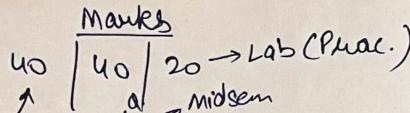


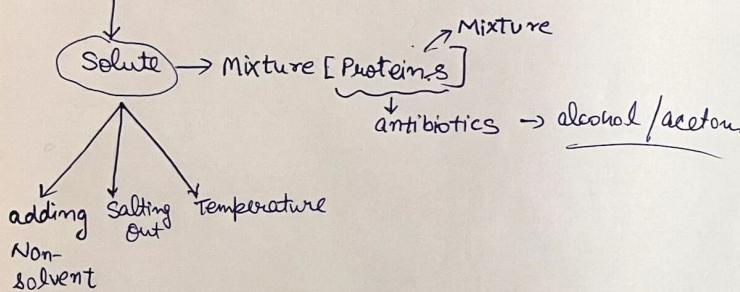
BT-306



↑
Bef Midsem (40+30)

Book: Bioseparations by Belter, Cussler and Hu

Precipitation:



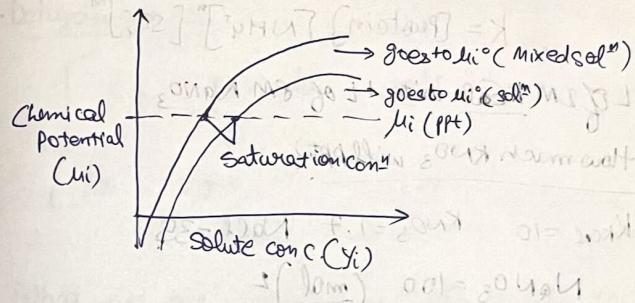
Feed Stream \rightarrow Solvent + Solute

Non-solvent \downarrow
Water

chemical potential
free energy

$$\begin{aligned} \mu_i(\text{ppt}) &= \mu_i(\text{sol}^m) \\ &= \mu_i^\circ(\text{sol}^m) + RT \ln Y_i \end{aligned}$$

Y_i = conc. of the solute

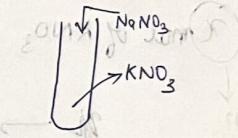


Precipitation w/ salt

electrolyte

$$K = [K^+][NO_3^-]$$

Solubility product



$$K = [K^+][NO_3^-] = K^\circ (solid) \cdot e^{-RT \ln [i] + Z_i F \phi}$$

ionic charge

$$\ln K = \ln K^\circ (solid) - \mu_K^\circ (solid) / RT - \mu_{NO_3^-}^\circ (solute) / RT$$

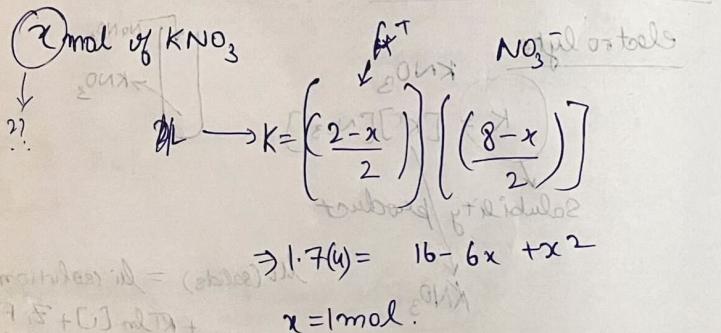
$$K = [\text{protein}] [NH_4^+]^m [SO_4^{2-}]^n$$

1L of 2M KCl with 1L of 8M NaNO₃

How much KNO₃ will ppt?

$$K_{\text{KCl}} = 10 \quad K_{\text{NaNO}_3} = 1.7 \quad K_{\text{NaCl}} = 35$$

$$NaNO_3 = 100 \quad \left(\frac{\text{mol}}{\text{L}}\right)^2$$



Temperature:

↳ selective denaturation
↓
(stability const.)

$$\frac{dP}{dt} = -K [P] \quad \xrightarrow{\text{Activation energy}} \quad ①$$

$$K = K_0 e^{-E_a/RT}$$

↓
const.

2 Dehydrogenase

$$K_A = \frac{5.0 \times 10^7}{sec} e^{-\frac{-380 \text{ kJ}}{RT}}$$

$$K_B = \frac{4.2 \times 10^{14}}{sec} e^{-\frac{-415 \text{ kJ}}{RT}}$$

What will the activity be after 10 minutes @ 20°C and 10 min @ 50°C?

Integrating ①

$$\frac{P}{P_0} = e^{-kt}$$

$$K_A \quad \frac{20^\circ C}{0.3 \times 10^{-11}}$$

$$K_B \quad \frac{50^\circ C}{4 \times 10^{-10}}$$

$$\frac{50^\circ C}{1.6 \times 10^{-4}}$$

$$\frac{3 \times 10^{-3}}{3 \times 10^{-3}}$$

$$\frac{[A]}{[A_0]} = e^{-\frac{KA}{P_0} + \frac{KB}{P_0}} = \left(\frac{1/b}{1/b} \right)$$

$$\frac{A}{A_0} \Big|_{20^\circ C} \xrightarrow{\text{arbitrary value}} 0.999 \text{ mol} = 1/b$$

$$= 0.91$$

Large Scale precipitation:

$$\text{"kinetics"} / \left(\frac{P_{\text{v}}}{V} \right)^* = \frac{f_0 \times 0.2}{4D} = K$$

- D Initial mixing $\rightarrow "t" = \frac{i^2}{4D}$ $i = \text{turbulent eddies avg size}$
- ii) Nucleation
- iii) Diffusion limited growth
- iv) Flow induced growth
- v) Flocculation
- vi) centrifugation.

$$D = \text{solute's diffusion coefficient}$$

$$L = \left(\frac{\rho \eta^3}{Pv} \right)^{1/4}$$

P = solution density

η = Kinematics viscosity

$Pv = \text{Power/volume of stirring.}$

Nucleation

Diffusion limited growth

$$\left(\frac{dy_i}{dt} \right) = -K y_i^2$$

$y_i = \text{conc. of solute particles}$

K = Rate const.

$$\frac{1}{y_i} = \frac{1}{y_0} + Kt$$

$$K = 8\pi D \bar{N}$$

D = diffusivity coeff

d = solute diameter (in micrometers)

\bar{N} = Avogadro's Number.

$$E_{\text{Mol}} f_0^2 \cdot 1 = \text{stochastic statistics!}$$

$$y_i \bar{M} = y_{i0} \bar{M}_0 \Rightarrow \bar{M} = \bar{M}_0 (1 + y_{i0} Kt)$$

$\bar{M} = \text{Mol. wt. of the precipitate}$

note: mol. wt. of precipitate = M_p / mol. wt. of solute

Flow induced growth

$$\frac{dy_i}{dt} = -K y_i^2$$

$$K = \frac{2}{3} \alpha \bar{N} d^3 \left[\frac{Pv}{\rho v} \right]^{1/2}$$

α = sticking coefficient

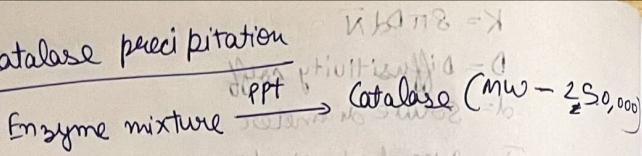
$$\phi \text{ (volume fraction of the solute)} = \left(\frac{1}{6} \pi d^3 \right) y_i \bar{N}$$

$$\frac{dy_i}{dt} = \frac{4 \alpha \phi \left[\frac{Pv}{\rho v} \right]^{1/2}}{(\alpha + 1) \pi d^3} y_i^2$$

$$\frac{y_i}{y_{i0}} = \exp \left(- \left(\frac{4 \alpha \phi \left[\frac{Pv}{\rho v} \right]^{1/2}}{(\alpha + 1) \pi d^3} \right) t \right)$$

22F =

Q: Catalase precipitation



$$\text{Precipitate density} = 1.3 \text{ g/cm}^3$$

$$(\frac{4}{3}\pi r^3) \rho M = \pi D^2 \text{ Diameter} \geq 10.4 \text{ nm}$$

$$D = 4.1 \times 10^{-7} \text{ cm}^2/\text{s}$$

Volume = 100 L / 3-flared with 0.1 rpm motor

$$\text{feed conc.} = 0.29 \text{ g/L}$$

- Assume solution has prop close to water
- time over which diffusion will limit growth
 - the conc. of particles at the end of this time
 - time req to grow 100 μm particles for centrifugation.

$$\text{Sol: } t = \frac{1}{4D} \left(\frac{\rho \pi^3}{P/V} \right)^{1/2}$$

$$\left(\frac{1}{4(4.1 \times 10^{-7} \text{ cm}^2/\text{s})} \right) \left[\frac{1 \text{ g/cm}^3 (0.01 \text{ cm}^2/\text{s})^3}{0.1 \text{ atm} (746 \times 10^9 \text{ g}) \left[\frac{(\text{sec}^3)}{\text{cm}^3} \right]} \right]^{1/2} = 7 \text{ sec}$$

$$\frac{1}{y_i} = \frac{1}{y_{i0}} + (8\pi D d N) t, \quad \text{where molar} \times$$

$$= \frac{10^3 \text{ cm}^2}{0.2 \text{ g}} \left(\frac{250,000 \text{ (g)}}{\text{mol}} \right) + \left[\frac{16\pi (4.1 \times 10^{-7})}{\times 5.2 \times 10^{-7} \text{ cm}} \times 6.02 \times 10^{23} \text{ (mol)} \right]$$

$$= 2.2 \times 10^{14} \text{ mol/cm}^3$$

$$\rightarrow d = 100 \mu\text{m}$$

$$\frac{y_{i0}}{y_i} = \left(\frac{4}{\pi} \right) \alpha \phi \left[\frac{80 P/V}{\rho g} \right]^{1/2} t$$

$$y_i = \frac{x_0 m_0}{M} \quad M = N P \left[\frac{1}{6} \pi d^3 \right]$$

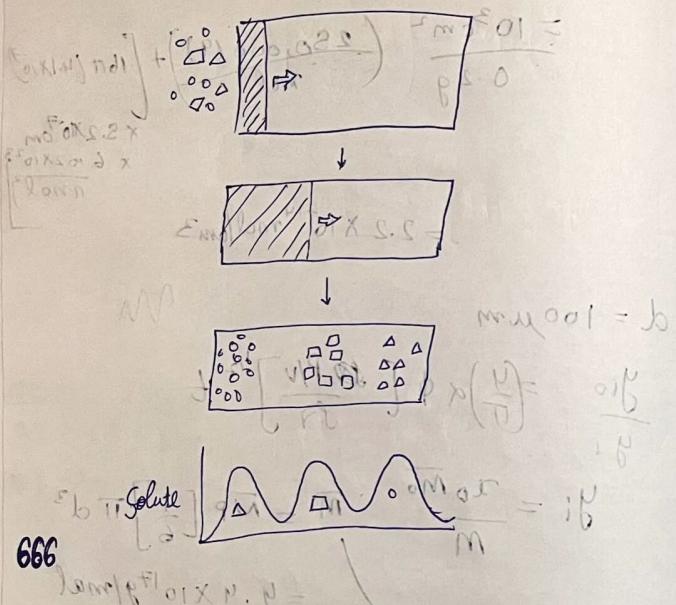
$$= 4.4 \times 10^{17} \text{ g/mol}$$

$$= \frac{0.2 \text{ g}}{10^3 \text{ cm}^3} \left(\frac{\text{mol}}{4.4 \times 10^{17} \text{ g}} \right)$$

$$= 4.5 \times 10^{22} \text{ mol/cm}^3$$

H2NCH2COOH
wolfranide-H
state lot

* Elution chromatography



666

Yield / Purity

$$\text{Amount eluted} = \int_{t'}^t y H dt$$

y = solution conc.

H = solvent flow

$$\text{total solute} = \int_0^t y H dt$$

8
60
6

$$\text{yield} = \frac{\int_{t'}^t y H dt}{\int_0^t y H dt} \quad \text{Purity} = \frac{\int_{t'}^t y_i H dt}{\sum_{j=t'}^t y_j H dt}$$

$$y = y_0 \exp \left(- \frac{[t/t_0 - 1]^2}{20^2} \right)$$

y_0 = Maximum conc.

t_0 = time at which this conc. exists

$$y = y_0 \exp \left[- \frac{[V/V_0 - 1]^2}{20^2} \right]$$

$\Rightarrow V_0$ = Volume req. to elute this maxm conc. y_0 at max conc. y

$$\text{Amount eluted} = \int_{t'}^t H y \exp \left(- \frac{[t/t_0 - 1]^2}{20^2} \right) dt$$

$$= \left[\sqrt{\frac{\pi}{2}} H y t_0 \sigma \right] y_0 \left\{ \exp \left(\frac{t/t_0 - 1}{\sqrt{20}} \right) - \exp \left(\frac{t/t_0 - 1}{\sqrt{20}} \right) \right\}$$

$$\text{Yield} = \frac{1}{2} \left\{ \exp \left[\frac{t/t_{0,-1}}{\sqrt{2\sigma}} \right] - \exp \left[\frac{t'/t_{0,-1}}{\sqrt{2\sigma}} \right] \right\}$$

$$= \frac{1}{2} \left\{ \exp \left[\frac{V/V_0 - 1}{\sqrt{2\sigma}} \right] - \exp \left[\frac{V/V_0 - 1}{\sqrt{2\sigma}} \right] \right\}$$

if $t/t_{0,-1} = 0$
↓
↓ stated

$$\text{Yield} = \frac{1}{2} \left\{ 1 + \exp \left(\frac{t/t_{0,-1}}{\sqrt{2\sigma}} \right) \right\}$$

V_0 .

$$t = t_{0,-1} \text{ maximum} = V$$

$$\text{Purity} = \frac{y_0(i) \text{ yield}(i)}{\sum_j y_0(j) \text{ yield}(j)}$$

$$\text{maximum elut. volume at pure sample} = V$$

Gel permeation chromatography

$$\text{e.g. volume eluted}(V) \text{ conc.}(A_V)$$

$$\begin{aligned} & \left[\frac{1-\alpha_f}{\alpha_f} \right] = 174 \\ & 190 \quad 0.0063 \\ & \text{bed volume} = 20 \text{ L} \\ & V = ? \quad \text{yield at } 190 \text{ or } 200 \text{ L?} \\ & \sigma = ? \end{aligned}$$

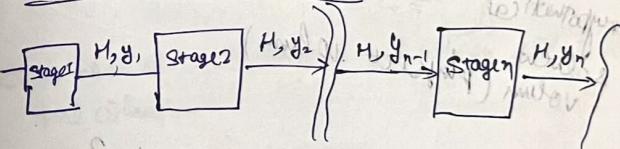
$$y = y_0 \exp \left(-\frac{[V/V_0]^2}{2\sigma^2} \right)$$

$$\Rightarrow \frac{0.0063}{0.0152} = \exp \left(-\frac{(174/190)^2 - 1}{2\sigma^2} \right)$$

$$\text{yield} = \frac{1}{2} \left[1 + \exp \left(\frac{V/V_0 - 1}{\sqrt{2\sigma}} \right) \right]$$

$$(C_p - C_n) H = \text{yield} \Big|_{V_0} = 80\%$$

Discrete Stage analysis

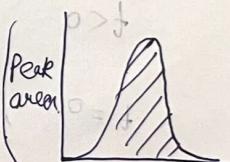


Solute mass balance for n :

$$\text{Solute IN} - \text{Solute OUT} = \text{accumulation, acc. in adsorber, inq}$$

$$H_n Y_{n-1} - H_n Y_n = (1-\varepsilon) V_s \frac{dy_n}{dt} + \varepsilon V_s \frac{dy_n}{dt}$$

mit salve vermis = 5



$$\varepsilon = \text{Volume frac. of liquid in column} = \beta$$

$$(1-\varepsilon) = \text{Volume frac. of the adsorbent}$$

$$V_s = \text{Stage Volume}$$

$$y_n = \text{solute / volume of solvent}$$

$$q_n = \text{solute / volume of adsorbent}$$

$$q_n = K \cdot y_n \quad \text{equilibrium.}$$

$$\left[(\varepsilon + (1-\varepsilon)K V_s) \frac{dy_n}{dt} \right] = H (y_{n-1} - y_n) \beta$$

hypothetical
solvent
volume (plus 10 l/m)

$$t < 0, \quad y_n = 0, \quad n = 1, 2, \dots, N$$

$$t = 0, \quad y_n(\text{feed stage}) = y_F$$

$$+ y_n = y_F \left(\frac{z^{n-1} e^{-\varepsilon z}}{1 - e^{-\varepsilon z}} \right)$$

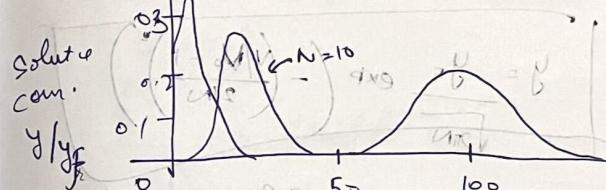
$\zeta = \text{dimensionless time.}$

$$\zeta = \frac{H t}{[(\varepsilon + (1-\varepsilon)K V_s) H]} = M$$

$$V_s = \frac{V_B}{M} \rightarrow \text{bed volume.}$$

$$\text{stage count (total)} = N$$

$$N=1$$



$$y = y_0 \exp \left[-\frac{(z - z_0)^2}{2z_0^2} \right]$$

$z_0 \rightarrow \text{mean dimensionless time at which solute leaves the column}$

$$\left(\frac{1}{z_0} = \int_0^\infty \zeta \left(\frac{y_m}{y_F} \right) dz \right) \frac{1}{y_F}$$

$$z_0 = N \frac{1}{y_F}$$

$$\frac{1}{z_0} = \frac{1}{\zeta_0} = \frac{1}{N}$$

$$M = \sum_{n=0}^{\infty} y_n + H = 3$$

$$= \int_0^{\infty} y H dt = \int_{-\infty}^{\infty} y n dt$$

column load

$M = \cancel{\text{total mass in the column}}$

$$y = \frac{y_0}{\sqrt{2N}} \exp \left(-\left(\frac{(N-1)}{2N} \right)^2 \right)$$

Eg: HPLC: stages in triglyceride separation.

peak leaving the column after 8.85 min

width of the peak when the conc is

half the max. is 3 min, $N=2$ means 5 minutes apart

Sol:

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

$$t = 8.85 + 3/2$$

$$t_0 = 8.85$$

$$\frac{y}{y_0} = 0.5$$

$$N = 1600$$

log albumin \rightarrow eluted from column. (80 L void fraction: 0.4. (d) (E.P. 2002)

The conc. in the column peaks after 470 L are eluted, this maximum conc. is 1.8% of that originally in the column.

a) $\epsilon K = ?$

b) $N = ?$

c) conc. profile.

solⁿ

no interaction with solid phase - 100% O/W

~~$$H_{to} = [\epsilon + (1-\epsilon)K] V_B$$~~

$$G_0 = N \left\{ \frac{H_{to} \text{ soln}}{[\epsilon + (1-\epsilon)K] V_B} \right\}$$

estimated elution time before start of elution

$$H_{to} = [\epsilon + (1-\epsilon)K] V_B$$

$$470 = [0.4 + (1-0.4)K] 80$$

K = 9.12

$K = \frac{q_m}{J_m}$ not for before \leftarrow method (d)

J_m has this in J_m before not much no effect (d)

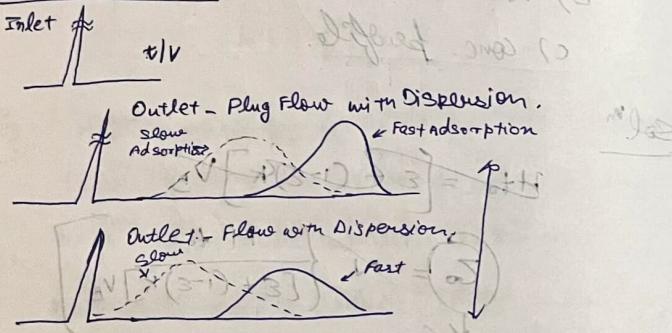
b) standard deviation is not given for
P.O. very big.

Source (7.3)

$$\text{mean ref to standard } \frac{y_0}{y_0} = \frac{1 + \ln(2\pi N)}{\sqrt{2\pi N}}$$

standard error approx $\sqrt{2\pi N}$
mean error $N = 490$

Kinetic Analysis



- 1) The solute is transferred from the bulk solution to the surface of the packing.
- 2) It diffuses into the packing.
- 3) It reacts reversibly with the packing.
- 4) Desorption \rightarrow surface of the packing
- 5) Diffusion from the surface to the bulk soln.

Mass balance on Solute

Solute accumulation = Solute dispersion + Solute in liquid & packing in-out
convection in-out

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

E = dispersion coefficient

v = superficial velocity

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

Initial cond

$$t=0 \text{ all } \begin{bmatrix} y \\ q \end{bmatrix} = \begin{bmatrix} y_0 \\ q_0 \end{bmatrix} \quad (1-\varepsilon) \frac{\partial q}{\partial t} =$$

$$\left(\frac{(1-\varepsilon)v}{E} \right) q + \text{all } q = 0$$

$$\left(\frac{(1-\varepsilon)v}{E} \right) q = 0$$

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

k_a = Mass transfer coeff

a = packing area / bed vol.

y^* = conc. of solute in soln which is in
stability + eq^m with packing elements which is
in solution

$$K_a (y - y^*) = - \frac{dy}{dz} - v \cdot \text{vol}$$

$$\int_0^L dz = \sqrt{v}(z - 1) + \frac{B_0}{v} z$$

$$= \left[\frac{v}{K_a} \right] \int_{y_0}^y \frac{dy}{y - y^*}$$

$\frac{v}{K_a}$ → Height of transfer unit

NTU → no. of transfer unit

$$f = HTU, NTU$$

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

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

$$NTU = \frac{1}{\sigma^2}$$

$$= \frac{1}{MTU}$$

$$y = \frac{M/A}{[\varepsilon + (1-\varepsilon)K] \sqrt{\frac{K_a}{vL}}} \exp \left(- \frac{K_a}{2v} \left(\frac{v}{v_0} - 1 \right)^2 \right)$$

$$y_0 = \frac{M/A}{[\varepsilon + (1-\varepsilon)K] \sqrt{\frac{K_a}{vL}}}$$

$\sigma^2 = \dots$

Eg:- Peak time to peak spread to
(min) (min)

dasparture	62	3
lastparture.	71	6

$$b = 25 \text{ cm} \quad d = 0.41 \text{ cm}$$

filled with 0.62 fraction of $45 \times 10^{-4} \text{ cm}$
silica gel sphere

flow rate of liquid $= 20 \text{ m}^3/\text{min}$

$$K = ? \left[\left(\frac{D}{20 \times 10^3} \right) \left(\frac{20}{0.41} \right) \right]$$

$$f = 1.17 \left(\frac{D}{v} \right)^{0.42} \left(\frac{v}{D} \right)^{-0.67} \left(\frac{0.7 \times 10^3}{s} \right)^{-0.7}$$

$$\text{Sol}^n \left(\frac{\text{Lat}}{\text{COK}} \right) = \text{NTU} \left(\frac{v}{aL} \right) \frac{A/M}{(3-1)+3} = 6$$

$$v = \frac{2/60}{\frac{\pi}{4} \times (0.41)^2} = 0.25 \text{ cm/s} \quad \frac{A/M}{(3-1)+3} = 6$$

~~desubstante~~

$$\Rightarrow \frac{t_0}{\sqrt{\text{NTU}}} = \text{peak spread} \quad t_0 = 62 \text{ min}$$

$\sqrt{\text{NTU}}$

$$2) \text{ NTU} = 427$$

Glyc.

$$\text{NTU for losartane} = 140$$

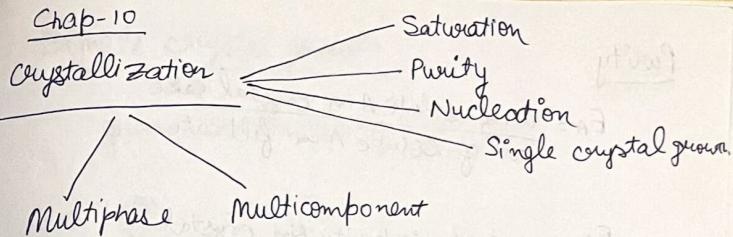
$$a = 6(1-\varepsilon)/d_{\text{particle}}$$

$$K_r = 427 \times 0.27$$

$$\left[\frac{6(0.62)}{(48 \times 10^{-4})} \right] 2S = 2$$

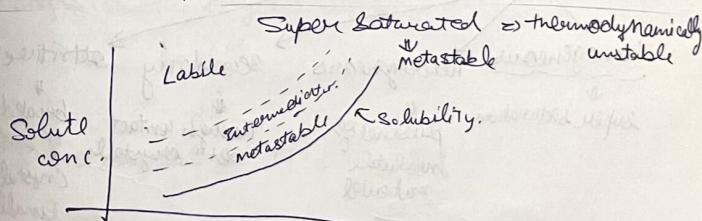
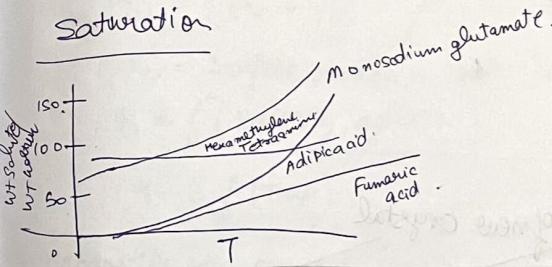
$$\left(\frac{v}{aL} \right) \left[\frac{v}{\sqrt{S}} \right] = 1.1 \times 10^{-3}$$

$$= 5.2 \times 10^{-3} \text{ cm/s}$$



Crystall? Space lattice

Saturation



temp.

$$T = (5-3) \text{ K} = \frac{10}{10} \text{ K}$$

Purity

$$E_A = \frac{\text{wt. of solute A in crystal cake}}{\text{wt. of Solute A in filtrate}}$$

$$E_B = \frac{\text{wt. of impurity B in crystal}}{\text{wt. of Impurity B in filtrate}}$$

$$\beta = \frac{E_A}{E_B}$$

separation
factor.

Nucleation

→ formation of new crystal

homogeneous
super saturation

$$\frac{dN}{dt} = K_n (c - c^*)^i = B$$

↓
solution saturation.

$K_n, i \rightarrow$ Empirical parameters.

heterogeneous
presence of insoluble material
secondary
attritive
Through contact b/w crystals
breakdown of existing crystal into small parti

Single crystal growth

growth is limited by diffusion.

$$\frac{dM}{dt} = -KA(c - c^*)$$

↓
crystal area.
mass fraction coeff.

$$\frac{dM}{dt} = \left(\frac{A}{1/k + 1/K} \right) (c - c^*)$$

K_r = surface reaction rate const.

$K = f$ (viscosity, agitation)

$$K = f(\text{Tamp})$$

characteristic crystal length

$$l = \frac{6M}{PA}$$

Cubic crystal $\rightarrow m = \rho s^3, A = 6s^2, l = \ell$

Sphere

Spherical crystal $\rightarrow m = \rho \phi, l^3, A = 6 \phi_A \ell^2$

$\phi_A \rightarrow$ geometric factors characteristics of crystal shape

$$\frac{d}{dt} (\rho \phi_v l^3) = \left[\frac{6 \phi_a l^2}{1/K + 1/K} \right] (c - c^*)$$

$$\frac{dl}{dt} = \left\{ \frac{(2 \phi_a / \phi_v l)}{1/K + 1/K} \right\} (c - c^*)$$

$$= b \text{ Kg} (c - c^*)$$

$$= G$$

rate const for
single crystal
growth

rate const for growth.

Example

Crystallisation of Adipic acid.

Adipic acid (10kg) + 13.1 Kg H₂O

90°C ↑, 10% of water evaporated

↓ 35°C → solubility. ~~- 0.05kg~~
13.1

wt. of crystal?

Water balance

$$13.1 = \text{water in soln} + 0.1 \times 13.1$$

$$\Rightarrow \text{Water} = 11.79 \text{ Kg}$$

water

10 kg = wt. of crystal + 0.05 (11.79)

$$\begin{aligned} \text{wt. of} \\ \text{crystal} \end{aligned} = 9.41 \text{ Kg}$$

example

Stigmastanol + Sisosterol

2040 kg

Original mixture = 86.5% Stigmastanol

Recovered crystal = 96.6%

wt = 11.73 kg

In liquid = 74.61% Stigmastanol
 $\beta = ?$

$$\begin{aligned} \text{Stigmastanol} &= \frac{113.7 \times 0.966 \text{ kg original/kg}}{(2040 - 113.7) \text{ kg} \times 0.746 \text{ kg original/kg}} \\ &= \frac{109.8}{673.6} = 1.63 \end{aligned}$$

$$\begin{aligned} \text{Sisosterol} &= \frac{113.7 \times (1.00 - 0.966) \text{ kg} + 0.05 \text{ kg}}{(2040 - 113.7) \times (1.000 - 0.746) \text{ kg original/kg}} \\ &= \frac{38.66}{2294.4} = 0.168 \end{aligned}$$

$$\begin{aligned} \beta &= \frac{E_{\text{strg}}}{E_{\text{iso}}} = \frac{1.63}{0.17} = 9.6 \end{aligned}$$

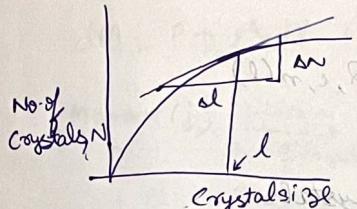
20-78

last year evaluation

2

288 Crystal Size Distribution

Population Density



$$\eta = \text{Population density} = \lim_{\Delta l \rightarrow 0} \frac{\Delta N}{\Delta l}$$

functional component of distribution

$$\mu_j = \frac{\int_l^j l^j n(l) dl}{\int_l^\infty l^n n(l) dl}$$

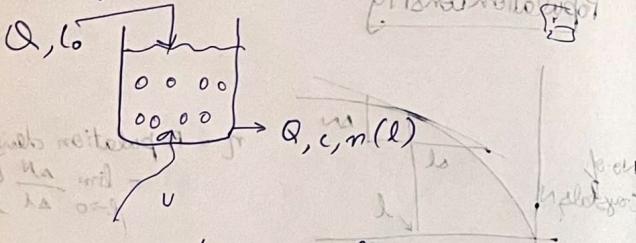
$$\mu_0 = \frac{\int_0^\infty n(l) dl}{\int_0^\infty n(l) dl} = 1$$

$$\mu_1 = \frac{\int_0^\infty l n(l) dl}{\int_0^\infty n(l) dl}$$

$$\mu_j = \frac{\rho \phi_v \int_0^\infty l^j n(l) dl}{\rho \phi_v \int_0^\infty l^n n(l) dl}$$

$$\mu_2 = \frac{\rho \phi_v \int_0^\infty l^2 n(l) dl}{\rho \phi_v \int_0^\infty l^n n(l) dl}$$

225
Crystal from a continuous process



mass balance of the crystals

accumulation = [crystal growing into range] +
 - [crystals growing out of range]
 steady state
 - [crystals of given range flowing out]

$$\frac{dI}{dt} = [V_n G]_l - [V_n G]_{l+dl} - Q n dl$$

$$V d(G_n) + Q_n = 0$$

$$\frac{dI}{dt} + \frac{Q_n}{G_n V} = 0$$

n is small

$$\eta_n = \frac{dN}{dt}$$

$$= \frac{dI}{dt}$$

$$= B \text{ nuclei}$$

G Single crystal growth

Dominant Crystal size

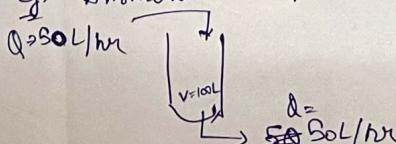
$$dM = \rho \phi_v l^3 n dl \quad (\text{Mass of a given size range})$$

- | | | |
|-------------------|-----------------|-------------------------------|
| Moment (ϕ) | Meaning | Total no. of crystallizer = 4 |
| 0 | No. of crystal | ρg^{284} |
| 1 | Size of crystal | <u>C-3</u> |
| 2 | Area of crystal | |
| 3 | Mass of crystal | |

$$M_t = 6 \phi_v \int n \left(\frac{G_n V}{\alpha} \right)^4$$

$$\begin{aligned} \text{Total mass of crystals, } \frac{dw}{dl} &= \frac{l^2}{6} \left(\frac{\phi}{G_n V} \right)^4 \frac{n}{n_0} \\ &= \frac{l^3}{6} \left(\frac{\phi}{G_n V} \right)^4 e^{-lQ/G_n V} \\ l_0 &= \frac{3G_n V}{\phi} \end{aligned}$$

Eg: Ammonium sulphate crystallization,



$$B = 7.18 \times 10^7 \text{ nuclei/L hr}$$

$$G = 0.056 \text{ mm/hr}$$

1) $l_D = ?$ 2) no. of crystals equal to or
 $\downarrow 36V$ smaller than this size (l_D)
 $\frac{0.336}{8}$ 6 is lot size to be increased

3) fraction of crystal in this range ($0 - 10$)

→ Product slurry conc'.

$$N = \int_0^L n dl = (\frac{\rho V}{A})(1 - e^{-\frac{L \rho g}{\rho V}})$$

steers 82512 — 1
heifers 6000 — 5
calves 2200 — 5

$$(\frac{v_1 d}{\theta}) \circ \varphi \circ \phi = M$$

$$\frac{10}{0.01} \left(\frac{D}{\sqrt{S}} \right) \frac{\pi L}{J} = \frac{Wb}{Lb}$$

$$\text{value} \rightarrow \left(\frac{0}{\sqrt{N}} \right) \text{ for } \rightarrow$$

reiterg. Datzen sterblich minimaal 30
mit einem F01X81. F = 8

NE 10th 320.0 - 12

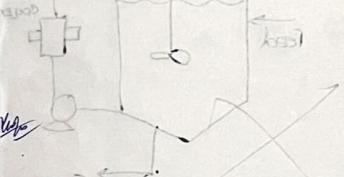
Berdesen Thermo stat and Bawostat

$$\frac{dT}{dt} = \frac{T_0 - T}{\tau}$$

reites illotus notho

Q8 Simulation time = time step x No. of steps.

$$= 0.002 \text{ sec} \times 10^{-9} \times 5 \times 10^6$$



yellowish
moderately
abundant

"swallowtail est"

"Les latques d'apr."
me iterante & que les foins me semblaient

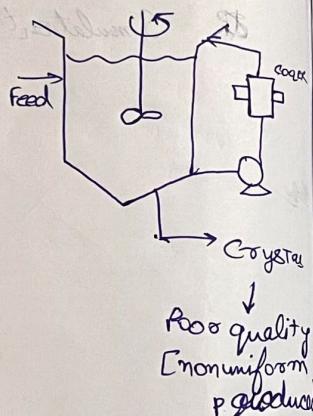
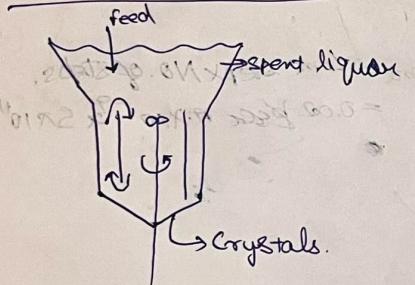
newt species) = *watercolorist's impression*

1900-1901

bottom road (and +

Gerard + Charles

Batch crystallization



"The Cooling Curve"

"Single crystal size"
balance amount of supersaturation.

Change in supersaturation = change from altered temp.
 + change from crystal growth + change from nucleation

$$O = \frac{Vdc^*}{dt} + \frac{A}{(1/k + 1/k)} (C - C^*)$$

$$\frac{dc^*}{dt} = \left(\frac{dc^*}{d\tau} \right) \left(\frac{d\tau}{dt} \right)$$

$\frac{d\tau}{dt} = f_r$

M

m A $= [m \text{ o. of crystals}] \left[\frac{\text{area}}{\text{crystal}} \right]$

~~$m =$~~ $m_s = 5$ $= \left[\frac{m_s}{P\Phi_A l_c^3} \right] \left\{ 6\Phi_A (l_s + q_t)^2 \right\}$

$$G_1 = \frac{dI}{dt}$$

$$= \left[\frac{2\phi_A / \phi_v g}{(K+1)/K} \right] (C - C^*)$$

$$\frac{dT}{dt} = - \left[\frac{m_s / v}{\frac{dc^*}{dT}} \right] \frac{\frac{3G_1}{L_s^3}}{(L_s + G_1 t)^2}$$

$$T = T_0 - \left[\frac{M_s / V}{\frac{dc^*}{dt} l_{st}} \right] \frac{3Gt}{l_s} \left(1 + \frac{Gt}{l_s} + \frac{1}{3} \left(\frac{Gt}{l_s} \right)^2 \right)$$

$$\{ = (+) \} = T$$

$$\frac{T - T_0}{T_p - T_0} = \frac{M_s}{M_p} \left(\frac{3\eta z}{1 + \eta z + \frac{1}{3}(\eta z)^2} \right)$$

$$M_p = (T_0 - T_p) v \frac{dc^*}{dT} \frac{ds}{dt}$$

$$\eta = \frac{\rho_p - \rho_s}{\rho_s}$$

$$\left[\frac{\text{mass}}{\text{volume}} \right] \left[\frac{\text{partial pressure}}{\text{total pressure}} \right] = \frac{1}{1 + \eta z}$$

$$\left[\frac{\rho_p + \eta z}{\rho_s + \eta z} \right] \left[\frac{z^{11}}{z^{11} + 1} \right] = \frac{z = \text{actual}}{\text{time / total time}}$$

Eg:- Initial temp = 20°C

Solubility change = 1.14×10^{-3} g tetra cycline

$$\text{Seed crystal} = 0.01 \text{ cm} \quad (\text{cubic})$$

$$f_s = 1.06 \text{ g/cm}^3$$

was added @ 23 ppm

Final Crystal size = 0.088 cm.

Super saturation is expected @ 0.077 g/cm³

$$K = 6.5 \times 10^{-5} \text{ cm}^3/\text{sec}$$

$$T = f(t) = ?$$

$$\eta = \frac{\rho_p - \rho_s}{\rho_s}$$

21st May 2019 (continued)

$\frac{0.088 - 0.010}{0.010} = 7.8$ hr (initially turbid, start to settle)

$$G_t = 2 K \left(\frac{\rho_A}{\rho_v \rho} \right) (c - c^*)$$

$$= 2 (6.5) \times 10^{-5} \frac{\text{cm}}{\text{sec}} \left(\frac{1}{1/(1.06 \text{ g/cm}^3)} \right) \frac{\text{cm}}{\text{hr}}$$

$$T = [0.034 \text{ cm/hr}] + 1$$

$$G_{tr} = \rho_p - \rho_s$$

$$(0.034 \text{ cm/hr})_{tr} = 0.088 \text{ cm} - 0.010 \text{ cm}$$

$$t_p = 2.3 \text{ hr}$$

$$T = T_0 - \left[\frac{M_s / V}{dc^* / dt} \right] \eta z \left[1 + \eta z + \frac{1}{3}(\eta z)^2 \right]$$

$$= 20 - \left[\frac{3.5 \times 10^{-6} \text{ g/m}^2 \text{ sec}^{-1}}{(1.14 \times 10^{-3} \text{ g/cm}^3)} \right] \frac{3 \times 7.8 t}{2.3 \text{ hr}} \left[1 + \frac{7.8 t}{2.3 \text{ hr}} + \frac{1}{3} \left(\frac{7.8 t}{2.3 \text{ hr}} \right)^2 \right]$$

$$= 20 - 0.312 t (1 + 3.39 t + 3.83 t^2)$$

* Drying

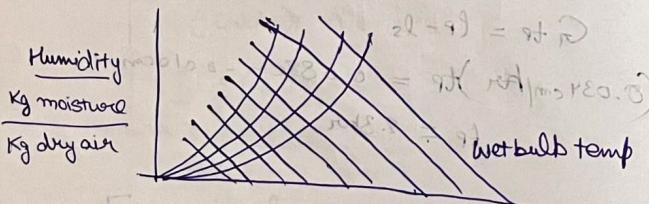
- 1) how much water content? \Rightarrow thermodynamics
- 2) how fast we can remove water? \Rightarrow Mass and heat transfer
- 3) how product degradation takes place \Rightarrow Reaction.

Water Content

$$(2-3) \left(\frac{18}{29} \right) \times S = P$$

humidity

$$G = \frac{P_i}{RT} = \frac{H}{1 + H \left[\frac{29 \text{ dalton}}{18 \text{ dalton}} \right] \frac{R}{R_p}}$$



$$\text{Relative humidity} = \frac{P_i / R_p}{P_i (\text{sat})} = \frac{V / \rho M}{18 + 29 H(\text{sat})}$$

$$\begin{aligned} \left(\frac{10F}{100} \right) \frac{1}{E} &= \frac{10F + 1}{100} - \frac{10F \times 8}{100} \\ &= \frac{10F + 1 - 80F}{100} = \frac{-70F + 1}{100} \\ &= \frac{1}{100} - \frac{7F}{10} \end{aligned}$$

$$\begin{aligned} \text{Relative humidity} &= \frac{H [18 + 29 H(\text{sat})]}{(100 - 7F) (18 + 29 H(\text{sat}))} \end{aligned}$$

H = actual humidity

H(sat) = saturation humidity

Evaporation and Heating Rates

J_c (evaporation / area, time)

$$= K (C_{si} - C_t)$$

C_{si} \Rightarrow water air interface

C_t \Rightarrow in bulk air

K = $\frac{D}{l}$ \Rightarrow length across which evaporation is taking place

$$q = n (T - T_i)$$

$$= \frac{n}{\rho C_p} \left(\hat{P} \hat{C}_p T(\text{bulk}) - \hat{P} \hat{C}_p T(\text{interface}) \right)$$

$$= \frac{k}{l} (T(\text{bulk}) - T(\text{interface}))$$

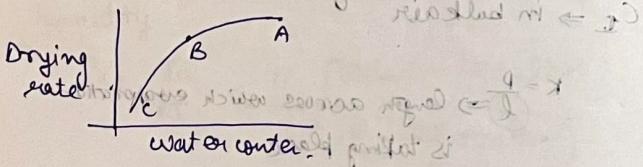
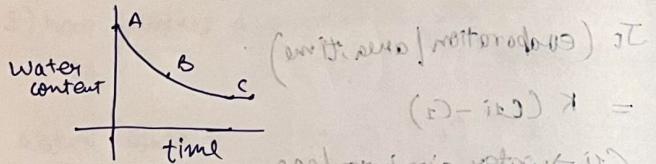
$$\frac{d(P)}{dt} = k e^{-E/RT} \left[\frac{P}{P_0} \right]$$

$$\ln \frac{P}{P_0} = \frac{E}{RT} - \frac{1}{l} \cdot \frac{1}{k} \cdot \frac{1}{C_p}$$

* 1 class missing

ftibular heat $\rightarrow H$
ftibular water $\rightarrow (H_w)$

Adiabatic drying



A \rightarrow B \Rightarrow constant rate drying

B \rightarrow C \Rightarrow Falling rate drying

$$(B \Rightarrow \text{critical } (T_{c,i}) \text{ or } \frac{\partial w}{\partial t} = 0)$$

constant rate drying

particle diameter: d

$$\frac{d}{dt} \left(\frac{\pi d^3 \rho_s w}{6} \right) = - \left(\pi d^2 \right) j_1 \quad \text{flux (1)}$$

mass water content

$$\pi d^2 \rho_s / 6 \rightarrow \text{solid mass}$$

$$j = k (c_{si} - c_s) \quad \text{loss of solid particle}$$

$$= k p (H_i - H) \quad \xrightarrow{\text{humidity}} \quad \text{wb} \quad \text{wb}$$

$\Rightarrow \text{eq 1 + 2}$ $w = w_c \rightarrow$ density of dry air

$$\frac{\pi d^3 \rho_s}{6} \frac{dw}{dt} = \frac{1}{k} \pi d^2 K_p (H_i - H)$$

$$\Rightarrow \frac{dw}{dt} = - \left(\frac{6 K_p}{\rho_s} \right) (H_i - H) \quad (3)$$

$$K = h \frac{dw}{dT}$$

$$q = h (T_f - T_i) \quad \text{or} \quad q = \dot{Q}$$

$$h (T_f - T_i) = K p (H_i - H)$$

$$\frac{dw}{dt} = - \left(\frac{6 K_p}{\rho_s d} \right) \left(\frac{C_p (T_f - T_i)}{d} \right) \quad (4)$$

Integrating (4)

$$\text{At } t = 0, w = w_0 \rightarrow w = w_0$$

$$t = t_c \Rightarrow w = w_c$$

t_c \rightarrow time to reach residual water content

$$t_c = \left(\frac{\rho_s d}{6 K_p} \right) \left(\frac{1}{C_p (T_f - T_i)} \right) (w_0 - w_c)$$

$$30d = t_c t_w$$

$$381 = \rho_w + \text{obitual}$$

$$0.5 t = \text{obitual} \rightarrow \text{ft. mass}$$

$$0.5 t = \text{obitual} \rightarrow \text{ft. mass}$$

Falling Rate Period $(t_0 - t_c) \rightarrow t = b$

$$\frac{dw}{dt} = -K_w (t - t_c) g_a =$$

$$\underline{\text{At}} \quad t = t_c \Rightarrow w = w_c$$

$$(H - iH)^{1/3} t_c = \left(\frac{1}{K_w} \right) \ln \left(\frac{w_0}{w_c} \right)^{1/3}$$

$$\underline{\text{②}} \quad (H - iH)^{1/3} \frac{t_c}{d} = - \frac{w_0 - w_c}{K_w d}$$

$$t = \left\{ \frac{f_s d}{6 K_p} \frac{1}{C_p (T - T_i)} \right\} = \left[\frac{w_0 - w_c + q_s \ln w_c}{\bar{w}} \right]$$

$$\underline{\text{③}} \quad \text{when } \rightarrow w_i = \frac{6 K_p}{f_s d} \frac{C_p (T - T_i)}{K_w g_s d}$$

Eg:- Spray Drying

Protease slurry $\rightarrow 45\%$ (wt) total

$$K = 7.1 \text{ cm/sec} \quad \downarrow \text{to be dried} \quad \omega = f$$

\rightarrow to a residual moisture content of 5%

$$\begin{aligned} & (\omega - \omega_i) \rightarrow \text{Inlet} = 90^\circ C \\ & \text{air temp} \rightarrow \text{outlet} = 60^\circ C \end{aligned}$$

Particle temp $= 18^\circ C$

\rightarrow gravity of slurry $= 1.20$

\rightarrow gravity of product $= 0.80$

Critical moisture content $= 0.083$

mass transfer coefficient $K = 7.1 \text{ cm/sec}$
rate const $K_w = 0.259 \text{ sec}^{-1}$

initial $d = 0.03 \text{ cm}$.

$$\boxed{d = \text{dinit.} \left[\left(\frac{f_s}{g} \right) \left(\frac{H + w_0}{1 + w_0} \right) \right]^{1/3}}$$