MATHEMATICAL CONTROL THEORY
FOR
LIQUID CHROMATOGRAPHY

Thesis by

Richard Lewis Martin Ammons

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ABSTRACT

A more comprehensive mathematical theory for liquid chromatography is set forth, incorporating dynamical models for mixed solvents and solutes, and new mathematical models for adsorption, including adsorbent and exchange processes. The equations for solvent and solute are shown to possess unique solutions, using so-called *energy methods.* The solvent modulation of local velocity is found theoretically, as is solvent control of solute adsorption, diffusivity, and dispersion. The theory for solvent control of solute adsorption is found to be very accurate against experiment, and offers a useful method of treating normal phase, reversed phase, ion exchange, and ion pair liquid chromatography in a unified mathematical framework, under the name *catalyzed adsorption.* The long-recognised problem of *solvent localization* is modelled, and the model shown to be consistent with experiment. Another classical problem, *solvent demixing,* is explained in terms of the nonlinear multicomponent solvent model, wherein solvent gradients steepen according to the adsorption and shock formation. Perturbation theory, based on a small *packing number* $d_p/L \ll 1$ (where d_p is substrate particle diameter, L is column length), is applied to the solvent-controlled pulsed solute dynamical equations. When moment techniques are used in conjunction with perturbation theory, very useful and simplified system control equations are obtained. These control equations are used in some model problems to discuss HETP (Height Equivalent to a Theoretical Plate) variations with Peclet number, with relative solvent concentration, and between solutes. Finally, numerical methods for the solvent and solute equations are discussed.

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INTRODUCTION

Probably the most commonly used method for organic quantitative and qualitative analysis in chemistry today is HPLC — High Performance Liquid Chromatography, used for the separation and analysis of chemical mixtures. Over the past several years many advances in instrumentation have been made leading to higher efficiency and better applicability of HPLC, but there always has been room for improvement. The variables most directly affecting the capabilities of HPLC for the separation of chemical mixtures are solvent type, solvent strength, flow rate, and column type. Though accurate models for the uncontrolled dynamics of solutes have been developed over the past forty years, no apparent attempt has been made to generalize them to controlled dynamics. A more comprehensive and unified model for the solvent–solute dynamics and control is developed here; it is apparent that the methods presented in this paper for liquid chromatography will find important applications also in thin layer chromatography, gas chromatography, ion exchange chromatography, electrophoresis, *et c.* Figure 1 depicts the various classes of chromatography. Column liquid chromatography is among the most popular, primarily in the form of Reversed Phase Liquid Chromatography (RPLC), which also presents perhaps the most difficulties theoretically and experimentally.

In HPLC, a cylindrical container typically of steel is filled with a substrate, for example porous silica particles or gel (see Figure 2). The substrate is then saturated with a solvent such as water, alcohols, hydrocarbons, *et c.* and a pressure gradient is applied across the ends of the column to establish a flow of solvent. At some time a (possibly unknown) mixture of chemicals dissolved in the chosen solvent is introduced to the "top" (the end at higher pressure) of the column, and these solutes subsequently flow down the column. The solutes may interact with

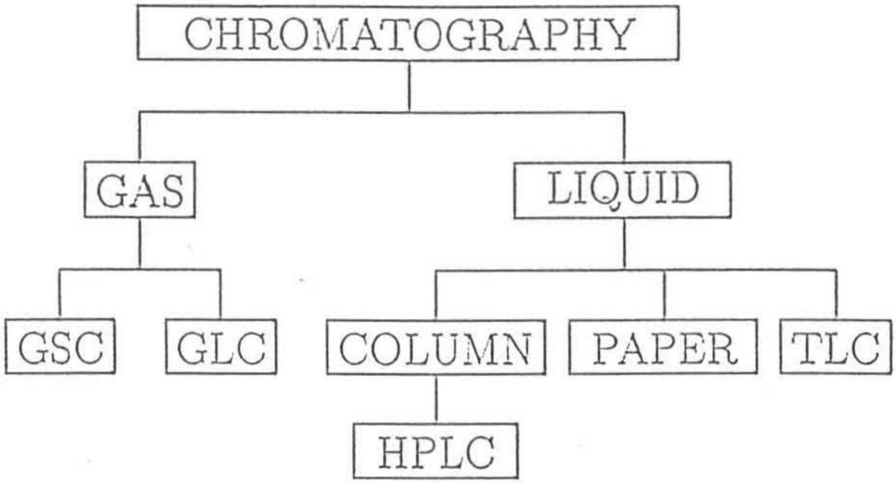

Figure 1: General Types of Chromatography.

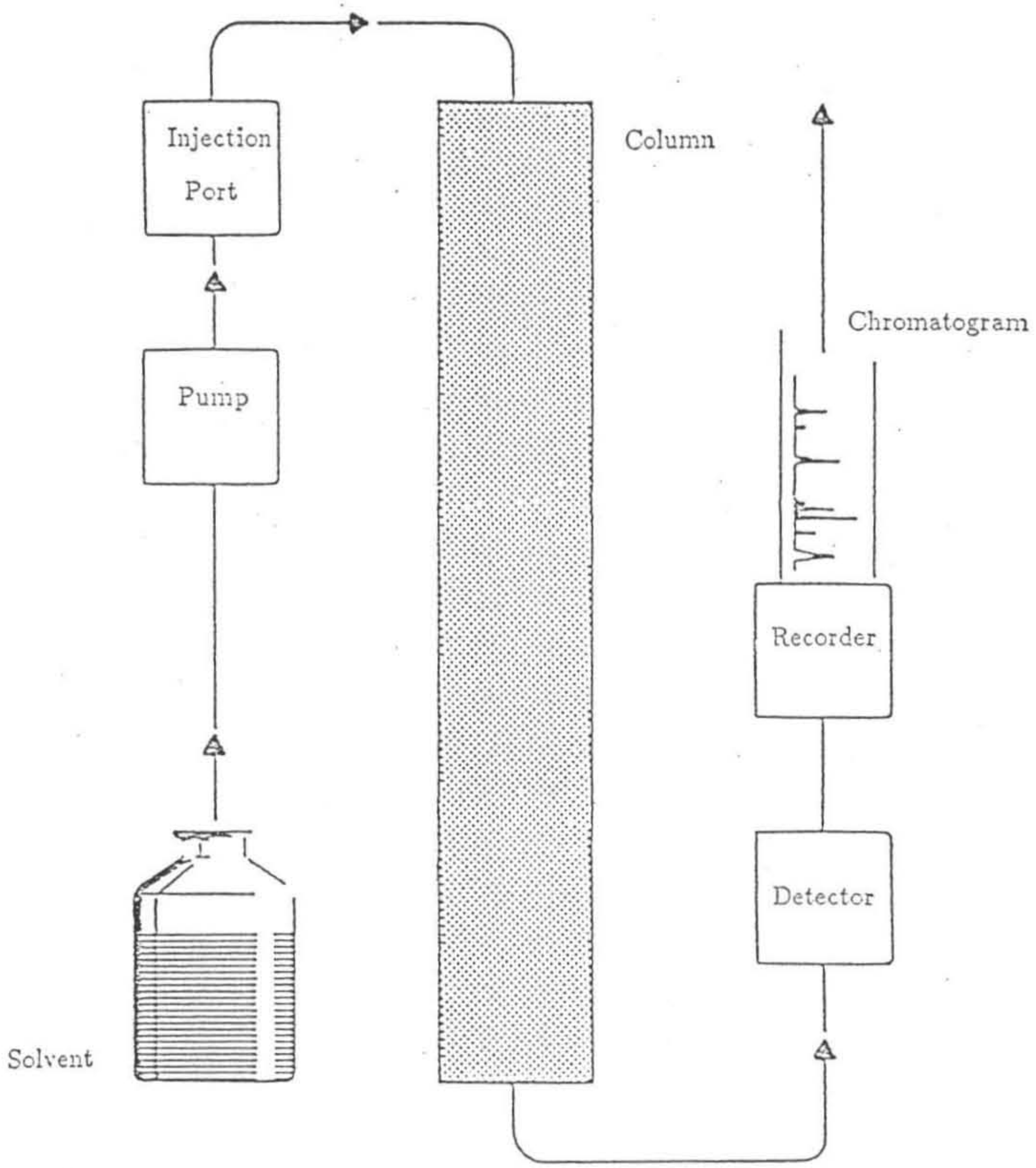

Figure 2: Typical experimental setup for chromatography.

the substrate, typically with different equilibrium reaction coefficients. This results in differing effective speeds down the column for each solute in the mixture, and hence the solutes gradually separate spatially from one another. Usually at the bottom of the column a detector of some sort (*e.g.*, using light absorbance at a single wavelength or over a range of wavelengths) registers the concentrations of solutes as they elute. Hopefully the chromatographic system is chosen such that all the solutes are resolved when they arrive at the bottom of the column; if not, the system should be changed in some manner. The more solutes there are in the mixture, the more difficult it is to *guess* how to change the system to improve performance. Figure 3 depicts an example of a complex mixture run through a column, with many solutes still confounded despite the long analysis time.

In HPLC the most important mechanisms acting inside the column to effect separation of solutes are as follows. The solute travels in the flow around particles (*i.e.*, the *mobile phase*). Near the surface of each particle there is a boundary layer in which the flow speed is sharply reduced, to zero at the particle surface. Thus there is mass transfer of the solute through each particle's fluid film. The surface of the particle is usually porous (see Figure 4) and the solute molecules diffuse into the pores, possibly adsorbing to the solid surface of the substrate. The molecule is said to be in the *stationary phase* when it enters the particles' boundary layer. The solvent may then displace the adsorbed molecule, which may in turn eventually diffuse out of the stationary phase back into the mobile phase. It is often the case that not all of these mechanisms need to be included in a model to accurately describe the system. That is, it may be that there are clearly rate limiting steps — those steps which are the slowest and thus limit the rate of the whole process. The substrate is not always a collection of porous particles, but sometimes a matrix of nonporous particles. In this case, we would delete the above steps involving

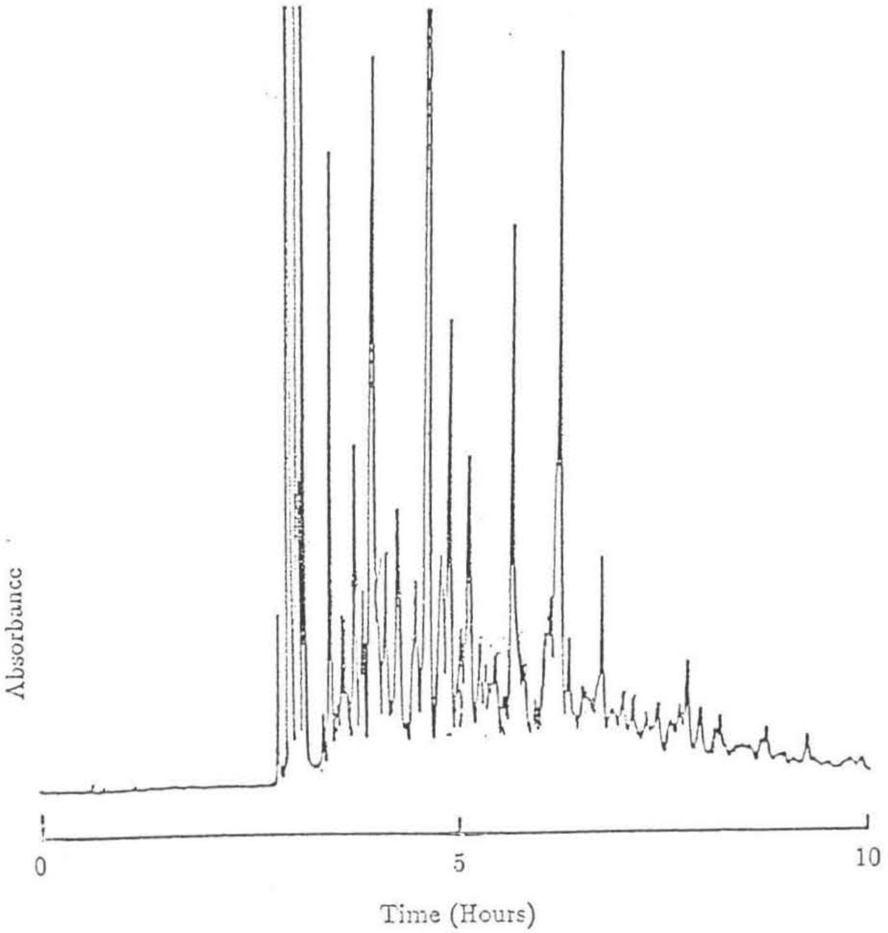

Figure 3: Typical example of a complex chromatogram, with many confounded components, even for a run time of several hours. Adapted from Snyder, Glajch, and Kirkland [ ].

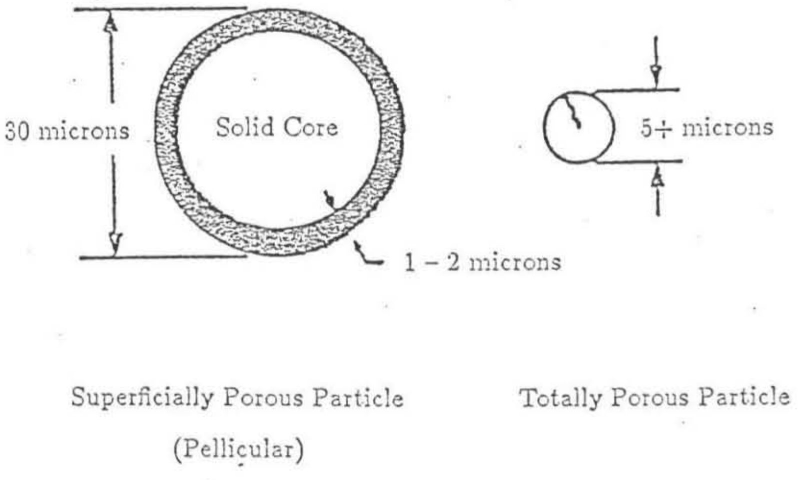

Figure 4: Typical Column Packing Supports.

diffusion into and out of particle pores.

The dynamical equations of mixed solvent systems flowing through a porous medium are found in chapter 1. The solvent equations are in part adapted from equations originating from the study of ground water flow; changes were made due to the markedly variable viscosity and density of many solvent systems utilized in chromatography. From the solvent equations comes the local velocity at which the mobile phase (unadsorbed solvent and solute molecules) travels. The calculated local solvent concentration controls solute adsorption, diffusivity, and dispersion in a specified manner. The solvent and solute dynamical equations are a system of fairly complicated second order nonlinear partial differential equations; the existence and uniqueness of solutions to these equations is shown in chapter 2 by means of "energy methods."

Chapters 3 and 4 briefly cover the simpler uncontrolled solute dynamical models and their solutions that have appeared in the literature.

Chapters 5 and 6 cover the basics of a theory of solvent modulation of solute adsorption, which is found to be quite accurate against experiment. The theory includes the effect of an inhomogeneous adsorbent surface – resulting in what has been called *solvent localization* in the experimental literature – and also provides a means of treating normal phase, reversed phase, ion exchange, and ion pair liquid chromatography in a unified mathematical framework, under the name *catalyzed adsorption*.

Due to the nature of the nonlinear solvent equation, a solvent gradient will steepen if the gradient is increasing in time, and will flatten if the gradient is decreasing in time. If the steepening is marked, it is (experimentally) known as *solvent demixing*. An increasing gradient that flows in a long enough chromatography column will form a "shock," or jump, in solvent concentration. Such solvent jumps are not desireable in chromatography, because they cause impurities in the column to be released as the jump travels down the column, producing spurious "sample" concentration peaks. When solvent jumps are disallowed, such impurities are released slowly and are typically lost in detector baseline "noise." One can find a mathematical constraint on the input solvent profile so as to disallow shock formation within the column (chapter 7).

The use of a control theory of chromatography is introduced and briefly discussed in chapter 7, for a simplified system.

In their partial differential equation form, the solute equations are too complicated to be solved practically for complex solute mixtures. Therefore these equations must be simplified as much as possible without losing relevant information. There are two mathematical methods utilized here, that together go far in simplifying the solute partial differential equations, covered in chapters 8 and 9. One method is to use moments, particularly the location (mean) of a sharp solute pulse, and its width (variance). The other method utilized is perturbation theory, based on a small *packing number* $d_p/L \ll 1$, where d_p is the average substrate particle diameter, and L is the column length. Typically in HPLC, $d_p/L \approx 10^{-4}$. It is shown that, after undimensionalizing the dynamical equations, the nondimensional parameters appearing in the equations are

$$\begin{aligned}
\epsilon_p &== \frac{d_p^2 v}{4D_i L} = \frac{1}{4}\varepsilon Pe \\
\epsilon_k &= \frac{v}{Lk_{for}} = \frac{\varepsilon}{St_k} \\
\delta\epsilon_p &= \frac{\varepsilon}{2St_f} \\
\epsilon_e &= \frac{D_e L}{V\vartheta} = \frac{\varepsilon}{\vartheta Pe_p},
\end{aligned}$$

where Pe is the Peclet number, Sh is the Sherwood number, St_k is the kinetics Stanton number, St_f is the fluid film mass transfer Stanton number, Pe_p is the packing Peclet number, or Bodenstein number, and we call ε the packing number. We see that the packing number occurs in each of the nondimensional numbers, thus restricting the validity of the perturbation analysis to values

$$
\begin{aligned}
Pe &\ll \frac{4}{\varepsilon} \\
St_k &\gg \varepsilon \\
St_f &\gg \frac{\varepsilon}{2} \\
Pe_p &\gg \frac{\varepsilon}{\vartheta}.
\end{aligned}
$$

The perturbation and moment techniques applied to the solute partial differential equations give rise to two first order ordinary differential equations for each solute, one for the pulse location, and one for the pulse width. For the case of a constant control (constant solvent conditions) the *HETP - Height Equivalent to a Theoretical Plate* is calculated. The HETP is a function that has been used classically to characterize the "efficiency" of a chromatographic system. In chapter 9 the HETP is calculated for a model system for a large range of Peclet numbers, for different constant solvent concentrations, and for different solutes. It is found that the HETP varies widely for different constant solvent concentrations and between different solutes, indicating most importantly that for complex multicomponent chromatography systems, computer control with comprehensive mathematical models are imperative, and that it is likely that the control theory developed in this paper will result in improved separations of complex solute mixtures.

CHAPTER 1

Hydraulic Properties of Porous Media and Rheology of Mixed Solvents

Introduction: In liquid chromatography, changing the relative concentrations of solvents is the most effective way to control the system, and so it is imperative to understand the flow characteristics of mixed solvents through chromatograph columns. In this chapter we develop a theory for such flows, based in part on the extant theory of the flow of groundwater through sandy soil [5,6]. The specific mathematical goal here is to find the formula for the local solvent velocity and specifically how this velocity depends on the local and transcolumn solvent densities and viscosities. Then, given empirical formulas relating mixed solvent density and viscosity to relative constituent solvent concentration, one obtains the dynamical equation for the mixed solvent.

With the above goal in mind, we proceed to develop the necessary concepts, find the equation for the piezometric head, give a simple example relevant to HPLC, and finally develop the required formula for the local velocity of the solvent mixture in the general case.

Porosity: The porosity of a porous substrate is a measurement of the extent to which it contains interstices. It can be expressed quantitatively as the ratio of the volume of interstices to the total volume (within a control volume):

$$\vartheta = \frac{v_i}{V} = \frac{v_w}{V} = \frac{V - v_m}{V} = 1 - \frac{v_m}{V} \qquad \text{[dimensionless]}$$

where

$\vartheta =$ porosity

$v_i =$ volume of interstices

$V =$ total volume

$v_w =$ volume of fluid in saturated sample

$v_m =$ volume of substrate particles.

An alternate expression is

$$\vartheta = \frac{\rho_m - \rho_d}{\rho_m} = 1 - \frac{\rho_d}{\rho_m} \qquad \text{[dimensionless]}$$

where

$\rho_m =$ mean density of particles

$\rho_d =$ density of dry substrate particles.

Considering spherical particles, the arrangement of particles can greatly affect porosity – Slichter (see [11]) shows that the most compact – rhombohedral – arrangement of particles gives a porosity of about .26, whereas for the least compact, cubical arrangement the porosity is about .48. The shape of the particles may increase or decrease the porosity, which is a local variable except for homogeneously graded, well-packed particles (as is usually the case in chromatography). The greater the range of sizes of particle sizes in the porous medium, generally the greater the porosity due to resulting non-compactness of the largest particles.

Void Ratio : The void ratio of a porous substrate is the ratio of the volume of its interstices to the volume of the particles:

$$\frac{v_i}{v_m} = \frac{v_w}{v_m} = \frac{\vartheta}{1 - \vartheta} \qquad \text{[dimensionless]}$$

Permeability : The permeability of a porous substrate measures its ability to transmit fluid under a potential gradient (see below); it is commonly found that permeability is proportional to the square of the mean particle diameter:

$$k_p = Cd^2 \qquad [L^2]$$

where

$k_p =$ intrinsic permeability

$C =$ dimensionless constant depending on porosity

$d =$ mean particle diameter.

Darcy's Law : Darcy [5,6] found empirically that the rate of viscous laminar flow of water through a porous medium (sand) is proportional to the hydraulic gradient (see Figure 5):

$$q = \frac{Q}{A} = -K\frac{d\phi}{dx} \qquad [\mathrm{L/T}]$$

where Q is the volume flux, A is the cross–sectional area of the medium, x is the distance down the column, and the constant of proportionality K is the *hydraulic conductivity*. Also, the form of the potential is $\phi = z + p/\gamma$ where p is pressure, and γ is the specific weight of the fluid, so

$$q = -K\frac{d\phi}{dx}$$

holds also for an inclined porous medium. p/γ is called the *pressure head* for an incompressible fluid. To understand this more fully, consider Figure 5. A test section of a porous medium is saturated with fluid which fills tanks at either end of the test section. An arbitrary reference level is chosen, and the heights z_i of the ends of the test section are measured. The test section is tilted, is of length L, cross section A, and has volume flux Q through it. There is a pressure head p_i/γ in the tank at either end of the test section, giving a potential

$$\phi_i = z_i + \frac{p_i}{\gamma}$$

at either end. In this experiment we maintain constant levels of fluid in each end tank, measuring inflow and outflow and hence Q. It is found that

$$Q = KA\frac{\phi_1 - \phi_2}{L}.$$

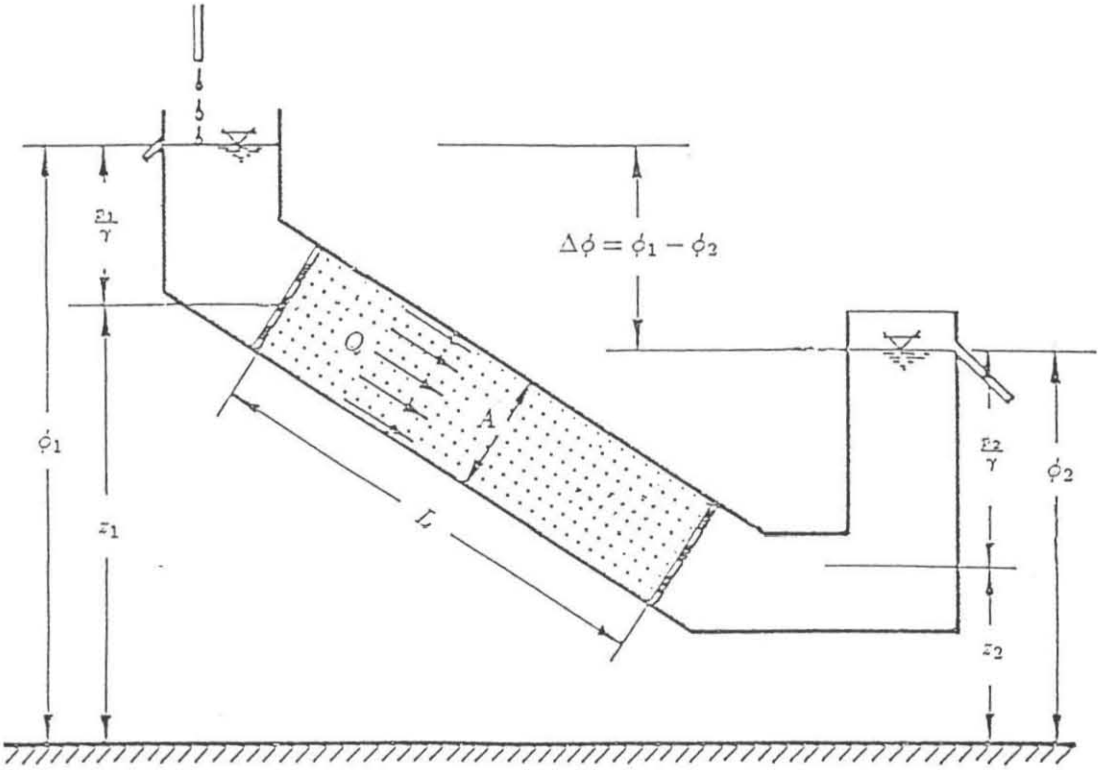

Figure 5: Flow through an inclined chromatograph column filled with a homogeneous porous medium. Adapted from Bear [ ].

Extension of Darcy's Law : When $K = K(x)$, the porous medium is assumed isotropic, but

$$q = -\frac{\partial}{\partial x}(K\phi).$$

As q increases the relation between the specific discharge and the hydraulic gradient deviates from Darcy's proportional law. It is found that Darcy's law is valid for $Re = qd/\nu < 10$, where Re is the Reynold's number (see Figure [6]). Above $Re \approx 10$ the interstices develop turbulent flow.

Hydraulic Conductivity : The hydraulic conductivity is defined as

$$K = \frac{kg}{\nu} = \frac{kg\rho}{\eta} \qquad [L/T]$$

where k $[L^2]$ is the permeability of the porous substrate, ν $[L^2/T]$ is the kinematic viscosity, g $[L/T^2]$ is gravitational acceleration, η $[M/LT]$ is the dynamic viscosity, and ρ $[M/L^3]$ is fluid density. For a compressible fluid in isothermal conditions, $\gamma = \gamma(p)$, so the pressure head is

$$\int_{p_0}^{p} \frac{dp}{\gamma(p)}$$

and hence the *piezometric head* (or *Hubbert's potential*) is

$$\phi^* = z + \int_{p_0}^{p} \frac{dp}{\gamma(p)}.$$

The length z represents elevation head (potential energy per unit weight of fluid.) The sum of pressure head and elevation head is the piezometric head ϕ^*.

Fluid Velocity : For a fluid which does not react with the substrate, the velocity depends on the porosity, hydraulic conductivity, and the hydraulic gradient:

$$v = -\frac{1}{\vartheta}K\frac{d\phi^*}{dx},$$

where v is the velocity averaged over the cross section perpendicular to the direction of flow. This formula is useful if the porous medium is quite homogeneous, as is the

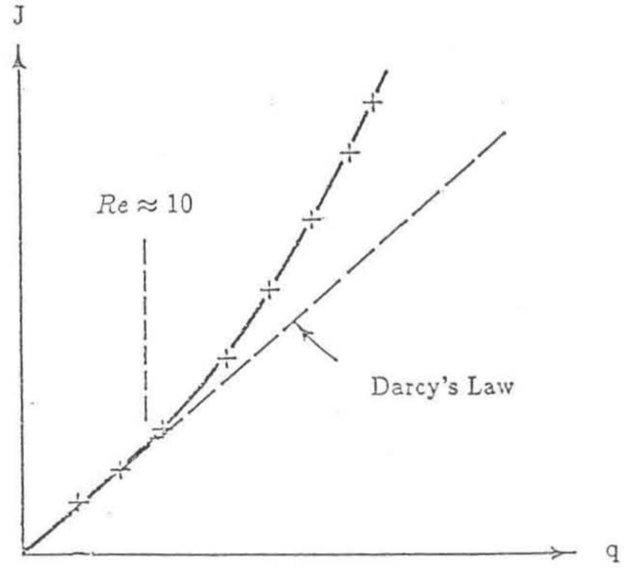

Figure 6: Deviation from Darcy's Law at high flow velocities. Adapted from Bear [ ].

case in chromatography. Since $K = k\rho g/\eta$, velocity is clearly inversely proportional to the viscosity η of the fluid.

Solvent Mixture Viscosity: In liquid chromatography, the most effective control variable is relative solvent composition in systems of two or more solvents. As mentioned before, RPLC is usually done with a water–organic solvent mixture. Such a mixture has long been known to have a rather large variation of viscosity over the range of possible relative concentrations. The viscosity may vary about a factor of three for water and methanol, ethanol, tetrahydrofuran, acetonitrile, or n-propanol (*e.g.*, Melander and Horvath, [34]), as shown in Figure 7.

From the figure, least square fits were calculated to estimate the mixed solvent viscosities for methanol–water and acetonitrile–water as

$$\eta_{MeOH}(s) = .01954s^3 - .03492s^2 + .00879s + .01017,$$

$$\eta_{ACN}(s) = .02525s^3 - .07603s^2 + .04676s + .09711,$$

(in Poise ($gm/cm\,sec$), at $25^o\,C$) where s is the percent volume organic solvent. The density variations at $25^o\,C$, in gm/cm^3, are

$$\rho_{MeOH}(s) = -.08287s^2 - .12104s + .99652,$$

$$\rho_{ACN}(s) = -.212s + .999,$$

where least squares fitting was done with data from Perry and Green [38]. Later the local velocities and diffusivities will be calculated using the above functions for a hypothetical variation of solvent composition within a chromatography column.

Diffusivity and Dispersion : The variability of solute diffusion coefficients with solvent mixture composition can be adequately predicted (Perkins and Geankopolis [37]) by a modified Wilke–Chang equation

$$D_j = 7.4 \times 10^{-8} \frac{(\phi M)^{\frac{1}{2}} T}{\eta_m V_b^{0.6}}$$

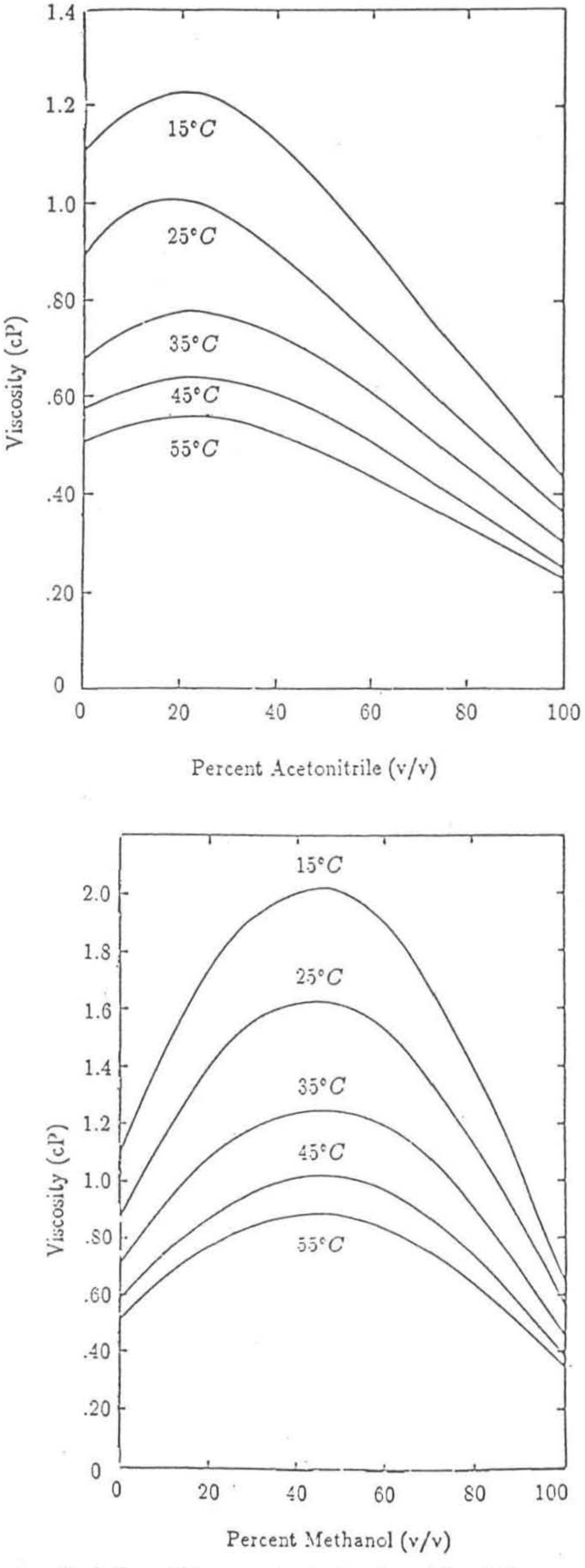

Figure 7: Variation of binary solvent viscosity with relative composition and temperature. Adapted from Melander and Horvath [ ].

where T^o (K) is temperature, η_m (cP) is the liquid mixture dynamic viscosity, V_b $(\frac{cm^3}{g \cdot mole})$ is the molal volume at normal boiling temperature, D_j $(\frac{cm^2}{sec})$ is the solute diffusion coefficient in the bulk liquid mixture, and

$$\phi M = \sum_{i \neq j} x_i \phi_i M_i,$$

where ϕ_j is the "association constant" for pure liquid i, x_i is the mole fraction of liquid i, and M_i is the molecular weight of liquid i. The molal volume at normal boiling temperature can be fairly accurately estimated (if not known empirically) by either the method of LeBas or the method of Schroeder [37].

Using the above relation for the bulk liquid diffusion coefficients, the coefficients for ethanol, hexanol, octyldecanol, and tritium tracer in methanol–water binary solvent are (at 25° C, η_m in centipoise)

$$\begin{aligned}
D_E &\approx 7.4 \times 10^{-8} \frac{(46.8 + 14s)^{\frac{1}{2}}}{\eta_m(s)11.57} \times 298 \\
D_H &\approx 7.4 \times 10^{-8} \frac{(46.8 + 14s)^{\frac{1}{2}}}{\eta_m(s)20.05} \times 298 \\
D_{OD} &\approx 7.4 \times 10^{-8} \frac{(46.8 + 14s)^{\frac{1}{2}}}{\eta_m(s)37.19} \times 298 \\
D_t &\approx 7.4 \times 10^{-8} \frac{(46.8 + 14s)^{\frac{1}{2}}}{\eta_m(s)7} \times 298,
\end{aligned}$$

shown in Figure 8.

Using the data of Greenkorn [17] (see Figure 9) one may estimate the dispersion coefficient D_e over a very large range of linear velocities for different solvent compositions. From Figure 9, we have approximately that

$$\frac{D_e}{D} \approx \alpha + \kappa Pe,$$

with $\kappa \approx 1.163$ and $\alpha \approx .7$, where D is the solute diffusion coefficient in the bulk solvent. Thus the packing Peclet number (or Bodenstein number) can be

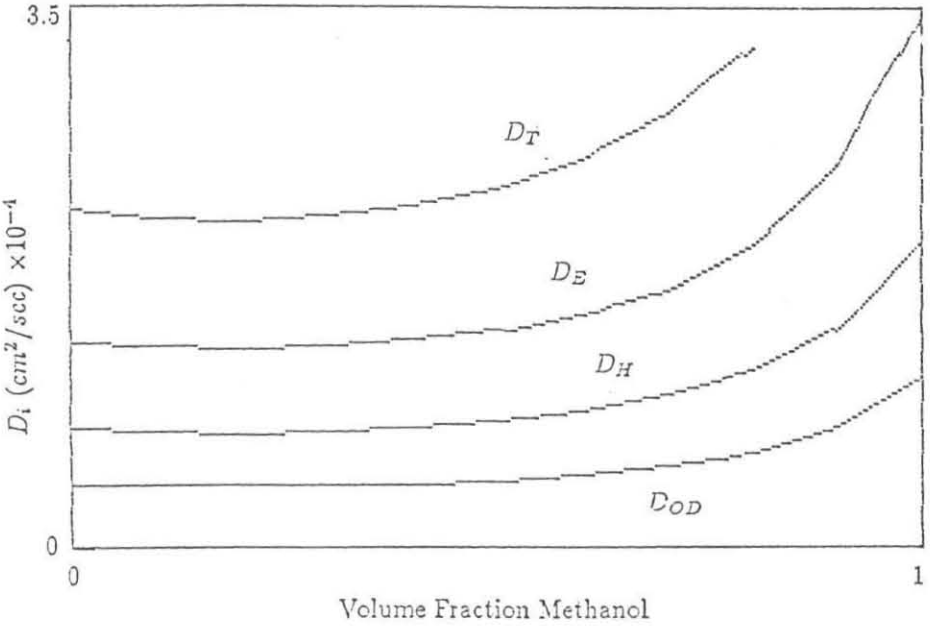

Figure 8: Theoretical bulk diffusion coefficients for trace octyldecanol, hexanol, ethanol, and tritium, at various volume fractions of methanol in water. At 25° C.

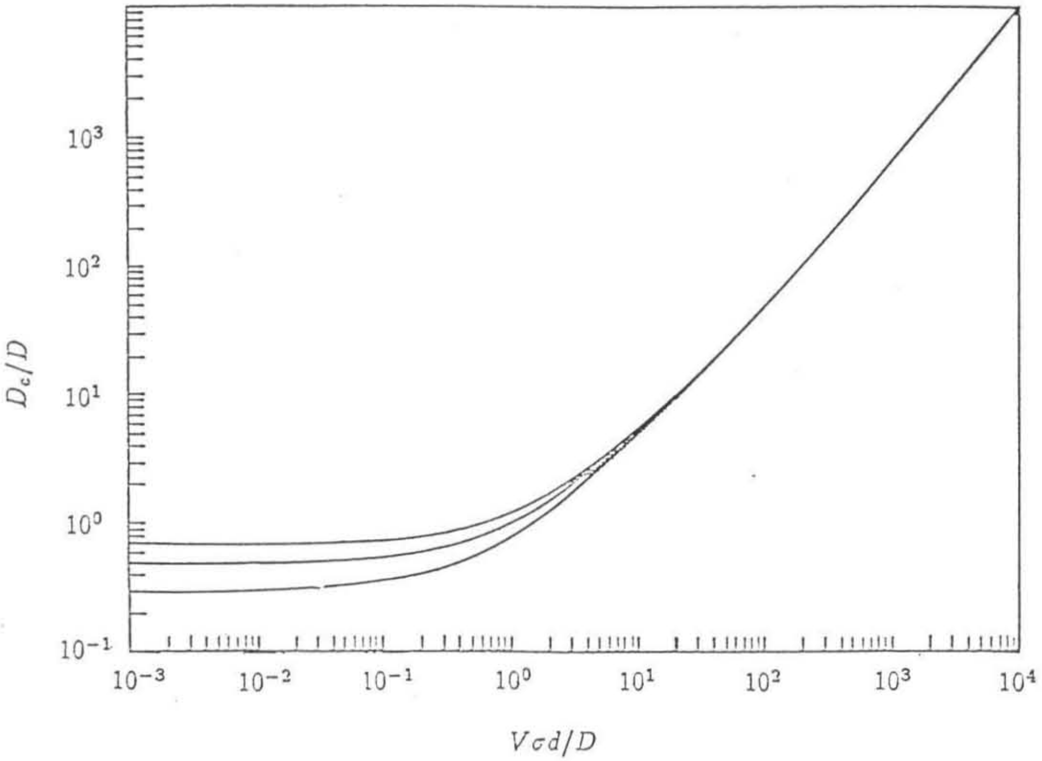

Figure 9: Dispersion correlation with velocity and diffusivity for typical porous media. Adapted from Greenkorn [ ].

approximated as

$$Pe_p = \frac{vd_p}{D_e} \approx (1.163 + .7Pe^{-1})^{-1}.$$

Solvent Continuity Equation: Here we consider the density of the entire, mixed solvent. Thus we need not worry about adsorption source terms in the equation, since they cancel. For a control volume we obtain, assuming $\vartheta = \vartheta(x,t)$, $\rho = \rho(x,t)$, $q = q(x,t)$, and $p = p(x,t)$,

$$\frac{\partial}{\partial t}(\rho\vartheta) = -\frac{\partial}{\partial x}(\rho q).$$

Thus if $\rho = \rho(p)$ only, then

$$\frac{\partial}{\partial t}(\rho\vartheta) = \rho\frac{\partial\vartheta}{\partial t} + \vartheta\frac{\partial\rho}{\partial t} = (\rho\frac{\partial\vartheta}{\partial p} + \vartheta\frac{\partial\rho}{\partial p})\frac{\partial p}{\partial t}.$$

The solvent in the column is slightly compressible; define a coefficient of compressibility β by

$$\beta = \frac{1}{\rho}\frac{\partial\rho}{\partial p}.$$

The substrate can be considered elastic — it can undergo deformation and thus change the porosity ϑ. This does not necessarily imply that the particles themselves are deformed, though deformation can be dramatic, as for Sephadex packings with high "G–numbers," with Janson and Hedman [24] finding exponential variation of permeability with pressure drop. The changes in porosity due to pressure changes are characterized by the coefficient

$$\alpha = \frac{1}{1-\vartheta}\frac{\partial\vartheta}{\partial p}.$$

From the above relations, we have

$$\frac{\partial}{\partial t}(\rho\vartheta) = (\rho\frac{\partial\vartheta}{\partial p} + \vartheta\frac{\partial\rho}{\partial p})\frac{\partial p}{\partial t} = \rho[\alpha(1-\vartheta) + \beta\vartheta]\frac{\partial p}{\partial t}.$$

Thus, using the relation between pressure and the Hubbert potential $\phi^* = z + p/\gamma$,

$$\frac{\partial \phi^*}{\partial t} = \frac{1}{\rho g}\frac{\partial p}{\partial t},$$

so that

$$\frac{\partial}{\partial t}(\rho \vartheta) = g\rho^2 \left[\alpha(1-\vartheta) + \beta\vartheta\right] \frac{\partial \phi^*}{\partial t}.$$

Set

$$S_0^* = g\rho^2 \left[\alpha(1-\vartheta) + \beta\vartheta\right],$$

which gives the mass of solvent added to or removed from storage in a unit volume of the porous medium per unit change of the potential ϕ^*. Then the continuity equation can be written

$$S_0^* \frac{\partial \phi^*}{\partial t} = -\frac{\partial}{\partial x}(\rho q).$$

At this point, typical assumptions made (Bear, [5]) for analysis of groundwater flow are: 1) Darcy's Law is valid; 2) S_0^*, K are independent of variability of ϑ and ρ (so $K = k_p \rho g/\mu \approx k_p \rho_0 g/\mu$); and 3) $q\frac{\partial \rho}{\partial x} \ll \vartheta \frac{\partial \rho}{\partial t}$. Then we have that

$$S_0 \frac{\partial \phi^*}{\partial t} = -\frac{\partial q}{\partial x}$$

where $\rho S_0 = S_0^*$. The second assumption would seem generally valid for NPLC solvent systems, but clearly not so for RPLC solvent systems. RPLC will be discussed shortly; first we consider a simpler problem of pressure variation within a chromatography column.

Using the above assumptions, using Darcy's law, we obtain

$$S_0 \frac{\partial \phi^*}{\partial t} = \frac{\partial}{\partial x}\left(K \frac{\partial \phi^*}{\partial x}\right)$$

for an isotropic porous medium. If the porous medium is also homogeneous, then K is constant:

$$S_0 \frac{\partial \phi^*}{\partial t} = K \frac{\partial^2 \phi^*}{\partial x^2}.$$

A typical chromatograph column for HPLC operates at high back pressure and has a very nearly homogeneous, isotropic porous substrate, so for an NPLC solvent Hubbert's potential will be governed by the equation

$$\frac{\partial \phi^*}{\partial t} = \frac{K}{S_0}\frac{\partial^2 \phi^*}{\partial x^2},$$

with boundary conditions

$$\phi^*(0,t) = f(t), \qquad \phi^*(L,t) = g(t),$$

where $f(t)$ and $g(t)$ are specified by specifying end pressures.

Example for HPLC : It is not uncommon for HPLC pumps to be capable of back pressures of about 10 to 6000 *psia* (or: 1 to 400 *atm*). Often it is desired to vary the type of solvent in time. This involves a variation in the viscosity of the solvent mixture, and hence by Darcy's Law either the pressure or the velocity must change; if one wishes to keep the velocity constant, the back pressure must be slowly changed.

Let's consider a situation at constant solvent composition in which we specify an acceptable initial pressure gradient and suddenly change the column end pressure. This situation is modelled by

$$\begin{aligned}
\frac{\partial \phi^*}{\partial t} &= \frac{K}{S_0}\frac{\partial^2 \phi^*}{\partial x^2} \qquad \text{for } 0 \le x \le L,\\
\phi^*(0,t) &= \phi_1 \quad \textit{constant}\\
\phi^*(L,t) &= \phi_2 \quad \textit{constant}\\
\phi^*(x,0) &= f(x) \quad \textit{given, such that}\\
&\phi_1 \neq f(0).
\end{aligned}$$

This type of problem is best solved by setting

$$\phi^* = u + w,$$

where

$$\frac{d^2u}{dx^2} = 0$$

$$u(0,t) = \phi_1$$

$$u(L,t) = \phi_2,$$

$$\frac{\partial w}{\partial t} = \frac{K}{S_0}\frac{\partial^2 w}{\partial x^2}$$

$$w(0,t) = 0$$

$$w(L,t) = 0$$

$$w(x,0) = f(x) - u(x),$$

Clearly then

$$u(x) = \phi_1 + (\phi_2 - \phi_1)\frac{x}{L}$$

$$w(x,t) = \sum_{n=1}^{\infty} a_n \sin(\frac{n\pi x}{L})\exp(-\frac{Kn^2\pi^2}{S_0L^2}t)$$

with

$$a_n = \frac{2}{L}\int_0^L [f(\xi) - \phi_1 - (\phi_2 - \phi_1)\frac{\xi}{L}]\sin(\frac{n\pi\xi}{L})d\xi$$

so that

$$\begin{aligned}\phi^* = \phi_1 + (\phi_2 - \phi_1)\frac{x}{L} + \frac{2}{L}\sum_{n=1}^{\infty}\frac{\phi_2(-1)^n - \phi_1}{n}\sin(\frac{n\pi x}{L})\exp(-\frac{Kn^2\pi^2}{S_0L^2}t)\\ + \sum_{n=1}^{\infty}\sin(\frac{n\pi x}{L})\exp(-\frac{Kn^2\pi^2}{S_0L^2}t)\int_0^L f(\xi)\sin(\frac{n\pi\xi}{L})d\xi\end{aligned}$$

If

$$f(x) = \Phi_1 + (\Phi_2 - \Phi_1)\frac{x}{L},$$

then

$$\int_0^L f(\xi)\sin(\frac{n\pi\xi}{L})d\xi = -\frac{L}{\pi}\sum_{n=1}^{\infty}\frac{\Phi_2(-1)^n - \Phi_1}{n}\sin(\frac{n\pi x}{L})\exp(-\frac{Kn^2\pi^2}{S_0L^2}t).$$

Since these sums are absolutely convergent we may combine the two as

$$\begin{aligned}\phi^* =& \phi_1 + (\phi_2 - \phi_1)\frac{x}{L}\\ &+ \frac{2}{\pi}\sum_{n=1}^{\infty}\frac{(\phi_2 - \Phi_2)(-1)^n - (\phi_1 - \Phi_1)}{n}\sin(\frac{n\pi x}{L})\exp(-\frac{Kn^2\pi^2}{S_0L^2}t),\end{aligned}$$

the sum of steady-state and transient parts. If only the back pressure (at $x = 0$) is changed, then $\phi_2 = \Phi_2$, and $\phi_1 \neq f(0)$. Then at around $x = 0$, $t = 0$ there is a boundary layer such that $| \partial\phi^* / \partial x | \gg 1$, as seen in Figure 10, implying that the instantaneous local average velocity is very large there, as is the pressure gradient. To avoid rearranging and possibly shattering the substrate particles due to the resulting large stresses over the length of a particle, (reaching critical values of α for the substrate) changes in prescribed pressure should be made smoothly and slowly.

Velocity Variations in RPLC Solvent Systems: The solvent is the carrier of the solutes in the mobile phase; as such, the solvent determines the limiting velocity of the mobile phase fluid through the column. Waves or local variations of solvent composition create corresponding changes in viscosity and density, though it is the overall solvent composition in the entire column that determines transcolumn pressure gradients and hence overall flow. This will be borne out by our next calculations. To find the dynamics of the solvent system we first need to consider the dynamics of the pressure gradient. In order to accomplish this, we need to consider S_0^* and K to be variable with ρ and η. In this case we use the equation

$$S_0^* \frac{\partial \phi^*}{\partial t} = -\frac{\partial}{\partial x}(\rho q),$$

with

$$S_0^* = \rho^2[\alpha(1-\vartheta) + \beta\vartheta], \qquad q = -K\frac{\partial \phi^*}{\partial x}, \qquad K = \frac{k\rho g}{\eta},$$

where $\beta = \frac{1}{\rho}\frac{\partial \rho}{\partial p}$ is the compressibility of the solvent and $\alpha = \frac{1}{1-\vartheta}\frac{\partial \vartheta}{\partial p}$ is the compressibility of the solid substrate. When gradients of binary solvent are used in the column, S_0^*, ρ, and η are dependent on the solvent concentration $s(x,t)$. This implies that in order to find the pressure gradient, the solvent concentration dynamics must be known, but to find the solvent dynamics, the pressure gradient has

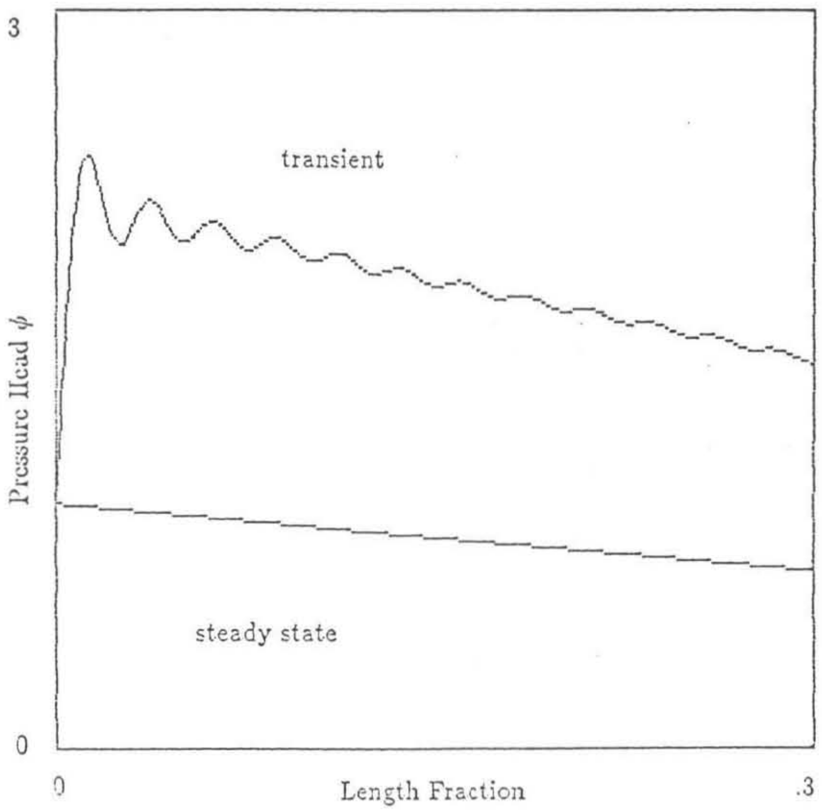

Figure 10: Effect of instantaneous change in end pressure head showing steep gradient near column end. (Eighty terms taken in summation – oscillations nonphysical.)

to be known. Thus the hydraulic and solvent dynamical equations must be solved simultaneously.

The dependences $\rho = \rho(s)$ and $\eta = \eta(s)$ should be found empirically, as well as dependencies on p and T, since there is no accurate means of estimating them. This is not an unreasonable task, given that there are only a few important solvent components typically used in RPLC and NPLC. We expect that the dependencies will be much less important in NPLC, as discussed earlier.

It should be noted also that pressure (essentially ϕ^*) dependencies of relevant parameters should be found, since pressure can vary a few hundred atmospheres down the column. Figure 11 depicts the variability of viscosity with pressure. We find that, for the solvents typically used in chromatography, viscosity can be considered constant with respect to pressure over typical column pressure gradients.

We consider density essentially constant with respect to pressure. The most dramatic variations of mixed solvent density and viscosity derive from changes in relative concentration of the solvent components.

The equation for the Hubbert potential for solvent gradient conditions in the case where the pressures are fixed at either end of the column can be calculated as follows. Assume that the solid substrate (*e.g.*, silica) compressibility α is essentially zero compared to solvent compressibility β. Then we have

$$\rho^2 \beta \vartheta \frac{\partial \phi^*}{\partial t} = \frac{\partial}{\partial x}\left(\frac{k\rho^2}{\eta}\frac{\partial \phi^*}{\partial x}\right)$$

with initial condition $(0 < x < L)$

$$\phi^*(x,0) = \phi_1 + (\phi_2 - \phi_1)\frac{x}{L}$$

with $\rho(s(x,0)) = constant$, $\beta(s(x,0)) = constant$, and $\eta(s(x,0)) = constant$ following from taking $s(x,0) = constant$. The boundary conditions are

$$\phi^*(0,t) = \phi_1 \quad \text{fixed}, \quad \phi^*(L,t) = \phi_2 \quad \text{fixed}.$$

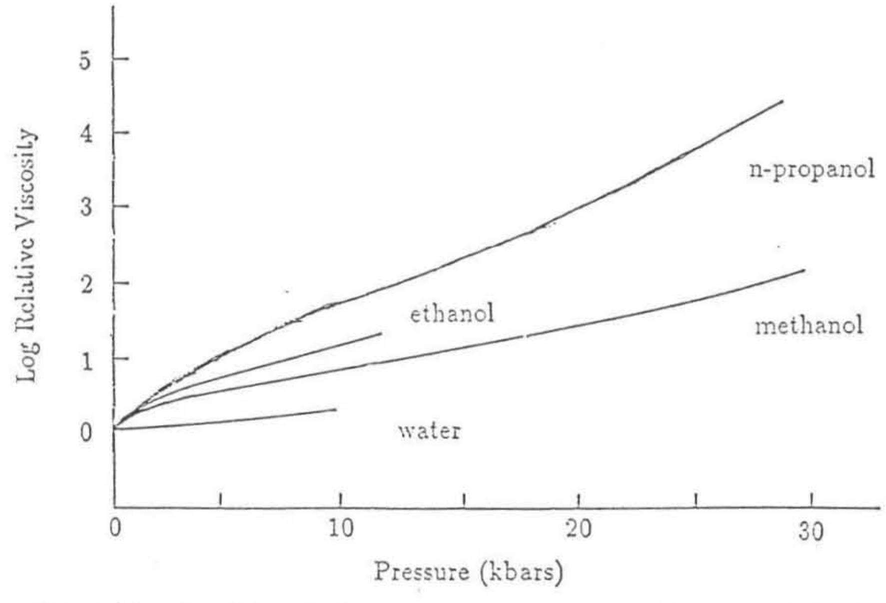

Figure 11: Viscosities of selected fluids as a function of pressure. Adapted from Bridgman [ ].

Since typical values (for the solvents of interest) of compressibility are less than $10^{-10}cgs$, volume fraction ϑ about 10^0, viscosity about $10^{-2}cgs$, and permeability about 10^{-5} to $10^{-6}cgs$, the coefficient of the time derivative can be seen to be a factor of about 10^{-6} smaller than the space derivative coefficient, so one may effectively consider the system to be always at steady state:

$$\frac{\partial}{\partial x}\left(\frac{k\rho^2}{\eta}\frac{\partial\phi^*}{\partial x}\right) = 0$$

so that

$$\frac{k\rho^2}{\eta}\frac{\partial\phi^*}{\partial x} = \bar{\alpha}_0 \qquad \text{constant.}$$

Thus the initial condition may be discarded since it will decay so fast onto the steady state solution. One may solve for ϕ^* now: we have

$$\frac{\partial\phi^*}{\partial x} = \frac{\bar{\alpha}_0\eta(s)}{k\rho^2(s)}.$$

Time enters in now only as a parameter. Thus one obtains

$$\phi^*(x,t) = \frac{\bar{\alpha}_0}{k}\int_0^x \frac{\eta(s)}{\rho^2(s)}\,dx + \phi_1;$$

but

$$\phi^*(L,t) = \frac{\bar{\alpha}_0}{k}\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx + \phi_1 = \phi_2,$$

implying that

$$\bar{\alpha}_0 = \frac{k(\phi_2-\phi_1)}{\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx}.$$

Therefore

$$\phi^*(x,t) = \frac{(\phi_2-\phi_1)}{\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx}\int_0^x \frac{\eta(s)}{\rho^2(s)}\,dx + \phi_1.$$

This calculation enters in the equation for solvent dynamics *via* the velocity, and hence $\frac{\partial\phi}{\partial x}^*$. Thus we use

$$\frac{\partial\phi^*}{\partial x} = \frac{\frac{1}{L}(\phi_2-\phi_1)\eta(s)}{\frac{\rho^2(s)}{L}\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx}.$$

The velocity of the mobile phase is thus

$$v = \frac{1}{\vartheta} q = \frac{k\rho g}{\vartheta\eta}\frac{\partial\phi^*}{\partial x} = \frac{kg(\phi_2 - \phi_1)/L}{\vartheta\rho(s)\frac{1}{L}\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx}.$$

Now this form of the linear velocity can be substituted in the solvent dynamical equation. The requirement of fixed end pressures is indeed physically reasonable.

Intracolumn Reynolds and Peclet Numbers: We found that the piezometric head in the case of an incompressible solvent varies as

$$\phi^*(x,t) = \frac{(\phi_2 - \phi_1)}{\int_0^L \frac{\eta(s)}{\rho^2(s)}\,dx}\int_0^x \frac{\eta(s)}{\rho^2(s)}\,dx + \phi_1.$$

Rewrite this in a normalized form (with $\xi = x/L$)

$$\hat{\phi}^*(x,t) = \frac{\phi^* - \phi_1}{\phi_2 - \phi_1} = \Big(\int_0^1 \frac{\eta(s)}{\rho^2(s)}\,d\xi\Big)^{-1}\int_0^\xi \frac{\eta(s)}{\rho^2(s)}\,d\xi.$$

The linear velocity within the column was found earlier; let

$$\hat{v} = \frac{v}{kg}\Big(\frac{\Delta\phi}{L}\Big)^{-1} = \Big(\rho\int_0^1 \frac{\eta}{\rho^2}\,d\xi\Big)^{-1}$$

the Reynold's number is

$$Re(x,t) = \frac{d_p v\rho}{\eta} = \frac{d_p kg}{\vartheta\eta}\frac{\phi_2 - \phi_1}{L\int_0^1 \frac{\eta}{\rho^2}\,d\xi},$$

and we consider the quantity

$$\hat{Re} = \frac{Re\,\vartheta}{d_p kg}\Big(\frac{\Delta\phi}{L}\Big)^{-1} = \Big(\eta\int_0^1 \frac{\eta}{\rho^2}\,d\xi\Big)^{-1}$$

Finally, we consider a Péclet number $\hat{Pe} = Pe/d_p$. To get a feeling for what the range of these variables might be, consider a methanol–water solvent system with hypothetical linear solvent composition variation within a column. We choose three hypothetical intracolumn composition variations, all increasing in methanol concentration from column bottom to top:

$$s_1(\xi) = 1 - \xi$$

$$s_2(\xi) = .37 - .37\xi$$

$$s_3(\xi) = 1 - .63\xi$$

Note that s_1 is associated with an increase, then a decrease in viscosity, s_2 is associated with an decrease in viscosity, and s_3 is associated with a increase in viscosity. The corresponding variations in ρ, η, v, D, $\hat{Re}$, and $\hat{Pe}$ are plotted in Figures 12, 13, 14, 15, 16, and 17. One may see that the variations in all of these variables are substantial. Of course, to get the *solvent dynamics* one must combine the velocity calculation obtained in the previous section with the solvent continuity equation. The solvent continuity equation, along with the solute equations, will be discussed in more detail in chapters 2, 3, 4, 8, and 9.

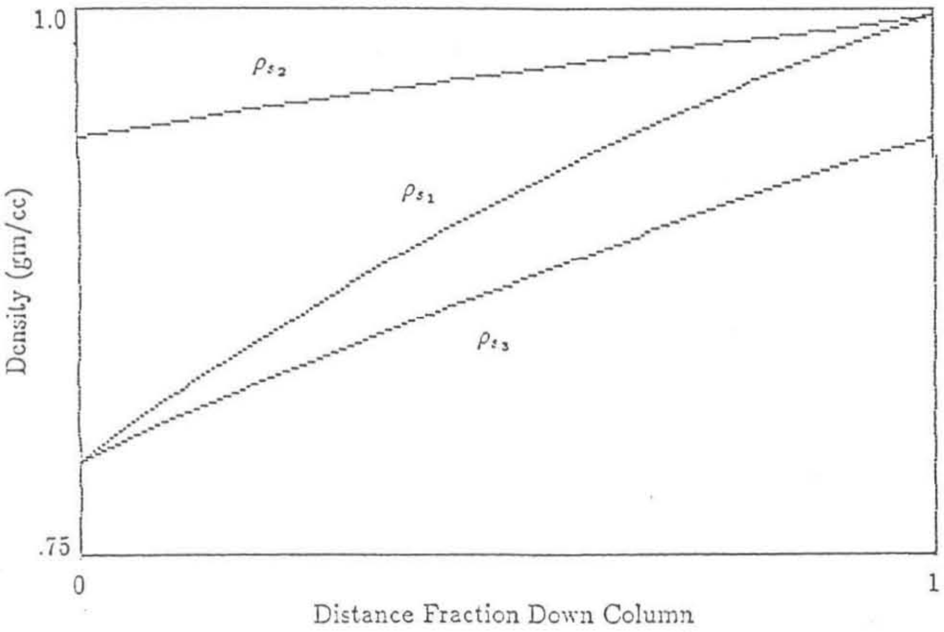

Figure 12: Intracolumn binary solvent density variation for three hypothetical solvent concentration distributions (see text). At 25° C.

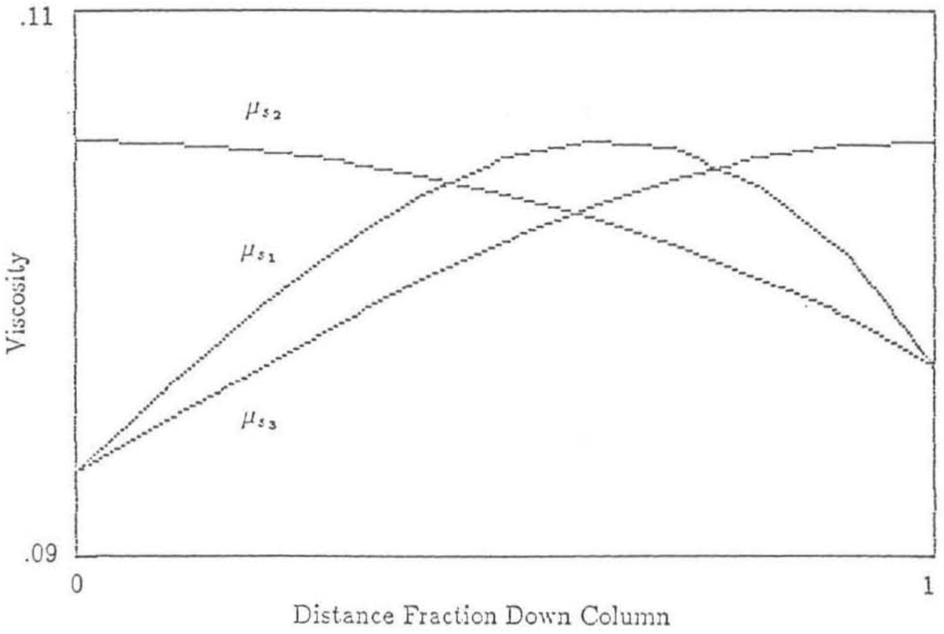

Figure 13: Intracolumn binary solvent kinematic viscosity variation for three hypothetical solvent concentration distributions (see text). At 25° C.

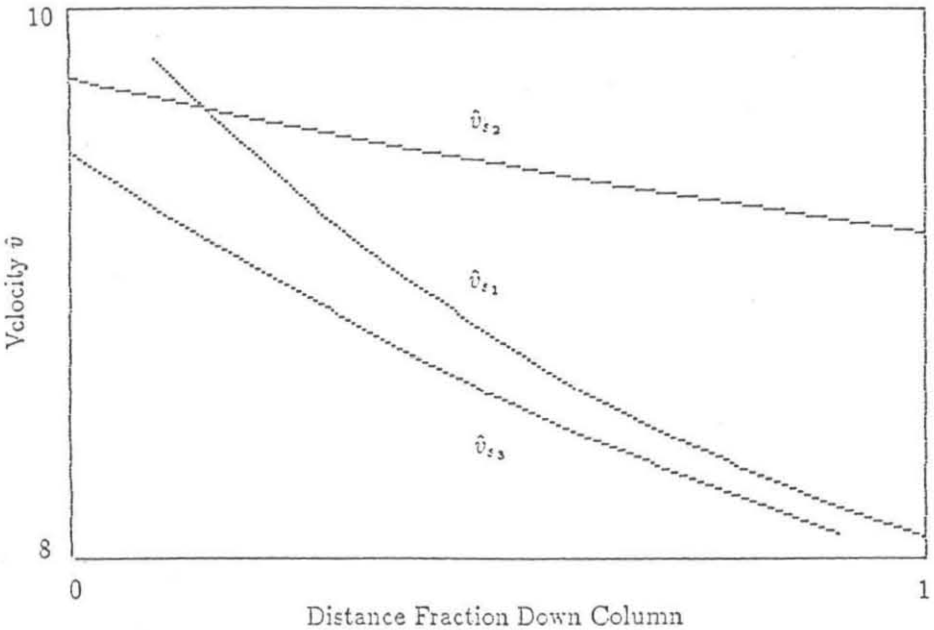

Figure 14: Intracolumn binary solvent velocity variation for three hypothetical solvent concentration distributions (see text). At 25° C.

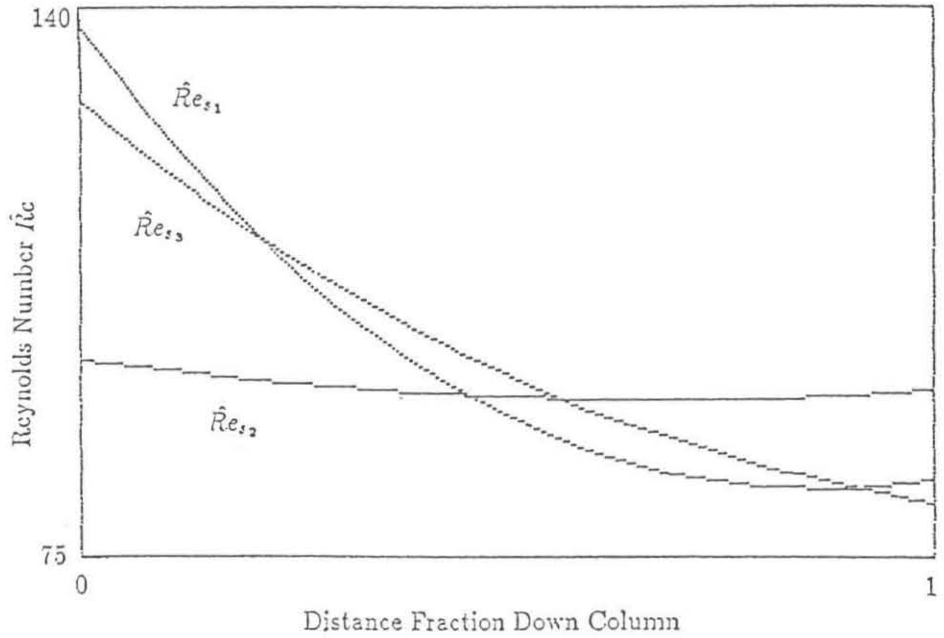

Figure 15: Intracolumn binary solvent Reynolds Number variation for three hypothetical solvent concentration distributions (see text). At 25° C.

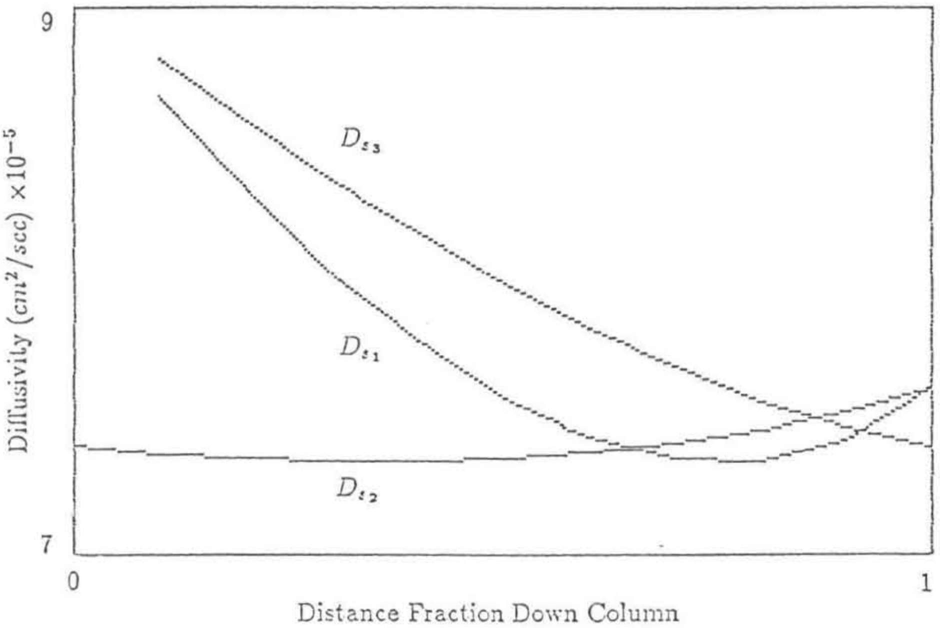

Figure 16: Intracolumn solute (hexanol) diffusivity variation for three hypothetical solvent concentration distributions (see text). At 25° C.

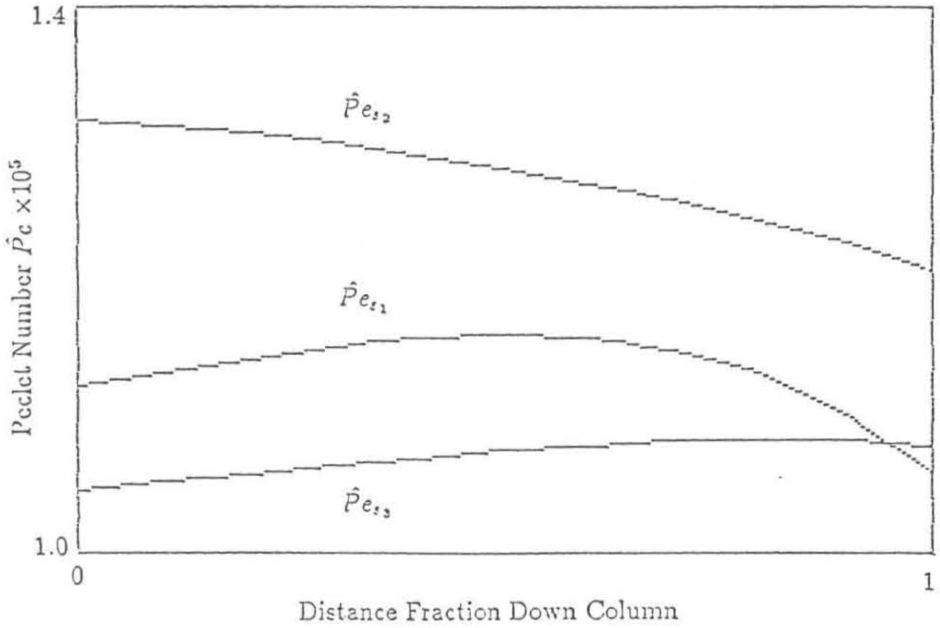

Figure 17: Intracolumn Peclet number (for hexanol) variation for three hypothetical solvent concentration distributions (see text). At 25° C.

CHAPTER 2

Existence and Uniqueness of Solutions to the Solvent and Solute Equations

Introduction: Here we examine the basic solvent and solute dynamical equations as to whether or not they possess solutions, and also if these solutions are unique. The actual form of these equations is discussed in more detail in chapters 3, 4, 8, and particularly 9, the latter chapter dealing also with numerical solutions. For this chapter, the mathematical structure of the equations is discussed in terms of Sobolev norms, and no mention is made of Sobolev norms outside of this chapter.

The chosen normalized form of the solvent equation is

$$\frac{\partial s}{\partial \tau} + \beta(s)\frac{\partial s}{\partial \xi} = 0,$$

with

$$\beta(s) = \frac{\hat{v}(s)}{1 + \frac{1-\vartheta}{\vartheta} b'(s)}$$

a bounded strictly positive function; effects of a nonlinear isotherm $b(s)$ are considered more important than the relatively very small effects of dispersion, fluid film mass transfer, or intraparticle diffusion. The coefficient $\hat{v}(\xi, \tau)$, the local velocity of the solvent, has been discussed in detail in chapter 1, and has the form

$$\hat{v} = \Big(\hat{\rho}(s)\int_0^1 \frac{\hat{\eta}(s)}{\hat{\rho}^2(s)}\,d\xi\Big)^{-1},$$

where $\hat{\rho} = \rho/\rho_0$ is normalized density, and $\hat{\eta} = \eta/\eta_0$ is the normalized dynamic viscosity. The chosen form (for this chapter) of the solute equation, which includes a linear isotherm, dispersion, and intraparticle diffusion, is

$$\vartheta\frac{\partial c}{\partial \tau} + v\frac{\partial c}{\partial \xi} + \frac{3D}{R}(1-\vartheta)\frac{\partial \hat{c}}{\partial \varrho}\Big|_{\varrho=1} = 0$$

$$\beta\frac{\partial\hat{c}}{\partial\tau}+\frac{\partial}{\partial\tau}(K(\hat{c}))-D(\frac{\partial^2\hat{c}}{\partial\varrho^2}+\frac{2}{\varrho}\frac{\partial\hat{c}}{\partial\varrho})=0$$

subject to the initial and boundary conditions

$$\begin{aligned}\hat{c}(\varrho,\xi,\tau)&=c(\xi,\tau)\\ \frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=0}&=0\\ c(\xi,0)&=0\\ \hat{c}(\varrho,\xi,0)&=0\\ c(0,\tau)&=\phi(\tau),\\ \text{with}\quad c,\hat{c}&\in L_2(0,\infty)\end{aligned}$$

(One may also include fluid film mass transfer effects, as in chapter 9, but here they are omitted for clarity.)

Mathematical Preliminaries: The reader is guided to reference [28] for a more thorough development of Sobolev spaces and existence of solutions to partial differential equations. Here we show (local) existence and uniqueness of the solvent and solute equations. Existence is shown by introducing an iterative solution technique, wherein each iterate possesses a unique, bounded solution, bounded independently of the iteration number, and then showing a Cauchy criterion holds for the sequence of iterates, together implying uniform convergence of the iteration to a solution.

We use the inner product and associated induced norm

$$(u_1,u_2)=(u_1(\cdot,\tau),u_2(\cdot,\tau))=\int_0^\infty u_1(\xi,\tau)u_2(\xi,\tau)\,d\xi,$$

$$\|u\|^2=(u,u),$$

in conjunction with the Sobolev classes of inner products and norms defined by

$$(u_1,u_2)_{H^p}=\sum_{j=0}^{p}(\frac{\partial^j u_1}{\partial\xi^j},\frac{\partial^j u_2}{\partial\xi^j});$$

$$\|u\|_{H^p}^2 = (u,u)_{H^p}.$$

For functions $a(\xi,\tau)$ we use the max norm

$$\mid a \mid_\infty = \max\{\mid a(\xi,\tau) \mid : 0 \le \xi < \infty\}.$$

We use the results that for u, $v \in L[0,\infty)$

$$(u_1, au_2) \le \|u_1\|\,\|au_2\| \le \mid a \mid_\infty \ \|u_1\|\,\|u_2\|$$

$$\|u_1\|\,\|u_2\| \le \frac{1}{2}(\|u_1\|^2 + \|u_2\|^2)$$

and the Sobolev inequality for $u \in C^1[0,\infty)$:

$$\mid u \mid_\infty^2 \le \|u\|^2 + 2\,\|u\|\,\|\frac{\partial u}{\partial \xi}\|$$

which implies that

$$\mid u \mid_\infty^2 \le \|u\|^2 + \|u\|^2 + \|\frac{\partial u}{\partial \xi}\|^2 \le 2\,\|u\|_{H^1}^2 \le 2\,\|u\|_{H^2}^2$$

We also will make use of the following versions of Gronwall's Lemma and Picard's Lemma, stated here without proof:

Gronwall's Lemma. Suppose $y \in C^1[0,T]$, $\psi \in C^0[0,T]$ satisfy

$$\frac{dy}{dt} \le cy(t) + \psi(t); \qquad 0 \le t \le T$$

for some $c \ge 0$. Then

$$y(t) \le e^{ct}\{y(0) + \int_0^t \mid \psi(\tau) \mid \, d\tau\}; \qquad 0 \le t \le T.$$

Picard's Lemma. Let $\{\eta^k(t)\}$, $k = 0, 1, 2, \ldots$ denote a sequence of nonnegative continuous functions such that

$$\eta^{k+1} \le a + b\int_0^t \eta^k(\tau)\,d\tau$$

for $0 \leq t \leq T$ and a, $b \geq 0$. Then the sequence is uniformly bounded; if $a = 0$, the sequence converges uniformly to zero.

Uniqueness of Solutions to the Solvent Equation. The solvent equation is

$$\frac{\partial s}{\partial \tau} + \beta(s)\frac{\partial s}{\partial \xi} = 0,$$

where we note again that $\beta(s)$ is bounded and strictly positive.

Lemma 1. *Solutions to the solvent equation are unique.*

Proof: Let u, v be solutions. Then $w = u - v$ satisfies

$$\frac{\partial w}{\partial \tau} + \beta(u)\frac{\partial u}{\partial \xi} - \beta(v)\frac{\partial v}{\partial \xi} = 0,$$

but

$$\beta(u)\frac{\partial u}{\partial \xi} - \beta(v)\frac{\partial v}{\partial \xi} = \beta(u)\frac{\partial w}{\partial \xi} + (\beta(u) - \beta(v))\frac{\partial v}{\partial \xi},$$

and by the mean value theorem,

$$(\beta(u_1) - \beta(u_2))\frac{\partial u_2}{\partial \xi} = \tilde{\beta}\frac{\partial u_2}{\partial \xi}w.$$

Thus we have

$$\frac{\partial w}{\partial \tau} + \beta(u)\frac{\partial w}{\partial \xi} - \tilde{\beta}\frac{\partial u_2}{\partial \xi}w = 0,$$

with

$$w(\xi, 0) = 0$$

$$w(0, \tau) = 0.$$

If the evolution of "energy" is calculated, we find

$$\begin{aligned}
\frac{1}{2}\frac{d}{d\tau}(w(\cdot,\tau), w(\cdot,\tau)) &= (w, \frac{\partial w}{\partial \tau}) \\
&= -(w, \beta(u_1)\frac{\partial w}{\partial \xi} + \tilde{\beta}\frac{\partial u_2}{\partial \xi}w) \\
&\leq - \mid \tilde{\beta}\frac{\partial u_2}{\partial \xi} \mid_\infty (w, w) + \frac{1}{2} \mid \beta(u_1) \mid_\infty (w, w) \\
&\leq \frac{1}{2} \mid \beta(u_1) \mid_\infty (w, w) = K\|w(\cdot,\tau)\|^2,
\end{aligned}$$

so by Gronwall's Lemma,

$$\|w(\cdot,\tau)\|^2 \leq e^{K\tau}\,\|w(\cdot,0)\|^2$$

and since $w(\xi,0) = 0$, the above implies $w(\xi,\tau) = 0$ on the entire domain, and hence $u_1 = u_2$.

Existence of Solutions to the Solvent Equation. In this section we introduce an iteration whose iterates s^n possess smooth solutions on $[0,L] \times [0,T]$, that the iterates are bounded independently of n, and satisfy a Cauchy criterion, so that the iteration converges.

The iteration is defined as

$$\frac{\partial s^{n+1}}{\partial \tau} + \beta^n \frac{\partial s^{n+1}}{\partial \xi} = 0,$$

where the coefficient is given by

$$\beta^n = \beta(s^n).$$

The initial and boundary conditions for each iterate is

$$s^{n+1}(0,\tau) = \phi(\tau)$$

$$s^{n+1}(\xi,0) = s_0 \quad \text{constant},$$

$$\phi(0) = s_0.$$

Lemma 2. *The iterates to the above problem are bounded independently of* n *in the* H^2 *norm.*

Proof: The iteration begins at $n = 1$, and we take $s^0 = s_0$. Clearly s^1 exists and is bounded. Assume s^n exists and is bounded. Note from its definition that the coefficient β is positive, smooth, and bounded. Note also that each iterate problem has a smooth, unique solution for a finite time; shocks will take time to develop if

ϕ is smooth. The evolution of the norm is given as

$$\begin{aligned}
\frac{1}{2}\frac{d}{d\tau}(s^{n+1}, s^{n+1}) &= \frac{1}{2}\frac{d}{d\tau}\|s^{n+1}\|^2 \\
&= (s^{n+1}, \frac{\partial s^{n+1}}{\partial \tau}) \\
&= -(s^{n+1}, \beta^n \frac{\partial s^{n+1}}{\partial \xi}) \\
&\leq | \gamma^n |_\infty | \frac{\partial s^n}{\partial \xi} |_\infty \|s^{n+1}\|^2 + \phi^2(\tau)\beta^n(0,\tau),
\end{aligned}$$

(using integration by parts as needed) where

$$\gamma^n = \frac{\partial \beta}{\partial s^n}.$$

This is not sufficient to bound the norm, because of the derivative of s^n appearing on the right hand side. We then use the solvent equation to find the evolution of the derivative $\frac{\partial s^{n+1}}{\partial \xi}$:

$$\frac{\partial^2 s^{n+1}}{\partial \xi \partial \tau} + \beta^n \frac{\partial^2 s^{n+1}}{\partial \xi^2} + \gamma^n \frac{\partial s^n}{\partial \xi}\frac{\partial s^{n+1}}{\partial \xi} = 0,$$

with boundary conditions

$$\begin{aligned}
\frac{\partial s^{n+1}}{\partial \xi}(0,\tau) &= -\frac{\phi'}{\beta^n(0,\tau)} \\
\frac{\partial s^{n+1}}{\partial \xi}(\xi,0) &= 0
\end{aligned}$$

which are obtained also from the original solvent equation. Using integration by parts and the usual inequalities, we find

$$\begin{aligned}
\frac{d}{d\tau}\|\frac{\partial s^{n+1}}{\partial \xi}(\cdot,\tau)\|^2 &= 2(\frac{\partial s^{n+1}}{\partial \xi}, \frac{\partial^2 s^{n+1}}{\partial \xi \partial \tau}) \\
&= -2(\frac{\partial s^{n+1}}{\partial \xi}, \beta^n \frac{\partial^2 s^{n+1}}{\partial \xi^2} + \gamma^n \frac{\partial s^n}{\partial \xi}\frac{\partial s^{n+1}}{\partial \xi}) \\
&\leq | \gamma^n |_\infty | \frac{\partial s^n}{\partial \xi} |_\infty \|\frac{\partial s^{n+1}}{\partial \xi}\|^2 + \beta^n(0,\tau)(\frac{\partial s^{n+1}}{\partial \xi}(0,\tau))^2,
\end{aligned}$$

but the max norm of the derivative of s^n can be approximated by the L_2 norm of the second derivative of s^n *via* the Sobolev inequality, so that we now need to find the evolution equation for the second derivative:

$$\begin{aligned}
\frac{1}{2}\frac{d}{d\tau}\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}(\cdot,\tau)\|^2 &= (\frac{\partial^2 s^{n+1}}{\partial\xi^2}, \frac{\partial^3 s^{n+1}}{\partial\xi^2\tau}) \\
&= -(\frac{\partial^2 s^{n+1}}{\partial\xi^2}, \beta^n\frac{\partial^3 s^{n+1}}{\partial\xi^3}) + (\frac{\partial^2 s^{n+1}}{\partial\xi^2}, 2\gamma^n\frac{\partial s^n}{\partial\xi}\frac{\partial^2 s^{n+1}}{\partial\xi^2}) + (\frac{\partial^2 s^{n+1}}{\partial\xi^2}, \gamma^n\frac{\partial s^{n+1}}{\partial\xi}\frac{\partial^2 s^n}{\partial\xi^2}) \\
&\quad + (\frac{\partial^2 s^{n+1}}{\partial\xi^2}, \alpha^n(\frac{\partial s^n}{\partial\xi})^2\frac{\partial s^{n+1}}{\partial\xi}) \\
&\le 5\mid\gamma^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2 + \mid\gamma^n\mid_\infty\mid\frac{\partial s^{n+1}}{\partial\xi}\mid_\infty\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|\|\frac{\partial^2 s^n}{\partial\xi^2}\| \\
&\quad + \mid\alpha^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty^2\|\frac{\partial s^{n+1}}{\partial\xi}\|\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\| + +\beta^n(0,\tau)(\frac{\partial^2 s^{n+1}}{\partial\xi^2}(0,\tau))^2.
\end{aligned}$$

To obtain an estimate we need to relate the above estimates to a Sobolev norm, as follows:

$$\begin{aligned}
\frac{d}{d\tau}\|s^{n+1}\|^2 &\le \mid\gamma^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty\|s^{n+1}\|^2 + \phi^2(\tau)\beta^n(0,\tau), \\
&\le K_0\|s^n\|_{H^2}\|s^{n+1}\|^2 + \phi^2(\tau)\beta^n(0,\tau),
\end{aligned}$$

$$\begin{aligned}
\frac{d}{d\tau}\|\frac{\partial s^{n+1}}{\partial\xi}(\cdot,\tau)\|^2 &\le K_1\mid\gamma^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty\|\frac{\partial s^{n+1}}{\partial\xi}\|^2 + \beta^n(0,\tau)(\frac{\partial s^{n+1}}{\partial\xi}(0,\tau))^2 \\
&\le K_2\|s^n\|_{H^2}\|\frac{\partial s^{n+1}}{\partial\xi}\|^2 + \beta^n(0,\tau)(\frac{\partial s^{n+1}}{\partial\xi}(0,\tau))^2,
\end{aligned}$$

$$\begin{aligned}
\frac{d}{d\tau}\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}(\cdot,\tau)\|^2 &\le 5\mid\gamma^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2 \\
&\quad + \mid\gamma^n\mid_\infty\mid\frac{\partial s^{n+1}}{\partial\xi}\mid_\infty\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|\|\frac{\partial^2 s^n}{\partial\xi^2}\| \\
&\quad + \mid\alpha^n\mid_\infty\mid\frac{\partial s^n}{\partial\xi}\mid_\infty^2\|\frac{\partial s^{n+1}}{\partial\xi}\|\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\| + \beta^n(0,\tau)(\frac{\partial^2 s^{n+1}}{\partial\xi^2}(0,\tau))^2 \\
&\le K_2\|s^n\|_{H^2}\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2 + K_3\|s^{n+1}\|_{H^2}[\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2 + \|\frac{\partial^2 s^n}{\partial\xi^2}\|^2] \\
&\quad + K_4\|s^n\|_{H^2}^2[\|\frac{\partial s^{n+1}}{\partial\xi}\|^2 + \|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2] + \beta^n(0,\tau)(\frac{\partial^2 s^{n+1}}{\partial\xi^2}(0,\tau))^2 \\
&\le K_5\|s^n\|_{H^2}\|\frac{\partial^2 s^{n+1}}{\partial\xi^2}\|^2 + \beta^n(0,\tau)(\frac{\partial^2 s^{n+1}}{\partial\xi^2}(0,\tau))^2,
\end{aligned}$$

so that, adding these three estimates, we obtain

$$\frac{d}{d\tau}\|s^{n+1}(\cdot,\tau)\|_{H^2}^2 \leq K_6\|s^n\|_{H^2}\|s^{n+1}\|_{H^2}^2 + \phi^2(\tau)\beta^n(0,\tau) + \beta^n(0,\tau)(\frac{\partial s^{n+1}}{\partial \xi}(0,\tau))^2$$

$$+\beta^n(0,\tau)(\frac{\partial^2 s^{n+1}}{\partial \xi^2}(0,\tau))^2,$$

this last step also following from the induction assumption. Let the forcing be denoted by

$$F(\tau) = \phi^2(\tau)\beta(0,\tau) + \beta(0,\tau)(\frac{\partial s}{\partial \xi}(0,\tau))^2 + \beta(0,\tau)(\frac{\partial^2 s}{\partial \xi^2}(0,\tau))^2$$

noting that for these boundary terms no superscripts are necessary, so the solution is

$$\|s^{n+1}(\cdot,\tau)\|_{H^2}^2 \leq \exp(K_6\|s^n\|_{H^2}\tau)\left[\|s(\cdot,0)\|_{H^2}^2 + \int_0^\tau F(\tau^*)\,d\tau^*\right],$$

so it is clear that a time T_1 can be found such that

$$\|s^{n+1}(\cdot,\tau)\|_{H^2}^2 \leq K^*, \qquad \text{for } 0 \leq \tau \leq T_1,$$

where K^* is independent of the iterate number. Thus the lemma is proven.

To prove convergence, we need to find the evolution of the norm of

$$\eta^{n+1}(\xi,\tau) = s^{n+1}(\xi,\tau) - s^n(\xi,\tau).$$

Lemma 3. *The iteration* $\eta^n \to 0$ *as* $n \to \infty$.

Proof: We have the equations

$$\frac{\partial s^{n+1}}{\partial \tau} + \beta(s^n)\frac{\partial s^{n+1}}{\partial \xi} = 0,$$

$$\frac{\partial s^n}{\partial \tau} + \beta(s^{n-1})\frac{\partial s^n}{\partial \xi} = 0$$

with the usual boundary conditions. Subtracting these two equations from each other, we obtain

$$\frac{\partial}{\partial \tau}(s^{n+1} - s^n) + \beta(s^{n-1})\frac{\partial}{\partial \xi}(s^{n+1} - s^n)(\beta(s^n) - \beta(s^{n-1}))\frac{\partial s^{n+1}}{\partial \xi} = 0,$$

Using the mean value theorem, we find the equation

$$\frac{\partial \eta^{n+1}}{\partial \tau} + \beta(s^{n-1})\frac{\partial \eta^{n+1}}{\partial \xi} = \phi^n \eta^n,$$

where

$$\phi^n \eta^n = -\tilde{\beta}(s^n)\frac{\partial s^{n+1}}{\partial \xi}\eta^n$$

with homogeneous initial and boundary conditions. Thus the norm satisfies

$$\begin{aligned}
\frac{1}{2}\frac{d}{d\tau}(\eta^{n+1}, \eta^{n+1}) &= \frac{1}{2}\frac{d}{d\tau}\|\eta^{n+1}\|^2 \\
&= (\eta^{n+1}, \frac{\partial \eta^{n+1}}{\partial \tau}) \\
&= (\eta^{n+1}, \phi^n \eta^n - \beta^n \frac{\partial \eta^{n+1}}{\partial \xi}) \\
&\leq |\phi^n|_\infty \|\eta^n\| \|\eta^{n+1}\| \\
&\leq K^0(\|\eta^n\|^2 + \|\eta^{n+1}\|^2)
\end{aligned}$$

on $0 \leq \tau \leq T_1$. Then by Gronwall's Lemma,

$$\|\eta^{n+1}\|^2 \leq \exp(K^0\tau)(\|\eta^{n+1}(\cdot, 0)\|^2 + K^1 \int_0^\tau \|\eta^n(\cdot, \tau^*)\|^2 \, d\tau^*),$$

but $\|\eta^n(\cdot, 0)\| = 0$, so

$$\begin{aligned}
\|\eta^{n+1}\|^2 &\leq K^* \int_0^\tau \|\eta^n(\cdot, \tau^*)\|^2 \, d\tau^* \\
&\Big(\leq K^* T_1 \|\eta^n(\cdot, \hat{\tau})\|^2\Big),
\end{aligned}$$

where $0 \leq \hat{\tau} \leq T_1$, so by Picard's Lemma (or note that we can choose T_1 such that $K^* T_1 = 1/2$), the sequence converges uniformly to zero:

$$\eta^n \to 0 \qquad \text{as} \qquad n \to \infty.$$

Uniqueness of Solutions to the Solute Equation. We have seen that the solution to the solvent equation is unique and exists; also, it can be shown [28, and references therein] that a unique solution exists for a linear partial differential equation of the type

$$\frac{\partial c}{\partial \tau} + v(\xi,\tau)\frac{\partial c}{\partial \xi} - \bar{D}(\xi,\tau)\frac{\partial^2 c}{\partial \xi^2} = F(\xi,\tau)$$

on $(\xi,\tau) \in [0,1] \times [0,\infty)$, $c(\xi,\tau) = 0$, $c(0,\tau) = \phi(\tau)$ $c(\cdot,\tau) \in L_2[0,\infty)$, where v, $\bar{D}$, F are all bounded C^2 functions with $\bar{D} > 2\delta > 0$, δ constant, for all ξ, τ.

Here we will show existence by converting the solute equations into an iterative problem with each iterate possessing an equation in the form of the above linear equation, so that each iterate exists and is smooth locally. Below we treat the case of the solute unaffected by fluid film mass transfer; basically the same method as below may be used when fluid film mass transfer is important.

Lemma 4. *The form of the solute equation as mentioned earlier*

$$\vartheta\frac{\partial c}{\partial \tau} + v\frac{\partial c}{\partial \xi} + \frac{3D}{R}(1-\vartheta)\frac{\partial \hat{c}}{\partial \varrho}\Big|_{\varrho=1} = 0$$

$$\beta\frac{\partial \hat{c}}{\partial \tau} + \frac{\partial}{\partial \tau}(K(\hat{c})) - D(\frac{\partial^2 \hat{c}}{\partial \varrho^2} + \frac{2}{\varrho}\frac{\partial \hat{c}}{\partial \varrho}) = 0$$

subject to the initial – boundary conditions

$$\hat{c}(\varrho,\xi,\tau) = c(\xi,\tau)$$

$$\frac{\partial \hat{c}}{\partial \varrho}\Big|_{\varrho=0} = 0$$

$$c(\xi,0) = 0$$

$$\hat{c}(\varrho,\xi,0) = 0$$

$$c(0,\tau) = \phi(\tau).$$

can be transformed into an equivalent form

$$\frac{\partial c^{n+1}}{\partial \tau} + v\frac{\partial c^{n+1}}{\partial \xi} - D_e\frac{\partial^2 c^{n+1}}{\partial \xi^2} + \int_0^\tau H(\xi,\tau-\hat{\tau})c^n(\xi,\hat{\tau})\,d\hat{\tau} = 0;$$

$$c(0,\tau) = \phi(t)$$

$$c(\xi,0) = 0$$

$$c \in L_2[0,\infty)$$

That is to say, the transformation is isomorphic.

Proof: We wish to solve the following problem:

$$\vartheta\frac{\partial c}{\partial\tau} + v\frac{\partial c}{\partial\xi} + \frac{3D}{R}(1-\vartheta)\frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=1} - D_e\frac{\partial^2 c}{\partial\xi^2} = 0$$

$$\beta\frac{\partial\hat{c}}{\partial\tau} + \frac{\partial}{\partial\tau}(K(\xi,\tau)\hat{c}) - D(\frac{\partial^2\hat{c}}{\partial\varrho^2} + \frac{2}{\varrho}\frac{\partial\hat{c}}{\partial\varrho}) = 0$$

subject to the initial – boundary conditions

$$\begin{aligned} \hat{c}(1,\xi,\tau) &= c(\xi,\tau) \\ \frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=0} &= 0 \\ c(\xi,0) &= 0 \\ \hat{c}(\varrho,\xi,0) &= 0 \\ c(0,\tau) &= \phi(\tau). \end{aligned}$$

First we note that the equation only for $\hat{c}$ above is equivalent to

$$\frac{\partial}{\partial\tau}(\Phi\varrho\hat{c}) - D\frac{\partial^2}{\partial\varrho^2}(\Phi\varrho\hat{c}) = 0$$

where $\Phi(\xi,\tau) = \beta + K(\xi,\tau)$ subject to

$$\begin{aligned} \varrho\hat{c}\big|_{\varrho=1} &= c(\xi,\tau) \\ \varrho\hat{c}\big|_{\varrho=0} &= 0 \\ \varrho\hat{c}\big|_{\tau=0} &= 0. \end{aligned}$$

One may solve for $\psi(\varrho,\xi,\tau) = \varrho\hat{c}(\varrho,\xi,\tau)$ in terms of the "boundary forcing" $\phi = c(\xi,\tau)$, using the Green's function for ψ. In order to carry this out, we need to express the boundary forcing ϕ above as a body forcing appearing in the partial differential equation instead of in the boundary conditions. Thus we need to find an *extended operator* A_e derived from the original operator A, where

$$A \equiv \frac{\partial}{\partial\tau}\gamma(\xi,\tau) - D\frac{\partial^2}{\partial\varrho^2}.$$

Let the domain of A be described by the set of functions $W(\varrho, \xi, \tau)$ satisfying

$$AW = 0$$

$$W(0, \xi, \tau) = 0$$

$$W(\varrho, \xi, 0) = 0$$

$$W(\varrho, \xi, \tau) = \hat{c}(1, \xi, \tau) = c(\xi, \tau).$$

In these equations ξ is merely a parameter. Introduce an inner product

$$\langle\langle V, W \rangle\rangle \overset{!}{=} \int_0^\infty \int_0^1 VW \, d\varrho \, d\tau,$$

where $V = V(\varrho, \xi, \tau)$ is an integrable function whose properties will be defined in the following development.

We will now define a problem for V adjoint to the one defined for W above, by using the inner product. Using integration by parts,

$$\begin{aligned}
\langle\langle V, AW \rangle\rangle &= \int_0^\infty \int_0^{\overset{1}{\varrho}} VA(W) \, d\varrho \, d\tau \\
&= \int_0^\infty \int_0^1 V[\frac{\partial}{\partial \tau}(\gamma(\xi, \tau)W) - D\frac{\partial^2 W}{\partial \varrho^2}] \, d\varrho \, d\tau \\
&= \int_0^1 \{V\gamma W]_0^\infty \, d\varrho - \int_0^\infty \int_0^1 \gamma \frac{\partial V}{\partial \tau} W \, d\varrho \, d\tau \\
&\quad + \int_0^\infty \{-DV\frac{\partial W}{\partial \varrho}]_0^1 d\tau - \int_0^\infty \int_0^1 (-D\frac{\partial V}{\partial \varrho}\frac{\partial W}{\partial \varrho}) \, d\varrho \, d\tau \\
&= \int_0^1 \{V\gamma W]_0^\infty \, d\varrho - \int_0^\infty \int_0^1 \gamma \frac{\partial V}{\partial \tau} W \, d\varrho \, d\tau \\
&\quad + \int_0^\infty \{-DV\frac{\partial W}{\partial \varrho}]_0^1 d\tau + \int_0^\infty \int_0^1 (-D\frac{\partial^2 V}{\partial \varrho^2} W) \, d\varrho \, d\tau
\end{aligned}$$

so we identify the adjoint operator A^* as

$$A^* \equiv -\gamma(\xi, \tau)\frac{\partial}{\partial \tau} - D\frac{\partial^2}{\partial \varrho^2},$$

and let the domain of A^* be described by the set of functions $V(\varrho, \xi, \tau)$ satisfying

$$A^* V = 0$$

$$V(\varrho, \xi, \tau \to \infty) = 0$$

$$V(0, \xi, \tau) = 0$$

$$V(1, \xi, \tau) = \hat{c}(1, \xi, \tau) = c(\xi, \tau)$$

This allows the equality

$$\langle\langle V, AW \rangle\rangle = \langle\langle A^* V, W \rangle\rangle.$$

Now we define the *extended operator* A_e such that

$$\langle\langle V, AW \rangle\rangle = \langle\langle A^* V, W \rangle\rangle \stackrel{!}{=} \langle\langle V, A_e W \rangle\rangle$$

Again using integration by parts, we obtain

$$\begin{aligned}
\langle\langle A^* V, W \rangle\rangle &= \int_0^\infty \int_0^1 A^*(V) W \, d\varrho \, d\tau \\
&= \int_0^\infty \int_0^1 [-\gamma(\xi, \tau) \frac{\partial V}{\partial \tau} W - D \frac{\partial^2 V}{\partial \varrho^2} W] \, d\varrho \, d\tau \\
= \int_0^1 \{-\gamma V W]_0^\infty \, d\varrho &- \int_0^\infty \int_0^1 (-V \frac{\partial}{\partial \tau}(\gamma W)) \, d\varrho \, d\tau \\
&+ \int_0^\infty \{-D \frac{\partial V}{\partial \varrho} W]_0^1 d\tau - \int_0^\infty \int_0^1 (-D \frac{\partial V}{\partial \varrho} \frac{\partial W}{\partial \varrho}) \, d\varrho \, d\tau \\
= \int_0^1 \{-\gamma V W]_0^\infty \, d\varrho &- \int_0^\infty \int_0^1 (-V \frac{\partial}{\partial \tau}(\gamma W)) \, d\varrho \, d\tau \\
&+ \int_0^\infty \{-D \frac{\partial V}{\partial \varrho} W]_0^1 d\tau - \int_0^\infty \int_0^1 (-D V \frac{\partial^2 W}{\partial \varrho^2}) \, d\varrho \, d\tau
\end{aligned}$$

so we identify the extended operator A_e as

$$A_e \equiv \frac{\partial}{\partial \tau} \gamma(\xi, \tau) - D \frac{\partial^2}{\partial \varrho^2} + 2D\delta'(\varrho - 1) c(\xi, \tau),$$

and let the domain of A_e be described by the set of functions $\tilde{W}(\varrho, \xi, \tau)$ satisfying

$$A_e \tilde{W} = 0$$

$$\tilde{W}(\varrho, \xi, 0) = 0$$

$$\tilde{W}(0, \xi, \tau) = 0$$

$$\tilde{W}(1, \xi, \tau) = 0.$$

Having found the body-forcing equivalent to the original problem, we now apply separation of variables to the homogeneous problem to find the Green's function.

$$\varrho\hat{c}(\varrho,\xi,\tau)=f(\tau)g(\varrho)h(\xi)$$

gives

$$\frac{\partial}{\partial\tau}(\gamma(\xi,\tau)f(\tau)g(\varrho))-D\frac{\partial^2}{\partial\varrho^2}(f(\tau)g(\varrho))=0$$

so that ($\kappa>0$)

$$\frac{(\gamma f)'}{f}=-\kappa=\frac{Dg''}{g}$$

with boundary conditions $g(0)=0=g(1)$, implying that, setting $\kappa=Dn^2\pi^2$,

$$g(\varrho)=\sin(n\pi\varrho).$$

Also, we have

$$f'+(\frac{\gamma'+\kappa}{\gamma})f=0,$$

so that

$$f(\tau)=A\exp(-\int_0^\tau(\frac{\gamma'+\kappa}{\gamma})d\tau),$$

which simplifies to

$$f(\tau)=\frac{A\gamma(\xi,0)}{\gamma(\xi,\tau)}\exp(-Dn^2\pi^2\int_0^\tau\frac{d\tau}{\gamma})$$

Thus we have the solution for the homogeneous initial and boundary conditions, and with body forcing $\ell(\xi,\varrho,\tau)$ as

$$\varrho\hat{c}(\varrho,\xi,\tau)=A\int_0^\tau\int_0^1\mathbf{G}(\varrho,\tau;\hat{\varrho},\hat{\tau})\ell(\xi,\hat{\varrho},\hat{\tau})\,d\hat{\varrho}\,d\hat{\tau},$$

where the Green's function $\mathbf{G}$ is given by

$$\mathbf{G}(\varrho,\tau;\hat{\varrho},\hat{\tau})=2\sum_{n=1}^{\infty}\frac{\gamma(\xi,0)\exp(-Dn^2\pi^2\int_0^{\tau-\hat{\tau}}\frac{d\sigma}{\gamma(\xi,\sigma)})}{\gamma(\xi,\tau-\hat{\tau})}\sin(n\pi\varrho)\sin(n\pi\hat{\varrho}).$$

Earlier we found that the body forcing we will be concerned with is

$$\ell(\xi, \varrho, \tau) = 2D\delta'(\varrho - 1)c(\xi, \tau).$$

Substituting this into the integral of the Green's function and integrating by parts, we obtain

$$\begin{aligned}\int_0^\tau \int_0^1 \mathbf{G}(\varrho, \tau; \hat{\varrho}, \hat{\tau}) 2D\delta'(\hat{\varrho} - 1)c(\hat{\xi}, \hat{\tau})\, d\hat{\varrho}\, d\hat{\tau} \\ &= \int_0^\tau (\mathbf{G}(\varrho, \tau; \hat{\varrho}, \hat{\tau}) 2D\delta(\hat{\varrho} - 1)c(\xi, \hat{\tau})]_0^1 d\hat{\tau} \\ &- \int_0^\tau \int_0^1 \frac{\partial \mathbf{G}}{\partial \varrho} \delta(\hat{\varrho} - 1) 2Dc(\xi, \hat{\tau})\, d\hat{\varrho}\, d\hat{\tau} \\ &= -\int_0^\tau \frac{\partial \mathbf{G}}{\partial \varrho}\Big|_{\varrho = 1} 2Dc(\xi, \hat{\tau})\, d\hat{\tau}.\end{aligned}$$

Also,

$$\frac{\partial \mathbf{G}}{\partial \varrho}\Big|_{\varrho = 1} = 2 \sum_{n=1}^{\infty} \frac{\gamma(\xi, 0) \exp(-Dn^2\pi^2 \int_0^{\tau - \hat{\tau}} \frac{d\sigma}{\gamma(\xi, \sigma)})}{\gamma(\xi, \tau - \hat{\tau})} \sin(n\pi\varrho)(-1)^n n\pi$$

so that we now have

$$\varrho\hat{c}(\varrho, \xi, \tau) = \gamma(\xi, 0) 4D\pi \int_0^\tau \sum_{n=1}^{\infty} \frac{\gamma(\xi, 0) \exp(-Dn^2\pi^2 \int_0^{\tau - \hat{\tau}} \frac{d\sigma}{\gamma(\xi, \sigma)})}{\gamma(\xi, \tau - \hat{\tau})} \sin(n\pi\varrho)(-1)^{n+1} nc(\xi, \hat{\tau})\, d$$

Clearly the series appearing in the integrand is uniformly convergent in $0 \leq \varrho \leq 1$ and $\tau > 0$, so we may differentiate $\hat{c}$ with respect to ϱ:

$$\frac{\partial \hat{c}}{\partial \varrho} = 4\pi D \int_0^\tau \sum_{n=1}^{\infty} I_n(\xi, \tau - \hat{\tau})(-1)^{n+1} n \frac{\partial}{\partial \varrho}(\frac{\sin(n\pi\varrho)}{\varrho}) c(\xi, \hat{\tau})\, d\tau.$$

Since

$$\frac{\partial}{\partial \varrho}(\frac{\sin(n\pi\varrho)}{\varrho}) = n\pi(-1)^n,$$

we obtain

$$\frac{\partial \hat{c}}{\partial \varrho}\Big|_{\varrho = 1} = -4\pi^2 D \int_0^\tau \sum_{n=1}^{\infty} n^2 I_n(\xi, \tau - \hat{\tau}) c(\xi, \hat{\tau})\, d\hat{\tau}.$$

With this expression the original equation for $c(\xi, \tau)$ can be written as

$$\vartheta \frac{\partial c}{\partial \tau} + V \frac{\partial c}{\partial \xi} - 12D^2\pi^2(1-\vartheta) \int_0^\tau \sum_{n=1}^{\infty} n^2 I_n(\xi, \tau - \hat{\tau}) c(\xi, \hat{\tau})\, d\hat{\tau} = 0.$$

The problem to be solved is now in the form

$$\vartheta \frac{\partial c}{\partial \tau} + V \frac{\partial c}{\partial \xi} + \int_0^\tau H(\xi, \tau - \hat{\tau}) c(\xi, \hat{\tau})\, d\hat{\tau} = 0$$

with boundary conditions

$$c(\xi, 0) = 0, \qquad c(0, \tau) = \phi(\tau),$$

and hence the lemma is proven. Note that

$$Q(\xi, \tau) = \int_0^\tau H c \, d\hat{\tau}$$

is bounded if c exists, since H is bounded on $[0, \tau)$ and c is assumed in $L_2[0, \infty)$.

Uniqueness of the Solution to the Solute Equation: For any two solutions c_1, c_2 $\eta = c_1 - c_2$ satisfies

$$\frac{\partial \eta}{\partial \tau} + v \frac{\partial \eta}{\partial \xi} + \int_0^\tau H(\xi, \tau - \hat{\tau}) \eta(\xi, \hat{\tau})\, d\hat{\tau} - D_e \frac{\partial^2 \eta}{\partial \xi^2} = 0;$$

with initial and boundary conditions

$$\eta(0, \tau) = 0$$

$$\eta(\xi, 0) = 0$$

$$\eta \in L_2[0, \infty)$$

Lemma 5. *The above equation and boundary and initial data for η implies* $\eta = 0$.

Proof: (Though the argument can be carried through with $D_e \neq 0$, here we take $D_e = 0$ for clarity of the argument.) The form of the solute above equation suggests using Laplace transformation in the variable τ. Introduce the transforms for c and initial condition ϕ as

$$\begin{aligned}\bar{\phi}(p) &= \int_0^\infty e^{-p\tau}\,\phi(\tau)\,d\tau\\ \bar{H}(\xi,p) &= \int_0^\infty e^{-p\tau}\,H(\xi,\tau)\,d\tau\\ \bar{c}_i(\xi,p) &= \int_0^\infty e^{-p\tau}\,c_i(\xi,\tau)\,d\tau, \qquad \text{giving}\\ \bar{\eta} &= \bar{c}_1 - \bar{c}_2\end{aligned}$$

and so

$$\vartheta p\bar{\eta} + V\frac{d\bar{\eta}}{d\xi} + \bar{H}\bar{\eta} = 0,$$

$$\text{with initial condition} \quad \bar{\eta}(0,p) = 0,$$

using the convolution theorem. The transformed solution can then be expressed as

$$\bar{\eta}(\xi,p) = \bar{\eta}(0,p)\exp\Big(-\int_0^x \Big(\frac{\vartheta p}{V} + \frac{1}{V}\bar{H}(\xi,p)\Big)\,dx\Big) = 0.$$

Thus $\bar{c}_1 = \bar{c}_2$, and hence $c_1 = c_2$ on the whole domain, and so the lemma is proven.

Existence of Solution to the Solute Equation: This follows by showing that the solution of the iteration equation given by

$$\frac{\partial c^{n+1}}{\partial\tau} + v\frac{\partial c^{n+1}}{\partial\xi} - D_e\frac{\partial^2 c^{n+1}}{\partial\xi^2} = G^n(\xi,\tau);$$

where the forcing is given by

$$G^n(\xi,\tau) = -\int_0^\tau H(\xi,\tau-\hat{\tau})c^n(\xi,\hat{\tau})\,d\hat{\tau} + F(\xi,\tau);$$

$$c^{n+1}(0,\tau) = \phi(\tau)$$

$$c^{n+1}(\xi,0) = 0$$

$$c^{n+1} \in L_2[0,\infty)$$

is bounded independently of n, and satisfies a Cauchy criterion; hence the sequence of twice differentiable functions $\{c^n\}$ converges, to a twice differentiable function $c(\xi, \tau)$.

With this in mind, we proceed to state some lemmas.

Lemma 6. *The above iteration at the $(n+1)$ step is bounded independently of n:*

$$| \, c^{n+1}(\cdot, \tau) \, |_{H^2} \leq K$$

where K depends on T_2, depends on up to the second derivative of the boundary data, and δ, (where $D_e \geq 2\delta > 0$).

Proof: See reference [28].

Lemma 7: *The sequence of solutions to the iterative problem satisfy*

$$\|\eta^{n+1}\|^2_{H^2} \leq K(\|\eta(\cdot, 0)\|^2_{H^2} + \int_0^\tau \|\eta^n(\cdot, \tau)\|^2_{H^2} \, d\hat{\tau})$$

where $\eta^{n+1}(\xi, \tau) = c^{n+1}(\xi, \tau) - c^n(\xi, \tau)$; since $\eta(\xi, 0) = 0$, the sequence $\eta^{n+1} \to 0$.

Proof: See reference [28].

Hence the iteration is bounded, satisfies a Cauchy criterion, and hence converges uniformly to a unique solution.

CHAPTER 3

Uncontrolled Solute Dynamical Equations

In this chapter typical uncontrolled dynamical models of solutes in chromatography that have appeared in the literature will be reviewed quickly. Solutions to the simpler equations will be found in Chapter 4; subsequent chapters discuss controlled dynamics.

Equations of conservation. For simplicity, let us consider only one solute in the sample mixture as it travels down the column. The mobile phase is considered to be in *plug flow* through a packed bed of porous particles, all assumed to be spheres of uniform radius R and porosity β. Plug flow refers to the case where the flow can be averaged over each cross–section down the column; the flow must be quasilaminar. The solute in the mobile phase has concentration $c(x,t)$, where t denotes time and x denotes distance down the column. The solute in the stationary phase within the particles has concentration $\hat{c}(r,x,t)$, where t and x are as before, and r denotes the radial distance from the center of the particles. The column is of length L and has a *void volume* fraction ϑ, the volume available to the liquid outside the particles relative to column volume. The concentration of adsorbed sample molecules in the average particle at distance x down the column is denoted $q(r,x,t)$, while the solute concentration inside the average particle is denoted $\hat{c}(r,x,t)$.

Conservation of mass across a control volume in the column gives the equation of continuity [2,9,11,14,29,30,32,33,41,50,51, 52,53]

$$\vartheta\frac{\partial c}{\partial t}+V\frac{\partial c}{\partial x}+(1-\vartheta)\frac{\partial \bar{s}}{\partial t}-D_e\frac{\partial^2 c}{\partial x^2}=0$$

where $\bar{s}=\bar{s}(x,t)$ is the average solute concentration inside the particles, whether adsorbed or not. The coefficient D_e takes into account axial dispersion and diffusion in the flow. If the particles are nonporous, the source term in the discussion above is instead $(1-\vartheta)\partial q/\partial t$, so the continuity equation is

$$\vartheta\frac{\partial c}{\partial t}+V\frac{\partial c}{\partial x}+(1-\vartheta)\frac{\partial q}{\partial t}-D_e\frac{\partial^2 c}{\partial x^2}=0.$$

Equations of Intraparticle Diffusion and Fluid Film Mass Transfer: For the average particle at position x down the column, the diffusion of solute into the particle and adsorption to the solid surface is given by

$$\beta\frac{\partial\hat{c}}{\partial t}+\frac{\partial q}{\partial t}-D_p\Big(\frac{\partial^2\hat{c}}{\partial r^2}+\frac{2}{r}\frac{\partial\hat{c}}{\partial r}\Big)=0,$$

where the adsorbent is of spherical particles of radius R and D_p is the diffusion coefficient inside the particles. For spherical particles, the surface area per unit bed volume is

$$\frac{3(1-\vartheta)}{R},$$

so that flux of solute into the particle pores gives the rate of change of the average particle concentration:

$$(1-\vartheta)\frac{\partial\bar{s}}{\partial t}=\Big[\frac{3(1-\vartheta)}{R}D_p\Big]\frac{\partial\hat{c}}{\partial r}\Big|_{r=R}\ .$$

The rate of mass transfer of solute across the fluid film surrounding each particle is given by

$$D_p\frac{\partial\hat{c}}{\partial r}\Big|_{r=R}=k_f\,[c(x,t)-\hat{c}(R,x,t)].$$

If the resistance to mass transfer is relatively small, at $r=R$ we may take $c(x,t)=\hat{c}(R,x,t)$.

Reaction equations (equilibrium theory). When V is not so large that we must use kinetics equations for reactions of sample molecules with the substrate, we assume a local equilibrium relation, called the *adsorption isotherm,* between adsorbed and unadsorbed molecules:

$$q(x,t)=h(c(x,t))\,.$$

The shape of the function $h(c)$ affects the profile of a concentration pulse travelling down the column.

In the *linear equilibrium* case, we have

$$q(x,t) = K_{th}\, c(x,t).$$

This relation is accurate whenever the solute concentration is quite small. A typical relation for higher concentrations is the Langmuir isotherm, which indeed reduces to the linear case for small $c(x,t)$

$$q(x,t) = \frac{k_f Q c(x,t)}{k_b C + (k_f - k_b) c(x,t)}$$

so that

$$K_{th} = \frac{k_f Q}{k_b C}.$$

Reaction equations (kinetic theory). For weak adsorbers or small solute concentration, there is a simple relation describing the rate of adsorption at (x,t) :

$$\left.\frac{\partial q}{\partial t}\right|_x = k_f Q c(x,t) - k_b C q(x,t),$$

where k_f is the forward reaction rate constant, Q is the adsorption capacity of the column, k_b is the backward reaction rate constant, and C is the "solvent capacity." At steady–state we arrive at the linear equilibrium relation

$$q(x,t) = K^{\circ} \frac{Q}{C} c(x,t),$$

where $K^{\circ} = k_f / k_b$.

If instead we assume the forward adsorption rate is proportional to the product of unadsorbed molecule concentration and the concentration of available adsorption sites, and that the backward reaction rate is proportional to the product of adsorbed molecule concentration and concentration of "available sites" in the solvent, we obtain the Langmuir kinetic equation

$$\frac{\partial q}{\partial t}\Big|_x = k_f\,(Q - q(x,t))\,c(x,t) - k_b\,(C - c(x,t))\,q(x,t).$$

This will lead to the Langmuir isotherm at steady–state conditions. If the solvent capacity is always much larger than the unadsorbed molecule concentration, then we have

$$\frac{\partial q}{\partial t}\Big|_x = k_f\,(A - q(x,t))\,c(x,t) - k_b C q(x,t).$$

Dynamical equations. We first consider the equilibrium dynamical equations. Combining the isotherm equation

$$q(x,t) = h(c(x,t))$$

with the conservation equation

$$\vartheta \frac{\partial c}{\partial t} + V \frac{\partial c}{\partial x} + (1-\vartheta)\frac{\partial q}{\partial t} = 0$$

yeilds the simple hyperbolic equation

$$\frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta}h')\,\frac{\partial c}{\partial t} + \frac{\partial c}{\partial x} = 0,$$

where $v = V/\vartheta$ is the linear velocity. For a Langmuir isotherm this has been shown to be an adequate model in circumstances with high solute concentrations (see Figure 18).

There are two primary sources of nonequilibrium that can be of importance – fast flow velocities v, and initial conditions not satisfying the equilibrium isotherm. Initially, at the introduction of the sample into the column, there are no adsorbed molecules. However, in using the equilibrium isotherm we actually are assuming that there is (*immediately*) a concentration of adsorbed molecules proportional (in

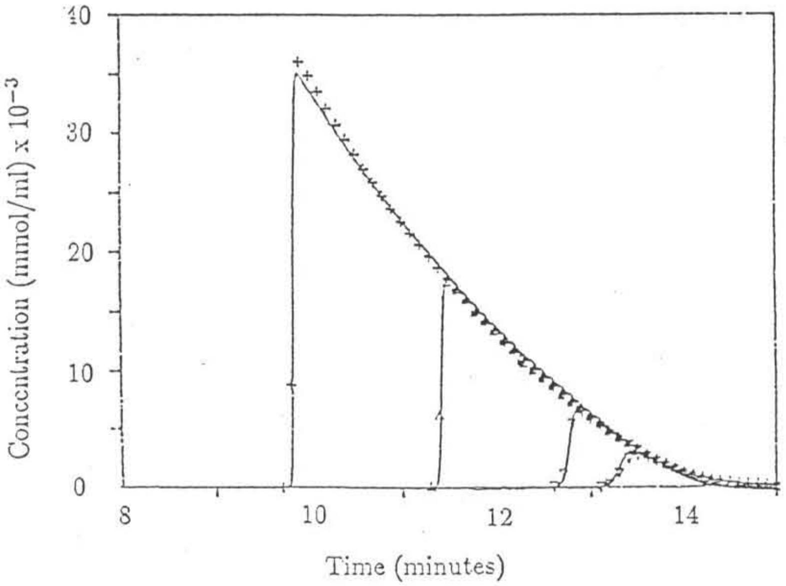

Figure 18: Predicted (solid curve) and experimental (+) concentration profiles for a corrected nonlinear hyperbolic model (see text). Sample sizes .0025 mmol, .00625 mmol, .025 mmol, and .075 mmol. Adapted from

the linear case) to the concentration of unadsorbed molecules introduced into the column.

There are two usual ways around this contradiction. One way is to go ahead and assume immediate equilibrium, so that the initial boundary value conditions are

$$c(x,0) = q(x,0) = 0,$$

$$c(0,t) = f(t),$$

and

$$q(0,t) = h(f(t))\,.$$

We then further assume that the decay of the "true" solution onto the approximate solution satisfying these unphysical conditions is quite fast compared to sample elution time. It is found experimentally that this is a reasonable assumption for the usual range of flow velocities v.

The second way is to abandon the isotherm equation and use a kinetics equation, such as for linear kinetics, and use the more physically accurate initial and boundary values

$$c(x,0) = q(x,0) = 0,$$

$$c(0,t) = f(t),$$

$$q(0,t) = 0.$$

One finds that for v not too large this solution decays onto the equilibrium solution in an exponentially short time.

To obtain the dynamical equation for the case involving the kinetics equation, it is easiest to change independent variables:

$$\bar{\tau} = \frac{x}{V} \quad \text{and} \quad \bar{\eta} = t - \frac{\vartheta x}{V}.$$

Then the conservation equation

$$\vartheta \frac{\partial c}{\partial t} + V \frac{\partial c}{\partial x} + \frac{\partial q}{\partial t} = 0$$

becomes

$$\frac{\partial c}{\partial \bar{\tau}} + \frac{\partial q}{\partial \bar{\eta}} = 0.$$

This relation implies the existence of a potential $F(\bar{\tau}, \bar{\eta})$ such that dF is an exact differential

$$dF = c\, d\bar{\eta} - q\, d\bar{\tau},$$

i.e.,

$$c(\bar{\tau}, \bar{\eta}) = \frac{\partial F}{\partial \bar{\eta}},$$
$$q(\bar{\tau}, \bar{\eta}) = -\frac{\partial F}{\partial \bar{\tau}}.$$

So, combining this with the linear kinetics equation

$$\left.\frac{\partial q}{\partial t}\right|_x = V \frac{\partial q}{\partial \bar{\eta}} = k_f Q c(\bar{\tau}, \bar{\eta}) - k_b C q(\bar{\tau}, \bar{\eta}).$$

we obtain

$$V \frac{\partial^2 F}{\partial \bar{\tau} \partial \bar{\eta}} + k_f Q \frac{\partial F}{\partial \bar{\eta}} + k_b C \frac{\partial F}{\partial \bar{\tau}} = 0.$$

For Langmuir kinetics, we instead obtain

$$V \frac{\partial^2 F}{\partial \bar{\tau} \partial \bar{\eta}} + k_f Q \frac{\partial F}{\partial \bar{\eta}} + k_b C \frac{\partial F}{\partial \bar{\tau}} - (k_f + k_b) \frac{\partial F}{\partial \bar{\tau}} \frac{\partial F}{\partial \bar{\eta}} = 0,$$

which can be put in the same form as the linear equation *via* the Thomas transformation, which will be discussed in the next chapter.

Dynamical equations for several solutes: equilibrium theory. In the linear theory, there are no interactions between solutes, so that the equations are decoupled:

$$\frac{\partial c_i}{\partial \bar{\tau}} + \frac{\partial}{\partial \bar{\eta}} \left(K_i c_i \right) = 0$$

for $i = 1 \dots n$, where n denotes the total number of solutes.

Assuming a Langmuir isotherm, we obtain a set of coupled nonlinear hyperbolic equations

$$\frac{\partial c_i}{\partial \bar{\tau}} + \frac{\partial}{\partial \bar{\eta}}\Big(h(K_i, c_1, \dots, c_n)\Big) = 0$$

where K_i is given by

$$K_i = \frac{(C - (\sum_j c_j))\, q_i}{(Q - (\sum_j q_j))\, c_i}.$$

Dynamical equations for several solutes: kinetic theory. Using the notion of potentials F_i as defined from the conservation equation

$$\frac{\partial c_i}{\partial \bar{\tau}} + \frac{\partial q_i}{\partial \bar{\eta}} = 0$$

for $i = 1 \dots n$, so that

$$c_i(\bar{\tau}, \bar{\eta}) = \frac{\partial F_i}{\partial \bar{\eta}}$$

$$q_i(\bar{\tau}, \bar{\eta}) = -\frac{\partial F_i}{\partial \bar{\tau}}$$

and so the linear kinetics dynamical equations are

$$V \frac{\partial^2 F_i}{\partial \bar{\tau} \partial \bar{\eta}} + k_{b,i} C \frac{\partial F_i}{\partial \bar{\tau}} + k_{f,i} Q \frac{\partial F_i}{\partial \bar{\eta}} = 0.$$

For Langmuir kinetics, the dynamical equations are a set of coupled, nonlinear hyperbolic equations

$$V \frac{\partial^2 F_i}{\partial \bar{\tau} \partial \bar{\eta}} + k_{b,i} C \frac{\partial F_i}{\partial \bar{\tau}} + k_{f,i} Q \frac{\partial F_i}{\partial \bar{\eta}} + (\sum_j k_{f,j} + k_{b,j})\big(\sum_{k,l} \frac{\partial F_k}{\partial \bar{\tau}} \frac{\partial F_l}{\partial \bar{\eta}}\big) = 0.$$

CHAPTER 4

Solutions to the Simpler Uncontrolled Dynamical Equations

In this chapter the easier uncontrolled solute dynamical models that have appeared in the literature will be solved. The more accurate dynamical models have analytical solutions too complex to include here, and indeed are generally in themselves too complicated to be very useful. As we will demonstrate in following chapters, other techniques can be more fruitfully implemented, namely perturbation and moment techniques.

Solution of the linear equilibrium dynamical equations. Recall from the third chapter that the equation for linear, local equilibrium theory of one solute is (where $v = V/\vartheta$)

$$\frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta}K_{th})\frac{\partial c}{\partial t} + \frac{\partial c}{\partial x} = 0,$$

with

$$c(x,0) = 0$$

and

$$c(0,t) = f(t).$$

Here we have assumed that the solvent is not changing with respect to x. This is simple to solve using the method of characteristics. Let $t = t(x)$. On the *characteristic curve* defined by

$$\frac{dt}{dx} = \frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta}K_{th}),$$

$$t(0) = t_0,$$

the concentration satisfies

$$\frac{dc}{dx} = 0,$$

$$c(0, t_0) = f(t_0).$$

Thus the characteristic curve is given by

$$t(x) = \frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta} K_{th}) x + t_0$$

and so the solution to the overall problem is

$$c(x,t) = f(t - \frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta} K_{th})x)$$

for

$$t \geq \frac{1}{v}\Big(1 + \frac{1-\vartheta}{\vartheta} K_{th}\Big) x.$$

The solution for several solutes is of course analogous, with due respect to each solute's different reaction coefficient:

$$c_i(x,t) = f_i\Big(t - \frac{1}{v}(1 + \frac{1-\vartheta}{\vartheta} K_{th,i})x\Big)$$

for

$$t \geq \frac{1}{v}\Big(1 + \frac{1-\vartheta}{\vartheta} K_{th,i}\Big) x.$$

Solution of the nonlinear equilibrium dynamical equations: one solute. Using the Langmuir isotherm to eliminate $q(\tau, \eta)$,we obtain

$$\frac{\partial c}{\partial \tau} + \frac{\partial}{\partial \eta}\Big(\frac{KQc}{C + [K-1]c}\Big) = 0.$$

(Again we assume that the solvent is not changing with respect to x.) Thus [50,54]

$$\Big(\frac{(C + [K-1]c)^2}{KQc}\Big) \frac{\partial c}{\partial \tau} + \frac{\partial c}{\partial \eta} = 0.$$

the characteristic curves are thus given by

$$\tau = \Big(\frac{(C+[K-1]f(\tau))^2}{KQf(\tau_0)}\Big)\eta + \tau_0.$$

Note that this is implicit in τ_0. Depending on the shape of $f(\tau_0)$, *shocks* can occur in the solution.

Solution of the nonlinear equilibrium dynamical equations: several solutes. This is not an easy solution, and there is no way to express the general solution. Helferrich and Klein [19] have written a book on the subject as it pertains to chromatography (see the review in appendix A).

Solution of the linear nonequilibrium dynamical equation: one solute. This equation

$$\frac{\partial^2 F}{\partial\tau\partial\eta} + \frac{k_f Q}{V}\frac{\partial F}{\partial\eta} + \frac{k_b C}{V}\frac{\partial F}{\partial\tau} = 0$$

which we will call the linearized Thomas equation, has been solved by Thomas [50,51] for some very simple boundary conditions, and investigated in detail by Goldstein [14,15]. Here it will be solved for a simple initial finite pulse.

Let $k = k_f$, $K = k_f/k_b$, $\mu = kQ\tau$, $\varrho = kC\eta$, $u(\mu,\varrho) = c(\mu,\varrho)/C$, $v(\mu,\varrho) = q(\mu,\varrho)/Q$, and $r = 1/K$. Then the linearized Thomas equation becomes

$$\frac{\partial^2 F}{\partial\mu\partial\varrho} + \frac{\partial F}{\partial\varrho} + r\frac{\partial F}{\partial\mu} = 0.$$

The boundary conditions are (assigning the arbitrary constant $F(0,0) = 1$)

$$\frac{\partial F}{\partial\mu} \equiv 0 \Rightarrow F \equiv 0$$

for $\mu \geq 0,\ \varrho = 0$, and

$$\frac{\partial F}{\partial \varrho} = f(\varrho) \Rightarrow F \equiv 1 + \int_0^\varrho f(\omega) d\omega$$

for $\varrho \geq 0,\ \mu = 0$, where

$$f(\varrho) = \begin{cases} c^0, & \text{if } 0 \leq \varrho \leq w; \\ 0, & \text{otherwise.} \end{cases}$$

This initial boundary value problem can be solved perhaps best by Heaviside transform with respect to ϱ.

The Heaviside transformation of $F(\mu, \varrho)$ with respect to ϱ is defined as

$$\hat{F}(\mu, p) = p \int_0^\infty e^{-p\varrho} F(\mu, \varrho) d\varrho,$$

and its inverse as

$$H(\varrho)F(\mu, \varrho) = \frac{1}{2\pi i} \int_{\mathcal{B}} e^{p\varrho} \hat{F}(\mu, p) \frac{dp}{p},$$

where $\mathcal{B}$ denotes the Bromwich contour and $H(\varrho)$ denotes the unit step function.

The dynamical equation then becomes

$$(p+1)\frac{\partial \hat{F}}{\partial \mu} + rp\hat{F} - p[\frac{\partial F}{\partial \mu}(\mu, 0) + rF(\mu, 0)] = 0,$$

or

$$(p+1)\frac{\partial \hat{F}}{\partial \mu} + rp\hat{F} - pr = 0.$$

The initial condition for this can be found from the boundary condition () by transforming it:

$$\hat{F}(0, p) = 1 + \hat{f}(p)/p,$$

and since $f(\varrho)$ can be written in terms of step functions

$$f(\varrho) = c^0 \left[H(\varrho) - H(\varrho - w) \right],$$

we have

$$\hat{f}(p) = c^0 \left[1 - exp(-pw) \right],$$

and so

$$\hat{F}(\mu, p) = 1 + \frac{c^0}{p} exp\Big(-\frac{pr\mu}{p+1}\Big) - \frac{c^0}{p} exp\Big(-\frac{pr\mu}{p+1}\Big)\, exp(-pw).$$

Taking the inverse transform of $\hat{F}$,

$$F(\mu, \varrho) = 1 + c^0 \int_0^{\varrho} J(r\mu, \omega) d\omega - c^0 \int_0^{\varrho - w \geq 0} J(r\mu, \omega) d\omega,$$

where

$$J(x, y) = \frac{1}{2\pi i} \int_{\mathcal{B}} exp\Big(\zeta y - \frac{\zeta x}{\zeta + 1}\Big) \frac{d\zeta}{\zeta}.$$

That the boundary conditions are indeed satisfied can be easily verified *via* one of the properties of $J(x, y)$:

$$J(0, y) = 1.$$

The original dependent variables satisfy

$$c = kC \frac{\partial F}{\partial \varrho}$$

$$q = -kQ \frac{\partial F}{\partial \mu},$$

thus

$$c(\tau, \eta) = kCc^0 \Big\{ J(kQ\tau/K, kC\eta) - J(kQ\tau/K, kC\eta - w \geq 0) \Big\}$$

$$q(\tau,\eta) = kQc^0/K\Big\{\int_{kC\eta - w}^{kC\eta} exp(-kQ\tau/K - \omega)\, I_0(2\sqrt{kQ\tau\omega/K})\, d\omega\Big\},$$

where I_0 is the zeroth order modified Bessel function.

Solution of the linear nonequilibrium dynamical equation: n solutes. Recall this case involves a set of uncoupled equations, so that we can use the solution found in the previous section:

$$\frac{\partial^2 F_i}{\partial\tau\partial\eta} + \frac{k_{f,i}Q}{V}\frac{\partial F_i}{\partial\eta} + \frac{k_{b,i}C}{V}\frac{\partial F_i}{\partial\tau} = 0$$

Let $k_i = k_{f,i}$, $K = k_{f,i}/k_{b,i}$, $\mu = k_i Q\tau$, $\varrho = k_i C\eta$, $u_i(\mu,\varrho) = c_i(\mu,\varrho)/C$, $v_i(\mu,\varrho) = q_i(\mu,\varrho)/Q$, and $r_i = 1/K_i$. Then the linearized Thomas equation becomes

$$\frac{\partial^2 F_i}{\partial\mu\partial\varrho} + \frac{\partial F_i}{\partial\varrho} + r_i\frac{\partial F_i}{\partial\mu} = 0.$$

The boundary conditions are

$$\frac{\partial F_i}{\partial\mu} = 0$$

for $\mu \geq 0$, $\varrho = 0$, and

$$\frac{\partial F_i}{\partial\varrho} = f_i(\varrho)$$

for $\varrho \geq 0$, $\mu = 0$. As before, the pulses at the boundary are

$$f_i(\varrho) = \begin{cases} c_i^0, & \text{if } 0 \leq \varrho \leq w; \\ 0, & \text{otherwise.} \end{cases}$$

Thus the solution to this set of equations is

$$c_i(\tau,\eta) = k_i C c_i^0\Big\{\, J(k_i Q\tau/K_i, k_i C\eta) - J(k_i Q\tau/K_i, k_i C\eta - w \geq 0)\Big\}$$

$$q(\tau,\eta) = k_i Q c_i^0/K_i\Big\{\int_{k_i C\eta - w}^{k_i C\eta} exp(-k_i Q\tau/K_i - \omega)\, I_0(2\sqrt{k_i Q\tau\omega/K_i})\, d\omega\Big\}.$$

Solution of the nonlinear nonequilibrium dynamical equation: one solute. As done previously, a potential is introduced; here we call it ψ:

$$c(\tau,\eta)=\frac{\partial\psi}{\partial\eta},$$
$$q(\tau,\eta)=-\frac{\partial\psi}{\partial\tau}.$$

so that the Thomas equation is

$$\frac{\partial^2\psi}{\partial\tau\partial\eta}+\frac{k_f Q}{V}\frac{\partial\psi}{\partial\eta}+\frac{k_b C}{V}\frac{\partial\psi}{\partial\tau}-(k_f+k_b)\frac{\partial\psi}{\partial\tau}\frac{\partial\psi}{\partial\eta}=0.$$

Making the same independent variable transformations as in the previous section, we obtain

$$\frac{\partial^2\psi}{\partial\mu\partial\varrho}+\frac{\partial\psi}{\partial\varrho}+\frac{k_b C}{V}r\frac{\partial\psi}{\partial\mu}+(1-r)\frac{\partial\psi}{\partial\mu}\frac{\partial\psi}{\partial\varrho}=0.$$

The boundary conditions are

$$\frac{\partial\psi}{\partial\mu}=0$$

for $\mu\geq 0$, $\varrho=0$, and

$$\frac{\partial\psi}{\partial\varrho}=f(\varrho)$$

for $\varrho\geq 0$,$\mu=0$. We assign the arbitrary $\psi(0,0)=1$. Then $\psi(\mu,0)=1$ for $\mu\geq 0$ and

$$\psi(0,\varrho)=1+\int_0^{\varrho}f(\omega)d\omega$$

for $\varrho\geq 0$.

We can arrive back at the linearized form of the Thomas equation by introducing a nonlinear transformation, the one used here being slightly different than the Thomas transformation [14,51]:

$$F(\mu,\varrho)=exp[(1-r)(\psi(\mu,\varrho)-\varrho+\mu-1)],$$

which gives

$$\psi(\mu,\varrho) = \frac{1}{1-r} ln(F(\mu,\varrho)) + \varrho - \mu + 1,$$

and

$$u = N/F,$$

$$v = M/F.$$

Here we have set

$$N = F + \frac{\partial F}{\partial \varrho}/(1-r),$$

$$M = F - \frac{\partial F}{\partial \mu}/(1-r).$$

The dynamical equation is then

$$\frac{\partial^2 F}{\partial \mu \partial \varrho} + \frac{\partial F}{\partial \mu} + r\frac{\partial F}{\partial \varrho} = 0.$$

The boundary conditions are

$$F(\mu, 0) = exp[(1-r)\mu],$$

$$F(0,\varrho) = exp[(1-r)\int_0^\varrho (f(\omega)-1)\,d\omega].$$

We use the Heaviside transformation again; the dynamical equation then becomes

$$(p+1)\frac{\partial \hat{F}}{\partial \mu} + rp\hat{F} - p[\frac{\partial F}{\partial \mu} + rF(\mu,0)] = 0,$$

or

$$(p+1)\frac{\partial \hat{F}}{\partial \mu} + rp\hat{F} - p[e^{(1-r)\mu}] = 0.$$

Thus the solution to the transformed equation is

$$\hat{F}(\mu,p) = \frac{p}{p-r+1}\Big[exp[(1-r)\mu] - exp\big(-\frac{pr\mu}{p+1}\big)\Big] + \chi(p)exp\big(-\frac{pr\mu}{p+1}\big),$$

where $\chi(p)$ is the Heaviside transform of $F(0,\varrho)$. The expressions for M and N are thus

$$N(\mu,p) = \Big[\chi(p) + \frac{p[\chi(p)-1]}{1-r}\Big]exp\big(-\frac{pr\mu}{p+1}\big)$$

and

$$M(\mu,p) = \Big[\frac{\chi(p)}{p+1} + \frac{p[\chi(p)-1]}{(1-r)(p+1)}\Big]exp\big(-\frac{pr\mu}{p+1}\big).$$

The solutions are expressed in terms of the function

$$J(x,y) = \frac{1}{2\pi i}\int_{B} exp\big(\zeta y - \frac{\zeta x}{\zeta+1}\big)\frac{d\zeta}{\zeta},$$

whose many properties can be found in Watson [54]. One can develop the asymptotic and Taylor expansions of $J(x,y)$, which can be of use for numerical work.

In this chapter we have covered solutions to the chromatography dynamical equations that can be fairly simply expressed, though the Thomas equation has a solution that is clearly not terribly simple. Solutions to the more complete equations, combining intraparticle diffusion and kinetics, *et c.* are not very useful in themselves. Instead, one should use only the "important" or "relevant" parts of the solutions, typically done by using moment techniques [29,30,32]. However, the manner in which moment formulas have been obtained in past literature is useless when dynamical control of the chromatography system is desired. In chapters 8 and 9 a new method is presented for arriving at moment formulas, called *moment integration by parts*, a method easily applied to any control case.

CHAPTER 5

Adsorbent and Binary Solvent Models

In chromatography, one or more solvents are always present in high concentrations; the number of adsorption sites on the solid substrate is quite small and is entirely covered by the solvent and solutes. The solvent system is well into the nonlinear range of the isotherm describing the relationship between adsorbed and unadsorbed components.

From thermodynamics, we define an *activity* a_i (normalized fugacity) which for regular mixtures is simply related to the mole fraction x_i of the solvent component i: $a_i = \gamma_i x_i$. *Ideal mixtures* satisfy $\gamma_i = 1$. For a regular, nonideal mixture (Isaacs [23]),

$$\frac{\partial \ln \gamma_i}{\partial p} = \frac{\Delta \bar{V}_i}{RT},$$

where p is pressure, R is the gas constant, T is temperature, and $\Delta \bar{V}_i$ is excess partial molar volume that is due to reaction, weakly dependent on solvent composition for small molecules, assumed negligibly so. Assuming that $\Delta \bar{V}_i$ is essentially independent of pressure in the range $1 - 300$ atmospheres, we can integrate:

$$\gamma_i = \exp(\frac{p \Delta \bar{V}_i}{RT}).$$

At equilibrium, a steady-state partition occurs between mobile-phase and stationary-phase concentrations. This is described by the reaction coefficient, which is calculated by finding a certain ratio of activities. Assume that we model the binary solvent stationary-phase displacement reaction as

$$S_1 + S_2 A \rightleftharpoons S_1 A + S_2,$$

where S_i represents a molecule of solvent i and A represents an adsorbent site. Here the solvents have been assumed to be of equivalent size on the adsorbent. Also, the excess volume may be nonzero, and the binary solvent system is assumed to satisfy

$$s_1 + s_2 = 1 \quad \text{and} \quad b_1 + b_2 = 1,$$

where s_i and b_i represent mole fractions of unadsorbed and adsorbed solvent i, respectively. Then the Langmuir reaction coefficient (a constant) is given by

$$K_L = \frac{a_{b_1} a_{s_2}}{a_{s_1} a_{b_2}} = \frac{b_1 \exp(\frac{p\Delta \bar{V}_{b_1}}{RT}) s_2 \exp(\frac{p\Delta \bar{V}_{s_2}}{RT})}{s_1 \exp(\frac{p\Delta \bar{V}_{s_1}}{RT}) b_2 \exp(\frac{p\Delta \bar{V}_{b_2}}{RT})},$$

where a_{s_i} is the activity of unadsorbed solvent i, and a_{b_i} is the activity of adsorbed solvent i, and $\Delta\bar{V}_j$ are the respective excess volumes. If the two solvents are similar in size and chemistry, the exponential terms cancel. Or if it is assumed instead that $\Delta\bar{V}_j$ is independent of solvent composition, all the exponentials may be divided into the K_L to define a new equilibrium constant. Since $s_1 + s_2 = 1$, we obtain

$$K_L = \frac{b_1(1 - s_1)}{s_1(1 - b_1)},$$

so that

$$b_1 = \frac{K_L s_1}{(K_L - 1)s_1 + 1} = \frac{K_L s_1}{K_L s_1 + s_2}.$$

Likewise,

$$K_L = \frac{(1 - b_2)s_2}{(1 - s_2)b_2},$$

so

$$b_2 = \frac{K_L^{-1} s_2}{(K_L^{-1} - 1)s_2 + 1} = \frac{K_L^{-1} s_2}{K_L^{-1} s_2 + s_1}.$$

Note that indeed $b_1 + b_2 = 1$, and *both solvents have Langmuir isotherms with inverse reaction coefficients.* Also, if $K_L = 1$, then the solvents are identical in chemistry and the isotherms are entirely linear. In general, in the linear region (s_i

small) $b_1 = K_L s_1$ and $b_2 = K_L^{-1} s_2$. There are analogous results for ternary or higher-order solvent systems.

The use of mole fractions in the above calculations presents some difficulties, primarily when combining the solvent reaction model into the solvent continuity equation. The difficulty is that unless the two solvents have essentially the same chemical makeup, the total number of moles cannot remain constant, because the volume in the column is constant. Thus we cannot simply divide each solvent's dynamical equation by the total number of solvent moles to obtain the dynamics of the solvent mole fractions. A more natural form of the concentrations is the volume fraction; there is a constant volume available to the mobile phase, and a constant "volume" available to the stationary phase. We may take the mole concentrations appearing in each solvent equation and multiply through by its partial molar volume, assumed constant, and so we obtain the volume fraction of solvent per cm^3 column volume. The partial molar volume is not truly constant; for example, consider the partial molar volumes for the ethanol– water mixture in Figure 19. However, we find satisfactory accuracy with experimental data, assuming that the partial molar volumes are constant, at least in the examples considered to date.

The form of the solvent isotherms in terms of volume fractions can be found to be essentially identical to those in terms of mole fractions, the only difference being in the reaction coefficient ("Langmuir coefficient"). Returning to the definition of the Langmuir reaction coefficient in terms of activities, and assuming that the activity coefficients cancel, then

$$K_L = \frac{b_1 s_2}{s_1 b_2},$$

where s_i, b_i are in mole fractions. If $\bar{s}_i$, $\bar{b}_i$ represent molar concentrations, then

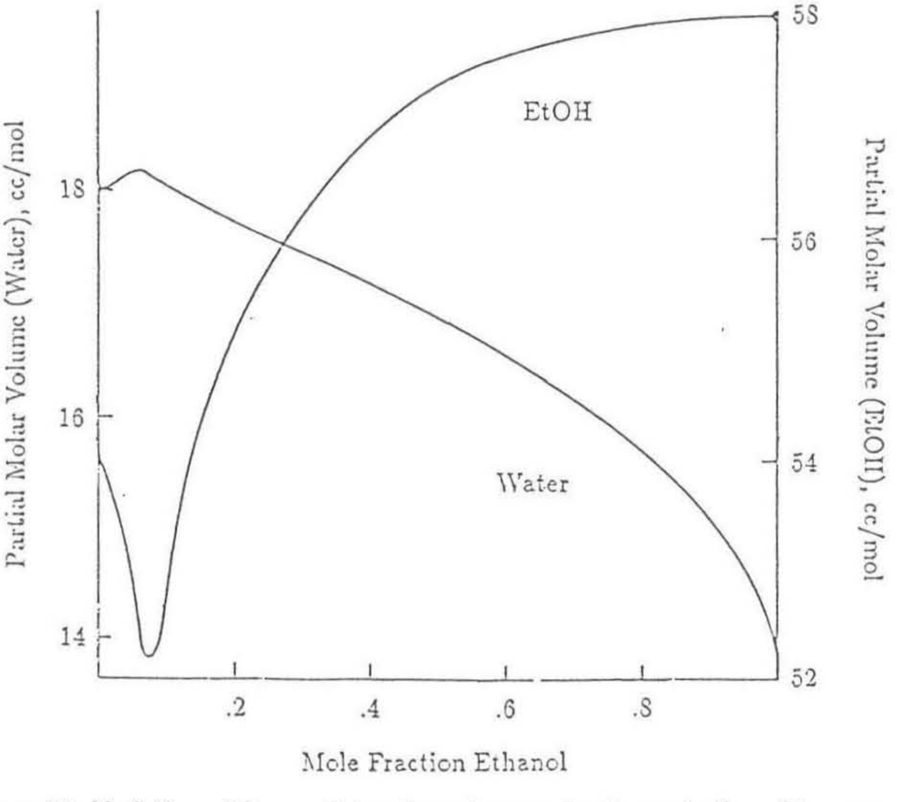

Figure 19: Variation of the partial molar volumes of water and ethanol in aqueous ethanol. Adapted from Atkins [ ].

from the above,

$$K_L = \frac{\frac{\bar{b}_1}{\bar{b}_1+\bar{b}_2}\,\frac{\bar{s}_2}{\bar{s}_1+\bar{s}_2}}{\frac{\bar{s}_1}{\bar{s}_1+\bar{s}_2}\,\frac{\bar{b}_2}{\bar{b}_1+\bar{b}_2}} = \frac{\bar{b}_1\,\bar{s}_2}{\bar{s}_1\,\bar{b}_2}.$$

From the definition of partial molar volumes and the presence of constant volumes in the stationary and mobile phases, we can write

$$\bar{s}_1\bar{V}_{s1} + \bar{s}_2\bar{V}_{s2} = 1$$

$$\bar{b}_1\bar{V}_{b1} + \bar{b}_2\bar{V}_{b2} = 1;$$

i.e., the sum of volume fractions is one in each phase. Thus

$$K_L = \Big(\frac{\bar{V}_{b2}}{\bar{V}_{s2}}\Big)\frac{\bar{b}_1(1-\bar{s}_1\bar{V}_{s1})}{\bar{s}_1(1-\bar{b}_1\bar{V}_{b1})}.$$

Thus the first solvent's isotherm is given in terms of volume fractions as

$$(\bar{V}_{b1}\bar{b}_1) = \frac{\bar{K}_L(\bar{V}_{s1}\bar{s}_1)}{1+[\bar{K}_L-1](\bar{V}_{s1}\bar{s}_1)}$$

where

$$\bar{K}_L = K_L\Big(\frac{\bar{V}_{s2}}{\bar{V}_{s1}}\Big)\Big(\frac{\bar{V}_{b1}}{\bar{V}_{b2}}\Big),$$

which is weakly dependent on s_1, but here is assumed constant in the isotherm. It is easy to see that the second solvent isotherm $(\bar{V}_{b2}\bar{b}_2)$ has a "Langmuir coefficient" of $\bar{K}_L^{-1}$.

If the solvents are not of similar size, and obey the displacement reaction

$$S_1 + zS_2\cdot A \rightleftharpoons S_1\cdot A + zS_2$$

then the equilibrium constant is

$$K_L = \Big(\frac{b_1}{s_1}\Big)\Big(\frac{s_2}{b_2}\Big)^z$$

in mole fractions, and

$$\bar{K}_L = K_L\Big(\frac{\bar{V}_{b1}}{\bar{V}_{s1}}\Big)\Big(\frac{\bar{V}_{s2}}{\bar{V}_{b2}}\Big)^z = \frac{(\bar{V}_{b1}\bar{b}_1)}{(\bar{V}_{s1}\bar{s}_1)}\Big(\frac{1-(\bar{s}_1\bar{V}_{s1})}{1-(\bar{b}_1\bar{V}_{b1})}\Big)^z$$

in volume fractions. Either of these formulas expresses an isotherm that must be calculated from the implicit equation

$$\frac{(1-\tilde{s}_1)^z}{\tilde{K}_L\,\tilde{s}_1} = \frac{(1-\tilde{b}_1)^z}{\tilde{b}_1},$$

where the terms are either for mole or volume fraction.

Adsorbent Models : Typical adsorbents for HPLC are based on uniformly sized silica beads, 5 to $50\mu m$ in diameter, usually treated so as to be superficially porous (pellicular) or totally porous (see Figure 4). NPLC methods utilize the bare silica surface as adsorbent, though steps should be taken so as to make the silica surface more "generic" with solvent additives 48. Even then, there are typically adsorbent sites of various activities. As reviewed by Little [31], the typical silica surface prepared for chromatography is composed of "free" silanol (SiOH) groups (Figure 20), "geminal" silanols (Figure 21), and hydrogen–bonded silanols (Figure 22). A two-dimensional schematic (Figure 23) of the adsorbent silanols and resulting polarity inhomogeneities shows what a polar solute might experience as it passes over the surface. An apolar solute would experience an essentially homogeneneous surface. The effects of inhomogeneities that are due to various types of silanols will be discussed in the next section in conjunction with solute and solvent equilibria.

RPLC adsorbents consist of silica beads with one of the usual functional groups attached to the silanols. Probably the most common of the functional groups are alkyl chains, often of length eight or eighteen carbons. Figure 24 shows a schematic of "octylsilica," or a hydrocarbonaceous ligand of length eight bonded to the silica surface. The silanols are never entirely covered, though the silanols are well beneath the alkyl "surface." Note that in contrast to the polar NPLC surface, the bonded RPLC surface is apolar and hydrophobic. Thus polar solutes will bind less than apolar solutes, in contradistinction to the NPLC adsorbent surface characteristics. The silanols within the "forest" of alkyl chains may or may not be accessible to a

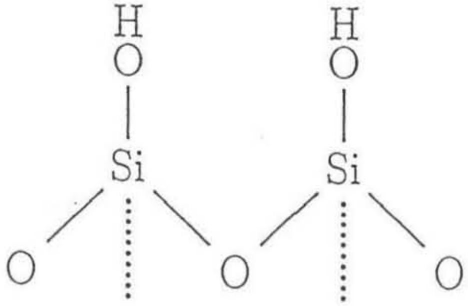

Figure 20: "Free" Silanol.

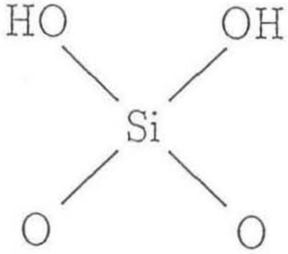

Figure 21: Geminal Silanol

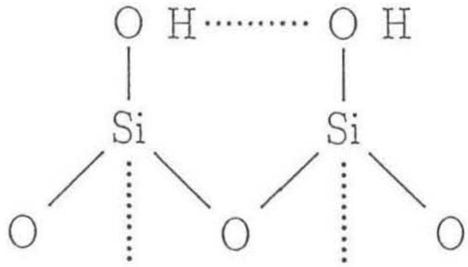

Figure 22: Hydrogen–Bonded Silanols

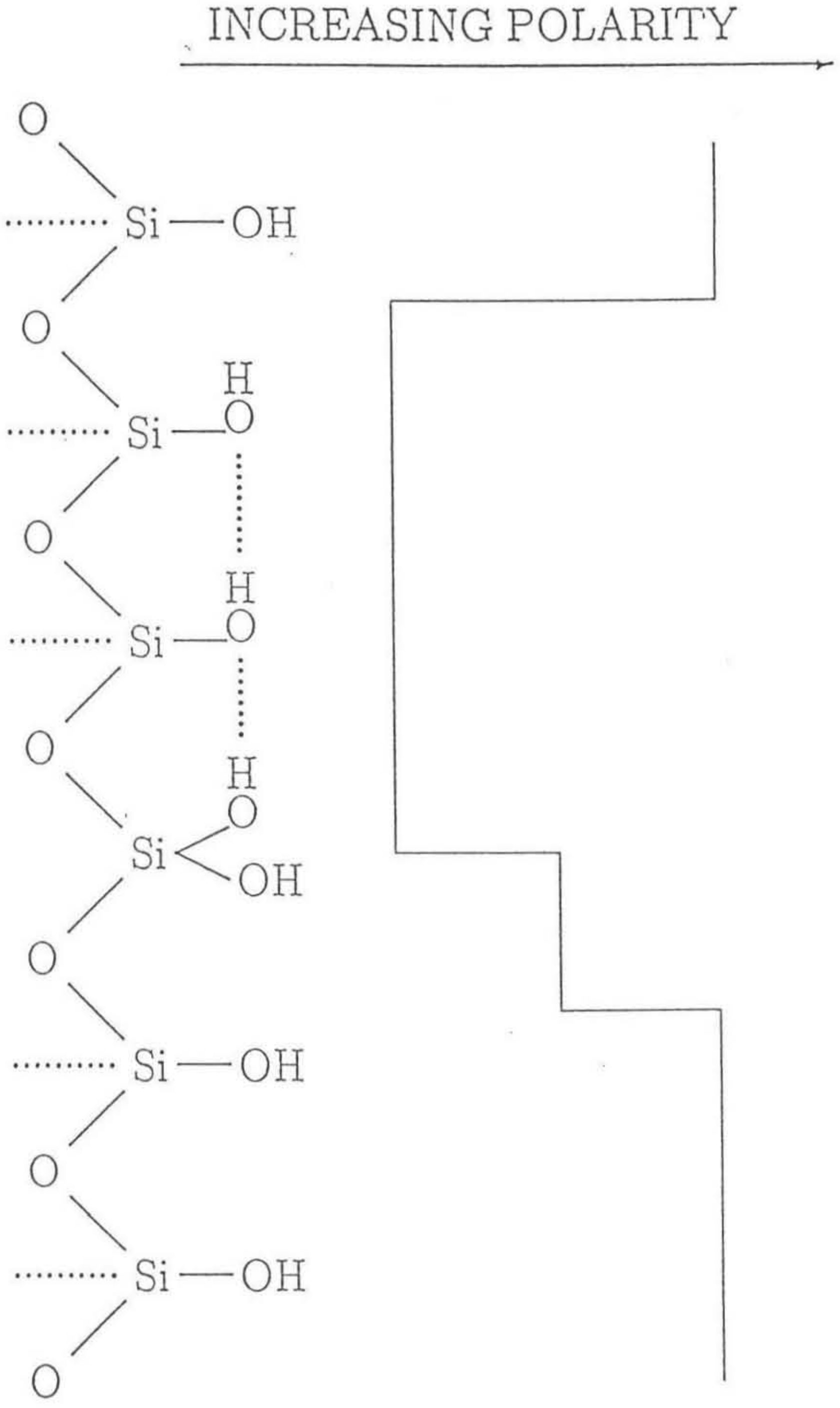

Figure 23: Schematic Silica Surface Inhomogeneities.

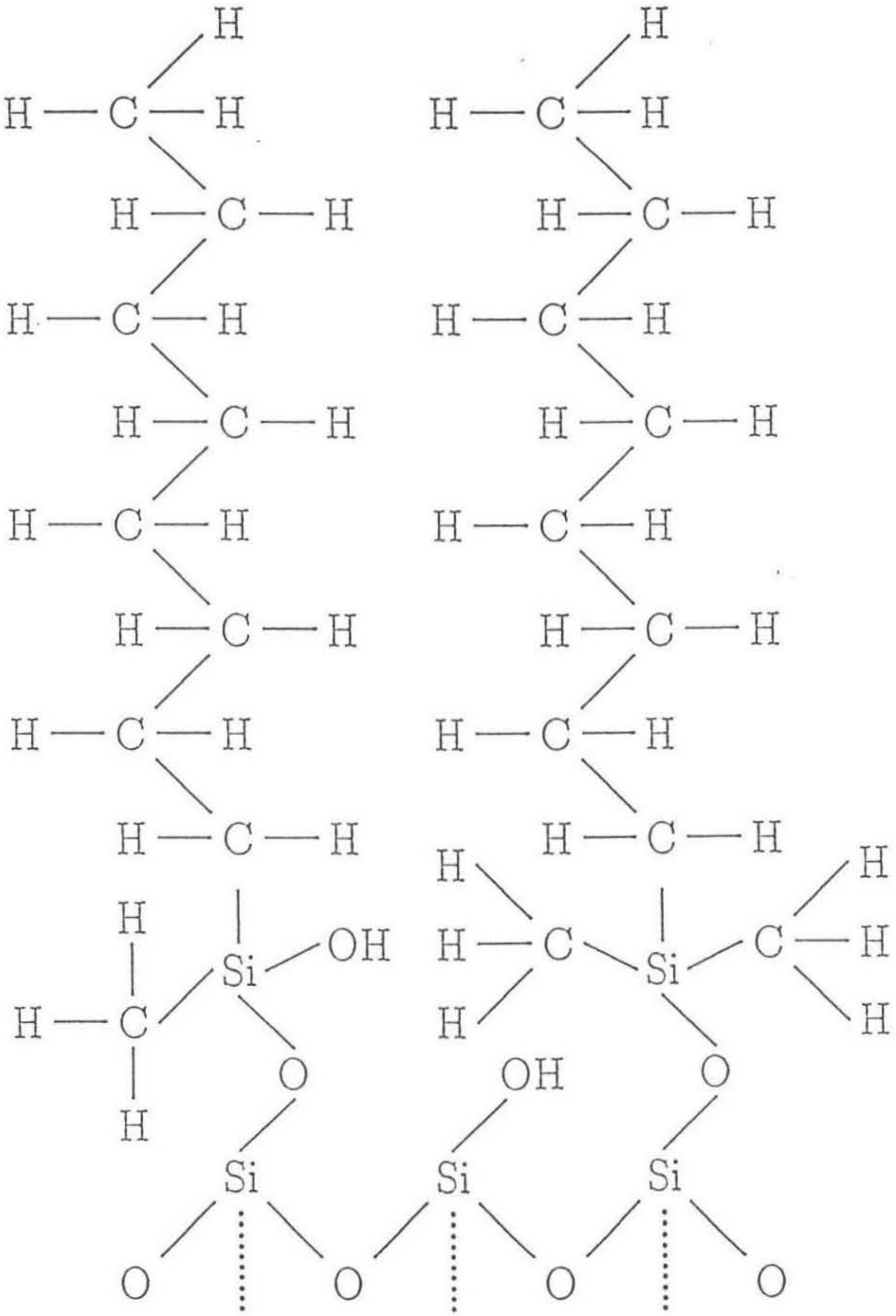

Figure 24: Schematic Bonded Stationary Phase.

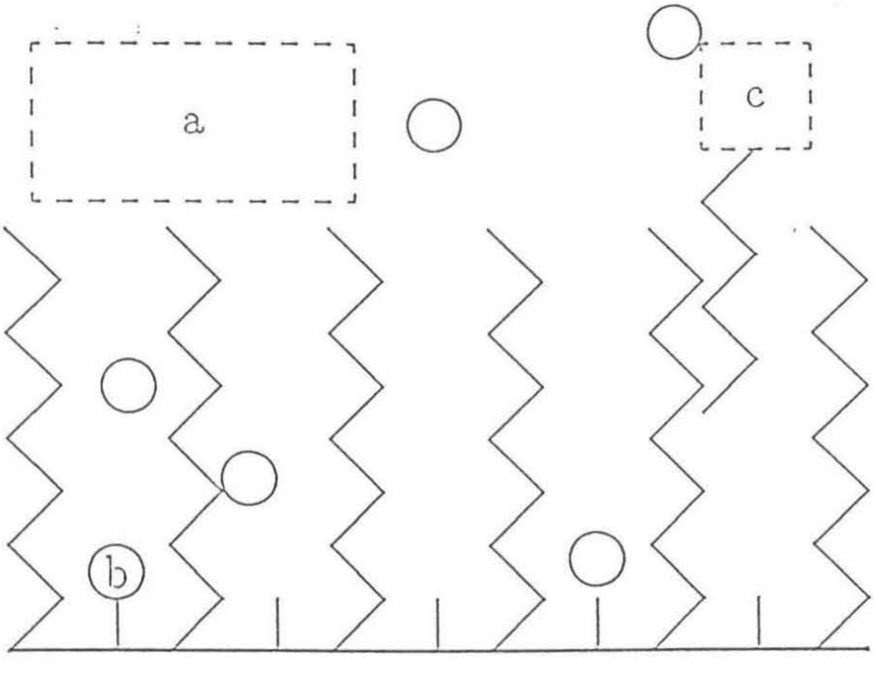

Figure 25: Mobile Phase Interaction with Bonded Phase.

solute, independently of its polarity, depending on its size. Figure [25] schematically shows how large molecules (a) may interact only with the surface of the hydrocarbonaceous adsorbent, and sterically restricted from entering into the alkyl chain "forest." Solutes or solvents (b) that are small enough might enter into the "forest" to interact with the silanols. (Sometimes such silanols are capped with smaller alkyl groups — however, the important aspect to note is the actuality of multiple adsorption site types for smaller molecules.) Thus the smaller molecules may experience a somewhat different porosity and slightly different dynamics (see Figure 26) than the larger molecules. Figure 25 shows a molecule (c) with an alkyl chain attached and a hydrophilic portion represented by the dashed square and shows how such a molecule would adsorb to the surface alkyl chains, with the hydrophilic portion outward. Such arrangements can effect strong binding and can modify the adsorbent characteristics if present in high concentrations (see the chapter on *catalyzed adsorption* for further discussion of this matter).

RPLC solvents must be chosen so as to "solvate" the ligands on the silica surface. For instance, if we choose pure water as solvent with no organic component, we commonly obtain "greasy patches" [34] of ligands that are due to the water molecules' energetically not being able to remain between the ligands, which then "fold up" on each other (see Figure 27). Thus it is important to keep a few percent of the organic component in the mixed solvent, which allows assumption of a constant adsorbent capacity.

Solvent Localization Models. In the previous section we assumed that all adsorbent sites are equivalent, and that no interactions occur between adsorbed solvent molecules. Little [31] reviewed apparent exceptions to this, when two or more types of adsorption sites exist on the substrate. Snyder [44,45] has called adsorption to the sites with higher reactivities (usually associated with surface silanols)

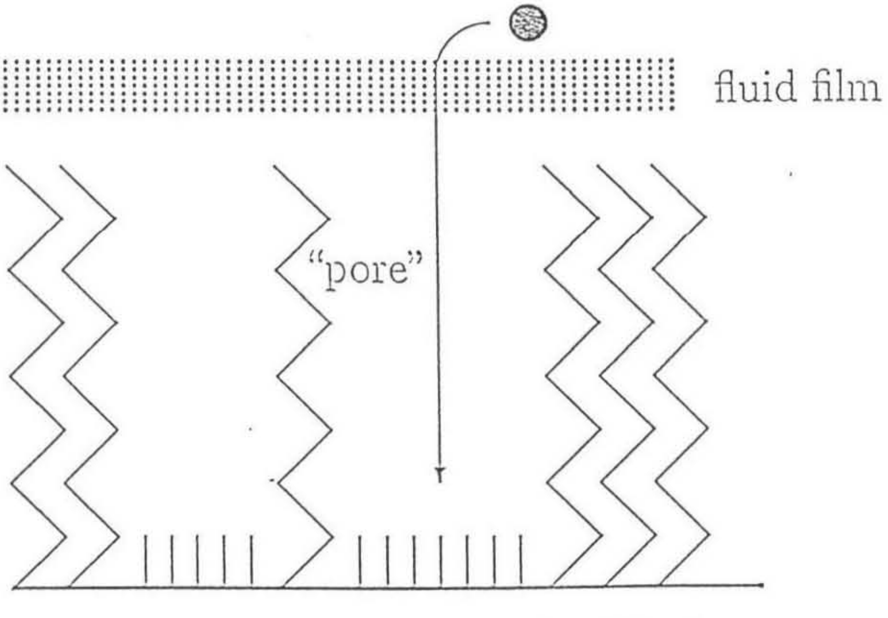

Figure 26: Dynamics of Mobile Phase Molecule.

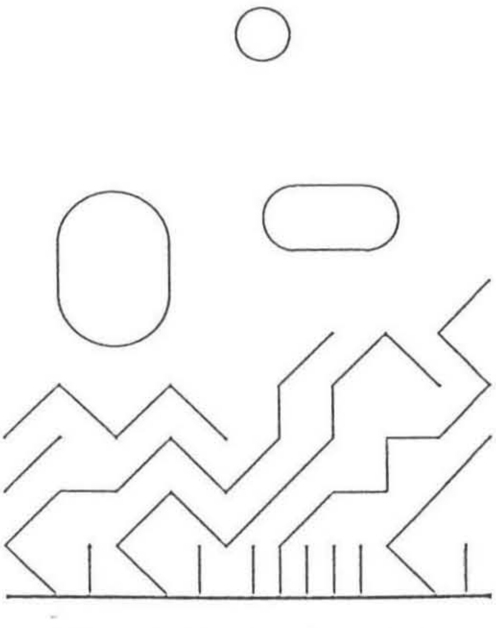

Figure 27: Unsolvated C–8 Silica.

localization.

Snyder [45] proposed a model in which one type of adsorption site exists for solvent 1, and two exist for (localizing) solvent 2. Let β_i represent the mole fraction of solvent 2 adsorbed to adsorbent site type i, the sites being present in a fraction N_i of the total number of sites. Let ψ represent the mole fraction of unadsorbed solvent 2, s the mole fraction of unadsorbed solvent 1, and b the mole fraction of adsorbed solvent 1. Snyder then proposed that when $s + \psi = 1$, $b + \beta = 1$, then $\beta = N_1\beta_1 + N_2\beta_2$, and

$$\beta_i = \frac{K_i\psi}{1 + K_i\psi}.$$

Snyder did not go further in the analysis, except to investigate the linear capacity of such a system. However, if we proceed to find the isotherm of the nonlocalizing solvent, we find

$$b = 1 - \beta = 1 - \frac{K_1N_1\psi}{1 + K_1\psi} - \frac{K_2N_2\psi}{1 + K_2\psi},$$

which gives (after some algebra)

$$b = \frac{N_1}{1 + K_1\psi} + \frac{N_2}{1 + K_2\psi} = b_1 + b_2,$$

where b_i are the "co-isotherms," which are notably *not* of Langmuir type. Thus (nonlocalizing) solvent 1 does not have the desired Langmuir isotherm.

The above difficulties with Snyder's proposal can be remedied, as will be shown, but it will be apparent that his idea that only one of the two solvents in a binary solvent system might show "localizing" behavior is erroneous.

To improve Snyder's model and take it further, assume a less approximate form for the β_i isotherms:

$$\beta_i = \frac{K_i\psi}{(K_i - 1)\psi + 1} = \frac{K_i\psi}{K_i\psi + s}.$$

An example isotherm is depicted in Figure 28, for $N_1 = .25$, $N_2 = .75$, $K_1 = 100$, and $K_2 = 2$. Note the sharp rise at low concentrations. To compare with some

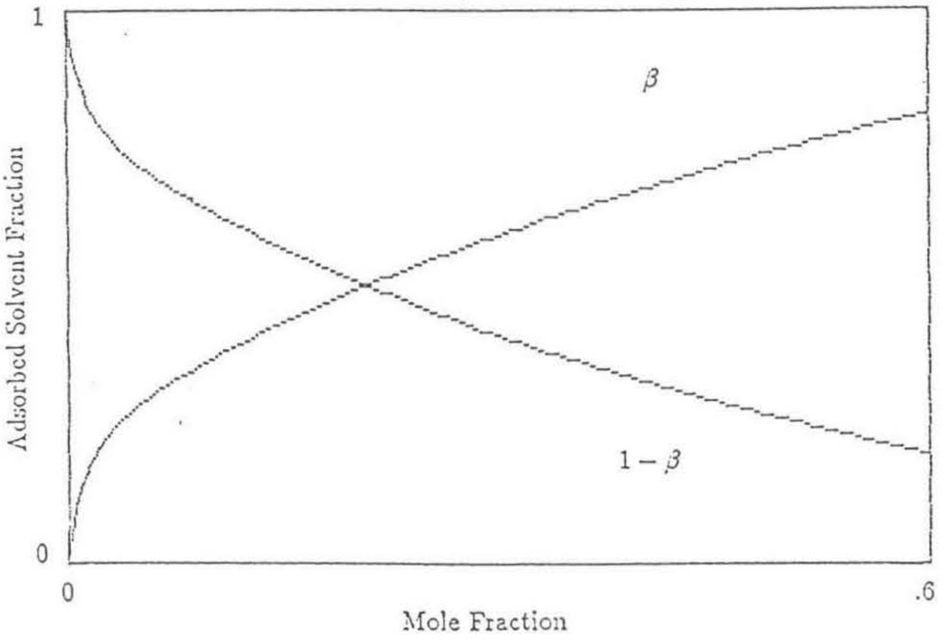

Figure 28: Complementary localizing solvent isotherms at lower mole fractions showing steepening effect.

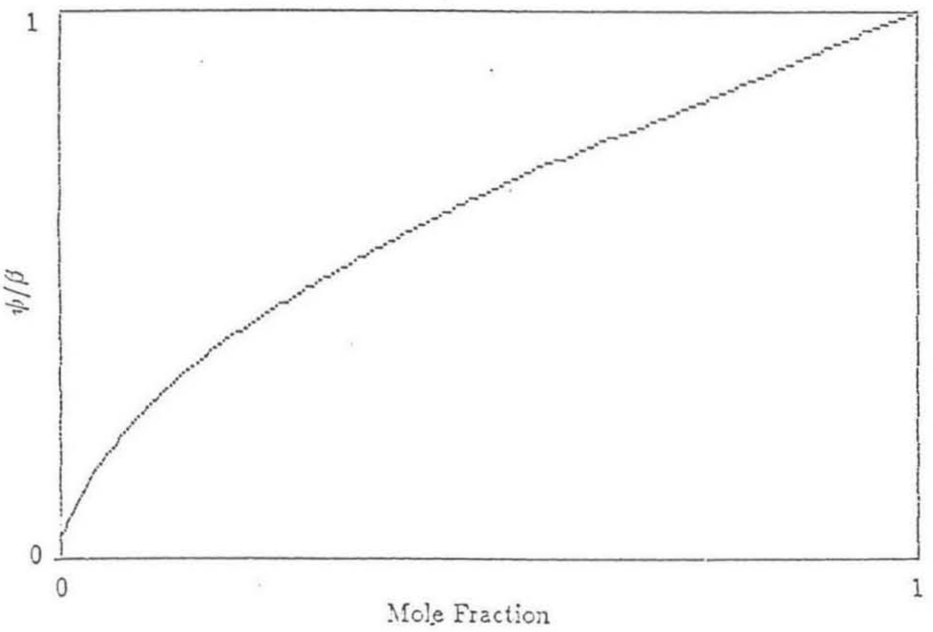

Figure 29: Non–Langmuir isotherm behavior (nonlinear) of localizing solvent showing two linear regions, at low and at high mole fractions.

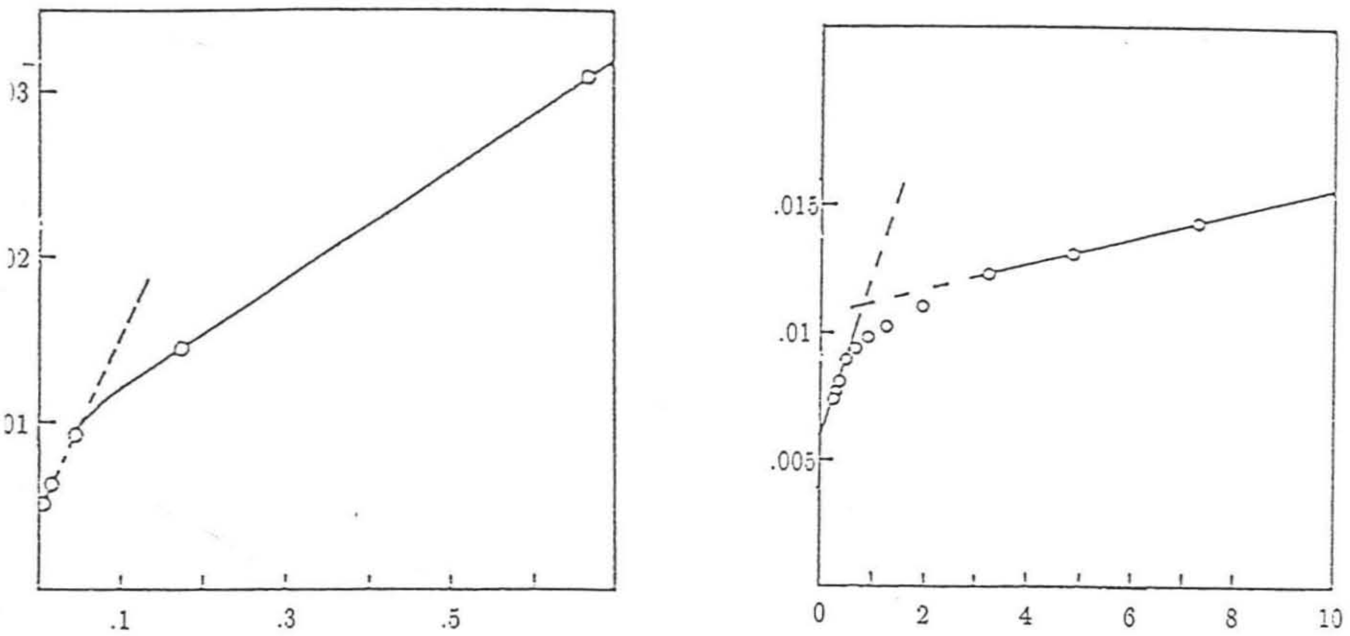

Figure 30: Experimental evidence for "hot" silanol sites: deviation from a Langmuir isotherm. Adapted from Snyder and Poppe [ ].

experimental data supposed to demonstrate localization, look at ψ/β qualitatively in Figures 29 and 30:

$$\frac{\psi}{\beta} = \frac{[1+[K_1-1]\psi]\,[1+[K_2-1]\psi]}{N_1K_1\,[1+[K_2-1]\psi] + N_2K_2\,[1+[K_1-1]\psi]}.$$

We see two regions of essentially linear behavior (instead of only one — as is the case for Langmuir-type isotherm) as the system first fills the more energetic sites according to a Langmuir scheme, and then fills the less energetic sites, also according to a (different) Langmuir scheme.

The b isotherm is calculated as

$$\begin{aligned}
b &= 1-\beta = 1 - N_1\beta_1 - N_2\beta_2 \\
&= 1 - N_1\frac{K_1\psi}{K_1\psi+s} - N_2\frac{K_1\psi}{K_1\psi+s} \\
&= \frac{(K_1\psi+s)(K_2\psi+s) - N_1K_1\psi(K_2\psi+s) - N_2K_2\psi(K_1\psi+s)}{(K_1\psi+s)(K_2\psi+s)} \\
&= \frac{[K_1K_2\psi^2 - (N_1+N_2)K_1K_2\psi^2] + (1-N_1)sK_1\psi + (1-N_2)sK_2\psi + s^2}{(K_1\psi+s)(K_2\psi+s)} \\
&= \frac{N_2sK_1\psi + N_1sK_2\psi + (N_1+N_2)s^2}{(K_1\psi+s)(K_2\psi+s)} \\
&= N_1\frac{s(K_2\psi+s)}{(K_1\psi+s)(K_2\psi+s)} + N_2\frac{s(K_1\psi+s)}{(K_1\psi+s)(K_2\psi+s)} \\
&= N_1\frac{K_1^{-1}s}{K_1^{-1}s+\psi} + N_2\frac{K_2^{-1}s}{K_2^{-1}s+\psi} \\
&= N_1\frac{K_1^{-1}s}{(K_1^{-1}-1)s+1} + N_2\frac{K_2^{-1}s}{(K_2^{-1}-1)s+1.}
\end{aligned}$$

This again is in "Langmuir form" if we look at the two terms independently, and we see each term is in the same form as the corresponding β_i except with a Langmuir reaction coefficient that is the inverse to the original. Also note that *both* solvents show the effects of localization, contrary to Snyder's thoughts. In the next section we study the effects of this solvent localization on the binding of solutes.

Note that, using the isotherm

$$\beta = N_1\frac{K_1\psi}{(K_1-1)\psi+1} + N_2\frac{K_2\psi}{(K_2-1)\psi+1}$$

to calculate $\frac{\partial \beta}{\partial t}$, we can then find the dynamical equation for ψ:

$$\frac{\partial \psi}{\partial t} + v \frac{\partial \psi}{\partial x} + \frac{1-\vartheta}{\vartheta} \frac{\partial \beta}{\partial t} = 0,$$

which becomes

$$\frac{1}{v}\Big[1 + (\frac{1-\vartheta}{\vartheta}) \frac{N_1 K_1}{[(K_1 - 1)\psi + 1]^2} + (\frac{1-\vartheta}{\vartheta}) \frac{N_2 K_2}{[(K_2 - 1)\psi + 1]^2}\Big] \frac{\partial \psi}{\partial t} + \frac{\partial \psi}{\partial x} = 0,$$

which can of course be dealt with by the method of characteristics.

Binary Solvent Modulation of Sample Retention: In Chapters 6 and (particularly) 7, we derive the equations describing how solvent concentration affects the solute retention (equilibrium reaction coefficient). For a binary solvent, we find that the equilibrium coefficient for a solute is

$$K_{sam} = \frac{q s^n}{c b^n},$$

where q, b are adsorbed solute and solvent concentrations, respectively, and c, s are unadsorbed solute and solvent concentrations, respectively, the balance equation following from the displacement reaction

$$C + n(S \cdot A) \overset{K_{sam}}{\rightleftharpoons} C \cdot (nA) + nS,$$

where A denotes an adsorption site. Thus

$$q = \Big(K_{sam} \frac{b^n}{s^n}\Big) c = K_{eff}\, c$$

and since

$$\frac{b^n}{s^n} = \Big(1 + [K_s - 1]s\Big)^{-n},$$

where K_s is the Langmuir coefficient for the solvent, we have

$$\ln(K_{eff}) = \ln(K_{sam}) - n \ln(1 + [K_s - 1]s).$$

This model can be rigorously tested against experimental data from Karger *et al.* [25], who found how n–hexanol and n–octanol retention on a C–18 bonded phase column depended on the methanol (MeOH) and acetonitrile (ACN) concentration varied in MeOH–water and ACN–water solvents, respectively. To find the parameters $K_{sam,h}$, $K_{sam,o}$, n_h, n_o, K_{MeOH}, and K_{ACN}, there is no need to do a least squares fit to obtain the outstanding curves in Figure 31. At $s = 0$ we can find $K_{sam,h} \approx 63$, $K_{sam,o} \approx 1000$. For the MeOH–water data, taking $s = 1$, we find the values for $n_h \ln(K_{MeOH})$ and $n_o \ln(K_{MeOH})$, noting at this point that $n_h/n_o \approx .75$. We make the assumption at this point that methanol $(CH_3) - OH$ and acetonitrile $(CH_3) - C \equiv CN$ are chemically the same size in the displacement of the n–hexanol and n–octanol from the adsorbent. Thus, using the ACN–water data, we find for $s = 1$ the values $n_h \ln(K_{ACN})$ and $n_o \ln(K_{ACN})$ (noting that also in this case $n_h/n_o \approx .75$). From the four values at $s = 1$, we find

$$\begin{aligned} K_{MeOH} &\approx 1.995 \\ K_{ACN} &\approx 7.872 \\ n_o &\approx 4.018 \\ n_h &\approx 3.015. \end{aligned}$$

Very interestingly, note that the ratio $n_h/n_o \approx .75$ is the same as the ratio of the number of carbon atoms in each alcohol (6/8), which is consistent with the picture of the alkyl group of the alcohol nesting into the alkyl forest of the bonded phase adsorbent. From this picture, we can predict the n_i's and $K_{sam,i}$'s for all alcohols from ethanol to n–octadecanol by interpolation and extrapolation. A more extensive analysis of this and of similar problems will appear in future papers.

Localizing Solvent Effects on Solute Retention: Assuming a solute the same size ($n = 1$) as the solvent molecules, we obtain the isotherm (as resulting

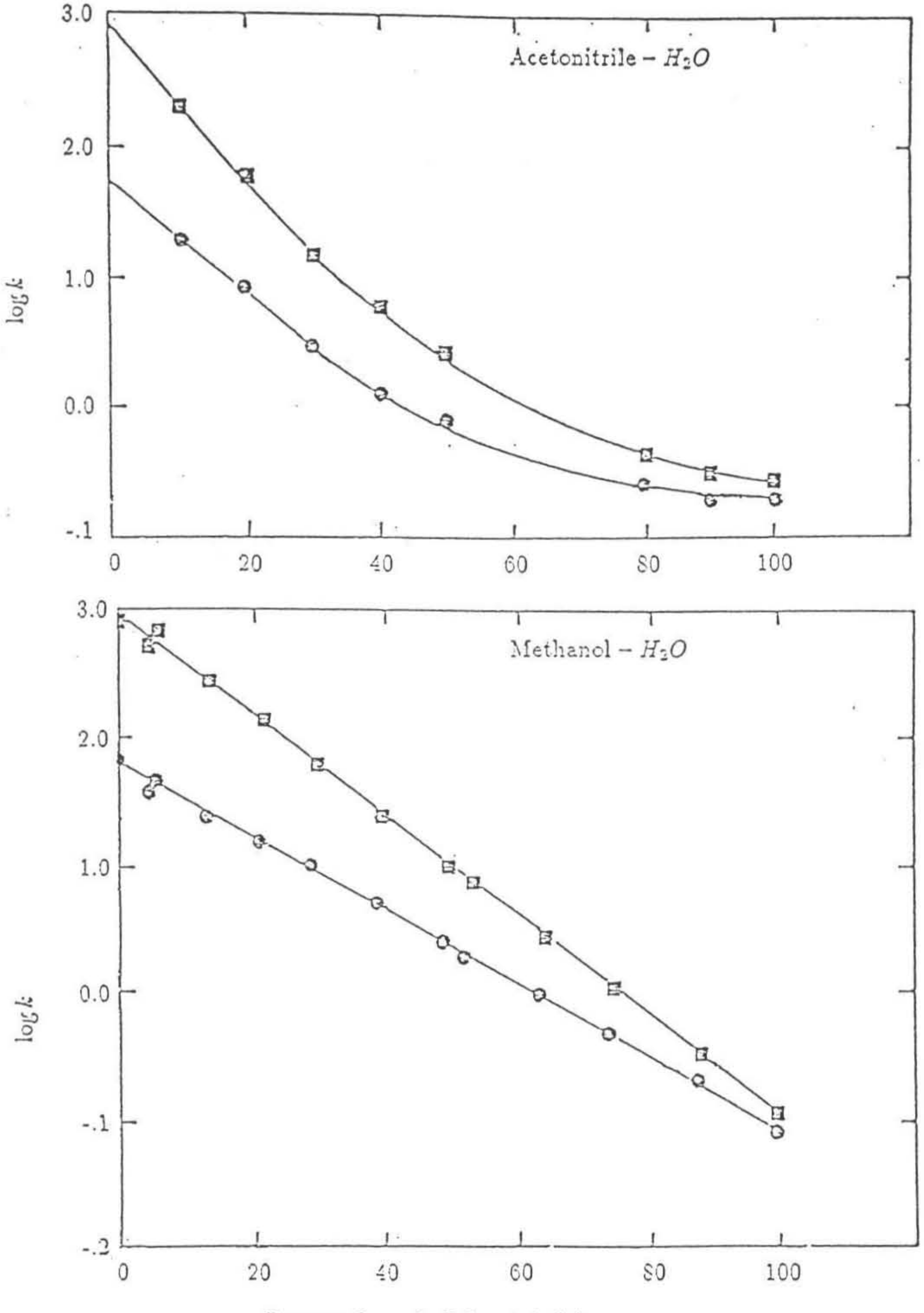

Figure 31: Experimental data from Karger *et al.* plotted against theoretical curves for two solutes (hexanol and octanol) in two different binary solvents (methanol–water and acetonitrile–water).

from a localizing solvent) as

$$K_{sam} = \frac{q\psi}{c\beta},$$

or

$$q = K_{sam}\left(\frac{\beta}{\psi}\right)c.$$

We find that

$$\frac{\beta}{\psi} = \frac{N_1 K_1 [1 + [K_2 - 1]\psi] + N_2 K_2 [1 + [K_1 - 1]\psi]}{[1 + [K_1 - 1]\psi]\,[1 + [K_2 - 1]\psi]}.$$

Thus

$$q = K_{sam}\Big[\frac{(N_1 K_1 + N_2 K_2) + N_1 K_1 [K_2 - 1]\psi + N_2 K_2 [K_1 - 1]\psi}{([K_1 - 1]\psi + 1)([K_2 - 1]\psi + 1)}\Big]c,$$

so the solute's effective reaction coefficient for the case of a binary localizing solvent is

$$K^{loc}_{eff}(\psi) = K_{sam}\Big[\frac{(N_1 K_1 + N_2 K_2) + N_1 K_1 [K_2 - 1]\psi + N_2 K_2 [K_1 - 1]\psi}{([K_1 - 1]\psi + 1)([K_2 - 1]\psi + 1)}\Big].$$

For a case where $N_1 = .25$, $N_2 = .75$, $K_1 = 100$, $K_2 = 2$, $\ln(K^{loc}_{eff}/K_{sam})$ is plotted in Figure 32.

If $n > 1$, so that several solvent molecules are displaced by one solute molecule, we obtain

$$K^{loc}_{eff}(\psi) = K_{sam}\Big[\frac{(N_1 K_1 + N_2 K_2) + N_1 K_1 [K_2 - 1]\psi + N_2 K_2 [K_1 - 1]\psi}{([K_1 - 1]\psi + 1)([K_2 - 1]\psi + 1)}\Big]^n,$$

so that

$$\ln[K^{loc}_{eff}(\psi)] = \ln(K_{sam}) + n\Big[\ln[(N_1 K_1 + N_2 K_2) + N_1 K_1 [K_2 - 1]\psi + N_2 K_2 [K_1 - 1]\psi] - \ln([K_1 - 1]\psi + 1) - \ln([K_2 - 1]\psi + 1)\Big].$$

The above example is shown again in Figure 33, except with $n = 4$.

The dynamical equation for the solute is easily found by obtaining $\partial q/\partial t$ and substituting it in the equation

$$\frac{\partial c}{\partial t} + v\frac{\partial c}{\partial x} + \frac{1-\vartheta}{\vartheta}\frac{\partial q}{\partial t} = 0.$$

An in–depth comparison with experimental data will be given in a future article.

In this chapter we have discussed binary solvents and their effects on solutes without solvent–solute binding in the mobile or stationary phases. In the next chapter higher-order solvent systems are discussed, along with the novel concept of *catalyzed adsorption,* which serves to unify notions of ion exchange and ion pairing in a form useful for the dynamical equations of chromatography under discussion.

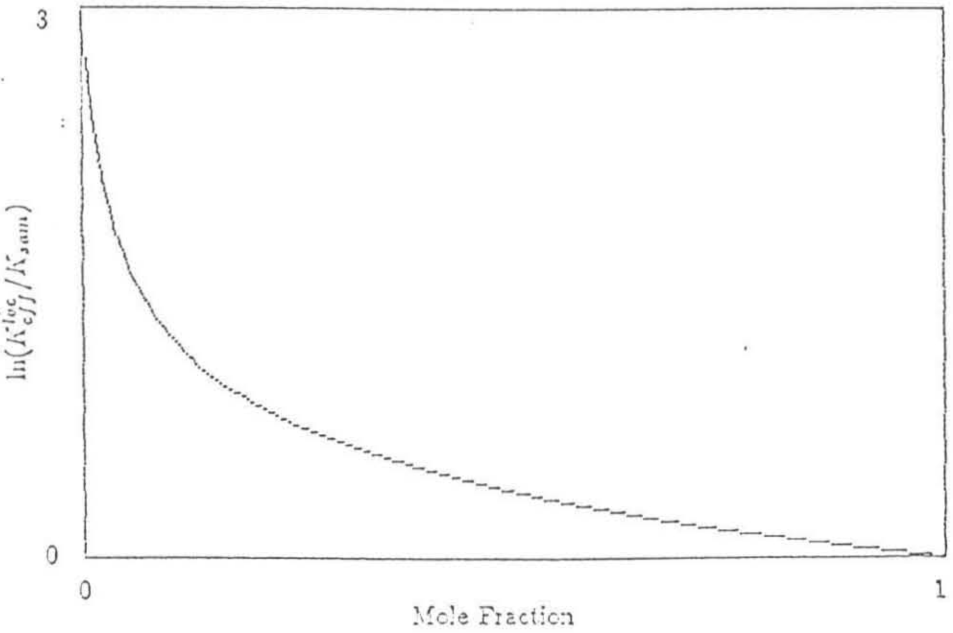

Figure 32: Effect of solvent localization on solute retention: variation with methanol mole fraction in water, $n = 1$, $N_1 = .25$, $N_2 = .75$, $K_1 = 100$, $K_2 = 2$.

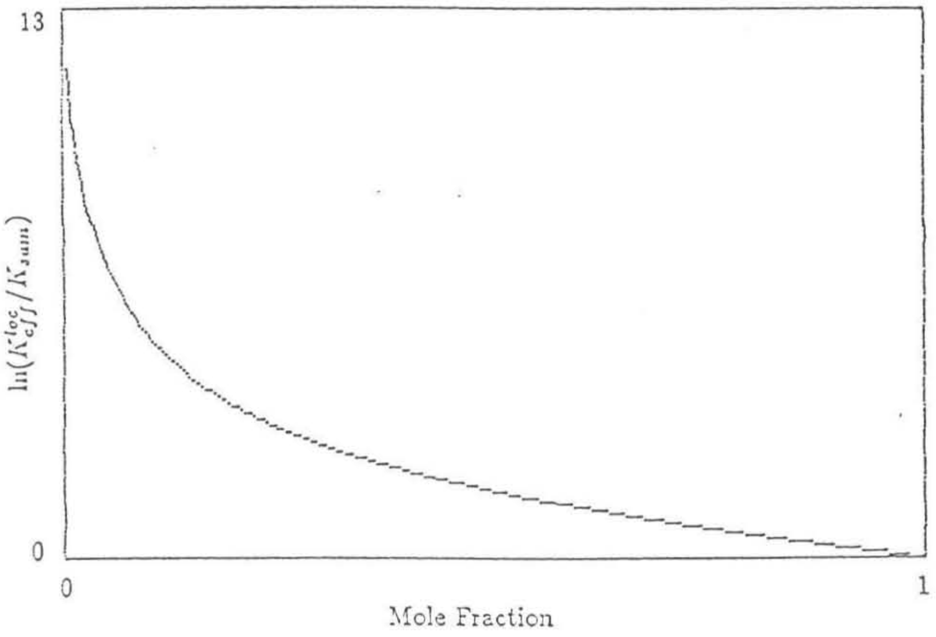

Figure 33: Effect of solvent localization on solute retention: variation with methanol mole fraction in water, $n = 4$, $N_1 = .25$, $N_2 = .75$, $K_1 = 100$, $K_2 = 2$.

CHAPTER 6

Multisolvent Systems and Catalyzed Adsorption Models

Introduction : In this chapter we will develop models for systems of more than two solvents. We note that for such systems, if we assume that solvent behavior is governed by only simple displacement effects, nothing is gained by having more than two solvents, except possibly a larger range of solvent strengths. That is, *selectivity*, or dispersion of the solutes' retention times, is not affected. In fact, for each solvent added to the system (over two), a higher-dimensional redundancy is created. Therefore, if we are to have three or more solvents in a system, we should introduce solvents that interact in chemical pathways other than simple displacement.

The following theoretical development includes new models appropriate for both normal and reversed-phase chromatography, including effects of *ion pairing*, *ion exchange*, *bases*, *acids*, *complex exchange*, and *hæteron chemistry*, all in a unified framework. All these effects are classified here under *catalyzed adsorption*, since they provide alternative chemical pathways parallel to simple displacement, either diminishing or enhancing adsorption at equilibrium. Selectivity may be enhanced by altering either the mobile phase or the stationary phase; catalyzed adsorption includes both of these options. *Localization* effects on the adsorptive surface (primarily associated with "hot" silanol sites) are discussed because of the effect on selectivity, though these effects are not classified under catalyzed adsorption.

First we will introduce multisolvent systems with simple displacement chemistry, then add in localization effects, and finally discuss catalyzed adsorption.

Though in one circumstance a less phenomenological theory exists for a particular adsorption process (Melander and Horvath's solvophobic theory for some RPLC cases [34]), we choose a level of description that can be applied to all forms of chromatography and easily integrated into the proper dynamical equations.

Multisolvent Displacement : Typically no more than three or four solvents are mixed together for a given chemical separation, so we confine the discussion to systems of that size. Assume that the different solvent molecules are of similar size, and that the volume change upon displacement (adsorption) is negligible. Then we can consider displacement to be described by simple binary reaction coefficients, expressed as ratios of mole fractions:

$$K_{ij} = \frac{b_i s_j}{s_i b_j},$$

where b_i are the adsorbed solvent species and s_i are the unadsorbed solvent species. Clearly,

$$K_{ji} = K_{ij}^{-1}, \qquad K_{ij} K_{jk} = K_{ik};$$

solving for b_i we obtain

$$b_i = \frac{s_i}{s_i + \sum_{j \neq i} K_{ji} s_j}.$$

Choosing solvent $i = 1$ to be the "weak" reference solvent (*e.g.*, water in RPLC, methylene chloride in NPLC),

$$b_i = \frac{K_{i1} s_i}{1 + \sum_{j \neq 1} [K_{j1} - 1] s_j},$$

using

$$s_1 = 1 - \sum_{j \neq 1} s_j.$$

The same form of isotherm holds for volume fractions (see Chapter 5) with different "equilibrium coefficients" $\bar{K}_{ij}$. The reference solvent is chosen such that all $K_{j1} \geq 1$;

$K_{j1} = 1$ implies that there is no difference in the displacement process between solvent j and solvent 1, and will force the $[K_{j1} - 1]s_j$ term to vanish.

Eluotropic Series : If the solvent coefficients K_{j1} are quite different, we may use three or four solvents to increase the available range of solute K_{eff} values; the K_{j1} then provide a basis for an eluotropic series of solvents.

Localization : A standard choice of NPLC solvent systems is now emerging [48], which includes two localizing solvents. Also, in RPLC we almost inevitably have to contend with silica surfaces unsaturated with hydrocarbonaceous ligand, though this effect can be largely controlled [34]. In gas chromatography, we also have similar localization problems [38]. Clearly, localization effects are important to consider. Call the two localizing solvents $i = 3$ and $i = 4$, implying that they are the two stronger (in NPLC) solvents — localizability is associated with the more polar solvents. (In RPLC, the more polar solvents are "weaker").

Suppose that there are only two types of adsorption sites, present in proportions N_1 and $N_2 = 1 - N_1$, respectively. Then for a four-component solvent system, we have

$$b_i = N_1 \frac{K_{i1}^1 s_i}{1 + \sum_{j \neq 1} [K_{j1}^1 - 1] s_j} + N_2 \frac{K_{i1}^2 s_i}{1 + \sum_{j \neq 1} [K_{j1}^2 - 1] s_j}$$

If solvents 1 and 2 are not localizing in themselves, then we require $K_{21}^1 = K_{21}^2$. Thus, when $s_4 = s_3$,

$$\begin{aligned} b_2 &= \frac{K_{21} s_2}{1 + [K_{21} - 1] s_2} \\ b_1 &= \frac{s_1}{1 + [K_{21} - 1] s_2} = \frac{s_1}{s_1 + K_{21} s_2} = \cdot \\ &= 1 - b_2 . \end{aligned}$$

These expressions must be rewritten if there is a possibility that $s_1 = 0$:

$$b_i = \frac{K_{i1} s_i}{s_1 + \sum_{j \neq 1} K_{j1} s_j}.$$

In NPLC or RPLC this is a possibility. However, the previous expression for the isotherm brings out the important aspects of the K_{ij} values.

Solvent Isotherm Effects on Solute Retention : The solute–solvent displacement

$$C + n(S \cdot A) \overset{K_{sam,1}}{\rightleftharpoons} C \cdot (nA) + nS$$

is described at equilibrium by the constant

$$K_{sam,1} = \frac{q s_1^n}{c b_1^n},$$

where we have chosen solvent 1 as the reference. Thus

$$q = K_{eff,1} c, \qquad \text{with} \qquad K_{eff,1} = K_{sam,1} \left(\frac{b_1}{s_1}\right)^n,$$

or

$$K_{eff,1} = K_{sam,1} [\sum_{i=1}^{P} N_i \{s_1 + K^i_{41} s_4 + K^i_{31} s_3 + K^i_{21} s_2\}^{-1}]^n,$$

where there are P distinct localized adsorption site types, four solvents of equal size, and the solute being discussed is the size equivalent of n solvent molecules.

Catalyzed Adsorption : A unified scheme will now be presented that includes effects of ion exchange, ion pair, and complex exchange effects on the displacement process; these effects we call *catalyzed adsorption* because they represent additional chemical pathways parallel to adsorption *via* displacement. Catalyzed adsorption can be utilized theoretically to good effect in any liquid chromatography, though ion-pair and ion-exchange chromatography are currently done in an RPLC setting.

Denote the displacement of solvent by solute as

$$C + n(S \cdot A) \overset{K_0}{\rightleftharpoons} C \cdot (nA) + nS.$$

Parallel chemical pathways can be introduced by two general means: liquid (mobile) phase solvent–solute interactions and solid (stationary) phase solvent–solute interactions, as follows. Note that the reactions are balanced with respect to the entire chemical system; though we use the same stoichiometric factor n throughout, it will in general be different at the various steps below.

$$\begin{tikzcd}
& C + 2n(S\cdot A) + nS \arrow[rr, shift left, harpoon, "K_0"] \arrow[dl, shift left, harpoon] & & C\cdot(nA) + 2nS + n(S\cdot A) \arrow[ll, shift left, harpoon] \arrow[dl, shift left, harpoon] \arrow[dr, shift left, harpoon] & \\
C\cdot(nS)+2n(S\cdot A) \arrow[ur, shift left, harpoon, "K_1"] \arrow[rr, shift left, harpoon, "K_4"] \arrow[drr, shift left, harpoon, "K_6"] & & (nS)\cdot C\cdot(nA)+n(S\cdot A)+nS \arrow[ll, shift left, harpoon] \arrow[ur, shift left, harpoon, "K_2"] \arrow[rr, shift left, harpoon, "K_5"] & & (n[S\cdot A])\cdot C\cdot(nA)+2nS \arrow[ll, shift left, harpoon] \arrow[ul, shift left, harpoon, "K_3"] \arrow[dll, shift left, harpoon] \\
& & C\cdot(n[S\cdot A])+n(S\cdot A)+nS \arrow[ull, shift left, harpoon] \arrow[urr, shift left, harpoon, "K_7"] & &
\end{tikzcd}$$

whereby we obtain the following expressions:

$$\begin{aligned}
K_0 &= \frac{qs^n}{cb^n} \\
K_1 &= \frac{c\sharp}{cs^n} \\
K_2 &= \frac{qs^n}{q\sharp} \\
K_3 &= \frac{qb^n}{q\flat} \\
K_4 &= \frac{s^n\, q\sharp}{c\sharp b^n} \\
K_5 &= \frac{s^n\, q\flat}{q\sharp b^n} \\
K_6 &= \frac{s^n\, c\flat}{c\sharp b^n} \\
K_7 &= \frac{s^n\, q\flat}{c\flat b^n},
\end{aligned}$$

where

$c\sharp =$ concentration of $C\cdot(nS)$

$c\flat =$ concentration of $C\cdot(n[S\cdot A])$

$q\sharp =$ concentration of $(nA)\cdot C\cdot(nS)$

$q\flat =$ concentration of $(nA)\cdot C\cdot(n[S\cdot A])$.

We may see that K_0 is the equilibrium coefficient associated with simple displacement, and that K_1 represents a competing pathway whereby "ion pairing" occurs in the mobile phase. From the ion–paired complex, various pathways are possible for adsorption — here we have a schematic representation showing either that the complexed solvent is adsorbed first, or that the complexed solute is adsorbed first. The more complex the shape of the solute, the more possible paths there are parallel to displacement. The total adsorbed solute A^{ip} can be written in terms of the K_i and c, the unadsorbed solute:

$$\begin{aligned} A^{ip}(s,c) &= q + q\flat + q\sharp + c\flat \\ &= K^{0}_{eff}\,[1 + (K_2^{-1} + \frac{K_6 K_1}{K_0})s^n + K_3^{-1} b^n]\,c \\ &= K^{ip}_{eff}\,c. \end{aligned}$$

Here $b = b(s)$ is the isotherm for that solvent, which may or may not be localizing; also,

$$K^{0}_{eff} = K_0\,(\frac{b}{s})^n.$$

Examples of $\log K^{ip}_{eff}$ curves are given below. We can use the alcohol series for which the K^{0}_{eff} were calculated (Chapter 5) to demonstrate how one might understand what the effective reaction coefficient would look like if methanol– catalyzed adsorption occurred along with the usual displacement reaction in methanol–water solvent. We compare these curves with the experimental curves for some phenylalanine oligomers (Figure 34), which apparently are affected by methanol–catalyzed adsorption. Note that the correction to $\ln K^{0}_{eff}$ that is due to catalyzed adsorption is

$$+\ln\Big(1 + \alpha_1 s^n + \alpha_2\,[\frac{s}{1 + [K_s - 1]s}]^n\Big),$$

where (for methanol on C–18 columns) $K_s = K_{MeOH} \approx 2$. In Figure 35 we see curves generated from the $\alpha_1 = 10$, $\alpha_2 = 0$ case, and the $\alpha_1 = 0$, $\alpha_2 = 100$ case in Figure 36. The solute isotherms are modulated by the solvent by raising $\ln(K_{eff})$ at high s values; the curve at higher s values becomes progressively more downturned (yet always monotonic) for larger α_2. A similar correction is apparent

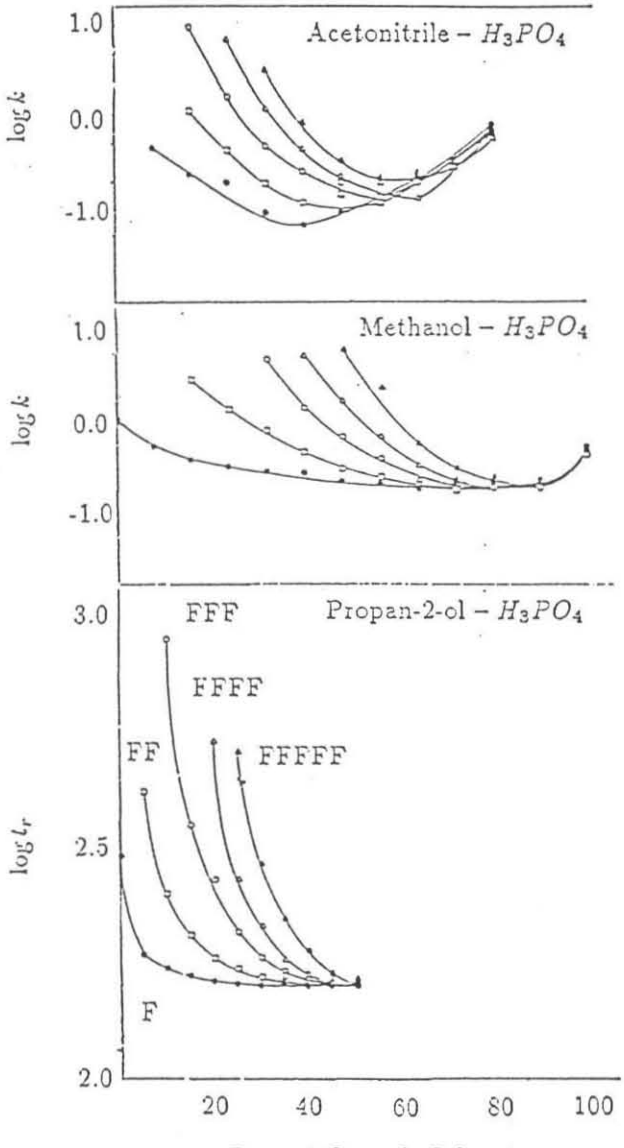

Figure 34: Retention behavior of phenylalanine oligomers on C-18 bonded phase for various indicated solvent compositions, with orthophosphoric acid modifier. The domain of solvent compositions is limited by the component miscibility of the binary solvents. Shown are data for oligomers of length 1 to 5.

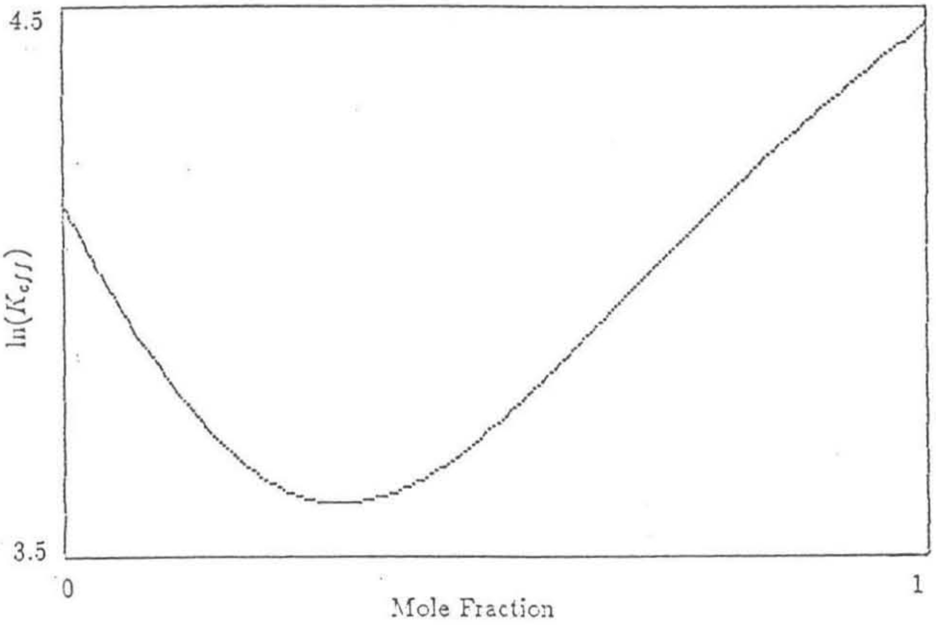

Figure 35: Effect of catalyzed adsorption on solute isotherms: variation with methanol mole fraction in water, $n = 3$, $K_{scly} = 2$, $K_{scm} = 63$, $\alpha_1 = 10$, $\alpha_2 = 0$.

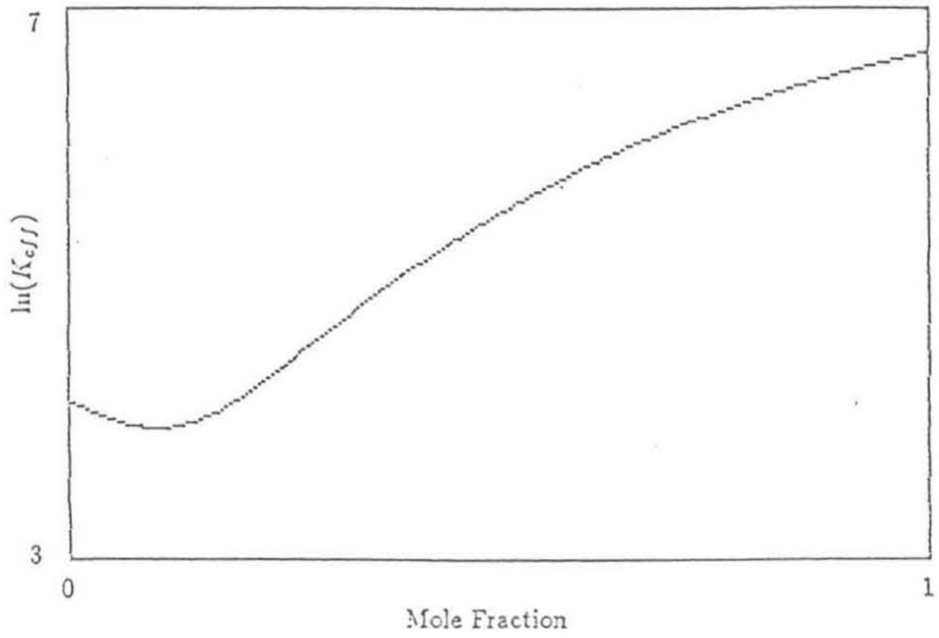

Figure 36: Effect of catalyzed adsorption on solute isotherms: variation with methanol mole fraction in water, $n = 3$, $K_{solv} = 2$, $K_{scm} = 63$, $\alpha_1 = 100$, $\alpha_2 = 0$.

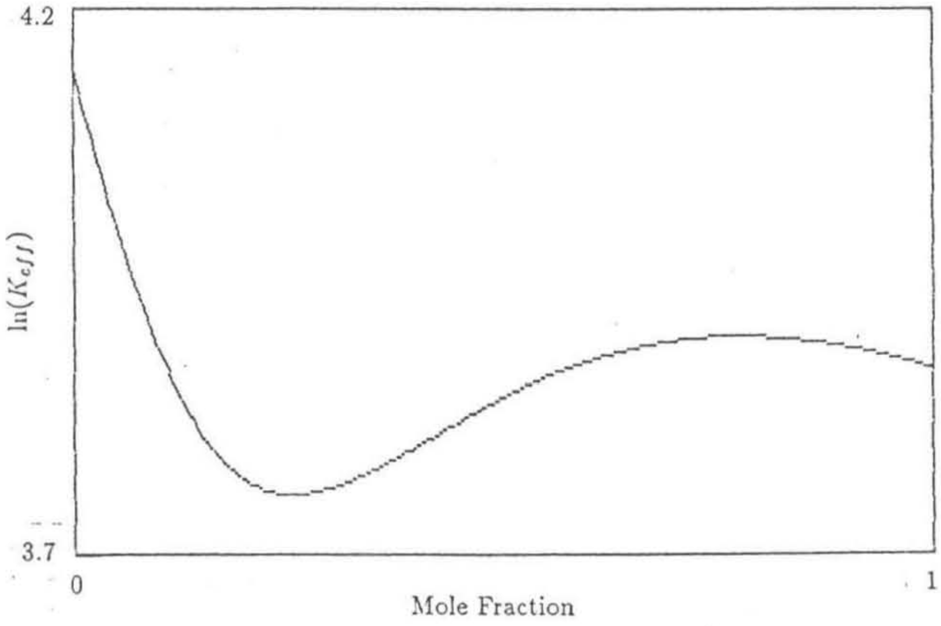

Figure 37: Effect of catalyzed adsorption on solute isotherms: variation with methanol mole fraction in water, $n = 3$, $K_{solv} = 2$, $K_{sam} = 63$, $\alpha_1 = 0$, $\alpha_2 = 40$.

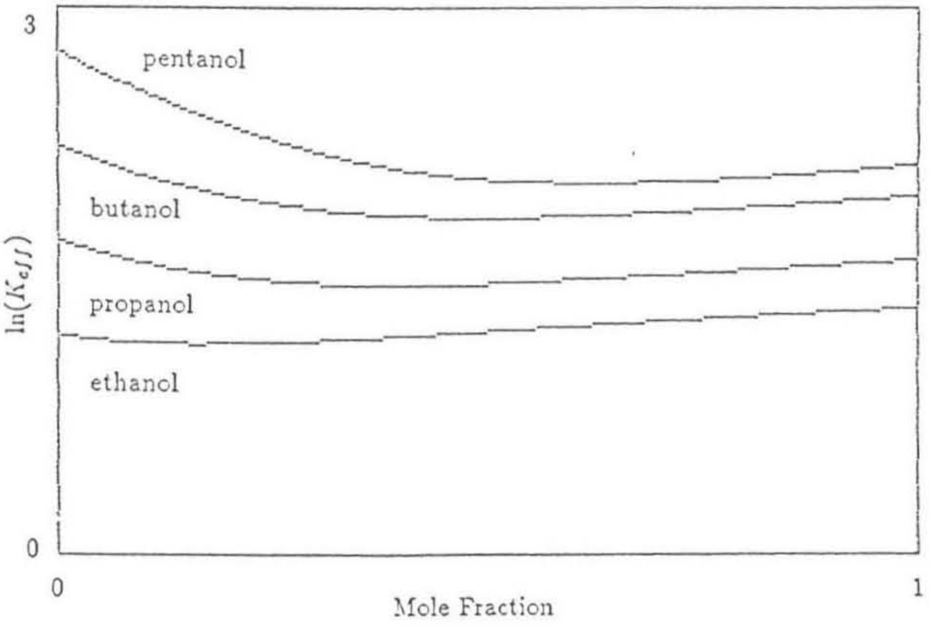

Figure 38: Effect of catalyzed adsorption on theoretical alcohol series isotherms: ethanol, propanol, butanol, and pentanol; variation with methanol mole fraction in water, $K_{solv} = 2$, $\alpha_1 = 0$, $\alpha_2 = 40$.

in Figure 37 where $\alpha_1 = 0$ and $\alpha_2 = 40$, and the alcohol series data are derived from the analysis in Chapter 5. Note that the alcohol series' curves are similar, with hypothetical catalyzed adsorption effects included, to the phenylalinine curve sets. In Figure 35 all alcohols were taken to have the same α_1 and α_2; such is unlikely, but no experimental values were available. Future papers will deal with detailed experimental data for oligomers and alcohol series; it appears that the theory holds good possibilities of explaining such curves.

For situations in which ion exchange is present parallel to displacement:

$$C + nS + 2n(S \cdot A) \overset{K_8}{\rightleftharpoons} C \cdot (n[S \cdot A]) + n(S \cdot A) + nS \overset{K_7}{\rightleftharpoons} (n[S \cdot A]) \cdot C \cdot (nA) + 2nS,$$

which gives

$$K_7 = \frac{q\flat s^n}{c\flat b^n} \qquad K_8 = \frac{c\flat}{cb^n}.$$

This in turn implies

$$\begin{aligned} A^{ie}(s,c) &= q + q\flat + c\flat \\ &= K^0_{eff}\,[1 + (\frac{K_8}{K_0})s^n + \frac{K_7 K_8}{K_0} b^n\,]\,c \\ &= K^{ie}_{eff}\,c. \end{aligned}$$

Note that A^{ie} has the same dependence on s, b that A^{ip} does, so that they are empirically indistinguishable.

In a system of four solvents, with the fourth giving catalyzed adsorption, we could have (assuming $K^i_{21} = K^j_{21}$ for every i, j, — *i.e.*, solvents 1 and 2 nonlocalizing)

$$K_{eff,1} = K_{sam,1}\,[\sum_{i=1}^{P} N_i(s_1 + K^i_{41}s_4 + K^i_{31}s_3 + K^i_{21}s_2)^{-1}]^n \cdot [1 + \alpha(K_j)s_4^n + \beta(K_j)b_4^n\,],$$

so that

$$\log K_{eff,1} = \log K^0_{eff,1} + \log[1 + \alpha(K_j)s_4^n + \beta(K_j)b_4^n\,],$$

where α and β represent appropriate functions of the equilibrium coefficients. In an optimization of resolution of a system of such solutes, we would find the dynamics of $s_j(x,t)$ to determine the equilibrium coefficients' actual values for each solute. It should be stressed that in the above catalysis schemes, various stoichiometries are possible; for simplicity it was assumed that the same stoichiometric factor n occurred in every reaction — generally, they seem to be different.

CHAPTER 7

Controlled Dynamics : Preliminaries

Introduction: There are various ways to control dynamics in chromatography, including varying solvent strength, temperature, pressure gradient, and substrate. However, the most useful and apparently effective way is to vary solvent strength through time as the sample solutes pass through the column; the next best way generally is to vary the velocity of the fluid (effected by changing the pressure drop across the length of the column.) We will focus our discussion primarily on solvent control, though in some cases in conjunction with velocity control. The idea of control is of course to arrive at a "better" or "best" separation, *via* optimization of control. In this chapter we introduce basic ideas of control of chromatographic dynamics using the simplest dynamical model. In chapter 9 we consider a thorough control model, though due to the complexity of the subject, a more complete discussion of optimization will be postponed to later papers.

Isocratic separations: Recall from the discussion in chapter 4 that the elution time for the simplest dynamical model of chromatography is given by

$$t_{b,i} = \frac{L}{V}(\vartheta + (1-\vartheta)K_i(s)) + \omega_0,$$

(where s is solvent concentration in a binary solvent mixture) which, when undimensionalized by the *experiment time* t_{exp} becomes

$$\tau_i := \frac{t_{b,i}}{t_{exp}} = \Delta(\vartheta_i + (1-\vartheta)K_i) + \delta,$$

where $\Delta = L/vt_{exp}$ and $\delta = \omega_0/t_{exp}$. This characteristic curve will be found to be essentially the same as the equation for the first moment (see chapter 9).

For a given i^{th} component, the width of its concentration pulse can be simply stated in terms of characteristic curves:

$$\omega = t_{b,i} - t_{f,i},$$

(where $t_{b,i}$ denotes the characteristic for the back of the pulse, and $t_{f,i}$ denotes the characteristic for the front of the pulse,) a constant throughout the column. Therefore the bisolute resolution $\mathcal{R}_i$ given by the difference in mean positions of two solutes divided by the sum of their individual widths is simply proportional to the difference in the mean positions:

$$\mathcal{R}_i = \frac{\Delta}{2\omega}\left([\vartheta_{i+1} - \vartheta_i] + [(1-\vartheta_{i+1})K_{i+1} - (1-\vartheta_i)K_i]\right).$$

We see that a cost function for optimization based on bisolute resolutions permits (for this model) independent adjustment of the reaction coefficient terms and Δ (the latter being usually equivalent to adjusting the mobile phase velocity since the length of the column usually is not considered variable.) This property may be used to advantage in the following way.

If we fix a desired overall experiment time (the duration of the entire chromatographic run) and then optimize (maximize) overall resolution – say

$$\mathcal{C} = \sum_i \mathcal{R}_i^2 = \frac{\Delta^2}{4\omega^2}\sum_i \left[(\theta_{i+1} - \theta_i) + [(1-\vartheta_{i+1})K_{i+1} - (1-\vartheta_i)K_i]\right]^2,$$

with respect to solvent effects on K_i, then we would obtain various $\mathcal{R}_i$ with possibly a large range of values. Thus there might be a very small value of $\min\{\mathcal{R}_i\}$. But one can rectify this by changing Δ (*i.e.* velocity or column length) so as to make the minimum resolution component comply with a desired minimum value r_i:

$$\min\{\mathcal{R}_i\} \overset{!}{=} r_i,$$

and so all other $\mathcal{R}_j$ $(j \neq i)$ scale accordingly.

One could also vary the velocity so as to make the $\mathcal{R}_i$ essentially equal once $\mathcal{C}$ is maximized. Note that for each solute, its characteristic equation is given by

$$\frac{dt}{dx} = \frac{(1-\vartheta_i)K_i + \vartheta_i}{\vartheta_i V},$$

so if $V = V(t)$, we obtain

$$\int_{t_0}^{t_i} V(t)dt = \frac{1}{\vartheta_i}\int_0^L ((1-\vartheta_i)K_i + \vartheta_i)dx = ([1-\vartheta]K_i + \vartheta_i)L.$$

One is then free to select $V(t)$, though one should limit $V(t)$ to experimentally achievable values, and indeed, well within the limits determined by acceptable dispersive effects.

Let us reconsider the cost function. If the overall experiment time is left unspecified and is optimized (along with solvent concentration) it is easily seen that for any given velocity V or solvent strength (concentration) s, longer experiment times lead to higher resolutions, so we expect the experiment time to increase without bound in an optimization (maximization) of $\mathcal{C}$. This problem might be resolved by subtracting the square of the overall experiment time from $\mathcal{C}$ and maximizing, but there is a compelling reason not to do this: there is no direct control over the minimum bisolute resolution $\min_i\{\mathcal{R}_i\}$, so it could conceivably be essentially zero. A way to handle this problem without varying the velocity (as we did above) is to introduce a new cost function which encourages the minimum resolution to be a given value; this should lead to phenomenologically better performance. To implement this thinking, we can try the new cost function

$$\hat{\mathcal{C}} = \sum_{n=1}^{M} \mathcal{R}_n^2 - M(\min_i\{\mathcal{R}_i\} - r_{min})^2,$$

where r_{min} is the specified minimum resolution, and we have weighted this objective proportionally to the number of components.

We note that the dependence of a solute reaction coefficient K_{sam} on solvent concentration s has by many researchers (*e.g.*, [43–48]) been taken to be

$$\ln(K_{sam}) = \eta - \alpha s,$$

where α and η are solute-dependent empirical parameters. However, it is well documented that this relation is only approximate (though less so for small solute molecules in aqueous methanol solvent,) and often quite inadequate. A way is now presented (also see chapter 5) to relate the effective sample reaction coefficient and s in a less empirical manner. Our model involves the assumptions that mobile phase solute-solvent interactions are negligible, the solvent is present in the system in large quantities, so as to be well into the nonlinear portion of the isotherm, and competes with the solute for adsorption sites on the substrate, following a Langmuir isotherm. We will develop the model here, where only constant solvent control is considered, but the model will be in a sense more important for the gradient control case; this is due to the fact that our model allows us to easily include the effect of solvent *dynamics* on the sample retention, including *gradient steepening,* or shock formation.

Assuming a binary solvent, the *solvent–solute* equations are, in mole fractions,

$$\left\{\begin{aligned} \vartheta s_t + V s_x + (1-\vartheta) b_t &= 0 \\ b_t = \kappa_f\left[s(1-b) - \frac{1}{K_{solv}} b(1-s)\right] &= 0 \end{aligned}\right\} \qquad \textit{(solvent equations)}$$

$$\left\{\begin{aligned} \vartheta c_t + V c_x + (1-\vartheta) q_t &= 0 \\ q_t = k_f\left[c(1-b) - \frac{1}{K_{sam}} q(1-s)\right] &= 0 \end{aligned}\right\} \qquad \textit{(solute equations)}$$

and consider the local equilibrium case $q_t = 0$, $b_t = 0$. Here $c = c(x,t)$ and $q = q(x,t)$ denote free and bound solute (respectively), and $s = s(x,t)$ and $b = b(x,t)$ denote free and bound solvent (respectively). Above we made the implicit approximations that $1-b-q \approx 1-b$, and $1-s-c \approx 1-s$. Note that only the solvent is in nonlinear quantities; the solute's second–order effects are negligible in the reaction equations due to the assumed small quantities present. We then can determine the isotherms for the solvent and the solute:

$$b = \frac{sK_{solv}}{[K_{solv}-1]s+1}$$

$$q = K_{sam}\,(\frac{1}{[K_{solv}-1]s+1})\,c.$$

Therefore an *effective reaction coefficient* K_{eff} can be defined for the solute:

$$K_{eff} := K_{sam}\,\frac{1}{[K_{solv}-1]s+1}.$$

Note that if $K_{solv}=1$ there is no dependence of K_{eff} on s, as expected since this would imply there is no effective difference between the two solvents in the system. This gives the new relation between the (effective) reaction coefficient for the solute and the solvent concentration:

$$\ln(K_{eff}) = \ln(K_{sam}) - \ln(1+[K_{solv}-1]s).$$

In the above we assumed implicitly that it took just one solvent molecule to displace one solute molecule, and *vice versa*. For the case where $n>1$ solvent molecules displace one solute molecule, which is often the case, we obtain instead

$$q_t = k_f\,[c(1-b)^n - \frac{1}{K_{sam}}q(1-s)^n\,] = 0,$$

which gives at steady state

$$q = K_{sam}\,[\frac{1-b}{1-s}]^n,$$

but since

$$b = \frac{sK_{solv}}{[K_{solv}-1]s+1}$$

we obtain

$$q = K_{sam} \left(\frac{1}{[K_{solv} - 1]s + 1}\right)^{n} c.$$

In this case, we have the relation

$$\ln(K_{eff}) = \ln(K_{sam}) - n \ln([K_{solv} - 1]s + 1).$$

If $[K_{solv} - 1]s(x,t) < 1$, this last formula is similar to the linear phenomenological model since $\ln(1+\epsilon) \sim \epsilon$ for ϵ small. For K_s large, there is a considerable discrepancy with the linear phenomenological model, but better correspondence with general experimental data (chapter 5). We take this to mean that our solvent–solute model has experimental validity. Using this new model we can include explicitly the influence of the dynamics of the solvent in the effective reaction coefficient of the solute.

We can use the simple dynamical model giving the solutes' characteristic curves, which depend on the effective reaction coefficient of the solute on the substrate, to demonstrate optimization of isocratic control. A very simple mixture of solutes is used, with effective reaction coefficients as shown in Figure 39. Assuming a constant peak width, the minimum bisolute resolutions are calculated and plotted in Figure 40. One can easily pick out the global maximum of the curve, at about $s = .3$. If one ran an experiment at this solvent concentration one obtains the optimum performance over the set of isocratic binary solvent controls, relative to the given cost function.

Gradient Control: Consider for a moment what is required in the case of a solvent gradient control. Experimental examples of solvent gradient controls applied to a test mixture of solutes is shown in Figure 41. To obtain $s(x,t)$, we need to solve

$$\vartheta \frac{\partial s}{\partial t} + V \frac{\partial s}{\partial x} + \frac{\partial}{\partial t}\left(\frac{sK_{solv}}{[K_{solv} - 1]s + 1}\right) = 0,$$

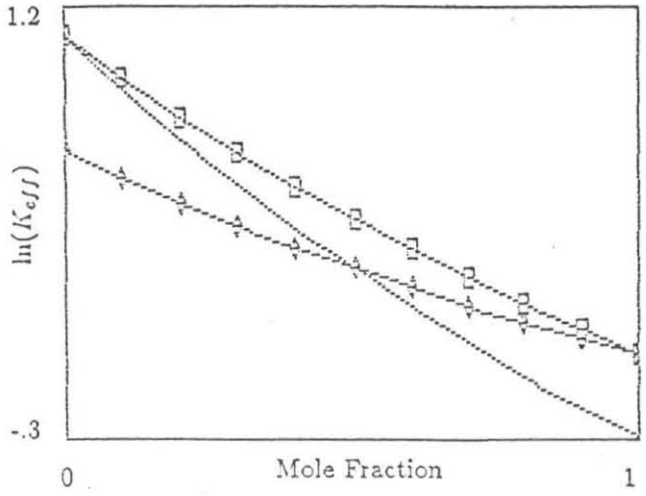

Figure 39: Modulation of reaction coefficients of three hypothetical solutes by binary solvent, for various mole fractions of reference solvent.

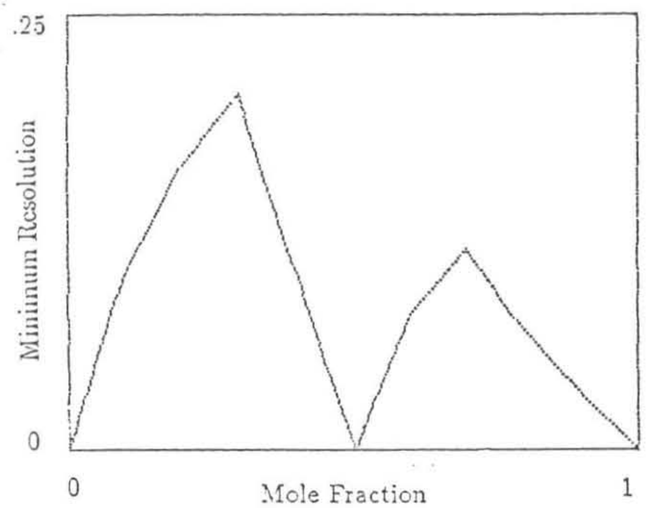

Figure 40: Minimum resolution function for three hypothetical solutes, showing local maxima at 30% and 70% reference solvent mole fraction.

or

$$\frac{1}{v}\Big[+\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{([K_{solv}-1]s+1)^2}\Big]\frac{\partial s}{\partial t}+\frac{\partial s}{\partial x}=0,$$

where v is the linear velocity. Using the method of characteristics, we obtain the set of equations

$$\frac{dt}{dx}=\frac{1}{v}+\frac{1}{v}\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{([K_{solv}-1]s+1)^2},\qquad t(0)=t_0$$
$$\frac{ds}{dx}=0,\quad s(0,t_0)=\phi(t_0)\quad \text{given.}$$

If we choose $\phi(t_0)$ to be a simple linear variation, one can solve these equations analytically. Note that we do not want the solvent gradient to develop into a shock – experimentally this results in spurious sample peaks – this corresponds mathematically to allowing only one solution to a cubic equation in the variable t_0: *i.e.,* the discriminant of the cubic must be positive.

Solvent Shock Constraints: We find the characteristic curves for the solvent are then

$$s=\text{constant}=\phi(t_0)$$
$$t(x)=\Big(\frac{1}{v}+\frac{1}{v}\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{([K_{solv}-1]\phi(t_0)+1)^2}\Big)x+t_0.$$

Shocks will form if the chosen $\phi(t_0)$ is increasing; it is important that shocks do not form inside the column: $x<L$ (see the introduction). To find the location of the shock, we describe two characteristic curves: (i) one passing through a given $t_1(0)=t_0$ and (ii) one nearby, passing through $t_2(0)=t_0+\Delta t$:

$$(i)\qquad t_1(x)=\Big(\frac{1}{v}+\frac{1}{v}\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{([K_{solv}-1]\phi(t_0)+1)^2}\Big)x+t_0$$
$$(ii)\qquad t_2(x)=\Big(\frac{1}{v}+\frac{1}{v}\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{([K_{solv}-1]\phi(t_0+\Delta t)+1)^2}\Big)x+t_0+\Delta t.$$

The envelope of intersecting characteristics is found by subtracting (i) from (ii), where we take $t_1(x^*)=t_2(x^*)$:

$$0=\frac{1-\vartheta}{\vartheta}\frac{K_{solv}}{v}\Big[\frac{1}{(1+[K_{solv}-1]\phi(t_0+\Delta t))^2}-\frac{1}{(1+[K_{solv}-1]\phi(t_0))^2}\Big]x^*+\Delta t.$$

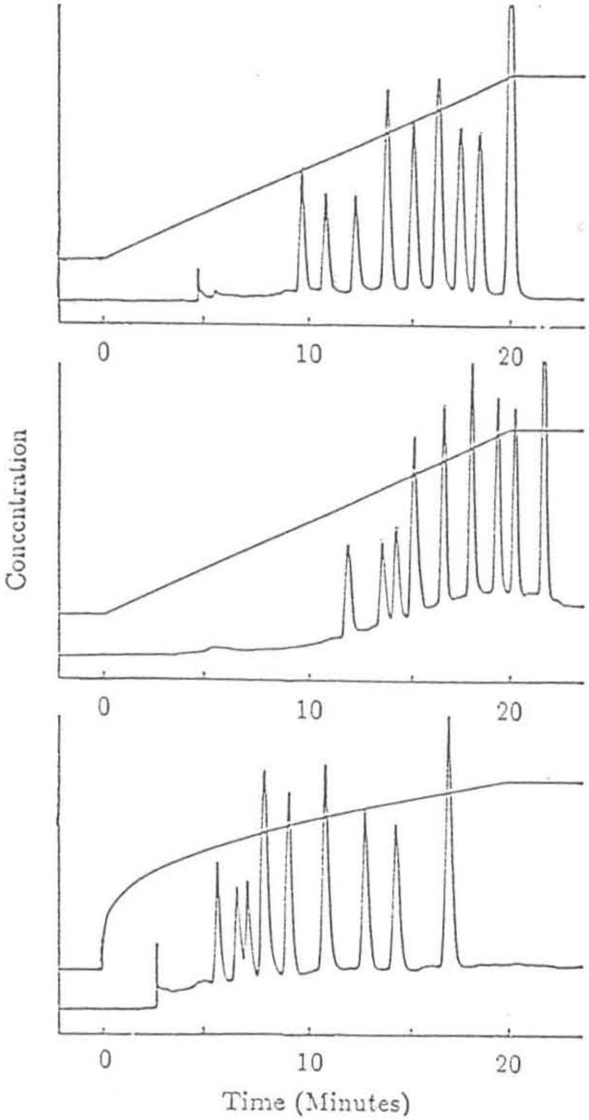

Figure 41: Test mixture separated with indicated solvent gradients. The top gradient is acetonitrile – water, and the bottom two gradients methanol – water. All gradients are from 0% to 100% organic solvent. Adapted from Schoenmakers, Billiet, and de Galan [ ].

Dividing by $\frac{1-\vartheta}{\vartheta}\frac{\Delta t K_{solv}}{v}$, we have

$$-\frac{\vartheta}{1-\vartheta}\frac{v}{K_{solv}} = \frac{1}{\Delta t}\Big[\frac{1}{(1+[K_{solv}-1]\phi(t_0+\Delta t))^2} - \frac{1}{(1+[K_{solv}-1]\phi(t_0))^2}\Big]x^*,$$

then taking the limit $\Delta t \to 0$, we obtain

$$\begin{aligned} -\frac{\vartheta}{1-\vartheta}\frac{v}{K_{solv}} &= \frac{d}{dt_0}(1+[K_{solv}-1]\phi(t_0))^{-2}x \\ &= -2x^*[K_{solv}-1]\phi'(t_0)[1+[K_{solv}-1]\phi(t_0)]^{-3} \end{aligned}$$

so that the value x^* at which the shock occurs is

$$x^* = \frac{\vartheta}{1-\vartheta}\frac{v}{2K_{solv}^2}\frac{[1+[K_{solv}-1]\phi(t_0)]^3}{\phi'(t_0)}.$$

Since the shock is not allowed inside the column, we require $x^* > L$; thus

$$\frac{[1+[K_{solv}-1]\phi(t_0)]^3}{K_{solv}^2\,\phi'(t_0)} \geq \frac{1-\vartheta}{\vartheta}\frac{2L}{v}$$

is a constraint on the choice of solvent, gradient slope, and concentration.

For example, if one chose a linear gradient

$$\phi(t_0) = \frac{\gamma_1-\gamma_0}{y_1}t_0 + \gamma_0$$

for $0 \leq t_0 \leq y_1$, the resulting constraint on the control parameters would be

$$\frac{[1+[K_{solv}-1](\frac{\gamma_1-\gamma_0}{y_1}t_0+\gamma_0)]^3}{K_{solv}^2(\frac{\gamma_1-\gamma_0}{y_1})} \geq \frac{1-\vartheta}{\vartheta}\frac{2L}{v}.$$

For such a choice in $\phi(t_0)$ we have $\phi(0) \leq \phi(t_0)$; for this choice in gradient t_0 is eliminated:

$$\frac{[1+[K_{solv}-1]\gamma_0]^3}{K_{solv}^2(\frac{\gamma_1-\gamma_0}{y_1})} \geq \frac{1-\vartheta}{\vartheta}\frac{2L}{v}.$$

Of course, the constraint is released when $\gamma_1 = \gamma_0$. Indeed, as long as ϕ is strictly monotonic in t_0, we have

$$\frac{[1+[K_{solv}-1]\phi(0)]^3}{K_{solv}^2\,\phi'_{max}} \geq \frac{1-\vartheta}{\vartheta}\frac{2L}{v},$$

or more generally

$$\frac{\left[1+[K_{solv}-1]\phi_{min}\right]^3}{K_{solv}^2\,\phi'_{max}} \geq \frac{1-\vartheta}{\vartheta}\frac{2L}{v},$$

where

$$\phi_{min} = \min_{t_0}\phi(t_0) \quad \text{and} \quad \phi'_{max} = \max_{t_0}\phi'(t_0).$$

There are some other introductory points to discuss concerning control function specification. For a linear gradient of solvent, we need to find a beginning solvent concentration γ_0 (at time $t = 0$,) the final solvent concentration γ_1, and the "gradient time" τ_1 which defines the slope of the gradient:

$$\textit{gradient slope} \quad = \quad \frac{\gamma_1 - \gamma_0}{\tau_1}$$

Let $\hat{\tau}_1$ denote the time at which the slowest solute elutes from the column. One may find a unique solvent characteristic $\tau^0(x)$ which at $x = L$ satisfies $\tau^0(L) = \hat{\tau}_1$. Call the value $\tau^0(0)$ the *control time*. For a well-defined γ_0, the sample is released into the column at $t = 0$ with simultaneous solvent concentration γ_0. For a well-defined γ_1 the gradient time should be taken to be identical to the control time:

$$\tau_1 = \tau_0(0).$$

Thus the solvent concentration that the slowest solute experiences as it elutes from the column is γ_1. Note that if $\tau_1 \neq \tau_0(0)$, γ_1 would of course *not* be the actual solvent concentration at the time of slowest solute elution, giving undesireable redundancy in the mathematical system through an ill-defined control function. Indeed, for arbitrary $\phi(t)$, one must make a similar definition as was done above for the control time.

CHAPTER 8

Perturbation Theory for Liquid Chromatography

Introduction. Perturbation theory can be applied very effectively and appropriately to HPLC models. In this chapter we cover two different developments of perturbation theory for the record, the first (Giddings' method) more of a heuristic method. The preferred development is done in chapter 9; the reader may skip to chapter 9 without loss of continuity of argument.

The reason that perturbation theory works is primarily due to the nature of modern column technology, which to a large extent prevents much sample or solvent concentration peak spreading, so one typically can express the effects from mechanisms such as intraparticle diffusion, fluid film mass transfer, and nonequilibrium reactions as perturbations of more easily solvable "equilibrium" dynamical equations. Recall that the sample solute equations are assumed linear due to the small sample concentrations, and though the solvent equations are nonlinear no solvent shocks are allowed to occur in the chromatography column, (effectively preventing spurious peak formation). Without the use of perturbation theory the controlled dynamical equations (having variable coefficients) are at best very tedious to solve and use, and apparently do not offer significant improvement over the perturbation solution. Finally, one may use representations of the perturbed solute control equations' solutions in the calculation of the "cost" functional in turn used for optimization of the control. In such a manner one has more control over peak spreading, primarily through the steepness of the solvent gradient. While kinetics, diffusion, dispersion, and fluid film mass transfer processes widen the solute peaks, solvent gradients of increasing concentration of the solvent component with larger reaction coefficient will cause the solute peak to narrow. This is a result of the rear of the solute peak experiencing a higher solvent concentration than the front, so the rear is moving faster than the front.

There are three ways we can obtain equilibrium solution perturbation terms. Giddings [11] originally found perturbation solutions for the uncontrolled linear kinetics and intraparticle diffusion cases, using a somewhat heuristic method derived from his research on flame diffusion–reaction flow systems. We review one of his solutions, extend it to the solvent–controlled case, but do not go further because the method does not suit the ultimate purpose in obtaining the perturbed equations – this will be discussed later. The other method we use in this chapter is simply from the standard perturbation techniques for partial differential equations (*e.g.* , Nayfeh [36], Kervorkian and Cole [26]), applied to the controlled dynamics equations (variable coefficients). These latter perturbed equations have not been reported before in the literature. We then show that they have a special structure which generically allows mass conservation in the system, something Giddings' resulting equations do not possess. Equations for the first two moments (peak location and width) are found, which are surprisingly simple, and allow effective optimization of the system. The third and best method, called *moment integration by parts* will be used to derive the "full" moment control equations in chapter 9.

Giddings' Method

Giddings and Hirschfelder [11,12] developed a method of determining the amount of spreading of a solute concentration pulse due to nonequilibrium effects and mass transfer. They noted that in actuality the stationary phase concentration profile lags behind that which exists at exact equilibrium, and the mobile phase concentration profile is displaced ahead of the exact equilibrium profile. That is, ahead of the center of the concentration profile the mobile phase concentration is greater than that of what would be expected at equilibrium, and behind the center of the concentration profile the mobile phase concentration is less than the equilibrium amount. Further, the rate of migration of the solute overall is proportional to the mobile phase concentration at any point. If R denotes the fraction of solute molecules in the mobile phase at equilibrium, the solute's mobile phase ahead of the profile center is actually travelling at a greater rate than Rv, where v is the linear velocity, and the mobile phase behind the center of overall concentration is travelling at a lesser rate than Rv. Thus the solute's overall concentration profile is widened, the the rate of which depends on the degree of nonequilibrium. Note that the larger v is, the more pronounced the nonequilibrium effects are.

One–site adsorption kinetics: constant solvent concentration. Though one can develop a theory for multiple types of adsorption sites, we only consider the solution process for adsorbents with a single type of adsorption site. Consider the concentration $c(x,t)$, the amount of solute per unit volume packing material, equal to the sum of solute per unit volume of column packing in the mobile phase c_m and stationary phase c_s. At complete equilibrium, we label these terms c_m^* and c_s^*. Next we introduce the "equilibrium departure" terms ϵ_m, ϵ_s *via*

$$c_m = c_m^*(1+\epsilon_m) \qquad c_s = c_s^*(1+\epsilon_s),$$

so that

$$\epsilon_m = \frac{c_m - c_m^*}{c_m^*} \qquad \epsilon_s = \frac{c_s - c_s^*}{c_s^*}.$$

We assume that $\epsilon_i << 1$. The sum of the component concentrations in both cases is c:

$$c_s + c_m = c, \qquad c_s^* + c_m^* = c, \text{ so } \quad c_s + c_m = c_s^* + c_m^*.$$

Thus

$$c_m^*(1+\epsilon_m) + c_s^*(1+\epsilon_s) = c_s^* + c_m^*,$$

$$\text{or} \qquad c_m^*\epsilon_m + c_s^*\epsilon_s = 0, \qquad \text{so that}$$

$$\epsilon_s = -\frac{c_m^*\epsilon_m}{c_s^*} = -\frac{R\epsilon_m}{1-R}.$$

Through adsorption and desorption, the rate of mass transfer between phases increases as nonequlibrium increases. For the mobile phase this rate of transfer is

$$s_m = (\frac{dc_m}{dt})_{mt},$$

the rate of increase in c_m purely due to mass transfer; thus

$$s_m = k_b c_s - k_f c_m$$

for the linear theory. At equilibrium,

$$s_m = 0 = k_b c_s - k_f c_m; \qquad c_s = c_s^*, \quad c_m = c_m^*.$$

Then

$$\begin{aligned} s_m &= k_b c_s^*(1+\epsilon_s) - k_f c_m^*(1+\epsilon_m) \\ &= (k_b c_s^* - k_f c_m^*) + k_b c_s^*\epsilon_s - k_f c_m^*\epsilon_m \\ &= k_b c_s^*\epsilon_s - k_f c_m^*\epsilon_m. \end{aligned}$$

Eliminating ϵ_s,

$$s_m = -c_m^*(k_b + k_f)\epsilon_m.$$

Then we relate s_m to flow properties. From the conservation of mass, we obtain

$$\frac{\partial c_m}{\partial \tau} = (\frac{dc_m}{dt})_{mt} + (\frac{dc_m}{dt})_{flow},$$

where

$$(\frac{dc_m}{dt})_{flow} = -v\frac{\partial c_m}{\partial x},$$

so we have

$$\begin{aligned}\frac{\partial c_m}{\partial \tau} &= s_m - v\frac{\partial}{\partial x}c_m\,, \quad \text{and}\\ s_m &= \frac{\partial c_m}{\partial \tau} + v\frac{\partial}{\partial x}c_m\\ &= [\frac{\partial c_m^*}{\partial \tau} + v\frac{\partial}{\partial x}c_m^*] + [\frac{\partial \epsilon_m c_m^*}{\partial \tau} + v\frac{\partial}{\partial x}\epsilon_m c_m^*]\\ &\approx \frac{\partial c_m^*}{\partial \tau} + v\frac{\partial}{\partial x}c_m^*,\end{aligned}$$

neglecting the terms of order ϵ_m. Now by definition, $c_m^* = Rc$, and the mass conservation equation for c is simpler; mass transfer effects leave $c = c_m + c_s$ unchanged. Thus any net gain in c in a control volume is due to influx of mobile phase:

$$\frac{\partial c}{\partial \tau} = -v\frac{\partial}{\partial x}c_m = -v\frac{\partial}{\partial x}[c_m^*(1+\epsilon_m)] \approx -v\frac{\partial}{\partial x}c_m^*.$$

But since $c_m^* = Rc$, then $R^{-1}\frac{\partial c_m^*}{\partial \tau} = \frac{\partial c}{\partial \tau}$, so we now have

$$\begin{aligned}\frac{\partial c_m^*}{\partial \tau} &\approx -Rv\frac{\partial c_m^*}{\partial \tau}; \qquad \text{thus}\\ s_m &= \frac{\partial c_m^*}{\partial \tau} + v\frac{\partial}{\partial x}c_m^*\\ &\approx -Rv\frac{\partial}{\partial x}c_m^* + v\frac{\partial}{\partial x}c_m^*\\ &= v(1-R)\frac{\partial}{\partial x}c_m^*\end{aligned}$$

Earlier it was found that

$$s_m = -c_m^*(k_f + k_b)\epsilon_m\,,$$

so now we have

$$-c_m^*(k_f + k_b)\epsilon_m = (1-R)v\frac{\partial}{\partial x}c_m^*, \quad \text{which implies}$$

$$\epsilon_m \approx -\frac{(1-R)v}{k_f + k_b}\frac{\partial}{\partial x}(\ln c_m^*).$$

(Note that ϵ_m is positive at the front of the concentration peak and negative at the back, as per the intuitive discussion earlier.)

Thus

$$\begin{aligned} c_m &= c^*_m(1+\epsilon_m) \approx c^*_m - \frac{(1-R)v}{k_f+k_b}\frac{\partial}{\partial x}c^*_m , \\ &= c^*_m - \frac{R(1-R)v}{k_b}\frac{\partial}{\partial x}c^*_m . \end{aligned}$$

The last step derives from

$$(k_f+k_b)/k_b = 1 + k_f k_b = 1 + c^*_s/c^*_m = c/c^*_m = 1/R.$$

Thus the nonequilibrium dynamics can be approximated by using only the equilibrium solution.

Adsorption kinetics: variable solvent concentration. We can also apply Giddings' method to the case where the solvent is varying, implying that k_f, k_b, and R all depend on x, t. Much of the analysis is unchanged from the previous derivations; we find that

$$\begin{aligned} s_m &= -c^*_m(k_f+k_b)\epsilon_m , \\ &= \frac{\partial c_m}{\partial \tau} + v\frac{\partial}{\partial x}c_m \\ &\approx \frac{\partial c^*_m}{\partial \tau} + v\frac{\partial}{\partial x}c^*_m , \end{aligned}$$

but now, since $c^*_m = Rc$,

$$\frac{\partial c^*_m}{\partial \tau} = \frac{\partial (Rc)}{\partial \tau} = c\frac{\partial R}{\partial \tau} + R\frac{\partial c}{\partial \tau},$$

so that

$$\frac{\partial c}{\partial \tau} = \frac{1}{R}[\frac{\partial c^*_m}{\partial \tau} - c\frac{\partial R}{\partial \tau}] = \frac{1}{R}[\frac{\partial c^*_m}{\partial \tau} - \frac{c^*_m}{R}\frac{\partial R}{\partial \tau}].$$

Hence

$$\frac{\partial c}{\partial \tau} \approx -v\frac{\partial}{\partial x}c^*_m$$

implies

$$\frac{\partial c^*_m}{\partial \tau} \approx \frac{c^*_m}{R}\frac{\partial R}{\partial \tau} - vR\frac{\partial}{\partial x}c^*_m ,$$

and so

$$s_m \approx \frac{\partial c^*_m}{\partial \tau} + v\frac{\partial}{\partial x}c^*_m \quad \text{gives}$$

$$\begin{aligned} s_m &\approx \frac{c^*_m}{R}\frac{\partial R}{\partial \tau} - vR\frac{\partial}{\partial x}c^*_m + v\frac{\partial}{\partial x}c^*_m \\ &= \frac{c^*_m}{R}\frac{\partial R}{\partial \tau} - v(1-R)\frac{\partial}{\partial x}c^*_m . \end{aligned}$$

Therefore

$$-c^*_m(k_b + k_f)\epsilon_m = s_m \approx \frac{c^*_m}{R}\frac{\partial R}{\partial \tau} - v(1-R)\frac{\partial}{\partial x}c^*_m ,$$

and so

$$\begin{aligned} \epsilon_m &\approx -\frac{1}{R(k_b + k_f)}\frac{\partial R}{\partial \tau} - \frac{(1-R)v}{k_b + k_f}\frac{\partial}{\partial x}\ln(c^*_m) \\ &= -\frac{1}{k_b)}\frac{\partial R}{\partial \tau} - \frac{R(1-R)v}{k_b}\frac{\partial}{\partial x}\ln(c^*_m), \end{aligned}$$

again using $1/(k_b + k_f) = R/k_b$. Finally,

$$c_m = c^*_m(1 + \epsilon_m) \approx c^*_m - \frac{c^*_m}{k_b}\frac{\partial R}{\partial \tau} - \frac{R(1-R)v}{k_b}\frac{\partial}{\partial x}c^*_m .$$

Since k_b, k_f depend on time through the mobile phase solvent concentration $s(x,t)$, we can use

$$\frac{\partial R}{\partial \tau} = \frac{dR}{ds}\frac{\partial s}{\partial \tau}.$$

Standard Perturbation Techniques. The equations of chromatography have been written down in previous sections, but for clarity they will be summarized here. We denote the mobile phase solute concentration by $c(x,t)$ and stationary phase sample concentration by $q(x,t)$. The mobile phase solvent concentration is denoted by $s(x,t)$ and the stationary phase solvent concentration by $b(x,t)$. Concentrations of solute and solvent internal to porous substrate particles are denoted by $\hat{c}$ and $\hat{s}$ respectively, both dependent on r, x, t.

The solute equations are

$$\begin{aligned}
\frac{1}{v}\frac{\partial c}{\partial t}+\frac{\partial c}{\partial x}+\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial}{\partial r}\hat{c}\big|_{r=R} &= \frac{D_e}{\vartheta v}\frac{\partial^2 c}{\partial x^2}\\
D_p\frac{\partial \hat{c}}{\partial r}\big|_{r=R} &= k_f\,(c-\hat{c}\big|_{r=R})\\
\beta\frac{\partial \hat{c}}{\partial t}+\frac{\partial q}{\partial t} &= D_p\nabla^2\hat{c}\\
\frac{\partial q}{\partial t} &= k_f\,(\hat{c}(1-b)-\frac{1}{K_{sam}}q(1-\hat{s}))
\end{aligned}$$

with boundary conditions

$$\begin{aligned}
\frac{\partial}{\partial r}\hat{c}\big|_{r=0} &= 0\\
c(0,t) &= \phi(t)\\
c(\cdot,t) &\in L_2(0,\infty),
\end{aligned}$$

and initial conditions

$$\begin{aligned}
c(x,0) &= 0\\
\hat{c}(x,0) &= 0\\
\hat{c}(r,x,0) &= 0\\
q(r,x,0) &= 0.
\end{aligned}$$

At equilibrium we obtain the linear isotherm

$$q=K_{eff}\,(x,t)\hat{c}.$$

(See chapter 5.) If the particles are not considered porous, the intraparticle diffusion equation is eliminated and the

$$\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{c}}{\partial r}\big|_{r=R}$$

term in the first equation is replaced by

$$\frac{1-\vartheta}{\vartheta\nu}\frac{\partial q}{\partial t}.$$

The solvent equations are (concentrations measured in mole fractions)

$$\begin{aligned}
\frac{1}{v}\frac{\partial s}{\partial t}+\frac{\partial s}{\partial x}+\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{s}}{\partial r}\Big|_{r=R} &= \frac{D_e}{\vartheta v}\frac{\partial^2 s}{\partial x^2}\\
D_p\frac{\partial \hat{s}}{\partial r}\Big|_{r=R} &= k_f\left(s-\hat{s}\big|_{r=R}\right)\\
\beta\frac{\partial \hat{s}}{\partial t}+\frac{\partial b}{\partial t} &= D_p\nabla^2\hat{s}\\
\frac{\partial b}{\partial t} &= \kappa_f\left[(1-b)s-\frac{1}{K_{sol}}b(1-s)\right]
\end{aligned}$$

with particle boundary condition $\frac{\partial \hat{s}}{\partial r}\Big|_{r=0}=0$

and initial–boundary conditions

$$\begin{aligned}
\hat{s}(r,x,t) &= s(x,t)\\
s(0,t) &= \Phi(t)\\
s(x,0) &= \quad \text{constant}\\
\hat{s}(x,0) &= \quad \text{constant.}\\
b(r,x,0) &= 0.
\end{aligned}$$

Note that, whereas K_{sam} is dependent on x and t, *via* its dependency on $s(x,t)$, K_{sol} is constant. The diffusion coefficient D_p and diffusion coefficient D_e will be in general different for solvent and each solute. At equilibrium we obtain the isotherm

$$q=\frac{K_{sol}\,\hat{s}}{[K_{sol}-1]\hat{s}+1}.$$

Again, if the particles are not considered porous, the intraparticle diffusion equation is disregarded and the

$$\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{s}}{\partial r}\Big|_{r=R}$$

term in the first equation is replaced by

$$\frac{1-\vartheta}{\vartheta\nu}\frac{\partial \hat{b}}{\partial t}.$$

These equations will now be investigated for the cases of one rate-limiting mechanism at a time. Dispersion effects will not be considered here; in chapter 9 they will be dealt with. In each solute case, the equations first will not be solved for constant K_{eff}, which solution is easily obtained from the variable K_{eff} case.

Solute Equations: equilibrium reaction, intraparticle diffusion, no fluid film mass transfer, variable K_{eff}. The continuity equation is

$$\frac{1}{v}\frac{\partial c}{\partial t}+\frac{\partial c}{\partial x}+\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{c}}{\partial r}\Big|_{r=R}=0;$$

the intraparticle diffusion equation is

$$\beta\frac{\partial \hat{c}}{\partial t}+\frac{\partial q}{\partial t}-D_p r^{-2}\frac{\partial}{\partial r}r^2\frac{\partial \hat{c}}{\partial r}=0$$

which can be written as

$$\frac{L}{v}\frac{\partial c}{\partial t}+L\frac{\partial c}{\partial x}+L\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{c}}{\partial r}\Big|_{r=R}=0,$$

$$\frac{L}{v}\beta\frac{\partial \hat{c}}{\partial t}+\frac{L}{v}\frac{\partial q}{\partial t}-\frac{L}{v}D_p r^{-2}\frac{\partial}{\partial r}r^2\frac{\partial \hat{c}}{\partial r}=0$$

or, introducing normalized variables $\tau=\frac{tv}{L}$, $\xi=x/L$, and $\varrho=r/R$,

$$\frac{\partial c}{\partial \tau}+\frac{\partial c}{\partial \xi}+\frac{3(1-\vartheta)}{\vartheta}\frac{4}{\varepsilon Pe}\frac{\partial \hat{c}}{\partial \varrho}\Big|_{\varrho=1}=0.$$

$$\frac{\partial \hat{c}}{\partial \tau}+\beta\frac{\partial q}{\partial \tau}-\frac{4}{\varepsilon Pe}\varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2\frac{\partial \hat{c}}{\partial \varrho}=0.$$

Here we have set what we call the *packing number* $\varepsilon=d_p/L$ and the *Peclet number* $Pe=\frac{vd_p}{D_p}$. We assume $q=K_{eff}\hat{c}$. We also assume $\epsilon\ll 1$, where $\epsilon=\varepsilon Pe/4$, and substitute $\hat{c}=\hat{c}_0+\epsilon\hat{c}_1+\epsilon^2\hat{c}_2+\cdots$ into the dynamical equations to find a regular perturbation series:

$$\beta\frac{\partial}{\partial \tau}(\hat{c}_0+\epsilon\hat{c}_1+\epsilon^2\hat{c}_2+\cdots)+\frac{\partial}{\partial \tau}[K_{eff}(\hat{c}_0+\epsilon\hat{c}_1+\epsilon^2\hat{c}_2+\cdots)]-$$
$$\frac{1}{\epsilon}\varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2\frac{\partial}{\partial \varrho}(\hat{c}_0+\epsilon\hat{c}_1+\epsilon^2\hat{c}_2+\cdots)=0.$$

Equating like powers of ϵ, we obtain

$$\epsilon^0 : \qquad \varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{c}_0 = 0$$

which implies that

$$\frac{\partial}{\partial\varrho}\hat{c}_0 = \frac{\lambda_0}{\varrho^2}$$

$$\frac{\partial\hat{c}_0}{\partial\varrho}\Big|_{\varrho=0} = 0 \quad \Rightarrow$$

$$\lambda_0 = 0,$$

$$\hat{c}_0 = c.$$

$$\epsilon^1 : \qquad \frac{\partial}{\partial\tau}[\beta\hat{c}_0 + K_{eff}\,\hat{c}_0] = \varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{c}_1,$$

but from the above result, $\hat{c}_0 = c$, so

$$\frac{\partial}{\partial\tau}[\beta c + K_{eff}\,c] = \varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{c}_1,$$

$$\frac{\varrho^3}{3}\frac{\partial}{\partial\tau}[\beta c + K_{eff}\,c] + \lambda_0 = \varrho^2\frac{\partial}{\partial\varrho}\hat{c}_1$$

$$\frac{\partial\hat{c}_1}{\partial\varrho}\Big|_{\varrho=0} = 0 \quad \Rightarrow$$

$$\lambda_0 = 0,$$

so that $$\frac{\varrho^2}{6}\frac{\partial}{\partial\tau}[\beta c + K_{eff}\,c] + \lambda_1 = \hat{c}_1$$

implies

$$\hat{c}_1 = \frac{\varrho^2 - 1}{6}\frac{\partial}{\partial\tau}[\beta c + K_{eff}\,c].$$

$$\epsilon^2 : \qquad \frac{\partial}{\partial\tau}[\varrho\hat{c}_1 + \beta K_{eff}\,\hat{c}_1] = \varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{c}_2.$$

or, substituting in the result for $\hat{c}_1$

$$\frac{\varrho^2 - 1}{6}\frac{\partial^2}{\partial\tau^2}[\varrho c + \beta K_{eff}\,c] = \varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{c}_2.$$

Now integrating, we obtain

$$(\frac{\varrho^5}{30}-\frac{\varrho^3}{18})\frac{\partial^2}{\partial\tau^2}[\beta c+K_{eff}\,c]+\lambda_0=\varrho^2\frac{\partial}{\partial\tau}\hat{c}_2;$$

but the boundary condition

$$\frac{\partial\hat{c}_2}{\partial\varrho}\Big|_{\varrho=0}=0$$

implies $\lambda_0=0$, so that

$$(\frac{\varrho^3}{30}-\frac{\varrho}{18})\frac{\partial^2}{\partial\tau^2}[\beta c+K_{eff}\,c]=\frac{\partial}{\partial\tau}\hat{c}_2,$$

and it is not necessary to find $\hat{c}_2$.

Evaluating the derivatives $\frac{\partial\hat{c}_i}{\partial\varrho}\big|_{\varrho=1}$, we find

$$\begin{aligned}\frac{1-\vartheta}{\vartheta}\frac{1}{\epsilon}\hat{c}\,\Big|_{\varrho=1}=&\frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon}\{0+\frac{\epsilon}{3}\frac{\partial}{\partial\tau}[\beta c+K_{eff}\,c]\\&-\frac{\epsilon^2}{45}\frac{\partial^2}{\partial\tau^2}[\beta c+K_{eff}\,c]+\ldots\},\\=&\frac{1-\vartheta}{\vartheta}[\beta\frac{\partial c}{\partial\tau}+K_{eff}\frac{\partial c}{\partial\tau}+\frac{\partial}{\partial\tau}(K_{eff}\,c)]\\-\frac{1-\vartheta}{\vartheta}\frac{\epsilon}{15}[\beta\frac{\partial^2 c}{\partial\tau^2}&+K_{eff}\frac{\partial^2 c}{\partial\tau^2}+2\frac{\partial K_{eff}}{\partial\tau}\frac{\partial c}{\partial\tau}+\frac{\partial^2 K_{eff}}{\partial\tau^2}c].\end{aligned}$$

The combination of continuity and intraparticle diffusion equations then yeilds

$$\begin{aligned}\Big[1+\frac{1-\vartheta}{\vartheta}(\beta+K_{eff}-\frac{2\epsilon}{15}\frac{\partial K_{eff}}{\partial\tau})\Big]\frac{\partial c}{\partial\tau}+\frac{\partial c}{\partial\xi}+\frac{1-\vartheta}{\vartheta}\Big[\frac{\partial K_{eff}}{\partial\tau}-\frac{\epsilon}{15}\frac{\partial^2 K_{eff}}{\partial\tau^2}\Big]c\\-\frac{1-\vartheta}{\vartheta}\frac{\epsilon}{15}[\beta+K_{eff}]\frac{\partial^2 c}{\partial\tau^2}=0.\end{aligned}$$

This form of dynamical equations indicates any pulse initial data obviously will travel while spreading. Note there seems to be a source term (the zeroth–order derivative) — however, as we soon will see, the "source" term serves to cancel the perturbed "wave velocity" and a "source" term from the diffusion. This will be clear once the special structure of the equation is seen. If we label

$$\begin{aligned}A(\xi,\tau)&=1+\frac{1-\vartheta}{\vartheta}(\beta+K_{eff}-\frac{2\epsilon}{15}\frac{\partial K_{eff}}{\partial\tau})\\B(\xi,\tau)&=\frac{1-\vartheta}{\vartheta}\frac{\epsilon}{15}[\beta+K_{eff}],\end{aligned}$$

then the dynamical equation becomes

$$A(\xi,\tau)\frac{\partial c}{\partial \tau}+\frac{\partial c}{\partial \xi}+\{\frac{\partial A}{\partial \tau}+\frac{\partial^2 B}{\partial \tau^2}\}c-B(\xi,\tau)\frac{\partial^2 c}{\partial \tau^2}=0.$$

One must retain the fundamental assumption of mass conservation; here it is not immediately clear that it is retained. It is easily shown that mass is conserved by integrating the equation throughout time, keeping in mind that the solute pulse is very narrow, so coefficients A and B are essentially constant over the nonzero portion of the pulse, located at $\tau=\tau^*(\xi)$:

$$\begin{aligned}\int_0^\infty A(\xi,\tau)\frac{\partial c}{\partial \tau}d\tau+\int_0^\infty \frac{\partial c}{\partial \xi}d\tau+\int_0^\infty \{\frac{\partial A}{\partial \tau}+\frac{\partial^2 B}{\partial \tau^2}\}c\,d\tau&\\ -\int_0^\infty B(\xi,\tau)\frac{\partial^2 c}{\partial \tau^2}d\tau&=0.\end{aligned}$$

Integrating by parts, with $0\le\xi\le1$, then

$$\begin{aligned}\int_0^\infty A(\xi,\tau)\frac{\partial c}{\partial \tau}d\tau&=[Ac]_0^\infty-\int_0^\infty \frac{\partial A}{\partial \tau}c\,d\tau\\ &\approx-\frac{\partial A}{\partial \tau}(\xi,\tau^*)\int_0^\infty c\,d\tau\\ &=-\frac{\partial A}{\partial \tau}(\xi,\tau^*)m_0.\end{aligned}$$

$$\begin{aligned}\int_0^\infty B(\xi,\tau)\frac{\partial^2 c}{\partial \tau^2}d\tau&=[B\frac{\partial c}{\partial \tau}]_0^\infty-\int_0^\infty \frac{\partial B}{\partial \tau}\frac{\partial c}{\partial \tau}d\tau\\ &=-[\frac{\partial B}{\partial \tau}c]_0^\infty+\int_0^\infty \frac{\partial^2 B}{\partial \tau^2}c\,d\tau\\ &\approx\frac{\partial^2 B}{\partial \tau^2}(\xi,\tau^*)\int_0^\infty c\,d\tau\\ &=\frac{\partial^2 B}{\partial \tau^2}(\xi,\tau^*)m_0.\end{aligned}$$

$$\begin{aligned}\int_0^\infty \frac{\partial c}{\partial \xi}d\tau&\approx\frac{\partial}{\partial \xi}\int_0^\infty c\,d\tau\\ &=\frac{\partial m_0}{\partial \xi}.\end{aligned}$$

$$\int_0^\infty \{\frac{\partial A}{\partial \tau} + \frac{\partial^2 B}{\partial \tau^2}\} c d\tau$$

$$\approx \{\frac{\partial A}{\partial \tau}(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*)\} \int_0^\infty c d\tau$$

$$= \{\frac{\partial A}{\partial \tau}(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*)\} m_0.$$

Thus the total mass satisfies

$$-\frac{\partial A}{\partial \tau}(\xi, \tau^*) m_0 + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) m_0 + \frac{\partial}{\partial \xi} m_0 + \{\frac{\partial A}{\partial \tau}(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*)\} m_0 = 0$$

or simply

$$\frac{\partial m_0}{\partial \xi} = 0,$$

so mass is clearly conserved in the dynamical equation. The location $\tau^*(\xi)$ is just the first moment: $\mu_1'(\xi) = \tau^*(\xi)$ (see appendix A for a discussion of moment techniques). Next we will determine the dynamical equations for μ_1'. Multiply the dynamical equation by τ and then integrate:

$$\int_0^\infty \tau A(\xi, \tau) \frac{\partial c}{\partial \tau} d\tau + \int_0^\infty \tau \frac{\partial c}{\partial \xi} d\tau + \int_0^\infty \tau \{\frac{\partial A}{\partial \tau} + \frac{\partial^2 B}{\partial \tau^2}\} c d\tau$$

$$- \int_0^\infty \tau B(\xi, \tau) \frac{\partial^2 c}{\partial \tau^2} d\tau = 0.$$

Integrating by parts, similar to the calculation for m_0:

$$\int_0^\infty \tau A(\xi, \tau) \frac{\partial c}{\partial \tau} d\tau = [\tau A c]_0^\infty - \int_0^\infty \frac{\partial}{\partial \tau}(\tau A) c d\tau$$

$$\approx -\frac{\partial A}{\partial \tau}(\xi, \tau^*) \int_0^\infty \tau c d\tau - A(\xi, \tau^*) \int_0^\infty c d\tau$$

$$= -\frac{\partial A}{\partial \tau}(\xi, \tau^*) m_1 - A(\xi, \tau^*) m_0.$$

$$\int_0^\infty \tau B(\xi, \tau) \frac{\partial^2 c}{\partial \tau^2} d\tau = [\tau B \frac{\partial c}{\partial \tau}]_0^\infty - \int_0^\infty \frac{\partial}{\partial \tau}(\tau B) \frac{\partial c}{\partial \tau} d\tau$$

$$= -[\frac{\partial}{\partial \tau}(\tau B) c]_0^\infty + \int_0^\infty \frac{\partial^2}{\partial \tau^2}(\tau B) c d\tau$$

$$\approx 2 \frac{\partial B}{\partial \tau}(\xi, \tau^*) \int_0^\infty c d\tau$$

$$+ \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) \int_0^\infty \tau c d\tau$$

$$= 2 \frac{\partial B}{\partial \tau}(\xi, \tau^*) m_0 + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) m_1.$$

$$\int_0^\infty \tau \frac{\partial c}{\partial \xi} d\tau \approx \frac{\partial}{\partial \xi} \int_0^\infty \tau c d\tau$$
$$= \frac{\partial m_1}{\partial \xi}.$$

$$\int_0^\infty \{ \frac{\partial A}{\partial \tau} + \frac{\partial^2 B}{\partial \tau^2} \} \tau c d\tau$$
$$\approx \{ \frac{\partial A}{\partial \tau}(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) \} \int_0^\infty \tau c d\tau$$
$$= \{ \frac{\partial}{\partial \tau} A(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) \} m_1.$$

Thus m_1 satisfies

$$-A(\xi, \tau^*) m_0 - \frac{\partial A}{\partial \tau}(\xi, \tau^*) m_1 + \frac{\partial m_1}{\partial \xi} + \{ \frac{\partial A}{\partial \tau}(\xi, \tau^*) + \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) \} m_1$$
$$- 2\frac{\partial B}{\partial \tau}(\xi, \tau^*) m_0 - \frac{\partial^2 B}{\partial \tau^2}(\xi, \tau^*) m_1 = 0$$

or simply

$$\frac{\partial m_1}{\partial \xi} = A(\xi, \tau^*) m_0 + 2\frac{\partial B}{\partial \tau}(\xi, \tau^*) m_0,$$

but $\mu_1' = m_1/m_0$ and $\tau^* = \mu_1'$, so

$$\frac{\partial \mu_1'}{\partial \xi} = A(\xi, \mu_1') + 2\frac{\partial B}{\partial \tau}(\xi, \tau^*).$$

Thus for the case where the equilibrium dynamics are perturbed by intraparticle diffusion,

$$\frac{\partial \mu_1'}{\partial \xi} = 1 + \frac{1 - \vartheta}{\vartheta}[\beta + K_{eff}(\xi, \mu_1')].$$

Next we will determine the dynamical equations for μ_2. Multiply the dynamical equation by τ^2 and then integrate:

$$\int_0^\infty \tau^2 A(\xi, \tau) \frac{\partial c}{\partial \tau} d\tau + \int_0^\infty \tau^2 \frac{\partial c}{\partial \xi} d\tau + \int_0^\infty \tau^2 \{ \frac{\partial A}{\partial \tau} + \frac{\partial^2 B}{\partial \tau^2} \} c d\tau$$
$$- \int_0^\infty \tau^2 B(\xi, \tau) \frac{\partial^2 c}{\partial \tau^2} d\tau = 0.$$

Integrating by parts,

$$\int_0^\infty \tau^2 A(\xi, \tau) \frac{\partial c}{\partial \tau} d\tau \approx -2A(\xi, \mu_1') m_1 - \frac{\partial A}{\partial \tau}(\xi, \mu_1') m_2.$$

$$\int_0^\infty \tau^2 B(\xi,\tau)\frac{\partial^2 c}{\partial\tau^2}d\tau \approx 2B(\xi,\mu_1')m_0 + 4\frac{\partial B}{\partial\tau}(\xi,\mu_1')m_1 + \frac{\partial^2 B}{\partial\tau^2}(\xi,\mu_1')m_2.$$

$$\int_0^\infty \tau^2\frac{\partial c}{\partial\xi}d\tau \approx \frac{\partial m_2}{\partial\xi}.$$

$$\int_0^\infty \{\frac{\partial A}{\partial\tau} + \frac{\partial^2 B}{\partial\tau^2}\}\tau^2 c d\tau \approx \{\frac{\partial A}{\partial\tau}(\xi,\mu_1') + \frac{\partial^2 B}{\partial\tau^2}(\xi,\mu_1')\}m_2.$$

Thus m_2 satisfies

$$\begin{aligned}-2A(\xi,\mu_1')m_1 - \frac{\partial}{\partial\tau}A(\xi,\mu_1')m_2 + \frac{\partial}{\partial\xi}m_2 + \{\frac{\partial}{\partial\tau}A(\xi,\mu_1') + \frac{\partial^2 B}{\partial\tau^2}(\xi,\mu_1')\}m_2 \\ -2B(\xi,\mu_1')m_0 - 4\frac{\partial B}{\partial\tau}(\xi,\mu_1')m_1 - \frac{\partial^2 B}{\partial\tau^2}(\xi,\mu_1')m_2 = 0,\end{aligned}$$

or simply (since $\mu_i' = m_i/m_0$)

$$\begin{aligned}\frac{\partial\mu_2'}{\partial\xi} &= 2A(\xi,\mu_1')\mu_1' + 2B(\xi,\mu_1') + 4\frac{\partial B}{\partial\tau}(\xi,\mu_1')\mu_1', \\ &= 2(A + 2\frac{\partial B}{\partial\tau})\mu_1' + 2B \\ &= 2\frac{d\mu_1'}{d\xi}\mu_1' + 2B \\ &= \frac{d}{d\xi}(\mu_1')^2 + 2B\end{aligned}$$

but $\mu_2 = \mu_2' - (\mu_1')^2$, so

$$\frac{d}{d\xi}\mu_2 = \frac{d}{d\xi}\mu_2' - \frac{d}{d\xi}(\mu_1')^2$$

implies

$$\frac{d\mu_2}{d\xi} = 2B(\xi,\mu_1').$$

For the case where the equilibrium dynamics are perturbed by intraparticle diffusion,

$$\frac{\partial\mu_2}{\partial\xi} = 2\frac{1-\vartheta}{\vartheta}\frac{\epsilon}{15}[\beta + K_{eff}] = \frac{1-\vartheta}{\vartheta}\frac{\varepsilon Pe}{30}[\beta + K_{eff}].$$

For a typical gradient solvent control, K_{eff} is monotonically decreasing — one can thus slow the growth of μ_2.

Solute Equations: nonequilibrium reaction, no diffusion or fluid film mass transfer, variable K_{eff}. Here the relevant continuity equation is

$$\frac{\partial c}{\partial \tau} + \frac{\partial c}{\partial \xi} + \frac{1-\vartheta}{\vartheta}\frac{\partial q}{\partial \tau} = 0.$$

The reaction kinetics equation is

$$\frac{\partial q}{\partial \tau} = \frac{L}{v} k_f \left[(1-b)c - \frac{1}{K_{sam}} q(1-s)\right]$$

which can be written as

$$\epsilon \frac{\partial q}{\partial \tau} = (1-b)c - \frac{1}{K_{sam}} q(1-s).$$

Where

$$\epsilon = \frac{v}{k_f L} = \frac{d_p}{L}\frac{v}{k_f d_p} = \varepsilon St_k,$$

ε is the packing number, and St_k is the kinetics Stanton number. (Recall $K_{sam} = k_f/k_b$.) We let $\tau = vt/L$ and $\xi = x/L$. Now, assuming that $\epsilon \ll 1$, we substitute $q = q_0 + \epsilon q_1 + \epsilon^2 q_2 + \cdots$ into the dynamical equations. Though this is truly a singular perturbation problem, we only consider the outer (regular) expansion, since the singular part of the q expansion is associated with initial conditions and very small times. The continuity equation gives

$$\frac{\partial c}{\partial \tau} + \frac{\partial c}{\partial \xi} + \frac{1-\vartheta}{\vartheta}\frac{\partial}{\partial \tau}(q_0 + \epsilon q_1 + \epsilon^2 q_2 + \cdots) = 0.$$

The reaction kinetics equation gives

$$\epsilon \frac{\partial}{\partial \tau}(q_0 + \epsilon q_1 + \epsilon^2 q_2 + \cdots) = (1-b)c - \frac{1}{K_{sam}}(1-s)(q_0 + \epsilon q_1 + \epsilon^2 q_2 + \cdots).$$

Equating like powers of ϵ, we obtain

$$\epsilon^0 : q_0 = \frac{(1-b)}{(1-s)} K_{sam}\, c$$

$$\epsilon^1 : \frac{\partial q_0}{\partial \tau} = -\frac{1}{K_{sam}}(1-s) q_1.$$

Combining these last two equations we obtain

$$q_1 = -\frac{K_{sam}^2}{(1-s)}\frac{\partial}{\partial\tau}[\frac{1-b}{1-s}c] = -\frac{K_{sam}}{(1-s)}\frac{\partial}{\partial\tau}[K_{eff}\,c].$$

Thus the combination of continuity and reaction equations yeilds

$$\begin{aligned}\frac{\partial c}{\partial\tau}+\frac{\partial c}{\partial\xi}+\frac{1-\vartheta}{\vartheta}\frac{\partial}{\partial\tau}\Big(&\frac{(1-b)}{(1-s)}K_{sam}\,c\\ &-\epsilon\frac{K_{sam}^2}{(1-s)}\frac{\partial}{\partial\tau}[\frac{(1-b)}{(1-s)}c]\Big)=0.\end{aligned}$$

Collecting terms,

$$\begin{aligned}&\Big(1+\frac{1-\vartheta}{\vartheta}K_{eff}-\epsilon\frac{1-\vartheta}{\vartheta}\frac{\partial}{\partial\tau}(\frac{K_{sam}}{1-s})K_{eff}-2\epsilon\frac{1-\vartheta}{\vartheta}\frac{K_{sam}}{1-s}\frac{\partial}{\partial\tau}K_{eff}\Big)\frac{\partial c}{\partial\tau}\\ &+\frac{\partial c}{\partial\xi}+\frac{1-\vartheta}{\vartheta}\Big(\frac{\partial}{\partial\tau}(K_{eff})-\epsilon\frac{\partial}{\partial\tau}(\frac{K_{sam}}{1-s})\frac{\partial}{\partial\tau}(K_{eff})-\epsilon(\frac{K_{sam}}{1-s})\frac{\partial^2}{\partial\tau^2}(K_{eff})\Big)c\\ &\qquad-\epsilon\frac{1-\vartheta}{\vartheta}(\frac{K_{sam}}{(1-s)})K_{eff}\frac{\partial^2 c}{\partial\tau^2}=0.\end{aligned}$$

This perturbed equation fits the generic equation type introduced in the last section, with

$$A(\xi,\mu_1')=1+\frac{1-\vartheta}{\vartheta}K_{eff}-\epsilon\frac{1-\vartheta}{\vartheta}\frac{\partial}{\partial\tau}(\frac{K_{sam}}{1-s})K_{eff}-2\epsilon\frac{1-\vartheta}{\vartheta}\frac{K_{sam}}{1-s}\frac{\partial}{\partial\tau}K_{eff}$$

and

$$B(\xi,\mu_1')=\epsilon\frac{1-\vartheta}{\vartheta}(\frac{K_{sam}}{(1-s)})K_{eff}$$

Thus the dynamics for $\mu_1'(\xi)$ and $\mu_2(\xi)$ can be determined with the same generic equations, which for this case are

$$\begin{aligned}\frac{\partial\mu_1'}{\partial\xi}&=1+\frac{1-\vartheta}{\vartheta}K_{eff}+\epsilon\frac{1-\vartheta}{\vartheta}K_{eff}\frac{\partial}{\partial\tau}\frac{K_{sam}}{1-s}\\ \frac{\partial\mu_2}{\partial\xi}&=2\frac{1-\vartheta}{\vartheta}\epsilon K_{eff}\frac{K_{sam}}{1-s}\end{aligned}$$

Note the location μ_1' of the concentration pulse is perturbed slightly by the kinetics. For the case of the solute being equivalent to n solvent molecules, in the above equations replace $(s-1)$ with $(s-1)^n$, and the appropriate K_{eff}.

Solvent Equations: equilibrium, intraparticle diffusion, no fluid film mass transfer. We will find the regular perturbation to the solvent equation, since the singular part only is important where the second derivative is large — *i.e.*, at shocks and "corners" of the control forcing. Recall that shocks are disallowed in the solvent profile within the column; also, with small perturbations we can do without the minimal corrections to the K_{eff} obtained by equilibrium theory entirely — the equations presented below are included just for comparison with the solute equations, and that indeed intraparticle diffusion affects the solvent also.

The continuity equation is

$$\frac{1}{v}\frac{\partial s}{\partial t}+\frac{\partial s}{\partial x}+\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{s}}{\partial r}\Big|_{r=R}=0.$$

The intraparticle diffusion equation is

$$\beta\frac{\partial \hat{s}}{\partial t}+\frac{\partial b}{\partial t}-D_p r^{-2}\frac{\partial}{\partial r}r^2\frac{\partial \hat{s}}{\partial r}=0$$

which can be written as

$$\frac{L}{v}\frac{\partial s}{\partial t}+L\frac{\partial s}{\partial x}+L\frac{3(1-\vartheta)D_p}{R\vartheta\nu}\frac{\partial \hat{s}}{\partial r}\Big|_{r=R}=0,$$

$$\frac{L}{v}\beta\frac{\partial \hat{s}}{\partial t}+\frac{L}{v}\frac{\partial b}{\partial t}-\frac{L}{v}D_p r^{-2}\frac{\partial}{\partial r}r^2\frac{\partial \hat{s}}{\partial r}=0$$

or, for $\tau=tv/L$, $\xi=x/L$, $\varrho=r/R$,

$$\frac{\partial s}{\partial \tau}+\frac{\partial s}{\partial \xi}+\frac{3(1-\vartheta)LD_p}{R^2\nu}\frac{\partial \hat{s}}{\partial \varrho}\Big|_{\varrho=1}=0.$$

$$\beta\frac{\partial \hat{s}}{\partial \tau}+\frac{\partial b}{\partial \tau}-\frac{LD_p}{vR^2}\varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2\frac{\partial \hat{s}}{\partial \varrho}=0.$$

Also, we assume

$$b=\frac{K_{sol}\hat{s}}{1+[K_{sol}-1]\hat{s}}$$

so that

$$\frac{\partial b}{\partial \tau}=\frac{K_{sol}}{(1+[K_{sol}-1]\hat{s})^2}\frac{\partial \hat{s}}{\partial \tau}.$$

Now, if $\epsilon \ll 1$, where

$$\epsilon = \frac{R^2 v}{D_p L} = \frac{1}{4}\frac{d_p}{L}\frac{d_p v}{D_p} = \frac{1}{4}\varepsilon Pe,$$

we substitute $\hat{s} = \hat{s}_0 + \epsilon \hat{s}_1 + \epsilon^2 \hat{s}_2 + \cdots$ into the dynamical equations:

$$\beta \frac{\partial}{\partial \tau}(\hat{s}_0 + \epsilon \hat{s}_1 + \epsilon^2 \hat{s}_2 + \cdots) + \frac{\partial}{\partial \tau}\Big[\frac{K_{sol}(\hat{s}_0 + \epsilon \hat{s}_1 + \epsilon^2 \hat{s}_2 + \cdots)}{1 + [K_{sol} - 1](\hat{s}_0 + \epsilon \hat{s}_1 + \epsilon^2 \hat{s}_2 + \cdots)}\Big] - \frac{1}{\epsilon}\varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2 \frac{\partial}{\partial \varrho}(\hat{s}_0 + \epsilon \hat{s}_1 + \epsilon^2 \hat{s}_2 + \cdots) = 0.$$

Equating like powers of ϵ, we obtain

$$\epsilon^0 : \qquad \varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2 \frac{\partial}{\partial \varrho}\hat{s}_0 = 0$$

which implies that $\hat{s}_0 = s$ (a constant with respect to ϱ), using the same argument as for the solute.

$$\epsilon^1 : \frac{\partial}{\partial \tau}\Big[\beta s + \frac{K_s s}{1 + [K_s - 1]s}\Big] = \varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2 \frac{\partial}{\partial \varrho}\hat{s}_1,$$

then integrating:

$$\frac{\varrho^3}{3}\frac{\partial}{\partial \tau}\Big[\beta s + \frac{K_s s}{1 + [K_s - 1]s}\Big] + \lambda_0 = \varrho^2 \frac{\partial \hat{s}_1}{\partial \varrho}$$

where λ_0 is a constant, but then the boundary condition

$$\frac{\partial \hat{s}_1}{\partial \varrho}\Big|_{\varrho = 0} = 0$$

implies $\lambda_0 = 0$, so

$$\frac{\varrho^2}{6}\frac{\partial}{\partial \tau}[\beta s + \frac{K_s s}{1 + [K_s - 1]s}] + \lambda_1 = \hat{s}_1$$

implies that (noting $\hat{s}_1 = 0$ at $\varrho = 1$)

$$\hat{s}_1 = \frac{\varrho^2 - 1}{6}\frac{\partial}{\partial \tau}[\beta s + \frac{K_s s}{1 + [K_s - 1]s}]$$

$$\epsilon^2 : \frac{\partial}{\partial \tau}[\beta s_1 + \frac{K_s s_1}{(1 + [K_s - 1]s})^2] = \varrho^{-2}\frac{\partial}{\partial \varrho}\varrho^2 \frac{\partial}{\partial \varrho}\hat{s}_2.$$

or, substituting in the result for $\hat{s}_1$,

$$\frac{\varrho^2-1}{6}\frac{\partial}{\partial\tau}\Big([\beta+\frac{K_s}{(1+[K_s-1]s)^2}]\frac{\partial}{\partial\tau}[\beta s+\frac{K_s s}{(1+[K_s-1]s)^2}]\Big)=\varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial}{\partial\varrho}\hat{s}_2.$$

Now integrating, we obtain

$$(\frac{\varrho^5}{30}-\frac{\varrho^3}{18})\frac{\partial}{\partial\tau}\Big([\beta+\frac{K_s}{(1+[K_s-1]s)^2}]\frac{\partial}{\partial\tau}[\beta s+\frac{K_s s}{(1+[K_s-1]s)^2}]\Big)+\lambda_0=\varrho^2\frac{\partial s_2}{\partial\varrho},$$

but the boundary condition

$$\frac{\partial\hat{s}_2}{\partial\varrho}\Big|_{\varrho=0}=0$$

implies $\lambda_0=0$, so

$$(\frac{\varrho^3}{30}-\frac{\varrho}{18})\frac{\partial}{\partial\tau}\Big([\beta+\frac{K_s}{(1+[K_s-1]s)^2}]\frac{\partial}{\partial\tau}[\beta s+\frac{K_s s}{(1+[K_s-1]s)^2}]\Big)=\frac{\partial}{\partial\tau}\hat{c}_2,$$

and it is not necessary to find $\hat{s}_2$.

Evaluating the derivatives $\frac{\partial\hat{s}_i}{\partial\varrho}\big|_{\varrho=1}$, we find

$$\begin{aligned}\frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon}\frac{\partial\hat{s}_i}{\partial\varrho}\Big|_{\varrho=1}=&\frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon}\Big\{0+\frac{\epsilon}{3}\frac{\partial}{\partial\tau}[\beta s+\frac{K_s s}{(1+[K_s-1]s)^2}]\\&-\frac{\epsilon^2}{45}\frac{\partial}{\partial\tau}\Big([\beta+\frac{K_s}{(1+[K_s-1]s)^2}]\frac{\partial}{\partial\tau}[\beta s+\frac{K_s s}{(1+[K_s-1]s)^2}]\Big)+\ldots\Big\},\end{aligned}$$

The combination of continuity and intraparticle diffusion equations then yeilds

$$\begin{aligned}\{1+\frac{1-\vartheta}{\vartheta}(\beta+\frac{K_s}{1+[K_s-1]s})\}\frac{\partial s}{\partial\tau}+\frac{\partial s}{\partial\xi}+\frac{4\epsilon}{15}\frac{1-\vartheta}{\vartheta}\frac{(K_s-1)K_s^2}{(1+[K_s-1]s)^5}(\frac{\partial s}{\partial\tau})^2&\\-\frac{1-\vartheta}{\vartheta}\frac{\epsilon}{15}\frac{K_s^2}{(1+[K_s-1]s)^4}\frac{\partial^2 s}{\partial\tau^2}&=0.\end{aligned}$$

Note that this is a singular perturbation problem, typical of the form of equation obtained when dispersion, fluid film mass transfer, or kinetics perturb the solvent system. It can be dealt with as a regular perturbation problem, ignoring the initial boundary layer, unless shocks are allowed in the solvent system. If shocks are disallowed, one simply uses the method of characteristics to solve the resulting hyperbolic subproblems. This will be considered at length in future papers; for most problems we simply use the unperturbed dynamics for the solvent equation, as appears in chapters 2 and 9.

CHAPTER 9

Moment Control Equations

When solvent concentrations are allowed to vary, the solute reaction coefficient can no longer be considered to be constant, so that the dynamical equations have variable coefficients. This renders Laplace transform techniques ineffectual for obtaining useful expressions for the moments. We found a method superior to Laplace Transforms for obtaining the moments from the constant coefficient equations, that can be applied effectively to the variable coefficient equations also, yielding extremely useful first–order ordinary differential equations for the moments. We will call this technique *moment integration by parts* since it relies on integration by parts of the dynamical equations, and to denote its difference from other extant techniques. Moment integration by parts is the most economical way of finding moment equations for pulsed systems. In the following development, the equilibrium reaction coefficient, diffusion coefficient, and other transfer coefficients will be considered variable, but the reader may easily see the corresponding solution for the constant coefficient case.

Central to the solution of the variable coefficient case is an understanding that coefficient variability comes from changes of solvent composition, pressure, temperature, or velocity on a much smaller time scale that the solute concentration pulse width. Therefore, one can make the very important assumption that, over the scale of the solute pulse width, the coefficients in the dynamical equations are *constant*.

The reader unacquainted with definitions of the moments and their significance to pulse analysis in chromatography is referred to appendices B and C. Also, we need to clarify some aspects of one of the dynamical equations, concerning solute adsorption kinetics modulated by solvent concentration (see also chapter 5):

$$\begin{aligned}\epsilon\frac{\partial}{\partial\tau}q &= (1-b)c - \frac{1}{K_{sam}}(1-s)q\\ &= \frac{1}{K_{sam}}(K_{eff}\,c - q)(1-s).\end{aligned}$$

Note that $\partial q/\partial\tau = 0$ when either $q = K_{eff}\,c$ (reaction is at equilibrium) or when $s = 1 \Rightarrow b = 1$ (adsorbent is saturated with the strong solvent). The latter case does not represent local equilibrium; at solvent saturation of the adsorbent the solute has no chance to adsorb. Since this is not a useful situation, we require that $s < 1$ and hence that $b < 1$. Actually, keeping in mind the approximations made in deriving the solute isotherm, we require $1 - s > c$ and $1 - b > q$. Thus it is important for the validity of our model to consider $s \le .95$. Also, in RPLC it is typically necessary to keep at least a few percent organic component in the solvent to keep the bonded phase adsorbent "solvated" (see chapter 5), so we require $s \ge .05$.

Now we proceed to derive the moment control equations. The most general form of equations considered here include solvent equilibrium modulation of the solute reaction coefficient, and perturbative spreading of the solute pulse due to reaction kinetics, interparticle and intraparticle diffusion, and fluid film mass transfer. All parameters may have dependence on solvent composition, though velocity dependence (due to changing viscosity) demands a different form of the dynamical equations (where v is not included in the independent variable), which will be treated later. The equations are (recall $\xi = x/L$, $\tau = Lt/v$, $\varrho = r/R$)

$$\frac{\partial c}{\partial\xi} + \frac{\partial c}{\partial\tau} + \frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon_p}\frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=1} - \epsilon_e\frac{\partial^2 c}{\partial\xi^2} = 0,$$

$$\text{with boundary conditions}\qquad \begin{aligned} &c(\xi,0) \equiv 0\\ &c(0,\tau) = f(\tau)\\ &c(\cdot,\tau) \in L_2(0,\infty),\end{aligned}$$

$$\beta\frac{\partial\hat{c}}{\partial\tau}+\frac{\partial q}{\partial\tau}-\frac{1}{\epsilon_p}\varrho^{-2}\frac{\partial}{\partial\varrho}\varrho^2\frac{\partial\hat{c}}{\partial\varrho}=0,$$

with boundary conditions

$$\frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=0}=0$$

$$\delta\frac{\partial\hat{c}}{\partial\varrho}\Big|_{\varrho=1}=c-\hat{c},$$

$$\epsilon_k\frac{\partial q}{\partial\tau}=(1-b)\hat{c}-\frac{1}{K_{sam}}(1-s)q.$$

The dimensionless parameters are defined by

$$\begin{aligned}\epsilon_p &= \frac{R^2v}{D_iL}=\frac{d_p^2v}{4D_iL}=\frac{1}{4}\varepsilon Pe\\ \epsilon_k &= \frac{v}{Lk_{for}}=\frac{\varepsilon}{St_k}\\ \delta &= \frac{D_i}{k_fR}=\frac{2D_i}{k_fd_p}=\frac{2}{Sh}\\ \delta\epsilon_p &= \frac{\varepsilon}{2St_f}\\ \epsilon_e &= \frac{D_eL}{V\vartheta}=\frac{\varepsilon}{\vartheta Pe_p},\end{aligned}$$

where Pe is the *Peclet number*, Sh is the *Sherwood number*, St_k is the *kinetics Stanton number*, St_f is the *fluid film mass transfer Stanton number*, Pe_p is the *packing Peclet number*, or *Bodenstein number*, and we call ε the *packing number*. Note that since D_i, v, and Pe_p vary with s, so do all of the above dimensionless quantities except ε. In HPLC, usually $\varepsilon\approx 10^{-4}$, so this limits the size of the multiplicative dimensionless quantity if perturbation technique is to be useful. In the following derivation, we use the moment notations

$$\begin{aligned}m_i'(\xi) &= \int_0^\infty \tau^i c(\xi,\tau)\,d\tau,\\ \hat{m}_i'(\xi) &= \int_0^\infty \tau^i \hat{c}(\xi,\tau)\,d\tau,\\ p_i'(\xi) &= \int_0^\infty \tau^i q(\xi,\tau)\,d\tau,\\ \mu_i'(\xi) &= \frac{m_i'(\xi)}{m_0'(\xi)}\\ \mu_2(\xi) &= \mu_2'(\xi)-(\mu_1'(\xi))^2.\end{aligned}$$

Calculation of m_0': The equation

$$\epsilon_k \frac{\partial}{\partial \tau} q = (1-b)\hat{c} - \frac{1}{K_{sam}}(1-s)q$$

gives

$$\epsilon_k \int_0^\infty \frac{\partial}{\partial \tau} q \, d\tau = \int_0^\infty (1-b)\hat{c}\, d\tau - \frac{1}{K_{sam}} \int_0^\infty (1-s) q \, d\tau.$$

Assuming s, b varying slowly over the concentration pulse for $\hat{c}$, q, and using integration by parts, this gives

$$0 = (1-b)\hat{m}_0' - \frac{1}{K_{sam}}(1-s)p_0',$$

$$\text{or} \qquad p_0' = K_{eff}\, \hat{m}_0'.$$

Then,

$$\beta \frac{\partial \hat{c}}{\partial \tau} + \frac{\partial q}{\partial \tau} - \frac{1}{\epsilon_p} \varrho^{-2} \frac{\partial}{\partial \varrho} \varrho^2 \frac{\partial \hat{c}}{\partial \varrho} = 0$$

gives through integration by parts

$$\frac{\partial}{\partial \varrho} \varrho^2 \frac{\partial}{\partial \varrho} \hat{m}_0' = 0,$$

$$\text{so that} \qquad \frac{\partial}{\partial \varrho} \hat{m}_0' = \frac{\gamma_0}{\varrho^2} \quad \Rightarrow \quad \gamma_0 = 0 \quad \text{from the boundary conditions.}$$

Thus $\hat{m}_0'$ is constant with respect to ϱ. From the fluid–film mass transfer equation, we then obtain

$$0 = \delta \frac{\partial}{\partial \varrho} \hat{m}_0' \,\Big|_{\varrho=1} = m_0' - \hat{m}_0' \,\Big|_{\varrho=1} = 0 \quad \Rightarrow \quad m_0' = \hat{m}_0'$$

for all ξ, τ. Now, from the continuity equation

$$\frac{\partial c}{\partial \xi} + \frac{\partial c}{\partial \tau} + \frac{3(1-\vartheta)}{\vartheta} \frac{1}{\epsilon_p} \frac{\partial \hat{c}}{\partial \varrho} \,\Big|_{\varrho=1} - \epsilon_e \frac{\partial^2 c}{\partial \xi^2} = 0$$

we obtain

$$\frac{dm_0'}{d\xi} - \epsilon_e \frac{d^2 m_0'}{d\xi^2} = 0,$$

$$\text{so that} \qquad \frac{dm_0'}{d\xi} = \frac{dm_0'}{d\xi}\Big|_0 \exp\left(\frac{1}{\epsilon_e}\xi\right).$$

Since $c(\cdot,\tau) \in L_2(0,\infty)$ (physically, mass is not added to the column), we must take $\frac{dm_0'}{d\xi}\big|_0 = 0$. Thus $m_0' =$ constant throughout the column (*i.e.*, for all ξ).

Calculation of m_1': The equation

$$\epsilon_k \frac{\partial}{\partial\tau} q = (1-b)\hat{c} - \frac{1}{K_{sam}}(1-s)q$$

gives

$$\epsilon_k \int_0^\infty \tau \frac{\partial q}{\partial \tau}\, d\tau = \int_0^\infty \tau(1-b)\hat{c}\, d\tau - \frac{1}{K_{sam}} \int_0^\infty \tau(1-s)q\, d\tau.$$

Assuming s, b varying slowly over the concentration pulse for $\hat{c}$, q, and using integration by parts, this gives

$$-\epsilon_k p_0' = (1-b)\hat{m}_1' - \frac{1}{K_{sam}}(1-s)p_1',$$

but since

$$p_0' = K_{eff}\,\hat{m}_0',$$

$$p_1' = \epsilon_k \frac{K_{sam} K_{eff}}{(1-s)} \hat{m}_0' + K_{eff}\,\hat{m}_1';$$

and also

$$-\beta m_0' - K_{eff}\, m_0' - \frac{1}{\epsilon_p} \varrho^{-2} \frac{\partial}{\partial\varrho} \varrho^2 \frac{\partial}{\partial\varrho} \hat{m}_1' = 0$$

which implies

$$-\epsilon_p \varrho^2 (\beta + K_{eff}) m_0' = \frac{\partial}{\partial\varrho} \varrho^2 \frac{\partial}{\partial\varrho} \hat{m}_1';$$

integrating and using the boundary conditions,

$$-\epsilon_p \frac{\varrho}{3} (\beta + K_{eff}) m_0' = \frac{\partial}{\partial\varrho} \hat{m}_1';$$

From the fluid–film mass transfer equation, we then obtain

$$\delta \frac{\partial}{\partial\varrho} \hat{m}_1' \Big|_{\varrho=1} = m_1' - \hat{m}_1' \Big|_{\varrho=1} = 0$$

which gives

$$-\delta\epsilon_p\frac{1}{3}(\beta+K_{eff})m_0' = m_1' + \epsilon_p\frac{1}{6}(\beta+K_{eff})m_0' - \gamma_1,$$

which gives the value of the constant γ_1; hence

$$\hat{m}_1' = m_1' + \delta\epsilon_p\frac{1}{3}(\beta+K_{eff})m_0' + \epsilon_p\frac{1-\varrho^2}{6}(\beta+K_{eff})m_0'$$

and so

$$\frac{\partial \hat{m}_1'}{\partial\varrho}\mid_{\varrho=1} = -\epsilon_p\frac{1}{3}(\beta+K_{eff})m_0'$$

Now, from the continuity equation we obtain

$$\frac{\partial m_1'}{\partial\xi} - m_0' + \frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon_p}\frac{\partial\hat{m}_1'}{\partial\varrho}\mid_{\varrho=1} - \epsilon_e\frac{\partial^2 m_1'}{\partial\xi^2} = 0$$

which upon substitution becomes

$$-\epsilon_e\frac{d^2 m_1'}{d\xi^2} + \frac{dm_1'}{d\xi} - m_0' + \frac{3(1-\vartheta)}{\vartheta}\frac{1}{\epsilon_p}\left[\frac{-\epsilon_p}{3}(\beta+K_{eff})\right]m_0' = 0,$$

so that we obtain an equation for μ_1':

$$\epsilon_e\frac{d^2\mu_1'}{d\xi^2} - \frac{d\mu_1'}{d\xi} + 1 + \frac{(1-\vartheta)}{\vartheta}(\beta+K_{eff}) = 0,$$

with the initial condition

$$\mu_1'(0) = \frac{1}{m_0'}\int_0^\infty \tau\phi(\tau)\,d\tau \qquad \text{given,}$$

and the initial value $\frac{d\mu_1'}{d\xi}(0)$ to be discussed momentarily.

Calculation of m_2': The equation

$$\epsilon_k\frac{\partial q}{\partial\tau} = (1-b)\hat{c} - \frac{1}{K_{sam}}(1-s)q$$

gives

$$\epsilon_k\int_0^\infty \tau^2\frac{\partial q}{\partial\tau}\,d\tau = \int_0^\infty \tau^2(1-b)\hat{c}\,d\tau - \frac{1}{K_{sam}}\int_0^\infty \tau^2(1-s)q\,d\tau.$$

Assuming s, b varying slowly over the concentration pulse for $\hat{c}$, q, and using integration by parts, this gives

$$-2\epsilon_k p_1' = (1-b)\hat{m}_2' - \frac{1}{K_{sam}}(1-s)p_2',$$

which would be used for the calculation of m_3. We found

$$p_1' = \epsilon_k \frac{K_{sam} K_{eff}}{(1-s)} \hat{m}_0' + K_{eff} \hat{m}_1';$$

using the internal diffusion equation we have

$$-2\beta \hat{m}_1' - 2p_1' - \frac{1}{\epsilon_p} \varrho^{-2} \frac{\partial}{\partial \varrho} \varrho^2 \frac{\partial}{\partial \varrho} \hat{m}_2' = 0$$

which implies (substituting for p_1' and $\hat{m}_1'$)

$$\begin{aligned} -2\epsilon_p ((\beta + K_{eff})[\varrho^2 m_1' + \epsilon_p \frac{\varrho^2 - \varrho^4}{6}(\beta + K_{eff}) m_0' + \delta \epsilon_p \frac{\varrho^2}{3}(\beta + K_{eff}) m_0'] \\ + \varrho^2 K_{eff} \epsilon_k \frac{K_{sam}}{1-s} m_0') = \frac{\partial}{\partial \varrho} \varrho^2 \frac{\partial}{\partial \varrho} \hat{m}_2'; \end{aligned}$$

integrating and using the boundary conditions,

$$\begin{aligned} -2\epsilon_p ((\beta + K_{eff})[\frac{\varrho}{3} m_1' + \epsilon_p (\frac{\varrho}{18} - \frac{\varrho^3}{30})(\beta + K_{eff}) m_0' \\ + \delta \epsilon_p \frac{\varrho}{3}(\beta + K_{eff}) m_0'] + \frac{\varrho}{3} K_{eff} \epsilon_k \frac{K_{sam}}{1-s} m_0') \frac{\partial}{\partial \varrho} \hat{m}_2'; \end{aligned}$$

We need not calculate $\hat{m}_2'$ itself, only its derivative as above.

Now, from the continuity equation we obtain

$$-\frac{\partial}{\partial \xi} m_2' + 2m_1' - \frac{3(1-\vartheta)}{\vartheta} \frac{1}{\epsilon_p} \frac{\partial}{\partial \varrho} \hat{m}_2' \mid_{\varrho = 1} + \epsilon_e \frac{\partial^2}{\partial \xi^2} m_2' = 0$$

which upon substitution becomes (also dividing by m_0'):

$$\epsilon_e \frac{d^2 \mu_2'}{d\xi^2} - \frac{d\mu_2'}{d\xi} + 2[1 + \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})] \mu_1' + F_2 = 0,$$

where F_2 is given by

$$F_2 = \frac{2}{15}\epsilon_p \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 + \frac{2}{3}\delta\epsilon_p \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 + 2\epsilon_k \frac{1-\vartheta}{\vartheta} K_{eff} \frac{K_{sam}}{1-s},$$

with the initial condition

$$\mu'_2(0) = \frac{1}{m'_0}\int_0^\infty \tau^2 \phi(\tau)\, d\tau \qquad \text{given,}$$

and the initial value $\frac{d\mu'_2}{d\xi}(0)$ to be discussed momentarily.

We now have, for each solute, equations for the moments μ'_1 and μ'_2, which will ultimately yeild the position and width of each solute's associated concentration pulse:

$$\epsilon_e \frac{d^2\mu'_1}{d\xi^2} - \frac{d\mu'_1}{d\xi} + F_1 = 0,$$

$$\epsilon_e \frac{d^2\mu'_2}{d\xi^2} - \frac{d\mu'_2}{d\xi} + 2F_1\mu'_1 + F_2 = 0,$$

where

$$F_1 = 1 + \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})$$

and F_2 is given as before. The F_i terms may be considered forcing in these second–order equations, determined by the solvent and system constants. These equations can be reduced to first–order differential equations by precluding nonphysical exponential growth (from the condition $c(\cdot,\tau) \in L_2(0,\infty)$). This is done similarly as in the solution to m'_0; we simply choose the values of the initial conditions appropriately. Integrating the equation for μ'_1 once, we obtain

$$\frac{d\mu'_1}{d\xi} = \exp(\frac{\xi}{\epsilon_e})[-\frac{1}{\epsilon_e}\int_0^\xi \exp(-\frac{\xi}{\epsilon_e})F_1\, d\xi + \eta_1].$$

Integrating by parts, we obtain

$$\frac{d\mu'_1}{d\xi} = \exp(\frac{\xi}{\epsilon_e})[\eta_1 - F_1(0) - \epsilon_e\frac{dF_1}{d\xi}(0) - \epsilon_e^2\frac{d^2F_1}{d\xi^2}(0) - \cdots - \epsilon^n\int_0^\xi \exp(-\frac{\xi}{\epsilon_e})\frac{d^nF_1}{d\xi^n}d\xi + \exp(-\frac{\xi}{\epsilon_e})(F_1(\xi) + \epsilon_e\frac{dF_1}{d\xi}(\xi) + \epsilon_e^2\frac{d^2F_1}{d\xi^2}(\xi) + \cdots)].$$

Choosing the previously undetermined derivative initial condition to be

$$\eta_1 = \frac{d\mu_1'}{d\xi}(0) = [\sum_{i=0} (\epsilon_e \frac{d}{d\xi})^i F_1]_{\xi=0},$$

the exponential behavior of μ_1' is eliminated, and now we have

$$\frac{d\mu_1'}{d\xi} = F_1(\xi) + \epsilon_e \frac{dF_1}{d\xi}(\xi) + \cdots.$$

(Note: if solvent concentration s is increasing in time, it is decreasing in space, so K_{eff} is increasing in space, as is F_1. Thus the solute is slowed by a very small amount.) Assuming $\epsilon_e \ll 1$, we approximate:

$$\frac{d\mu_1'}{d\xi} \approx F_1(\xi).$$

This is the appropriate dynamical equation for μ_1', and now we can more easily find the associated dynamical equation for

$$\mu_2 = \mu_2' - (\mu_1')^2,$$

since from this identity

$$\frac{d\mu_2}{d\xi} = \frac{d\mu_2'}{d\xi} - 2\mu_1' \frac{d\mu_1'}{d\xi} \approx \frac{d\mu_2'}{d\xi} - 2\mu_1' F_1.$$

The equation for μ_2' can likewise be reduced to a first-order differential equation; using precisely the same kind of argument as for the μ_1' equation, we obtain

$$\frac{d\mu_2'}{d\xi} = 2F_1\mu_1' + F_2 + \epsilon_e \frac{d}{d\xi}(2F_1\mu_1' + F_2) + \cdots$$

with initial condition

$$\frac{d\mu_2'}{d\xi}(0) = 2F_1(0)\mu_1'(0) + F_2(0) + \epsilon_e \frac{d}{d\xi}(2F_1\mu_1' + F_2)\,|_{\xi=0} + \cdots$$

so, dropping the smaller-order terms, we have finally the approximate equation

$$\frac{d\mu_2'}{d\xi} \approx 2F_1\mu_1' + F_2 + \epsilon_e \frac{d}{d\xi}(2F_1\mu_1'),$$

and hence the approximate equation for the "variance" term μ_2 is

$$\begin{aligned}\frac{d\mu_2}{d\xi} &\approx F_2 + 2\epsilon_e(\mu_1' \frac{dF_1}{d\xi} + F_1 \frac{d\mu_1'}{d\xi}) \\ &= F_2 + 2\epsilon_e \mu_1' \frac{dF_1}{d\xi} + 2\epsilon_e F_1^2.\end{aligned}$$

The final set of approximate equations for each solute are thus

$$\begin{aligned}\frac{d\mu_1'}{d\xi} &= 1 + \frac{(1-\vartheta)}{\vartheta}(\beta + K_{eff}) \\ \frac{d\mu_2}{d\xi} &= \frac{2}{15}\epsilon_p \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 + \frac{2}{3}\delta\epsilon_p \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 \\ &\quad + 2\epsilon_k \frac{1-\vartheta}{\vartheta} K_{eff} \frac{K_{sam}}{1-s} + 2\epsilon_e \mu_1' \frac{1-\vartheta}{\vartheta} \frac{\partial K_{eff}}{\partial \xi} + 2\epsilon_e (1 + \frac{1-\vartheta}{\vartheta}(\beta + K_{eff}))^2.\end{aligned}$$

The last term in the expression for $d\mu_2/d\xi$ contains the factor $dK_{eff}/d\xi$, which will be negative for the typical solvent gradient, and hence will reduce the growth of the peak width. In fact, in the absence of dominating peak width growth parameters ϵ_p, ϵ_e, ϵ_k, or δ, the width will actually narrow under the influence of a solvent gradient. Such an effect in experiment has long been acknowledged.

In terms of standard dimensionless variables as reviewed earlier this chapter, we have

$$\begin{aligned}\frac{d\mu_2}{d\xi} &= \frac{1}{30}\varepsilon Pe \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 + \frac{\varepsilon}{3St_f} \frac{1-\vartheta}{\vartheta}(\beta + K_{eff})^2 \\ &\quad + 2\frac{\varepsilon}{St_k} \frac{1-\vartheta}{\vartheta} K_{eff} \frac{K_{sam}}{1-s} + \frac{2}{\vartheta} \frac{\varepsilon}{Pe_p} \Big[\mu_1' \frac{1-\vartheta}{\vartheta} \frac{\partial K_{eff}}{\partial \xi} + (1 + \frac{1-\vartheta}{\vartheta}(\beta + K_{eff}))^2\Big].\end{aligned}$$

If, as generally happens in RPLC, the linear velocity v is variable, we go back to dimensional moments

$$\tilde{\mu}_1' = \frac{L}{v}\mu_1' \qquad \text{and} \qquad \tilde{\mu}_2 = (\frac{L}{v})^2 \mu_2.$$

The expressions for $d\mu_1'/d\xi$ and $d\mu_2/d\xi$ may be used to find directly the dynamics of the *Height Equivalent to a Theoretical Plate* (HETP – see appendix C) for a given solute:

$$\begin{aligned}H &:= \frac{\mu_2 L}{(\mu_1')^2} \\ \frac{dH}{d\xi} &= \frac{L}{(\mu_1')^2}\frac{d\mu_2}{d\xi} - 2\frac{\mu_2 L}{(\mu_1')^3}\frac{d\mu_1'}{d\xi}.\end{aligned}$$

The HETP has been used classically to characterize the "efficiency" of columns – the smaller the HETP, the more "efficient" the column. Define the *normalized HETP* as $\hat{H} = H/L$ and the *reduced HETP* as $h = \hat{H}/\varepsilon = H/d_p$. For the constant–parameter case, the reduced HETP is

$$\frac{1}{\varepsilon}H(1) = \frac{2}{\vartheta Pe_p} + \frac{1-\vartheta}{\vartheta}\Big(\frac{\beta + K_{eff}}{1 + \frac{1-\vartheta}{\vartheta}[\beta + K_{eff}]}\Big)^2 \Big[\frac{1}{30}Pe + \frac{1}{3St_f}\Big]$$
$$+ \frac{1-\vartheta}{\vartheta}\Big(\frac{2}{1 + \frac{1-\vartheta}{\vartheta}[\beta + K_{eff}]}\Big)^2 \frac{1}{St_k} K_{eff} \frac{K_{sam}}{1-s}.$$

This agrees with the HETP found by moments derived by means of Laplace transforms, as discussed in detail by Arnold *et al.* [3] (see appendix C), the only differences being the explicit dependencies on Pe, St_k, St_f, and the nature of the dependence of the reaction coefficient on the solvent concentration.

We can write (as *per* the discussion in chapter 1) the packing Peclet number as

$$Pe_p^{-1} \approx 1.16 + 2.8\, Pe^{-1};$$

the fluid film Stanton number can be expressed as

$$St_f = \frac{1}{d_p}\, Sh\, Pe^{-1},$$

and so (from [3,21,22,39])

$$St_f \approx \frac{\Omega(\vartheta)}{d_p}(Pe)^{-\frac{2}{3}}$$

for $Pe > 50$, and

$$St_f \approx \frac{\Omega(\vartheta) 50^{\frac{1}{3}}}{d_p}(Pe)^{-1}$$

for $Pe < 50$.

Thus for a tracer solute with no binding

$$\frac{1}{\varepsilon}H(1) = \frac{2}{\vartheta}(1.16 + 2.8\, Pe^{-1}) + \frac{1-\vartheta}{\vartheta}\Big(\frac{\beta}{1 + \frac{1-\vartheta}{\vartheta}\beta}\Big)^2 \Big[\frac{1}{30} + \frac{d_p}{3\Omega 50^{\frac{1}{3}}}\Big]\, Pe$$

for $Pe < 50$, and

$$\frac{1}{\varepsilon}H(1) = \frac{2}{\vartheta}(1.16 + 2.8\,Pe^{-1}) + \frac{1-\vartheta}{\vartheta}\Big(\frac{\beta}{1+\frac{1-\vartheta}{\vartheta}\beta}\Big)^2\Big[\frac{1}{30}\,Pe + \frac{d_p}{3\Omega}\,Pe^{\frac{2}{3}}\Big]$$

for $Pe > 50$. This combined expression for the plate height is close to the Van Deemter form, obtained by a heuristic argument [11]:

$$H = A + \frac{B}{\nu} + C\nu,$$

where ν is a form of the velocity.

For the isocratic control case, we need not worry about solvent dynamics; using the predicted HETP for the case of methanol–water solvent in a C–18 column, with n–hexanol as solute, we obtain the following results. We take $\vartheta = 1/4$, $\beta = 1/4$, $D_i = 6D$ for the relation of intraparticle diffusivity to bulk diffusivity, $\Omega = 1$, $d_p = 10\,\mu m$, and $L = 10\,cm$. Assuming the forward reaction rate to be $k_{for} = .5\,sec^{-1}$, we obtain the curves in Figures 42 and 43, showing HETP dependence on s and Pe. Note that as Pe gets smaller, s has less influence on the system. Increasing k_{for} to 100, as in Figures 44 and 45, we see s has little effect on the system unless we look at much higher Peclet numbers (velocities). Figure 46 shows HETP curves for two different molecules (assumed with the same k_{for}, for lack of experimental data), as functions of the hexanol Pe. We see substantially different curves.

These HETP curves would seem to indicate that it is not a simple matter to choose an overall best flow velocity, since the HETP minimum changes dramatically for different molecules and different relative solvent concentrations. This underscores the necessity of developing an advanced optimization theory for solvent control.

Gradient Control : As mentioned in chapter 7, when using a solvent gradient for solute dynamical control, it is useful to define a *control time* (the duration of the control scheme), which has to depend on the *experiment time* (the column exit

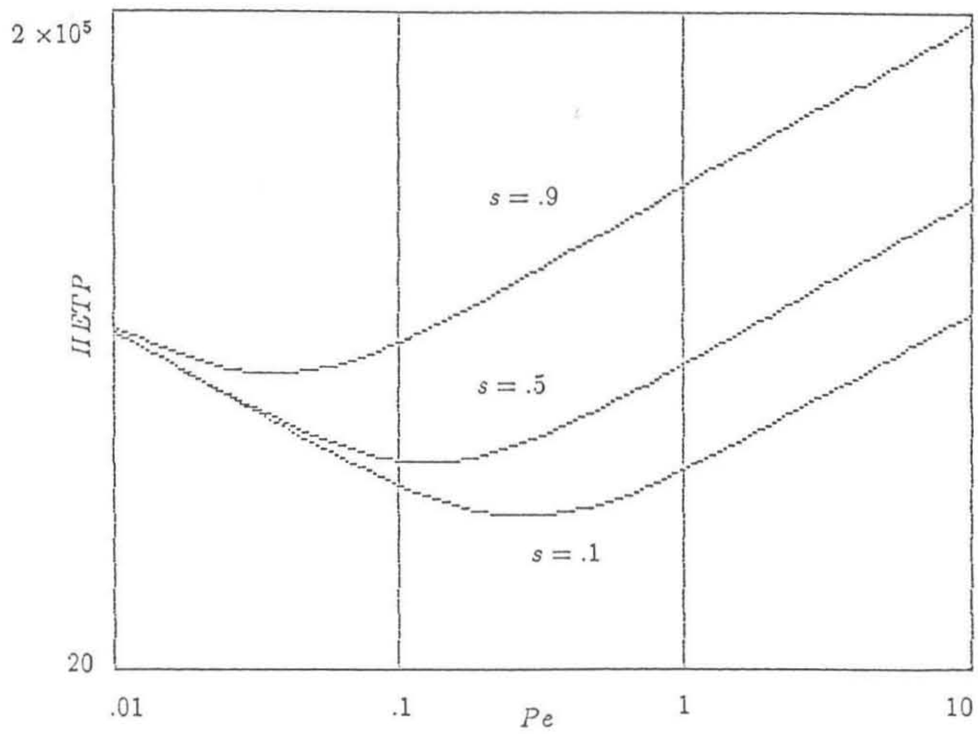

Figure 42: Hexanol HETP variation with Peclet number Pe at various mole fractions s of methanol in methanol–water solvent; $k_{fcr} = .5$.

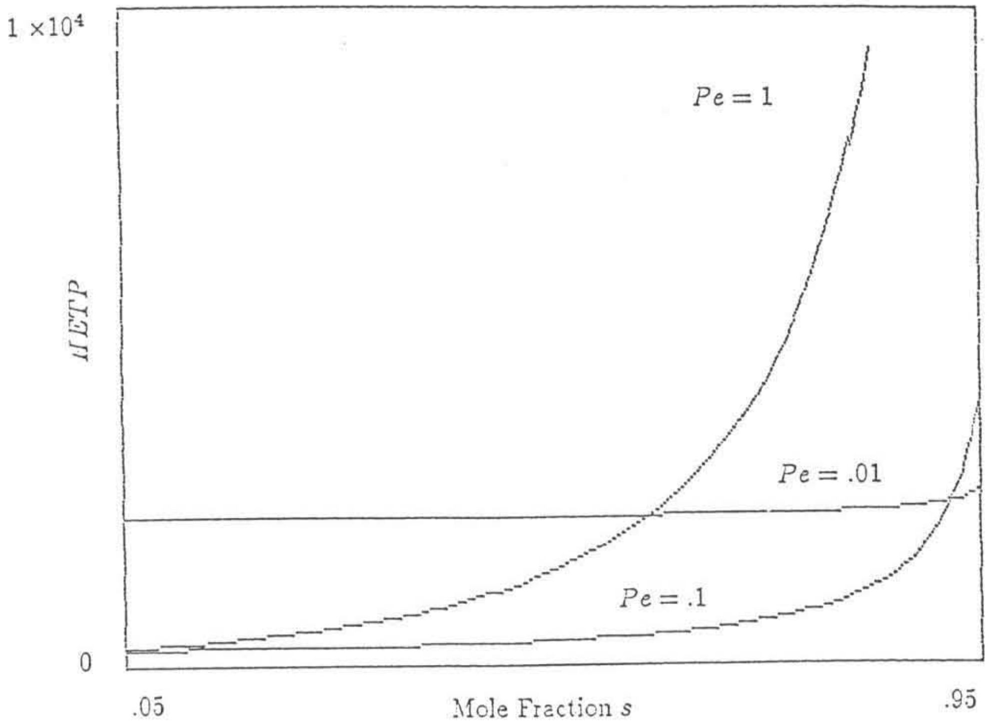

Figure 43: Hexanol HETP variation with mole fraction s of methanol in methanol–water solvent for Peclet numbers $Pe = .01$, $Pe = .1$, and $Pe = 1$; $k_{for} = .5$.

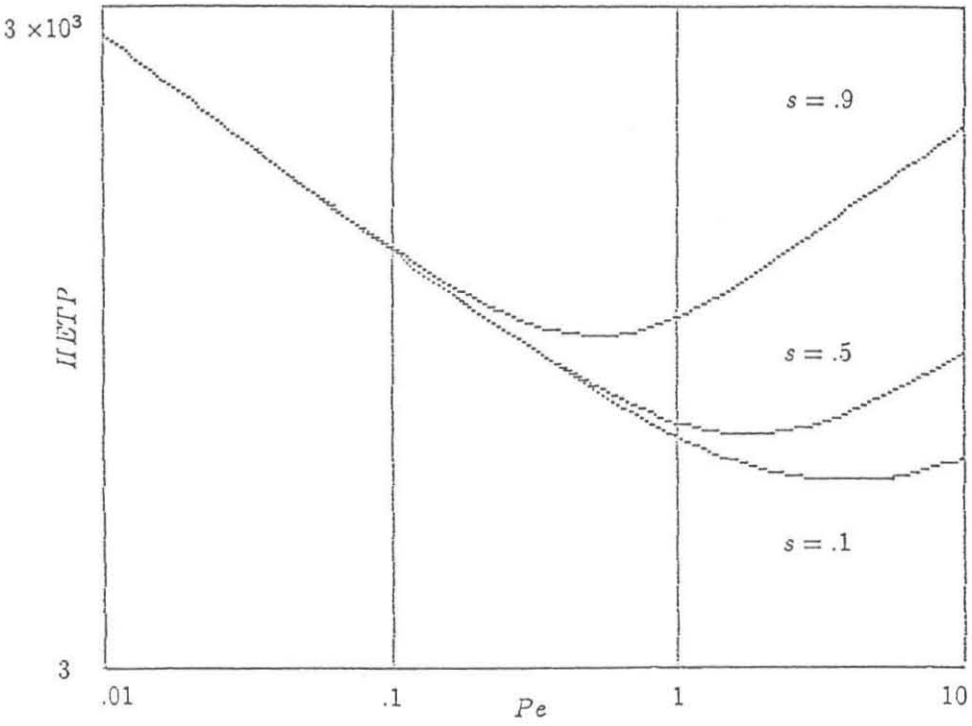

Figure 44: Hexanol HETP variation with Peclet number Pe at various mole fractions s of methanol in methanol–water solvent; $k_{for} = 100$.

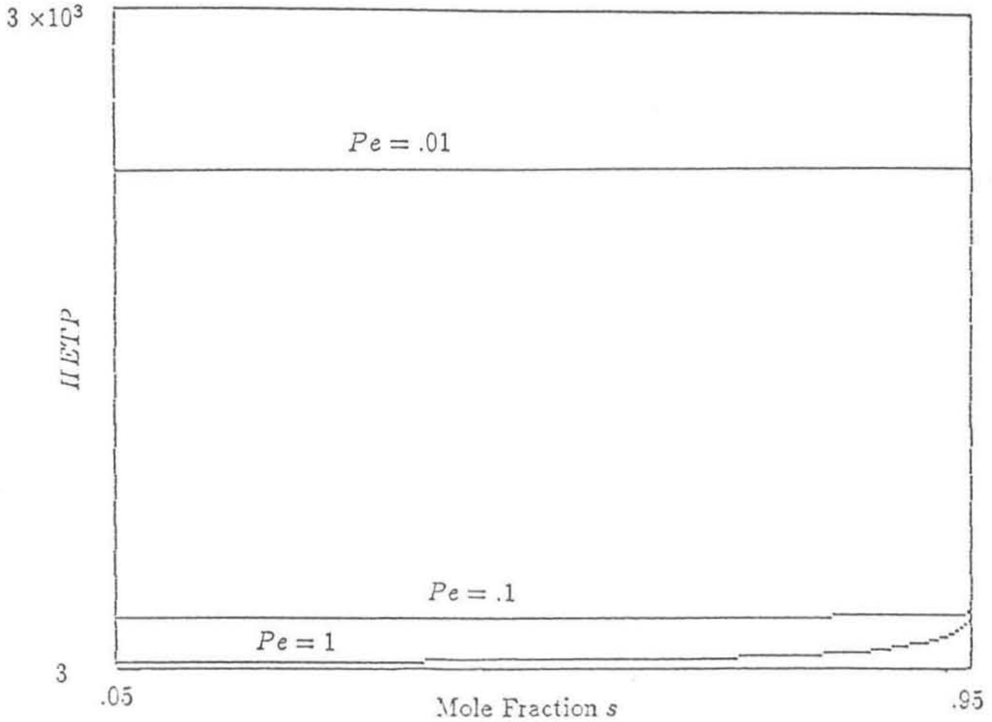

Figure 45: Hexanol HETP variation with mole fraction s of methanol in methanol–water solvent for Peclet numbers $Pe = .01$, $Pe = .1$, and $Pe = 1$; $k_{for} = 100$.

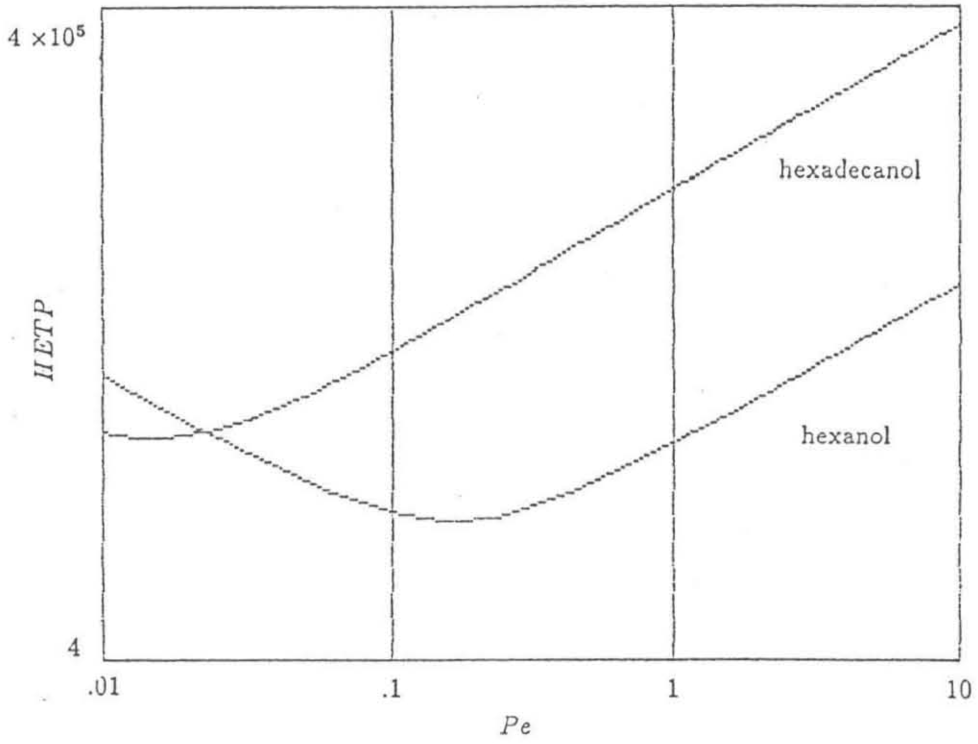

Figure 46: Hexanol and hexadecanol HETP variation with hexanol Peclet number Pe at mole fraction $s = .5$ of methanol in methanol–water solvent; $k_{for} = .5$ assumed for both molecules.

time of the slowest solute). Suppose $\mu_1'(1)$ is the largest column exit time of all the solutes. We want this time to be the same as the time when the end of the solvent gradient exits the column. Clearly $\mu_1'(1)$ depends on solvent dynamics. Solvent dynamics depend on the velocity through the column, which depends itself on the solvent dynamics. This will now be expressed mathematically.

Solvent dynamics for nonporous particles is expressed as

$$\frac{\partial s}{\partial t} + v(s)\frac{\partial s}{\partial x} + \frac{1-\vartheta}{\vartheta}\frac{\partial b}{\partial t} = 0$$

where

$$b = \frac{K_s s}{1 + [K_s - 1]s},$$

and $s(x,0) = 0$, $s(0,t) = \phi(t)$, and the linear velocity v is determined by end pressures, density, and dynamic viscosity:

$$v = \frac{kg\Delta\phi/L}{\vartheta\rho(s)\int_0^1 \frac{\eta(s)}{\rho^2(s)}\,d\xi}.$$

Notice that v is a *global* operator on s, so the equation for s is *not* hyperbolic. Let v_0 be the linear velocity of some standard isocratic solvent mixture. Define a normalized velocity as

$$\hat{v} = \Big(\hat{\rho}(s)\int_0^1 \frac{\hat{\eta}(s)}{\hat{\rho}^2(s)}\,d\xi\Big)^{-1},$$

where $\hat{v} = v/v_0$, $\hat{\eta} = \eta/\eta_0$, and $\hat{\rho} = \rho/\rho_0$. Then the solvent equation can be put in the form

$$\Big(\hat{\rho}(s)\int_0^1 \frac{\hat{\eta}(s)}{\hat{\rho}^2(s)}\,d\xi\Big)\Big(1 + \frac{1-\vartheta}{\vartheta}\frac{K_s}{(1+[K_s-1]s)^2}\Big)\frac{\partial s}{\partial \tau} + \frac{\partial s}{\partial \xi} = 0$$

where $\tau = v_0 t/L$ and $\xi = x/L$. The initial and boundary conditions are

$$s(\xi,0) = 0, \quad \text{and} \quad s(0,\tau) = \phi(\tau L/v_0),$$

with ϕ some arbitrary function. However, we are only interested in ϕ on the interval $0 \leq \tau \leq \tau_{con}$, the control time, so define $\sigma = \tau/\tau_{con} = t/t_{con}$, so

$$s(0,\sigma) = \phi(\sigma\tau_{con}\,L/v_0) = \hat{\phi}(\sigma).$$

The trouble with the above use of τ_{con} is that it is not known *á priori.* It must be calculated in conjunction with $\tau_{exp} = \mu_1'(1)$.

Let

$$Q(s;\sigma) = \int_0^1 \frac{\hat{\eta}(s)}{\hat{\rho}^2(s)}\,d\xi,$$

with $\tau_{con} = \hat{\tau}_{con}$ as an initial guess. If $\hat{\tau}_{con}$ turns out to be incorrect, a new guess is made, so that $\hat{\phi}(\sigma)$ is rescaled. Given $\hat{\tau}_{con}$, an iterative technique might be tried such as

$$\hat{\rho}(s_{i+1})Q(s_i;\sigma)\Big(1 + \frac{1-\vartheta}{\vartheta}\frac{K_s}{(1+[K_s-1]s_{i+1})^2}\Big)\frac{\partial s_{i+1}}{\partial \tau} + \frac{\partial s_{i+1}}{\partial \xi} = 0,$$

(as was used to prove existence of a solution to the solvent equation) starting with constant s_0, so as to give a hyperbolic structure to each subproblem, but then it would be awkward to calculate $\mu_1'(1)$, because one would have to store and interpolate over many s values across its domain. Instead, it is best to calculate the solvent equation numerically as a partial differential equation (for instance using finite differences), simultaneously calculating $\mu_1'(\xi)$.

The solvent equation can be solved numerically to obtain estimates of s for all ξ at each time step, and so approximate $Q(s;\sigma)$ at each σ. One takes a grid in space with constant stepsize $\Delta\xi$, but a variable sized time step $\Delta\sigma$, being careful not to violate any stepsize constraints imposed by conditional convergence (*e.g.*, Courant–Friedrich–Levy condition). The time step size is determined by the calculation of $\Delta\sigma = \mu_1'(\xi+\Delta\xi) - \mu_1'(\xi)$ *via* an ordinary differential equation solver. This technique is used to calculate the reduced HETP of n–hexanol in a methanol–water solvent (see Figure 47).

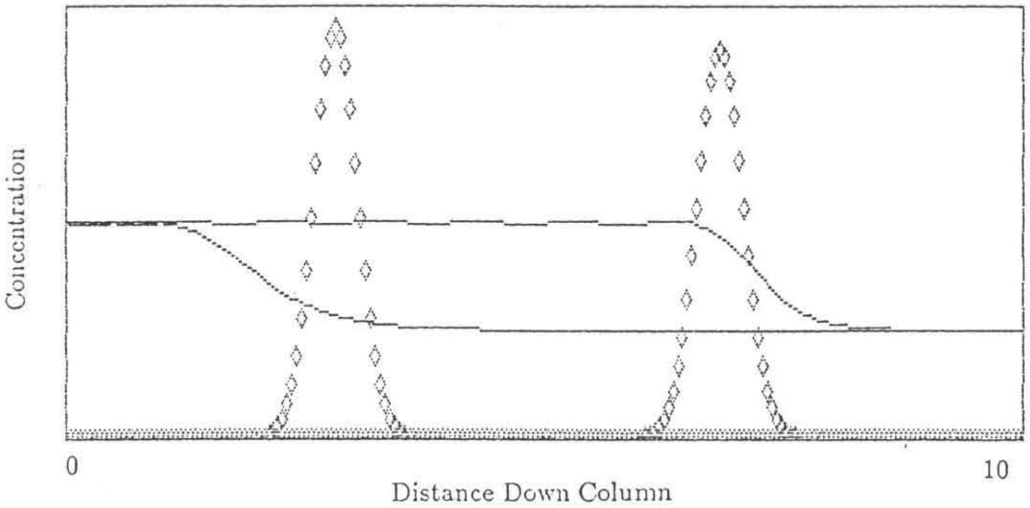

Figure 47: Theoretical dynamics of aqueous methanol solvent and hexanol solute. Concentration profiles are shown at two times within the column of length 10 cm; solute profiles exaggerated horizontally and vertically. Note steepening of smooth solvent gradient, and very little spreading of the solute pulse. Conditions are: $T = 25^o$ C, $d_p = 10$ microns, $Pe = 400$, $\beta = .25$, $\vartheta = .25$, cubic spline initial solvent gradient from .25 to $s = .50$.

Use of Average Velocities : If one estimates the density and viscosity of the solvent mixture as constant, one may use an easier technique, utilizing only characteristic equations. We solve the equation

$$\frac{d\mu_1'}{d\xi} = F_1(s)$$

using, say an explicit ordinary differential equation solver, stepping from ξ to $\xi + \Delta\xi$ using the value of $s(\xi, \mu_1'(\xi)/t_{con})$ to obtain $\sigma = \mu_1'(\xi + \Delta\xi)/t_{con}$. Then one follows a solvent characteristic ℓ back to σ_0 at $\xi = 0$ to find the new value of s along that characteristic. Hence we can step again in space.

To obtain σ_0 at each step one must solve the equations for the solvent characteristic

$$\begin{aligned}\frac{d\sigma}{d\xi} &= \frac{1}{\tau_{con}}\hat{\rho}(s)\bar{Q}(s)(1 + \frac{1-\vartheta}{\vartheta}\frac{K_s}{(1+[K_s-1]s)^2}) \\ &= F(s; \tau_{con}),\end{aligned}$$

with initial condition $\sigma(0) = \sigma_0$;

$$\frac{ds}{d\xi} = 0,$$

with initial condition $s(0, \sigma_0) = \phi(\sigma_0)$. where $\bar{Q}(s)$ is an averaged value assuming constant viscosity and density of solvent over a certain time.

Thus

$$s(\xi, \sigma(\xi)) = \phi(\sigma_0) = \quad \text{constant}$$

on the characteristic curve, so we obtain the nonlinear equation

$$\sigma = F(\phi(\sigma_0); \tau_{con})\xi + \sigma_0$$

to solve. In the integration scheme, we know that $\sigma = \mu_1'(\xi_0 + \Delta\xi)$ and the space location $\xi = \xi_0 + \Delta\xi$ and hence can use a Newton iterative technique to find σ_0. Once $\mu_1'(1)$ and the corresponding σ_0 is estimated, if $\sigma_0 \neq 1$ one must try a new τ_{con}; this process can be cast into a numerical "shooting" technique.

APPENDIX A

Nonlinear Multicomponent Stoichiometric Systems

In this appendix the theory of Helfferich and Klein [19] is briefly covered, particularly with regard to how it fits in with our formalism for general chromatographic systems.

Considering mobile and stationary phases of a set of solutes to be at equilibrium in the column, we define (using Helfferich and Klein's notation)

$$C_i = \vartheta c_i \qquad \text{and} \qquad \bar{C}_i = \varrho q_i ,$$

where we now have both stationary phase concentration $\bar{C}_i$ and mobile phase concentration C_i given *per* unit volume of the column rather than of the respective phase. We also define total concentrations of sorbable species' phases as

$$C = \sum_i C_i , \qquad \bar{C} = \sum_i \bar{C}_i .$$

If the system has C and $\bar{C}$ constant, we may conveniently define the normalized concentrations y_i, z_i as

$$\begin{gathered} y_i = \frac{C_i}{C} , \qquad z_i = \frac{\bar{C}_i}{\bar{C}} , \\ \text{so that} \quad \sum_i y_i = 1 , \qquad \sum_i z_i = 1 . \end{gathered}$$

Thus, if there are n components in a system, we can represent the mobile or stationary phase concentration state as a point on an $(n-1)$–dimensional simplex. Further, a *normalized distribution ratio* is defined as:

$$\frac{z_i}{y_i} = \frac{C}{\bar{C}} \frac{\bar{C}_i}{C_i}$$

and a *binary separation factor*

$$\alpha_{ij} = \frac{\bar{C}_i C_j}{C_i \bar{C}_j} = \frac{y_i x_j}{x_i y_j}.$$

Note that

$$\alpha_{ji} = \alpha_{ij}^{-1}, \qquad \alpha_{ii} = 1.$$

The n components are ordered in terms of their *affinity* $\bar{C}_i / C_i$, such that

$$\frac{\bar{C}_i}{C_i} > \frac{\bar{C}_j}{C_j} \qquad \text{for} \quad j > i.$$

Hence $\alpha_{ij} > 1$, for $j > i$. We call this an *affinity sequence*, with decreasing values of affinity.

If in this system sorption of one component implies desorption of another, this process is called *exchange sorption*; if the sorbent has a constant capacity for sorbable components, then the exchange sorption is *stoichiometric* (i.e., the amount sorbed is equal to the amount desorbed). A physical example of such a system is ion exchange chromatography of dilute systems, according to the authors. Of importance to the developments of the present research is that the authors note that systems of n components having Langmuir isotherms can be represented as an $(n+1)$–component stoichiometric system. That a Langmuir system of the type the authors consider is not in itself stoichiometric is easy to demonstrate; consider for the following development that

$$q_j = \frac{Q_j K_j c_j}{1 + \sum_i K_i c_i}, \quad \text{for} \quad j = 1 \ldots n.$$

For this to be stoichiometric, we must have the total sorbed concentration constant:

$$\sum_j q_j = \sum_j \frac{Q_j K_j c_j}{1 + \sum_i K_i c_i} = \quad \text{constant},$$

which clearly only holds for c_i infinitely large.

Also of importance is that the α_{ij} are constant in a Langmuir system:

$$\alpha_{ij} = \frac{Q_i K_i}{Q_j K_j}$$

so that indeed the authors' formalism can be applied.

To convert such a Langmuir system into a stoichiometric system, note that

$$\frac{q_j}{c_j} = \frac{Q_j K_j}{1 + \sum_i K_i c_i}, \quad \text{for} \quad j = 1 \ldots n,$$

and that a stoichiometric system can be written as

$$\frac{q_j}{c_j} = \frac{\alpha_{jk} R}{1 + \sum_{i \neq k} (\alpha_{ik} - 1) x_i}, \quad \text{for} \quad j = 1 \ldots n,$$

where

$$R = \frac{\sum_i q_i}{\sum_i c_i} = \quad \text{constant.}$$

Thus such an n–component Langmuir system is equivalent to an $(n+1)$–component stoichiometric system *via*

$$Q_i K_i = R\alpha_{i,k} \qquad \text{for} \quad i = 1 \ldots k-1,$$

$$K_i c_i = (\alpha_{i,k} - 1) x_i \qquad \text{for} \quad i = 1 \ldots k-1,$$

$$Q_i K_i = R\alpha_{i+1,k} \qquad \text{for} \quad i = k \ldots n,$$

$$K_i c_i = (\alpha_{i+1,k} - 1) x_{i+1} \qquad \text{for} \quad i = k \ldots n,$$

so take

$$\alpha_{i,k} = \frac{Q_i K_i}{R} \qquad \text{for} \quad i = 1 \ldots k-1,$$
$$\frac{x_i}{c_i} = \frac{R K_i}{Q_i K_i - R} \qquad \text{for} \quad i = 1 \ldots k-1,$$
$$\alpha_{i+1,k} = \frac{Q_i K_i}{R} \qquad \text{for} \quad i = k \ldots n,$$
$$\frac{x_{i+1}}{c_i} = \frac{R K_i}{Q_i K_i - R} \qquad \text{for} \quad i = k \ldots n,$$

If we want the same scale for measuring concentration in both phases, we the have

$$\frac{y_i}{q_i} = \frac{K_i}{Q_i K_i - R} \qquad \text{for} \quad i = 1 \ldots k-1,$$
$$\frac{y_{i+1}}{q_i} = \frac{K_i}{Q_i K_i - R} \qquad \text{for} \quad i = k \ldots n.$$

We are free to choose R; if we choose

$$0 < R < Q_n K_n ,$$

then all x_i, y_i will be positive; so we choose R within this interval and such that

$$\sum_{i \neq n+1} x_i < 1.$$

In this way, the pseudocomponent will have lowest affinity, and is labelled with index $n+1$. To demonstrate this procedure, we carry out calculations for Langmuir systems with one and two components.

The dynamical equations

$$\frac{\partial C_i}{\partial t} + u_0 \frac{\partial C_i}{\partial x} + \frac{\partial \bar{C}_i}{\partial t} = 0$$

can be undimensionalized using the previous normalizations:

$$\frac{\bar{C}}{u_0 C} \frac{\partial y_i}{\partial t} + \frac{1}{u_0} \frac{\partial z_i}{\partial t} + \frac{\partial \bar{z}_i}{\partial x} = 0.$$

Defining

$$\begin{aligned}
\tau &= \frac{C}{\bar{C}} u_0 (t - \frac{x}{u_0}) \\
\tilde{x} &= x \\
\frac{\partial}{\partial t} &= \frac{\bar{C}}{u_0 C} \frac{\partial}{\partial \tau} \\
\frac{\partial}{\partial x} &= -\frac{C}{\bar{C}} \frac{\partial}{\partial \tau} + \frac{\partial}{\partial \tilde{x}}
\end{aligned}$$

so that our equation is now

$$\frac{\partial y_i}{\partial \tau} + \frac{\partial z_i}{\partial \tilde{x}} = 0$$

with equilibrium isotherms

$$y_j = \frac{z_j}{1 + \sum_{i \neq j} \alpha_{ij} z_i}, \quad \text{for} \quad j = 1 \ldots n$$

Another way to represent the dependent variables is through the so-called *H-Transform,* which reduces to the problem of finding the "H-roots" of

$$\sum_{i=1}^{n}\left(\frac{K_iC_i}{\frac{hQ_iK_i}{Q_1K_1}-1}\right)=1$$

which can be shown to satisfy

$$C_j=\frac{\prod_{i=1}^{n}\left(\frac{h_iQ_jK_j}{Q_1K_1}-1\right)}{K_j\prod_{i=1,i\neq j}^{n}\left(\frac{Q_jK_j}{Q_iK_i}-1\right)}$$

for the mobile phase variables. The H–transform is remarked to be similar to Binet's Transformation for the description of homofocal surfaces in differential geometry [35].

For instance, in a three component space for an ordinary stoichiometric system, we can represent the available compositions in a simplex as shown in Figure 48. The interior solid and dashed lines are called *composition paths,* which satisfy

$$\frac{\partial\bar{C}_i}{\partial C_i}=\frac{\partial\bar{C}_j}{\partial C_j}\qquad\text{for all } i,j.$$

In a three component system, there are two such paths through each composition point. These paths are important in the representation of *coherence*, which constitutes quasi–steady state behavior for the nonlinear waves in the system. Helfferich and Klein give a complete characterization of coherence in such systems. Schematically, one may represent the attainment of coherence as a sort of "vector projection." Suppose the system has an initial state of a square pulse, as in Figure 449.

Then through time we see a development in which the respective pulses find and retain the same *general* shape and relative positions – the scales of the pulse lengths and heights will change dynamically. If the dependent variables are viewed on the simplex, we see in time that the noncoherent initial state resolves itself into two "vectors" lying along the composition paths which intersect at the base

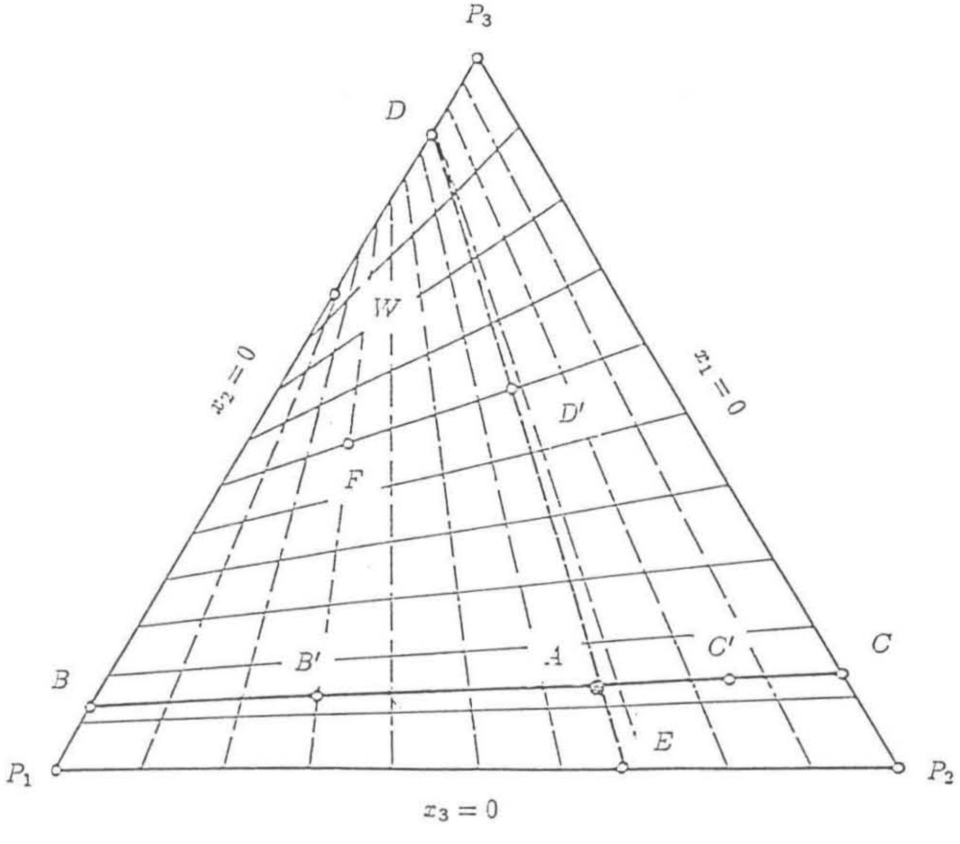

Figure 48: Path grid for mobile phase compositions for a three component system with separation factors $\alpha_{12} = 2$, $\alpha_{13} = 4$. Adapted from Helfferich and Klein [ ].

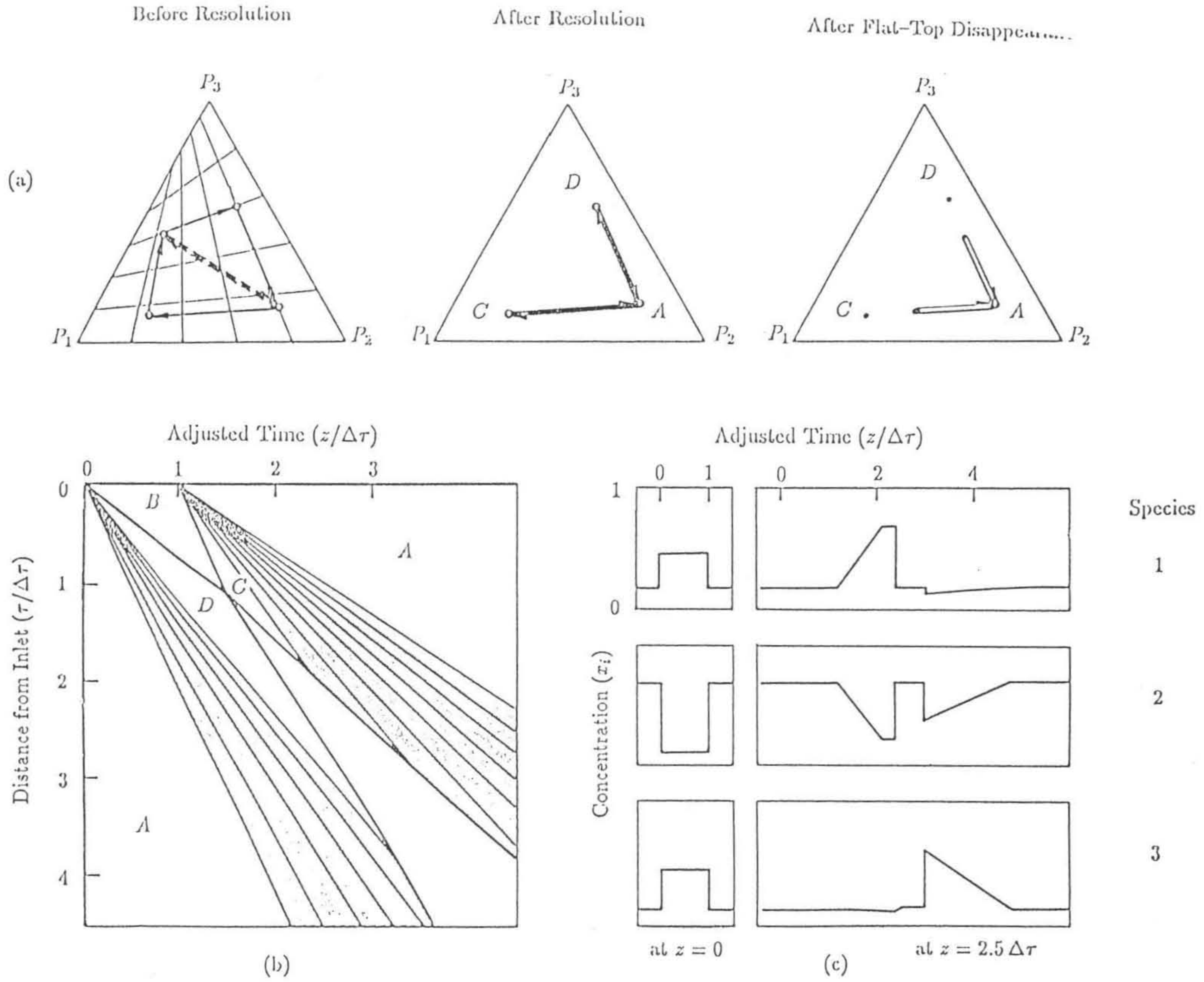

Figure 49: Evolution of initial square pulse, showing root trajectories, and concentration histories for a typical three- component case. $\alpha_{12} = 2$, $\alpha_{13} = 4$; $x_1' = 0.18$, $x_2' = 0.68$, $x_3' = 0.14$, $x_1^0 = 0.45$, $x_2^0 = 0.10$, $x_3^0 = 0.45$. Adapted from Helfferich and Klein [ ].

composition point for the initial composition variation. Note that the composition paths are solely determined by the equilibrium properties of the system, and are independent of space, time, and experimental conditions.

In the next section the applicability of the authors' formalism to our MPLC control problem will be discussed.

Application to Process Modelling in MPLC. First of all, the idea of coherence mentioned in the previous section implies the formation of various shocks in the concentration profiles. Recall that shocks are not to be allowed in the chromatographic column, and so coherence is never allowed to develop. For this reason Helfferich and Klein's formalism has no applicability to the control problems discussed in this paper. The present problem deals with nonlinear concentrations only for the solvent system; the solutes are assumed in small, linear concentrations. The solvent control will generally be assumed monotonic; shocks would indeed form within the column if the control were allowed to vary nonmonotonically, or if the solutes were in very high concentrations. The latter situation points to the importance of being aware of the linear capacity of the column. In future papers we will discuss the control problem wherein such shocks are allowed in the system, which has its importance in multicomponent affinity chromatography, along with the important aspects of the so–called coherent states. Roughly speaking, the situation for fully nonlinear dynamics is as follows. There will be n solute components to be separated, and two or three solvents to control the separation. The concept of coherence is intimately related with that of component resolution, since a coherent state will be seen to represent the maximum attainable resolution for a given control.

All solutes begin their history within the column as pulses of equal width, with solvents possessing the least affinity and solutes with progressively higher affinities –

if a component has lower affinity than the solvents, ther is no solvent control possible for that component. Though the solutes are generally in nonlinear concentrations, there also might be those that are in small, linear concentrations.

More general nonlinear problems involving fluid film mass transfer, porous–particle diffusion, and nonequilibrium reactions can be approached as perturbations from the above equilibrium problem.

APPENDIX B

Moment Techniques

Moment techniques are used in various physical theories for pulsed systems, as they ignore some of the detail of solving the overall partial differential equations, while not leaving out the essentials. Essentially following Kubín [29] and Kučera [30], the form of the solution to a set of equations for chromatography is postulated to be

$$c(x,t) = \sum_{n=0}^{\infty} a_n \mathcal{H}_n(\tau),$$

where

$$\tau = \frac{t - \mu_1'}{\sqrt{2\mu_2}},$$

$$a_k = \frac{m_0}{2^k k! \sqrt{2\pi\mu_2}} \int_0^{\infty} c(x,t)\mathcal{H}_k(\tau)dt,$$

$$m_k(x) = \int_0^{\infty} t^k c(x,t)dt,$$

$$\mu_k'(x) = \frac{m_k(x)}{m_0},$$

$$\mu_k = \frac{1}{m_0}\int_0^{\infty} (t - \mu_1')^k c(x,t)dt,$$

and $\mathcal{H}_k$ is the k^{th} Hermite polynomial

$$\mathcal{H}_k(\tau) = (-1)^k exp(\tau)^2 \frac{d^k}{d\tau^k} exp(-\tau^2).$$

The quantities μ_k' and μ_k are called *moments.* The first few coefficients a_k can be calculated as being

$$a_0(x) = \frac{m_0}{\sqrt{2\pi\mu_2(x)}},$$

$$a_1 = a_2 = 0,$$

$$a_3 = (\frac{m_0}{2^2 3! \sqrt{\pi}}) \frac{\mu_3}{\mu_2^2},$$

and further terms involving higher and higher moments:

$$a_n = \frac{m_0}{\sqrt{2\pi\mu_2}} \sum_{k=0}^{[\frac{n}{2}]} \frac{(-1)^k \mu_{n-2k} \mu_2^k}{2^k k!(n-2k)!(2\mu_2)^{[\frac{n}{2}]}}$$

where for even n

$$[\frac{n}{2}] = \frac{n}{2}$$

and for odd n

$$[\frac{n}{2}] = \frac{n-1}{2}.$$

Kubín applied moment techniques to a linear model of partition chromatography with a finite pulse as initial condition, whereas Kučera considered the same equations but with a delta function initial condition. Recall that in chapter 4 explicit solutions to these problems were reviewed. The value of the moment method becomes clear when we try to interpret the analytical solution and compare with experimental data, for the first moments have much physical and mathematical significance. The solution method involved the Heaviside transformation; it turns out that one can avoid taking the inverse transform of the entire solution and relatively easily find the moments instead. This is indeed an advantage in terms of relative simplicity and clarity, when comparing with the full analytical solution, if it can be found. Kubín notes that

$$m_k = (-1)^k \lim_{s \to 0} \frac{d^k}{ds^k} [\frac{c(x,s)}{s}]$$

where s is the transform variable, and any moment μ_j or μ'_j can be expressed in terms of combinations of m_k for $k = 1 \cdots \infty$. Here we note that the *moment integration by parts* method found in this paper is much easier to implement than Kubin and Kucera's method for their constant coefficient equations; their method is not viable for the controlled equations considered in this paper.

For the case of equilibrium chromatography such that there is only axial dispersion, no mass transfer and delta function initial conditions the first few moments are (from Kučera)

$$\mu_0 = \mu_0' = 1$$

$$\mu_1 = 0$$

$$\mu_1' = \frac{L}{u_{ef}} + \frac{2D_{ef}}{u_{ef}^2}$$

$$\mu_2 = \frac{2D_{ef}\,L}{u_{ef}^3} + \frac{8D_{ef}^2}{u_{ef}^4}$$

$$\mu_3 = \frac{12D_{ef}^2\,L}{u_{ef}^5} + \frac{64D_{ef}^3}{u_{ef}^6}$$

where Kucera has the "effective velocity" u_{ef} and "effective diffusion" D_{ef} as

$$u_{ef} = \frac{u}{1+\epsilon K_c}$$

$$D_{ef} = \frac{D_p}{1+\epsilon K_c}.$$

For the more complete linear problem with longitudinal diffusion, radial diffusion in the particles, mass transfer, completing the inverse transform has proven intractable so far, and yet the moments can be calculated. The first few are as follows:

$$\mu_0 = \mu_0' = 1$$

$$\mu_1 = 0$$

$$\mu_1' = \Big(\frac{L}{u} + \frac{2D}{u^2}\Big)\Big[1+\epsilon/K_c(1+K_n)\Big]$$

$$\begin{aligned}\mu_2 = {} & \Big(\frac{2D_p L}{u^3} + \frac{8D_p^2}{u^4}\Big)\left[1+\epsilon/K_c(1+K_n)\right]^2 \\ & + \Big(\frac{2L}{u} + \frac{4D}{u^2}\Big)\epsilon K_c\Big[\frac{R^2(1+K_n)^2}{D_r\,\nu(\nu+2)} + \frac{\epsilon(1+K_n)^2}{H_c} + \frac{K_n}{H_n}\Big]\end{aligned}$$

Note that the first moment μ_1' does not depend on the effective shape of the substrate particles ν the radial diffusion D_r or the mass transfer coefficients H_c and H_n, but only on the equilibrium reaction coefficients K_c and K_n, the solute velocity V, and axial dispersion D_l.

A pertinent question about the Hermite expansion is how many terms are needed to obtain satisfactory results, and indeed, what *are* satisfactory results? This brings us back to considering the primary concern in chromatography: we would like to have a clear separation of the different solutes. The expression of this goal involves a definition of *resolution,* which is agreed to depend on the width of each solute peak and the relative retention times of the different solutes. This means that the moments μ_1' and μ_2 are crucial to the problem. But can we get away with using only these moments? That is, if we substitute the Hermite expansion into the chromatography equations of our choice, are we forced to solve equations involving any other moments if we try to find μ_1' and μ_2? For all the linear equations considered, we find that the answer is no — higher moments are not needed. However, this answer should be qualified somewhat. If a Gaussian distribution of concentration is assumed, and this distribution is decomposed into Hermite modes, we should only need to consider the first term in the expansion, since that is all that is needed to model the peak perfectly. However, if for instance a "box" function is modelled with the expansion, there are of course more terms in the expansion having a nonzero contribution. More generally, if the function is symmetric, its Hermite expansion will have odd terms zero; if the function is odd, the even terms in the Hermite expansion will be zero. Asymmetries in a function will make both even and odd terms important. If we consider only the width and retention time important for a solute's peak, then we can fit a Gaussian shape to that peak, ignoring further structure of the solution.

APPENDIX C

Relation of Moments to Physical Parameters

Kučera [30] notes that if a detector measuring the concentration of solutes eluting from the chromatographic column is at distance $x = L$ down the column, then we can define various significant times. First, there is the time t_R of peak maximum such that

$$\frac{\partial c(L,t)}{\partial t}\Big|_{t=t_R} = 0,$$

and the time t_S of the peak median defined as

$$\int_0^{t_S} c(L,t)dt = \frac{1}{2}\int_0^{\infty} c(L,t)dt$$

which is when half the area of the peak is registered, the time t_C of the mean (center of "gravity") of the peak given by

$$t_C = \mu_1'(L) = \int_0^{\infty} tc(L,t)dt,$$

and the time t_0 when the concentration peak's maximum passes by the point $x = L$:

$$\frac{\partial c(x,t_0)}{\partial x}\Big|_{x=L} = 0.$$

For the uncontrolled case, it makes good sense to define an effective velocity u_{ef}, and hence to define the retention time as $t_R^* = L/u_{ef}$. It is generally known that $t_R^* = t_0$; the relation between t_S and t_R^* can be had from the relation

$$\operatorname{erfc}\Big(\sqrt{\frac{u_{ef}^2(t_R^*)^2}{4D_{ef}t_S}} - \sqrt{\frac{u_{ef}^2 t_S}{4D_{ef}}}\Big) - \exp\Big(\frac{u_{ef}^2 t_R^*}{D_{ef}}\Big)\operatorname{erfc}\Big(\sqrt{\frac{u_{ef}^2(t_R^*)^2}{4D_{ef}t_S}} + \sqrt{\frac{u_{ef}^2 t_S}{4D_{ef}}}\Big) = 1$$

which gives approximately that

$$t_R^* \doteq t_S - \frac{D_{ef}}{u_{ef}^2}.$$

Kučera [ ] also shows that

$$t_R^* \doteq t_R + \frac{D_{ef}}{u_{ef}^2},$$

and the relation

$$t_R^* = t_C - \frac{2D_{ef}}{u_{ef}^2}$$

is directly from the first moment, and gives for large times a difference between the two times which can be neglected. The retention time is important to determine accurately because it gives the partition coefficient.

The second moment μ_2 is the variance of a Gaussian peak shape and clearly depends on all the important parameters in the chromatographic system. For dynamics without a change in solvent strength, μ_2 increases with length of the column, with longitudinal diffusion, and the size of the substrate particles; it decreases with larger radial diffusion in the particles, with an increase in the mass transfer across the particle boundary, and increased symmetry of the particles.

The definition of u_{ef} and D_{ef} as constants is invalid when the partition coefficient changes as it does in the case of solvent strength control. The first moments are still useful, though, and really the above times can all be obtained from the moment μ_1'.

There is a question as to whether or not the popular phenomenological expressions for the HETP have more accuracy and predictability than HETP expressions based on moments. In this section it is argued that moments offer as much accuracy and perhaps better predictability; also, moments are derived from an underlying dynamic model of chromatography, so giving overall a more complete and detailed understanding of the chromatographic system.

Arnold *et al.* [3] have made a careful study of the HETP and its relationship to moments, particularly in the context of measuring equilibrium binding constants and rate constants of biochemical reactions. Horváth and Lin's *[21,22] plate height* expression

$$H = \frac{a}{1 + bv^{1/3}} + \frac{\mathrm{B}}{v} + \mathrm{C}v$$

commonly used in such cases is taken to task, as the expression is sometimes inappropriate to the situation. We note that yet another popular form for the HETP is

$$h = \mathrm{A}v^{1/3} + \mathrm{B}/v + \mathrm{c}v$$

put forth by Knox [27]. Clearly there is disagreement as to what the proper form is for the A term. Knox does not give a theoretical derivation for this term, but rather merely states that if one assumes a functional form of the plate height contribution from flow anisotropy – dispersion coupled with solute diffusion outside the particles as

$$h_{flow} = \frac{1}{\eta + \gamma v^{-z}}$$

with $z < 1$, $v = u_0 d_p / D_m$, $h = H/d_p$, and η, γ constants then we can fit experimental data rather closely. The value of z seems to be between 0.2 and 0.5, yet for the reason that this form is "cumbersome" Knox suggests the form

$$h_{flow} = \mathrm{A}v^{1/3}.$$

It might be inferred that Knox's reasoning behind this was based on the following: note that $0.2 < 1/3 < 0.5$; as $v \to 0$, and $z = 1/3$,

$$h_{flow} = \frac{1}{\eta + \gamma v^{-z}} \to \frac{1}{\gamma} v^{\frac{1}{3}},$$

giving Knox's final form for h_{flow}. However, it is quite clear that if v is not small, Knox's expression is in large error. Indeed, for v large,

$$h_{flow} = \frac{1}{\eta + \gamma v^{-z}} \to \frac{1}{\eta},$$

clearly a constant.

Overall, Knox's arguments do not seem compelling, partly because of the lack of sensitivity of his expression for h_{flow} to changes in the exponent z — with enough parameters it seems that relevant data could always be fitted, and partly because there is no rigorous quantitative theoretical reasoning behind his choice of the functional form of h_{flow}. Knox has found that only very high quality data over a range of two magnitudes of v give an accurate estimation of h. On the other hand, Horváth and Lin's expression is backed by a theoretical argument. We would like to relate the phenomenological plate height to physical parameters with as few free parameters as possible; while Horváth and Lin present a more physical argument for their plate height expression, Arnold *et al.* [3] take exception to the extent to which their model is typically taken. Further, they find that for the effective region of applicability of Horváth and Lin's model, there is a model given from moment techniques which gives an essentially identical expression.

Let us consider Arnold's arguments. In the case that the peak profile is Gaussian, so that μ_2 is identified with the variance, the HETP can be expressed as

$$H = \frac{\mu_2 L}{{\mu'_1}^2}.$$

If the column characteristics are already set, H can be written in terms of mobile phase velocity u. One such expression that has been in use for quite some time is the Van Deemter equation

$$H = \mathrm{A} + \frac{\mathrm{B}}{u} + \mathrm{C}u$$

where the effects of molecular diffusion and dispersion determine the first two coefficients, and mass transfer, intraparticle diffusion, and sorption kinetics determine the last coefficient. As Arnold remarks, Giddings [11] explained that the Van Deemter equation did not take into account flow and diffusive coupling in the space between particles, and that A should have flow rate dependence. Horváth and Lin [21,22] suggested a form for this dependence, which was subsequently used by many researchers. Arnold has made suggestions as to the proper form of the flow rate dependence and for what values of u.

For terms other than for the flow and diffusion coupling, it happens that Horváth and Lin's model agrees in detail (see Arnold [3]) with the plate height equation derived from the moment expressions found by Kučera [30] and Furusawa *et al.* [9]. Arnold questions the need for the term introduced by Horváth and Lin, as the calculation from using the moments would seem to include any coupling between axial mixing and diffusion. Using Arnold's notation, the moments and resulting HETP are

$$\mu_1' = \frac{L}{u_0}[\epsilon + (1-\epsilon)\beta + (1-\epsilon)\varrho_p K$$

$$\mu_2 = \frac{2L}{u_0}\Big(\frac{E_x}{u_0^2}\big[\epsilon+(1-\epsilon)\beta(1+\frac{\varrho_p K}{\beta})\big]^2+(1-\epsilon)\big[\frac{\varrho_p K}{k_d}+\frac{d_p\beta^2}{60}(1+\frac{\varrho_p K}{\beta})^2(\frac{1}{D_i}+\frac{10}{k_f\, d_p})\big]\Big)$$

so that the HETP defined by $H = \mu_2 L/{\mu_1'}^2$ is

$$H = \frac{2d_p}{\mathrm{Pe}_p} + \frac{2(1-\epsilon)\big[\frac{\varrho_p K}{k_d} + (\beta+\varrho_p K)^2\frac{d_p^2}{60}(\frac{1}{D_i}+\frac{10}{k_f\, d_p})\big]}{[\epsilon+(1-\epsilon)(\beta+\varrho_p K]^2}u_0$$

where $\mathrm{Pe}_p = u_0 d_p/E_x$ is the *packing Peclet* number.

APPENDIX D

"Fast Method Development"

Here we give a short description of the philosophy and method behind what is called "Fast Method Development" (FMD) in order to show contrast with the techniques presented in this paper and highlight certain important issues.

Fast Method Development. FMD has developed over the past five years as a primarily personal computer–based process whereby two to seven initial chromatograph experiments (see Figure 50), each at a different solvent strength, are done to identify the retention properties of the solutes in a mixture of chemicals to be separated. The isocratic retention of each solute can then be predicted using a well–known linear relationship between solvent strength and the logarithm of retention. A standard algebraic approximation of the dependence of isocratic bi–peak resolution on "capacity factor", "column plate number," and peak spacing is then used by computer software to predict resolution at any solvent strength thereby giving a map of minimum bi–peak resolution for all solute pairings (Figure 51). Then the experience of the chromatographer is called into play along with more software to help improve separation by changing column type, particle size, and flow rate.

Recently [48] FMD has been upgraded to include the possibility of a linear variation in solvent strength during the chromatographic experiment, not only isocratic (constant) solvent conditions. Thus FMD presents an increase in ease of developing what is now considered an acceptable chromatogram.

We start by defining the resolution between two consecutive solutes' peaks. The peak shape is assumed to be Gaussian, which turns out to be quite acceptable for most cases. The bisolute resolution R is

$$R = 2\frac{t_{R,2} - t_{R,1}}{W_2 + W_1}$$

1) Do two gradient runs.
2) Do solvent strength simulation.
3) Find relative resolution map.
4) Select solvent.
5) Do column simulation–optimization.
6) Fine tune final procedure.

Figure 50: Guidelines for Fast Method Development.

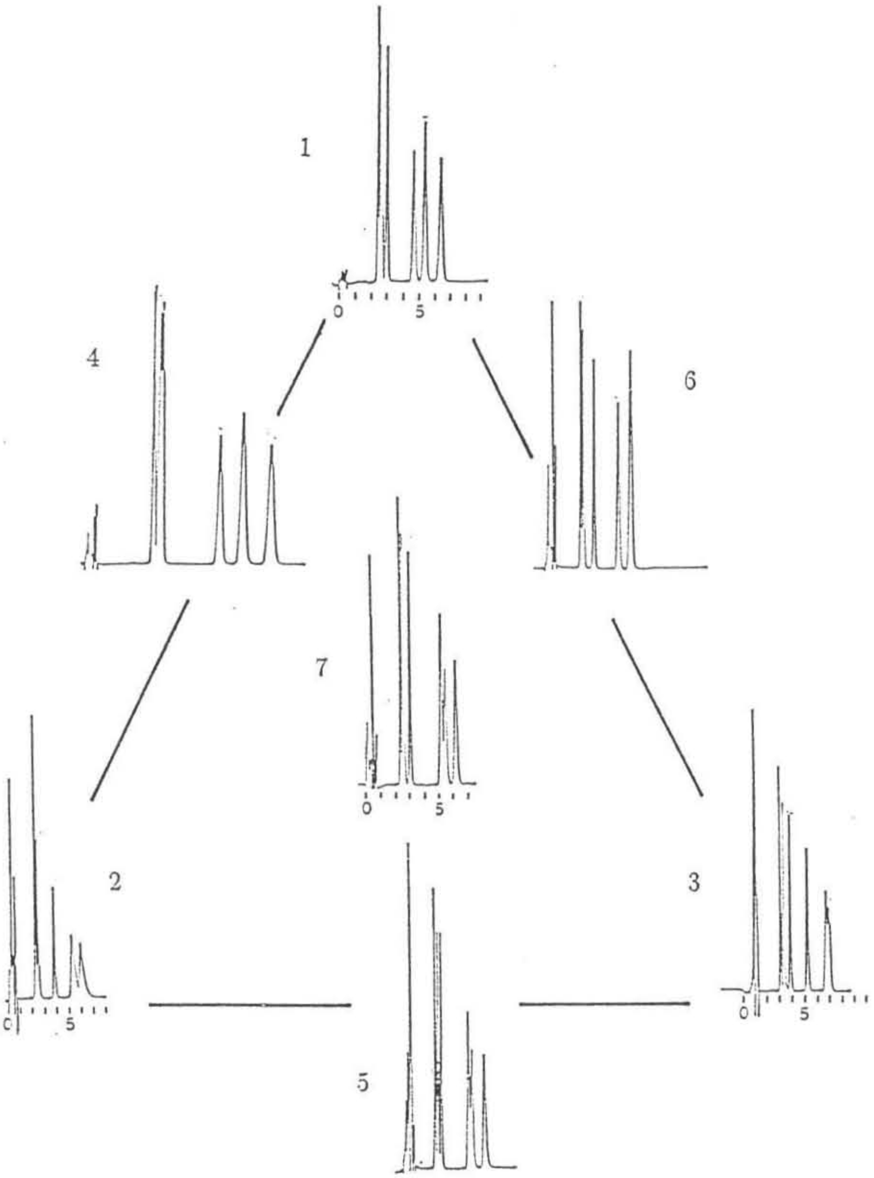

Figure 51: Fast Method Development applied to RPLC separation of six steroids (see text). Adapted from Snyder, Glajch, and Kirkland [ ].

where $t_{R,i}$ is the retention time and W_i is the peak width for solute i. If we define the *plate number* as

$$N = 16(t_R/W)^2$$

$$\alpha = \frac{t_{R,2} - t_0}{t_{R,1} - t_0} = \frac{t'_{R,2}}{t'_{R,1}} = \frac{k'_2}{k'_1}$$

where

$$t'_{R,i} = t_{R,i} - t_0$$

and

$$k'_i = \frac{t'_{R,i}}{t_0}.$$

Since the peak shape is Gaussian, we interpret $W = 4\sigma$, *i.e.*, the width is four standard deviations. From these relations we can easily find that the bisolute resolution is

$$R = \frac{\sqrt{N}}{4}\frac{\alpha - 1}{\alpha}\frac{k'_2}{1 + k'_2}.$$

The primary importance of k' is that it is proportional to the equilibrium partition coefficient (Giddings [11].) Note that the definition of N assumes that it is a well – defined *constant* for the column, which we will show is often incorrect and would lead us to err in some important situations; N is dependent on such things as solute type, solvent type and concentration, solvent gradient, and solute concentration.

If we accept the above phenomenological relationship then we can state that the plate number N_c of the column must satisfy

$$N_c \geq N_{req} = 16R^2(\frac{\alpha}{\alpha - 1})^2(\frac{1 + k'}{k'})^2$$

where R is the resolution required to separate any two of the solutes. Thus we will have to know how N_c depends on column length, particle diameter, and flow velocity. For short columns, often times peak profile is markedly disturbed; this is probably a nonequilibrium phenomenon which can be modelled by including kinetics in the system equations — this cannot be dealt with in FMD. So, a column length is assumed that does not give rise to such perturbations; then generally N_c is found to be roughly proportional to column length. Another parameter closely related to N is H, the *Height Equivalent to a Theoretical Plate* (HETP) given by

$$H = L/N.$$

The bandwidth near the end of the column can be expressed in units of length relative to column length, so giving us the expression

$$N = (L/\sigma)^2$$

where σ^2 is the Gaussian peak variance. Then the expression for H becomes

$$H = \sigma^2/L.$$

Further, σ^2 can be considered to be the sum of variances (peak spreading) originating from assumed independent mechanisms such as diffusion, fluid flow through the column, mass transfer resistance between mobile and stationary phases, and adsorption kinetics (Giddings [11]). Diffusion in the mobile phase arises from the solute concentration gradient, and gives rise to a variance of

$$\sigma^2_{D,m} = 2\gamma_m D_m L/u$$

where γ is the tortuosity coefficient due to the structure of the substrate. Stationary phase diffusion gives a variance contribution of

$$\sigma^2_{D,s} = 2k\gamma_s D_s L/u$$

Variance contribution from the fluid flow derives from differing streamlines and microchannel diameters in the substrate — local fluid velocities depend on the structure. This contributes a factor

$$\sigma^2_F = aLu^{1/3}$$

where a is a constant depending on particle diameter and mobile phase diffusion. Finally, since diffusion across the boundary between mobile and stationary phases takes a finite time, there is a variance due to mass transfer resistance

$$\sigma_{tr}^2 = \frac{CLd_p^2u}{D_m}$$

where C is a function of solute retention. (Here again we see that the plate height is really solute – dependent). Since adsorption kinetics contributes a variance proportional to Ld_p^2u/D_m its coefficient can be included in C.

The above variances summed up give an expression for the HETP of

$$H = \frac{2}{u}(\gamma_m D_m + k'\gamma_s D_s) + au^{1/3} + \frac{Cd_p^2u}{D_m}$$

It should be noted, however, that at large enough velocities the flow characteristics change considerably, as turbulence sets in within the microchannels (Giddings [11]).

A solvent model is necessary for the formulation of any theory of chromatography. Snyder, *et al.* [44,45,47] has improved nondynamical models of the behavior of solvents on various chromatograpic packings. This model is primarily for columns with silica or alumina as substrate, though simpler versions of the model are quite adequate for other substrates as long as only certain combinations of solvents are used. It is assumed that the measured effect of solvent on solute behavior is due not to interactions in the mobile phase but rather due to competition for for adsorbing sites on the substrate. A phenomenological parameter *solvent strength* ϵ is postulated to affect the solute retention coefficient as

$$log(k_1/k_2) = \alpha A_s(\epsilon_2 - \epsilon_1)$$

where k_i denotes the value of k' for a mobile phases 1 and 2, α is a substrate activity constant, and A_s refers to the cross–sectional area of the adsorbing molecule.

The surface of the typical substrate, or adsorbent, has isolated polar (*i.e.*, with dipole moment) groups scattered across its surface in addition to the generalized reactability of all exposed surface. These polar areas can react differently with a given mobile phase molecule if the molecule is itself polar. With silica as substrate, the polar areas are silanols (Si–OH) randomly scattered. The column can be pretreated with a depolarizer to incapacitate the polar groups, but polar groups can actually aid the separation of some solutes. For two solutes of similar retention in a nonpolar environment, changing to a polar solvent can create large changes in the solutes' relative retention if one is more polar than the other. The formula above already includes effects of localization of solvent and solute: a change in solvent localization changes ϵ whereas a change in localization of solute changes apparent A_s value. What the equation does not include is the effect of *interactions* of the two types of localization. Snyder, *et al.* [45] found that for silica adsorbents and localizing solvent/solute combinations the following equation holds:

$$log(k_1/k_2) = \alpha A_s(\epsilon_2 - \epsilon_1) + \Delta_1.$$

Δ_1 depends both on the properties of solute (X) and mobile phase M_i. Suppose Δ_X is the measure of relative localization of X. Let the coefficient m_i increase both with the amount of localization of some mobile phase solvent S_j and with its proportion of coverage θ_j of the adsorbent. An experimentally – verified linear free energy relationship between these parameters is

$$\Delta_1 = -\Delta_X m_i.$$

Here increased localization results in decreased solute retention. On the other hand, Δ_X increases with increasing X localization. m_i can be varied to help control solutes' retention times, *via* changing solvent composition. m can be calculated by determining the polarity coefficient m^0 of a pure solvent which localizes and specifying the fraction θ_j of the polar solvent:

$$m = m^0 f(\theta_j).$$

The function f is empirical, taking values between zero (for $\theta_j = 0$) and one (for $\theta = 1$.)

Still another factor was found to be of importance, though less so than solvent strength and solvent/solute localization. The relative basicity of a solvent is thought to give rise to a noticeable effect on solute retention. Snyder, *et al.* call this effect *solvent-specific localization* which gives rise to a term Δ_2:

$$log(k_1/k_2) = \alpha A_s(\epsilon_2 - \epsilon_1) + \Delta_1 + \Delta_2.$$

We see then that solvent strength, solvent/solute localization, and solvent-specific localization can be varied independently, allowing a great deal of control of the selectivity of the chromatographic system. It should be noted, however, that these parameters have upper and lower bounds; indeed, the maximum value of m_i increases as the solvent strength increases. The proposition is then to include, say, four solvents in the mobile phase, changing respective concentrations in order to institute solute retention control. For example, we choose solvents A,B,C,D, where A in nonpolar, B is weakly polarized, and C and D are increasingly polar. Also, C and D have basicity, increasing from C to D. In such a way we can predict the retention characteristics for solutes, and use this predictability to improve separation. Snyder, *et al.* [48] suggest for example hexane (a saturated hydrocarbon) for A, methylene chloride for B, an ether like methyl *tert.*– butyl ether for C, and acetonitrile for D.

These results have been found useful for the case where solvent characteristics are changed only from experiment to experiment — not for solvent changes during the chromatographic run — except for the case when only solvent strength ϵ is varied. This is not to say that one could not obtain superior results by considering changes in Δ_1 and Δ_2, just that methods utilizing these other aspects of the solvent model have not been developed. Rather, Snyder and his colleagues have focussed on simpler techniques for improving solute separation *via* Fast Method Development. It appears that FMD cannot handle more parameters gracefully or easily.

Snyder's equations express what occurs with a static solvent – solute model. To help take into account the dynamics when the solvent charcteristics change during the experiment, Snyder [47] uses an averaging of the solvent gradient to give effective relative retentions. This approach fails if anything more complicated than a linear solvent strength gradient is modelled. In fact, it is very likely the case that a large amount of controllability of the system is lost through averaging.

There is still another very important aspect that the model fails to address: the nature of high concentrations of solvent in the mobile phase. It is perfectly natural to consider the solvents present in the mobile phase as solutes, in light of the mechanisms of solvent action (*i.e.*, competition for attachment sites on the adsorbent; mobile phase effects negligible) shown to hold true by experiment. This behavior can be modelled by nonlinear dynamical equations (Thomas [50,51], Walter [52,53], Goldstein [14,15]) the nonlinearity deriving from the high concentrations. Thus we would expect to find that the implicitly linear model used in FMD to fail to show peculiarly nonlinear effects. Most notable among these effects are gradient spreading and "shock" formation from gradients. Which effect will occur depends on the particulars of variations in the solvent concentration; for the simple type of solvent gradients used in FMD, the solvent gradient will tend to increase its slope as it travels down the chromatographic column. This means that solutes near the top of the column experience a solvent gradient that is not as steep as the solutes further down the column. Exactly how important this nonlinear effect is to the control of the solute separation will have to be investigated.

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