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Fundamentals of Biological Engineering Formula Sheet

INSIDE

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Reaction and enzyme kinetics: rate laws, Michaelis-Menten and inhibition

POWER-LAW RATE LAW

$$-r_A = -\frac{dC_A}{dt} = k\,C_A^{\alpha}\,C_B^{\beta}, \qquad n = \alpha + \beta$$

Constant-volume batch. k does not depend on concentration; it varies with temperature. Its units are $(\mathrm{mol/L})^{1-n}\,\mathrm{time}^{-1}$.

FRACTIONAL CONVERSION

$$X_A = \frac{C_{A0} - C_A}{C_{A0}}, \qquad C_A = C_{A0}(1 - X_A)$$

Constant volume. C_{A0} is the initial concentration of reactant A.

ZERO ORDER

$$C_A = C_{A0} - kt \quad \left(t \le \frac{C_{A0}}{k}\right), \qquad t_{1/2} = \frac{C_{A0}}{2k}$$

The rate does not depend on concentration. Valid only while $C_A > 0$: A is used up completely at $t = C_{A0}/k$ and stays at zero after that.

FIRST ORDER

$$\ln\frac{C_{A0}}{C_A} = kt, \qquad t_{1/2} = \frac{\ln 2}{k}$$

Equivalently $C_A = C_{A0}e^{-kt}$, or $-\ln(1 - X_A) = kt$ in terms of conversion. The half-life does not depend on C_{A0}, and A never quite reaches zero.

SECOND ORDER (SINGLE REACTANT, OR EQUAL FEEDS)

$$\frac{1}{C_A} - \frac{1}{C_{A0}} = kt, \qquad t_{1/2} = \frac{1}{kC_{A0}}$$

Applies when $-r_A = kC_A^2$, for example $2A \to P$ with k defined on A, or $A + B \to P$ with $-r_A = kC_AC_B$ and $C_{A0} = C_{B0}$ (so $C_B = C_A$ throughout). The half-life is inversely proportional to C_{A0}.

NTH ORDER, INTEGRATED FORM

$$C_A^{1-n} - C_{A0}^{1-n} = (n-1)\,kt$$

Any $n \neq 1$. Gives the zero-order result for $n = 0$ and the second-order result for $n = 2$. For $n < 1$ it holds only until A is used up, at $t = \dfrac{C_{A0}^{1-n}}{(1-n)\,k}$.

NTH ORDER, HALF-LIFE

$$t_{1/2} = \frac{2^{\,n-1} - 1}{(n-1)\,k\,C_{A0}^{\,n-1}} \quad \Rightarrow \quad t_{1/2} \propto C_{A0}^{1-n}$$

Any $n \neq 1$. The proportionality is the basis of the half-life method for finding the order.

ARRHENIUS EQUATION

$$k = A\,e^{-E_a/(RT)}, \qquad \ln k = \ln A - \frac{E_a}{R}\cdot\frac{1}{T}$$

T in kelvin, $R = 8.314\,\mathrm{J\,mol^{-1}\,K^{-1}}$, E_a in J/mol. A plot of $\ln k$ against $1/T$ is a straight line of slope $-E_a/R$.

ARRHENIUS, TWO TEMPERATURES

$$\ln\frac{k_2}{k_1} = \frac{E_a}{R}\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

Eliminates A. When $T_2 > T_1$ and $E_a > 0$, $k_2 > k_1$.

MICHAELIS–MENTEN EQUATION

$$v = -\frac{d[S]}{dt} = \frac{d[P]}{dt} = \frac{V_{max}\,[S]}{K_m + [S]}$$

K_m has concentration units, the same as [S] (mM, mol/L or g/L). v and V_{max} are concentration per time (e.g. µmol L^{-1} min^{-1}).

MICHAELIS CONSTANT (QUASI-STEADY STATE)

$$K_m = \frac{k_{-1} + k_2}{k_1}$$

From $d[ES]/dt \approx 0$. Because $k_2 > 0$, K_m is always larger than the dissociation constant k_{-1}/k_1.

MAXIMUM RATE AND TURNOVER NUMBER

$$V_{max} = k_2[E]_0 = k_{cat}[E]_0$$

k_{cat} (s^{-1}) is the turnover number: substrate molecules converted per active site per unit time when the enzyme is saturated. $[E]_0$ is the molar concentration of active sites.

CATALYTIC EFFICIENCY

$$\text{efficiency} = \frac{k_{cat}}{K_m}, \qquad v \approx \frac{k_{cat}}{K_m}[E]_0[S] \;\; ([S] \ll K_m)$$

Units L mol^{-1} s^{-1}, a second-order rate constant. It compares substrates for the same enzyme. For the one-intermediate mechanism, $k_{cat}/K_m = k_1k_2/(k_{-1} + k_2)$, which is less than k_1, so it cannot exceed the rate constant for enzyme and substrate meeting by diffusion, of the order of 10^8 to 10^9 L mol^{-1} s^{-1}.

LIMITING FORMS

$$v \approx \frac{V_{max}}{K_m}[S] \;\; ([S] \ll K_m), \qquad v \approx V_{max} \;\; ([S] \gg K_m)$$

At low substrate the reaction is first order in S with rate constant V_{max}/K_m. At high substrate it is zero order.

SUBSTRATE NEEDED FOR A GIVEN FRACTION OF VMAX

$$[S] = K_m\,\frac{f}{1-f}, \qquad f = \frac{v}{V_{max}}$$

At $[S] = K_m$, $v = V_{max}/2$. This is the working definition of K_m under either assumption.

LINEWEAVER–BURK (DOUBLE RECIPROCAL)

$$\frac{1}{v} = \frac{K_m}{V_{max}} \cdot \frac{1}{[S]} + \frac{1}{V_{max}}$$

Plot $1/v$ against $1/[S]$: slope K_m/V_{max}, y-intercept $1/V_{max}$, x-intercept $-1/K_m$.

EADIE–HOFSTEE

$$v = V_{max} - K_m\,\frac{v}{[S]}$$

Plot v against $v/[S]$: slope $-K_m$, y-intercept V_{max}, x-intercept V_{max}/K_m.

HANES–WOOLF

$$\frac{[S]}{v} = \frac{1}{V_{max}}\,[S] + \frac{K_m}{V_{max}}$$

Plot $[S]/v$ against [S]: slope $1/V_{max}$, y-intercept K_m/V_{max}, x-intercept $-K_m$.

MIXED INHIBITION, GENERAL RATE LAW

$$v = \frac{V_{max}[S]}{\alpha K_m + \alpha'[S]}$$

Competitive: $\alpha' = 1$. Uncompetitive: $\alpha = 1$. Pure non-competitive: $K_i = K_i'$, so $\alpha = \alpha'$.

MIXED INHIBITION, APPARENT PARAMETERS

$$V_{max,app} = \frac{V_{max}}{\alpha'}, \qquad K_{m,app} = \frac{\alpha}{\alpha'} K_m$$

The inhibited reaction still follows the Michaelis–Menten form, with these apparent constants at a fixed [I].

COMPETITIVE INHIBITION

$$v = \frac{V_{max}[S]}{K_m\left(1 + \frac{[I]}{K_i}\right) + [S]}$$

I binds only free E, competing with S for the active site. $K_{m,app} = K_m(1 + [I]/K_i)$ increases and V_{max} is unchanged, so enough substrate overcomes the inhibition.

UNCOMPETITIVE INHIBITION

$$v = \frac{V_{max}[S]}{K_m + [S]\left(1 + \frac{[I]}{K_i'}\right)}$$

I binds only ES. $V_{max,app}$ and $K_{m,app}$ both fall by the factor $1 + [I]/K_i'$, so their ratio V_{max}/K_m is unchanged. The inhibition grows as [S] rises.

PURE NON-COMPETITIVE INHIBITION

$$v = \frac{V_{max}[S]}{(K_m + [S])\left(1 + \frac{[I]}{K_i}\right)}$$

I binds E and ES with equal affinity, at a site other than the active site. $V_{max,app} = V_{max}/(1 + [I]/K_i)$ and K_m is unchanged. The fractional inhibition is the same at every [S].

SUBSTRATE INHIBITION, RATE LAW

$$v = \frac{V_{max}[S]}{K_m + [S] + [S]^2/K_{SI}}$$

A second substrate molecule binds ES to form an inactive ES_2, with $K_{SI} = [ES][S]/[ES_2]$. At low [S] this reduces to Michaelis–Menten. At very high [S], $v \approx V_{max}K_{SI}/[S]$, so the rate falls. On a Lineweaver–Burk plot the points curve upward near the $1/v$ axis.

SUBSTRATE INHIBITION, OPTIMUM

$$[S]_{opt} = \sqrt{K_m K_{SI}}, \qquad v_{peak} = \frac{V_{max}}{1 + 2\sqrt{K_m/K_{SI}}}$$

From $dv/d[S] = 0$. v_{peak} is the highest rate the enzyme can reach and is always below V_{max}.

INTEGRATED MICHAELIS–MENTEN EQUATION

$$V_{max}\, t = ([S]_0 - [S]) + K_m \ln \frac{[S]_0}{[S]}$$

Natural log. V_{max} in concentration per time; K_m and [S] in the same concentration unit.

INTEGRATED FORM IN TERMS OF CONVERSION

$$V_{max}\, t = [S]_0\, X + K_m \ln \frac{1}{1 - X}, \qquad X = \frac{[S]_0 - [S]}{[S]_0}$$

Same assumptions. Gives the batch time for a target conversion X.

Ideal reactors: batch, mixed flow and plug flow

CONVERSION (CONSTANT DENSITY)

$$X_A = \frac{C_{A0} - C_A}{C_{A0}}, \qquad C_A = C_{A0}(1 - X_A)$$

The fraction of fed A that has reacted. The concentration form holds only at constant density (liquid-phase systems).

SPACE TIME AND SPACE VELOCITY

$$\tau = \frac{V}{v_0} = \frac{C_{A0}V}{F_{A0}}, \qquad s = \frac{1}{\tau}$$

The time needed to process one reactor volume of feed, measured at feed conditions (h). The space velocity s is its reciprocal (h^{-1}).

DILUTION RATE

$$D = \frac{F}{V} = \frac{1}{\tau}$$

The bioprocess name for the reciprocal space time of a continuous stirred vessel. F is the volumetric feed rate (L h^{-1}, the same quantity as v_0) and D is in h^{-1}.

CHEMOSTAT STEADY STATE (MONOD GROWTH)

$$S = \frac{K_s D}{\mu_{\max} - D}, \qquad x = Y_{X/S}(S_0 - S), \qquad D_{\text{crit}} = \frac{\mu_{\max} S_0}{K_s + S_0}$$

Steady-state chemostat with Monod growth $\mu = \mu_{\max} S/(K_s + S)$, a sterile feed, no cell death or maintenance, and a constant yield $Y_{X/S} = -dx/dS$ (g cells per g substrate). x is the cell concentration (g L^{-1}), written in lower case here so that it is not confused with conversion. S, S_0 and K_s are in g L^{-1}; $\mu_{\max}$ and D are in h^{-1}. The residual substrate S does not depend on S_0, and the cell productivity is Dx (g L^{-1} h^{-1}). These results hold for $D < D_{\text{crit}}$; at $D \geq D_{\text{crit}}$ the only steady state is washout, $x = 0$ and $S = S_0$.

BATCH REACTOR

$$t = N_{A0} \int_0^{X_A} \frac{dX_A}{(-r_A)V}$$

$$t = C_{A0} \int_0^{X_A} \frac{dX_A}{-r_A} = \int_{C_A}^{C_{A0}} \frac{dC_A}{-r_A} \quad \text{(constant volume)}$$

N_{A0} is the moles of A charged. This is the reaction time needed to reach X_A. It does not include the time to charge, empty or clean the vessel.

MIXED FLOW REACTOR (CSTR)

$$\frac{V}{F_{A0}} = \frac{X_A}{(-r_A)_f}, \qquad \tau = \frac{C_{A0}X_A}{(-r_A)_f} = \frac{C_{A0} - C_A}{(-r_A)_f}$$

Steady state, with a feed that contains no converted A. The rate is evaluated at exit (f) conditions, which equal the reactor contents. The last form holds only at constant density.

PLUG FLOW REACTOR (PFR)

$$\frac{V}{F_{A0}} = \int_0^{X_A} \frac{dX_A}{-r_A}, \qquad \tau = C_{A0} \int_0^{X_A} \frac{dX_A}{-r_A} = \int_{C_A}^{C_{A0}} \frac{dC_A}{-r_A}$$

Steady state, with no mixing along the length and a feed that contains no converted A. The rate varies along the reactor, so it stays inside the integral. The concentration form holds only at constant density.

FIRST ORDER: BATCH AND PFR

$$k\tau = \ln\frac{C_{A0}}{C_A} = -\ln(1 - X_A), \qquad X_A = 1 - e^{-k\tau}$$

For $-r_A = kC_A$ with k in h^{-1}. For a batch reactor, replace τ with t. The dimensionless group $k\tau$ is the first-order Damköhler number. The result does not depend on C_{A0}.

FIRST ORDER: CSTR

$$k\tau = \frac{X_A}{1 - X_A}, \qquad X_A = \frac{k\tau}{1 + k\tau}, \qquad \frac{C_A}{C_{A0}} = \frac{1}{1 + k\tau}$$

For $-r_A = kC_A$ at constant density and steady state. The result does not depend on C_{A0}.

SECOND ORDER ($-R_A = KC_A^2$)

$$\text{PFR or batch: } kC_{A0}\tau = \frac{X_A}{1 - X_A}$$

$$\text{CSTR: } kC_{A0}\tau = \frac{X_A}{(1 - X_A)^2}$$

Also covers $A + B \rightarrow$ products with $-r_A = kC_AC_B$ and equimolar feed ($C_{A0} = C_{B0}$), because the 1 : 1 stoichiometry then keeps $C_B = C_A$. k is in L mol^{-1} h^{-1}.

MICHAELIS–MENTEN RATE

$$-r_S = \frac{V_{\max}S}{K_m + S}$$

$V_{\max} = k_{cat}E_0$ stays constant only if the enzyme concentration is constant and the enzyme does not deactivate.

MICHAELIS–MENTEN: BATCH AND PFR

$$V_{\max}\tau = (S_0 - S) + K_m\ln\frac{S_0}{S} = S_0X + K_m\ln\frac{1}{1 - X}$$

The integrated Michaelis–Menten equation. For a batch reactor, replace τ with t. The first term is the zero-order part and the second is the first-order part.

MICHAELIS–MENTEN: CSTR

$$\tau = \frac{(S_0 - S)(K_m + S)}{V_{\max}S}$$

Steady state. The rate is evaluated at the exit substrate concentration S.

CSTR-TO-PFR VOLUME RATIO

$$\text{First order: } \frac{V_{\text{CSTR}}}{V_{\text{PFR}}} = \frac{X_A/(1 - X_A)}{-\ln(1 - X_A)}$$

$$\text{Second order: } \frac{V_{\text{CSTR}}}{V_{\text{PFR}}} = \frac{1}{1 - X_A}$$

Same feed and same conversion, constant density. Neither ratio depends on k, and the second-order ratio does not depend on C_{A0} either.

N EQUAL CSTRS IN SERIES, FIRST ORDER

$$\frac{C_{AN}}{C_{A0}} = \frac{1}{(1 + k\tau_i)^N}, \qquad \tau_i = \frac{\tau}{N}$$

First order, constant density, with N equal tanks each of space time τ_i. The total space time is $\tau = N\tau_i$. For unequal tanks, multiply the stage factors: $C_{AN}/C_{A0} = 1/[(1 + k\tau_1)(1 + k\tau_2)\cdots(1 + k\tau_N)]$.

SIZE OF EACH TANK FOR A TARGET CONVERSION

$$k\tau_i = (1 - X_A)^{-1/N} - 1$$

First order, with N equal CSTRs in series reaching an overall conversion X_A.

PFR WITH RECYCLE (GENERAL)

$$\tau = \frac{C_{A0}V}{F_{A0}} = (R+1)\,C_{A0}\int_{X_{A1}}^{X_{Af}}\frac{dX_A}{-r_A}$$

$$X_{A1} = \frac{R}{R+1}X_{Af}$$

τ is based on the fresh feed v_0, which contains no converted A. X_{A1} is the conversion at the reactor inlet after mixing with the recycle stream.

PFR WITH RECYCLE, FIRST ORDER

$$\frac{k\tau}{R+1} = \ln\left[\frac{C_{A0}+RC_{Af}}{(R+1)C_{Af}}\right]$$

First order, constant density, with $\tau = V/v_0$ based on the fresh feed. $R = 0$ gives the PFR result, and $R \to \infty$ gives $k\tau = X_A/(1-X_A)$.

Enzyme immobilisation and diffusion effects

ELECTROSTATIC PARTITIONING AND THE APPARENT KM

$$K_{m,app} = K_m \exp\left(\frac{zF\psi}{R_gT}\right), \qquad S_{local} = S_b \exp\left(-\frac{zF\psi}{R_gT}\right)$$

z = signed charge number of the substrate, ψ = signed electrostatic potential of the support (V), $F = 96485$ C/mol, $R_g = 8.314$ J mol^{-1} K^{-1}, T in K. Assumes a uniform potential in the enzyme's microenvironment and Boltzmann partitioning; the effect is largest at low ionic strength, because added salt screens the charge. Same signs ($z\psi > 0$): substrate repelled, $K_{m,app} > K_m$. Opposite signs: substrate attracted, $K_{m,app} < K_m$. Partitioning alone leaves V_{max} unchanged. More generally, any partition coefficient $K_p = S_{local}/S_b$ (electrostatic or hydrophobic) gives $K_{m,app} = K_m/K_p$ with V_{max} unchanged.

FILM–REACTION BALANCE AT THE SURFACE

$$k_L\,(S_b - S_s) = \frac{V'_{max}\,S_s}{K_m + S_s}$$

Steady state; enzyme on the external surface only, no internal diffusion. Solve for S_s; the observed rate per unit area is either side of the equation.

DAMKÖHLER NUMBER

$$\mathrm{Da} = \frac{V'_{max}}{k_L\,S_b} = \frac{\text{maximum reaction rate}}{\text{maximum mass-transfer rate}}$$

Dimensionless. The maximum mass-transfer rate is $k_L S_b$, reached when $S_s = 0$. Large Da favours film control, small Da favours reaction control (see the criteria below).

DIMENSIONLESS SURFACE CONCENTRATION (EXACT)

$$1 - x = \mathrm{Da}\,\frac{x}{\kappa + x}, \quad x = \frac{S_s}{S_b},\ \kappa = \frac{K_m}{S_b} \ \Rightarrow\ x = \frac{-(\mathrm{Da}+\kappa-1) + \sqrt{(\mathrm{Da}+\kappa-1)^2 + 4\kappa}}{2}$$

Exact for Michaelis–Menten kinetics. It comes from the quadratic $x^2 + (\mathrm{Da}+\kappa-1)x - \kappa = 0$; take the positive root ($0 < x < 1$).

EXTERNAL EFFECTIVENESS FACTOR

$$\eta_E = \frac{\text{observed rate}}{\text{rate at } S_b} = \frac{v(S_s)}{v(S_b)} = \frac{S_s\,(K_m + S_b)}{S_b\,(K_m + S_s)}$$

Referred to the bulk concentration. Always ≤ 1 for Michaelis–Menten kinetics, because $S_s \leq S_b$.

FIRST-ORDER LIMIT (S MUCH SMALLER THAN KM)

$$\eta_E = \frac{S_s}{S_b} = \frac{1}{1+\mathrm{Da}_1}, \qquad \mathrm{Da}_1 = \frac{V'_{max}}{K_m\, k_L} = \frac{k_s}{k_L}, \qquad \text{rate} = \frac{S_b}{\dfrac{1}{k_L} + \dfrac{1}{k_s}}$$

$k_s = V'_{max}/K_m$ (m/s) is the surface first-order rate constant. Film and reaction act as resistances in series. Note $\mathrm{Da}_1 = \mathrm{Da}/\kappa$: it uses K_m in place of S_b.

EFFECTIVENESS FACTOR (INTERNAL)

$$\eta = \frac{\text{observed rate with internal diffusion}}{\text{rate if all the enzyme saw } S_s} = \frac{v_{obs}}{v(S_s)}$$

Referred to the **surface** concentration S_s, not the bulk. $0 < \eta \leq 1$ for first-order and Michaelis–Menten kinetics.

THIELE MODULUS, FIRST ORDER (CHARACTERISTIC LENGTH VP/AP)

$$\phi = \frac{V_p}{A_p}\sqrt{\frac{k_1}{D_e}}, \qquad \frac{V_p}{A_p} = L\ (\text{slab}), \quad \frac{R}{2}\ (\text{long cylinder}), \quad \frac{R}{3}\ (\text{sphere})$$

ϕ^2 compares the characteristic reaction rate with the characteristic diffusion rate. For a slab, L is the half-thickness when both faces are exposed (the full thickness when one face is sealed). R is a radius, not a diameter.

EFFECTIVENESS FACTOR, SLAB, FIRST ORDER

$$\eta = \frac{\tanh\phi}{\phi}, \qquad \phi = L\sqrt{\frac{k_1}{D_e}}$$

L = half-thickness with both faces exposed. Exact for isothermal first-order kinetics.

EFFECTIVENESS FACTOR, SPHERE, FIRST ORDER

$$\eta = \frac{1}{\phi}\left(\frac{1}{\tanh 3\phi} - \frac{1}{3\phi}\right), \qquad \phi = \frac{R}{3}\sqrt{\frac{k_1}{D_e}}$$

R = particle radius. Exact for isothermal first-order kinetics.

SAME SPHERE RESULT, OTHER COMMON CONVENTION

$$\eta = \frac{3}{\phi_s^2}\left(\phi_s \coth\phi_s - 1\right), \qquad \phi_s = R\sqrt{\frac{k_1}{D_e}} = 3\phi$$

Gives identical numbers; only the modulus is defined without the factor 1/3. In this convention the large-modulus limit is $\eta \approx 3/\phi_s$.

LIMITS (ANY SHAPE, MODULUS BASED ON VP/AP)

$$\phi \to 0:\ \eta \to 1; \qquad \phi \gg 1:\ \eta \approx \frac{1}{\phi} \quad \left(\text{sphere: } \eta \approx \frac{1}{\phi}\left(1 - \frac{1}{3\phi}\right)\right)$$

Small ϕ: reaction is slow compared with diffusion and the whole particle sees S_s. Large ϕ: substrate is consumed in a thin shell near the surface and the core is starved. For a slab $\tanh\phi/\phi$ is within 1% of $1/\phi$ once $\phi \geq 2.65$ ($\tanh 3 = 0.995$). A sphere converges more slowly (at $\phi = 3$, $1/\phi$ overestimates η by about 12%), hence the correction term, which is within 1% of the exact value for $\phi \geq 1$.

GENERALISED MODULUS FOR MICHAELIS–MENTEN KINETICS

$$\Phi = \phi_1 \frac{\beta}{(1+\beta)\sqrt{2\left[\beta - \ln(1+\beta)\right]}}, \qquad \beta = \frac{S_s}{K_m}, \qquad \phi_1 = \frac{V_p}{A_p}\sqrt{\frac{V_{max}}{K_m D_e}}$$

ϕ_1 is the first-order modulus; $\ln$ is the natural logarithm. The factor multiplying ϕ_1 tends to 1 as $\beta \to 0$ and to $1/\sqrt{2\beta}$ as $\beta \to \infty$, and decreases steadily in between, so Φ falls as S_s rises.

OBSERVABLE (WEISZ) MODULUS

$$\Phi_W = \left(\frac{V_p}{A_p}\right)^2 \frac{v_{obs}}{D_e\, S_s} = \eta\, \phi^2$$

v_{obs} = measured rate per unit particle volume. The identity $\Phi_W = \eta\phi^2$ holds for first-order kinetics with ϕ based on V_p/A_p.

EXTERNAL FILM PLUS INTERNAL DIFFUSION, FIRST ORDER

$$v_{obs} = \frac{S_b}{\dfrac{1}{k_L a_p} + \dfrac{1}{\eta\, k_1}}, \qquad a_p = \frac{A_p}{V_p} = \frac{3}{R}\ \text{(sphere)}$$

Rate per unit particle volume, from $k_L a_p (S_b - S_s) = \eta k_1 S_s$. For isothermal first-order kinetics η does not depend on S_s, so the two resistances simply add.

SAME RESULT IN TERMS OF THE MASS-TRANSFER BIOT NUMBER

$$\frac{1}{\eta_o} = \frac{1}{\eta} + \frac{\phi^2}{\mathrm{Bi}_m}, \qquad \mathrm{Bi}_m = \frac{k_L\,(V_p/A_p)}{D_e}$$

First order, with ϕ based on V_p/A_p and η_o referred to S_b. Bi_m compares film transport with internal diffusion; the identity $k_1/(k_L a_p) = \phi^2/\mathrm{Bi}_m$ turns the series-resistance result into this form. If a question defines $\mathrm{Bi} = k_L R/D_e$ for a sphere together with $\phi_s = R\sqrt{k_1/D_e}$, the second term is $\phi_s^2/(3\,\mathrm{Bi})$. Large Bi_m: the film is negligible and $\eta_o \to \eta$.

OVERALL EFFECTIVENESS FACTOR

$$\eta_o = \frac{v_{obs}}{v(S_b)} = \eta_E\, \eta, \qquad \eta_E = \frac{v(S_s)}{v(S_b)}$$

Referred to the bulk concentration. It is the product of the external and internal factors because $v_{obs} = \eta\, v(S_s)$.

OBSERVED RATE UNDER STRONG INTERNAL LIMITATION, FIRST ORDER

$$v_{obs} \approx \frac{k_1 S_s}{\phi} = \frac{A_p}{V_p}\sqrt{k_1 D_e}\; S_s$$

Valid for $\phi \gg 1$. The observed rate scales with $\sqrt{k_1}$, hence with the square root of the enzyme loading (uniformly spread enzyme), and inversely with particle size.

APPARENT ACTIVATION ENERGY

$$E_{app} = \frac{E + E_D}{2} \approx \frac{E}{2}$$

Strong internal diffusion limitation ($\phi \gg 1$) in an isothermal particle, where $v_{obs} \propto \sqrt{k_1 D_e}$. E = intrinsic activation energy of the enzyme reaction; E_D = activation energy of diffusion, usually small. Under external film control the apparent value falls further, to the low value of liquid-film mass transfer.

APPARENT REACTION ORDER

$$n_{app} = \frac{n+1}{2}$$

Strong internal limitation ($\phi \gg 1$), isothermal particle, intrinsic power-law order n ($n > -1$): first order stays first order and zero order appears as half order. A Michaelis–Menten enzyme that is saturated at the surface ($\beta \gg 1$) under strong limitation therefore shows $v_{obs} \propto S_s^{1/2}$.

BULK CONCENTRATION AT HALF THE MAXIMUM RATE (EXTERNAL FILM, EXACT)

$$S_{b,1/2} = K_m + \frac{V'_{max}}{2k_L} = K_m\left(1 + \frac{\mathrm{Da}_1}{2}\right)$$

Surface-bound enzyme with Michaelis–Menten kinetics and a liquid film. The plateau is still V'_{max}; half of it needs $S_s = K_m$ at the surface, and the film must then carry $V'_{max}/2$, so $k_L(S_b - K_m) = V'_{max}/2$. This bulk half-saturation concentration is what the measured curve shows as its apparent K_m. Because the whole curve is not exactly Michaelis–Menten, a K_m fitted by linearisation depends on the substrate range used.

Cell growth, substrate utilisation and product formation

SPECIFIC GROWTH RATE

$$\mu = \frac{1}{X}\frac{dX}{dt} = \frac{d\ln X}{dt}$$

Definition, valid in any phase; units h^{-1}. X is the biomass concentration (g/L). When death is negligible this is the growth rate itself; when death or endogenous decay is significant, the measured $(1/X)\,dX/dt$ is the net rate $\mu - k_d$ (see below). The number-based rate μ_N uses the cell number concentration N instead of X.

EXPONENTIAL GROWTH AT CONSTANT SPECIFIC GROWTH RATE

$$X = X_0\, e^{\mu (t - t_0)} \quad \Longleftrightarrow \quad \ln\frac{X}{X_0} = \mu\,(t - t_0)$$

Applies to the exponential phase only: constant μ, no lag inside the interval, death neglected ($X = X_0$ at $t = t_0$). If death is significant, use the net rate $\mu - k_d$ in place of μ. Use the natural log. A plot of $\ln X$ against t is a straight line of slope μ.

DOUBLING TIME

$$t_d = \frac{\ln 2}{\mu} \approx \frac{0.693}{\mu}$$

Time for the biomass to double at constant μ (use $\mu - k_d$ if death is significant). The units follow μ: μ in h^{-1} gives t_d in h.

NUMBER OF GENERATIONS AND GENERATION TIME

$$n = \frac{\ln(N/N_0)}{\ln 2} = \log_2\frac{N}{N_0} \approx 3.32\log_{10}\frac{N}{N_0}, \qquad t_g = \frac{t}{n} = \frac{\ln 2}{\mu_N}$$

Based on cell NUMBER N (cells/mL): after n generations, $N = N_0\,2^n$. The relation $t_g = \ln 2/\mu_N$ holds for exponential growth at constant μ_N. The generation time t_g equals the biomass doubling time t_d only during balanced growth, when the mass per cell is constant.

DEATH AND NET GROWTH

$$\frac{dX}{dt} = (\mu - k_d)\,X, \qquad \text{death phase: } N = N_0\,e^{-k_d t}$$

In the biomass balance, k_d (h^{-1}) is a first-order constant for loss of biomass by death or endogenous decay, and $\mu_{\mathrm{net}} = \mu - k_d$ is the net specific growth rate; in the stationary phase $\mu_{\mathrm{net}} = 0$. In the death-phase expression, N is the viable cell concentration, N_0 is its value when the death phase starts and t is the time since then; there k_d is the specific death rate of viable cells, which need not equal the biomass decay constant.

MONOD EQUATION

$$\mu = \frac{\mu_{\max}\,S}{K_s + S}$$

Assumes one growth-limiting substrate, all other nutrients in excess, no inhibition and negligible death. $\mu_{\max}$ is in h^{-1}; K_s and S are in the same concentration units. At $S = K_s$, $\mu = \mu_{\max}/2$.

LIMITING CASES OF THE MONOD EQUATION

$$S \gg K_s:\ \mu \approx \mu_{\max}\ (\text{zero order in } S); \qquad S \ll K_s:\ \mu \approx \frac{\mu_{\max}}{K_s}\,S\ (\text{first order in } S)$$

Use these to simplify batch and chemostat problems. In batch culture with $S_0 \gg K_s$, growth stays near $\mu_{\max}$ until the substrate is almost exhausted.

SUBSTRATE CONCENTRATION FOR A GIVEN GROWTH RATE

$$S = \frac{K_s\,\mu}{\mu_{\max} - \mu}$$

The Monod equation solved for S; valid only for $\mu < \mu_{\max}$. In a chemostat at steady state with sterile feed and negligible death, $\mu = D = F/V$, so this gives the residual substrate concentration $S = K_s D/(\mu_{\max} - D)$, which does not depend on the feed substrate concentration.

LINEAR FORMS FOR ESTIMATING MONOD PARAMETERS

$$\frac{1}{\mu} = \frac{1}{\mu_{\max}} + \frac{K_s}{\mu_{\max}} \cdot \frac{1}{S}$$
$$\frac{S}{\mu} = \frac{K_s}{\mu_{\max}} + \frac{S}{\mu_{\max}}$$
$$\mu = \mu_{\max} - K_s\,\frac{\mu}{S}$$

Double-reciprocal (Lineweaver-Burk) plot: $1/\mu$ against $1/S$, with intercept $1/\mu_{\max}$, slope $K_s/\mu_{\max}$ and x-intercept $-1/K_s$. Second form: S/μ against S, with slope $1/\mu_{\max}$ and intercept $K_s/\mu_{\max}$. Third form: μ against μ/S, with slope $-K_s$ and intercept $\mu_{\max}$. In the double-reciprocal plot the low-S points (small μ, large $1/S$) lie far from the axis, and taking reciprocals magnifies their errors, so they dominate the fitted line.

LOGISTIC EQUATION

$$\frac{dX}{dt} = k\,X\left(1 - \frac{X}{X_\infty}\right) \;\Rightarrow\; X = \frac{X_\infty}{1 + \left(\dfrac{X_\infty}{X_0} - 1\right) e^{-kt}}$$

An unstructured model that needs no substrate balance: growth slows as X approaches the carrying capacity X_∞. X_0 is the biomass at $t = 0$, and k ($\mathrm{h^{-1}}$) is the specific growth rate when $X \ll X_\infty$. The volumetric growth rate dX/dt is highest at $X = X_\infty/2$, so the curve is sigmoidal when $X_0 < X_\infty/2$.

ANDREWS SUBSTRATE INHIBITION: OPTIMUM SUBSTRATE LEVEL

$$S^* = \sqrt{K_s K_I}, \qquad \mu(S^*) = \frac{\mu_{\max}}{1 + 2\sqrt{K_s/K_I}}$$

Found by setting $d\mu/dS = 0$. Below S^*, raising S speeds growth; above it, raising S slows growth. $\mu(S^*)$ is always below $\mu_{\max}$.

YIELD COEFFICIENTS

$$Y_{X/S} = -\frac{dX}{dS}, \qquad Y_{P/S} = -\frac{dP}{dS}, \qquad Y_{X/O_2} = -\frac{dX}{d[\mathrm{O_2}]}, \qquad Y_{P/X} = \frac{dP}{dX}$$

Units are g/g, C-mol/C-mol or mol/mol; always state which. Here $[\mathrm{O_2}]$ stands for the oxygen still available to the cells per litre of culture, which falls as it is consumed; it is not the dissolved-oxygen concentration. So Y_{X/O_2} is the biomass formed per unit of oxygen consumed. Yields taken over the same interval combine as ratios: $Y_{P/X} = Y_{P/S}/Y_{X/S}$ and $Y_{S/X} = 1/Y_{X/S}$.

BIOMASS-SUBSTRATE BALANCE IN BATCH CULTURE

$$X - X_0 = Y_{X/S}\,(S_0 - S), \qquad X_{\max} = X_0 + Y_{X/S}\,S_0$$

Assumes a constant yield and negligible maintenance. $X_{\max}$ is reached when the limiting substrate is used up ($S = 0$).

SPECIFIC RATES

$$q_S = -\frac{1}{X}\frac{dS}{dt}, \qquad q_P = \frac{1}{X}\frac{dP}{dt}, \qquad q_{O_2} = \frac{\mathrm{OUR}}{X}, \qquad q_S = \frac{\mu}{Y_{X/S}}$$

Rates per unit biomass, e.g. g substrate/(g cells·h). OUR is the volumetric oxygen uptake rate, e.g. mol $\mathrm{O_2}$/(L·h). The last relation uses the instantaneous observed yield and neglects death, since then $Y_{X/S} = (dX/dt)/(-dS/dt) = \mu/q_S$. A volumetric rate is the specific rate times X, e.g. $r_S = q_S X$.

PIRT MAINTENANCE MODEL

$$q_S = \frac{\mu}{Y^M_{X/S}} + m_S, \qquad q_{O_2} = \frac{\mu}{Y^M_{X/O_2}} + m_{O_2}$$

Y^M is the true (maximum) growth yield, the yield if no substrate went to maintenance. m_S is the maintenance coefficient, in g substrate/(g cells·h), taken as constant; m_{O_2} is the same for oxygen. Maintenance is energy spent on turnover of cell components, osmotic and ion gradients, and motility, not on making new cells.

OBSERVED YIELD WITH MAINTENANCE

$$\frac{1}{Y^{\text{obs}}_{X/S}} = \frac{1}{Y^M_{X/S}} + \frac{m_S}{\mu}$$

Follows from $Y^{\text{obs}}_{X/S} = \mu/q_S$ (death neglected). A plot of $1/Y^{\text{obs}}$ against $1/\mu$ is a straight line with slope m_S and intercept $1/Y^M_{X/S}$. In a chemostat at steady state with sterile feed and negligible death, $\mu = D$, so the plot is against $1/D$. Whenever $m_S > 0$, $Y^{\text{obs}} < Y^M$, and the gap widens as μ falls.

LUEDEKING-PIRET EQUATION

$$q_P = \frac{1}{X}\frac{dP}{dt} = \alpha\,\mu + \beta \quad \Longleftrightarrow \quad \frac{dP}{dt} = \alpha\,\frac{dX}{dt} + \beta\,X$$

α is the growth-associated coefficient (g P/g X). β is the non-growth-associated coefficient (g P/(g X·h)). The two forms are equivalent when $dX/dt = \mu X$ (death neglected). To find both constants, plot q_P against μ: the slope is α and the intercept is β.

DEGREE OF REDUCTION

$$\gamma = 4 + x - 2y - 3z \quad \text{for } \mathrm{CH_xO_yN_z}$$

Available electrons per C-mol, counting C = +4, H = +1, O = -2 and N = -3 (ammonia as the nitrogen reference). The reference compounds $\mathrm{CO_2}$, $\mathrm{H_2O}$ and $\mathrm{NH_3}$ all have $\gamma = 0$. If nitrate is the nitrogen source, count N as +5; if $\mathrm{N_2}$ is, count it as 0. One mole of $\mathrm{O_2}$ accepts 4 electrons.

ELECTRON BALANCE

$$\gamma_S - 4a = c\,\gamma_B + f\,j\,\gamma_P$$

Per C-mol of substrate. γ_S, γ_B and γ_P are the degrees of reduction of substrate, biomass and product per C-mol, and $f\,j$ is the C-mol of product formed. Electrons in the substrate end up in biomass, product or oxygen; $\mathrm{CO_2}$, $\mathrm{H_2O}$ and the nitrogen source carry none, provided γ_B is computed with the valence of N for that source.

FATE OF AVAILABLE ELECTRONS AND YIELD LIMITS

$$\eta = \frac{c\,\gamma_B}{\gamma_S}, \quad \zeta = \frac{f\,j\,\gamma_P}{\gamma_S}, \quad \varepsilon = \frac{4a}{\gamma_S}, \quad \eta + \zeta + \varepsilon = 1; \qquad c \le \min\left(1,\ \frac{\gamma_S}{\gamma_B}\right)$$

η, ζ and ε are the fractions of the substrate's available electrons that go to biomass, product and oxygen. For a heterotroph growing on one organic carbon source (no $\mathrm{CO_2}$ fixation), the biomass yield in C-mol/C-mol can never exceed the carbon limit of 1 or the electron limit γ_S/γ_B. The electron limit is reached only with no oxygen uptake and no product. The same reasoning bounds the product: $f\,j \le \min(1, \gamma_S/\gamma_P)$.

RESPIRATORY QUOTIENT AND YIELD CONVERSIONS

$$\mathrm{RQ} = \frac{d}{a}, \qquad Y_{X/S}\,[\mathrm{g/g}] = c\,\frac{M_X}{M_S}, \qquad Y_{X/O_2}\,[\mathrm{g/g}] = \frac{c\,M_X}{32\,a}$$

RQ is the mol of $\mathrm{CO_2}$ formed per mol of $\mathrm{O_2}$ consumed. M_X and M_S are masses per C-mol (g/C-mol). To express the coefficients a to e per mole of substrate instead of per C-mol, multiply them by the number of carbon atoms in the substrate; the g/g yields and the RQ do not change.

Batch, fed-batch and continuous bioreactors, and scale-up

MONOD KINETICS

$$\mu = \frac{\mu_m S}{K_s + S}$$

μ_m = maximum specific growth rate (h^{-1}); K_s = saturation constant, the substrate concentration at which $\mu = \mu_m/2$ (g/L). For $S \gg K_s$, $\mu \approx \mu_m$. Every result below that contains K_s assumes this form, with a single growth-limiting substrate.

EXPONENTIAL GROWTH AND DOUBLING TIME

$$X = X_0\, e^{\mu_m t}, \qquad t_d = \frac{\ln 2}{\mu_m}$$

Exponential phase of a batch culture, where $S \gg K_s$ so that $\mu \approx \mu_m$; no lag and no death.

BATCH YIELD BALANCE

$$X - X_0 = Y_{X/S}\,(S_0 - S)$$

Constant yield, substrate used only for growth. When the substrate is exhausted ($S = 0$) the biomass reaches its maximum, $X_m = X_0 + Y_{X/S} S_0$.

BATCH GROWTH TIME

$$t_b = \frac{1}{\mu_m} \ln \frac{X_m}{X_0}$$

Time to grow from X_0 to X_m if the cells grow at μ_m the whole time (K_s negligible, lag ignored).

BATCH PRODUCTIVITY

$$Q_{X,b} = \frac{X_m - X_0}{t_b + t_L}$$

Averaged over the whole cycle. t_L = turnaround time per cycle: harvesting, cleaning, sterilising, filling and lag.

CHEMOSTAT BIOMASS BALANCE

$$\frac{dX}{dt} = \mu X - D X$$

No cells in the feed (sterile), cell death neglected. At steady state with $X \neq 0$ this gives $\mu = D$: the feed rate sets the growth rate.

CHEMOSTAT SUBSTRATE BALANCE

$$\frac{dS}{dt} = D\,(S_0 - S) - \frac{\mu X}{Y_{X/S}}$$

Substrate used only for growth (no maintenance term), with $Y_{X/S}$ constant.

STEADY-STATE SUBSTRATE CONCENTRATION

$$\bar{S} = \frac{K_s D}{\mu_m - D}$$

Monod kinetics with $\mu = D$. It does not depend on S_0 and holds only for $D < D_c$.

STEADY-STATE BIOMASS CONCENTRATION

$$\bar{X} = Y_{X/S}\,(S_0 - \bar{S}) = Y_{X/S}\left(S_0 - \frac{K_s D}{\mu_m - D}\right)$$

From the substrate balance at steady state. Proportional to $Y_{X/S}$; it rises linearly with S_0, and nearly in proportion to it when $S_0 \gg \bar{S}$.

WASHOUT (CRITICAL) DILUTION RATE

$$D_c = \frac{\mu_m S_0}{K_s + S_0} \approx \mu_m \quad (S_0 \gg K_s)$$

Found by setting $\bar{S} = S_0$ (so $\bar{X} = 0$). For $D \geq D_c$ cells leave faster than they can grow and the culture washes out. Without recycle, $D_c < \mu_m$ for any finite S_0.

FINDING THE MONOD CONSTANTS FROM CHEMOSTAT DATA

$$\frac{1}{D} = \frac{1}{\mu_m} + \frac{K_s}{\mu_m}\frac{1}{\bar{S}}$$

Monod kinetics with $\mu = D$ at each steady state. Measure $\bar{S}$ at several dilution rates: a plot of $1/D$ against $1/\bar{S}$ is a straight line with intercept $1/\mu_m$ and slope K_s/μ_m.

VOLUMETRIC BIOMASS PRODUCTIVITY

$$Q_X = D\,\bar{X}$$

Grams of cells per litre of reactor per hour. For a product, $Q_P = D\,\bar{P}$.

DILUTION RATE FOR MAXIMUM PRODUCTIVITY

$$D_{opt} = \mu_m\left(1 - \sqrt{\frac{K_s}{K_s + S_0}}\right)$$

From $d(D\bar{X})/dD = 0$ with Monod kinetics, no maintenance and no death. It lies below D_c, and close to it when $S_0 \gg K_s$.

MAXIMUM CHEMOSTAT PRODUCTIVITY

$$(D\bar{X})_{max} = Y_{X/S}\,\mu_m\left(\sqrt{S_0 + K_s} - \sqrt{K_s}\right)^2$$

Productivity at D_{opt}. The substrate concentration there is $\bar{S} = \sqrt{K_s(K_s + S_0)} - K_s$.

GROWTH RATE WITH CELL RECYCLE

$$\mu = D\,(1 + \alpha - \alpha C)$$

From the steady-state biomass balance on the reactor (no death). A balance on the separator shows that $1 + \alpha - \alpha C = X_e/\bar{X}$, where X_e is the cell concentration in the effluent that leaves the system, so the factor lies between 0 and 1: cells grow more slowly than the liquid is diluted.

STEADY STATE WITH CELL RECYCLE

$$\bar{S} = \frac{K_s D(1 + \alpha - \alpha C)}{\mu_m - D(1 + \alpha - \alpha C)}, \qquad \bar{X} = \frac{Y_{X/S}\,(S_0 - \bar{S})}{1 + \alpha - \alpha C}$$

Monod kinetics. Same form as the simple chemostat, with D replaced by $D(1 + \alpha - \alpha C)$ in $\bar{S}$. $\bar{X}$ is raised by the factor $1/(1 + \alpha - \alpha C)$.

MAINTENANCE (PIRT) RELATION

$$\frac{1}{Y^{obs}_{X/S}} = \frac{1}{Y_G} + \frac{m_s}{\mu}$$

Y_G = true growth yield; m_s = maintenance coefficient (g substrate per g cells per h). In a chemostat $\mu = D$ and $Y^{obs}_{X/S} = \bar{X}/(S_0 - \bar{S})$, so a plot of $1/Y^{obs}$ against $1/D$ is a straight line with slope m_s and intercept $1/Y_G$.

PRODUCT IN A CHEMOSTAT

$$D\,\bar{P} = q_P\,\bar{X}, \qquad q_P = \alpha\mu + \beta \;\; (\mu = D)$$

Product-free feed, no product degradation. q_P = specific product formation rate (g product per g cells per h), written in the Luedeking–Piret form with growth-associated α and non-growth-associated β (this α is unrelated to the recycle ratio). So $\bar{P} = \alpha\bar{X} + \beta\bar{X}/D$.

VOLUME IN FED-BATCH

$$\frac{dV}{dt} = F, \qquad V = V_0 + Ft \ \ (\text{constant } F)$$

Liquid is only added, never withdrawn.

FED-BATCH BALANCES ON TOTAL AMOUNTS

$$\frac{d(XV)}{dt} = \mu XV, \qquad \frac{d(SV)}{dt} = FS_0 - \frac{\mu XV}{Y_{X/S}}$$

No biomass in the feed, nothing withdrawn, substrate used only for growth. Write fed-batch balances on total amounts (XV, SV), because V changes.

TOTAL BIOMASS UNDER CONSTANT FEED

$$\frac{d(XV)}{dt} = F\,Y_{X/S}\,S_0 \ \Rightarrow \ X_t = X_{t0} + F\,Y_{X/S}\,S_0\,t$$

Holds once substrate is used as fast as it is fed (S small and steady, $S \ll S_0$). $X_t = XV$ is the total mass of cells, and under constant feed it rises linearly, not exponentially.

QUASI-STEADY STATE (CONSTANT FEED)

$$\mu \approx D = \frac{F}{V_0 + Ft}, \qquad X \approx Y_{X/S}\,S_0$$

Approached as the run proceeds: with constant feed $XV = X_{t0} + FY_{X/S}S_0t$, so X tends to $Y_{X/S}S_0$, after which $dX/dt \approx 0$ and $dS/dt \approx 0$. Because V keeps rising, D and so μ fall with time, and the residual $S \approx K_sD/(\mu_m - D)$ falls too.

EXPONENTIAL FEEDING FOR CONSTANT GROWTH RATE

$$F(t) = \frac{\mu_{set}\,X_0V_0}{Y_{X/S}\,(S_0 - S)}\,e^{\mu_{set}t}$$

Holds μ at a chosen $\mu_{set} < \mu_m$, with S kept constant at $K_s\mu_{set}/(\mu_m - \mu_{set})$. X_0V_0 is the total biomass when exponential feeding starts ($t = 0$). It follows from $XV = X_0V_0e^{\mu_{set}t}$ and the substrate balance with S constant. If maintenance matters, replace $\mu_{set}/Y_{X/S}$ by $\mu_{set}/Y_G + m_s$. If $S \ll S_0$, use S_0 in the denominator.

HENRY'S LAW

$$p_{O_2} = H\,C^*, \qquad C^* = \frac{y_{O_2}\,P}{H}$$

C^* = dissolved O_2 concentration in equilibrium with the gas; H = Henry's constant for O_2 in the medium at the operating temperature (pressure per concentration, for example atm L/mmol); y_{O_2} = mole fraction of O_2 in the gas (0.21 for air); P = total pressure. C^* rises in proportion to the O_2 partial pressure (O_2-enriched air, higher head pressure). It falls with temperature and with dissolved salts and sugars. Air-saturated pure water at 25 °C and 1 atm holds only about 8 mg/L (about 0.26 mmol/L), and less at higher temperatures.

OXYGEN TRANSFER RATE (OTR)

$$\text{OTR} = k_La\,(C^* - C_L)$$

C_L = dissolved O_2 in the broth. With C in mmol/L and k_La in h^{-1}, OTR is in mmol/(L h). The maximum OTR is $k_La\,C^*$, reached when $C_L = 0$.

OXYGEN UPTAKE RATE (OUR)

$$\text{OUR} = q_{O_2}\,X$$

q_{O_2} = specific O_2 uptake rate (mmol O_2 per g cells per h). It does not depend on C_L above the critical dissolved-oxygen concentration C_{crit}, and falls below it.

DISSOLVED-OXYGEN BALANCE

$$\frac{dC_L}{dt} = k_L a\,(C^* - C_L) - q_{O_2} X$$

Well-mixed liquid. At steady state OTR = OUR.

OXYGEN-LIMITED DESIGN

$$(k_L a)_{min} = \frac{q_{O_2} X}{C^* - C_{crit}}, \qquad X_{max} = \frac{k_L a\,(C^* - C_{crit})}{q_{O_2}}$$

The smallest $k_L a$ that keeps $C_L \geq C_{crit}$ at a given cell density, or the largest cell density a given $k_L a$ can support.

STATIC GASSING-OUT (NO OXYGEN UPTAKE)

$$\ln \frac{C^* - C_{L0}}{C^* - C_L} = k_L a\, t$$

Cell-free medium: strip the O_2 with N_2, then aerate starting from C_{L0}. The slope of $\ln(C^* - C_L)$ against t is $-k_L a$. Valid when the DO probe responds much faster than $1/k_L a$.

KLA FROM SULPHITE OXIDATION

$$k_L a = \frac{\mathrm{OTR}}{C^*} = \frac{\frac{1}{2}\left(-d[\mathrm{SO_3^{2-}}]/dt\right)}{C^*}$$

2 mol of sulphite consume 1 mol of O_2, and $C_L \approx 0$ throughout.

IMPELLER REYNOLDS NUMBER

$$\mathrm{Re}_i = \frac{\rho N D_i^2}{\mu_L}$$

N in rev/s (not rad/s, not rpm). In a baffled tank, flow is laminar below about 10 and fully turbulent above about 10^4.

POWER NUMBER

$$N_P = \frac{P}{\rho N^3 D_i^5}$$

P = ungassed shaft power (W, with ρ in kg/m^3, N in rev/s and D_i in m). For a given impeller and baffled-tank geometry, N_P depends only on Re_i.

LAMINAR REGIME

$$N_P = \frac{k_1}{\mathrm{Re}_i} \;\Rightarrow\; P = k_1\, \mu_L N^2 D_i^3$$

Power does not depend on density (k_1 is a geometry constant).

TURBULENT REGIME

$$N_P = \text{constant} \;\Rightarrow\; P = N_P\, \rho N^3 D_i^5$$

Fully turbulent, baffled tank: power does not depend on viscosity. For a six-blade Rushton turbine N_P is about 5 to 6. Doubling N multiplies P by 8; doubling D_i multiplies it by 32.

SUPERFICIAL GAS VELOCITY, AERATION RATE AND TIP SPEED

$$u_s = \frac{Q_g}{\pi D_T^2/4}, \qquad \mathrm{vvm} = \frac{Q_g}{V}, \qquad \text{tip speed} = \pi N D_i$$

D_T = tank diameter; vvm = volume of gas per volume of liquid per minute, so Q_g in the vvm expression is per minute. Tip speed is a common index of the highest shear, which occurs near the impeller.

MIXING TIME, TURBULENT REGIME

$$N\, t_m = \text{constant}$$

Geometrically similar tanks, fully turbulent: mixing time is inversely proportional to impeller speed. Circulation time scales as $V/(N D_i^3)$.

GENERAL SCALE-UP RULE FOR IMPELLER SPEED

$$\frac{N_2}{N_1} = \left(\frac{D_{i1}}{D_{i2}}\right)^n$$

$n = 2/3$ for constant P/V; $n = 1$ for constant tip speed (ND_i); $n = 2$ for constant Re_i; $n = 0$ for constant mixing time (constant N). Turbulent regime at both scales, geometric similarity, ungassed power.

CONSTANT POWER PER UNIT VOLUME

$$\frac{P}{V} \propto N^3 D_i^2 \;\Rightarrow\; N_2 = N_1 \left(\frac{D_{i1}}{D_{i2}}\right)^{2/3}$$

Turbulent regime, geometric similarity. Tip speed then rises as $D_i^{1/3}$ and mixing time as $D_i^{2/3}$.

BATCH ENZYME REACTOR (INTEGRATED MICHAELIS–MENTEN)

$$V_{max}\, t = K_m \ln\frac{S_0}{S} + (S_0 - S)$$

Constant enzyme activity, no inhibition. In conversion form: $V_{max}t = S_0 x - K_m \ln(1-x)$.

PLUG-FLOW (PACKED-BED) ENZYME REACTOR

$$V_{max}\,\tau = K_m \ln\frac{S_0}{S} + (S_0 - S), \qquad \tau = \frac{V}{F}$$

The batch equation with residence time τ in place of t (ideal plug flow). Use V and V_{max} on the same basis. For an immobilized enzyme limited by diffusion, the local rate is η times the intrinsic rate; because η varies with S, this integrated form then holds only where η is roughly constant along the bed.

CSTR ENZYME REACTOR

$$V_{max}\,\tau = \frac{(S_0 - S)(K_m + S)}{S}$$

Well mixed, with the enzyme kept in the vessel; the whole reactor runs at the outlet concentration S. In conversion form: $V_{max}\tau = S_0 x + K_m x/(1-x)$.

FIRST-ORDER LIMIT (S MUCH SMALLER THAN KM)

$$\ln\frac{S_0}{S} = \frac{V_{max}}{K_m}\,\tau \;\;(\mathrm{PFR}), \qquad \frac{S_0}{S} = 1 + \frac{V_{max}}{K_m}\,\tau \;\;(\mathrm{CSTR})$$

Natural log. In the zero-order limit ($S \gg K_m$), $S_0 - S = V_{max}\tau$ for both reactors.

ENZYME DEACTIVATION

$$V_{max}(t) = V_{max,0}\, e^{-k_d t}, \qquad t_{1/2} = \frac{\ln 2}{k_d}$$

First-order loss of active enzyme; k_d in h^{-1} or min^{-1}.

Media formulation and sterilisation

SUBSTRATE NEEDED FOR A BIOMASS TARGET

$$S_0 - S_f = \frac{X_f - X_0}{Y_{X/S}}, \qquad Y_{X/S} = -\frac{\Delta X}{\Delta S}$$

X and S in g/L, $Y_{X/S}$ in g dry cells per g substrate. For a limiting substrate used up completely, $S_f \approx 0$. Maintenance and product formation lower the observed yield, so use the yield measured under the same conditions.

ELEMENT BALANCE FOR A NUTRIENT COMPOUND

$$m_{\text{nutrient}} = \frac{w_E \, \Delta X}{f_E}$$

m_{nutrient} in g/L; w_E = mass fraction of element E in dry biomass, ΔX = biomass to be formed (g/L), f_E = mass fraction of E in the nutrient compound (for N in $(NH_4)_2SO_4$, $f_N = 28/132$). This is a minimum: it assumes the compound is the only source of E and that all of it is taken up.

MAIN EFFECT IN A TWO-LEVEL DESIGN

$$E_i = \bar{Y}_{(x_i=+1)} - \bar{Y}_{(x_i=-1)}$$

Mean response over all runs at the high level minus the mean over all runs at the low level. A positive effect means that raising the factor raises the response within the range tested. An interaction effect E_{ij} is found the same way, grouping the runs by the sign of the product $x_i x_j$. In a regression on coded variables the coefficient is half the effect, $\beta_i = E_i/2$, because x_i changes by 2 between the levels.

RESPONSE SURFACE (QUADRATIC) MODEL

$$Y = \beta_0 + \sum_{i=1}^{k} \beta_i x_i + \sum_{i=1}^{k} \beta_{ii} x_i^2 + \sum_{i<j} \beta_{ij} x_i x_j$$

Number of coefficients $= \dfrac{(k+1)(k+2)}{2}$ (10 for $k = 3$). Fitted by least squares; the stationary point comes from setting every $\partial Y/\partial x_i = 0$, and it may be a maximum, a minimum or a saddle point, so its nature must be checked before it is called the optimum.

FIRST-ORDER THERMAL DEATH

$$\frac{dN}{dt} = -k_d N \quad \Rightarrow \quad N = N_0 \, e^{-k_d t}, \qquad \ln \frac{N_0}{N} = k_d t$$

N = number of viable organisms (use the total number in the vessel for design, not the concentration); k_d = specific death rate constant in min^{-1} or s^{-1}. Holds at constant temperature.

DECIMAL REDUCTION TIME (D VALUE)

$$D = \frac{\ln 10}{k_d} = \frac{2.303}{k_d}, \qquad \log_{10} \frac{N_0}{N} = \frac{t}{D}$$

Time at a fixed temperature for a 90% kill (one log cycle). D and k_d must refer to the same temperature.

TEMPERATURE DEPENDENCE OF THE DEATH RATE (ARRHENIUS)

$$k_d = A \, e^{-E_d/(RT)}, \qquad \ln \frac{k_{d2}}{k_{d1}} = \frac{E_d}{R} \left(\frac{1}{T_1} - \frac{1}{T_2} \right)$$

T in kelvin, $R = 8.314$ J mol^{-1} K^{-1}, E_d = activation energy for death in J mol^{-1}, A has the units of k_d.

Z VALUE

$$\log_{10} \frac{D_{T_1}}{D_{T_2}} = \frac{T_2 - T_1}{z}$$

z = temperature rise that reduces D tenfold, assuming $\log_{10} D$ falls linearly with temperature. It is a temperature difference, so its value is the same in °C and K.

DEL (DESIGN) FACTOR

$$\nabla = \ln \frac{N_0}{N} = \int_0^t k_d \, dt = A \int_0^t e^{-E_d/(R\,T(t))} \, dt$$

Dimensionless, natural log. $N_0 = n_0 V$ (spore concentration × medium volume), N = acceptable number of survivors per batch (for example 10^{-3}).

BATCH CYCLE: HEATING, HOLDING AND COOLING

$$\nabla_{\text{total}} = \nabla_{\text{heat}} + \nabla_{\text{hold}} + \nabla_{\text{cool}}, \qquad t_{\text{hold}} = \frac{\nabla_{\text{total}} - \nabla_{\text{heat}} - \nabla_{\text{cool}}}{k_d(T_{\text{hold}})}$$

∇_{heat} and ∇_{cool} are the integrals of k_d over the heating and cooling temperature–time profiles; the holding period at constant temperature supplies the rest.

HOLDING TUBE IN PLUG FLOW

$$\nabla = k_d\,\bar{t} = \frac{k_d L}{\bar{u}}, \qquad L = \frac{\bar{u}\,\nabla}{k_d}, \qquad \bar{u} = \frac{Q}{\pi d^2/4}$$

$\bar{u}$ = mean velocity, Q = volumetric flow rate, d = tube internal diameter, L = holding-tube length, k_d at the holding temperature. Valid for a flat (turbulent) velocity profile, negligible axial dispersion and near-instant heating and cooling; otherwise add ∇_{heat} and ∇_{cool}.

DEPTH-FILTER PENETRATION

$$\frac{dN}{dx} = -KN \quad \Rightarrow \quad \ln\frac{N_0}{N} = KL, \qquad L_{90} = \frac{\ln 10}{K} = \frac{2.303}{K}$$

K = filter constant (per unit depth), which depends on air velocity, fibre diameter and packing; L_{90} = bed depth that removes 90%, so $\log_{10}(N_0/N) = L/L_{90}$. Collection efficiency $\eta_{\text{filter}} = 1 - N/N_0$, so $\ln\dfrac{1}{1-\eta_{\text{filter}}} = KL$.

FILTER BED DEPTH FOR A WHOLE FERMENTATION

$$N_0 = n_0\,Q\,t, \qquad L = \frac{1}{K}\ln\frac{n_0\,Q\,t}{N}$$

n_0 = organisms per m^3 of air, Q = air flow rate (m^3 per unit time), t = duration of the fermentation, N = acceptable number of organisms passing in that time (for example 10^{-3}).

Downstream processing: filtration, centrifugation, chromatography, extraction

SPECIFIC ACTIVITY

$$\text{Specific activity} = \frac{\text{total activity (U)}}{\text{total protein (mg)}}$$

In U/mg, where 1 U (enzyme unit) is the amount of enzyme that converts 1 µmol of substrate per minute under the stated assay conditions. It rises as contaminating protein is removed and is the working measure of purity for an enzyme or other active protein.

STEP YIELD AND OVERALL YIELD

$$Y_{\text{step}} = \frac{\text{total activity after the step}}{\text{total activity before the step}}, \qquad Y_{\text{overall}} = \frac{\text{total activity (final)}}{\text{total activity (crude)}} = \prod_i Y_i$$

Yields use TOTAL activity (or total product mass), never specific activity. The overall yield is the product of the step yields.

PURIFICATION FOLD

$$\text{Purification fold} = \frac{\text{specific activity at a step}}{\text{specific activity of the crude extract}}$$

Uses SPECIFIC activity; dimensionless, equal to 1 for the crude extract. The fold for one step alone is the ratio of specific activities after and before that step, and step folds multiply.

FIRST-ORDER RELEASE (BATCH BEAD MILL)

$$\ln\left(\frac{R_m}{R_m - R}\right) = k\,t$$

R = protein released at time t, R_m = maximum releasable protein, k = first-order rate constant (for example min^{-1}). Natural log. Equivalently $R/R_m = 1 - e^{-kt}$.

HIGH-PRESSURE HOMOGENISER

$$\ln\left(\frac{R_m}{R_m - R}\right) = k\,N\,P^a$$

N = number of passes, P = operating pressure, a = empirical pressure exponent that depends on the organism and its growth conditions, k = rate constant (its numerical value depends on the units of P and on temperature). Release is first order in the number of passes.

STOKES' LAW (GRAVITY SETTLING VELOCITY)

$$v_g = \frac{d^2(\rho_p - \rho_f)\,g}{18\,\mu}$$

d = particle diameter (m), ρ_p and ρ_f = particle and fluid densities (kg/m³), μ = fluid viscosity (Pa s), g = 9.81 m/s². Valid for a rigid sphere settling freely in a dilute suspension (no hindered settling) when the particle Reynolds number $Re_p = \rho_f v d/\mu$ is below about 1 (creeping flow). If $\rho_p < \rho_f$ the particle rises.

CENTRIFUGAL SETTLING VELOCITY

$$v_c = \frac{d^2(\rho_p - \rho_f)\,\omega^2 r}{18\,\mu} = v_g\,\frac{\omega^2 r}{g}$$

r = radial position (m), ω = angular speed (rad/s); Stokes' regime assumed. The velocity grows with radius, so the particle speeds up as it moves outward.

RELATIVE CENTRIFUGAL FORCE (G-NUMBER)

$$Z = \frac{\omega^2 r}{g}, \qquad \omega = \frac{2\pi n}{60}$$

n in rpm, ω in rad/s, r in m. Z is quoted as 'times g': the factor by which the centrifuge speeds up settling compared with gravity. In practical units, $Z = 1.118 \times 10^{-5}\,r\,n^2$ with r in cm and n in rpm.

SIGMA FACTOR AND CENTRIFUGE SCALE-UP

$$Q = v_g\,\Sigma, \qquad \frac{Q_1}{\Sigma_1} = \frac{Q_2}{\Sigma_2}$$

Σ (m²) is the area of a gravity settling tank that would do the same separation; Q is the feed rate at which particles of gravity settling velocity v_g are just completely captured. For the same broth and the same separation, Q/Σ is kept constant on scale-up between machines of the same type; comparing different types needs an efficiency correction.

TUBULAR-BOWL CENTRIFUGE

$$\Sigma_{\text{tubular}} = \frac{\pi\,\omega^2 b\,(r_1^2 - r_0^2)}{g\,\ln(r_1/r_0)}$$

b = bowl length, r_0 = radius of the liquid surface (inner), r_1 = radius of the bowl wall (outer). Derived from Stokes' law, assuming uniform (plug) axial flow, for complete capture of a particle entering at the liquid surface. For a thin liquid layer ($r_0 \to r_1 = r$) it reduces to $2\pi r b \times \omega^2 r/g$: the wall area times the G-number.

DISC-STACK CENTRIFUGE

$$\Sigma_{\text{disc}} = \frac{2\pi\,\omega^2 (N-1)\,(r_1^3 - r_0^3)}{3\,g\,\tan\theta}$$

N = number of discs ($N-1$ settling channels), r_1 and r_0 = outer and inner radii of the discs, θ = half-cone angle, measured between the disc surface and the axis of rotation. Same complete-capture basis as the tubular-bowl expression.

SEDIMENTATION COEFFICIENT

$$s = \frac{v}{\omega^2 r} = \frac{d^2(\rho_p - \rho_f)}{18\,\mu}$$

v = sedimentation velocity at radius r: the velocity per unit centrifugal field. s has units of time and is quoted in svedbergs, 1 S $= 10^{-13}$ s. The second form is Stokes' law for a sphere. For a macromolecule, $s = M(1 - \bar{v}\rho_f)/(N_A f)$, where M = molar mass, $\bar{v}$ = partial specific volume, f = frictional coefficient and N_A = Avogadro's number, so s depends on mass, density and shape.

SVEDBERG EQUATION (MOLAR MASS FROM S AND D)

$$M = \frac{s\,R\,T}{D\,(1 - \bar{v}\rho_f)}$$

R = gas constant (8.314 J mol^{-1} K^{-1}), T = absolute temperature (K), D = diffusion coefficient (m²/s), $\bar{v}$ = partial specific volume (m³/kg), ρ_f = solvent density (kg/m³), s in seconds; M then comes out in kg/mol. It follows from $s = M(1 - \bar{v}\rho_f)/(N_A f)$ and $D = RT/(N_A f)$, with s and D measured in the same solvent and at the same temperature.

TIME TO PELLET AND THE CLEARING FACTOR (K-FACTOR)

$$t = \frac{\ln(r_{\max}/r_{\min})}{s\,\omega^2}, \qquad k = \frac{2.53 \times 10^{11}\,\ln(r_{\max}/r_{\min})}{n^2}, \qquad t\,(\mathrm{h}) = \frac{k}{s\,(\mathrm{S})}$$

From $dr/dt = s\omega^2 r$ at constant s: the time for a particle to travel from $r_{\min}$ (top of the liquid) to $r_{\max}$ (bottom of the tube). The clearing factor k of a rotor at speed n (rpm) gives the pelleting time in hours when s is in svedbergs. For the same particle, run times on two rotors scale as $t_1/t_2 = k_1/k_2$.

CAKE FILTRATION RATE (DARCY FORM)

$$\frac{dV}{dt} = \frac{A\,\Delta P}{\mu\left(\dfrac{\alpha\,c\,V}{A} + R_m\right)}$$

V = filtrate volume (m³), A = filter area (m²), ΔP = pressure drop (Pa), μ = filtrate viscosity (Pa s), α = specific cake resistance (m/kg), c = mass of dry cake solids per volume of filtrate (kg/m³), R_m = filter-medium resistance (m^{-1}). α is constant for an incompressible cake; for a compressible one see below.

CONSTANT-PRESSURE FILTRATION (RUTH EQUATION)

$$\frac{t}{V} = \frac{\mu\,\alpha\,c}{2A^2\,\Delta P}\,V + \frac{\mu\,R_m}{A\,\Delta P}$$

Integrated form for constant ΔP with $V = 0$ at $t = 0$. A plot of t/V against V is a straight line: the slope gives α and the intercept gives R_m. With R_m negligible, $t = \mu\alpha c V^2/(2A^2\Delta P)$, so $V \propto \sqrt{t}$.

CONSTANT-RATE FILTRATION

$$\Delta P = \frac{\mu\,\alpha\,c\,Q^2}{A^2}\,t + \frac{\mu\,R_m\,Q}{A}$$

At a constant filtrate rate $Q = V/t$ (m³/s) and constant α (incompressible cake), the pressure drop must rise linearly with time.

COMPRESSIBLE CAKE

$$\alpha = \alpha_0\,(\Delta P)^s$$

s = compressibility index: $s = 0$ for an incompressible cake, typically between 0 and 1 for the compressible cakes formed by cells, so raising the pressure gives less gain in rate than an incompressible cake would.

MEMBRANE FLUX AND TRANSMEMBRANE PRESSURE

$$J = \frac{\Delta P_{TM}}{\mu\,(R_m + R_f)}, \qquad \Delta P_{TM} = \frac{P_{\text{in}} + P_{\text{out}}}{2} - P_{\text{permeate}}$$

J = permeate volume per membrane area per time (m³ m^{-2} s^{-1}, often quoted in L m^{-2} h^{-1}); R_m = membrane resistance, R_f = resistance of the fouling or polarised layer; P_{in} and P_{out} = feed-side pressures at the module inlet and outlet. When the retained solute exerts an osmotic pressure, the driving force becomes $\Delta P_{TM} - \sigma\Delta\pi$ (σ = reflection coefficient).

GEL-POLARISATION (LIMITING FLUX) MODEL

$$J = k\,\ln\left(\frac{C_G}{C_B}\right)$$

k = boundary-layer mass-transfer coefficient (m/s), C_G = gel (wall) concentration, C_B = bulk concentration. In this regime flux is independent of pressure. It is the film model $J = k\ln[(C_w - C_p)/(C_B - C_p)]$ with full rejection ($C_p = 0$) and $C_w = C_G$.

OBSERVED REJECTION (RETENTION) COEFFICIENT

$$R = 1 - \frac{C_p}{C_B}$$

C_p = permeate concentration, C_B = bulk (retentate) concentration. $R = 1$: fully retained; $R = 0$: passes freely. The intrinsic rejection uses the wall concentration C_w in place of C_B.

BATCH CONCENTRATION BY ULTRAFILTRATION

$$\frac{C}{C_0} = \left(\frac{V_0}{V}\right)^{R}$$

Well-mixed retentate reduced in volume from V_0 to V at constant observed rejection R. The fraction of solute still in the retentate is $CV/(C_0V_0) = (V/V_0)^{1-R}$.

CONSTANT-VOLUME DIAFILTRATION

$$\frac{C}{C_0} = \exp\left[-(1-R)\,N_D\right], \qquad N_D = \frac{V_{\text{buffer}}}{V}$$

Buffer is added as fast as permeate leaves, so the well-mixed retentate volume V stays constant; N_D = number of diavolumes. A freely permeating solute ($R = 0$, such as a salt being exchanged out) falls to e^{-N_D} of its starting level: about 5 % after 3 diavolumes and under 1 % after 5.

PARTITION COEFFICIENT

$$K = \frac{C_E}{C_R}$$

Equilibrium concentration in the extract (or top) phase divided by that in the raffinate (or bottom) phase. Treated as constant for dilute solutions.

APPARENT PARTITION COEFFICIENT OF AN IONISABLE SOLUTE

$$K_{\text{app}} = \frac{K_0}{1 + 10^{\,\text{pH}-\text{p}K_a}}\ \text{(weak acid)}, \qquad K_{\text{app}} = \frac{K_0}{1 + 10^{\,\text{p}K_a-\text{pH}}}\ \text{(weak base)}$$

K_0 = partition coefficient of the uncharged form, assuming only that form enters the organic phase; for the base, $\text{p}K_a$ is that of its conjugate acid BH^+. At pH = pK_a the apparent coefficient is $K_0/2$; once the pH is more than about one unit on the ionising side of the pK_a, each further pH unit cuts it roughly tenfold.

EXTRACTION FACTOR

$$E = K\,\frac{V_E}{V_R}$$

The ratio of solute AMOUNTS in the two phases at equilibrium; V_E and V_R = extract and raffinate volumes (or volumetric flow rates in continuous operation).

SINGLE EQUILIBRIUM STAGE

$$\text{fraction extracted} = \frac{E}{1+E}, \qquad \text{fraction left in raffinate} = \frac{1}{1+E}$$

For an ATPS the yield in the top phase is $Y_T = E/(1+E)$ with $E = KV_T/V_B$, where V_T and V_B are the top and bottom phase volumes.

N CROSS-CURRENT STAGES

$$\frac{\text{solute left in raffinate}}{\text{solute in feed}} = \frac{1}{(1+E)^n}$$

Each stage contacts the raffinate with an equal volume of fresh solvent; E is the extraction factor of one stage (based on the solvent used in that stage).

N COUNTERCURRENT STAGES (KREMSER)

$$\frac{\text{solute left in raffinate}}{\text{solute in feed}} = \frac{E-1}{E^{\,n+1}-1} \;\; (E \neq 1), \qquad = \frac{1}{n+1} \;\; (E = 1)$$

Feed enters stage 1 and solvent enters stage n; E is based on the total solvent and feed flows, with constant K and immiscible phases. For $n = 1$ it reduces to $1/(1+E)$.

LANGMUIR ISOTHERM

$$q = \frac{q_{\max} K C}{1 + K C}$$

Assumes a monolayer on identical, independent sites. $q_{\max}$ = monolayer capacity; K = association constant (for example L/g). Written equivalently $q = q_{\max} C/(K_d + C)$ with $K_d = 1/K$, so $q = q_{\max}/2$ at $C = K_d$. At low C it becomes linear, $q = q_{\max} K C$. Linearised: $1/q = 1/q_{\max} + 1/(q_{\max} K C)$.

FREUNDLICH ISOTHERM

$$q = K_F \, C^{1/n}$$

Empirical, for heterogeneous surfaces; it has no saturation limit. $n > 1$ indicates favourable adsorption. Linearised: $\log_{10} q = \log_{10} K_F + (1/n) \log_{10} C$, so a log-log plot has slope $1/n$.

BATCH ADSORPTION MASS BALANCE

$$V \, (C_0 - C^*) = m \, q^*$$

V = liquid volume, m = mass of adsorbent (initially free of solute), C_0 = initial concentration. The equilibrium point (C^*, q^*) lies on both this straight operating line and the isotherm.

COHN EQUATION (SALTING OUT) AND IONIC STRENGTH

$$\log_{10} S = \beta - K_s \, I, \qquad I = \frac{1}{2} \sum_i c_i z_i^2$$

S = protein solubility; β = intercept (depends on the protein, pH and temperature); K_s = salting-out constant; I = ionic strength (mol/L), with c_i the molar concentration and z_i the charge of ion i. Base-10 logarithm. Applies in the salting-out region (high I).

RETENTION TIME AND RETENTION FACTOR

$$t_R = t_0 \, (1 + k'), \qquad k' = \frac{t_R - t_0}{t_0} = K \, \frac{V_s}{V_m}$$

t_0 = elution time of an unretained species (dead time); k' = retention (capacity) factor; K = distribution coefficient (stationary/mobile concentration); V_s and V_m = stationary- and mobile-phase volumes. Retention volumes obey the same relation, $V_R = V_m(1 + k')$.

SELECTIVITY (SEPARATION FACTOR)

$$\alpha = \frac{k_2'}{k_1'} \geq 1$$

Component 2 elutes later. $\alpha = 1$ means no separation is possible, however efficient the column. (Not the specific cake resistance of filtration.)

PLATE NUMBER AND PLATE HEIGHT (HETP)

$$N = 16\left(\frac{t_R}{w_b}\right)^2 = 5.54\left(\frac{t_R}{w_{1/2}}\right)^2, \qquad H = \frac{L}{N}$$

For a Gaussian peak: w_b = baseline width between the tangents ($= 4\sigma$), $w_{1/2}$ = width at half height ($5.54 = 8\ln 2$). t_R and w in the same units; L = column length. Smaller H means a more efficient column.

RESOLUTION

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

$R_s = 1.5$ gives baseline separation of two Gaussian peaks of similar size (about 99.7 % separation); $R_s = 1.0$ still leaves a small overlap (about 98 % separation).

RESOLUTION EQUATION (EFFICIENCY, SELECTIVITY, RETENTION)

$$R_s = \frac{\sqrt{N}}{4}\left(\frac{\alpha - 1}{\alpha}\right)\left(\frac{k_2'}{1 + k_2'}\right)$$

N is the plate number for the later peak. Resolution grows only as $\sqrt{N}$, that is as $\sqrt{L}$ at fixed plate height.

VAN DEEMTER EQUATION

$$H = A + \frac{B}{u} + C\,u, \qquad u_{\text{opt}} = \sqrt{\frac{B}{C}}, \qquad H_{\min} = A + 2\sqrt{BC}$$

u = linear velocity of the mobile phase. A = eddy diffusion (independent of u; smaller for small, uniformly packed particles), B/u = longitudinal molecular diffusion, Cu = resistance to mass transfer between the phases (also smaller for smaller particles). Large proteins diffuse slowly, so the C term dominates and their optimum velocity is low.

GEL FILTRATION PARTITION COEFFICIENT

$$K_{av} = \frac{V_e - V_0}{V_t - V_0}$$

V_e = elution volume, V_0 = void volume (liquid outside the beads, found with a fully excluded marker such as blue dextran), V_t = total bed volume. $K_{av} = 0$ for a fully excluded molecule, approaching 1 for one that permeates all the pores. (A related coefficient, $K_d = (V_e - V_0)/V_i$, uses the internal pore volume V_i and runs from 0 to 1 exactly.) Within the fractionation range, K_{av} is approximately linear in log(molecular mass) for molecules of similar shape, such as globular proteins, which is the basis of the calibration curve.

CONSTANT-RATE DRYING TIME

$$t_c = \frac{m_s\,(X_0 - X_c)}{A\,N_c}$$

m_s = mass of dry solid, A = drying area, N_c = constant drying rate (kg water m^{-2} h^{-1}), X_0 = initial moisture content (dry basis). Applies while $X > X_c$.

FALLING-RATE DRYING TIME (RATE LINEAR IN FREE MOISTURE)

$$t_f = \frac{m_s\,(X_c - X^*)}{A\,N_c}\,\ln\left(\frac{X_c - X^*}{X_f - X^*}\right)$$

Assumes the rate falls linearly from N_c at X_c to zero at X^*; X_f = final moisture content ($X_f > X^*$). Total drying time $= t_c + t_f$.

Measurement, dynamics and process control

PH ELECTRODE (NERNST)

$$E = E^0 - \frac{2.303\,RT}{F}\,\mathrm{pH}, \qquad \frac{2.303\,RT}{F} = 59.16\ \mathrm{mV\ per\ pH\ at\ 298\ K}$$

E^0 is a constant of the electrode pair, fixed by calibration with buffers. $R = 8.314$ J mol^{-1} K^{-1}, $F = 96485$ C mol^{-1}, T in K. The slope is proportional to absolute temperature.

ORIFICE OR VENTURI FLOW METER

$$Q = C_d A_0 \sqrt{\frac{2\,\Delta P}{\rho\,(1-\beta^4)}}, \qquad \beta = \frac{d_0}{D}$$

SI units: Q in m^3 s^{-1}, ΔP in Pa, ρ (fluid density) in kg m^{-3}. A_0 and d_0 are the orifice (or venturi throat) area and diameter, D is the pipe diameter and C_d the discharge coefficient. Because $Q \propto \sqrt{\Delta P}$, a 10 : 1 flow range needs a 100 : 1 pressure-drop range.

VALVE FLOW EQUATION

$$q = C_v\, f(x) \sqrt{\frac{\Delta P_v}{\mathrm{s.g.}}}$$

US customary units: q in US gal/min, ΔP_v (pressure drop across the valve) in psi. C_v is the valve coefficient (the flow of water in US gal/min through the fully open valve at a 1 psi drop), s.g. the specific gravity of the liquid, and $f(x)$ the inherent characteristic.

INHERENT VALVE CHARACTERISTICS

$$\text{Linear: } f = x$$

$$\text{Equal percentage: } f = R^{x-1}, \quad \frac{1}{f}\frac{df}{dx} = \ln R$$

$$\text{Quick opening: } f = \sqrt{x}$$

At constant valve pressure drop; the quick-opening form is one common idealisation. For an equal-percentage valve, equal increments of stem travel give equal *fractional* changes in flow. The ideal equal-percentage curve gives $f = 1/R$ at $x = 0$, the minimum controllable flow; a real valve departs from the curve near closure and shuts off.

LAPLACE TRANSFORMS USED IN PROCESS DYNAMICS

$$\mathcal{L}\{M\,u(t)\} = \frac{M}{s}, \quad \mathcal{L}\{a\,t\} = \frac{a}{s^2}, \quad \mathcal{L}\{A\,\delta(t)\} = A$$

$$\mathcal{L}\{e^{-at}\} = \frac{1}{s+a}, \quad \mathcal{L}\{\sin \omega t\} = \frac{\omega}{s^2+\omega^2}$$

$$\mathcal{L}\left\{\frac{dy}{dt}\right\} = sY(s) - y(0), \quad \mathcal{L}\left\{\int_0^t y\,dt\right\} = \frac{Y(s)}{s}$$

$$\mathcal{L}\{f(t-\theta)\,u(t-\theta)\} = e^{-\theta s}F(s)$$

One-sided transforms of functions defined for $t \geq 0$. $u(t)$ is the unit step and $\delta(t)$ the unit impulse. $e^{-\theta s}$ is a pure dead time (transport lag) of θ.

FINAL AND INITIAL VALUE THEOREMS

$$\lim_{t\to\infty} y(t) = \lim_{s\to 0} sY(s), \qquad \lim_{t\to 0^+} y(t) = \lim_{s\to\infty} sY(s)$$

The final value theorem holds only if $y(t)$ settles, i.e. every pole of $sY(s)$ has a negative real part. Applied to an unstable or sustained-oscillation response, it returns a meaningless number.

BLOCK-DIAGRAM ALGEBRA

Series: $G_1 G_2$, Parallel: $G_1 \pm G_2$, Negative feedback: $\dfrac{G}{1+GH}$, Positive feedback: $\dfrac{G}{1-GH}$

G is the forward-path and H the feedback-path transfer function.

CLOSED-LOOP RESPONSE OF A FEEDBACK LOOP

$$Y(s) = \frac{G_c G_v G_p}{1 + G_c G_v G_p G_m} Y_{sp}(s) + \frac{G_d}{1 + G_c G_v G_p G_m} D(s)$$

G_c = controller, G_v = valve, G_p = process, G_m = measuring element, G_d = disturbance path. $G_{OL} = G_c G_v G_p G_m$ is the open-loop transfer function. The equation assumes the set point and the measurement are in the same units. If the set point is entered in process units while $K_m \neq 1$, the servo numerator carries an extra factor K_m.

FIRST-ORDER TRANSFER FUNCTION

$$G(s) = \frac{Y(s)}{U(s)} = \frac{K}{\tau s + 1}$$

K = steady-state gain; τ = time constant (in time units). The pole is at $s = -1/\tau$.

LINEARISED OUTFLOW RESISTANCE

$$q_o = C\sqrt{h} \;\Rightarrow\; R = \left(\frac{dq_o}{dh}\right)^{-1}_{\bar{h}} = \frac{2\sqrt{\bar{h}}}{C} = \frac{2\bar{h}}{\bar{q}_o}$$

Taylor linearisation about the steady state $\bar{h}$. Valid only for small deviations. Then $\tau = AR$.

STEP RESPONSE (INPUT STEP OF SIZE M)

$$y(t) = KM\left(1 - e^{-t/\tau}\right), \qquad t_f = \tau \ln \frac{1}{1-f}$$

y reaches 63.2% of its final change KM at $t = \tau$, 86.5% at 2τ, 95.0% at 3τ, 98.2% at 4τ and 99.3% at 5τ. The initial slope is KM/τ, so the tangent at $t = 0$ meets the final value at $t = \tau$. t_f is the time to reach a fraction f of the final change (natural log).

IMPULSE RESPONSE (IMPULSE OF AREA A)

$$y(t) = \frac{KA}{\tau} e^{-t/\tau}$$

The output jumps to KA/τ at $t = 0^+$ and then decays back to the old steady state.

RAMP RESPONSE (INPUT U = A T)

$$y(t) = Ka\left(t - \tau + \tau e^{-t/\tau}\right) \;\to\; Ka\,(t-\tau) \;\text{ for } t \gg \tau$$

After the transient dies out, the output follows the ramp but lags it by a time τ. For a sensor ($K = 1$) the reading trails the true value by $a\tau$.

SINUSOIDAL (FREQUENCY) RESPONSE

$$u = A\sin\omega t \;\Rightarrow\; y = \hat{A}\sin(\omega t + \phi), \qquad \frac{\hat{A}}{A} = \frac{K}{\sqrt{1+\omega^2\tau^2}}, \qquad \phi = -\tan^{-1}(\omega\tau)$$

Ultimate periodic response, after the transient has decayed. ω in rad per unit time. This amplitude ratio includes the gain K; dividing by K gives the normalised amplitude ratio. The lag is 45° at $\omega\tau = 1$ and approaches, but never reaches, 90°.

FIRST ORDER PLUS DEAD TIME (FOPDT)

$$G(s) = \frac{K\, e^{-\theta s}}{\tau s + 1}$$

The standard model fitted to a process reaction curve. Dead time adds a phase lag of $\omega\theta$ rad (a phase angle of $-\omega\theta$, with no upper limit) and leaves the amplitude ratio unchanged.

INTEGRATING (PURE CAPACITIVE) PROCESS

$$G(s) = \frac{H(s)}{Q_i(s)} = \frac{1}{As}$$

A tank whose outflow is fixed by a pump: a step in inflow gives a ramp in level that never settles. The process is **not self-regulating**, and the final value theorem does not apply to it ($sY(s)$ has a pole at $s = 0$).

TWO TANKS IN SERIES

$$\text{Non-interacting: } \frac{H_2(s)}{Q_i(s)} = \frac{R_2}{(\tau_1 s + 1)(\tau_2 s + 1)}$$

$$\text{Interacting: } \frac{H_2(s)}{Q_i(s)} = \frac{R_2}{\tau_1\tau_2 s^2 + (\tau_1 + \tau_2 + A_1 R_2)\, s + 1}$$

Linear outflow resistances, $\tau_1 = A_1 R_1$, $\tau_2 = A_2 R_2$. In the non-interacting case tank 1 drains freely into tank 2. In the interacting case the flow between the tanks is $(h_1 - h_2)/R_1$. Both are overdamped, and interaction adds the term $A_1 R_2$, which makes the response more sluggish. The steady-state gain is R_2 in both.

STANDARD SECOND-ORDER TRANSFER FUNCTION

$$G(s) = \frac{K}{\tau^2 s^2 + 2\zeta\tau s + 1} = \frac{K\omega_n^2}{s^2 + 2\zeta\omega_n s + \omega_n^2}, \qquad \omega_n = \frac{1}{\tau}$$

K = gain, ζ = damping ratio, ω_n = natural frequency (rad per unit time), and $\tau = 1/\omega_n$, which is conventionally called the natural period of oscillation (the undamped oscillation actually repeats every $2\pi\tau$). Put the constant term of the denominator equal to 1 before reading off K, τ and ζ.

UNDERDAMPED STEP-RESPONSE CHARACTERISTICS

$$\text{Overshoot} = \frac{A}{B} = \exp\left(\frac{-\pi\zeta}{\sqrt{1-\zeta^2}}\right)$$

$$\text{Decay ratio} = \frac{C}{A} = (\text{overshoot})^2 = \exp\left(\frac{-2\pi\zeta}{\sqrt{1-\zeta^2}}\right)$$

$$\text{Period } T = \frac{2\pi\tau}{\sqrt{1-\zeta^2}} = \frac{2\pi}{\omega_d}, \quad \omega_d = \frac{\sqrt{1-\zeta^2}}{\tau}$$

$$\text{Time of first peak } t_p = \frac{\pi\tau}{\sqrt{1-\zeta^2}}$$

$$\text{Rise time } t_r = \frac{\tau(\pi - \phi)}{\sqrt{1-\zeta^2}}$$

B = final change (KM), A = height of the first peak above the final value, C = height of the second peak above it. The rise time here is the first time the response reaches its final value, with $\phi = \cos^{-1}\zeta$ in radians. Overshoot and decay ratio depend only on ζ, while the period and peak times also need τ. A quarter decay ratio corresponds to $\zeta \approx 0.215$ and an overshoot of 0.5.

SETTLING TIME (APPROXIMATE)

$$t_s \approx \frac{3\tau}{\zeta}\ (\pm 5\%), \qquad t_s \approx \frac{4\tau}{\zeta}\ (\pm 2\%)$$

From the decay envelope $e^{-\zeta t/\tau}$. An estimate for the underdamped case, not an exact result.

SECOND-ORDER FREQUENCY RESPONSE

$$\frac{\hat{A}}{A} = \frac{K}{\sqrt{(1-\omega^2\tau^2)^2 + (2\zeta\omega\tau)^2}}, \qquad \phi = -\tan^{-1}\frac{2\zeta\omega\tau}{1-\omega^2\tau^2}$$

The phase runs from 0 to −180° and is −90° at $\omega\tau = 1$ (for $\omega\tau > 1$, take the angle in the range −90° to −180°). For $\zeta < 1/\sqrt{2}$ the amplitude ratio has a resonant peak at $\omega_r\tau = \sqrt{1-2\zeta^2}$ of height $K/\left(2\zeta\sqrt{1-\zeta^2}\right)$.

BODE-PLOT ASYMPTOTES

$$\text{First order: } AR_N \to 1 \ (\omega\tau \ll 1), \quad AR_N \approx \frac{1}{\omega\tau} \ (\omega\tau \gg 1), \quad \omega_c = \frac{1}{\tau}$$

$$\text{Second order: } AR_N \to 1 \ (\omega\tau \ll 1), \quad AR_N \approx \frac{1}{(\omega\tau)^2} \ (\omega\tau \gg 1)$$

$$\text{Decibels: } AR_{\text{dB}} = 20\log_{10} AR$$

$AR_N = \hat{A}/(KA)$ is the normalised amplitude ratio. On log–log axes the high-frequency asymptote has slope −1 for a first-order system (−20 dB per decade) and −2 for a second-order system (−40 dB per decade). The two first-order asymptotes meet at the corner frequency $\omega_c = 1/\tau$, where the true value is $1/\sqrt{2}$ (about −3 dB) and the phase is −45°. For elements in series, amplitude ratios multiply (their dB values add) and phase angles add.

CONTROLLER LAWS (IDEAL, PARALLEL FORM)

$$\text{P: } p(t) = \bar{p} + K_c e(t), \qquad G_c = K_c$$

$$\text{PI: } p(t) = \bar{p} + K_c\left[e + \frac{1}{\tau_I}\int_0^t e\,dt\right], \qquad G_c = K_c\left(1 + \frac{1}{\tau_I s}\right)$$

$$\text{PID: } p(t) = \bar{p} + K_c\left[e + \frac{1}{\tau_I}\int_0^t e\,dt + \tau_D\frac{de}{dt}\right], \quad G_c = K_c\left(1 + \frac{1}{\tau_I s} + \tau_D s\right)$$

$e = y_{sp} - y_m$. $\bar{p}$ = bias (the output when $e = 0$), K_c = controller gain, τ_I = integral (reset) time, τ_D = derivative time; τ_I and τ_D are in time units. $G_c = P'(s)/E(s)$ in deviation variables. Some controllers are set in repeats per minute $= 1/\tau_I$ (with τ_I in minutes).

PROPORTIONAL BAND

$$PB = \frac{100}{K_c}\ \%$$

For a dimensionless K_c (input and output both as % of span). PB is the % change in the measured variable that moves the output through its full range. A narrow band means a high gain.

P CONTROL OF A FIRST-ORDER PROCESS: GAIN, TIME CONSTANT AND OFFSET

$$\frac{Y}{Y_{sp}} = \frac{K_{OL}}{1 + K_{OL}} \cdot \frac{1}{\tau' s + 1}, \quad \tau' = \frac{\tau}{1 + K_{OL}}, \quad K_{OL} = K_c K_v K_p K_m$$

$$\text{Servo offset} = \frac{M}{1 + K_{OL}}, \qquad |\text{Load offset}| = \frac{|K_d|\,M}{1 + K_{OL}}$$

For $G_p = K_p/(\tau s + 1)$ with $G_v = K_v$ and $G_m = K_m$ pure gains and $K_{OL} > 0$ (a stable loop); the servo expression takes $K_m = 1$. M is the step in set point (servo) or in the disturbance (load, $G_d = K_d/(\tau s + 1)$). The closed loop stays first order, is faster by the factor $1 + K_{OL}$, and has an offset that shrinks, but never vanishes, as K_c increases.

P CONTROL OF A SECOND-ORDER PROCESS

$$\tau' = \frac{\tau}{\sqrt{1 + K_{OL}}}, \qquad \zeta' = \frac{\zeta}{\sqrt{1 + K_{OL}}}, \qquad \text{servo offset} = \frac{M}{1 + K_{OL}}$$

For $G_p = K_p/(\tau^2 s^2 + 2\zeta\tau s + 1)$ with pure-gain valve and sensor, $K_m = 1$ and $K_{OL} > 0$. Raising K_c makes the closed loop faster and less damped (more overshoot). With $\zeta > 0$ and no dead time or extra lags, P control cannot make this loop unstable.

IDEAL AND STATIC FEED-FORWARD CONTROLLERS

$$G_f = -\frac{G_d}{G_t G_v G_p}, \qquad \text{static: } K_f = -\frac{K_d}{K_t K_v K_p}$$

G_t = transmitter on the disturbance. Perfect compensation needs a perfect model. The feed-forward block is outside the feedback loop, so it does not change the characteristic equation or the stability.

STABILITY OF A CUBIC CHARACTERISTIC EQUATION

$$a_0 s^3 + a_1 s^2 + a_2 s + a_3 = 0 \text{ is stable } \iff \text{ all } a_i > 0 \text{ and } a_1 a_2 > a_0 a_3; \qquad \text{at the limit } \omega_u^2 = \frac{a_2}{a_0} = \frac{a_3}{a_1}$$

The Routh test worked out for $n = 3$, for example three first-order lags under P control.

BODE STABILITY CRITERION, GAIN AND PHASE MARGINS

$$\angle G_{OL}(j\omega_{co}) = -180^\circ: \quad \text{stable if } AR_{OL}(\omega_{co}) < 1; \qquad K_u = \frac{1}{AR_{OL}(\omega_{co})\big|_{K_c=1}}, \quad P_u = \frac{2\pi}{\omega_{co}}$$

Applies when the open loop is itself stable and its phase crosses −180° only once (as for lags plus dead time); the K_u expression is for a P controller. ω_{co} = crossover (phase −180°) frequency. Gain margin $GM = 1/AR_{OL}(\omega_{co})$. Phase margin $PM = 180^\circ + \phi$ at the frequency where $AR_{OL} = 1$. Typical design guidelines are GM of 1.7 to 2 and PM of 30° to 45°. For three identical lags, each contributes −60° at crossover, so $\omega_{co}\tau = \sqrt{3}$, each lag has $AR = 1/2$, and $K_u K = 8$ (K = product of the other gains in the loop).

COHEN–COON SETTINGS (FOPDT K, T, Θ)

$$\text{P: } K_c = \frac{1}{K}\frac{\tau}{\theta}\left(1 + \frac{\theta}{3\tau}\right)$$

$$\text{PI: } K_c = \frac{1}{K}\frac{\tau}{\theta}\left(0.9 + \frac{\theta}{12\tau}\right), \quad \tau_I = \theta\,\frac{30 + 3\theta/\tau}{9 + 20\theta/\tau}$$

$$\text{PID: } K_c = \frac{1}{K}\frac{\tau}{\theta}\left(\frac{4}{3} + \frac{\theta}{4\tau}\right)$$

$$\tau_I = \theta\,\frac{32 + 6\theta/\tau}{13 + 8\theta/\tau}, \quad \tau_D = \frac{4\theta}{11 + 2\theta/\tau}$$

Designed, like the Ziegler–Nichols settings, for roughly a quarter decay ratio. Cohen–Coon corrects the Ziegler–Nichols reaction-curve gains with θ/τ terms, so the two methods differ most when dead time is not small compared with τ.

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