Michaelis Menten

$$S + E \underset{k_1'}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} P + E$$

$S + E \underset{k_1'}{\overset{k_1}{\rightleftharpoons}} C \quad ; \quad C \xrightarrow{k_2} P + E$

$$\frac{d[S]}{dt} = -k_1 [S][E] + k_1' [C]$$

$$\frac{d[E]}{dt} = -k_1 [S][E] + k_1' [C] + k_2 [C]$$

$$\frac{d[C]}{dt} = k_1 [S][E] - k_1' [C] - k_2 [C]$$

$$\Rightarrow \frac{d}{dt}\left([E] + [C]\right) = 0$$

$$\underbrace{[E] + [C]}_{\text{const}} = e_0$$

$$\frac{d[P]}{dt} = k_2 [C]$$

$$V = \frac{d[P]}{dt}$$

2)
$$\begin{cases} \dfrac{d[S]}{dt} = -k_1 [S](e_0 - [C]) + k'_1 [C] \\ \dfrac{d[C]}{dt} = k_1 [S](e_0 - [C]) - (k'_1 + k_2)[C] \end{cases}$$

- Aprox cuasi estacionaria -
- Adimensionalización

$\sigma = \dfrac{[S]}{S_0}$ con $S_0 = [S](t=0)$; $\dfrac{[C]}{e_0} = x$; $\tau = k_1 e_0 t$ $\uparrow$ tiempo adim

$$\frac{d\sigma}{d\tau} = \frac{d[S]/S_0}{d(k_1 e_0 t)} = -\frac{k_1}{k_1} \frac{[S]}{S_0} \frac{(e_0 - [C])}{e_0} + \frac{k'_1}{k_1 S_0} \frac{[C]}{e_0}$$

$$\frac{df}{dt} = \frac{df}{d\tau} \frac{d\tau}{dt} = k_1 e_0 \frac{df}{d\tau} \Rightarrow \frac{df}{d\tau} = \frac{1}{k_1 e_0} \frac{df}{dt} =$$

$$\frac{d\sigma}{d\tau} = -\frac{\cancel{k_1}}{\cancel{k_1}} \underbrace{\frac{[S]}{S_0}}_{\sigma} \underbrace{\left(\frac{e_0 - [c]}{e_0}\right)}_{=(1-x)} + \frac{k'_1}{k_1 S_0} \underbrace{\frac{[c]}{e_0}}_{x}$$

$$\frac{dx}{d\tau} = \frac{d\,[c]/e_0}{d(k_1 e_0 t)} = S_0 \frac{\cancel{k_1} [S]}{\cancel{k_1} e_0 S_0} \underbrace{\left(\frac{e_0 - [c]}{e_0}\right)}_{=\sigma(1-x)} - S_0 \frac{(k'_1 + k_2)}{k_1 e_0 S_0} \frac{[c]}{e_0}$$

$$\frac{dx}{d\tau} = \frac{S_0}{e_0} \sigma (1-x) - \frac{S_0}{e_0} \cdot \frac{(k'_1 + k_2)}{k_1 S_0} x$$

$$\frac{d\sigma}{d\tau} = -\sigma(1-x) + \frac{k'_1}{k_1 S_0} x$$

$e_0 \ll S_0$

$\frac{e_0}{S_0} = \epsilon \ll 1$

$$S + E \underset{k'_1}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2}$$

$$\frac{d\sigma}{d\tau} = -\sigma(1-x) + \frac{k'_1}{k_1 S_0} x$$

$$\epsilon \frac{dx}{d\tau} = \sigma(1-x) - \frac{k'_1 + k_2}{k_1 S_0} x$$

$$\left|\frac{dx}{d\tau}\right| \sim \frac{1}{\epsilon}\left|\frac{d\sigma}{d\tau}\right| \qquad \epsilon \ll 1 \Rightarrow$$ x varía muy rápido comparado con σ

$\sigma \cong$ constante en la escala de variación de x

$$\frac{dx}{d\tau} = \frac{1}{\epsilon}\left[\sigma - \left(\sigma + \frac{k'_1 + k_2}{k_1 S_0}\right) x\right]$$

$$\frac{dx}{d\tau} + \frac{1}{\epsilon}\left(\sigma + \frac{k'_1 + k_2}{k_1 S_0}\right) x = \sigma / \epsilon$$

$$\frac{dx}{d\tau} + \frac{1}{\epsilon}\left(\sigma + \frac{k_1' + k_2}{k_1 S_0}\right)x = 0$$

$$\rightarrow \quad x = A^{\lambda\tau} \rightarrow \quad \lambda + \frac{1}{\epsilon}\left(\sigma + \frac{k_1' + k_2}{k_1 S_0}\right) = 0$$

$$\Rightarrow \lambda = -\frac{1}{\epsilon}\left(\sigma + \frac{k_1' + k_2}{k_1 S_0}\right)$$

sol + gral

$$x = A e^{\lambda\tau} + x_p$$

$$\frac{dx}{d\tau} + \frac{1}{\epsilon}\left(\sigma + \frac{k_1' + k_2}{k_1 S_0}\right)x = \frac{\sigma}{\epsilon}$$

$$\frac{1}{\cancel{\epsilon}}\left(\sigma + \frac{k_1' + k_2}{k_1 S_0}\right)x_p = \sigma/\cancel{\epsilon}$$

$$x_p = \frac{\sigma}{\sigma + \frac{k'_1 + k_2}{k_1 S_0}}$$

$$x = A e^{-\frac{1}{\epsilon}\left(\sigma + \frac{k'_1 + k_2}{k_1 S_0}\right)\tau} + \frac{\sigma}{\sigma + \frac{k'_1 + k_2}{k_1 S_0}}$$

Para $\tau \sim (2-3)\,\epsilon$

$$x \simeq \frac{\sigma}{\sigma + \frac{k'_1 + k_2}{k_1 S_0}}$$

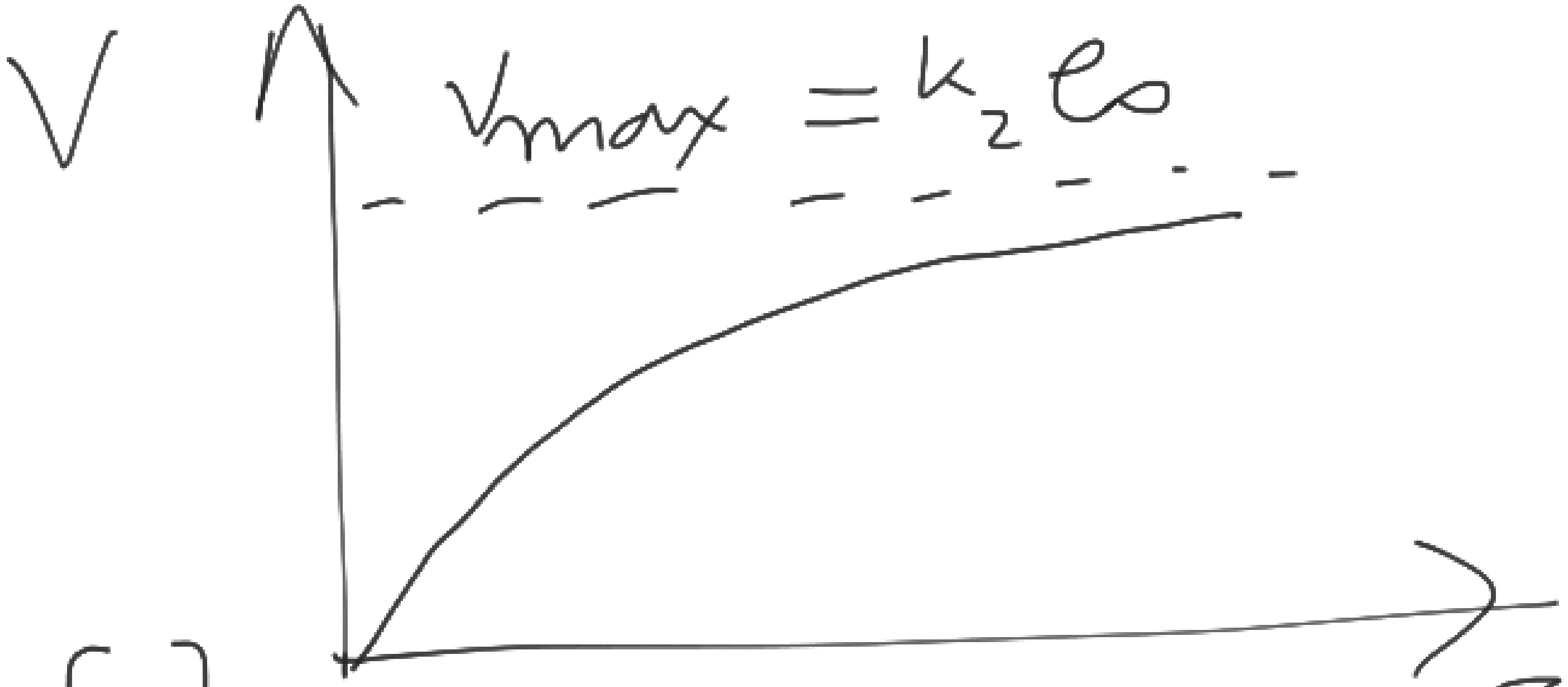
$$\epsilon \frac{dx}{d\tau} = \sigma - x\left(\sigma + \frac{k'_1 + k_2}{k_1 S_0}\right) \cong 0$$

$\Rightarrow$ [illegible] $\quad x = \dfrac{\sigma}{\sigma + \dfrac{k'_1 + k_2}{k_1 S_0}}$

$$V = k_2 [C] = d[P]/dt$$

$$x = \frac{[C]}{e_0} \Rightarrow [C] = e_0 x \Rightarrow$$

$$V = k_2 e_0 \frac{\sigma}{\sigma + \dfrac{k'_1 + k_2}{k_1 S_0}} = k_2 e_0 \frac{[S]}{[S] + \dfrac{k'_1 + k_2}{k_1}}$$



$$k_2 e_0 \frac{[S]}{[S] + \frac{k'_1 + k_2}{k_1}}$$

$$e_0 = [E] + [C]$$

$$S + E \rightleftharpoons C \xrightarrow{k_2} P + E \; ; \quad x \simeq \frac{\sigma}{\sigma + \frac{k'_1 + k_2}{k_1 s_0}}$$

$$\frac{d\sigma}{d\tau} = -\sigma + x\left(\frac{k'_1}{k_1 s_0} + \sigma\right) = -\sigma + \frac{\sigma}{\sigma + \frac{k'_1 + k_2}{k_1 s_0}} \cdot \left(\frac{k'_1}{k_1 s_0} + \sigma\right)$$

$$S + E \underset{k'_1}{\overset{k_1}{\rightleftharpoons}} C \xrightarrow{k_2} P + E$$

$$k_1[S][E] \cong k'_1[C]$$

$$e_0 = [E] + [C] \Rightarrow k_1[S](e_0 - [C]) = k'_1[C]$$

$$\Rightarrow e_0 k_1 [S] = (k_1[S] + k'_1)[C]$$

$$[C] = \frac{\cancel{k_1}\, e_0 [S]}{\cancel{k_1}([S] + k'_1/k_1)}$$

Aprox wanted

$$[C] = \frac{e_0[S]}{[S] + \frac{k'_1 + k_2}{k_1}}$$

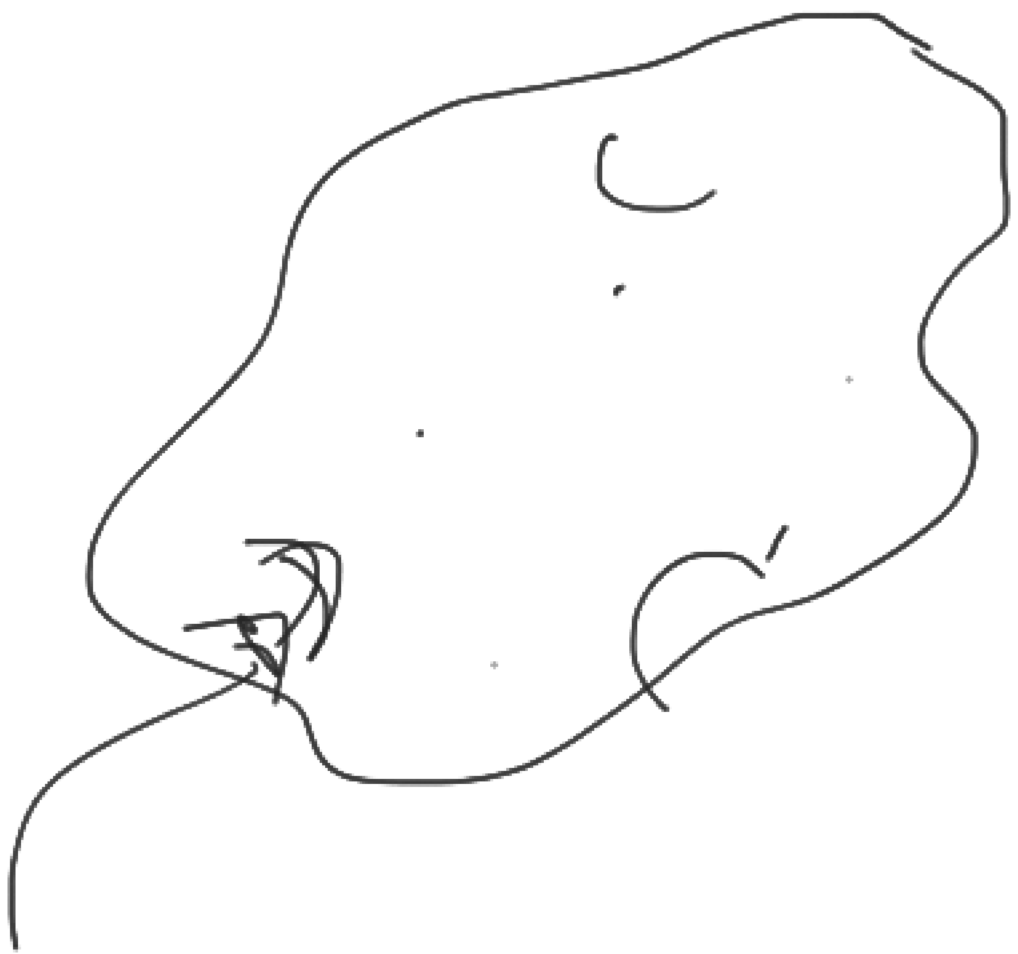
$$V = \frac{\overset{V_{max}}{k_2 e_0}\,[S]}{[S] + \frac{k'_1 + k_2}{k_1}} \; ; \; V_{max} = k_2 e_0$$

$$\frac{V_{max}}{V} = 1 + \frac{k'_1 + k_2}{k_1 [S]} \rightarrow \frac{1}{V} \text{ vs } \frac{1}{[S]}$$

$\frac{1}{V}$

$$\frac{1}{V} = \frac{1}{V_{max}} + \frac{k_1}{k'_1 + k_2} \cdot \frac{1}{V_{max}[S]}$$

$\frac{1}{[S]}$



Enzimas moléculas muy grandes

Tienen muchos sitios delgados y pueden sufrir cambios conformacionales

La actividad enzimática puede ser activada o inhibida por distintos factores

Algunos modelos de inhibición enzimática.

competición

Inhibición por competencia.
Molécula de un inhibidor que compite con el sustrato por el mismo sitio de unión

$$S + E \underset{k_1'}{\overset{k_1}{\rightleftharpoons}} C_1 \xrightarrow{k_2} P + E$$

$$I + E \underset{k_3'}{\overset{k_3}{\rightleftharpoons}} C_2$$

$$\frac{d[I]}{dt} = -k_3[I][E] + k_3'[C_2]$$

$$\frac{d[S]}{dt} = -k_1[S][E] + k_1'[C_1]$$

$$\frac{d[C_1]}{dt} = k_1[S][E] - k_1'[C_1] - k_2[C_1]$$

$$d[C_2]/dt = k_3[I][E] - k_3'[C_2]$$

$$\frac{d[E]}{dt} = -k_1[S][E] + k_1'[C_1] + k_2[C_1] - k_3[I][E] + k_3'[C_2]$$

$$\frac{d}{dt}([E] + [C_1] + [C_2]) = 0 \rightarrow e_0 = [E] + [C_1] + [C_2]$$

$$[E] = e_0 - [C_1] - [C_2] \qquad S + E \xrightarrow{k_1} C_1 \; ; \; I + E \xrightarrow{k_3} C_2$$

Adimensionalización $\sigma = \frac{[S]}{S_0}$; $x_1 = \frac{[C_1]}{e_0}$, $x_2 = \frac{[C_2]}{e_0}$, $\tau = k_1 e_0 t$

$i = [I]/i_0$

$$\frac{d[S]/S_0}{d(t k_1 e_0)} = -\frac{k_1}{k_1}\frac{[S]}{S_0}\frac{\left(e_0 - [C_1] - [C_2]\right)}{e_0} + \frac{k'_1}{S_0 k_1}\frac{[C_1]}{e_0} =$$

$$= -\sigma\,(1 - x_1 - x_2) + \frac{k'_1}{k_1 S_0}\,x_1$$

$$\frac{d[C_2]/e_0}{d(t k_1 e_0)} = \frac{S_0 k_3 i_0}{S_0 k_1 e_0}\frac{[I]}{i_0}\frac{\left(e_0 - [C_1] - [C_2]\right)}{e_0} - \frac{k'_3}{k_1 e_0 S_0}\frac{[C_2]}{e_0} S_0$$

$$\frac{dx_2}{d\tau} = \underbrace{\frac{S_0}{e_0}}_{= 1/\epsilon} \cdot \underbrace{\frac{k_3 i_0}{k_1 S_0}}_{\sim 1}\, i\,(1 - x_1 - x_2) - \underbrace{\frac{S_0}{e_0}}_{= 1/\epsilon}\frac{k'_3}{k_1 S_0}\,x_2$$

$$\frac{dx_2}{d\tau} = \frac{1}{\epsilon}\underbrace{\left(- \cdots \right)}_{\cong 0}$$

$$\frac{dx_1}{d\tau} = \frac{1}{\epsilon}\underbrace{\left(\cdots \right)}_{\cong 0}$$

Aprox warunku

$$\epsilon_1 = \frac{e_0}{s_0} \; ; \quad \epsilon_2 = \frac{e_0}{i_0}$$

$$0 \cong \frac{1}{\epsilon_1}\sigma(1 - x_1 - x_2) - \frac{k'_1}{k_1 s_0}\frac{1}{\epsilon_1}x_1 - \frac{k_2}{k_1 s_0}\frac{x_1}{\epsilon_1}$$

$$0 \cong \frac{k_3}{k_1}\frac{1}{\epsilon_2}\, i\,(1 - x_1 - x_2) - \frac{k'_3}{k_1 i_0}\frac{1}{\epsilon_2}x_2$$

obtener x_1 y x_2 como funciones de σ y de i y pasando a

$[C_1] = x_1 e_0$; $[C_2] = x_2 e_0$

$$[C_1] = \frac{(k'_3/k_3)\, e_0 [S]}{\frac{k'_1+k_2}{k_1}[I] + \frac{k'_3}{k_3}[S] + \frac{k'_1+k_2}{k_1} \cdot \frac{k'_3}{k_3}} \quad ; \quad \frac{d[P]}{dt} = k_2 [C_1]$$

$$[C_2] = \frac{k'_3/k_3\, e_0 [I]}{- - - - -}$$

$V_{max} = k_2 e_0$

Modelo de inhibición por alosterismo

$$\begin{array}{ccccc} E & \underset{k'_1}{\overset{k_1[S]}{\rightleftharpoons}} & ES & \xrightarrow{k_2} & E+P \\ k_3[I] \downarrow \uparrow k'_3 & & k_3[I] \downarrow \uparrow k'_3 & & \\ EI & \underset{k'_1}{\overset{k_1[S]}{\rightleftharpoons}} & EIS & & \end{array}$$

$[E]+[ES]+[EI]+[EIS] = const = e_0$

$$E+I \underset{k'_3}{\overset{k_3}{\rightleftharpoons}} EI$$

$$E+S \underset{k'_1}{\overset{k_1}{\rightleftharpoons}} ES$$

$k_1[S][E] = k'_1[ES]$

$k_3[I][ES] = k'_3[EIS]$

$k_1[S][EI] = k'_1[EIS]$

$k_3[I][E] = k'_3[EI]$

$$[E] = e_0 - \left([EI] + [ES] + [EIS]\right)$$

$$k_1 [S][E] = k'_1 [ES]$$

$$k'_3 [EIS] = k_3 [I][ES]$$

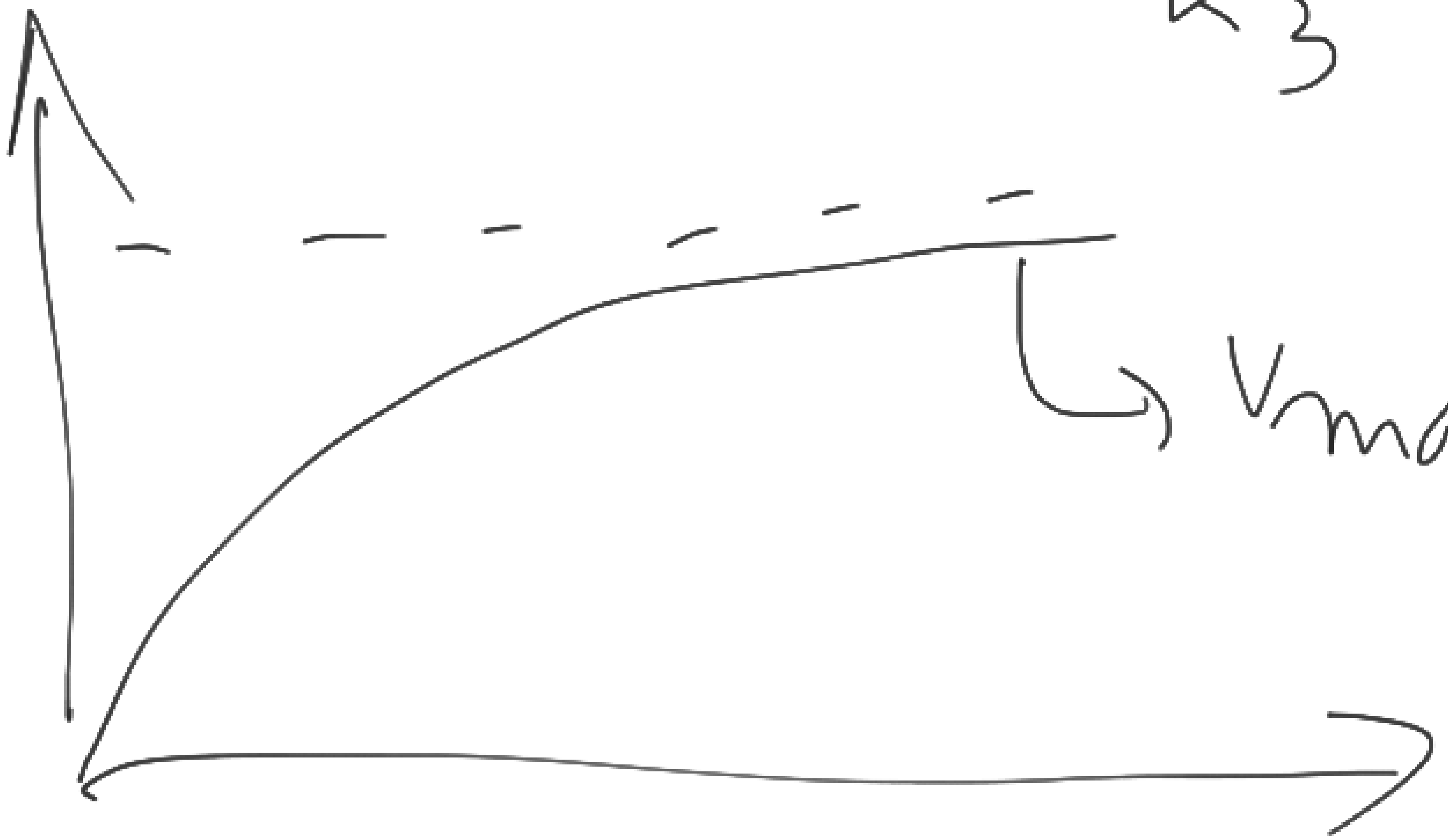
$$k_1 [S][EI] = k'_1 \frac{k_3 [I]}{k'_3} [ES]$$

$$e_0 = [ES] + [E] + [EIS] + [EI]$$

$$= [ES]\left(1 + \frac{k'_1}{k_1 [S]} + \frac{k_3 [I]}{k'_3} + \frac{k'_1 k_3 [I]}{k'_3 k_1 [S]}\right)$$

$$V = k_2[ES] = \frac{k_2 e_0 \, [S]}{[S] + \frac{k_3}{k'_3}[I][S] + \left(\frac{k'_1}{k_3}\,\frac{k_3[I]}{k_1} + \frac{k'_1}{k_1}\right)}$$

V



$$V_{max} = \frac{k_2 e_0}{1 + \frac{k_3}{k'_3}[I]}$$

$[S]$