Chromatographic reactors

Andreas Seidel-Morgenstern

- **Reactor Concepts**
- **Preparative Chromatography**
- **Discontinuously operated Chromatographic Reactor**
- **Simulated Moving Bed Reactor**
- **Conclusions**

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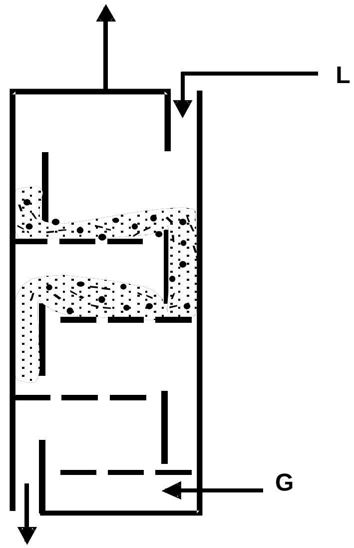
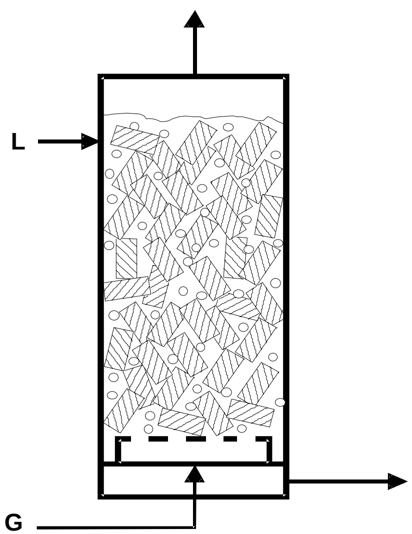
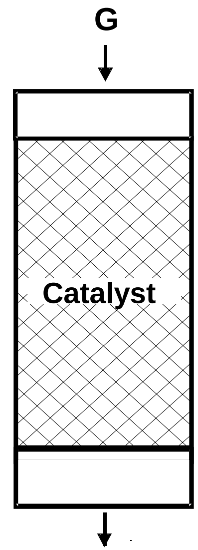
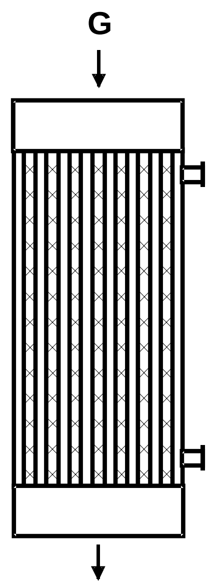
Gas/liquid reactors



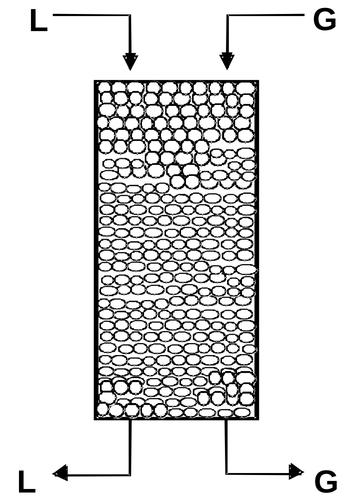


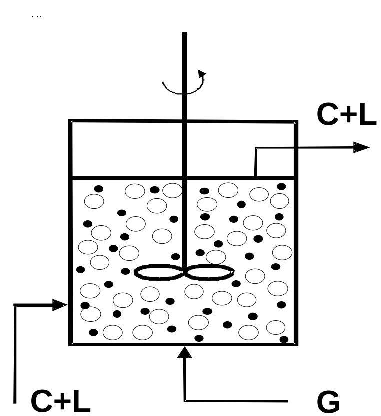
Fixed-bed reactors





Three phase reactors





Why more ?

Typical problems

A) Reversibility

$$A + B \rightleftarrows C + D$$

Total conversion of A desired

Removal of C and D advantageous

B) Limited selectivity

$$A + B \longrightarrow C$$

C is target (D undesired)

$$A + C \longrightarrow D$$

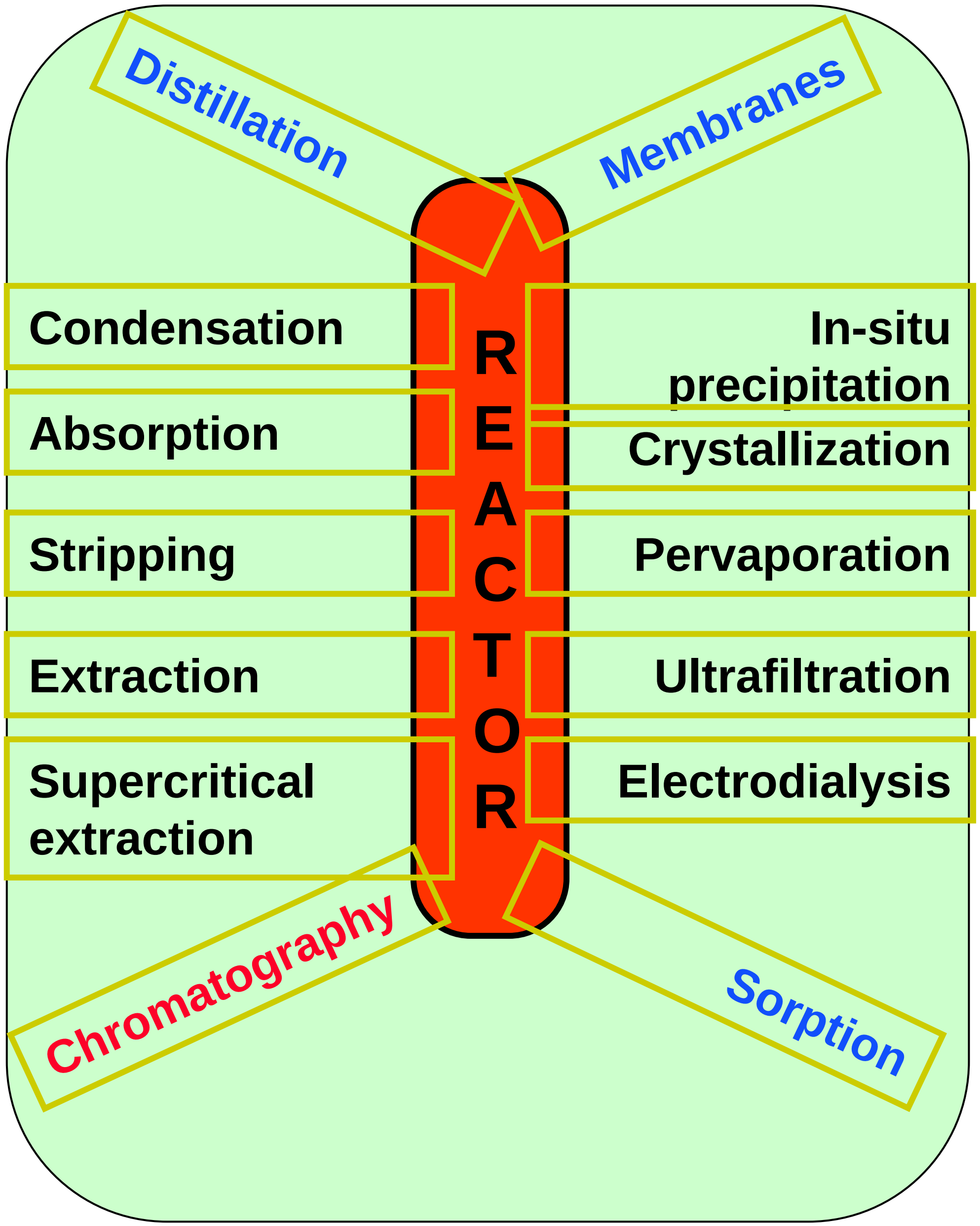
Tendencies

- search for alternative chemistry (other feedstocks and/or reaction pathways)

- improving reaction engineering

→ intelligent coupling of reaction and separation

Possibilities of coupling reaction and separation



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Features of preparative chromatography

- small particles - low diffusion resistances
- isothermal conditions - no energy balance required
- well packed columns - no radial gradients (1D)
- distribution equilibria established

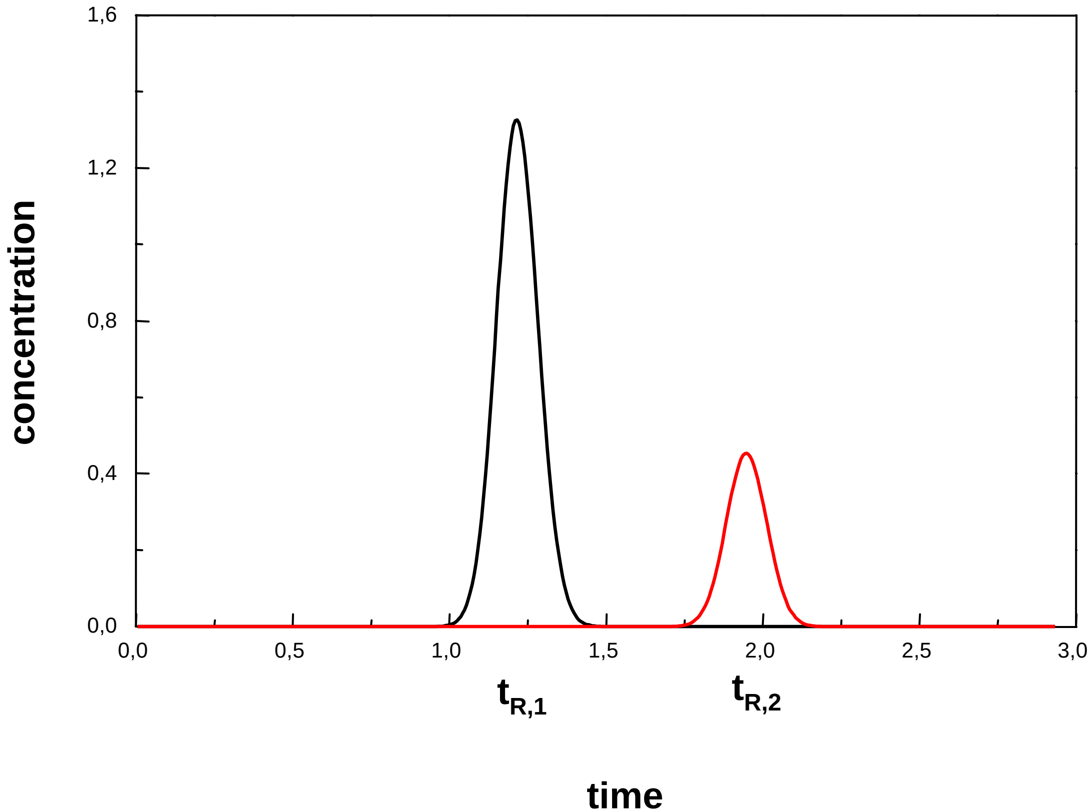
<u>Equilibrium dispersion model</u>

$$\frac{\partial c}{\partial t} + \frac{1-\varepsilon}{\varepsilon} \frac{\partial \overline{q}(c)}{\partial t} + w \frac{\partial c}{\partial z} = D_{ap} \frac{\partial^2 c}{\partial z^2}$$

D_{ap} - apparent dispersion coefficient,
lumps all kinetic effects,
related to plate number: $N = wL/2D_{ap}$

$q(c)$ - <u>adsorption isotherms</u>

Analytical Chromatography



$$t_{R,i} = t_0\left(1+\frac{1-\varepsilon}{\varepsilon}K_i\right) \quad \text{with} \quad t_0 = \frac{H}{w}$$

$$\alpha_{21} = \frac{K_2}{K_1}$$

Efficiency

$$N = \frac{\mu^2}{\sigma^2} \qquad \text{with} \qquad \mu = \frac{\int_0^\infty c(t)t\,dt}{\int_0^\infty c(t)\,dt} \qquad \sigma^2 = \frac{\int_0^\infty (t-\mu)^2 c(t)\,dt}{\int_0^\infty c(t)\,dt}$$

$$N = 5.54\left(\frac{t_R}{w_{0.5}}\right)^2$$ for Gaussian peaks

$$\mu = t_R = t_0\left(1 + \frac{1-\varepsilon}{\varepsilon}K\right) = t_0(1+k')$$ depends on thermodynamics

$$\sigma^2 = \frac{2D_{ax}(D_{mol,}R_P, w, \gamma_1, \gamma_2)}{Hw} t_R^2 + \ldots$$ depends on the kinetics of various effects

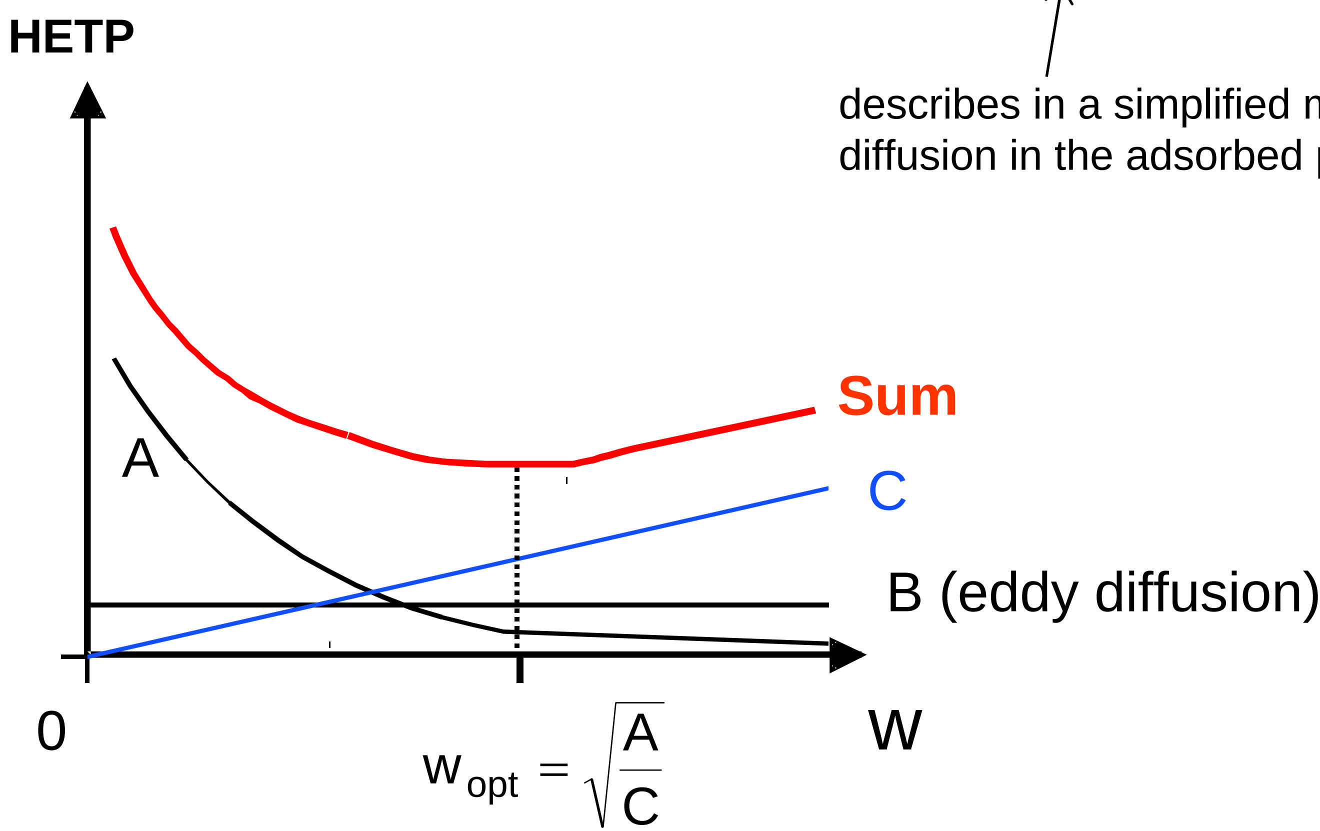
$$\boxed{HETP(w) = \frac{H}{N} = \frac{A}{w} + B + Cw}$$

e.g.: $$\mathbf{HETP} = \frac{2\gamma_1 D_{mol}}{w} + 4\gamma_2 R_P + 2w\frac{\varepsilon}{1-\varepsilon}\frac{1}{\beta_{LDF}K}\left(1 + \frac{\varepsilon}{(1-\varepsilon)K}\right)^{-2}$$

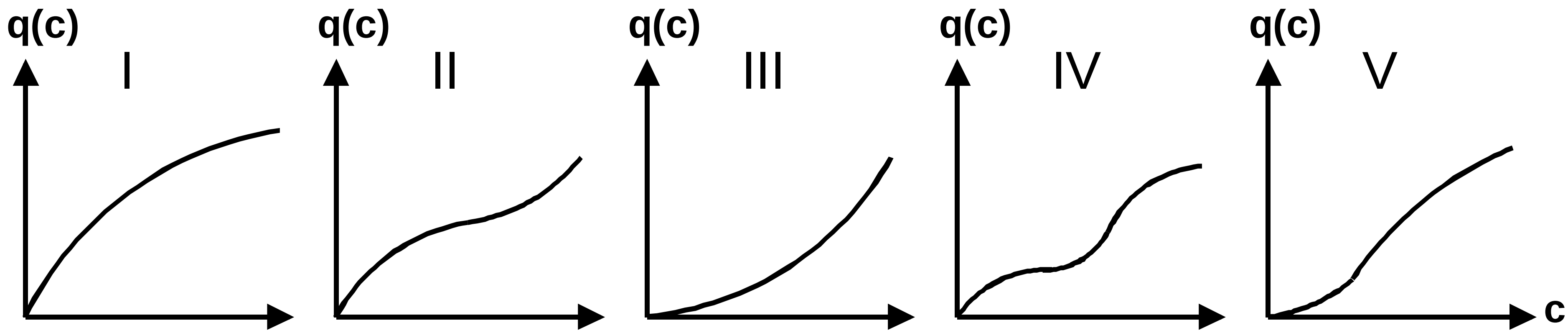
van Deemter Analysis

e.g.: $$\mathbf{HETP} = \frac{\mathbf{A}}{\mathbf{w}} + \mathbf{B} + \mathbf{Cw} = \frac{2\gamma_1 D_{mol}}{w} + 4\gamma_2 R_P + 2w \frac{\varepsilon}{1-\varepsilon} \frac{1}{\beta_{LDF} K} \left(1 + \frac{\varepsilon}{(1-\varepsilon)K}\right)^{-2}$$

describes in a simplified manner diffusion in the adsorbed phase



Adsorption isotherms



Brunauer classification

Mixtures even more complex !

Equilibrium theory

- assumes infinite efficiency (optimistic limiting case)
- explains shapes and migration speeds of characteristic fronts

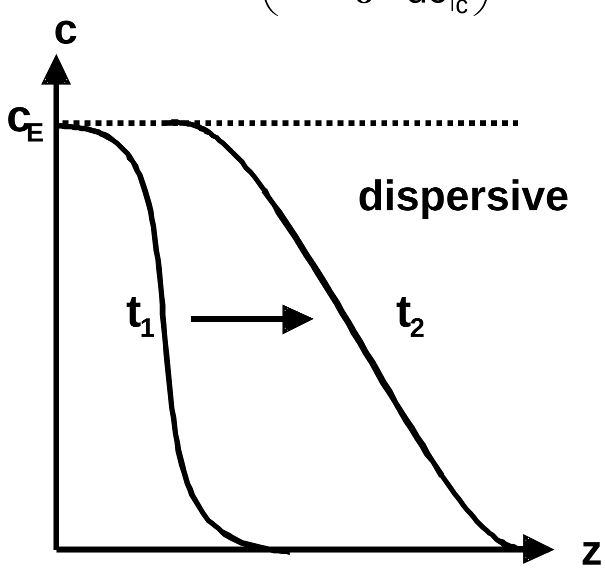
$$\frac{\partial c}{\partial t} + \frac{1-\varepsilon}{\varepsilon}\frac{\partial q(c)}{\partial t} + w\frac{\partial c}{\partial z} = 0$$

$$t_R(c) = \frac{H}{w}\left(1 + \frac{1-\varepsilon}{\varepsilon}\left.\frac{dq}{dc}\right|_c\right)$$

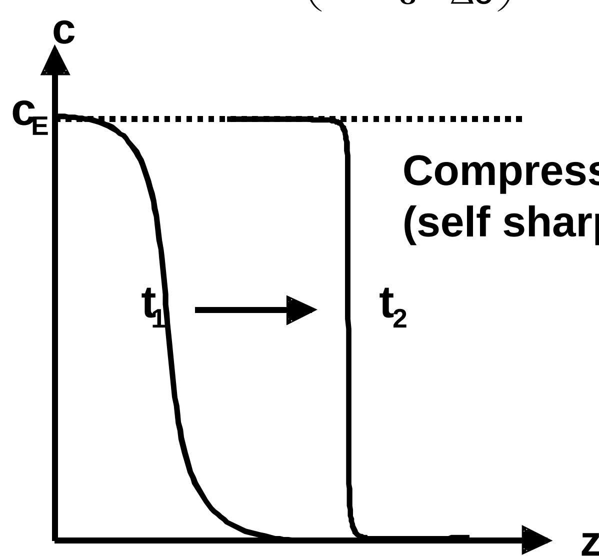
$$t_{R,shock} = \frac{H}{w}\left(1 + \frac{1-\varepsilon}{\varepsilon}\frac{\Delta q}{\Delta c}\right)$$

$$w_c(c) = \frac{w}{\left(1 + \frac{1-\varepsilon}{\varepsilon}\left.\frac{dq}{dc}\right|_c\right)}$$

$$w_{shock} = \frac{w}{\left(1 + \frac{1-\varepsilon}{\varepsilon}\frac{\Delta q}{\Delta c}\right)}$$

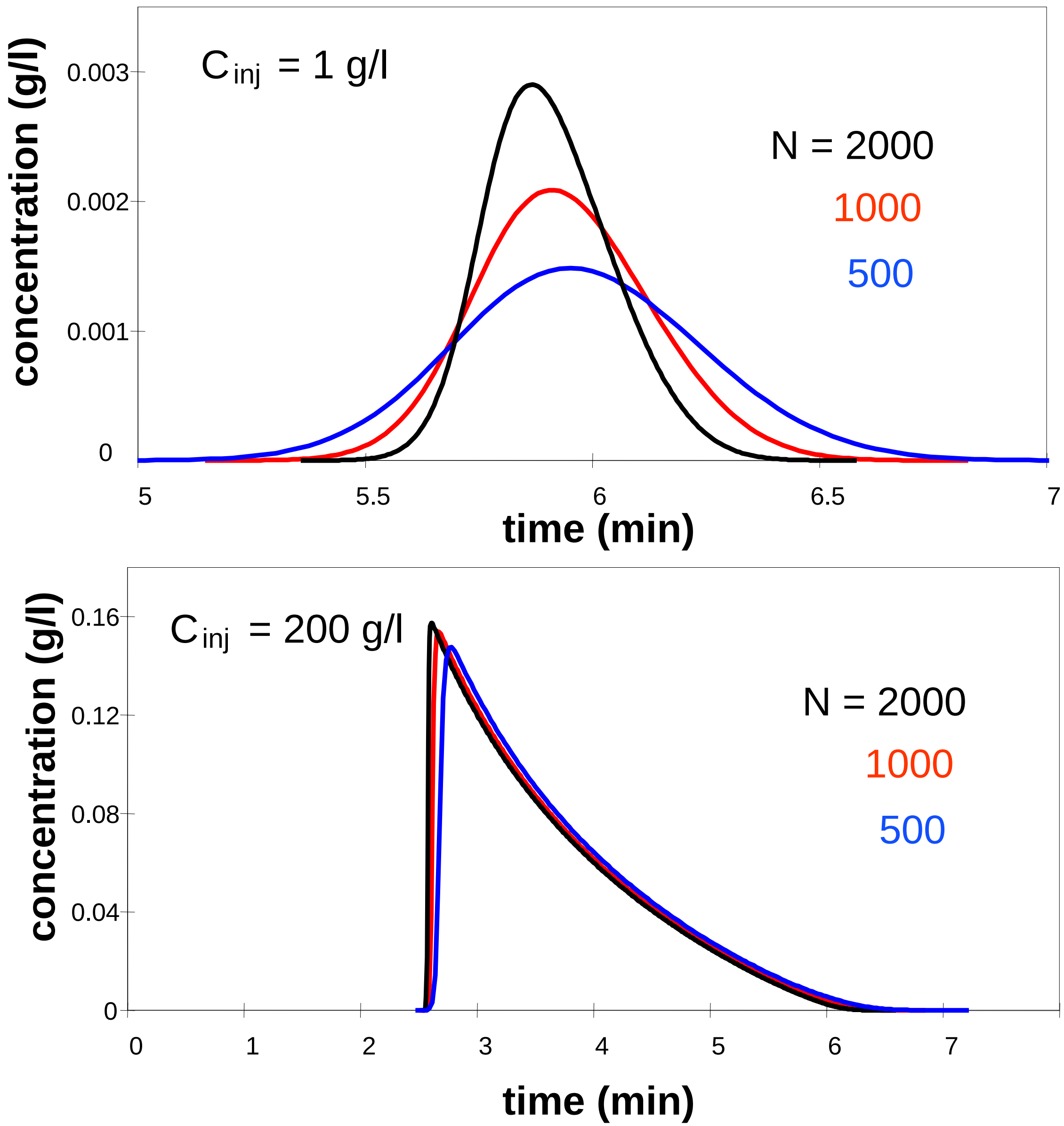


dispersive

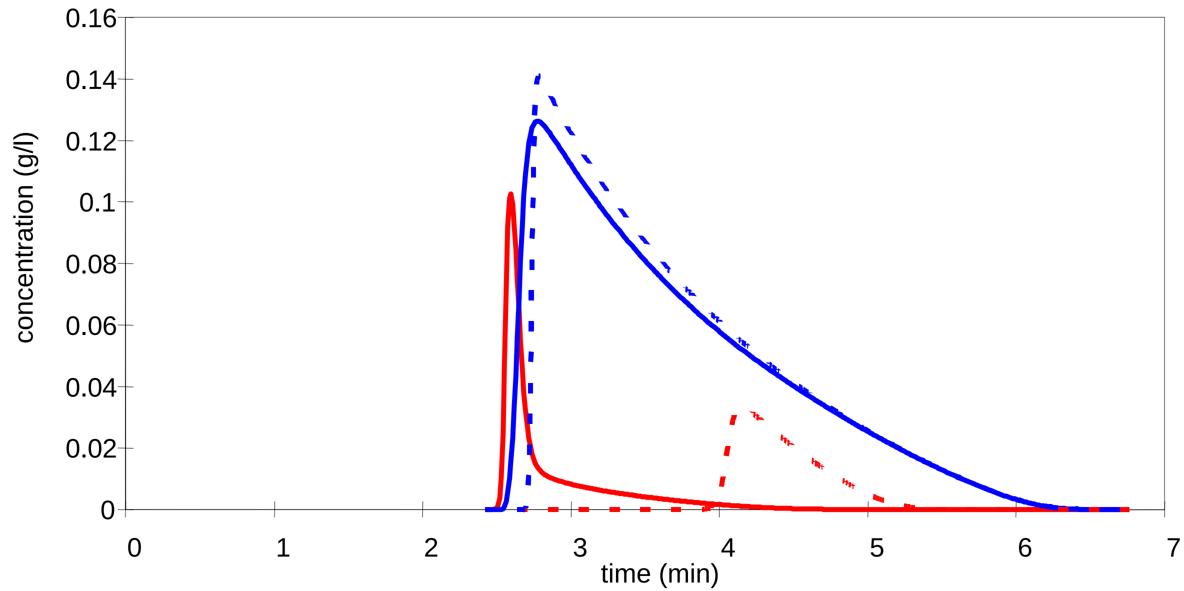


Compressive, “shock“
(self sharpening)

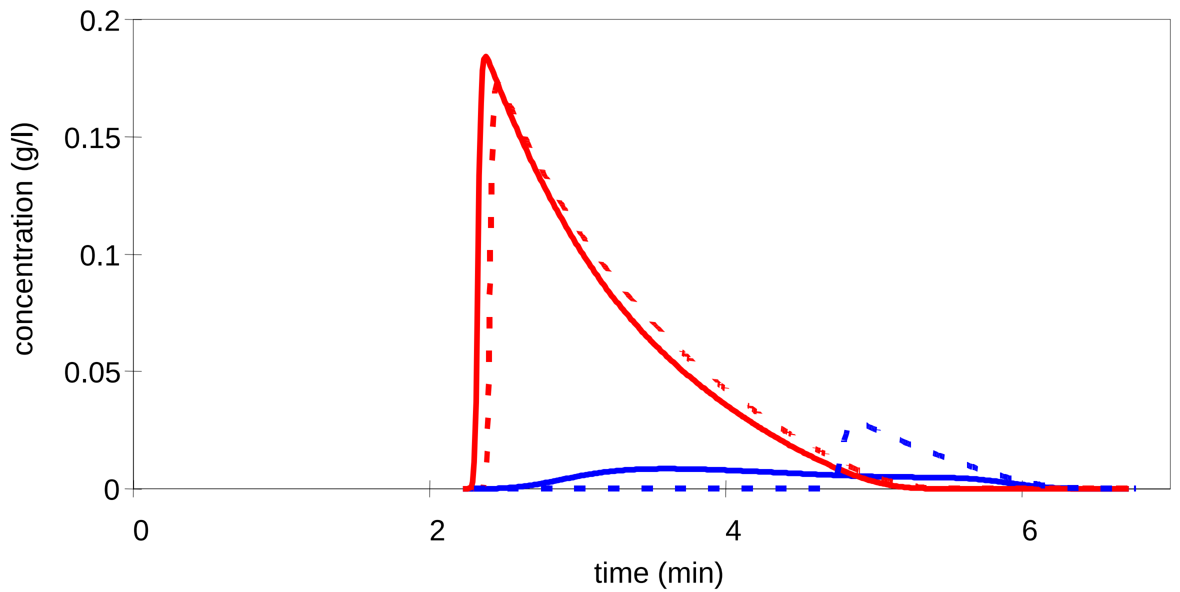
Dominance of thermodynamics in preparative chromatography



Influence of competition in preparative chromatography



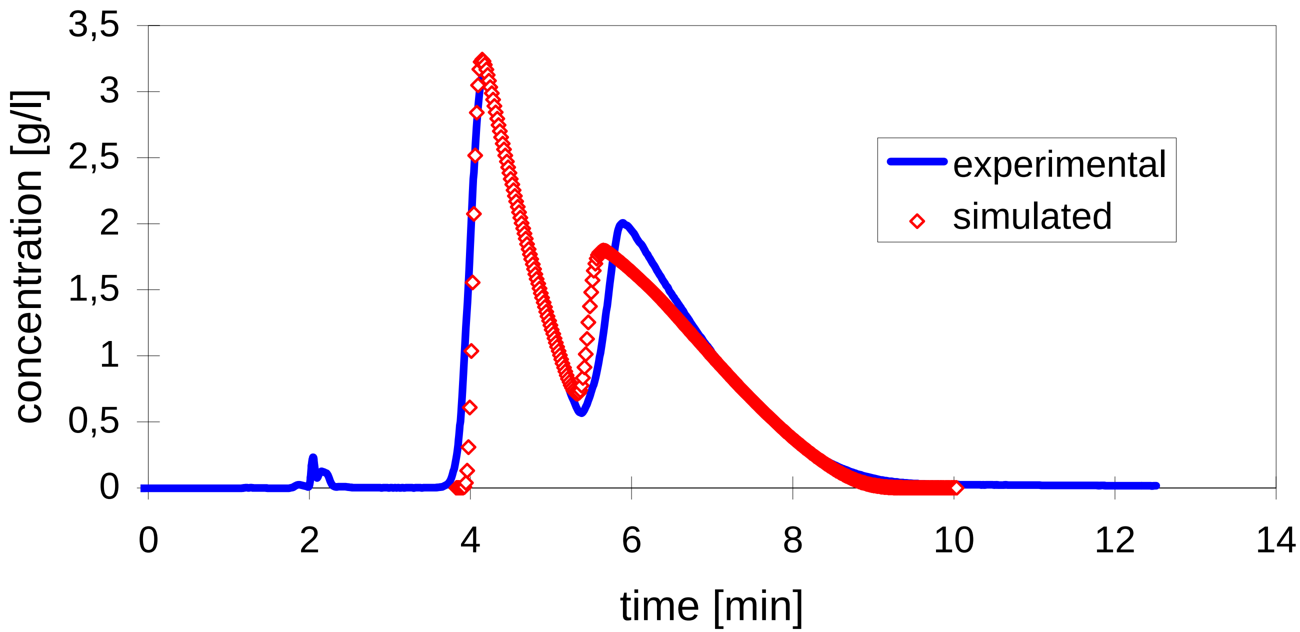
1 : 9 mixture
example of displacement



9 : 1 mixture
example of tag along

Elution profiles for the same amounts injected in a mixture and alone

Model validation

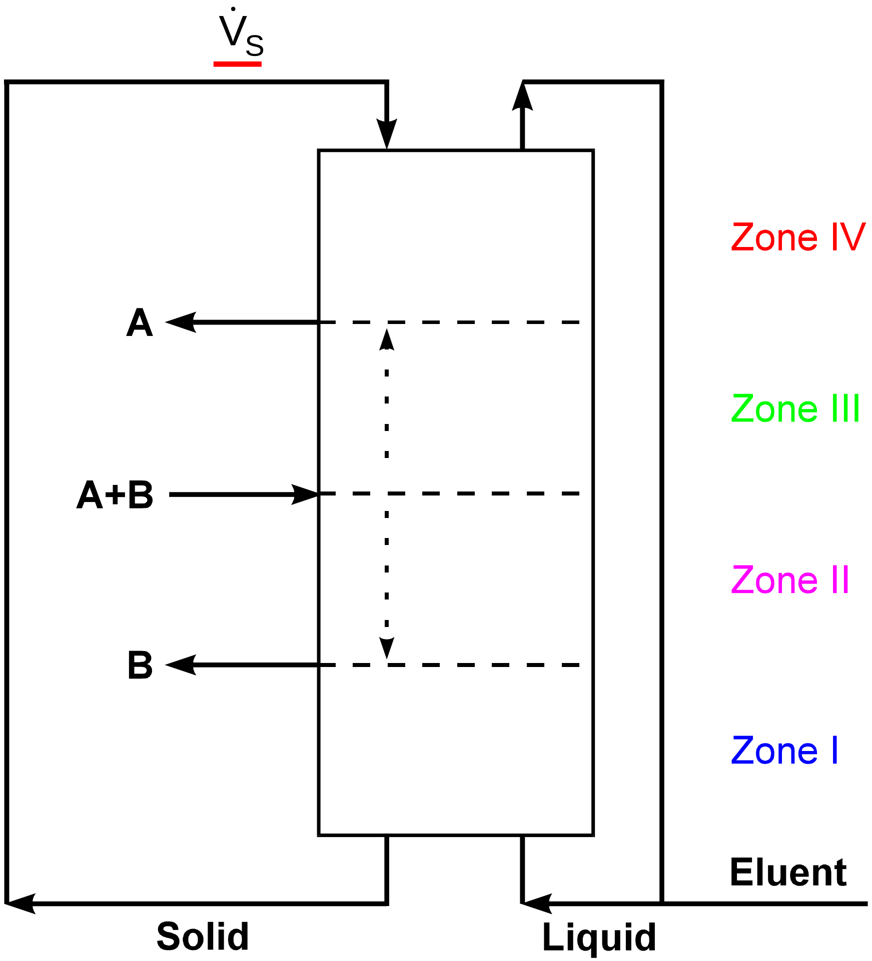


Separation of cyclopentanone and cyclohexanone on silica
mobile phase: hexane : ethylacetate = 85 : 15, T=20°C

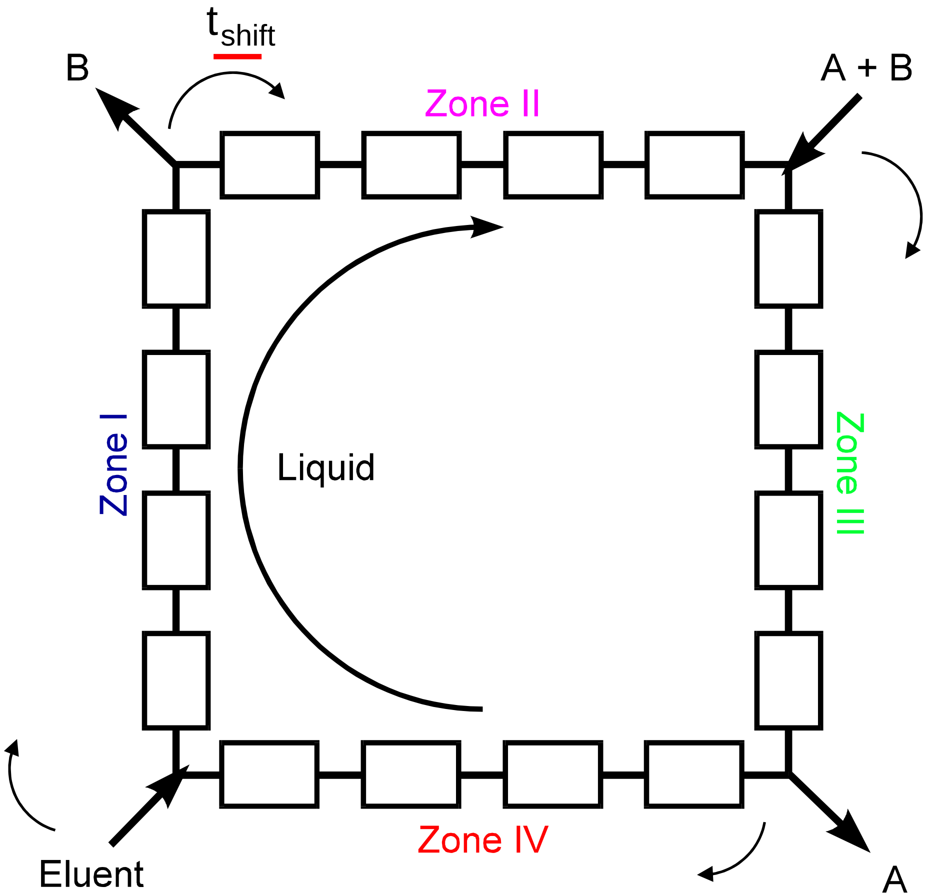
(H. Kniep, Ph. D. thesis, Magdeburg, 1998)

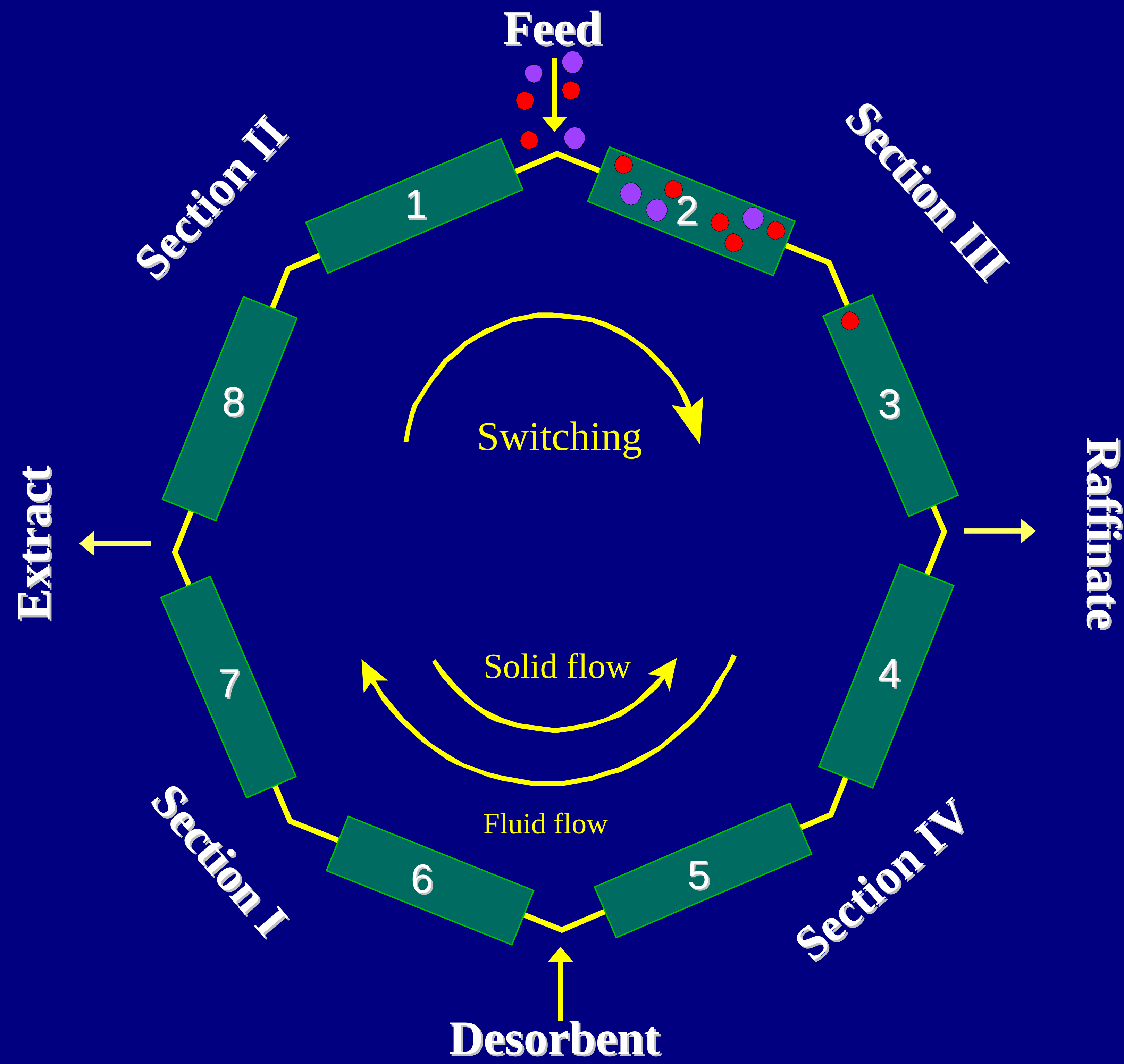
Continuous chromatography

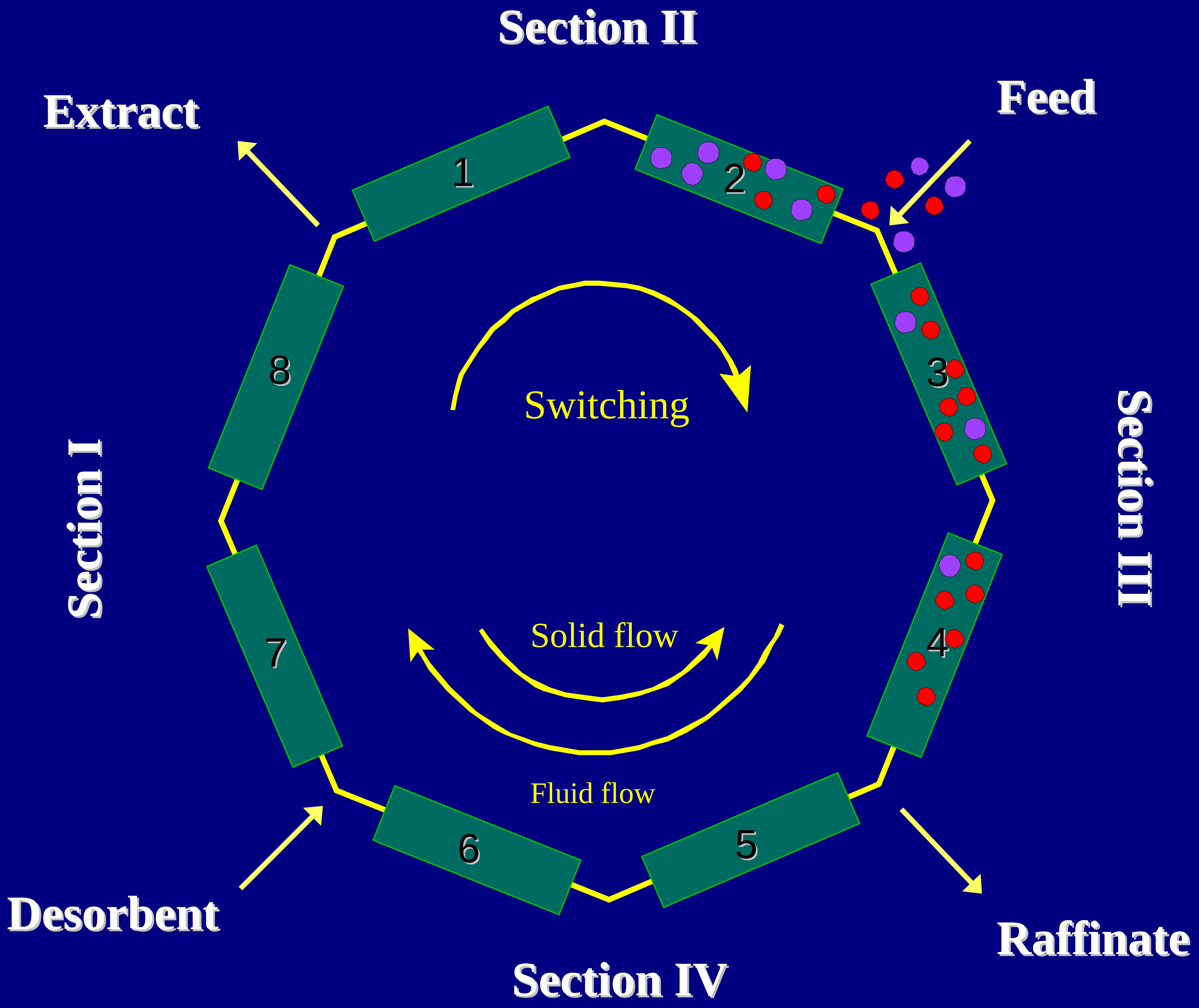
True Moving Bed



Simulated Moving Bed




Feed
Section II
Section III
1
2
3
4
5
6
7
8
Switching
Extract
Raffinate
Solid flow
Fluid flow
Section I
Section IV
Desorbent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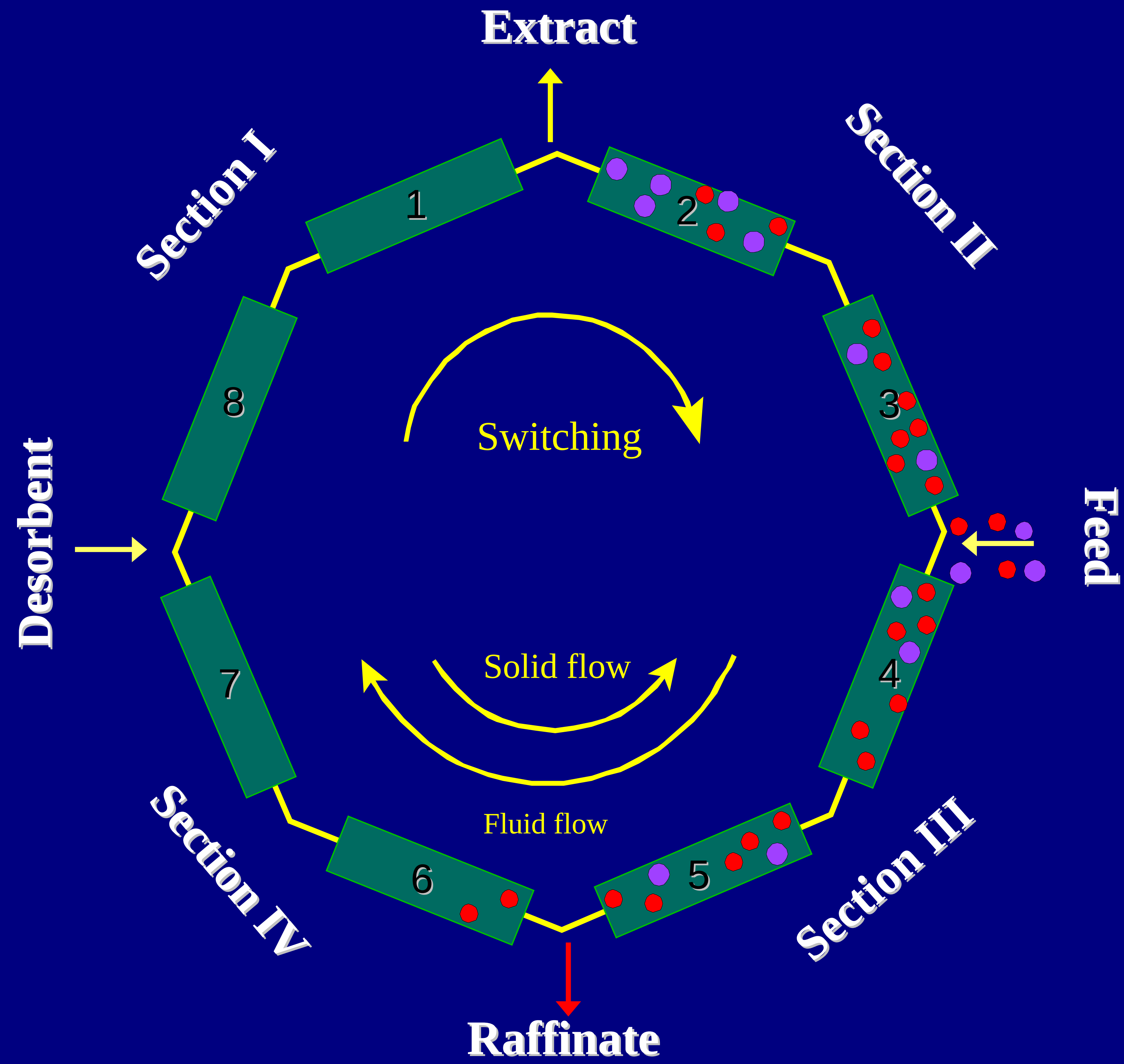
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Section I
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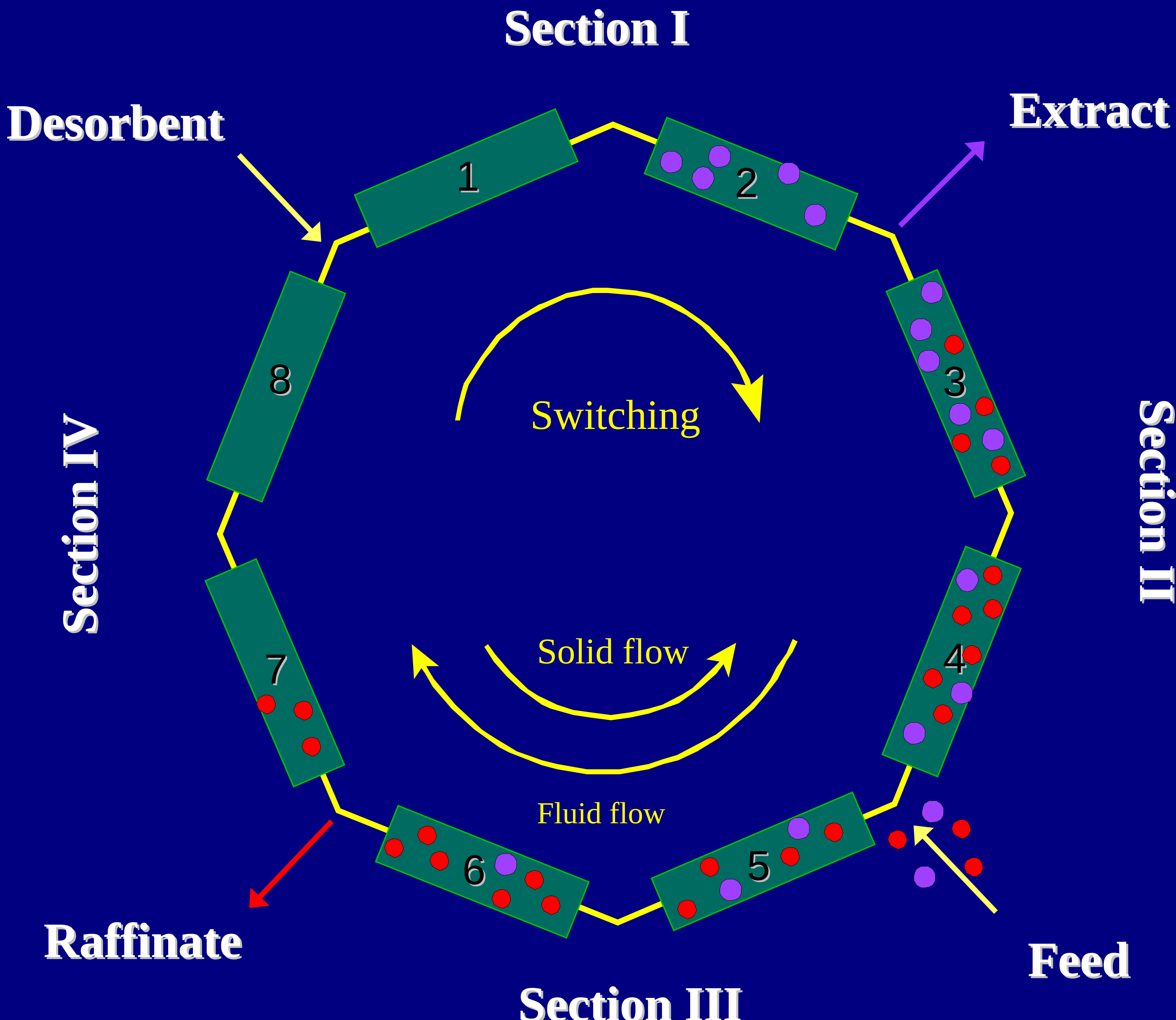

Section I
Desorbent
Extract
1
2
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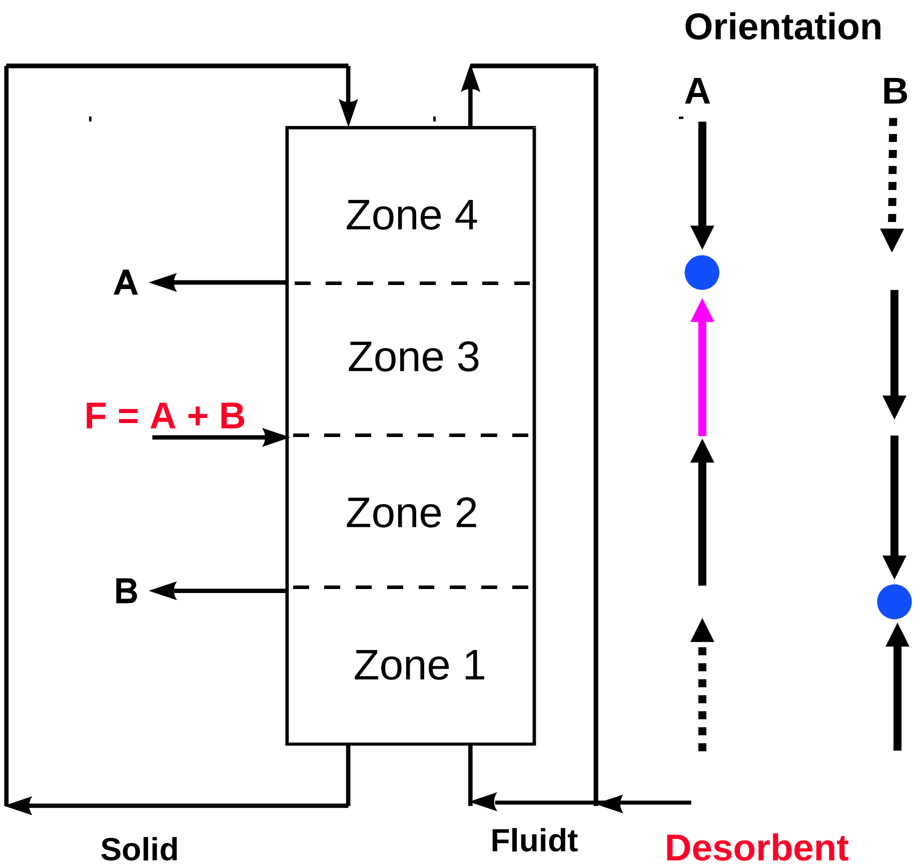
Switching
Solid flow
Fluid flow
Section II
Section III
Section IV
Raffinate
Feed

Design of TMB - Equilibrium Theory



$$\dot{V}_4 c_A < \dot{V}_S K_A c_A$$

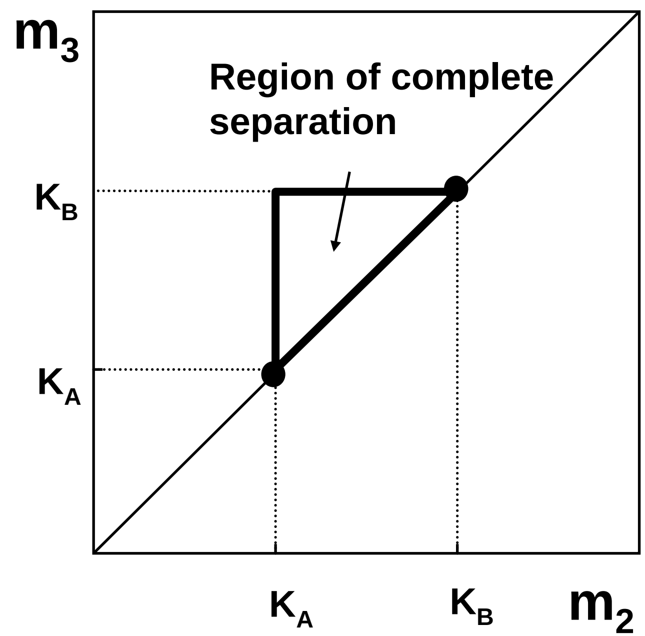
$$\dot{V}_S K_A c_A < \dot{V}_3 c_A$$

$$\dot{V}_3 c_B < \dot{V}_S K_B c_B$$

$$\dot{V}_S K_A c_A < \dot{V}_2 c_A$$

$$\dot{V}_2 c_B < \dot{V}_S K_B c_B$$

$$\dot{V}_S K_B c_B < \dot{V}_1 c_B$$

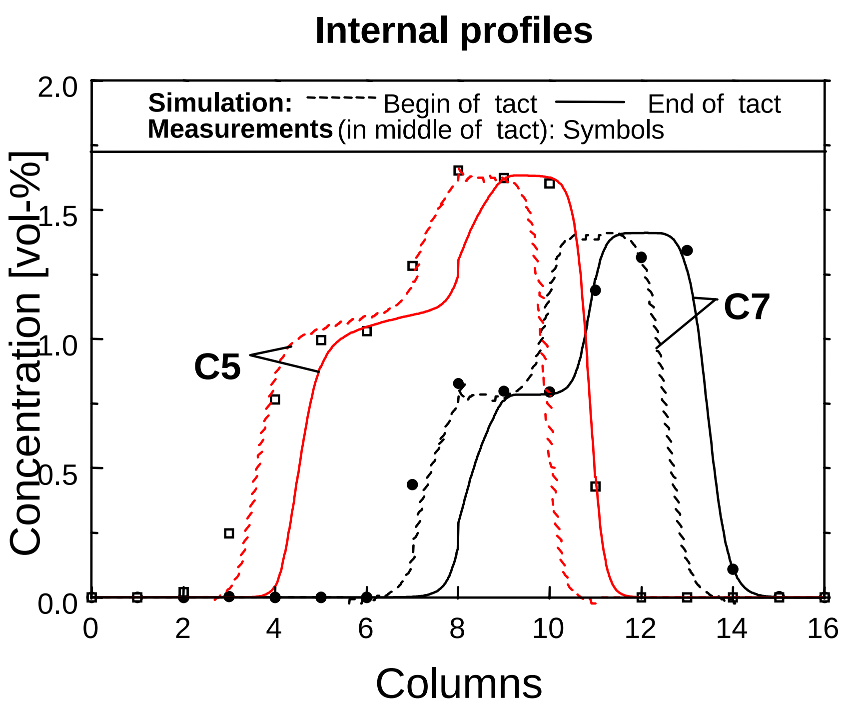


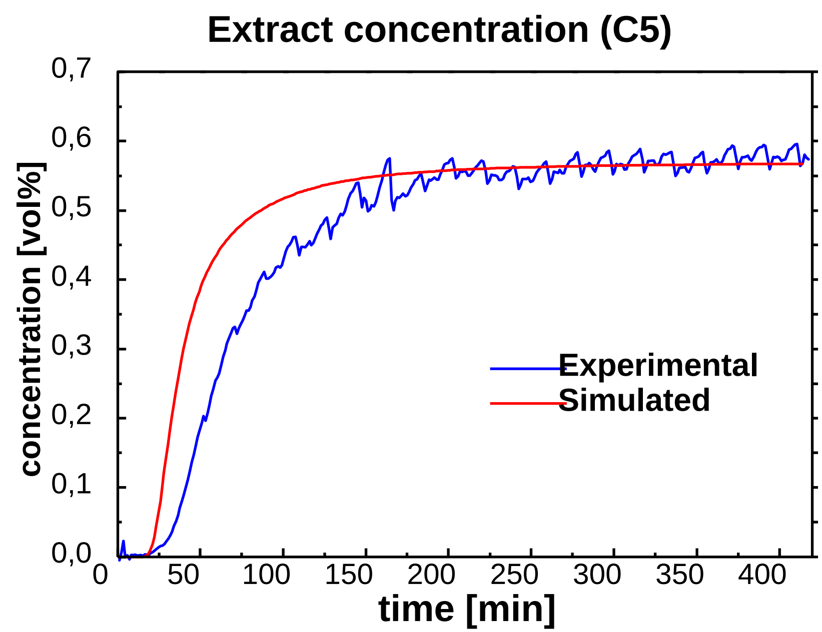
Flow rate ratios m_i *(Mazzotti, Storti, Morbidelli)*

$$m_i = \frac{\dot{V}_i}{\dot{V}_S} \qquad m_4 < K_A < K_B < m_1$$

$$i = 1,2,3,4 \qquad \left.\begin{array}{l} K_A < m_2 < K_B \\ K_A < m_3 < K_B \end{array}\right\} \text{„Triangle“}$$

SMB - Model Validation





2 Cycloketones (C5 and C7), Silica, Hexan, c^{mod} =15% EA

(Kniep, 1998)

Optimization

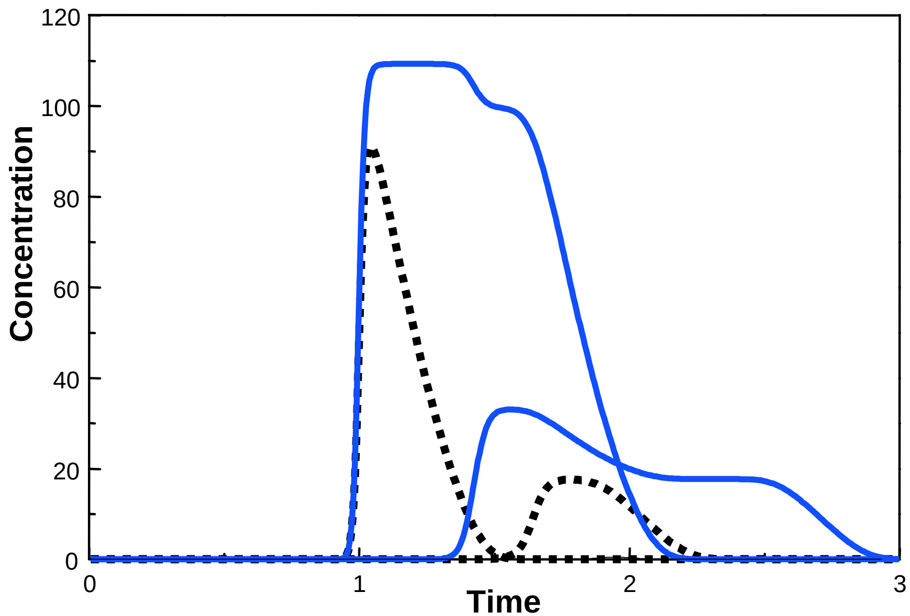
- determination of optimal operating points
- comparison between rivaling modes

Proper objective function needs to be specified

- Yield	g_{Prod} / g_{Feed}
- Production rate	g_{Prod} / scale s
- Solvent consumption	g_{Prod} / $l_{Solvent}$
- Diluation	c_{Prod} / c_{Feed}
- . . .	
- Costs	money / g_{Prod}

→ numerical calculations necessary

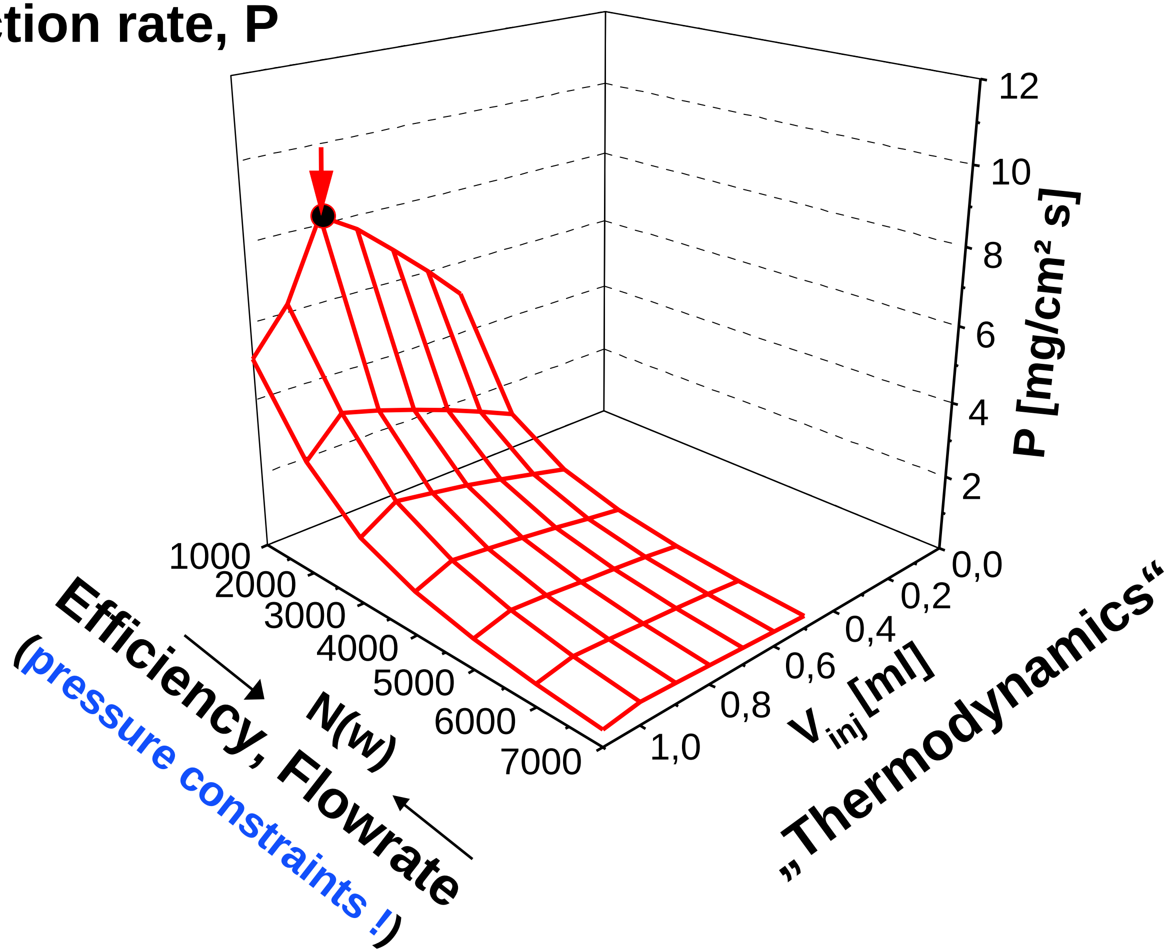
Touching Bands vs. „Radical“- Overloading



Do not be afraid of overloading in elution chromatography !

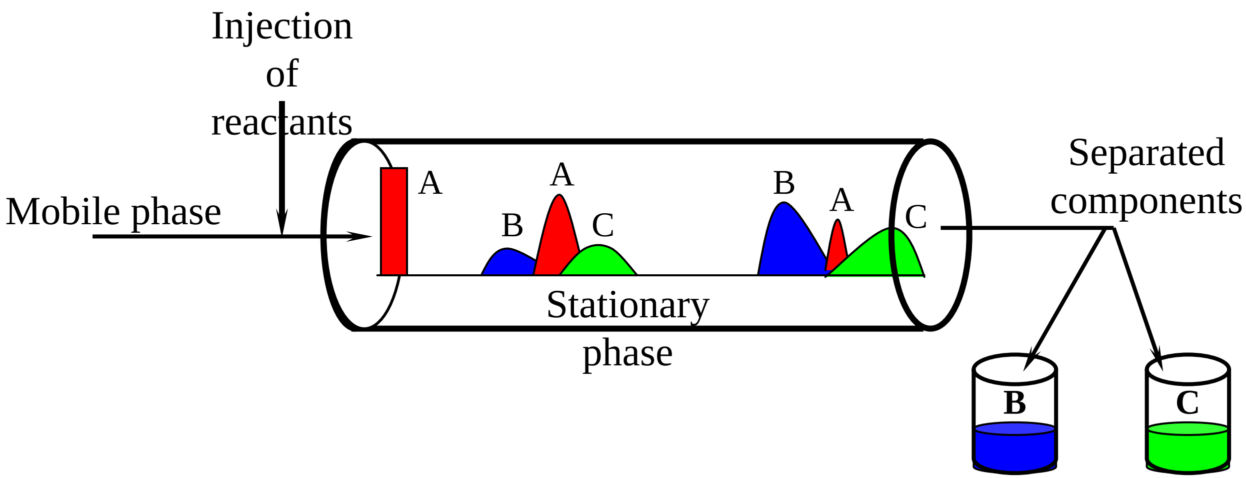
Optimizing overloaded elution chromatography

Production rate, P



- highest flowrate often most favorable for productivity
- injected amount needs to be carefully adjusted

Principle of chromatographic fixed-bed reactor



- **First patents in 60th (Magee, Gaziev)**
- **Goals:**
  - **- determination of parameters**
  - **- higher conversion**
  - **- improved selectitivity**
- **Essential design parameter:**
  - **- residence time**
  - **- feed (concentration, volume, cycle time)**
- **Requirements**
  - **- reversible reactions (K_{eq} small)**
  - **- separation of products, not of reactants**
  - **- reaction and separation at the same temperature**
- **Potential applications**
  - **- esterifications, transesterifications, hydrolysis reactions**

Model reactions and experimental

$$A + B \overset{H^+}{\Leftrightarrow} C + D$$

	1	2	3	4
A	Methyl formate (MF)	Methyl acetate (MA)	Ethyl formate (EF)	Ethyl acetate (EA)
B	Water (W)	Water (W)	Water (W)	Water (W)
C	Formic acid (FA)	Acetic acid (AA)	Formic acid (FA)	Acetic acid (AA)
D	Methanol (M)	Methanol (M)	Ethanol (E)	Ethanol (E)

- **Catalyst and adsorbens: Dowex 50 W-X8 (acidic cation exchanger)**
  - **- Particle size: 32 - 45 or 38 – 78 µm**
  - **- mobile phase: H_2O (Carrier and reactant)**
- **Dimension of fixed-bed: 250 x 4,6 mm**
- **Dosing: Ester (between 20 µl and several ml)**
- **Detection: UV, RI and conductivity**
- **Additional experiments with suspended catalyst in BR to quantity kinetics**

Catalysts

Characteristics	Cat. 1	Cat. 2
Particle size, μm	32-45	38-75
Feature	In use already for 5 years (T. Falk)	New sample (2003)
Active group (Sulfonic acid)*	3.9×10^{-3} eq/g	4.8×10^{-3} eq/g
Density, kg/m^3 **	1500	1450
Type	Dowex 50W-X8	
Matrix	Styrene-Divinylbenzene	
Ionic form	H^+	

(*) Determined by titration with sodium solution
(**) Determined by Micromeritics Helium-pycnometer

Hydrolysis of methyl formate

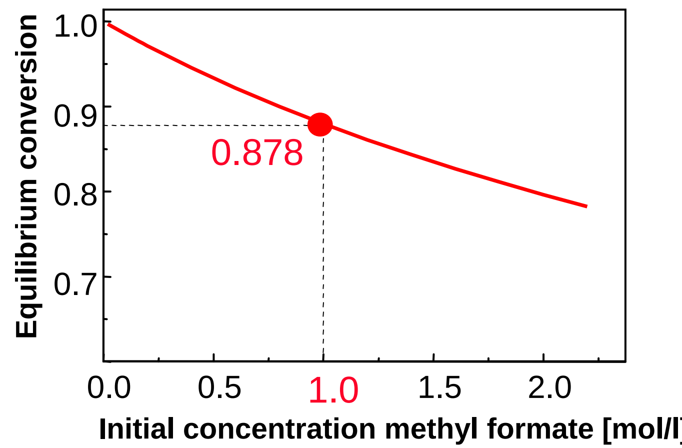
$$HCOOCH_3 + H_2O \overset{H^+}{\rightleftarrows} HCOOH + CH_3OH$$

Technical relevance: production of formic acid

(1988: 330.000 t/a, 49% by $HCOOCH_3$-hydrolysis):

$$CH_3OH + CO \overset{70°C,\ 2\text{-}20\ MPa}{\rightleftarrows} HCOOCH_3 \overset{+H_2O,\ H^+,\ 80\text{-}140\ °C,\ 0{,}3\text{-}1{,}8\ MPa}{\rightleftarrows} HCOOH + CH_3OH$$

Equilibrium constant: T = 298 K, K_{eq} = 0,12



Simplified fixed-bed model

Assumptions:

- constant temperature
- permanent equilibrium over the whole column
- no radial concentration gradients

➢For each component:

$$\varepsilon \frac{\partial c_i}{\partial t} + (1-\varepsilon)\frac{\partial q_{av,i}(c_i)}{\partial t} = -\varepsilon u \frac{\partial c_i}{\partial x} + \varepsilon D_{ap} \frac{\partial^2 c_i}{\partial^2 x} + \varepsilon \nu_i r^{hom}(\bar{c}) + (1-\varepsilon)\nu_i r^{het}(\bar{c}, \bar{q}_{av}) \qquad i = 1, N_c$$

➢If the adsorption isotherms are linear $q_{av,i} = K_i c_i$, this equation can be simplified as follows:

$$\frac{\partial c_i}{\partial t} = \left(1 + \frac{1-\varepsilon}{\varepsilon} K_i\right)^{-1} \left[-u \frac{\partial c_i}{\partial x} + D_{ap} \frac{\partial^2 c_i}{\partial^2 x} + \varepsilon \nu_i r^{hom}(\bar{c}) + \frac{1-\varepsilon}{\varepsilon} \nu_i r^{het}(\bar{c}) \right] \qquad i = 1, N_c$$

Initial conditions:

$$c_i(x, t=0) = 0$$

Standard Danckwerts boundary conditions:

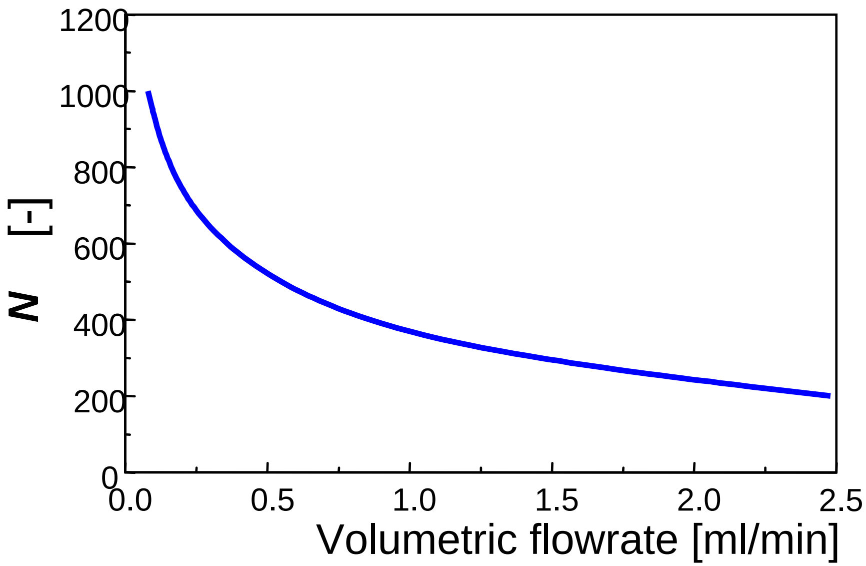
$$c_i(x=0,t) = \begin{cases} c_i^{inj} - \dfrac{D_{ap}}{u} \left.\dfrac{\partial c}{\partial x}\right|_{x=0,t} & \text{for } 0 \le t \le t^{inj} \\ -\dfrac{D_{ap}}{u} \left.\dfrac{\partial c}{\partial x}\right|_{x=0,t} & \text{for } t \ge t^{inj} \end{cases} \quad \text{and} \quad \left.\frac{\partial c}{\partial x}\right|_{x=L,t} = 0$$

Porosity and plate number

Porosity: from retention time of nonretained component (dextrane blue)

→ $\varepsilon_{FB} = 0{,}313$

Plate number: $$\mathbf{N\ (V)} = \frac{\mu^2}{\sigma^2} \approx 5{,}54\left(\frac{t_R}{w_{0,5}}\right)^2$$

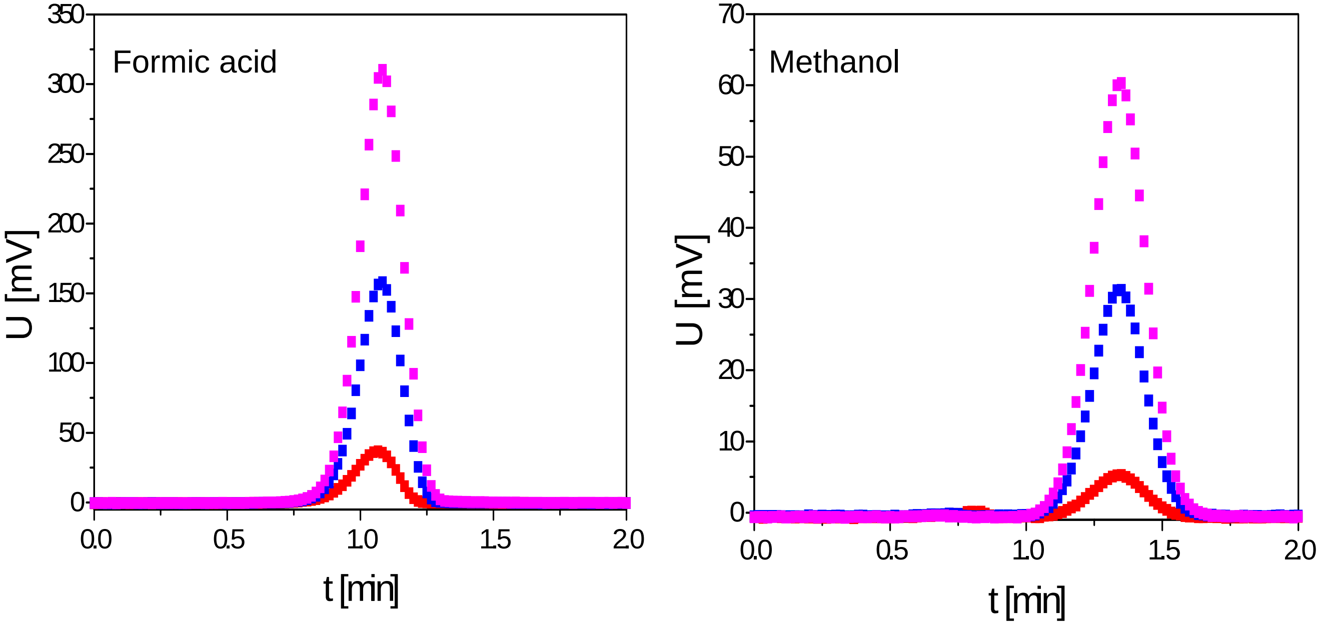


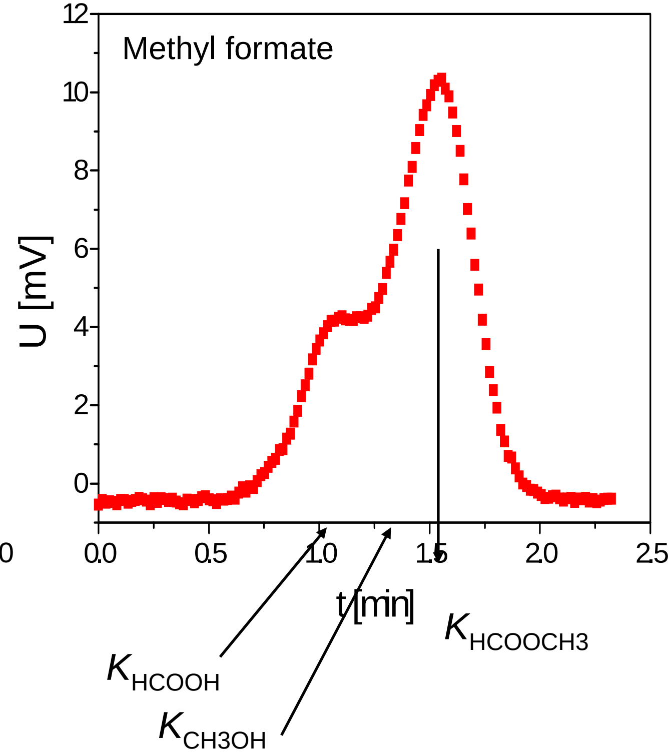
Typical values:

ca. 1000 for 0,1 ml/min

ca. 200 for 2,5 ml/min

Puls experiments



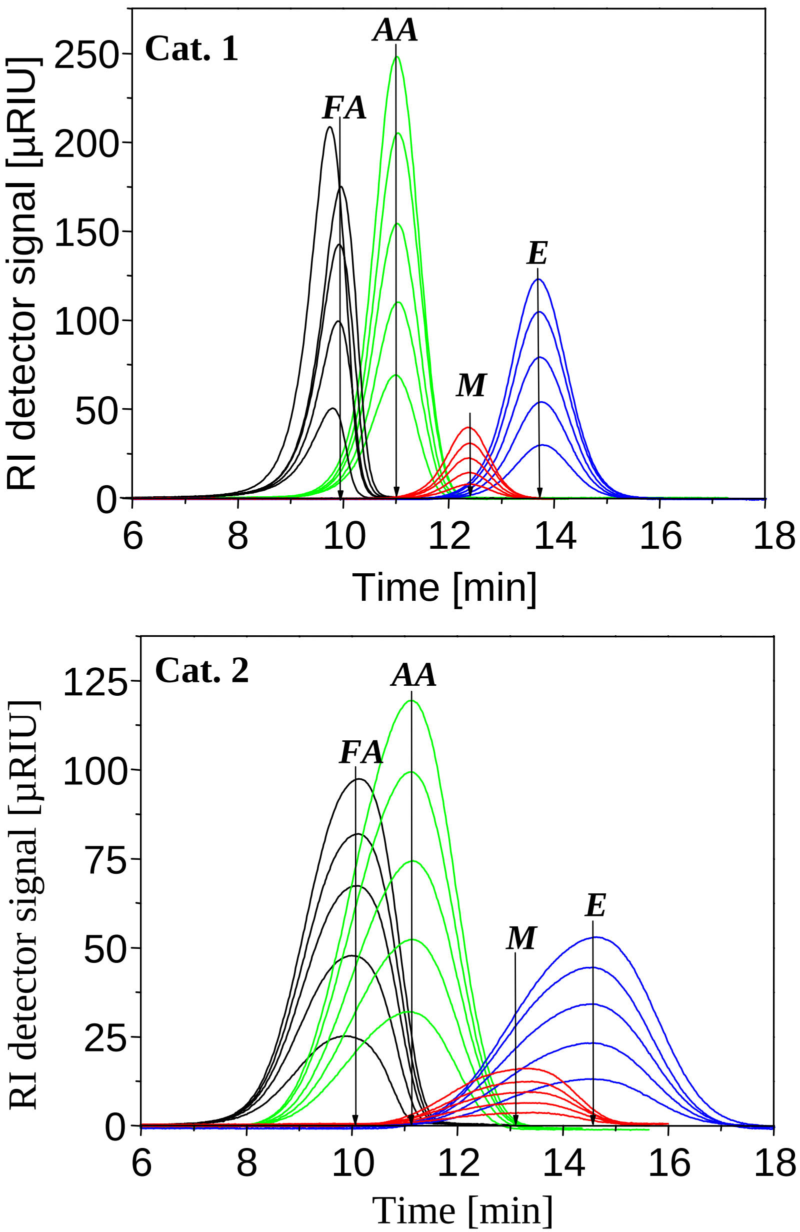


- varied: residence time and concentration

$$\frac{dq}{dc} = K = 1 + \frac{t_R \dot{V} - \varepsilon_{FB} V}{(1 - \varepsilon_{FB}) V}$$

- Almost linear equilibrium functions (q = K c)
- $K_{HCOOCH3}$ = 0,913, K_{HCOOH} = 0,476, K_{CH3OH} = 0,693 (T = 298 K)

Adsorption equilibrium constants



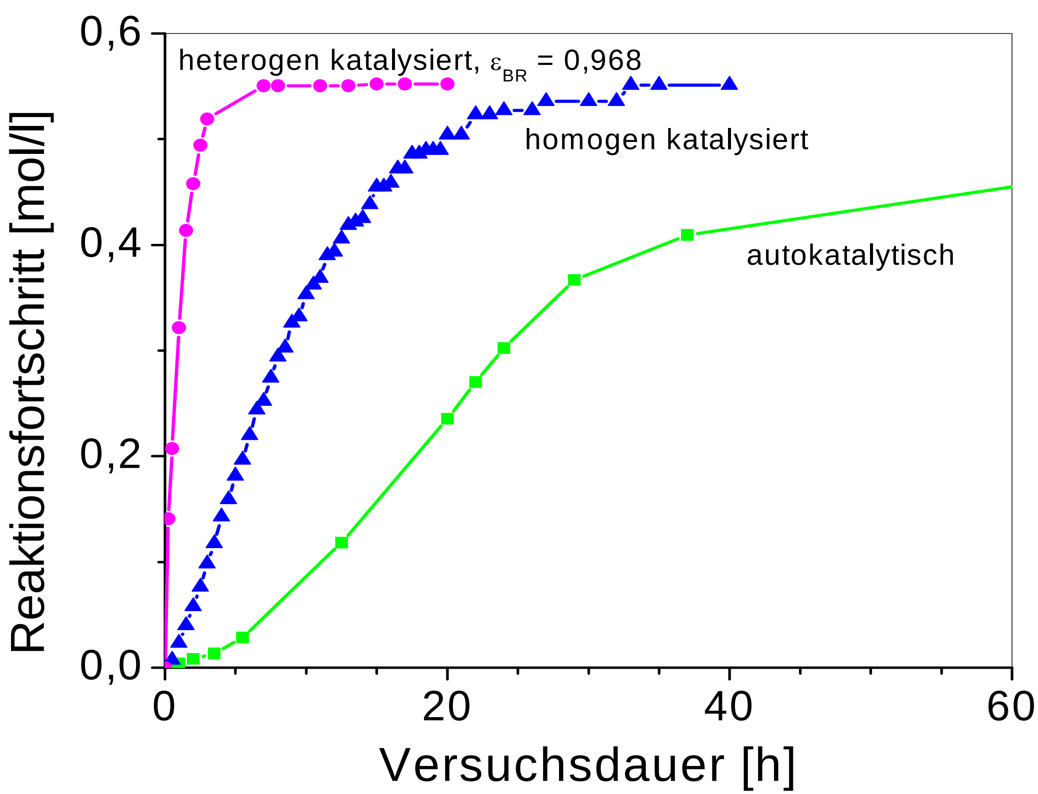
Elution profiles for various injection concentrations (0.1…0.5 mol/l)

(flow rate: 0.75 ml/min, injection volume: 100µl, temp.: 25ºC).

Component	Cat. 1 (Falk, T.)	Cat. 1	Cat. 2
Formic acid	0.476	0.432	0.380
Acetic acid		0.520	0.476
Methanol	0.693	0.628	0.673
Ethanol		0.736	0.781
Methyl format	0.913	0.850	≈ 0.65
Methyl acetate		0.995	0.819
Ethyl format		1.085	1.009
Ethyl acetate		1.327	1.219

Reaction kinetics (Batch reactor)

- Catalysts: a) Formic acid
  b) HCl (homogen)
  c) Dowex 50W-X8 (heterogen, ε_{BR} = 1 ... 0,925)
- Initial concentration of methyl formate: 0,3 - 2,5 mol/l

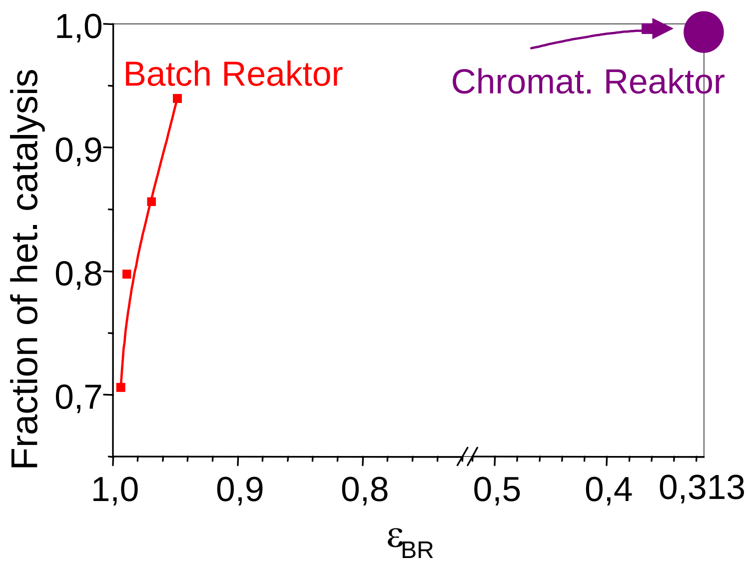


Rate of homogeneously and heterogeneously catalysed reactions (MF hydrolysis)

$$r = \varepsilon_{BR}\, r_{hom} + (1-\varepsilon_{BR})\, r_{het}$$

$$= \varepsilon_{BR}\,(k_0 + k_1 c_{H^+})\left(c_{HCOOCH_3}\, c_{H_2O} - \frac{c_{HCOOH}\, c_{CH_3OH}}{K_c}\right) +$$

$$+ (1-\varepsilon_{BR})\, k_2 \left(K_{HCOOCH_3} c_{HCOOCH_3}\, c_{H_2O} - \frac{K_{HCOOH} c_{HCOOH}\, K_{CH_3OH} c_{CH_3OH}}{K_c\,^*}\right)$$



k_0 = 4 x 10^{-4} (l/(mol h))

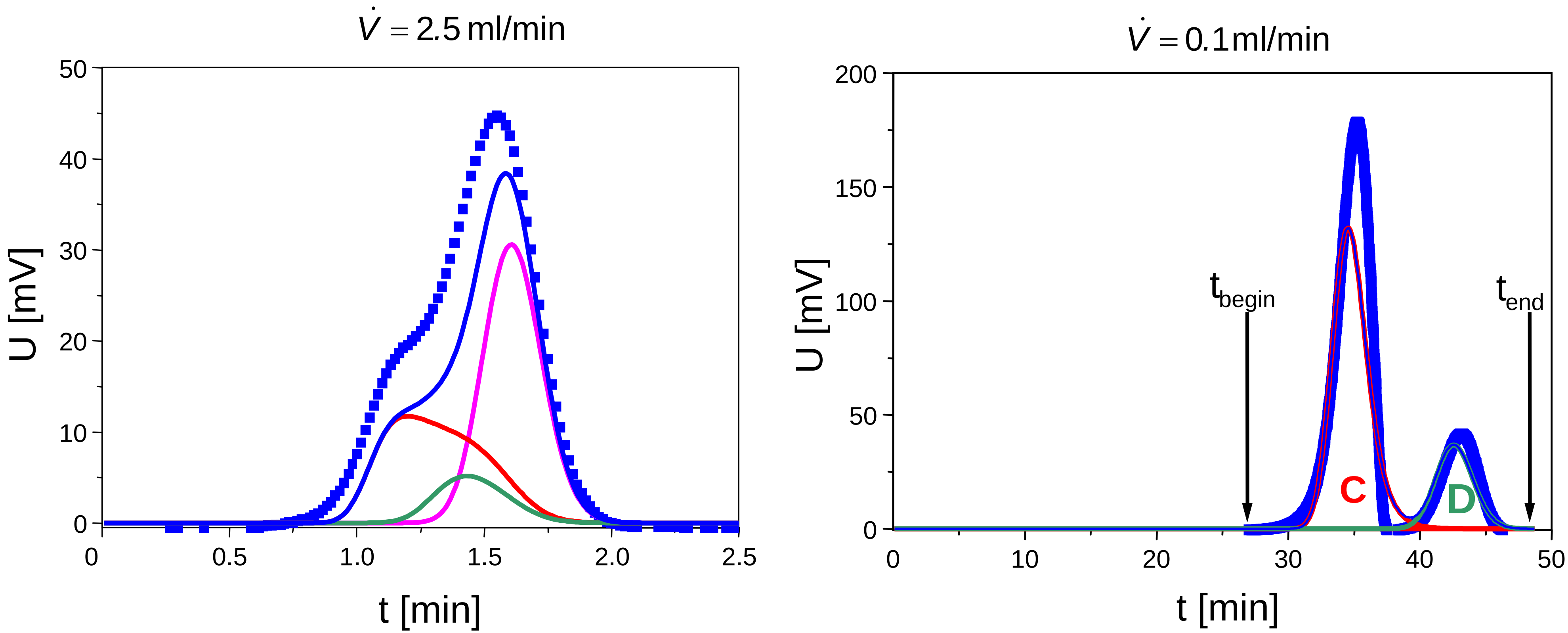
k_1 = 0,2 (l^2/mol^2 h))

k_2 = 0,47 (l/(mol h))

heterogeneously catalysed reaktion dominates in chromatographic fixed-bed reactor

Influence of residence time (hydrolysis of MF (A))

A + B ⇄ C + D



$c^{Inj} = 0.725$ mol/l, $V^{Inj} = 20$µl

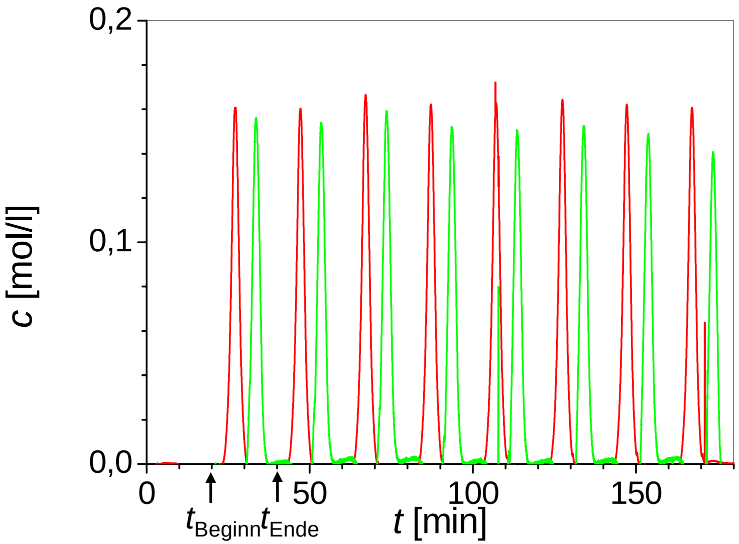
(Thomas Falk, 2003)

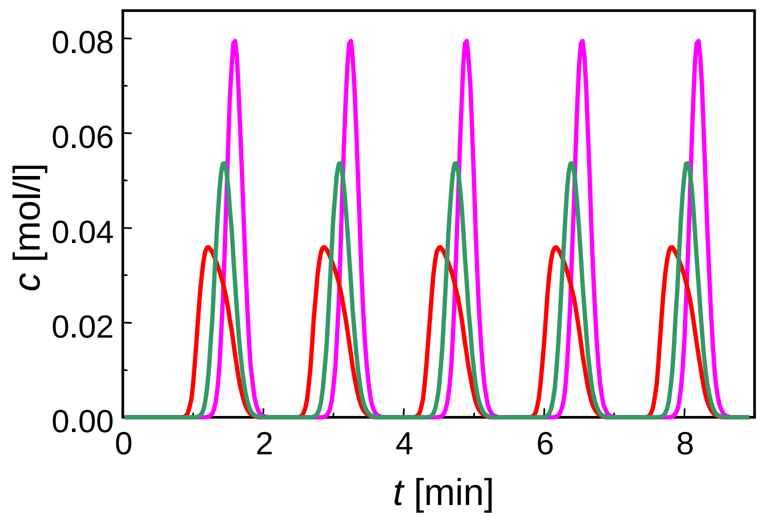
Periodic operation

0,1 ml/min, „large“ Damköhler number (experimental)

2,5 ml/min, „small“ Damköhler number (simulated)

$$\text{Da} = \frac{\text{residence time}}{\text{"charact. reaction time"}}$$





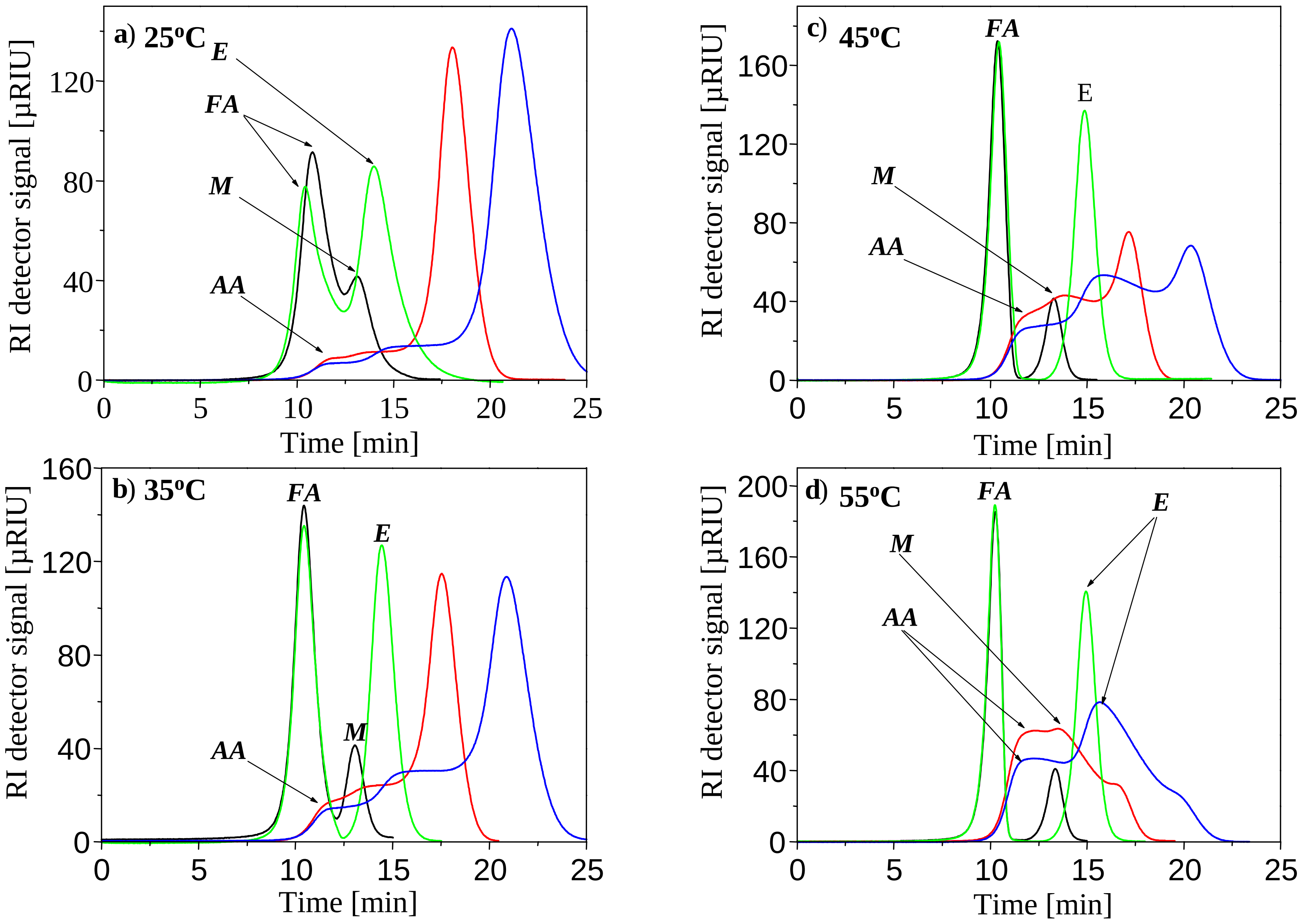
$V_{inj} = 50\ \mu l$

$c_{HCOOCH_3,\,inj} = 0{,}94\ mol/l$

$V_{inj} = 50\ \mu l$

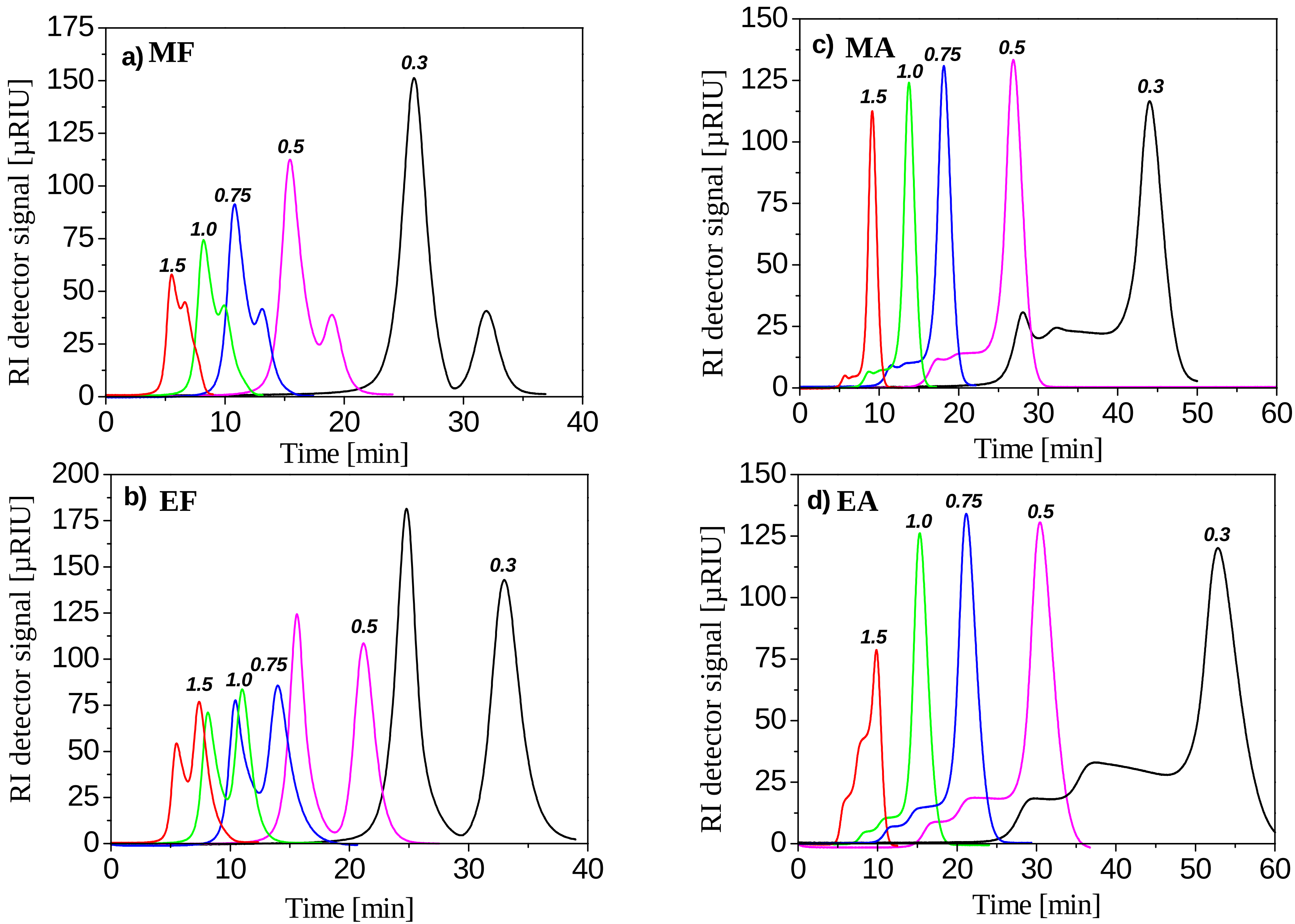
$c_{HCOOCH_3,\,inj} = 0{,}94\ mol/l$

Influence of feed components and temperature



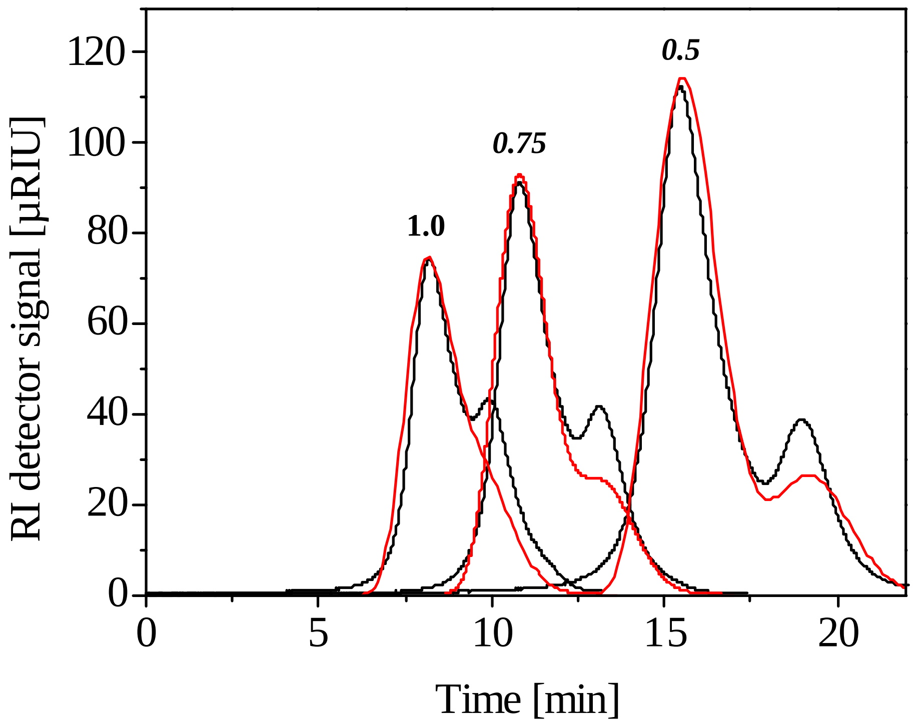
Comparison of elution profiles for hydrolysis reactions of MF (black), EF (green), MA (red) and EA (blue) at each temperature: (flow rate: 0.75 ml/min, injection volume: 100µl,)

Influence of flow rate on hydrolysis of esters



Influence of flow rate (0.3 … 1.5ml/min) on hydrolysis reactions of esters.
(injection volume: 100µl, concentration: 0.5 mol/l, temperature: 25°C).

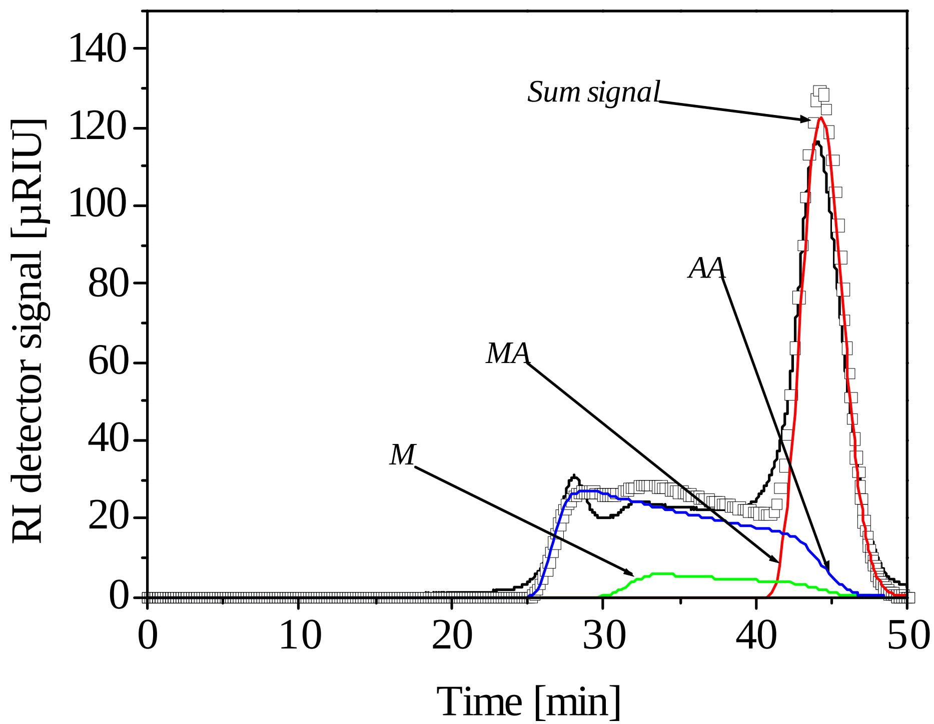
Simulations of elution profiles (flow rate effect)



Reactants	k_{eq}^{het}	$10^5\ k_{het}$, l/(mol s)	
		Cat. 1	Cat. 2
Methyl format	0.22	23.4	35.7
Ethyl format	0.38	12.1	22.6
Methyl acetate	0.14	0.64	1.26
Ethyl acetate	0.33	0.60	1.08

Comparison of response detector signals for MF: (symbol) measured, (red) simulated using k_{het}=2.34x10^{-4} l/(mol.s) quantified from the shape of elution (Cat. 1, flow rate: 0.5, 0.75 and 1.0 ml/min, injection volume: 100μl, concentration: 0.5 mol/l, temperature: 25^{o}C)

More simulations results

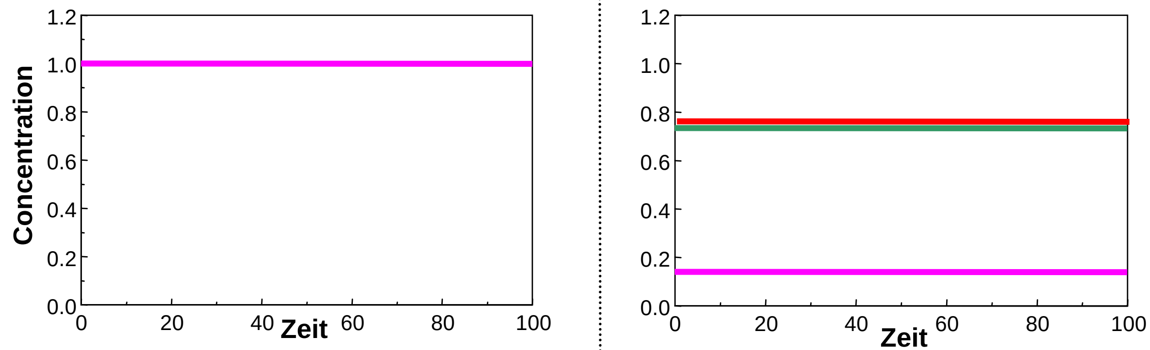


Comparison of response detector signals for MA hydrolysis: (solid) measured, (□) simulated using obtained k_{het} (Cat. 1, flow rate: 0.3 ml/min, injection volume: 100µl, concentration: 0.5 mol/l, temperature: 25°C)

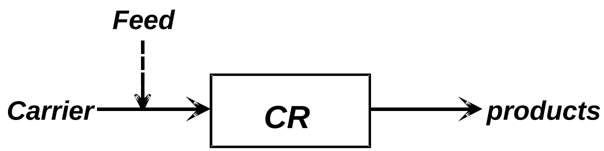
Comparison between various reactor concepts

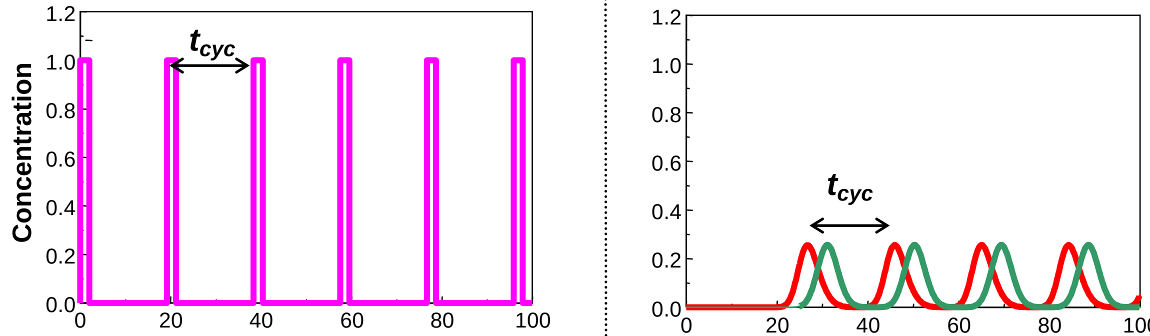
A + B ⇄ C + D

Conventional fixed-bed reactor

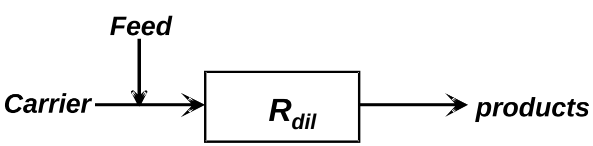


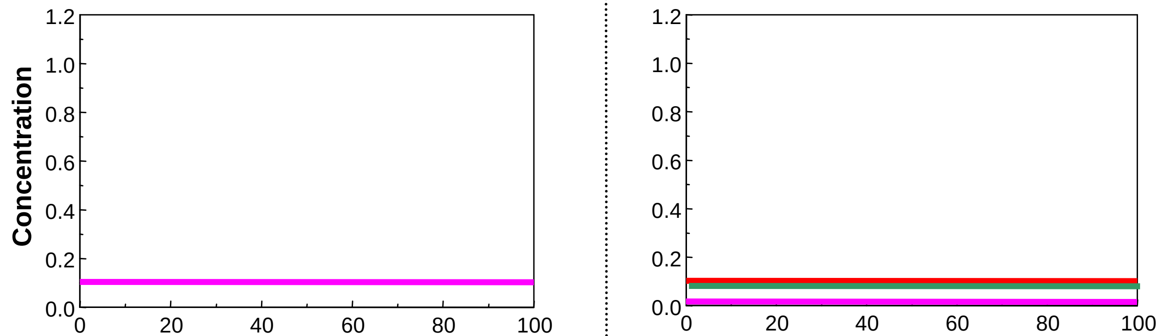
Chromatographic reactor



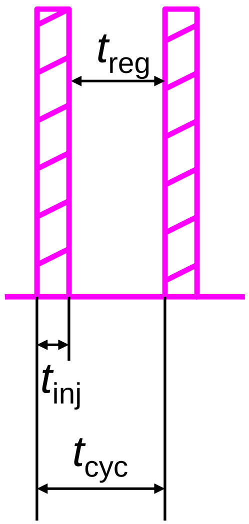


„Diluted“ fixed-bed reactor





Cycle time (t_{cyc}) and Degree of Dilution (φ)

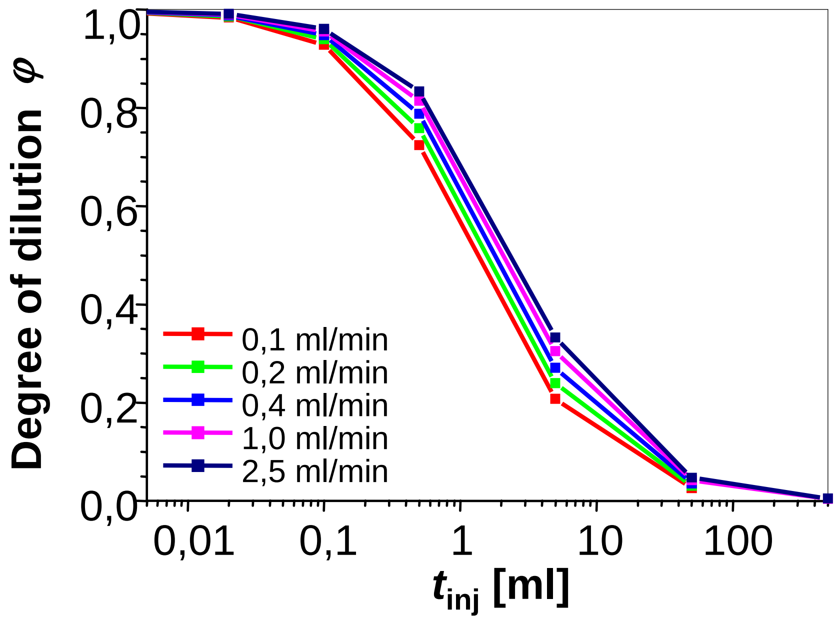


$$\varphi = 1 - \frac{t_{inj}}{t_{cyc}}$$

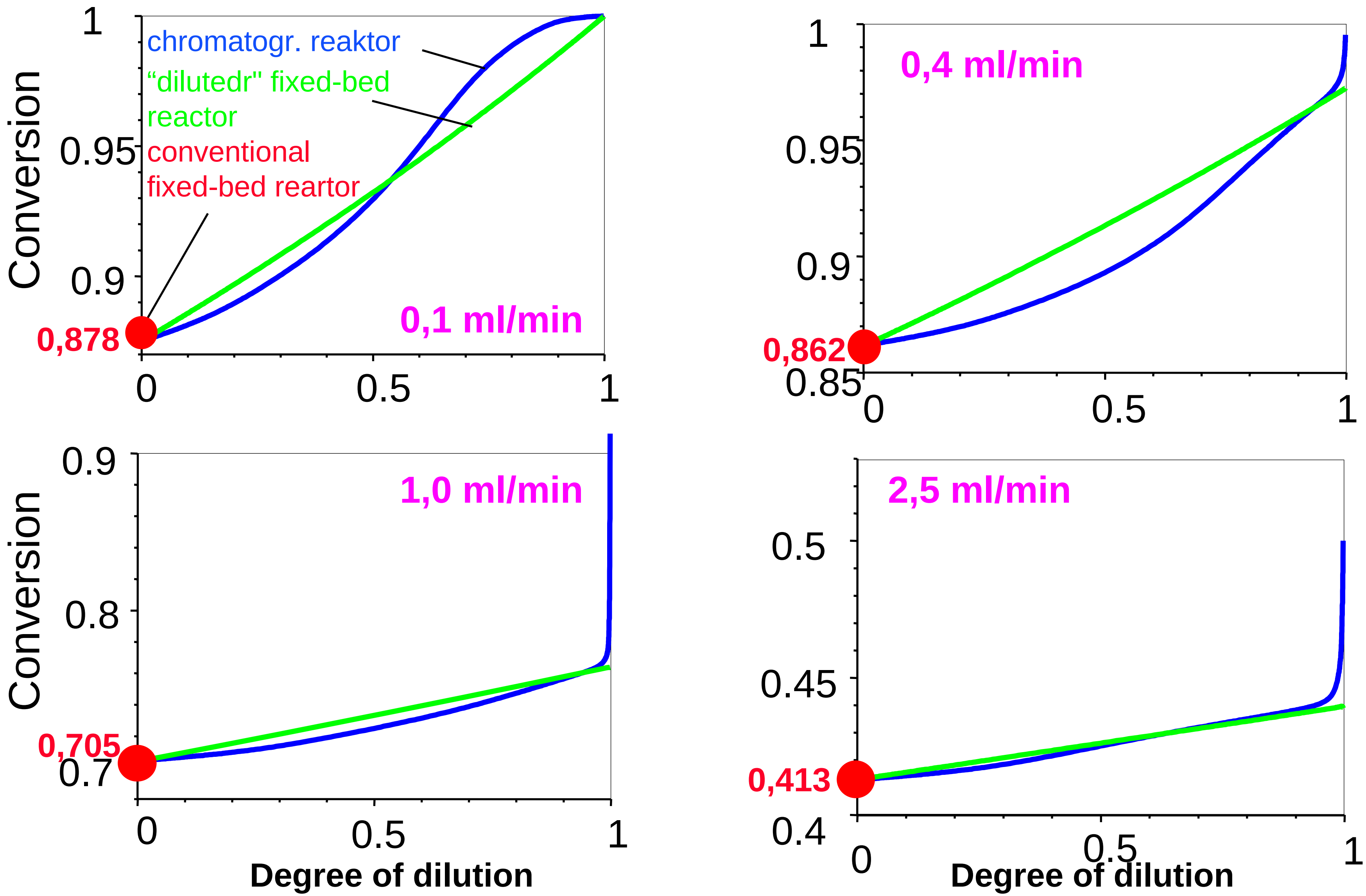
$$t_{cyc} = t_{cyc}(t_{inj}, N_c, K_i)$$

$\varphi = 0$: conventional fixed-bed reactor
(steady state, no separation, no dilution)

$0 < \varphi < 1$: chromatographic reactor

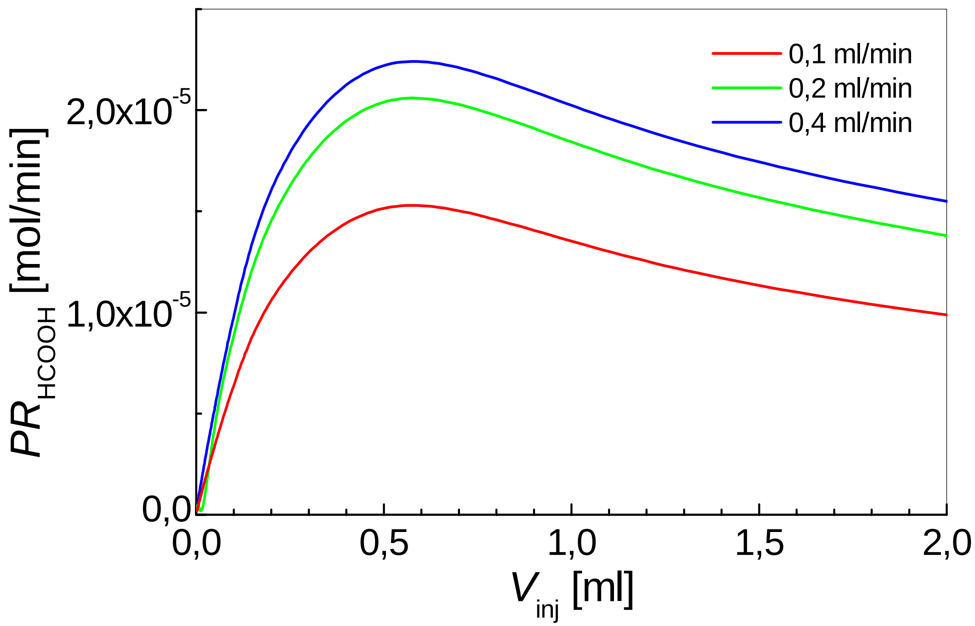


Conversion and Degree of Dilution (φ) ($c_{HCOOCH3,inj}$ = 1 mol/l)



Productivity (*PR*)

$$PR_i = \frac{n_{i,cyc}}{t_{cyc}} = \dot{n}_i$$



Produkt: HCOOH (Reinheit > 99%)

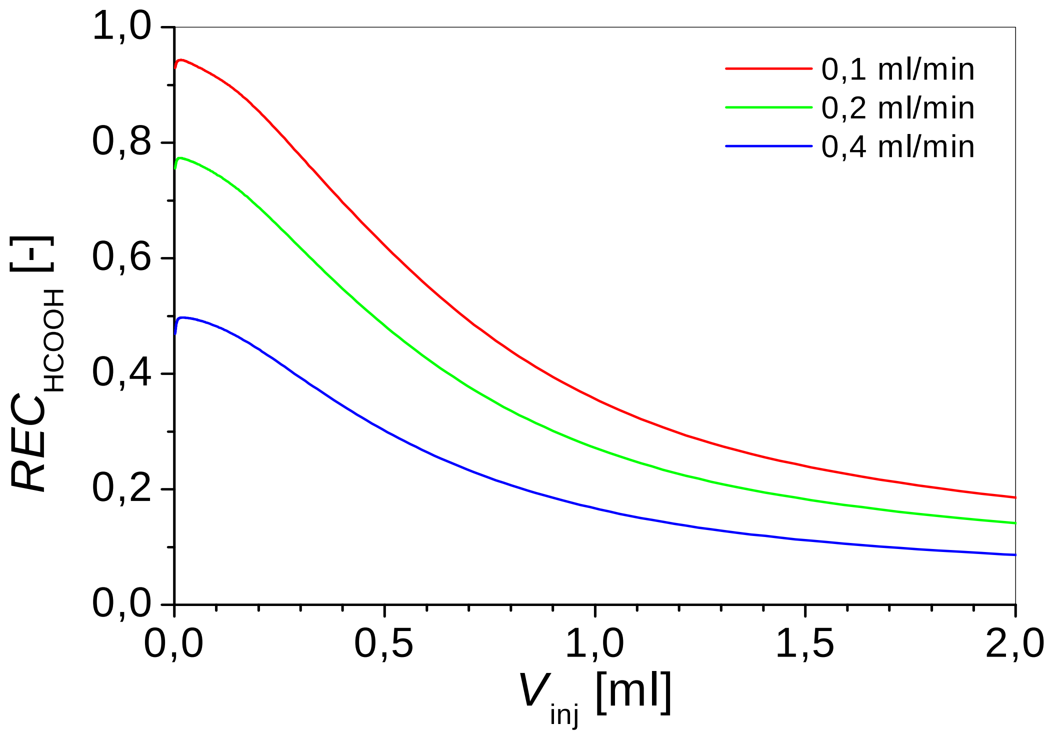
$c_{HCOOCH_3,inj} = 1\,mol/l$

$(n_{HCOOCH_3} : n_{H_2O} \approx 1:50)$

$T = 298\,K$

Recovery yield (*REC*)

$$REC = \frac{\dot{n}_C}{\dot{n}_A} = \frac{\dot{n}_{HCOOH}}{\dot{n}_{HCOOCH_3}}$$



Produkt: HCOOH (Reinheit $> 99\%$)

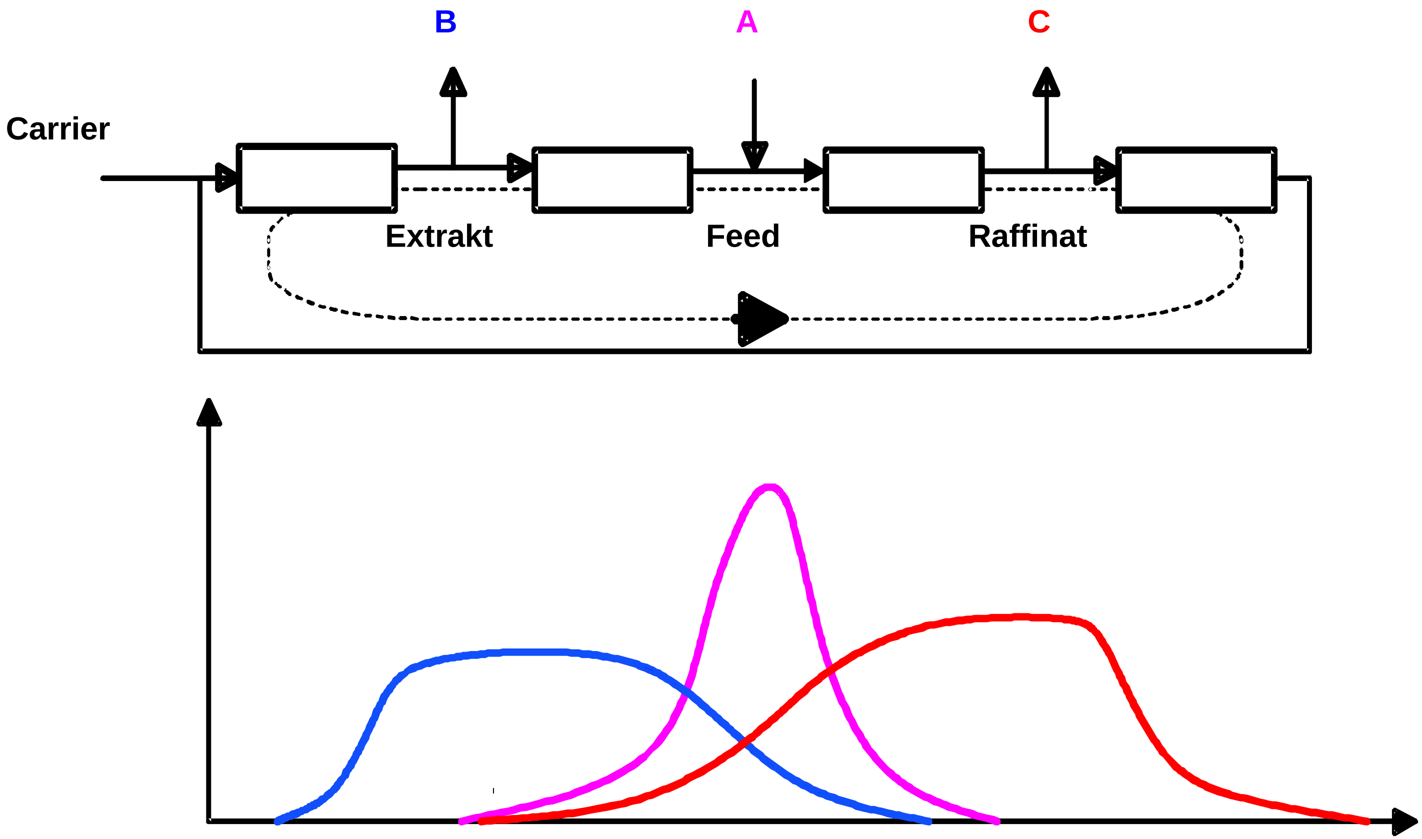
$c_{HCOOCH_3,inj} = 1\,\text{mol/l}$

$(n_{HCOOCH_3} : n_{H_2O} \approx 1:50)$

$T = 298\,\text{K}$

Continuous chromatographic reactors

$A \rightleftarrows B + C$



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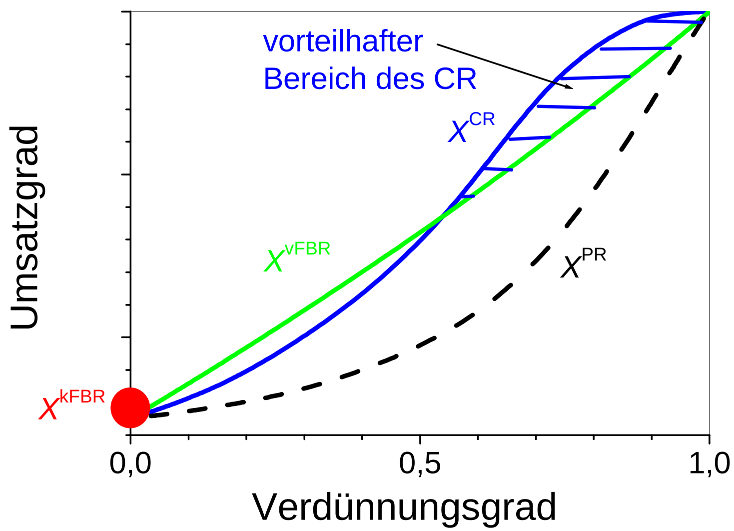
Conclusions

- **Exploitation of potential of chromatographic reators requires careful design and optimization**



- **Continuous operating modes are promising and challenging**

Acknowledgement

Thomas Falk, Phong T. Mai, Tien D. Vu, Andreas Schlinkert