DESIGNING INDUSTRIAL CHROMATOGRAPHIC PROCESSES

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- Selective separation technology at TNO
- Continuous chromatography: simulated moving bed (SMB)
- Designing industrial chromatographic processes
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  - SMB validation
  - CAPEX & OPEX
SEPARATION TECHNOLOGY AT TNO

› Focus on chromatography and membrane based separations in agro, food and bio-process industry

› For industry (large scale, food value) we develop separation technology to
  › Separate and fractionate proteins, peptides, saccharides and other (functional) ingredients
  › Remove unwanted components (e.g. salts, polyphenols, colour, toxic compounds, calories)

› From lab scale solutions to industrially feasible processes, with a focus on
  › Mild process conditions to preserve functional properties
  › Weak interactions → water as (food grade) eluent
  › Low/medium cost resins to improve economy
TNO REFERENCES

- Protein purifications
- Oligosaccharides fractionations
- Sugar recovery from process streams
- Sugar and acid removal from fruit juices
- Product recovery from fermentation broths
- Detoxification of biomass hydrolysate
- Salt removal from process streams
- Alkaloids recovery from process streams
- Off-flavour removal from product streams
**BATCH VERSUS CONTINUOUS CHROMATOGRAPHY**

**Batch**
- High selectivity & resolution
- High capacity
- Minor components (low conc)

- Recovery typically < 80%
- Limited productivity → large resin volume
- High dilution and water consumption
- Limited recycling → waste streams
- Multiple (product) fractions

**Continuous**
- Low-high selectivity & resolution
- Low-high capacity
- Bulk components (high conc)

- High recovery up to 100%
- High productivity → small resin volume
- Limited dilution and water consumption
- Up to 90% recycling → limited waste streams
- Two (product) fractions
CONTINUOUS CHROMATOGRAPHY
SIMULATED MOVING BED (SMB)

Component S: stronger interaction
Component W: weaker interaction

Component S
Component W

Feed Component S + W
Raffinate Component W

Column rotation

Extract
Eluens

eluens
extract feed
raffinate

Column length [m]
SIMULATED MOVING BED (SMB)

Advantages SMB (continuous counter-current process):
- More efficient use of adsorbent → smaller resin volume (€)
- Higher product yield, purity and concentration (€)
- Lower eluens consumption and reduced waste volume (€)
- Low selectivity (cheap) adsorbents can be used (€)

Drawbacks SMB:
- Complex process requiring robust control of flows
- Relatively long start-up times
FULL-SCALE APPLICATIONS OF SMB

› Pharma and biotech
  › Chiral separations
  › Purification of antibiotics, vitamins, amino acids
› Agro / food
  › Sugar separations (glucose/fructose, oligosaccharides)
  › Sugar recovery from molasses
  › Protein fractionation
DESIGNING INDUSTRIAL CHROMATOGRAPHIC PROCESSES

- Case definition
- Adsorbent selection and characterization
- SMB sizing and optimization
- SMB validation
- CAPEX & OPEX
CASE DEFINITION

- Defining separation problem
  - Feed flow and composition
  - Desired product(s)

- Defining performance indicators and constraints
  - Product recovery
  - Purity product stream
  - Dilution product stream
  - Productivity
  - Water consumption
Pre-selection of suitable adsorbents (depending on separation mechanism)
Selection of key components
Experiments on single column to determine column characteristics, separation performance and mass transfer kinetics → model input parameters
Selection of most promising adsorbents
Experiments on single column to determine column characteristics, separation performance and mass transfer kinetics → model input parameters

- Bed and total porosity
- Isotherms (frontal analysis)
- Mass transfer (Van Deemter curves)


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SMB SIZING AND OPTIMIZATION

- SMB chromatography is a complicated process
  - Large number of operating conditions (flows, switch time)
  - Conflicting objectives (purity, recovery, dilution, productivity)

- Dynamic model and multi-objective optimization used to determine optimal size and operating conditions
  1. Model chromatographic column
  2. Modelling SMB process
  3. Working point and sizing
  4. SMB optimization
1. MODEL CHROMATOGRAPHIC COLUMN

- Different kinetic models to describe adsorption in column
- General rate model (GRM) most elaborate model
- Lumped kinetic model → mass transfer resistances lumped into one overall mass transfer coefficient

\[
\frac{1}{k_{lumped}} = \frac{r_p}{3k_f} + \frac{r_p^2}{15D_p}
\]

- \( k_{lumped} \) overall mass transfer coefficient [1/s]
- \( r_p \) average radius of the stationary phase particles [m]
- \( k_f \) external mass transfer coefficient [m/s]
- \( D_p \) pore diffusivity coefficient [m²/s]

- Lumped kinetic model as good as GRM if \( D_p \gg 10^{-14} \text{ m}^2/\text{s} \)
2. MODELLING SMB PROCESS

- Simulating moving bed is a discontinuous process
- Switching can be modelled in gProms using SCHEDULE or TASKS
- Scheme can be relatively easy made for different number of columns and different number of columns per section (VARICOL)
- “Would like to have”

3. WORKING POINT AND SIZING

- Working point: triangle theory [Mazzotti et al., 1997] sets the solid/liquid flow ratios in the different sections of the TMB (!)
- Pure products are obtained for a maximum feed
- However…

\[
\begin{align*}
\Lambda_A &> 1 \\
\Lambda_B &> 1 \\
\Lambda_A &< 1 \\
\Lambda_B &< 1
\end{align*}
\]

\[
\Lambda = \frac{\Phi_S K_{aff}}{\Phi_L}
\]
It is developed for binary mixtures and binary separation → complex mixtures?

Performance indicator purity → dilution or other?

It does not take mass transfer resistance into account → safety margin?

It is based on a TMB resulting in solid flow m³/h → for SMB size (m³) and cycle time (min) needed

Dynamic model including optimization mandatory

Working point used as starting point for sizing and optimization
4. SMB OPTIMIZATION

- Single scalar objective function (e.g. €/kg) using weight factors
- Drawbacks single-objective optimization
  - Result dependent on weight factors
  - Optimal solutions are risked to be lost
- Multi-objective optimization overcomes these drawbacks
- Multi-objective optimization results in an optimum Pareto set of operating conditions

Trade off between productivity and dilution (water use)
OPTIMIZATION IN GPROMS

- Objective: max productivity and min water use
- Inequality constraints: purity and recovery
- Controls: velocities in four sections (I, II, III and IV)
  - Cycle time is calculated by maintaining constant velocity in section I (given by the maximum pressure drop in the column)
- Problems encountered:
  - SCHEDULE is out $\rightarrow$ TASKS is out $\rightarrow$ everything was modelled within MODEL
  - Calculation of the performance is done after each cycle: time horizon is fixed and therefore cycle time
- “Would like to have” full-discretization both in spatial and temporal domain
Trade-off between productivity and dilution (water use)

Example
- Comparison of three different resins
- Sensitivity for removal of main impurity
- For whole product range “red” resin is superior
SMB VALIDATION

- SMB experiments on lab-scale
  - Validation of model calculations
  - Production of test samples
  - Evaluation of performance and operational issues (e.g. fouling)

- SMB pilot facilities at TNO
  - Fixed columns combined with switching valves to simulate column movement
  - Rotating columns (on turntable) with multiport distributor valve
SMB PILOT FACILITY WITH FIXED COLUMNS
SMB PILOT FACILITY WITH ROTATING COLUMNS

[Image of an SMB pilot facility with rotating columns]
SMB VALIDATION

› Production of samples within specifications customer
› Fine-tuning settings experimentally required (cycle time ± 15%)
› Improvement: mass transfer resistance
CAPEX & OPEX

- CAPEX & OPEX calculations to evaluate economic feasibility of processes
- New developments to reduce CAPEX of chromatographic processes by size reduction of installation
  - Smaller resin particles combined with shorter cycles
  - Highly concentrated (viscous) feed streams
  → PhD project with WUR and ISPT
TO CONCLUDE

- Strong combination of lab facilities and model tools
- Feasibility, development & innovation
- Tools applicable at unit operation, process and factory level
THANK YOU FOR YOUR ATTENTION