Separation Methods Based on Distributions in Discrete Stages (02/04/15)

1. Chemical Separations: The Big Picture

   Classification and comparison of methods

2. Fundamentals of Distribution Separations

3. Separation Methods Based on Distributions in Discrete Stages

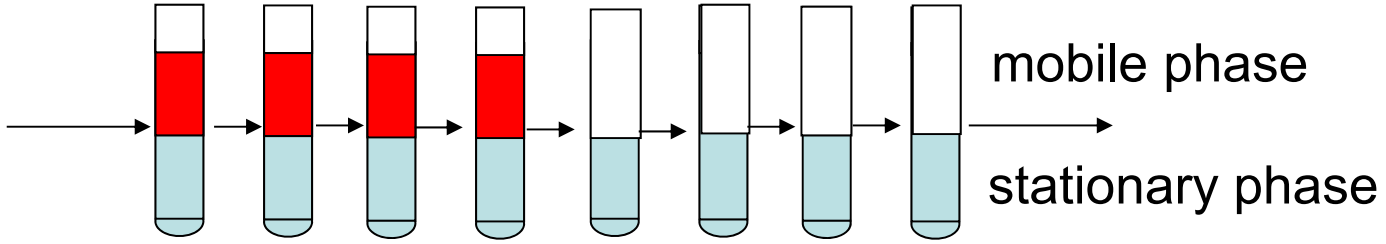
   Such as solvent extraction and distillation

4. Introduction to Distribution Separations in chromatographic methods. The plate theory, the rate theory; van Deemter's equation.

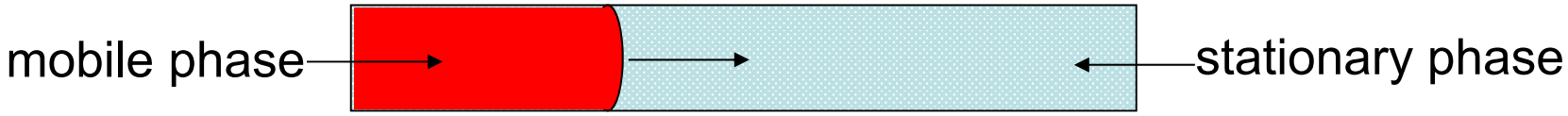
Basics of Chromatography

A. Chromatography vs. Countercurrent distribution

1. Both techniques involve the interaction of solutes with a mobile phase and stationary phase



Countercurrent distribution



Chromatography

2. Countercurrent distribution is based on a well-defined number of contacts between the mobile and stationary phases (i.e. discrete contact method)

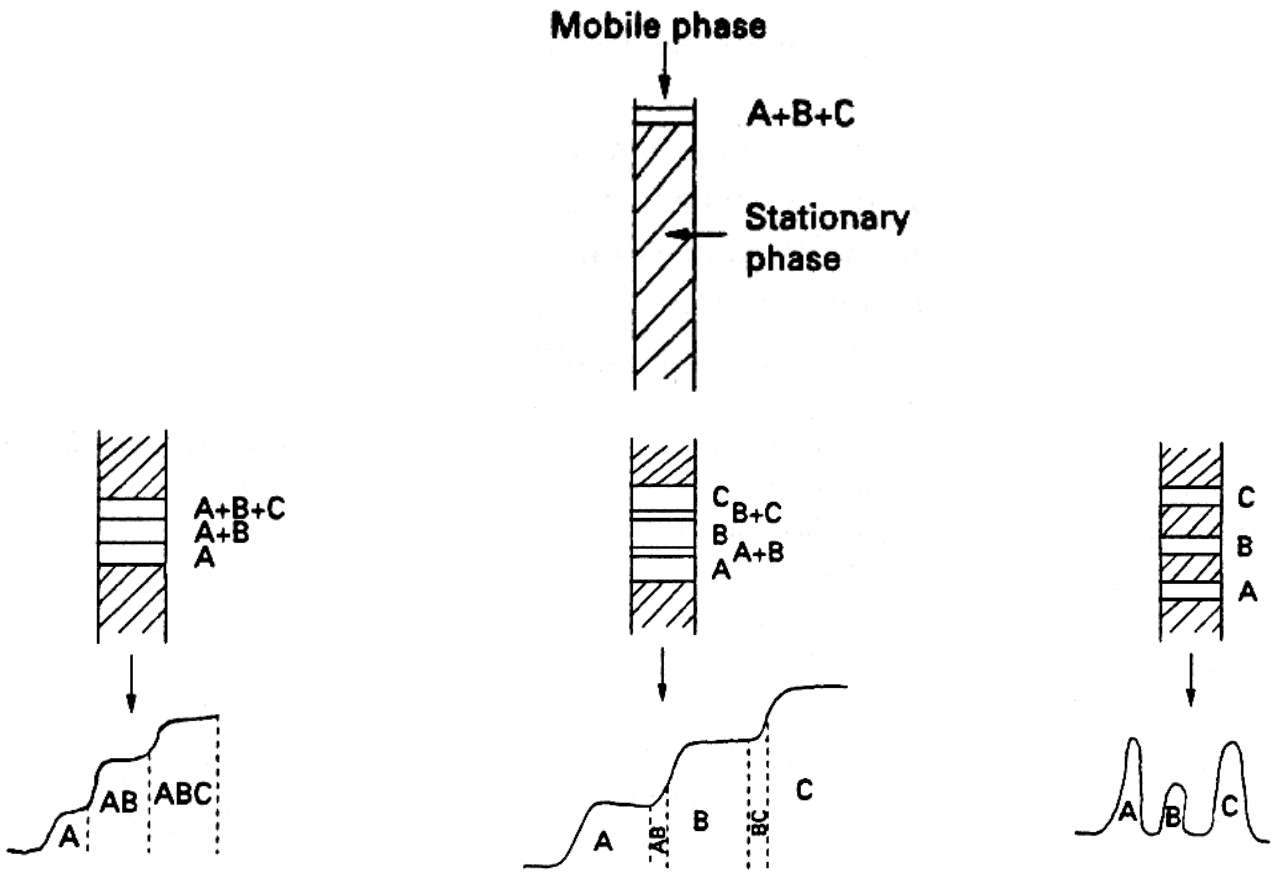
Chromatography involves continuous contact between the mobile and stationary phase (i.e. continuous contact method)

3. Separation of solution in both methods depends on
   a. *differences* in the retention of solute (i.e. their interaction with mobile and stationary phase, *distribution coefficients*).
   b. The *efficiency* of the the system (i.e., *the number of transfers* or the width of the solute peaks).

B. Type of Chromatography

1. Based on type of mobile phase:
   a. Gas chromatography
   b. Liquid chromatography
   c. supercritical fluid chromatography
2. Based on type of support
   a. Packed bed (column) chromatography
   b. Open tubular (capillary) chromatography
   c. Open bed (planar) chromatography
3. Based on the elution method:
   a. Constant column condition (e.g., isocratic conditions = constant mobile phase composition, isothermal conditions (T), or isobaric conditions (pressure).
   b. Variable column conditions (e.g., gradient elution, stepwise elution, temperature programming, pressure programming).

4. Based on the type of sample development:



Frontal development (solutes continuously Introduced with mobile phase).

Displacement development (with displacer in the Mobile phase)

Elution development (under equilibrium)

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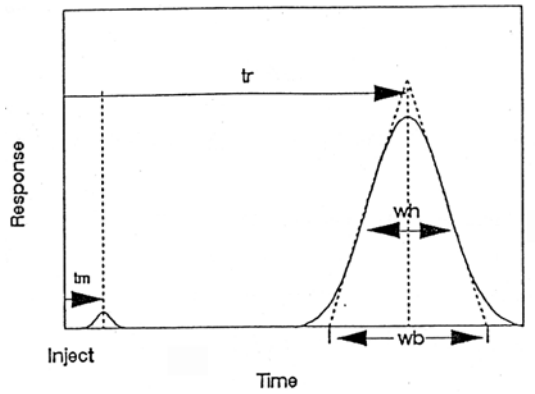
C. Chromatography Parameters:

(1) Time vs. detector response:



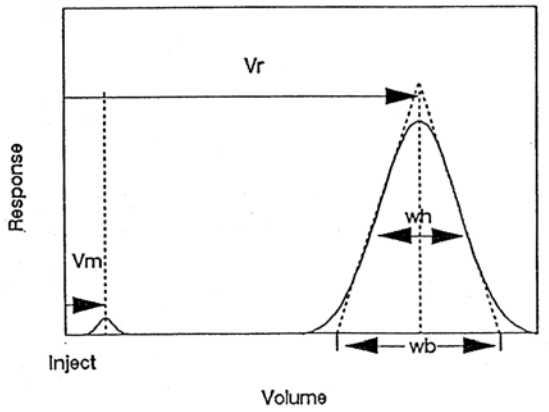
Where: t_R = Retention time

t_M= Void time (or dead time, hold-up time) time for mobile phase entering column reach the detector.

W_b = Baseline width of the peak (<u>in time units</u>)

W_h = Half-height width of the peak (<u>in time units</u>)

(2) Volume vs. detector response:



Where: V_R = Retention volume

V_M= Void volume of mobile volume (volume of mobile phase filling the column)

W_b = Baseline width of the peak (<u>in volume units</u>)

W_h = Half-height width of the peak (<u>in volume units</u>)

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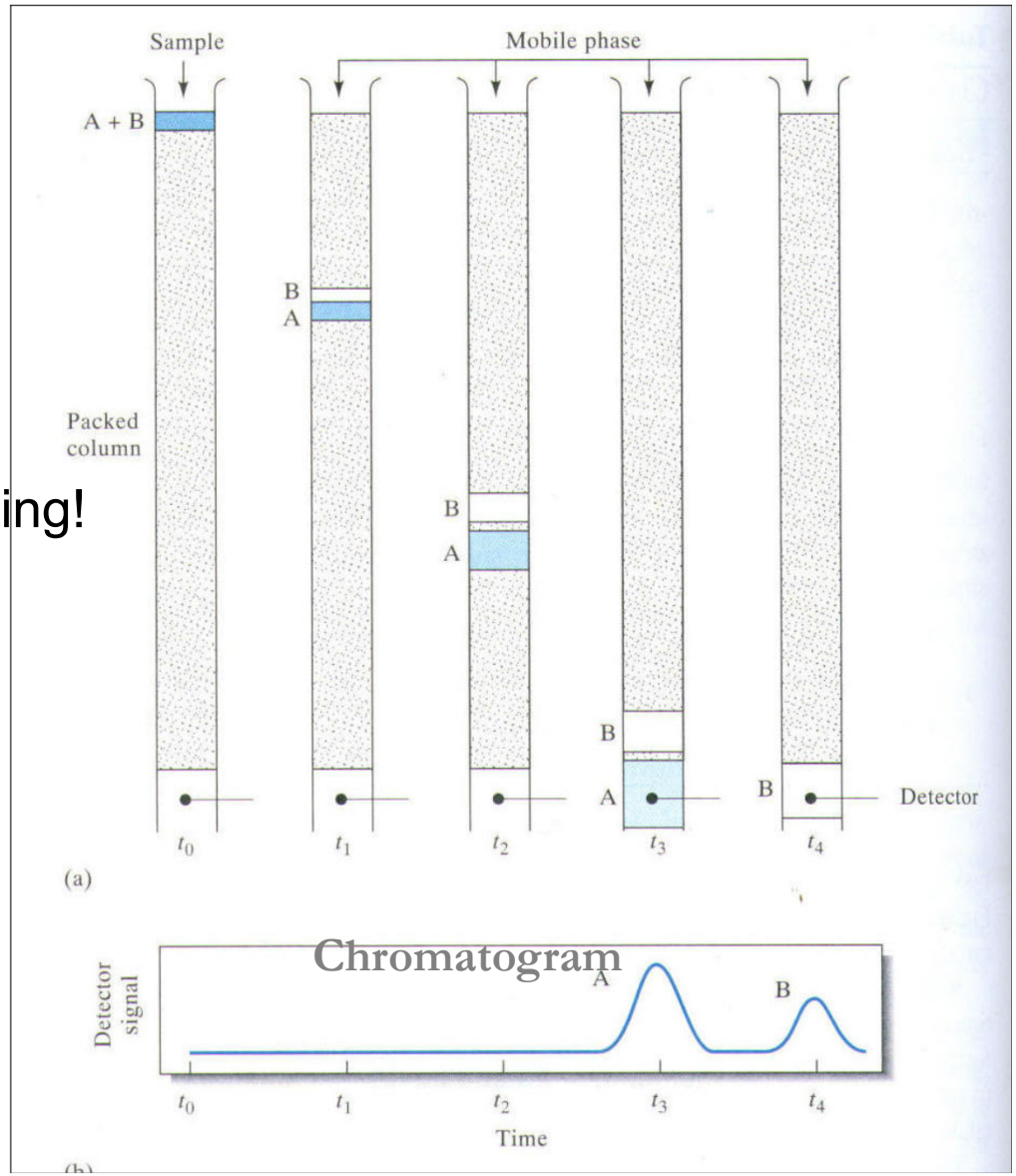
Column Chromatography

Dilution &
Peak broadening!



(3) Relationship of volume and time response:

$$V_R = t_R \text{ X } F$$
$$V_M = t_M \text{ X } F$$

Where: F = Flow-rate of solvent through the column

(4) Adjust retention times and volumes

Adjusted retention time (t_R') = $t_R - t_M$

Adjusted retention Volume (V_R') = $V_R - V_M$

These adjusted parameters are useful in that they better reflect the true retention of solute one the system (i.e. they correct for the void time contribution to the solute's total elution time).

D. Solute Retention:

(1) A solute's retention time or volume is important since it is related to the strength of a solute's interactions with the mobile and stationary phases.

(2) The capacity factor (k) is commonly used in chromatography as a measure of solution retention, where

$$k = \frac{\text{Moles A}_{\text{stationary phase}}}{\text{Moles A}_{\text{mobile phase}}} = q / p$$

(3) k can be experimentally related to t_r' or V_r' by the following equations:

$$k = t_R'/t_M = (t_R - t_M)/t_M \longrightarrow t_R = t_M(1+k) = (L/u)*(1+k)$$

$$k = V_R'/V_M$$

L : length of column
u: the average mobile phase velocity

E. Efficiency of Chromatography and Plate Theory:

1. Efficiency in chromatography is related experimentally to solute's peak width (e.g., an efficient system will present narrow peaks)

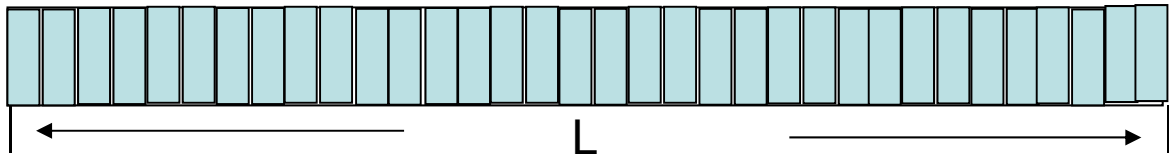
2. Efficiency in Chromatography is related theoretically to various kinetic and thermodynamic process occurring in the column: e.g., equilibrium, diffusion, and fluid (mobile phase) flow.

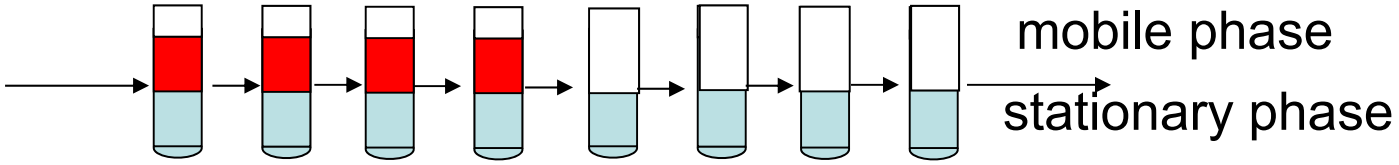
3. Plate theory for describing the efficiency of chromatography (proposed by Martin and Synge). Plate theory has contributed significantly in understanding the formation of bands and band broadening.

Assumptions: ***a.*** *Chromatography column can be divided into s number of volume elements or imaginary sections,* ***called plates***. ***b.*** At each plate the partitioning of the solute between stationary and mobile phase is rapid and equilibrium reached before the solute goes to the next plate. ***c.*** The solution distribution is constant and is independent with the solute concentration.

This theory has been replaced by rate theory. However, the number of plats (**N**) and plate height (**H**) are stilled used to evaluate the efficiency of chromatography.

Column





Craig apparatus

(a) After given number of transfers (r), the relative amount of A in any tube n is

$$P_{r,n} = \frac{r!}{n!\,(r-n)!}\, p^n\, q^{r-n}$$

Where: $P_{r,n}$ = Fraction of A in tube n after transfer r.

(b) The binomial can be expended as Gaussian distribution when n larger than 20 (rpq>3).

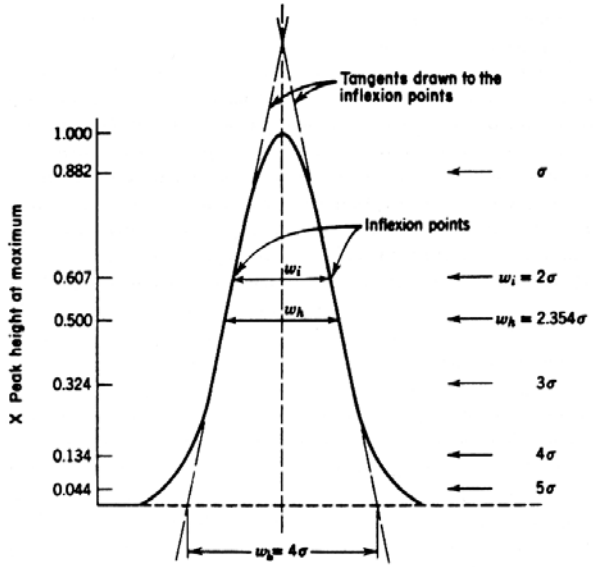
$$P_{r,n} = \frac{1}{\sqrt{2\pi} * \sqrt{rqp}}\ \text{Exp}\,[-(n-rp)^2/2rpq)]$$

Where: $P_{r,n}$ = Fraction of A in tube n after transfer r.

4. Properties of Gaussian curve.

(a). The general form of a Gaussian curve is shown below:

$y = y_0 \, Exp[-x^2/2\sigma^2]$



Where: y = Height of curve at position x

y_0 = Maximum height of the curve (at x = 0)

σ = standard deviation of the curve

(b). Measures of σ in Gaussian curves.

W_i = 2 σ (width at peak's inflection points, y = 0.607 y_0)

W_h = 2.354 σ (width at half-height of the peak. y = 0.5 y_0)

W_b = 4 σ (measured by drawing tangents to the curve at peak's inflection points. and measuring the peak width where they intersect the baseline.

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5. Theoretical plates

(a). The peak width, or variance, is related to column efficiency, but also increase with solutes retention (i.e., k, t_R, or V_R).

(b). To compare the efficiencies of the solute with different retentions, the number of theoretical plates (N) is often used, where

$$\mathbf{N = (t_R / \sigma_t)^2}$$

(c). N is used as a measure of the number of equilibration that must have occurred on the column to give the corresponding peak width. This is analogous to the number of tubes in a Craig apparatus.

(d). Experimentally, N is measured by using t_R and one of the variance measures of σ.

$$W_h = 2.354\ \sigma \longrightarrow N = 5.54*(t_R / W_h)^2$$

$$W_b = 4\ \sigma \longrightarrow N = 16*(t_R / W_b)^2$$

(e). To give a more value of the column efficiency, other measures of plate number are used. A common one is N_{eff} (the effective plate number), where

$$\mathbf{N_{eff} = (t_R' / \sigma_t)^2}$$

$$N_{eff} = 5.54*(t_R' / W_h)^2$$

$$N_{eff} = 16*(t_R' / W_b)^2$$

(f). The relationship between N and N_{eff}:

$$\mathbf{N_{eff} = N\,[k/(1+k)]^2}, \text{ k, retention factor}$$

$$k = t_R'/t_M = (t_R')/(t_R - t_R') \longrightarrow t_R'/t_R = k/(k+1)$$

For weak retained systems (k is small), N_{eff} could be quiet different than N.

(g). The height of a theoretical plate (H or HETP: height equivalent to a theoretical plate)

$$\mathbf{H = L/N}$$

Where: L = Column length

H is useful in comparing the efficiencies of different sized columns or different support materials. It is also heavily used in chromatography theory to relate various chromatographic parameters to the kinetic processes occurring in the column.

F. Measures of Solute Separation:

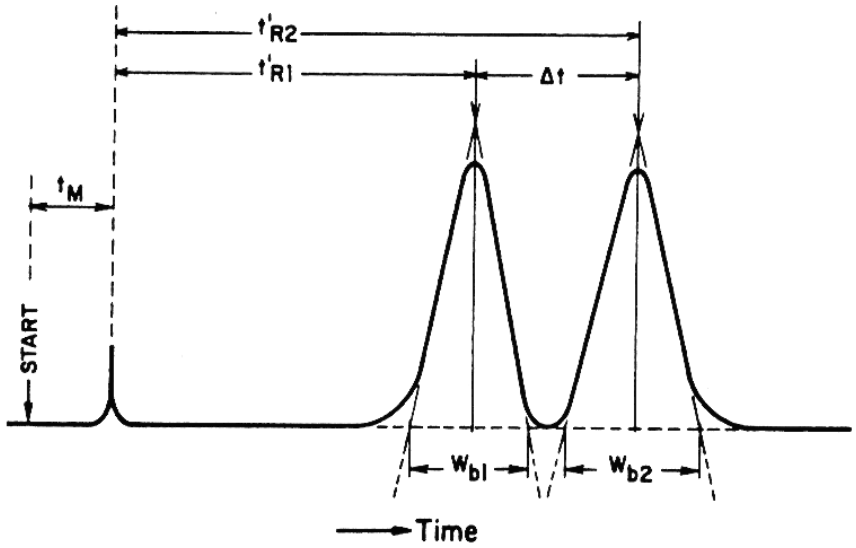
1. **The separation factor (α)** is one parameter used in describing how well two solutes are separated on a chromatographic system.

$$\alpha = t_R'_2 / t_R'_1 = k_2/k_1$$

Where: k_1 = The capacity factor of the first solute.
k_2= the capacity factor of the second solute.

The separation factor measures how well two solute are separated based on their retention (k values), but does not consider the effect of column efficiency, or peak widths on a separation.

2. The resolution (R_s) between two peaks is a second measure of how two peaks are separated.



$$R_s = \frac{t_{R2} - t_{R1}}{(W_{b2}+W_{b1})/2}$$

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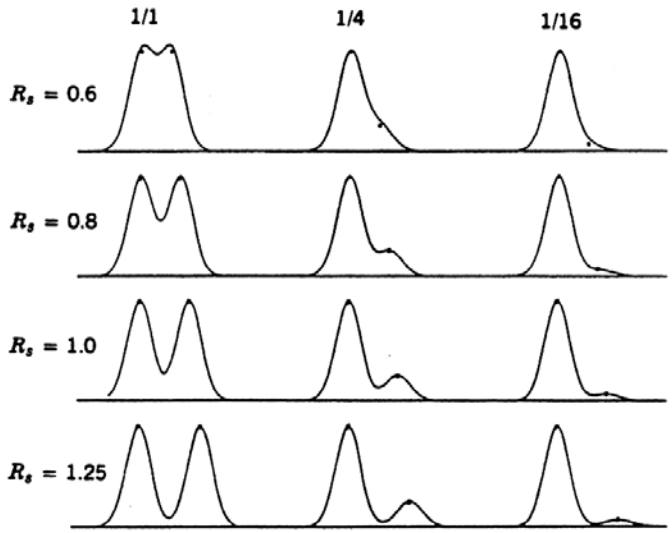
$$R_s = \frac{t_{R2} - t_{R1}}{(W_{b2}+W_{b1})/2} = \frac{2*\Delta t}{(W_{b2}+W_{b1})} = \frac{1.18 *\Delta t}{(W_{h2}+W_{h1})}$$

$$W_h = 2.354\ \sigma$$

$$W_b = 4\ \sigma$$

The resolution considers both retention (t_{R2}) and column efficiency (W_b) in defining how well two peaks are separated.

c. The effective peak size and degree of separation on R_s is shown below.



d. $1.5 > R_s > 1.0$ is adequate for most separations, especially if the peaks are about the same size and quantity is based on peak height height rather that areas.

e. For most cases, ***$R_s \geqslant 1.5$ is considered baseline resolution***. This represents quantitative (>99%) separation of two solutes.

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G. Fundamental factors affecting resolution:

Assuming N is same for the two peaks, and α >1.

$$R_s = \frac{t_{R2} - t_{R1}}{(W_{b2}+W_{b1})/2}$$

$N = (t_R/\sigma_t)^2$

$W_h = 2.354\ \sigma$

$W_b = 4\ \sigma$

$$R_s = [N^{1/2}/2][(k_2-k_1)/(2+k_1+k_2)]$$

$$\alpha = t_R'_2 / t_R'_1 = k_2/k_1$$

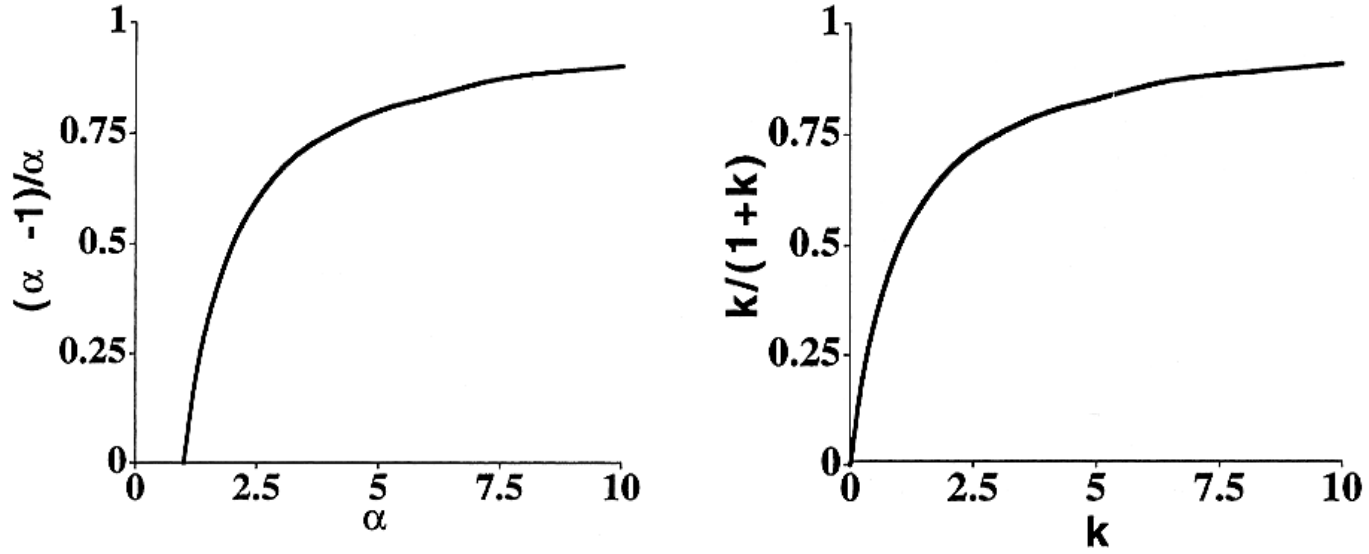
$$R_s = [N^{1/2}/4]*[(\alpha -1)/(\alpha+1)]*[k_{AV}/1+ k_{AV}], \quad k_{AV} = (k_1+k_2)/2$$

Assuming $W_{b2} = W_{b1}$

$$\mathbf{R_s = [N^{1/2}/4]*[(\alpha -1)/(\alpha)]*[k_2/(1+ k_2)],}$$

2. This equation shows how the resolution of a separation is affected by the efficiency of the system (N) as well as both retention of both solute (k and α).

3. Properties of the functions:



$$R_s = [N^{1/2}/2]*[(\alpha -1)/(\alpha)]*[k_2/(1+ k_2)],$$

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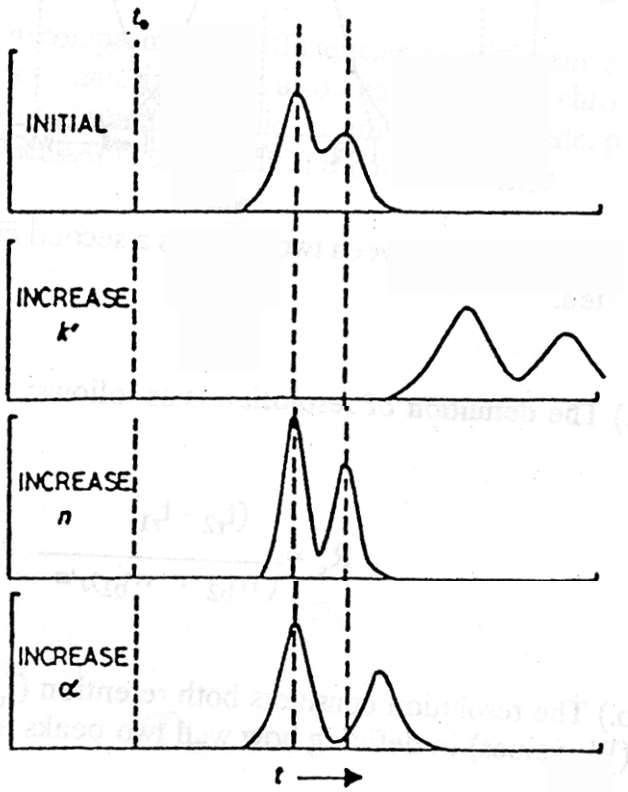
4. This equation also shows that the separation between two solutes can be improved in one of three ways:

(a) By increasing n (using longer ore more efficient columns)

(b) By increasing k (increasing solute retention on the system)

(c) By increasing α (increasing the selectivity of the system, or the relative retention of the second solute vs. the first one).



A Question for the discussion next class!

$$R_s = [N^{1/2}/4]*[(\alpha - 1)/(\alpha)]*[k_2/(1+ k_2)], \qquad N = (t_R/ \sigma_t)^2$$