Modelling and simulation in chemical engineering: 
Tools for process innovation

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Available online: 19 March 2005

1. Introduction—the Chemical Engineering Science movement

The Chemical Engineering Science movement illustrated in the book of Bird, Stewart, and Lightfoot “Transport Phenomena” (2002) follows the approach initiated by Kramers at Delft in his lecture notes “Physische Transporterscheinungen” (Kramers, 1958). It contains the basic material to help in developing a mathematical model defined by Aris (1994) as “a complete set of mathematical equations which are supposed to correspond to some entity – its prototype – which can be a physical, biological, social . . . entity although here we deal with physicochemical systems”.

A process model is a relation between “outputs” and “inputs” (feed conditions, design parameters and process adjustable parameters) in view of (i) scale-up from lab to industrial scale, (ii) prediction of process dynamics and (iii) optimization of operating conditions (Shinnar, 1978).

Keywords: Chemical Engineering Science; Process innovation; Technology; Perfusion chromatography; Simulated Moving Bed; Multifunctional reactors

Abstract

The Chemical Engineering Science movement has served well in solving problems from micro to macro scales. Ultimately, as Professor R. Sargent pointed out, it would be better if translated in “Scientific Engineering”.

Examples of innovation as a combination of science (concept), technology and process/product will be presented.

The first example is perfusion chromatography based on the concept of “diffusivity augmented by convection” and on the technology of fabrication of large-pore packings. The second example, Simulated Moving Bed (SMB), is based on a concept developed to overcome the difficulties in implementing True Moving Bed processes. Technological contributions come from adsorbent materials and rotary valve to simulate the solid movement. SMB is now a key technology for chiral separations. Modelling/Simulation tools provide sound basis for design/operation by using the concept of “separation volume”.

The third example is from the area of multifunctional reactors. The SMB technology is extended to the simultaneous reaction/separation.

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I remember the statement of Professor Le Goff (1970) when I was a student in Nancy “Le Génie Chimique c’est pas de la plomberie” and the philosophy of modelling that a chemical engineer uses when solving a new problem involving the writing of:

- conservation equations (mass, energy, momentum and electric charge);
- equilibrium laws at the interface(s);
- constitutive laws (e.g., ideal gas law);
- kinetic laws of transport and reaction;
- initial and boundary conditions;
- optimization criteria.

This methodology has been useful to analyze problems at various scales involved in chemical engineering:

- pore scale (catalyst and absorbent): 1–1000 nm;
- particle scale: 10 μm–1 cm;
- reactor/separater scale: 1–10 m;

Models can be guided by objectives, which can seem contradictory: simplification of the reality/idealization and de-
tailed models to “better” know the reality. On one side they aim at simplification of reality or idealization; this is conditioned in the words of Denbigh (1951): “In science it is always necessary to abstract from the complexity of the real world, and in its place to substitute a more or less idealized situation that is more amenable to analysis” and led to the creation of new, simplified models which are a “digital impression” of our profession: boundary layer theory, film model for heat/mass transfer, residence time distribution (RTD) theory (Levenspiel, 2002). On the other hand, detailed models are necessary when simple models fail to capture essential behaviour of real systems; this is illustrated by the Maxwell–Stefan treatment of multicomponent diffusion (Maxwell, 1952):

\[ d_0 = \nabla q = \sum_{j=1}^{n} x_j N_j - x_j N_j c_i D_{ij} \]

The basic laws of momentum transfer (Newton’s law: \( \tau = \mu \frac{d^2}{dt^2} \)), heat transfer by conduction (Fourier’s law: \( q_y = -k \frac{d^2}{dx^2} \)), mass transfer by diffusion (Fick’s law: \( j_y = -D \frac{d}{dx} c \)) assume infinite velocity of propagation of the signal; this problem is eliminated following the proposal of Maxwell (1952) for momentum transfer

\[ \frac{1}{\tau_y} + \frac{\partial^2}{\partial t^2} = -\mu \frac{\partial^2}{\partial t^2} \]

where \( \tau \) is the time constant and the shear stress \( \sigma_{yy} \) in a fluid or solid body \( \sigma_{yy} \); similarly for mass transfer (Westerterp, Kronberg, Benneker, & Dilman, 1996) and heat transfer (Liu, Chen, & Xu, 1999) one should write: \( j + \tau \frac{d}{dx} = -D \frac{d^2}{dx^2} \) and \( \mu + \tau \frac{d}{dt} = -\frac{d^2}{dt^2} \) (Vernott and Cattaneo—VC equation). In homogeneous substances, the relaxation time is \( 10^{-8} \) to \( 10^{-14} \) s and Fourier’s law works for real life situations.

A philosophy of modelling can be based in four points:

- start with simple models; obtain from such models information which remains valid for more complex models (US$ 10 approach of Levenspiel (2002): “Always start by trying the simplest model and then only add complexity to the extent needed”); the validity of a model is not just a result of a “good fit”; more important is the capability to predict the system behaviour under operating conditions different from those used to get model parameters;
- good results can only be obtained if the model “well” represents the system;
- use models to obtain useful design parameters and their dependence on operating conditions; use independent experiments if possible to get model parameters.

In short, model development is a task to be carefully done to avoid waste of energy in the next simulation step. “Keep things as simple as possible, but not simpler” (Einstein).

2. The “art” of modelling

Chemical engineers use some techniques in modelling such as: adimensionalization and scaling, averaging, appropriate choice of independent variables. However, physical insight is gained as a consequence of such manipulations. A further step is transforming model results into useful tools for real life situations.

2.1. Scaling and dimensionless groups

Chemical engineers have some habits as normalization of variables; as a consequence of that mathematical operation dimensionless groups appear with a physical meaning. Consider the problem of diffusion/reaction in an isothermal porous catalyst with slab geometry. The mass balance in steady-state for irreversible reaction of order \( n \) is:

\[ D_{0} \frac{d^2 c_i}{dx^2} - k_{e} c_{i}^{n} = 0 \]  

with boundary conditions (symmetry condition in the centre and surface condition)

\[ z = 0, \quad \frac{dc}{dz} = 0 \]  

\[ z = \ell, \quad c_{i} = c_{i0} \]

The normalization of space variable \( z = z/\ell \) and concentration variable \( f_{n} = c_{i}/c_{i0} \) leads to:

\[ \frac{d^2 f_{n}}{dx^2} - \frac{n}{D_{0}} f_{n}^{n-1} = 0 \]

The dimensionless group \( \phi \) (Thiele modulus) governing the reaction/diffusion problem is:

\[ \phi = \frac{z \ell}{D_{0} \ell} = \frac{z}{D_{0} \ell} \]

The physical meaning of the dimensionless group is: \( \phi^{2} = \frac{D_{0} \ell}{D_{n} \ell} = \frac{D_{0}}{D_{n}} \)

(a) reaction rate \( \gg \) diffusion rate—concentration profile inside the catalyst is almost equal to the surface concentration; the catalyst works on “chemical regime”;

(b) reaction rate \( \geq \) diffusion rate—the catalyst works in “diffusional regime”.

![Fig. 1. Chemical regime and diffusional regime in an isothermal catalyst.](image-url)
2.2. Averaging

The linear driving force (LDF) model of Glueckauf (1955) sketched in Fig. 2 is a good example. For a spherical "homogeneous" adsorbent particle the mass conservation equation is:

\[ \frac{\partial c_i}{\partial t} = D_i \frac{1}{R^2} \frac{\partial}{\partial R} \left( R^2 \frac{\partial c_i}{\partial R} \right) \]  

with boundary conditions (symmetry at the centre and equilibrium at the surface through the adsorption equilibrium isotherm with the fluid concentration at the surface through the adsorption equilibrium isotherm):

\[ R = 0, \quad \frac{\partial c_i}{\partial R} = 0 \]
\[ R = R_p, \quad c_i = f(c_i) \]

Multiplying both members by \( R^2 dR \), integrating over the particle volume (between 0 and \( R_p \)) and introducing the average concentration \( \langle c_i \rangle \) leads to:

\[ \frac{\partial \langle c_i \rangle}{\partial t} = \frac{3 D_i}{q_i a R_p} \frac{\partial}{\partial R} \langle q_i \rangle = \frac{3 D_i}{q_i a R_p} (q_i - \langle q_i \rangle) = k_i (q_i - \langle q_i \rangle) \]  

\[ \hat{q}_i = \frac{K_i}{1 + (K - 1) \xi} \]  

A first dimensionless parameter appears: the “capacity parameter” \( \zeta_n = \frac{q_i}{\langle q_i \rangle} \) of the adsorption column. A combination of the independent variables \( z \) and \( t \) in only one variable \( T \) (throughput parameter of Vermeulen (1958)) defined as the ratio of moles of solute passed through the bed section located at \( v = \xi z \) and the number of moles retained in the adsorbent contained in the volume \( v \). The new variable \( T = \frac{z}{\xi} \left( \frac{\xi}{z} - 1 \right) \) allows us to write the mass balance as \( \frac{\partial c_i}{\partial t} = T \) and taking into account the adsorption equilibrium isotherm \( \hat{q}_i = \frac{\delta}{1 + K \xi} \) we get the breakthrough curve shown in Fig. 3:

\[ \xi_i = \frac{1 - \sqrt{T}}{1 - K}, \quad K \leq T \leq 1/K \]  

2.4. From model results to real life

Back to the reaction/diffusion problem for first order reaction in isothermal slab catalyst. The concentration profile is \( f = \frac{a c(\xi)}{a c(0)} \) and the effectiveness factor of the catalyst is \( \eta = \frac{a c(\xi)}{a c(0)} \). It is important to know the effectiveness factor to calculate the amount of catalyst in the reactor needed to get a given reactant conversion. But the Thiele modulus requires that the kinetic constant \( k \) must be known (and many times it is not). Hopefully, there are always bright people around to transform theoretical results in practical tools. Weisz and Prater (1954) changed \( \eta = g(\phi^d) \) in a more useful plot \( \eta = g(\phi^2) \), where \( \phi^2 \) does not require the knowledge of \( k \); but only measurable quantities since \( \phi^2 = \frac{a c(\xi)}{a c(0)} \) (Fig. 4).

2.5. Obtaining useful relations between dependent variables

Consider the diffusion/reaction/conduction problem in a non-isothermal slab catalyst. For slab geometry and first order irreversible reaction conservation equations of mass/energy are:

\[ \frac{\partial c_i}{\partial t} + \frac{\partial}{\partial x} \left( \frac{1}{\varepsilon} \xi a c_i \right) = 0 \]  

\[ \frac{\partial}{\partial x} \left( \frac{1}{\varepsilon} \xi a \right) = 0 \]  

\[ \frac{\partial}{\partial x} \left( \frac{1}{\varepsilon} \xi a c_i \right) = 0 \]  


Fig. 2. LDF model.

Fig. 3. Breakthrough curves for unfavourable isotherms.
3. Models of US$ 10, 100 and 1000 (Levenspiel, 2002)

3.1. US$ 10 models

3.1.1. Equilibrium theory for adsorption columns.

Physical concepts from simple models

The simplest model of an adsorption column model assumes isothermal operation, plug fluid flow, infinitely fast mass transfer between fluid and solid phases (instantaneous equilibrium at the interface) and trace system (Rodrigues & Tondeur, 1981). Model equations are the mass balance in a bed volume element and the equilibrium law at fluid/solid interface:

$$\frac{\partial c_i}{\partial t} + \frac{u_i}{1 - \varepsilon} \frac{\partial \langle q_i \rangle}{\partial t} = 0$$ (20)

$$\langle q_i \rangle = q_i^* = f(c_i)$$ (21)

where $$\langle q_i \rangle$$ is the average concentration in the adsorbent and $$q_i^* = f(c_i)$$ is the concentration at the particle surface in equilibrium with the fluid concentration $$c_i$$. Using the cyclic relation between partial derivatives we get De Vaault equation (1943):

$$c_i = \left( \frac{\partial z}{\partial t} \right) c_i = u_i + \frac{1}{1 - \varepsilon} f'(c_i)$$ (22)

Those interested in understanding adsorptive and chromatographic processes will recognize this is the most important result to retain. It shows that adsorption in fixed beds is a phenomenon of propagation of concentration waves. The simplest model shows that the nature of the equilibrium isotherm is the main factor influencing the shape of the breakthrough curve (Fig. 6). The physical concepts to be retained are: dispersive waves are formed when isotherms are unfavourable; each concentration propagates with a velocity given by De Vaault equation. Compressive waves are formed for favourable isotherms and the physical limit is a shock, which propagates with a velocity $$u_{sh} = \frac{u_i}{1 + \frac{\partial f(c_i)}{\partial c_i}}$$, where the slope of the chord linking the feed state and the bed initial state appear instead of the local slope of the equilibrium isotherm.

3.1.2. Fluid flow in chemical reactors: residence time distribution and tracer technology

Danckwerts (1953) approached the study of fluid flow in reactors in a brilliant and simple way: "introduce a pulse of tracer into the fluid entering the reactor and see when it leaves". The normalized outlet concentration versus time is related with the residence time distribution.

The study of RTD of flowing fluids and its consequences can be put under the umbrella of tracer technology. This is important for chemical engineers, researchers in the medical field, environment, etc., to diagnose the reactor behaviour, drug distribution in the body, etc. Danckwerts built a theory based on the characterization of fluid elements of a population inside the reactor (age and life expectation) and leaving

Fig. 4. (a) Effectiveness factor vs. Thiele modulus and (b) effectiveness factor vs. $$\eta \phi^2$$.

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Fig. 5. Concentration and temperature profiles in a non-isothermal catalyst.
the reactor (residence time). Then, he introduced the “distribution” relative to each character; the residence time distribution $E(t)$ is then defined as $E(t)$ being the fraction of fluid elements leaving the reactor with residence time between $t$ and $t + dt$. The next question is how to experimen-
tally have access to $E(t)$. This brings the tracer technology to the center of the arena. The normalized response to an impulse of tracer $C(t)$ is directly related with the RTD, i.e., $C(t) = e(t)$; or the normalized response to a step input of tracer $C(t)$ curve of Danckwerts is $E(t) = dC(t)/dt$. This is a characteristic of linear systems: the response to an impulse is the derivative of the response to a step input. How this linearity appears in this macroscopic vision of fluid flow where Navier–Stokes equation (1959) holds.

$\frac{d^2 f}{dx^2} - 2m \frac{df}{dx} - 4k^2 f = 0$ (24)

with boundary conditions: $f = 1$ at $x = 0$ and $x = 1$. Model parameters are: Thiele modulus $\phi = \frac{L}{D}$ and intraparticle Peclet number $\lambda_m = \frac{m}{D}$ (ratio between time constants for pore diffusion and convection). The concentration profile inside the catalyst is:

$f = \frac{\text{sh} \alpha_2 e^{\lambda_2 (2s - 1)} - \text{sh} \alpha_1 e^{\lambda_1 (2s - 1)}}{\text{sh} (\alpha_2 - \alpha_1)}$ (25)

where $\alpha_{1,2} = \frac{D_2e^{\phi_1} \pm \sqrt{4D_2e^{\phi_1} - 1}}{2}$. Asymmetric profiles (Fig. 7) can be viewed as a result of mass transfer by convection inside pores. The effectiveness factor is:

$\eta_{dc} = \frac{1/\alpha_1 - 1/\alpha_2}{\coth \alpha_1 - \coth \alpha_2}$ (26)

When convection is not important, i.e., $\lambda_m = 0$, the effectiveness factor becomes $\eta_{dc} = \frac{\text{sh} \alpha_2}{\text{sh} \alpha_1}$. The effect of convection can be seen in Fig. 8 where $\eta_{dc}/\eta_B$ is plotted versus $\lambda_m$ and $\phi$. In the intermediate region of Thiele modulus (similar reaction and diffusion rates), the effectiveness of the catalyst is improved by convection. The pore convection will apparently increase diffusivity and move the working regime of the catalyst from diffusion to “chemical” controlled. The message is: intuition is not enough!
3.3. USS 1000 models: Computational Fluid Dynamics (CFD)

Levenspiel (2002) summarizes the progress on the study of fluid flow: “In the 19th century there were two approaches to study fluid flow: hydrodynamics (dealt with ideal frictionless fluid; highly mathematical stuff) and hydraulics developed by civil engineers who amassed mountains of tables of pressure drop and head loss of fluids in open and closed channels of all sort . . .”. At the beginning of the 20th century, Prandtl said “Hydrodynamics has little significance for the engineer because of the great mathematical knowledge required for an understanding of it and the negligible possibility of applying its results. Therefore, engineers put their trust in the mass of empirical data collectively known as the ‘science of hydraulics’. As Levenspiel says, ‘Prandtl was the genius who patched together these different disciplines with his simple boundary layer theory. The result is modern fluid mechanics’.

Numerical methods for the solution of PDE’s are available and the combination of two solid disciplines appears with a new name: “Computational Fluid Dynamics”. Twenty years ago, we published in ISCRE8 “Residence time distribution in laminar flow through reservoirs from momentum and mass transport equations” (Brunier, Zoulalian, Antonini, & Rodrigues, 1984). It is a problem of 2D flow in a reservoir of length $L$ and height $H$, where a stationary laminar flow exists between inlet and outlet (Fig. 9). The formulation is made in terms of vorticity and stream function; the flow field is obtained and the RTD is obtained by solving the mass conservation equation:

$$\frac{\partial (u\Omega)}{\partial x} + \frac{\partial (v\Omega)}{\partial y} = \frac{\partial^2 \Omega}{\partial x^2} + \frac{\partial^2 \Omega}{\partial y^2}$$

$$u = \frac{\partial \psi}{\partial y}; \quad v = -\frac{\partial \psi}{\partial x}$$

$$\left(\frac{\partial^2 \psi}{\partial x^2} + \frac{\partial^2 \psi}{\partial y^2}\right) = -\Omega$$

(27)

This problem was recently solved with modern tools (Fluent) (Madeira, Alves, & Rodrigues, 2004). Results are available at the following web address http://www.fe.up.pt/~mmalves/cfd/reactor/index.htm.

The following pictures (Fig. 10) illustrate the concentration evolution of a tracer inside the reactor. Initially, the reactor is full of water (blue), and a step profile in the con-

![Fig. 9. Two-dimensional flow in a reservoir (a) and RTD (b).](image1)

![Fig. 10. Time evolution of tracer concentration in a 2D reservoir.](image2)
The concentration of a tracer (red) is imposed at the inlet boundary. The reduced time is defined as $\theta = t/\tau$, where $\tau$ represents the space-time. The streamlines are shown in black.

These pictures clearly illustrate that approximately at $\theta = 0.22$ one starts to ‘see’ tracer at the reservoir outlet. In addition, even for a very long time of operation (about five times the residence time), the reservoir is not completely full of tracer, due to the large stagnant zone. The movie of concentration evolution is available at the following web address: http://paginas.fe.up.pt/~mmalves/cfd/reactor/movies.htm.

4. Process simulation

The processes to be discussed below illustrate how science and technology ingredients contribute to process innovation. In the area of proteins separation the concept of “diffusivity augmented by convection” combined with the manufacture of large-pore adsorbents lead to the development of a process—perfusion chromatography (Afeyan et al., 1990). Interestingly enough the development was made by a spin-off company of MIT and not by the traditional resin manufacturers. Also the development of SMB processes by UOP was based on the concept of simulating the solid movement by keeping it fixed combined with a technology development of rotary valve to allow switching of the position of fluid streams entering/leaving the system. Again the recent introduction of this technology in pharmaceutical industry was lead by a small company and not by the traditional owners of SMB technology.

4.1. Perfusion chromatography

The first chromatographic experiment (1903) was reported in 1905 by M. Tswett (Fig. 11a) to the Warsaw Society of Natural Sciences: “On a category of adsorption phenomena and their application to biochemical analysis” (Rondest, 1972). He coined the term “chromatography” inspired in the experiment: elution of a sample of green leaves extract through a column of calcium carbonate which was separated in a yellow fraction (carotenes) and green fraction (chlorophyll). This study was rediscovered in 1931 by the Nobel Prize R. Kuhn working on natural pigments. The theory of adsorption chromatography was developed in 1940 by Tiselius and partition chromatography in 1941 by Martin and Synge (all Nobel) (1941). Another vision of history shows David Talbot Day (Heines, 1971), geologist and engineer at the Mineral Resources of the US Geological Survey, who presented at the First International Petroleum Congress in Paris (1900) one experiment where “crude oil forced upward through a column packed with limestone changed in color and composition” (Fig. 11b). This is the basis of PONA analysis established in 1914 and still used in petroleum industry. The factors influencing the behaviour of a fixed bed column can be classified in two categories: equilibrium and kinetic factors (hydrodynamics, heat/mass transfer) (Fig. 12).
transport and smaller pores to provide adsorption capacity and catalytic sites. My interest in this area started with a problem of measurement of effective diffusivity in large-pore catalysts using a chromatographic method and tracer technology. The analysis of results obtained by Ahn (1980) with a conventional model led to the conclusion that effective diffusivity was changing with flow rate. Results were reanalyzed by assuming transport not only by diffusion, $D$, but also by convection (pore velocity $v_0$) and the equivalence with the conventional model where both mechanisms were lumped in an apparent $D_e$ allowed us to show that (Rodrigues, Ahn, & Zoulalian, 1982):

$$D_e = \frac{D}{f(\lambda)}$$ (28)

where the intraparticle Peclet number is $\lambda = \frac{v_0/\epsilon}{D_e}$ is the separation of proteins.

Based on the work of Nir and Pismen (1977) on diffusion, convection and reaction in large-pore catalysts (5000 Å) data from Ahn (1980) were analyzed. For a non-adsorbable tracer the “lumped” diffusion/convection model for transient state is:

$$\frac{\partial g_s(x)}{\partial t} = \frac{\partial}{\partial x}\left(\bar{v}g_s(x)\right) = \frac{\tilde{D}_e}{\epsilon} \frac{\partial^2 g_s(x)}{\partial x^2}$$ (29)

The particle transfer function is:

$$f(\lambda) = \frac{\lambda}{1 + \frac{\epsilon}{\epsilon_b} + \frac{\epsilon_b}{\epsilon} + \frac{\epsilon}{\epsilon_b}}$$ (30)

with an apparent diffusion time constant $\tau_d = \frac{\epsilon}{\epsilon_b}\frac{\epsilon_b}{\epsilon}$. The detailed diffusion/convection model is:

$$\frac{\partial^2 g_s(x)}{\partial x^2} = \frac{\epsilon}{\epsilon_b} \frac{\partial^2 g_s(x)}{\partial x^2} + \frac{\epsilon_b}{\epsilon} \frac{\partial^2 g_s(x)}{\partial x^2}$$ (31)

and

$$g_s(x) = \left(\frac{2}{\lambda}\right) \frac{1 + \frac{\epsilon}{\epsilon_b} + \frac{\epsilon_b}{\epsilon}}{\frac{\epsilon}{\epsilon_b} + \frac{\epsilon_b}{\epsilon}} \left(\frac{1 + \frac{\epsilon}{\epsilon_b}}{\frac{\epsilon}{\epsilon_b}} \right) \frac{\tau_d}{\epsilon}$$ (32)

with $\tau_{1,2} = \frac{\lambda}{2} \frac{1}{\lambda} \frac{1}{\tau_d}$. $\epsilon = \frac{\epsilon}{\epsilon_b}\frac{\epsilon_b}{\epsilon}$, $\epsilon_b = \frac{v_0/\epsilon}{D_e}$, is the slope of the equilibrium isotherm:

$$\frac{\partial g_s(x)}{\partial x} = \frac{\epsilon}{\epsilon_b} \frac{\partial^2 g_s(x)}{\partial x^2} + \frac{\epsilon_b}{\epsilon} \frac{\partial^2 g_s(x)}{\partial x^2}$$ (33)

The practical application of this concept was developed in 1990 for the separation of proteins (perfusion chromatography). The pore velocity can be estimated from the equality between bed pressure drop relative to the bed length and particle pressure drop assuming that Darcy’s law is valid; the result is: $v_0 = \frac{u}{\epsilon}$, where $\epsilon$ is the ratio of particle and bed permeabilities. Van Deemter, Zuiderweg, & Klinkenberg’s equation (1956) for conventional packings for the Height Equivalent to a Theoretical Plate (HETP) is:

$$\text{HETP} = A + \frac{B}{u} + \frac{C}{u}$$ (34)

where $\epsilon_p$, is the particle porosity, $\epsilon_b$, the interparticle porosity, $b = 1 + (1 - \epsilon_p)\frac{m}{\epsilon_p}$ and $m$ is the slope of the equilibrium isotherm:

$$\text{HETP} = A + \frac{B}{u} + Cu$$ (35)

For large-pore particles (Rodrigues, 1993) an extension of the Van Deemter equation was presented:

$$\text{HETP} = A + \frac{B}{u} + C\bar{v}$$ (36)

Equation (36) shows that at low velocities $f(\lambda) \approx 1$, HETP is reduced to the classic Van Deemter equation (diffusion-controlled limit): at high velocities $f(\lambda) \approx \pi i$, and the last term of Rodrigues equation (Eq. (36)) becomes constant since the velocity inside pores $v_0$ is proportional to the bed superficial velocity $u$. The HETP reaches a plateau, which does not depend on the solute diffusivity but only on the particle permeability and pressure gradient (convection-controlled limit). In large-pore supports the column performance is improved since HETP is lower than with conventional supports (the C term of Van Deemter equation is reduced) and the speed of separation is increased without losing efficiency (Fig. 15).

Fig. 13. Enhancement factor for diffusivity due to convection, $f(\lambda)$.

Fig. 14. Model equivalence: (a) diffusion and convection and (b) “lumped” diffusion.
Fig. 15. HETP vs. $u$ (Van Deemter equation and Rodrigues equation).

The objective achieved with the use of large-pore packing materials as shown in Fig. 16 is to reduce intraparticle mass transfer resistances. Examples of packing materials are in Fig. 17.

4.2. Simulated Moving Bed (SMB) processes

4.2.1. The concept of SMB

Simulated Moving Bed is a powerful technique for preparative scale chromatography known since 1961 (first patent by UOP, Broughton & Gerhold, 1961). This technology was originally developed in the areas of petroleum refining and petrochemicals, known as the Sorbex process. Recently, SMB technology has found new applications in the areas of biotechnology, pharmaceuticals and fine chemistry; the first industrial unit was installed at UCB Pharma (Belgium) in 1999 by Novasep. SMB is now considered a key technology for chiral separations. It is interesting to compare “old” and “new” applications of SMB technology. In the Parex process (Fig. 18), for $p$-xylene recovery from a mixture of xylene...
isomers column diameter is \( D = 10 \text{ m} \) (maximum) and bed height \( H = 1 \text{ m} \) and particles are of 600 \( \mu \text{m} \) diameter; in chiral separations (Fig. 19), \( D = 1 \text{ m} \) (maximum) and \( H = 0.1 \text{ m} \) (similar \( D/H \) ratio) with particles of 20 \( \mu \text{m} \) diameter. The adsorbent capacity is 200 kg/m\(^3\) in the Parex process compared with 10 kg/m\(^3\) in chiral separations; the productivity is 120 kg/m\(^3\) h in the Parex and 1–10 kg/m\(^3\) h in chiral separations.

The principle of SMB operation can be best understood by analogy with the equivalent True Moving Bed (TMB) process. The TMB unit (Fig. 20) is divided into four sections: section 1, between the eluent and extract ports; section 2, between the extract and feed ports; section 3, between feed and raffinate points; section 4, between the raffinate and the eluent inlet. In the ideal TMB operation, liquid and solid flow in opposite directions, and are continuously recycled: the liquid flowing out of section 4 is recycled to section 1, while the solid coming out of section 1 is recycled to section 4. In the TMB operation, the solid flow rate is constant all over the unit; however, the liquid flow rates differ from section to section. Let us consider a feed mixture containing species A, the more retained component and recovered in the extract (Fig. 19a) and species B, the less adsorbed species and preferentially recovered in the raffinate. In sections 2 and 3, the two components must move in opposite directions. The less retained component B must be desorbed and carried with the liquid phase, while the more retained species A must be adsorbed and carried with the solid phase. Section 2 is the zone of desorption of the less retained species B, while section 3 is the zone of adsorption of the more retained component A. The role of section 4 is to clean the eluent, which is then recycled to the section 1 where the adsorbent is regenerated. The operation of this ideal TMB has several drawbacks associated with the movement of the solid phase. A Simulated Moving Bed technique was developed in order to retain the advantages of continuous and countercurrent flow without introducing the problems associated with the actual movement of the solid phase. In the SMB system, the adsorbent is fixed and the positions of the inlet and outlet streams move periodically.

This shift, carried out in the same direction of the liquid phase, simulates the movement of the solid phase in the opposite direction. The four liquid access lines between each column can be used to perform a discrete movement of the inlet and outlet streams in the same direction of the liquid phase.

In the Sorbex SMB technology developed by UOP (Fig. 18), a rotary valve is used to periodically change the position of the eluent, extract, feed and raffinate lines along the adsorbent bed. At any particular moment, only four lines between the rotary valve and the adsorbent bed are active. However, there are alternative techniques to perform the port switching, like the one developed by NovaSep (France), which uses a set of individual on-off valves connect-
4.2.2. Modelling of SMB

The SMB can be modelled as an equivalent TMB where the solid movement is taken into account and equivalence relations are used to relate the results with a real SMB (Table 1) or as a real SMB; each bed is analyzed individually and the periodic change in boundary conditions is taken into account.

With reference to Fig. 20, the TMB unit is divided by inlet and outlet ports into four zones. The TMB steady-state internal concentration profiles are presented in Fig. 21. On the other hand, the SMB approach examines each column individually. Due to the switching of inlet and outlet ports, each column plays a different role during whole cycle, depending on its location. The model of the SMB unit is constituted of \( k \) (\( k = \text{number of the columns} \)) identical models of the column.

Table 1

<table>
<thead>
<tr>
<th>Equivalence relations between a SMB and a TMB</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMB</td>
</tr>
<tr>
<td>Solid phase velocity ( u_s )</td>
</tr>
<tr>
<td>Liquid phase velocity ( v_{\text{LMB}} )</td>
</tr>
</tbody>
</table>

\( t^* \) is the switching time and \( L_c \) is the column length.
connected with each other by simple material balances on the connecting nodes. With each switching of the inlet and outlet ports each column should be updated in terms of flow rate and inlet concentration. The flow rate in each column, according to its location (section), can be calculated by mass balance around the inlet and outlet nodes. The inlet concentration of each column is equal to the outlet concentration of the previous column, except for the feed and desorbent nodes.

The main difference between TMB and SMB approach is that the stationary regime of the unit. The time dependence of the boundary conditions in the SMB leads to cyclic steady-state instead of a real steady-state present in the TMB model. The cyclic steady-state is reached after a certain number of cycles, but the system states are still varying over the time because of the periodic movement of the inlet and outlet ports along the columns (Fig. 22).

Whatever modelling approach is considered, the degree of complexity of the model may vary significantly according to the description of the unit operation (staged or distributed plug flow system), the mass transfer resistance (equilibrium stage or mass transfer resistance within the fluid and/or solid phase) and adsorption equilibrium (linear, Langmuir, bi-Langmuir or modified Langmuir).

The SMB and TMB model equations when axial dispersion plug flow for the liquid phase, plug flow for the solid phase, homogeneous LDF for internal mass transfer and any multicomponent adsorption isotherm are assumed is presented in Table 2.

4.2.3. Design of SMB

Due to the relative complexity of its physical implementation, the definition of operating conditions (flow rates and switching time) of a SMB adsorber is not a straightforward task. Some constraints have to be met to recover the more strong adsorbed species (A) in the extract and the less adsorbed species (B) in the raffinate. These constraints are expressed in terms of net fluxes of components in each section considering an equivalent TMB. In section 1, the species A must move upward to the extract port, in sections 2 and 3, the species A must move downward to the extract port and the species B must move to the raffinate port and in section 4, the net flux of the species B has to be downwards (Fig. 20).

\[
\begin{align*}
Q_{S, A1} & > 1 \\
Q_{S, B1} & > 1 \quad \text{and} \quad Q_{S, A2} & < 1 \\
Q_{S, B2} & > 1 \quad \text{and} \quad Q_{S, A3} & < 1 \\
Q_{S, B3} & < 1 \\
Q_{S, B4} & < 1
\end{align*}
\]  

(37)

The simplest case may be formulated for systems with linear uncoupled adsorption isotherms. The region of complete separation (100% extract and raffinate purity) predicted by
the equilibrium theory is a triangle shown in Fig. 23a. The section constraints are explicit inequality relations between solid and liquid flow rates in the four TMB sections (Ruthven & Chung, 1989; Storti, Mazzotti, Morbidelli, & Carrà, 1993):

\[ m_1 > K_A \quad K_B < m_2 , \quad m_3 < K_A \quad m_4 < K_B \]  \hspace{1cm} (38)

For non-linear isotherms the “triangle” is distorted as shown in Fig. 23b.

Higher mass transfer resistances lead to a decrease of the separation region as shown in Fig. 24 (Pais, 1999).

For the systems where mass transfer resistance inside particles is important, the “triangle theory” can only give initial guesses for a feasible operating point of the process, since it is based on the assumption of the equilibrium model. Very often, 100% purity in both extract and raffinate is either unnecessary or would require an extremely large adsorbent inventory to be accomplished. Furthermore, the approach based on equilibrium model does not allow explicit prediction of the product purities that are generally the main constraints for a feasible operating point.

These are the reasons why the concept of separation volume was introduced (Azevedo & Rodrigues, 1999). The “separation volume” methodology uses realistic mathematical model and explore the influence of the flow rates in zones 1 and 4 (desorbent flow rate). The “separation volume” methodology offers two possibilities: if the flow rate in zone 1 \((m_1)\) is fixed, the design leads to a \((m_3 \times m_2 \times m_4)\) volume for a given separation requirement; if the flow rate in zone 4 \((m_4)\) is fixed, the design will result in a \((m_2 \times m_3 \times m_1)\) volume for a given separation requirement (see Fig. 25). In previous works (Azevedo & Rodrigues, 1999; Minceva & Rodrigues, 2002; Rodrigues & Pais, 2004) it was found that the flow rate in zone 4 has less influence on the separation performance.

4.2.4. Optimization of SMB

The optimization of SMB unit considers selection of the operating conditions and/or geometric parameters that minimize/maximize a given objective function(s), in the frame of previously defined constraints. Most commonly the objective is to maximize the SMB productivity and minimize the eluent (desorbent) consumption, for a given constraints defined in terms of minimum required product purity and/or recovery. Maximum productivity implies maximum feed flow rate, \(\max(Q_F) = \max(\gamma_3 - \gamma_2)\) and minimum eluent (desorbent) consumption implies minimum eluent flow rate \(\min(Q_E) = \min(\gamma_1 - \gamma_4)\), where \(\gamma_j = (1 - \varepsilon)\varepsilon m_j\), \(j = 1, 2, \ldots\).
Simulated Moving Bed model equations

Mass balance over a volume element of the bed $k$
\[
\frac{dC_k}{dt} = \frac{1}{V_k} \left( \frac{1}{D_{eqi}} \frac{dC_i}{dt} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)
\]

Mass balance in the particle
\[
\frac{dC_i}{dt} = w_i (C_{ik} - q_{ik})
\]

Initial conditions
\[
\theta = 0: \quad C_{ik} = q_{ik} = 0
\]

Boundary conditions for column $k$
\[
\begin{align*}
\frac{dC_k}{dx} &= 0, \quad x = 0: \quad C_k = \frac{1}{V_k} \int_0^1 (C_{ik} + \frac{1}{r_i^2} q_i) \frac{dz}{D_{eqi}} \\
&s = 1: C_k = C_{i0}
\end{align*}
\]

where $C_{i0}$ is the inlet concentration of species $i$ in column $k$

For eluent inside a section and for extract and raffinate nodes:
\[
C_k = C_{i0}
\]

For the eluent node:
\[
C_k = \frac{C_{i0}^2}{C_{i0}^2 - \frac{1}{r_i^2} \int_0^1 C_{ik} \frac{dz}{D_{eqi}}} - \frac{1}{r_i^2} q_i
\]

For the feed node:
\[
C_k = \frac{C_{i0}^2}{C_{i0}^2 - \frac{1}{r_i^2} \int_0^1 C_{ik} \frac{dz}{D_{eqi}}} - \frac{1}{r_i^2} q_i
\]

Global balances
Eluent node: $C_k = C_{i0}$, extract node: $C_{ik} = C_{i0}$ - $\frac{1}{r_i^2} q_i$
Feed node: $C_{ik} = C_{i0}$ - $\frac{1}{r_i^2} q_i$

Multicomponent adsorption equilibrium isotherm
\[
q_{ik} = f_i(C_{ik}, C_{i0})
\]

True Moving Bed model equations

Mass balance over a volume element of the section $j$
\[
\frac{dC_j}{dt} = \frac{1}{V_j} \left( \frac{1}{D_{eqi}} \frac{dC_i}{dt} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)
\]

Mass balance in the particle
\[
\frac{dC_i}{dt} = \frac{1}{V_j} \left( C_{ik} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)
\]

Initial conditions
\[
\theta = 0: \quad C_{ik} = q_{ik} = 0
\]

Boundary conditions for section $j$
\[
\begin{align*}
\frac{dC_j}{dx} &= 0, \quad x = 0: \quad C_j = \frac{1}{V_j} \int_0^1 (C_{ik} + \frac{1}{r_i^2} q_i) \frac{dz}{D_{eqi}} \\
&s = 1: C_j = C_{i0}
\end{align*}
\]

where $C_{i0}$ is the inlet concentration of species $i$ in section $j$

For the eluent node:
\[
C_j = \frac{1}{V_j} \int_0^1 C_{ij} \frac{dz}{D_{eqi}}
\]

For the feed node:
\[
C_j = \frac{1}{V_j} \int_0^1 C_{ij} \frac{dz}{D_{eqi}}
\]

Global balances
Eluent node: $C_{ij} = \gamma_{1j} + \gamma_{2j}$, extract node: $C_{ij} = \gamma_{1j}$
Feed node: $C_{ij} = \gamma_{1j}$

Multicomponent adsorption equilibrium isotherm
\[
q_{ik} = f_i(C_{ik}, C_{i0})
\]

Table 2

<table>
<thead>
<tr>
<th>SMB model equations</th>
<th>TMB model equations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simulated SMB model equations</td>
<td>True SMB model equations</td>
</tr>
<tr>
<td>Mass balance over a volume element of the bed $k$</td>
<td>Mass balance over a volume element of the section $j$</td>
</tr>
<tr>
<td>$\frac{dC_k}{dt} = \frac{1}{V_k} \left( \frac{1}{D_{eqi}} \frac{dC_i}{dt} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)$</td>
<td>$\frac{dC_j}{dt} = \frac{1}{V_j} \left( \frac{1}{D_{eqi}} \frac{dC_i}{dt} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)$</td>
</tr>
<tr>
<td>Mass balance in the particle</td>
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</tr>
<tr>
<td>$\frac{dC_i}{dt} = w_i (C_{ik} - q_{ik})$</td>
<td>$\frac{dC_i}{dt} = \frac{1}{V_j} \left( C_{ik} - \frac{1}{r_i^2} q_i (C_{ik} - q_{ik}) \right)$</td>
</tr>
<tr>
<td>Initial conditions</td>
<td>Initial conditions</td>
</tr>
<tr>
<td>$\theta = 0: \quad C_{ik} = q_{ik} = 0$</td>
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</tr>
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<td>Boundary conditions for column $k$</td>
<td>Boundary conditions for section $j$</td>
</tr>
<tr>
<td>$\frac{dC_k}{dx} = 0, \quad x = 0: \quad C_k = \frac{1}{V_k} \int_0^1 (C_{ik} + \frac{1}{r_i^2} q_i) \frac{dz}{D_{eqi}}$</td>
<td>$\frac{dC_j}{dx} = 0, \quad x = 0: \quad C_j = \frac{1}{V_j} \int_0^1 (C_{ij} + \frac{1}{r_i^2} q_i) \frac{dz}{D_{eqi}}$</td>
</tr>
<tr>
<td>$s = 1: C_k = C_{i0}$</td>
<td>$s = 1: C_j = C_{i0}$</td>
</tr>
</tbody>
</table>

Fig. 23. Separation region for: (a) linear isotherms and (b) non-linear isotherm.

3.4. The influence of $\gamma_1$ and $\gamma_4$ on the SMB productivity and eluent consumption is presented in Fig. 26. The separation region increases by increasing $\gamma_1$ up to some value and the vertex moves from lower to higher values of $(\gamma_2, \gamma_3)$, higher productivity could be reached. When the separation region size does not increase more, further increment in $\gamma_1$ will lead just to increase of the eluent consumption, since $(\gamma_2 - \gamma_4)$ increases. When the value of $\gamma_1$ is fixed (Fig. 26b) the separation regions are similar until some value of $\gamma_2$ and then they start to decrease if the value of $\gamma_4$ further increases. The value of the flow rate in zone 4 ($\gamma_4$) does not influence the feed flow rate and SMB unit productivity, but it affects the desorber consumption. We proposed a two-level optimization procedure based on the concept of “separation volume” and equivalent TMB design (Minceva, 2004).
4.3. Future directions in SMB: multicomponent, SMBR

Although the SMB technology offers many advantages over preparative chromatography (leading to cleaner, smaller, safer and faster processes) (Nicoud, 1997) the main disadvantage of this process is the limitation to the separation of binary mixtures or of one component from a multicomponent mixture.

The pseudo-Simulated Moving Bed process—JO process of Japan Organo Co. (Ando, Tanimura, & Tamura, 1990; Masuda, Sonobe, Matsuda, & Horie, 1993) has been successfully applied in separation of a ternary mixture. The process cycle is divided into two steps (Fig. 27). In step 1, feed and eluent streams are introduced into the system, equivalent to a series of preparative chromatographic columns, and the intermediate component is produced. In step 2, similar to a Simulated Moving Bed, there is no feed and the less adsorbed species is collected in the raffinate while the more retained species is collected in the extract (Mata & Rodrigues, 2001).

The combination of the chemical or biochemical reaction with Simulated Moving Bed chromatographic separator has been subject of considerable attention in the scientific research the last 10 years. This integrated reaction–separation technology adopts the name Simulated Moving Bed Reactor (SMBR) technology. The first application of SMBR in zeolite catalyzed alkylation reaction was patented by Zabransky and Anderson (1977). Integration of reaction and separation steps in one single unit has the obvious economical advantage of reducing the cost of unit operations for downstream purification steps. In the case of reversible reaction, where the conversion is limited by the chemical equilibrium removal of products as they are formed allows achieving conversions well beyond equilibrium values. For reactions in series or in parallel, it may be possible the selective separation of desired intermediate species. When a reaction product has an inhibiting or poisoning effect, its removal from the reaction medium also promotes enhanced yield.

The inversion of sucrose (\(A \rightarrow B + C\)) was studied in a SMBR (Azevedo & Rodrigues, 2001). Sucrose is introduced in the middle of the unit with the feed stream. The reaction is catalyzed by the enzyme invertase introduced in the unit with the eluent stream. The sucrose reacts near to the feed
port; fructose and glucose are formed and separated in the extract and raffinate, respectively. The internal concentration profiles are presented in Fig. 28.

Asynchronous shifting of the inlet/outlet ports has been proposed in the Varicol process (Ludemann-Hombourger, Nicoud, & Bailly, 2000) as well as manipulation of feed concentration and flow rate.

5. Conclusions

The area of Modelling/Simulation characterizes a generation of chemical engineers associated with the Second Paradigm of Chemical Engineering. Today, simulation tasks can be simplified with the availability of friendly user software; the question of validation of results remains and in principle more time will be available to analyze results.

The Third Paradigm of Chemical Engineer should come out soon (is it Molecular Transformations/Modelling/Simulation?), in the meantime we keep the reflection of Astarita: "the amount of information available grows continuously but the amount of information that any one of us can usefully digest does not grow".

References


