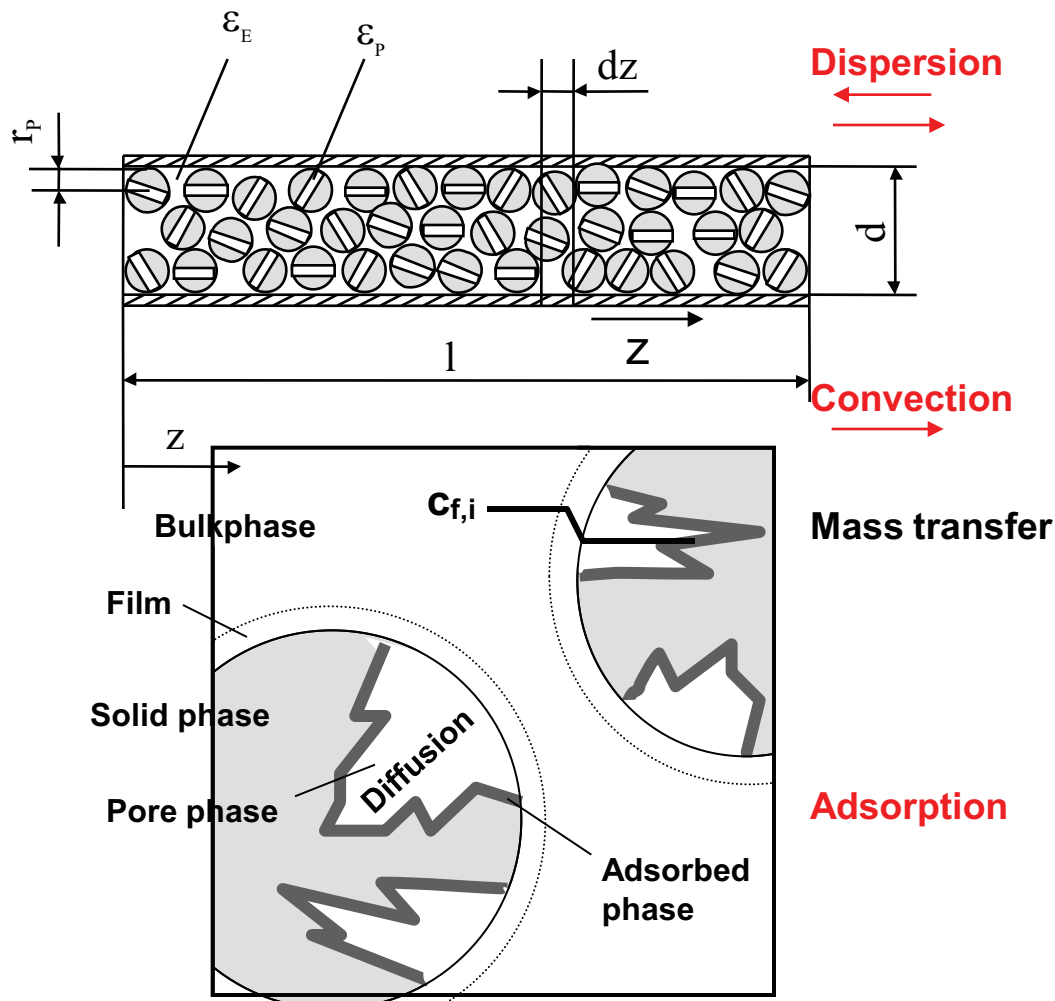
- ◆ Langmuir behaviour
- ◆ cubic Hill isotherm
- ◆ no influence of pressure in the range investigated
- ◆ R-enantiomer stronger adsorbed than S-enantiomer

$$q = \frac{q_s}{3} \times \frac{b_1 \times c + 2 \times b_2 \times c^2 + 3 \times b_3 \times c^3}{1 + b_1 \times c + b_2 \times c^2 + b_3 \times c^3}$$

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Model assumptions



Used balance equation:

- Equilibrium dispersive model
- Mobile phase velocity is considered to be variable

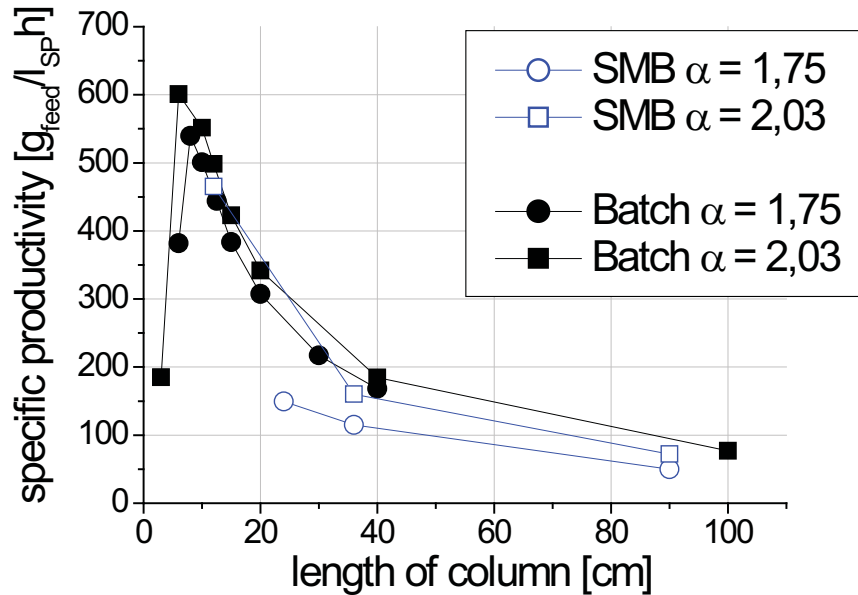
Adsorption:

- Single component isotherms determined (cubic Hill isotherm)
- Describing binary adsorption by the ideal adsorbed solution theory (IAST)

Specific productivities

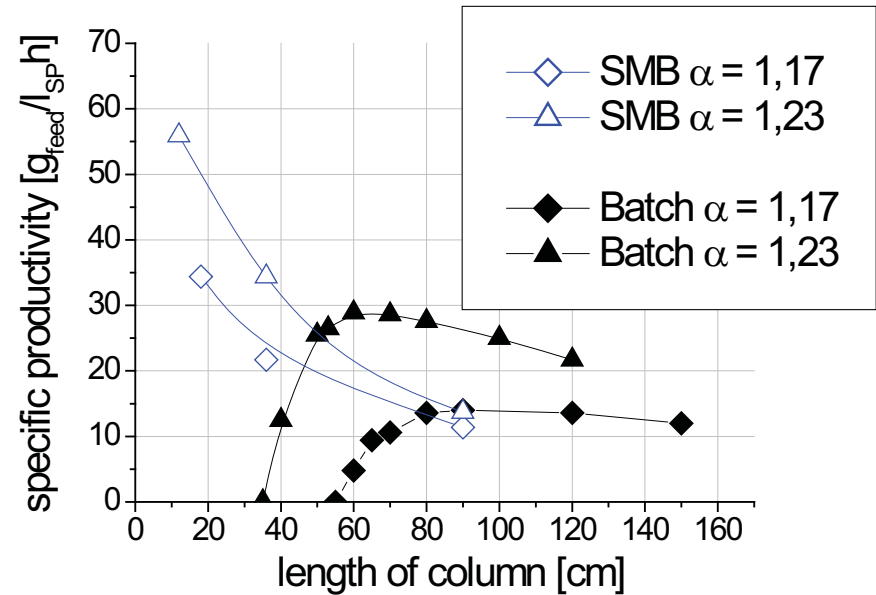
$N_{th} = 2500 \text{ m}^{-1}$, $u_{max} = 0.84 \text{ cm/s}$; SMB column configuration: 1/2/2/1

High separation factor



- **High separation factor:** Specific productivities nearly the same for both processes (Batch and SMB)

Low separation factor



- **Low separation factors:** Specific productivities of the SMB-process significant higher

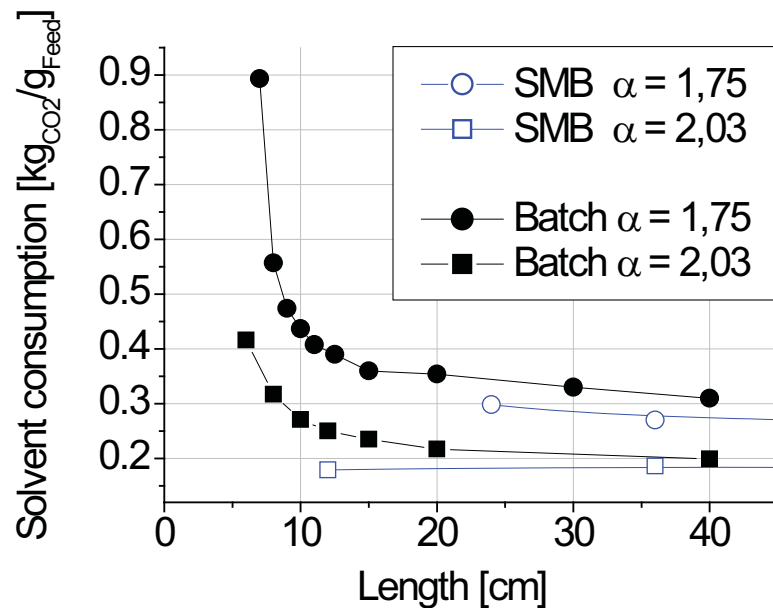
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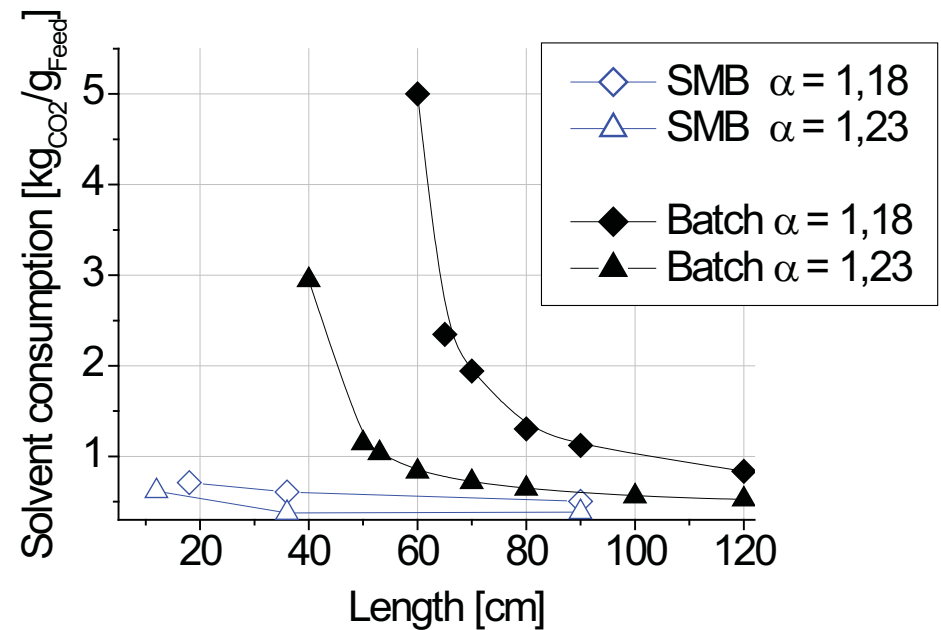
Solvent consumption

$N_{th} = 2500 \text{ m}^{-1}$, $u_{max} = 0.84 \text{ cm/s}$; SMB column configuration: 1/2/2/1

High separation factor



Low separation factor

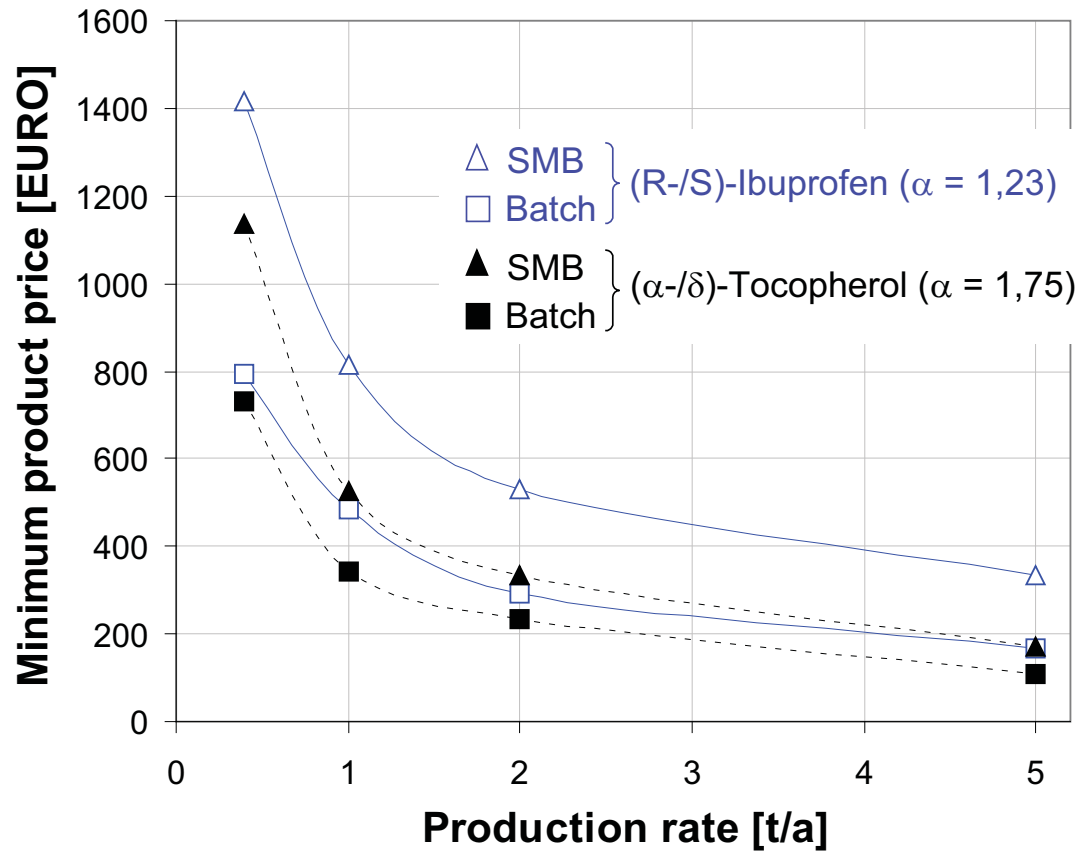


- The solvent consumption depends on the separation factor
- Solvent consumption of SMB-process significant lower

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Analysis of profitability



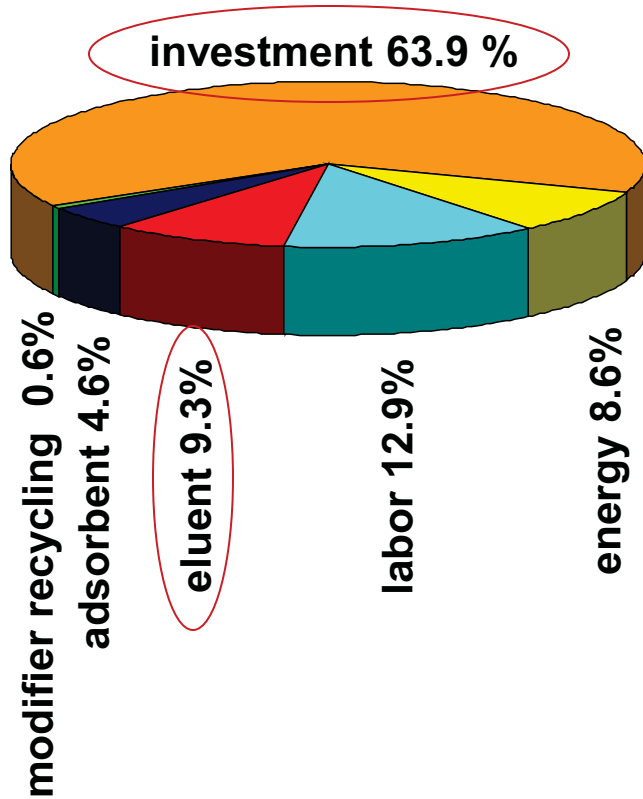
- In the range of investigated production rates, the Batch-process is the cheaper process

Distribution of costs

Separation of (R,S)-ibuprofen: 5 t/a (eluent: CO₂ + 2-propanol)

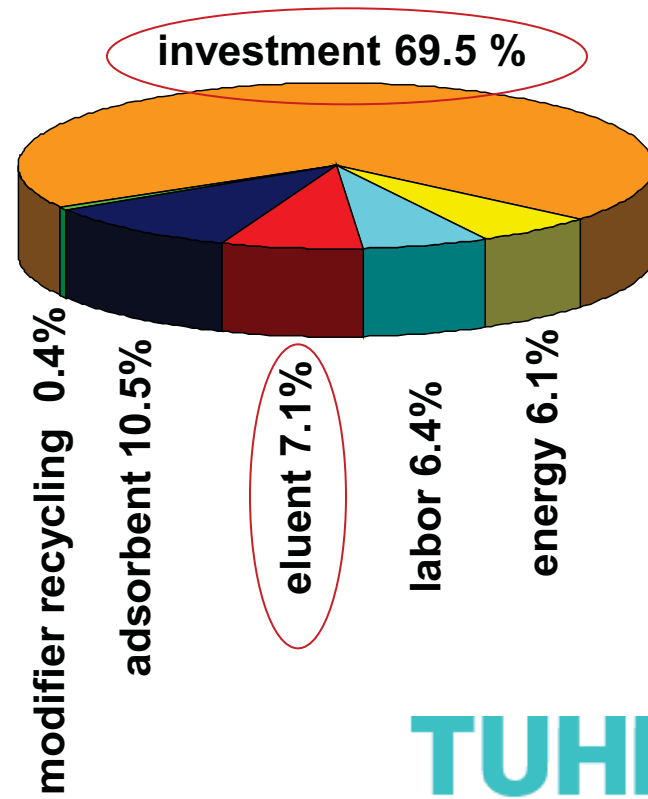
Batch-SFC

167 €/kg



SMB-SFC

337 €/kg

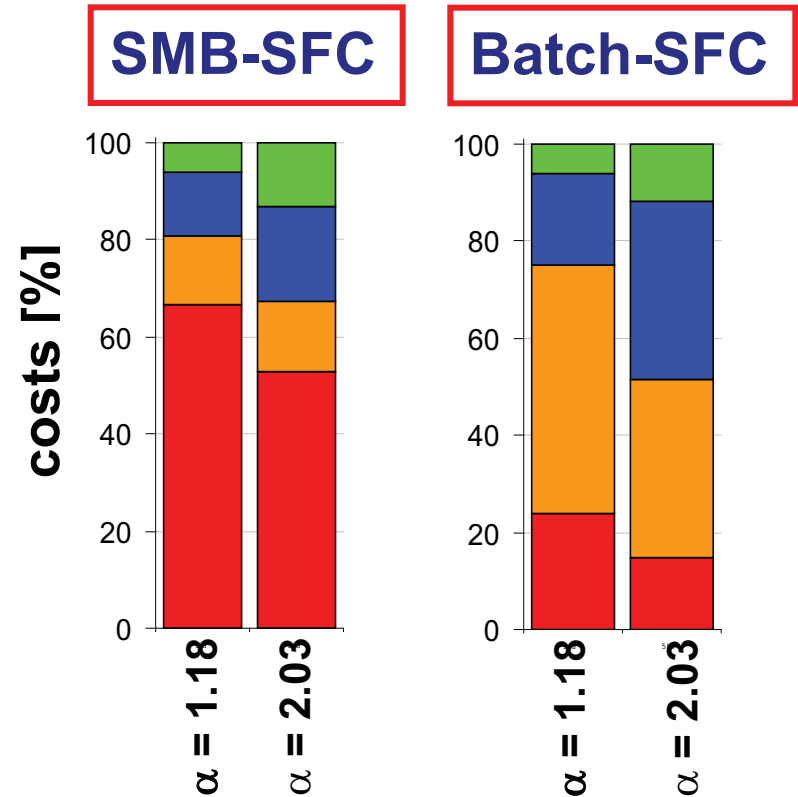
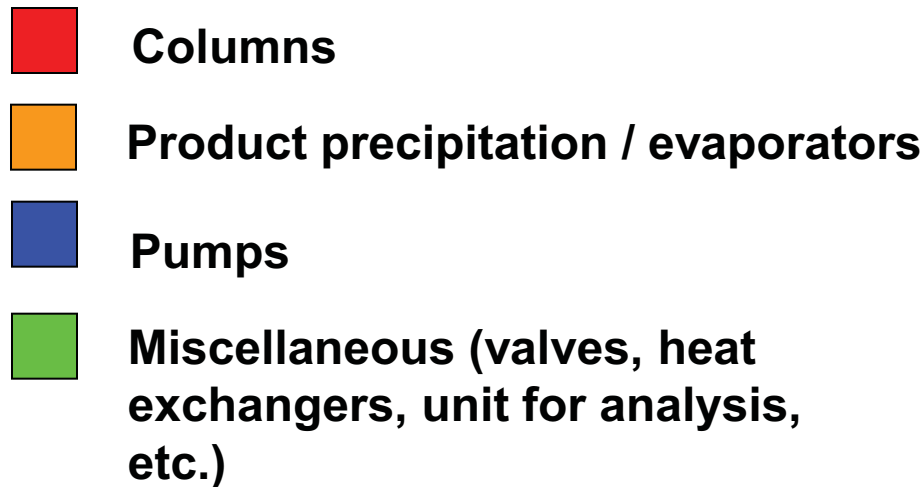


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Composition of fixed-capital investment

5 t/a



- **SMB-process: Costs dominated from costs of columns**
- **Batch-process: Costs dominated from costs of product precipitation and evaporators**
- **Investment costs of SMB are higher (factor 2 to 3)**

Summary

- Instruments for SFC at different scales are commercially available
- Batch-SFC (250 g st. phase) and SFC-SMB with up to 8 axial compressed columns (700 g st. phase) at TUHH
- Miscellaneous preparative SFC separations were carried out at TUHH successfully
- Adsorption equilibria as basis for optimisation of chromatographic processes
- Methods for process optimisation in SFC (Batch and SMB) are at hand
- In the range of the investigated production rates, the Batch-SFC is the more profitable process compared to SMB-SFC (cheap and easy!)

THANKS

Coworker: Matthias Lübbert
Dennis Bolten
Stephanie Peper
Meng-Han Chuang

Deutsche Forschungsgemeinschaft



YOU !

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