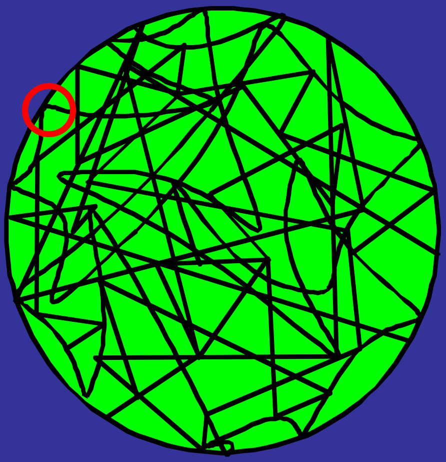
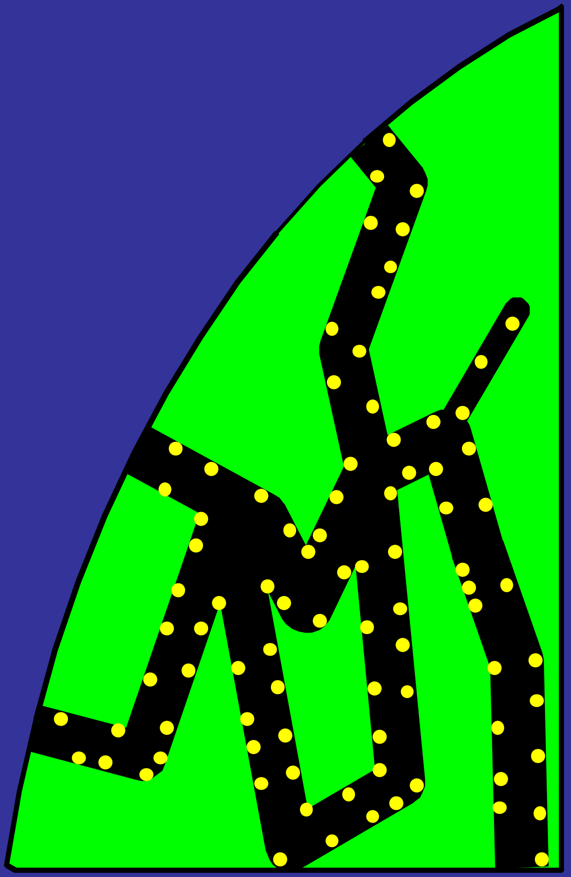
3. Internal Mass Transfer Effects

a. General Derivation

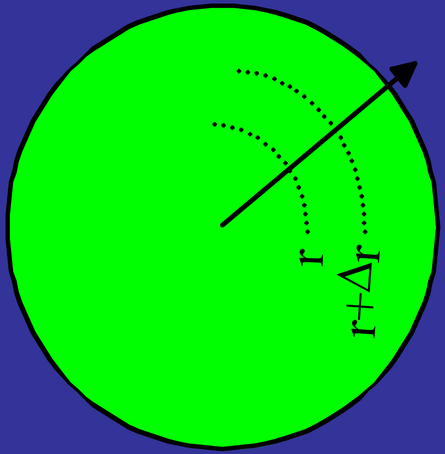
- Enzymes are immobilized to a porous support having large internal surface areas.





Assumptions: Immobilized enzyme is distributed uniformly; reaction involves no change in pH and electrostatic effects are negligible

Substrate (S) material balance on representative shell:



Rate of accum of S = Rate of S in - Rate of S out + Rate of S generation

At steady-state….

Rate of accum of S = Rate of S in - Rate of S out + Rate of S generation

$$0 = (A\Phi_S)|_r - (A\Phi_S)|_{r+\Delta r} \ominus v\cdot V_{SHELL}$$

S is consumed

A = surface area of shell = $4\pi r^2$
v = rate of reaction (moles/time·volume)
V_{SHELL} = volume of shell = $4\pi r^2\Delta r$
Φ_S = flux of S (moles/time·area)

So, $0 = (4\pi r^2\Phi_S)|_r - (4\pi r^2\Phi_S)|_{r+\Delta r} - v\cdot 4\pi r^2\Delta r$

Divide by $4\pi\Delta r$ and take limit as $\Delta r \rightarrow 0$ ….

$$0 = \frac{-d(r^2\boxed{\Phi_S})}{dr} - vr^2$$

Result of material balance

From Fick’s Law:

$$\Phi_S = -cD_{eff}\nabla X_S + X_S\sum_{\text{ALL } i}\Phi_i$$

$S = f(r)$ only

$$\Phi_S = \boxed{-D_{eff}\frac{dS}{dr}}$$

D_{eff} = effective diffusion coefficient

For constant D_{eff}:

$$vr^2 = D_{eff}\frac{d}{dr}\left(r^2\frac{dS}{dr}\right)$$

Note: $$\frac{d}{dr}\left(r^2\frac{dS}{dr}\right) = r^2\frac{d^2S}{dr^2} + 2r\frac{dS}{dr}$$

So, $$\boxed{v = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)}$$

This equation is general, and we now can define the system kinetics

$$D_{eff} = D_S \frac{\varepsilon_P}{\tau} H$$

D_S = Diffusion coefficient of S in bulk fluid

ε_P = Particle porosity
(some of a particle's cross section is occupied by solid matrix and hence is not available for diffusion)

τ = Tortuosity (range is 1.4 – 7)
(pore network is complex and entangled so diffusion occurs only in certain allowed directions)

H = Hindrance factor
(pores have small diameter – same scale as size of molecules – and this hinders diffusion)

Renkin Equation (good for $\gamma<0.4$)

$$H = (1-\gamma)^2(1-2.104\gamma+2.09\gamma^3-0.95\gamma^5)$$

γ = solute radius/pore radius

[E. M. Renkin, *J. Gen. Physiol.* 38 (1954) 225-243]

Mass transfer rates often depend on surface chemistry and charge! Can be quite complicated!

b. Michaelis-Menten Kinetics

If local reaction kinetics follows Michaelis-Menten kinetics, then:

$$v = \frac{V_{MAX}''S}{K_M + S}$$

I'll discuss later what happens if reaction follows first order kinetics

V_{MAX}'' = max. reaction rate per unit <u>volume</u> support

So,

$$\frac{V_{MAX}''S}{K_M + S} = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)$$

$$\frac{V_{MAX}''S}{K_M + S} = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)$$

Boundary Conditions:

A) $\frac{dS}{dr} = 0$ @ $r = 0$

No concentration gradient at center of catalyst

B) $S = S_{SURF}$ @ $r = R$

Concentration at surface of particle is known

Assign Dimensionless Variables:

$x = \frac{S}{S_{SURF}}$ Fractional concentration ($\bar{S}$ in book*)

$\beta = \frac{S_{SURF}}{K_M}$ Fractional Michaelis Constant ($1/\beta$ in book*)

$\xi = \frac{r}{R}$ Fractional radius ($\bar{r}$ in book*)

* Shuler, Kargi, Bioprocess Engineering, 1st edition, p. 87

Make Differential Equation Dimensionless:

$$\frac{V_{MAX}''S}{K_M + S} = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)$$

$$\frac{V_{MAX}''xS_{SURF}}{S_{SURF}/\beta + xS_{SURF}} = D_{eff}\left(\frac{S_{SURF}\,d^2x}{R^2\,d\xi^2} + \frac{2}{R\xi}\frac{S_{SURF}\,dx}{R\,d\xi}\right)$$

$$\frac{\beta V_{MAX}''x}{1 + \beta x} = D_{eff}\frac{S_{SURF}}{R^2}\left(\frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}\right)$$

$$\frac{x}{1 + \beta x} = \frac{D_{eff}S_{SURF}}{R^2\,\beta\,V_{MAX}''}\left(\frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}\right)$$

$$\frac{9x}{1+\beta x} = \frac{9D_{eff}S_{SURF}}{R^2\,\beta\,V_{MAX}''}\left(\frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}\right)$$

$$\frac{9x}{1+\beta x} = \frac{9D_{eff}K_M}{R^2\,V_{MAX}''}\left(\frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}\right)$$

Let $\phi^2 = \dfrac{R^2\,V_{MAX}''}{9D_{eff}K_M}$

Or $\boxed{\phi = \dfrac{R}{3}\sqrt{\dfrac{V_{MAX}''}{D_{eff}K_M}}}$

<u>Dimensionless Group</u>
“Thiele Modulus” for
Michaelis-Menten
Kinetics

Equation Becomes (Note book is slightly different, p. 87):

$$\phi^2 \frac{9x}{1 + \beta x} = \frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}$$

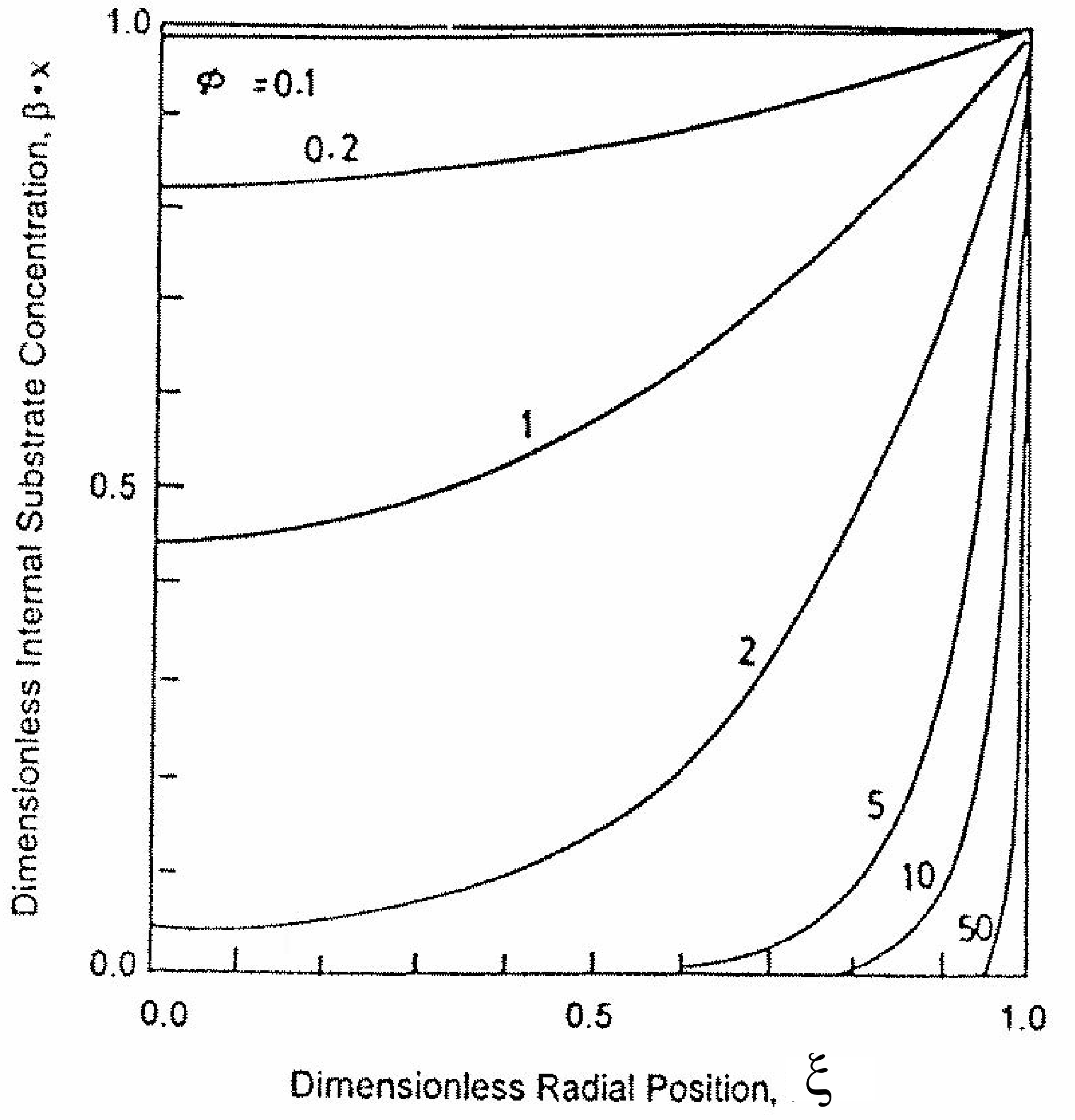
Boundary Conditions Become:

A) $\frac{dx}{d\xi} = 0$ @ $\xi = 0$

B) $x = 1$ @ $\xi = 1$

Solution of this Differential Equation (numerically) yields the concentration of x (or real variable S) as a function of ξ (or r)

For example, for β=1:



Blanch, Clark, Biochemical Engineering, (1997) p. 131

At steady-state:

Rate of substrate consumed inside sphere	=	Rate of substrate entering sphere

$$v_{ACTUAL}V_{SPHERE} = A_{SPHERE}\,(-\Phi_S|_{r=R})$$

v_{ACTUAL} = Actual, observed reaction rate (moles/volume·time)

V_{SPHERE} = Volume of sphere

A_{SPHERE} = Surface area of sphere

$-\Phi_S|_{r=R}$ = Flux of S at surface (Note: Φ_S is defined as flux in the r direction; we want flux <u>into</u> sphere)

Recall:

$$\Phi_S = -D_{eff}\frac{dS}{dr}$$

Or:

$$\Phi_S\Big|_{r=R} = -D_{eff}\frac{dS}{dr}\Big|_{r=R}$$

So:

$$v_{ACTUAL} = \frac{A_{SPHERE}}{V_{SPHERE}} D_{eff}\frac{dS}{dr}\Big|_{r=R}$$

← The actual moles S reacted per volume sphere per time

$$v_{MAX} = \frac{V_{MAX}''S_{SURF}}{K_M + S_{SURF}}$$

← The maximum reaction rate, assuming $S=S_{SURF}$ throughout sphere

Internal Effectiveness Factor = η_I

$$\eta_I = \frac{\text{Observed Reaction Rate}}{\text{Maximum Reaction Rate}}$$

$$\eta_I = \frac{v_{ACTUAL}}{v_{MAX}}$$

$$\eta_I = \frac{A_{SPHERE}}{V_{SPHERE}} \; \frac{\left(D_{eff} \left. \frac{dS}{dr} \right|_{r=R} \right)}{V_{MAX}'' S_{SURF} / (K_M + S_{SURF})}$$

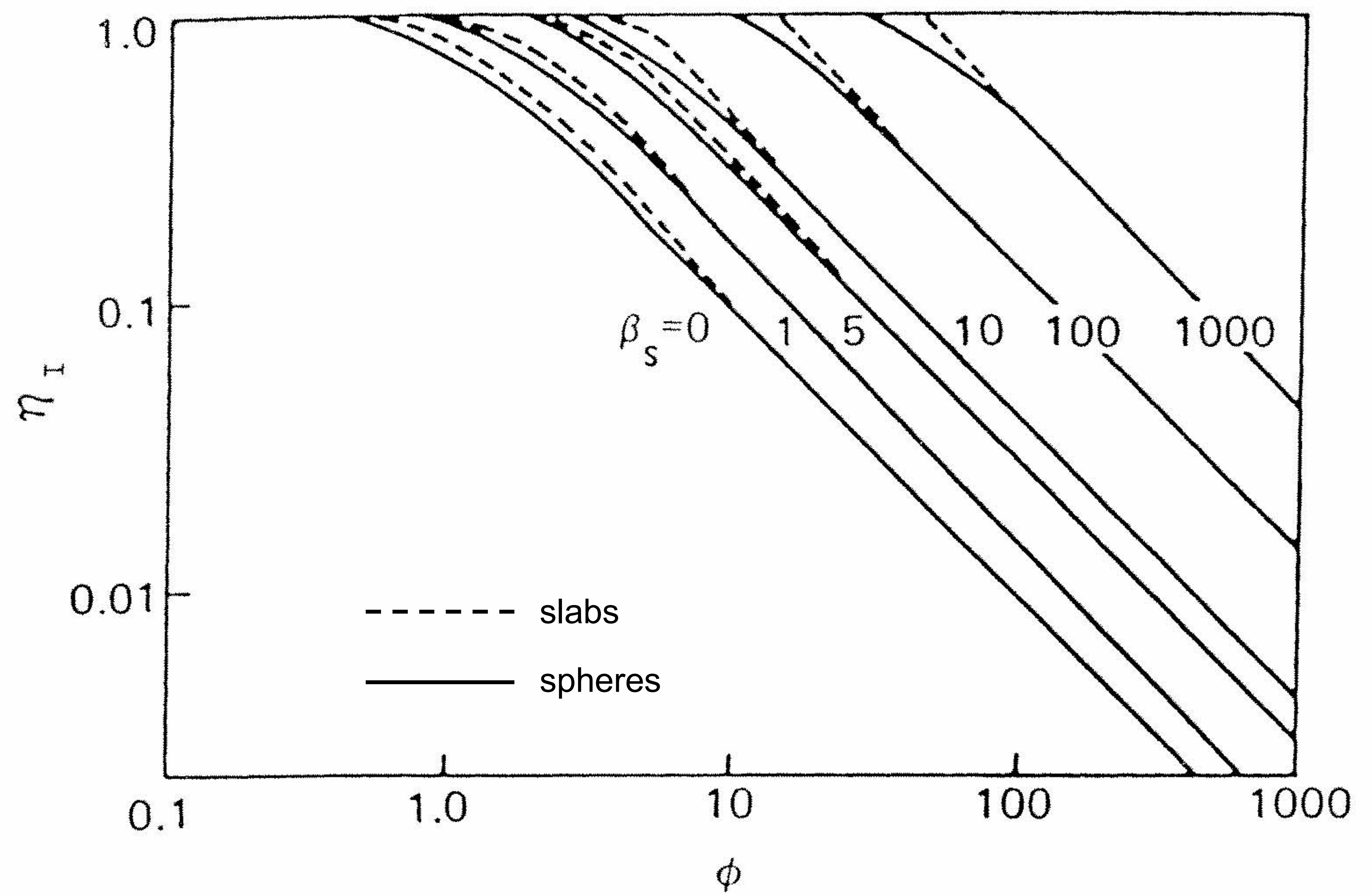
$$\eta_I = \frac{A_{SPHERE}}{V_{SPHERE}} \frac{\left(D_{eff} \left.\frac{dS}{dr}\right|_{r=R}\right)}{V_{MAX}''S_{SURF}/(K_M + S_{SURF})}$$

$$\frac{A_{SPHERE}}{V_{SPHERE}} = \frac{3}{R}$$

Using dimensionless variables, this equation becomes:

$$\eta_I = \frac{\left.\frac{dx}{d\xi}\right|_{\xi=1}}{3\,\phi^2\,[1/(1+\beta)]} = f(\phi, \beta)$$

The result is….



Blanch, Clark, Biochemical Engineering, (1997) p. 132

Special Cases

As $\beta \rightarrow 0$ ($S_{SURF} << K_M$) the effectiveness factor approaches…

$$\eta_I = \frac{1}{\phi}\left[\frac{1}{\tanh(3\phi)} - \frac{1}{3\phi}\right]$$

As $\phi \rightarrow 0$ (V_{MAX}'' small, D_{eff} large) …

(slow reaction, fast diffusion)

$$\eta_I = 1$$

In this case, the substrate diffuses far into the pore structure before being consumed. Concentration of substrate is nearly uniform throughout catalyst

As $\phi \rightarrow \infty$ (V_{MAX}'' large, D_{eff} small) …

(fast reaction, slow diffusion)

In this case, the substrate is consumed before it diffuses very far. Reaction is limited to a thin region near periphery of particle.

η_I is greater for greater values of β (when S_{SURF} is higher relative to K_M).

η_I is close to 1 if S_{SURF} is really large, in which case reaction rate is close to V_{MAX}'' everywhere in particle.

Difficulty…

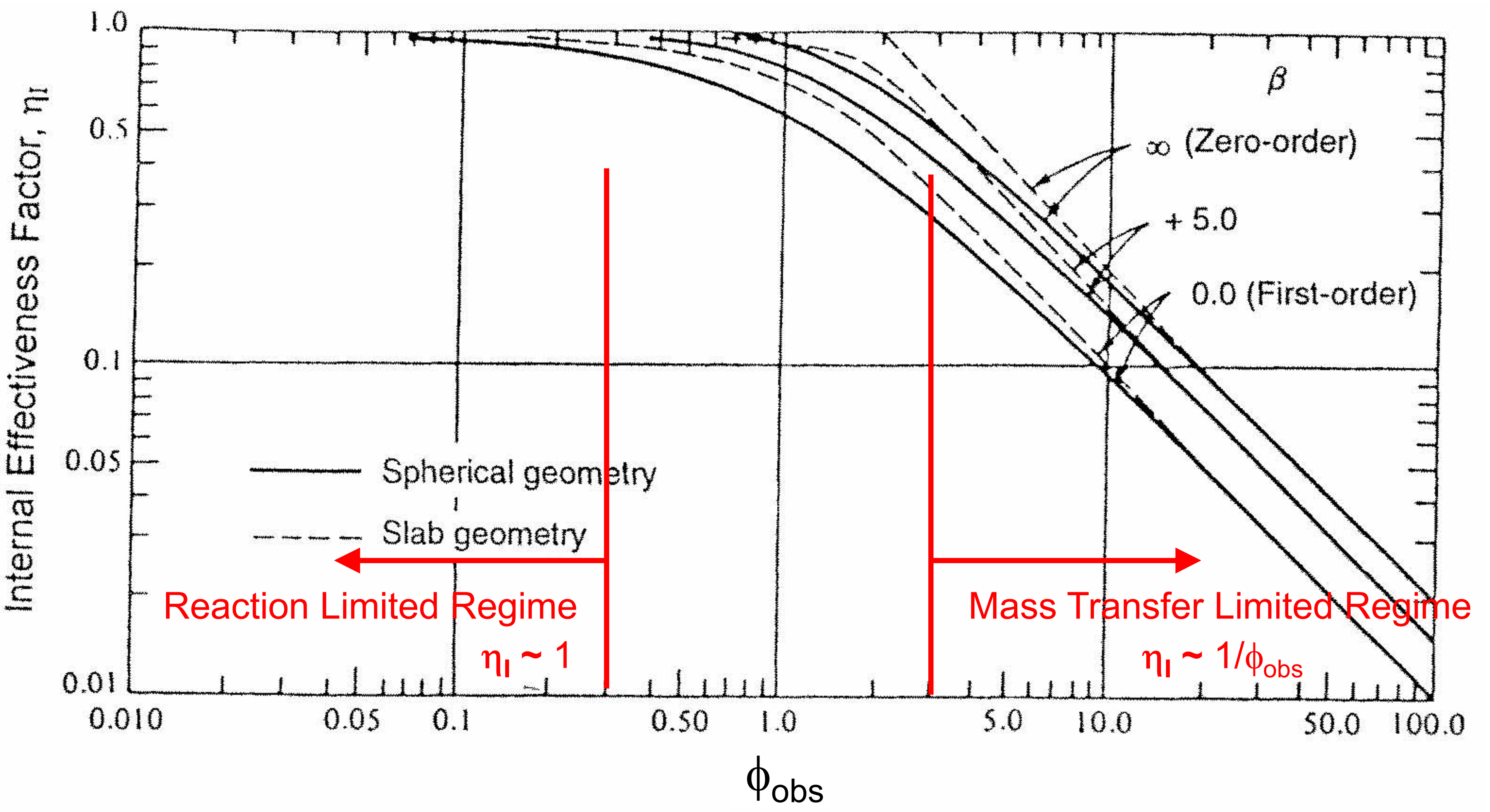
ϕ and β must be known to calculate η_I !

However, in order to calculate ϕ and β we must know V_{MAX}'' and K_M. These parameters are not readily obtained from a diffusion-disguised reaction. Also, these values for an immobilized enzyme may be different than the values for the free enzyme.

We therefore define an observable modulus, ϕ_{OBS}:

Let $$\boxed{\phi_{obs} = \frac{R^2 V_{obs}}{9 D_{eff} S_{SURF}}}$$

notice that ϕ_{obs} is not squared



Reaction Limited Regime

$\eta_I \sim 1$

Mass Transfer Limited Regime

$\eta_I \sim 1/\phi_{obs}$

Note that ϕ_{obs} is not as strong a function of β as ϕ

Blanch, Clark, Biochemical Engineering, (1997) p. 135

Example:

Chymotrypsin is immobilized in a spherical porous support. In preliminary studies of the immobilized enzyme's activity, reaction rates were measured using the substrate N-acetyl-L-tyrosine ethyl ether (ATEE):

Enzyme Loading: 1.27 mg/g particle
S_{SURF}: 1 mmol ATEE/L
D_{eff}: 3.8×10^{-6} cm^2/s
R: 60 μm
ρ_{PART}: 0.41 g particle/cm^3 particle
V_{obs}: 498 μmol ATEE/mg enzyme·min

1) Find η_I
2) What particle size is necessary to ensure kinetic properties of system will be studied under reaction-limited conditions?

1) Find η_I

V_{obs} = (498 μmol ATEE/mgE·min)(1.27 mgE/g Part)(0.41 g Part/cm^3 Part)

V_{obs} = 259.3 μmol ATEE/cm^3 Part·min

S_{SURF} = (1 mmol/L)(1000 μmol/mmol)(L/1000 cm^3)

S_{SURF} = 1 μmol/cm^3

D_{eff} = (3.8 × 10^{-6} cm^2/s)(60 s/min)

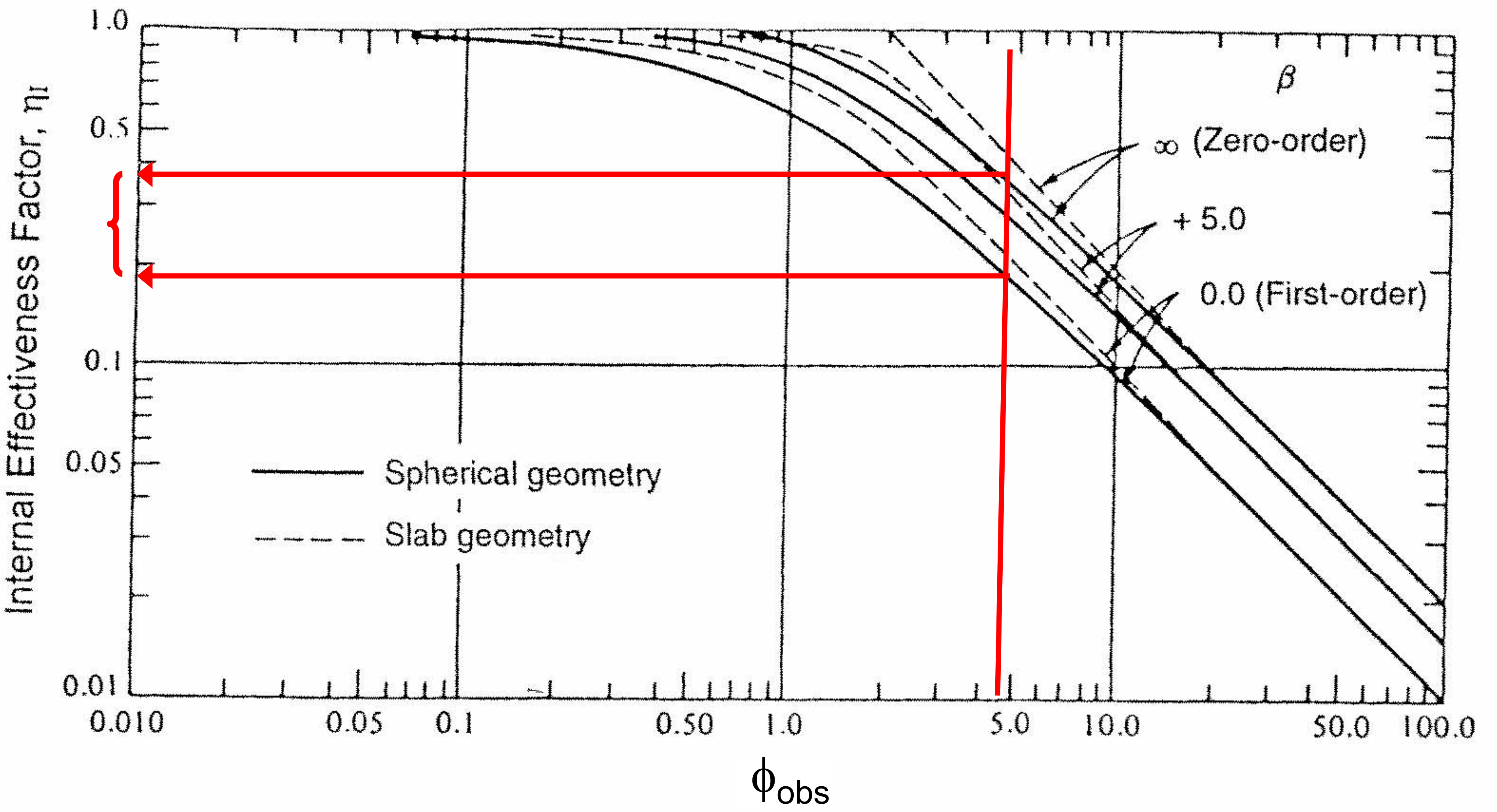
D_{eff} = 2.28 × 10^{-4} cm^2/min

$$\phi_{obs} = \frac{R^2 V_{obs}}{9 D_{eff} S_{SURF}}$$

$$\phi_{obs} = \frac{(60 \times 10^{-4}\ \mathrm{cm})^2 (259.3\ \mu\mathrm{mol\ ATEE/cm^3\ Part \cdot min})}{9(2.28 \times 10^{-4}\ \mathrm{cm^2/min})(1\ \mu\mathrm{mol/cm^3})}$$

$\phi_{obs} = 4.5$ Must be dimensionless!

Fairly large value of ϕ_{obs} indicates reaction rate is diffusion limited. β is unknown. Also, since the system is diffusion-limited, we cannot find K_M in the conventional manner. However, we know that $0 \le \beta \le \infty$, so we can obtain a range for β from figure.



We know that ϕ_{obs} is 4.5

So, we know that $0.17 \leq \eta_I \leq 0.35$.

Soluble enzyme has $K_M = 0.73$ mM; $\beta = 1.4$; $\eta_I = 0.29$.

2) What particle size is necessary to ensure kinetic properties of system will be studied under reaction-limited conditions?

Effectiveness factor η_l is ~1 when $\phi_{\mathbf{obs}} < 0.3$…

$$\phi_{obs} = \frac{R^2 V_{obs}}{9 D_{eff} S_{SURF}}$$

$$0.3 = \frac{R^2 (259.3\ \mu\text{mol ATEE/cm}^3\ \text{Part} \cdot \text{min})}{9(2.28 \times 10^{-4}\ \text{cm}^2/\text{min})(1\ \mu\text{mol/cm}^3)}$$

$$R = 0.00154\ \text{cm} = 15.4\ \mu\text{m}$$

c. First Order Kinetics

If local reaction kinetics follows first order kinetics, then:

$v = kS$

Remember we included the negative sign in the original material balance

So,

$$kS = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)$$

$$kS = D_{eff}\left(\frac{d^2S}{dr^2} + \frac{2}{r}\frac{dS}{dr}\right)$$

Same Boundary Conditions:

A) $\frac{dS}{dr} = 0$ @ $r = 0$

No concentration gradient at center of catalyst

B) $S = S_{SURF}$ @ $r = R$

Concentration at surface of particle is known

Same Dimensionless Variables:

$$x = \frac{S}{S_{SURF}}$$ Fractional concentration

$$\xi = \frac{r}{R}$$ Fractional radius

(Don’t define a β since we don’t have a two-parameter kinetic equation)

Thiele Modulus:

$$\phi^2 = \frac{R^2 k}{9D_{eff}}$$

$$\boxed{\phi = \frac{R}{3}\sqrt{\frac{k}{D_{eff}}}}$$

Differential Equation Becomes:

$$9\phi^2 x = \frac{d^2x}{d\xi^2} + \frac{2}{\xi}\frac{dx}{d\xi}$$

And the solution is:

$$\boxed{x = \frac{\sinh(3\phi\xi)}{\xi \sinh(3\phi)}}$$

$$S = f(\xi, \phi)$$

Note at center ($\xi = 0$):

$$x = \frac{\sinh(0)}{0 \sinh(3\phi)}$$

$$x = \frac{3\phi}{\sinh(3\phi)}$$

And from definition of Internal Effectiveness factor:

$$\eta_I = \frac{v_{ACTUAL}}{v_{MAX}}$$

$$\eta_I = \frac{A_{SPHERE}}{V_{SPHERE}} \frac{\left(D_{eff} \left. \frac{dS}{dr} \right|_{r=R} \right)}{kS_{SURF}}$$

$$\boxed{\eta_I = \frac{1}{\phi}\left[\frac{1}{\tanh(3\phi)} - \frac{1}{3\phi}\right]}$$

Problem

S → B by a first order reaction in a porous catalyst. The following data are available:

S_{SURF}: 2 mmol/L
D_{eff}: 5.1 ×10^{-6} cm^2/s
R: 100 μm
k: 125 /min

1) Find S at R = 50 μm
2) Find η_I

$$\phi = \frac{R}{3}\sqrt{\frac{k}{D_{eff}}}$$

$$\phi = \frac{100 \times 10^{-4}\ \text{cm}}{3}\sqrt{\frac{(125\ /\text{min})(\text{min}/60\ \text{s})}{5.1 \times 10^{-6}\ \text{cm}^2/\text{s}}}$$

$$\phi = 2.1$$

1) Find S at R = 50 μm

$$\xi = \frac{r}{R}$$

$$\xi = \frac{50}{100} = 0.5$$

$$x = \frac{\sinh(3\phi\xi)}{\xi \sinh(3\phi)}$$

$$x = \frac{\sinh(3 \times 2.1 \times 0.5)}{0.5 \sinh(3 \times 2.1)} = 0.086$$

$S = xS_{SURF} = (0.086)^*(2 \text{ mmol/L}) = \underline{0.172 \text{ mmol/L}}$

2) Find η_I

$$\eta_I = \frac{1}{\phi}\left[\frac{1}{\tanh(3\phi)} - \frac{1}{3\phi}\right]$$

$$\eta_I = \frac{1}{2.1}\left[\frac{1}{\tanh(3 \times 2.1)} - \frac{1}{3 \times 2.1}\right]$$

$\underline{\eta_I = 0.40}$

4. Simultaneous External & Internal Mass Transfer Resistance

A complex problem

S_{SURF} is not equal to S_{BULK}

Biot Number is key dimensionless group:

$$Bi = \frac{k_S R}{D_{eff}} = \frac{\text{External Mass Transfer Rate}}{\text{Internal Diffusion Rate}}$$

k_S is the mass transfer coefficient

If Bi>100 then external resistance is negligible