

Elution Chromatography

Kinetic Analysis and Scaling up

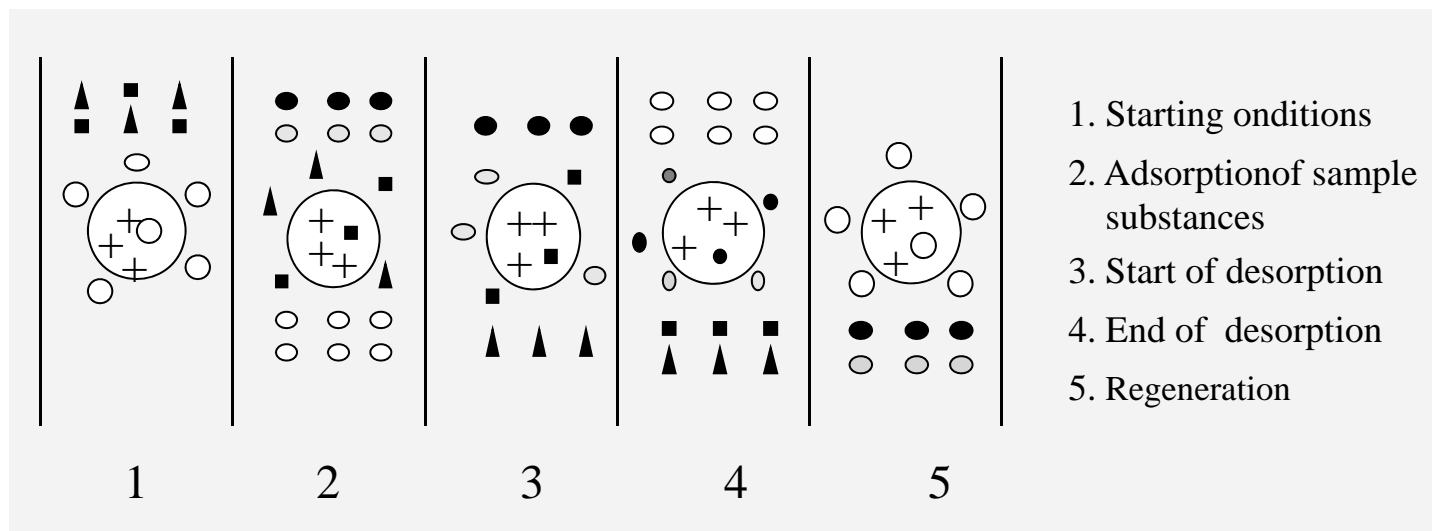
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Kinetic Analysis

• Introduction

- The column contains equilibrium stages
- The concentration profile is the result of diffusion and chemical reaction
- The actual diffusion and chemical reaction between solute and packing(5 step)



- To see the effects of diffusion and reaction, a solute pulse fed into a packed column

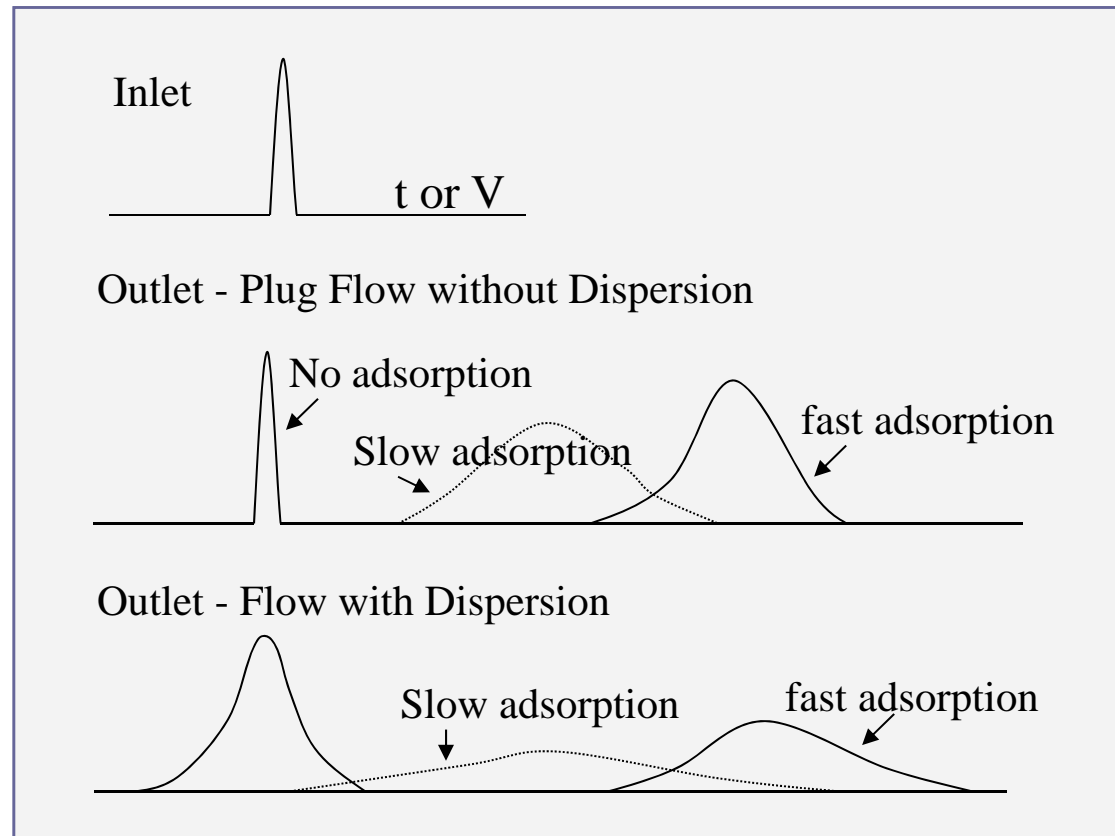


Figure 1. Modeling elution chromatography with rate processes

- **A quantitative approximation**

Mass balance equation

$$\varepsilon \frac{\partial y}{\partial t} + (1 - \varepsilon) \frac{\partial q}{\partial t} = E \frac{\partial^2 y}{\partial z^2} - v \frac{\partial y}{\partial z}$$

y, q = concentration of the solutes in mobile and stationary phase
 z = column length
 t = time
 v = linear velocity of the mobile phase
 ε = void fraction
 E = apparent axial dispersion coefficient

- initial condition

$$t = 0, \quad z = 0, \quad y = \left(\frac{M}{A} \right) \delta(z)$$
$$\text{all } z, \quad q = 0$$

- to solve these equation

- if mass transfer is controlling

$$(1 - \varepsilon) \frac{\partial q}{\partial t} = ka(y - y^*)$$

K = mass transfer coefficient
 a = packing area per bed volume
 y^* = concentration in solution at equilibrium

- if diffusion within pores is rate controlling

$$(1 - \varepsilon) \frac{\partial q}{\partial t} = \sqrt{\frac{D}{t'}} a(y - y^*)$$

D = effective diffusion coefficient
t' = some characteristic time

- if reversible chemical reaction is rate controlling

$$(1 - \varepsilon) \frac{\partial q}{\partial t} = ky = k'q$$

k, k' = forward and reverse rate constants of this reaction

$$l = \int_0^l dz = \left[\frac{v}{ka} \right] \int_{y_0}^y \frac{dy}{y - y^*}$$

$$l = HTU \cdot NTU$$

Number of transfer units(NTU)

Height of a transfer unit(HTU)

$$y = y_0 \exp \left(- \left(\frac{t/t_0 - 1}{\sqrt{2}\sigma} \right)^2 \right)$$

$$= y_0 \exp \left(- \left(\frac{t/t_0 - 1}{\sqrt{2/NTU}} \right)^2 \right)$$

$$NTU = \frac{1}{\sigma^2} = \frac{l}{HTU} = \frac{kal}{v}$$

The concentration at the peak

$$\int_{-\infty}^{\infty} yHdt = M$$

The result

$$y_0 = \frac{M / Ht_0}{\sqrt{2\pi(NTU)}} = \frac{M}{[\varepsilon + (1 - \varepsilon)K]V_B} \sqrt{\frac{kal}{v}} = \frac{M / A}{[\varepsilon + (1 - \varepsilon)K]} \sqrt{\frac{ka}{lv}}$$

$$y = \left[\frac{M / A}{[\varepsilon + (1 - \varepsilon)K]} \sqrt{\frac{ka}{lv}} \right] \exp \left(- \frac{kal}{2v} \left(\frac{t}{t_0} - 1 \right)^2 \right)$$

$$y = \left[\frac{M / A}{[\varepsilon + (1 - \varepsilon)K]} \sqrt{\frac{ka}{lv}} \right] \exp \left(- \frac{kal}{2v} \left(\frac{V}{V_0} - 1 \right)^2 \right)$$

- **Example**

- ▶ **Aspartame Isomer Separation**

	Peak Time t_0 (min)	Peak Spread $t_0\sigma$ (min)
<i>d</i> aspartame	62	3
<i>l</i> aspartame	71	6

column length : 25cm
diameter : 0.41cm
particle diameter : 45×10^{-4} cm
particle volume fraction : 0.62

Problem : Find the apparent rate constant k for this separation and compare these rate constants with those expected from the mass transfer correlation

$$\frac{k}{v} = 1.17 \left(\frac{d v}{\nu} \right)^{-0.42} \left(\frac{v}{D} \right)^{-0.67}$$

d : packing diameter
 v : solvent velocity
 ν : kinematic viscosity
 D : diffusion coefficient
 0.7×10^{-5} cm²/sec

Solution

$$\begin{aligned}\frac{y}{y_0} &= \exp\left(-\left(\frac{t/t_0 - 1}{\sqrt{2/NTU}}\right)^2\right) \\ &= \exp\left(-\frac{(t-t_0)^2}{2t_0^2/NTU}\right)\end{aligned}$$

For the *d* aspartame

$$\begin{aligned}\frac{t_0}{\sqrt{NTU}} &= \text{Peak spread} \\ \frac{62 \text{ min}}{\sqrt{NTU}} &= 3 \text{ min}, \quad NTU = 427\end{aligned}$$

for the *l* aspartame, $NTU = 140$

$$k = NTU \left(\frac{v}{al}\right)$$

The velocity under the conditions given

$$\begin{aligned}v &= \frac{H}{((\pi/4)d^2)} \\ &= \frac{2.0 \text{ cm}^3 / 60 \text{ sec}}{[\pi/4(0.41 \text{ cm})^2]} \\ &= 0.25 \text{ cm / sec}\end{aligned}$$

Therefore

$$\begin{aligned}a &= 6(1-\epsilon)/d \\ &\text{for the } d \text{ aspartame}\end{aligned}$$

$$\begin{aligned}k &= \frac{427 (0.25 \text{ cm / sec})}{[6(0.62) / 45 \times 10^{-4} \text{ cm}] 25 \text{ cm}} \\ &= 5.2 \times 10^{-3} \text{ cm / sec}\end{aligned}$$

for the *l* aspartame,

$$k = 1.7 \times 10^{-3} \text{ cm / sec}$$

The values for the mass transfer coefficient

$$k = 1.17 \left(0.25 \frac{\text{cm}}{\text{sec}} \right) \left[\frac{0.01 \text{ cm}^2 / \text{sec}}{45 \times 10^{-4} (0.25 \text{ cm} / \text{sec})} \right]^{0.42} \\ \times \left[\frac{0.7 \times 10^{-5} \text{ cm}^2 / \text{sec}}{0.01 \text{ cm}^2 / \text{sec}} \right]^{0.67} = 5.6 \times 10^{-3} \text{ cm} / \text{sec}$$

► The Effects of Axial Dispersion

Problem : For slow (laminar) flow in a long thin tube, the concentration profile of a pulse injected at $t = 0$ and $z = 0$ is given by

$$y = \frac{M / (\pi / 4) d^2}{\sqrt{4Et\pi}} \exp\left(-\frac{(z - tv)^2}{4Et}\right)$$

E : dispersion coefficient, $E = v^2 d^2 / 192D$

D : solute's diffusion coefficient

v : velocity, t : time

z : tube length, $z = l = vt_0$

d : diameter

Find NTU expression

Solution

rewriting

$$z = l = v t_0$$
$$y = \frac{M / (\pi / 4) d^2}{\sqrt{4Et\pi}} \exp\left(-\frac{tv^2}{4Et} \left(\frac{t}{t_0} - 1\right)^2\right)$$

Using the expression for E

$$y = 4.98 \frac{M}{d^3} \sqrt{\frac{D}{lv}} \exp\left(-\frac{48Dl}{d^2v} \left(\frac{t}{t_0} - 1\right)^2\right)$$

$$NTU = \frac{96Dl}{d^2v}$$

Scaling up

- **Introduction**

- At the larger scale, we want a bigger capacity but with the same yield and purity
- To increase the capacity, we are able to increase the solute concentration in the feed and the flow through the column

$$y = y_0 \exp\left(-\left(\frac{V}{V_0} - 1\right)^2 / 2\sigma^2\right)$$

- parameter : y_0 , V/V_0 , σ

- **Changes in the standard deviation**

$$\sigma^2 = \frac{v}{k_l a l}$$

- it is a function of the velocity, column length, rate constant
- d : sphere's diameter

rate constant k :

- solute와 packing사이의 상호작용이 지배되는 단계에서 변화

- if the controlling step by diffusion and fast reaction within the particles

$$k \propto \frac{1}{d} \Rightarrow \sigma^2 \propto \frac{d^2 v}{l}$$

- if the controlling step by mass transfer between the bulk and the particle

$$k \propto \left(\frac{v}{d}\right)^{1/2} \Rightarrow \sigma \propto \frac{v^{1/2} d^{3/2}}{l}$$

- it may also change because of dispersion

$$\sigma = \sqrt{\frac{2E}{lv}} \propto d \sqrt{\frac{v}{lD}}$$

Table 1. Changes in the Standard Deviation

Controlling step	The quantity σ^2 is Proportional to	Remarks
Internal diffusion and reaction	$\frac{d^2 v}{l}$	Probably the most common case
External mass transfer	$\frac{v^{1/2} d^{3/2}}{l}$	Supported by the most complete analysis
External(Taylor) dispersion	$\frac{d^2 v}{Dl}$	Likely to become more important at large scale
Axial diffusion	$\frac{D}{lv}$	Rarely important
Column of actual equilibrium stages	$\frac{1}{l}$	Assumes the number of stages N is proportional to the length

- **Scale up the separation**

- ▶ Keep the ratio of packing diameter to column diameter
 - preserve the character of the flow in the packed bed
 - use larger, cheaper packing
- ▶ Fix d and increase both v and l at constant (v/l)
 - at this case, the pressure drop can increase dramatically
 - because of small constant d , the pressure drop is already high
- ▶ use short fat columns
 - v and l used in the small scale separation
 - increased capacity is due to their greater cross sectional area

- **Example**

- ▶ **Fumarase Chromatography**

10g of the enzyme fumarase are being purified in an ion exchange column. At a velocity of 30cm/hr, the peak in concentration exits the column in 93min and the standard deviation of this peak is given as 12min

(a) how long must we purify for a 90% yield

$$\frac{y}{y_0} = \exp\left(-\left(\frac{t/t_0 - 1}{\sqrt{2}\sigma}\right)^2\right) = \exp\left(-\frac{(t - 93 \text{ min})^2}{2(12 \text{ min})^2}\right)$$

Thus $\sigma = 0.129$,

$$yield = \frac{1}{2} + erf \frac{t - t_B}{\sqrt{2}t_B\sigma} \quad 0.9 = 0.5 + erf \frac{t - 93}{\sqrt{2}93(0.129)}$$

$$t = 115 \text{ min}$$

We must wait 115/93(-1.24) times longer then the peak time to get a 90% yield

(b) If we increase the flow to 60cm/hr, how long must we run for this same yield if the process is controlled by diffusion and reaction?

$t_0 = 46.5\text{min}$
from Table 1

$$\sigma = 0.129 \left[\frac{60}{30} \right]^{1/2} = 0.182$$

Thus Eq. (7.2-12)

$$0.9 = 0.5 + \text{erf} \frac{t - 46.5}{\sqrt{2} 46.5(0.182)}$$

$$t = 61.8 \text{ min}$$

We must wait $61.8/46.5 (=1.33)$ times the peak time to get a 90% yield

(c) How long must we wait if the process is controlled by mass transfer

If the process is controlled by mass transfer,

$$t_0 = 46.5\text{min}$$

$$\sigma \propto v^{1/4}$$

$$\sigma = 0.129 \left[\frac{60}{30} \right]^{1/4} = 0.153$$

$$0.9 = 0.5 + \text{erf} \frac{t - 46.5}{\sqrt{2} 46.5(0.153)}$$

$$t = 59.4 \text{ min}$$

We must wait only 1.28 times the peak time for a 90% yield

(d) How long must we wait if Taylor dispersion controls?

If Taylor dispersion is rate controlling

$$\sigma \propto v^{1/2}$$

The results are exactly the same as part(b)

(e) How long must we wait if the column actually contains equilibrium stages

Thus $\sigma = 0.129$

$$\frac{t}{46.5 \text{ min}} = \frac{115 \text{ min}}{93 \text{ min}}$$

Thus t is 57.5min, 1.24 times the time for the peak

► Transferrin Desalting

A dilute feed in which 80% of the total solute is transferrin and 20 % behaves like sodium chloride is to be desalted on a dextran gel column. Operation the column at 10cm/hr gives the following results:

	Peak Time t_0 (min)	$t_0\sigma$ (min)
Void volume	27	-
Transferrin	41	4
Salts	88	4

Problem : What is the maximum velocity and the time which will give a 99% yield of thransferrin which is 98% pure

Solution :

$$\sigma = \frac{t_0 \sigma}{t_0} = a v^{1/2}$$

$$\sigma(\text{transferrin}) = \frac{4 \text{ min}}{41 \text{ min}} = a \left(\frac{10 \text{ cm}}{\text{hr}} \right)^{1/2}$$

$$a = 0.0309 \sqrt{\text{hr} / \text{cm}}$$

$$\sigma(\text{salt}) = \frac{4 \text{ min}}{88 \text{ min}} = a \left(\frac{10 \text{ cm}}{\text{hr}} \right)^{1/2}$$

$$a = 0.0144 \sqrt{\text{hr} / \text{cm}}$$

$$\text{purity of } i = \frac{y_0(i) \text{ yield}(i)}{\sum_j y_0(i) \text{ yield}(i)}$$

$$0.02 = \frac{(\text{yield salt})(0.2)}{0.99(0.8)}$$

$$\text{yield salt} = 0.08(8\%)$$

$$0.99 = \frac{1}{2} \left[1 + \operatorname{erf} \frac{vt / ((10 \text{ cm} / \text{hr}) 41 \text{ min}) - 1}{\sqrt{2} \cdot 0.0309 \sqrt{\text{hr} / \text{cm}} \sqrt{v}} \right]$$

$$0.08 = \frac{1}{2} \left[1 + \operatorname{erf} \frac{vt / ((10 \text{ cm} / \text{hr}) 88 \text{ min}) - 1}{\sqrt{2} \cdot 0.0144 \sqrt{\text{hr} / \text{cm}} \sqrt{v}} \right]$$

$$v = 93 \text{ cm} / \text{hr}$$

$$t = 7.4 \text{ min}$$