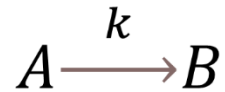
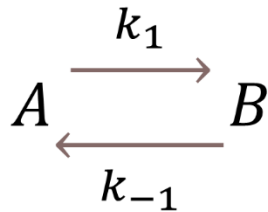


## Unimolecular, irreversible reaction



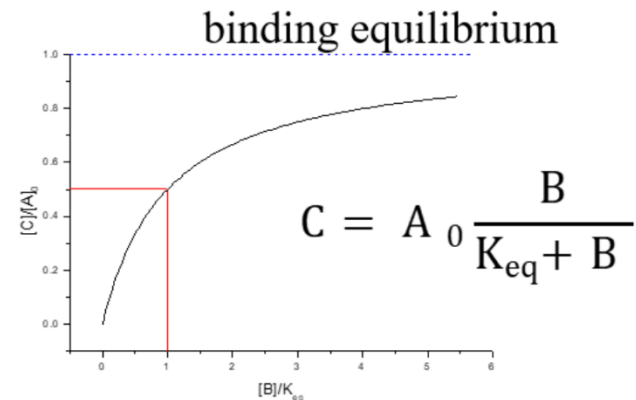
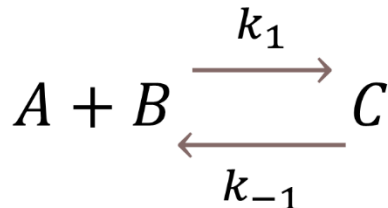
$$[A](t) = [A]_0 * \exp(-kt)$$

## Unimolecular, reversible reaction

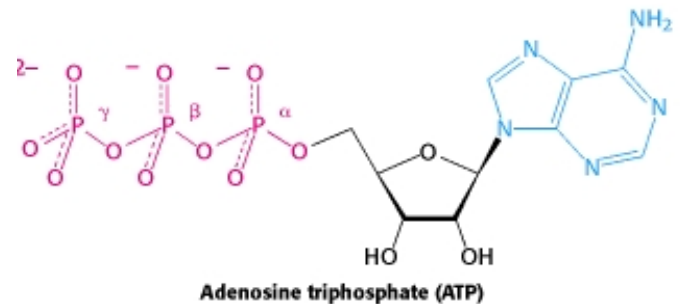
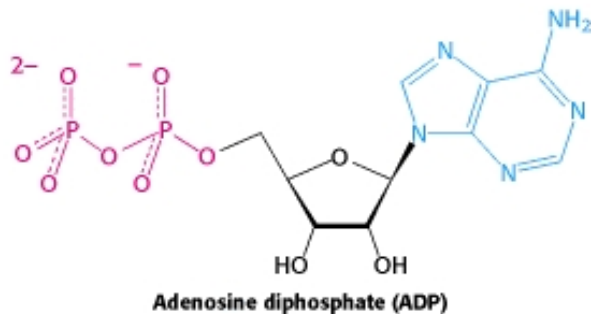
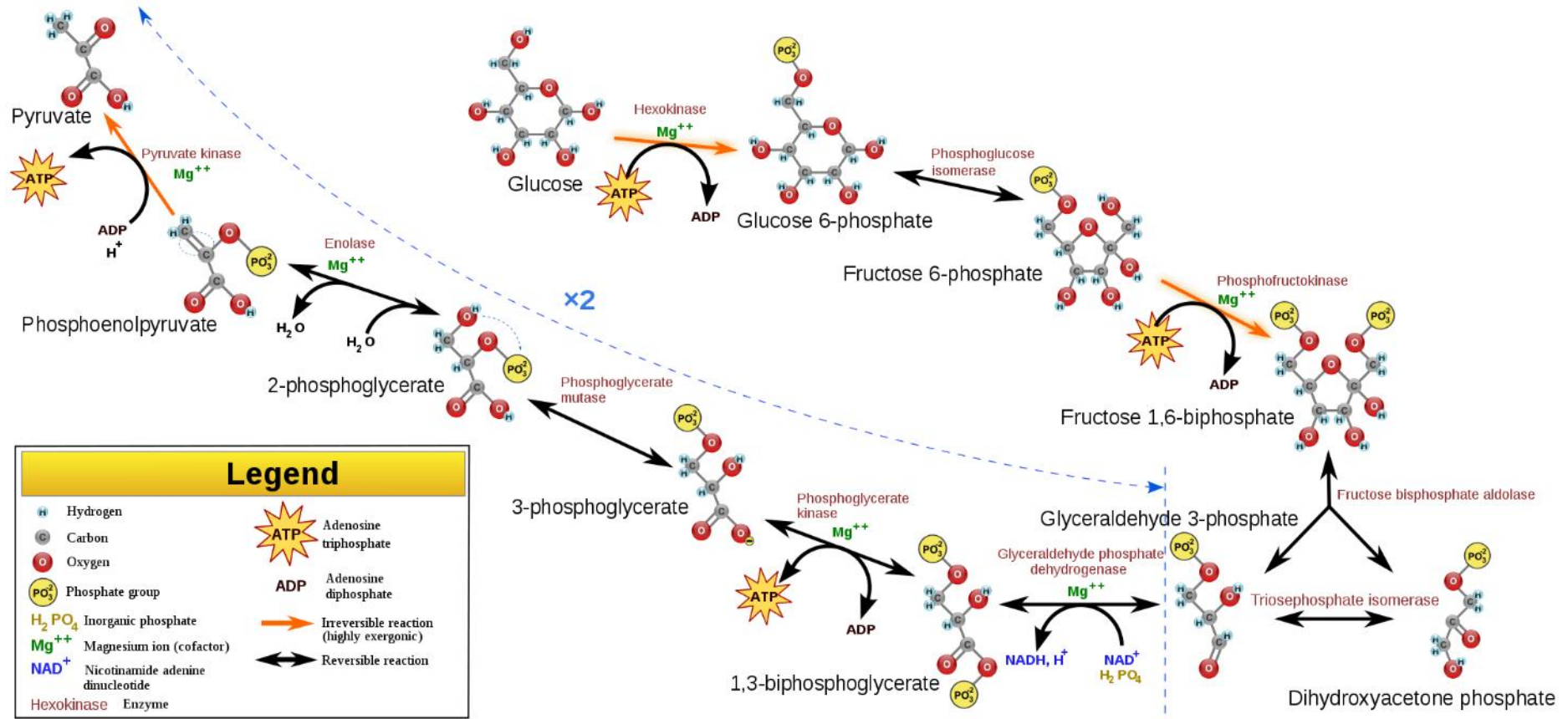


$$a(t) = C \exp(-(k_1 + k_{-1})t) + \frac{k_{-1}}{(k_1 + k_{-1})} a_0$$
$$C = \frac{k_1}{(k_1 + k_{-1})} a_0$$

## Bimolecular, reversible reaction

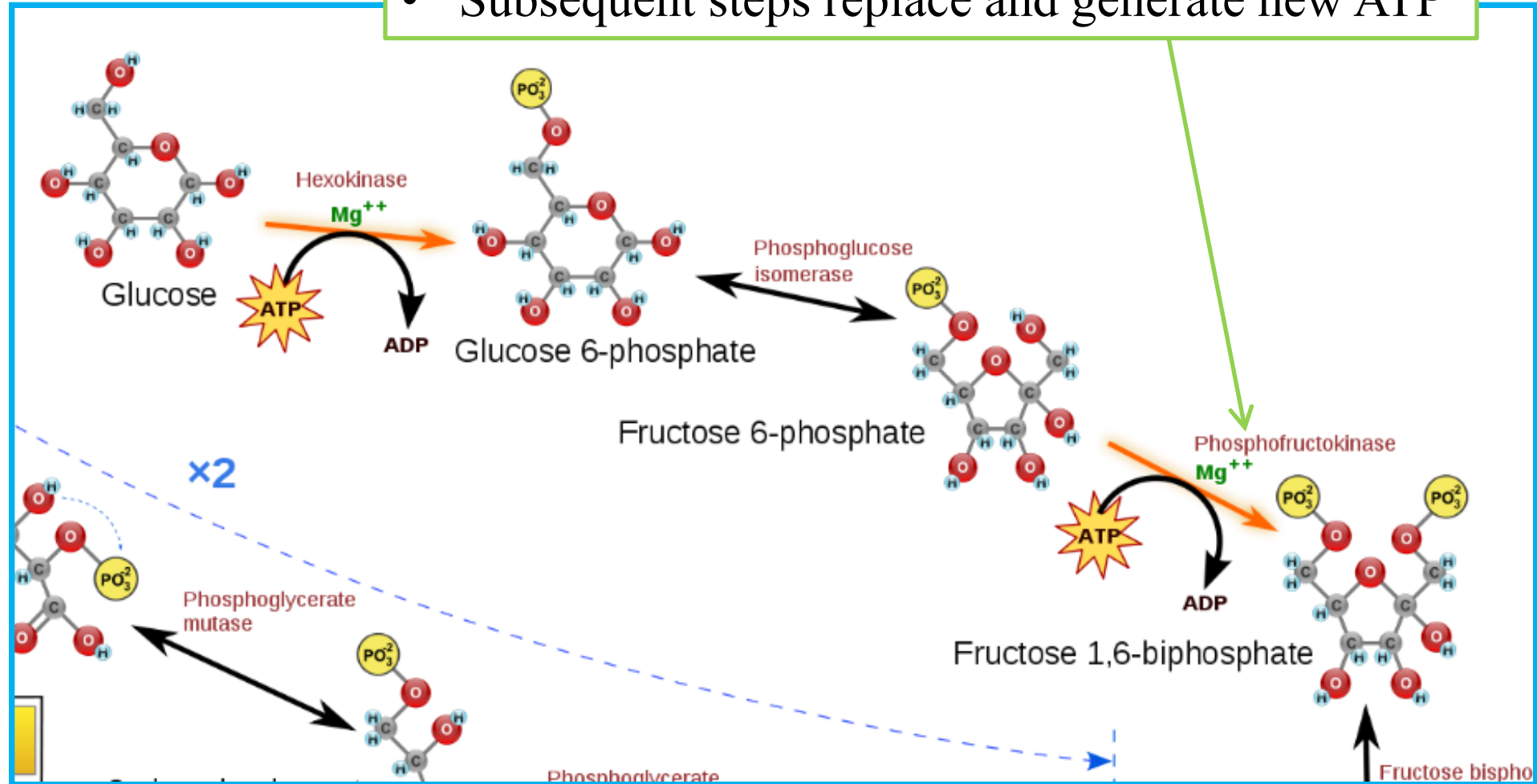


# Glycolysis

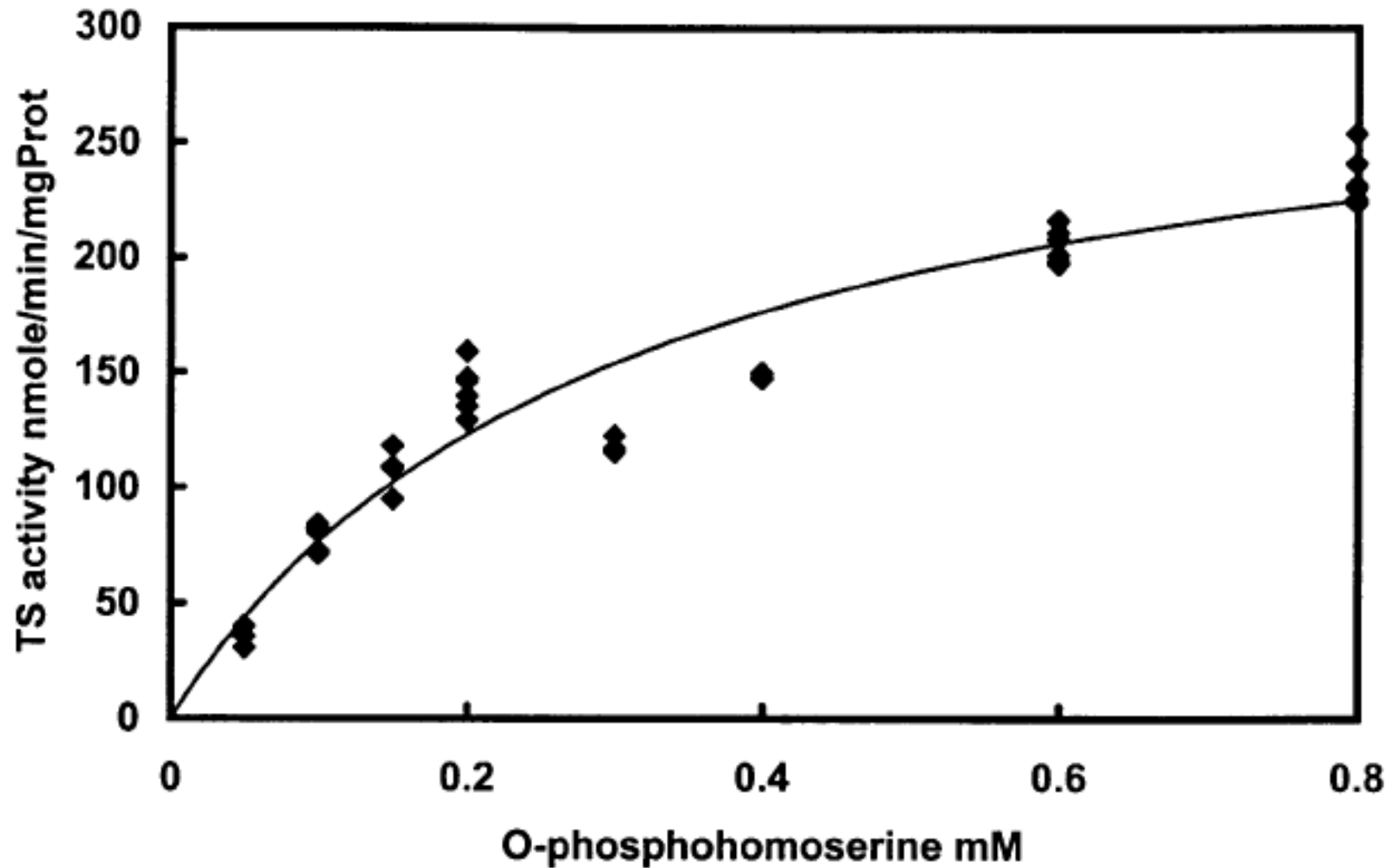


## Phosphofructokinase

- Adds a second phosphate to F6-P
- Uses ATP to produce F1,6-P.
- Subsequent steps replace and generate new ATP



# Threonine synthase





## Quasi-steady-state approximation – non-dimensionalization

Make the following substitutions:

$$\sigma = \frac{s}{s_0}; \quad \chi = \frac{c}{e_0}; \quad \tau = k_1 e_0 t; \quad \kappa = \frac{k_{-1} + k_2}{k_1 s_0}; \quad \varepsilon = \frac{e_0}{s_0}; \quad \alpha = \frac{k_{-1}}{k_1 s_0}$$

Which convert the ODEs to a non-dimensionalized equivalent:

$$\frac{d\chi}{d\tau} = \frac{dc}{dt} \left( \frac{d\chi}{dc} \right) \left( \frac{dt}{d\tau} \right) = \frac{1}{k_1 e_0^2} \frac{dc}{dt}$$

$$\frac{dc}{dt} = +s e_0 k_1 - c s k_1 - c k_{-1} - c k_2; (\text{using } e = e_0 - c)$$

$$\frac{dc}{dt} = +s e_0 k_1 - \left[ c(s k_1 + k_{-1} + k_2) \xrightarrow{\text{pull out } k_1 s_0} c k_1 s_0 \left( \frac{s}{s_0} + \left( \frac{k_{-1} + k_2}{k_1 s_0} \right) \right) \right]$$

$$\frac{d\chi}{d\tau} = \frac{dc}{dt} \left( \frac{d\chi}{dc} \right) \left( \frac{dt}{d\tau} \right) = \frac{1}{k_1 e_o^2} \frac{dc}{dt}$$

$$\frac{dc}{dt} = +se_0 k_1 - csk_1 - ck_{-1} - ck_2; (\text{using } e = e_0 - c)$$

$$\frac{dc}{dt} = +se_0 k_1 - \left[ c(sk_1 + k_{-1} + k_2) \xrightarrow{\text{pull out } k_1 s_0} ck_1 s_0 \left( \frac{s}{s_0} + \left( \frac{k_{-1} + k_2}{k_1 s_0} \right) \right) \right]$$

now, making the non - dimensionalized equivalents as possible

$$\frac{dc}{dt} = +\sigma * s_0 * e_0 * k_1 - c * k_1 * s_0 * (\sigma + \kappa)$$

and, multiplying by the terms to get to the nondimensional differential

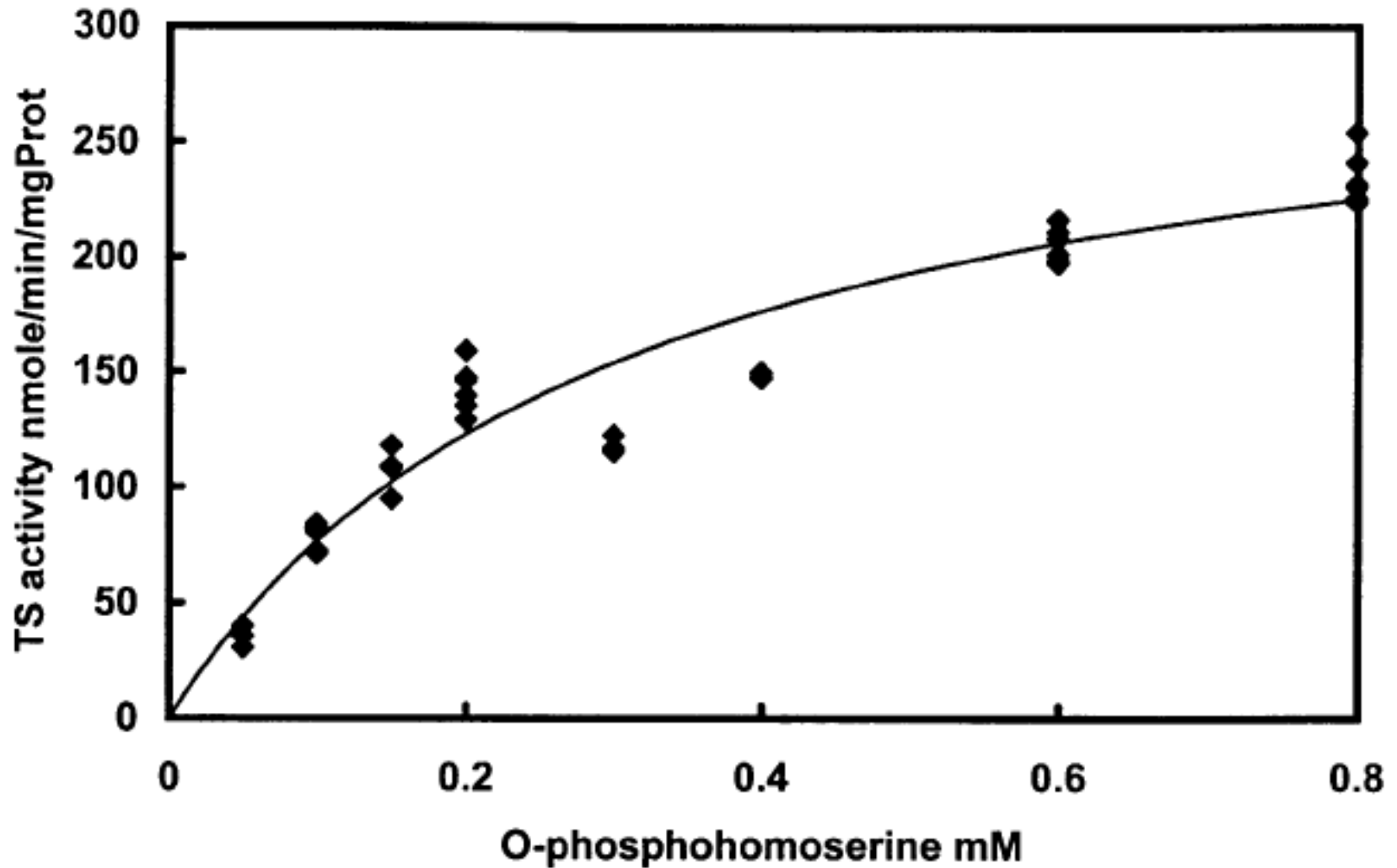
$$\frac{d\chi}{d\tau} = \left( \sigma \left( \frac{s_0}{e_0} \right) - \frac{c}{e_0} \left( \frac{s_0}{e_0} \right) (\sigma + \kappa) \right)$$

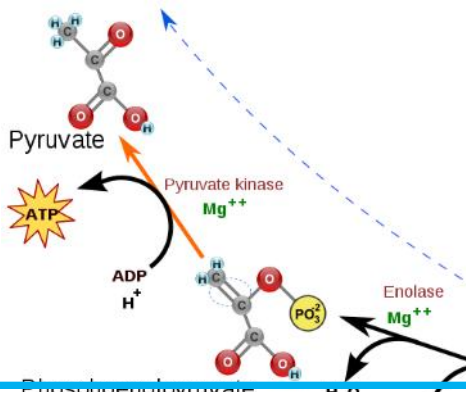
$$\frac{d\chi}{d\tau} = \frac{1}{\varepsilon} (\sigma - \chi(\sigma + \kappa))$$





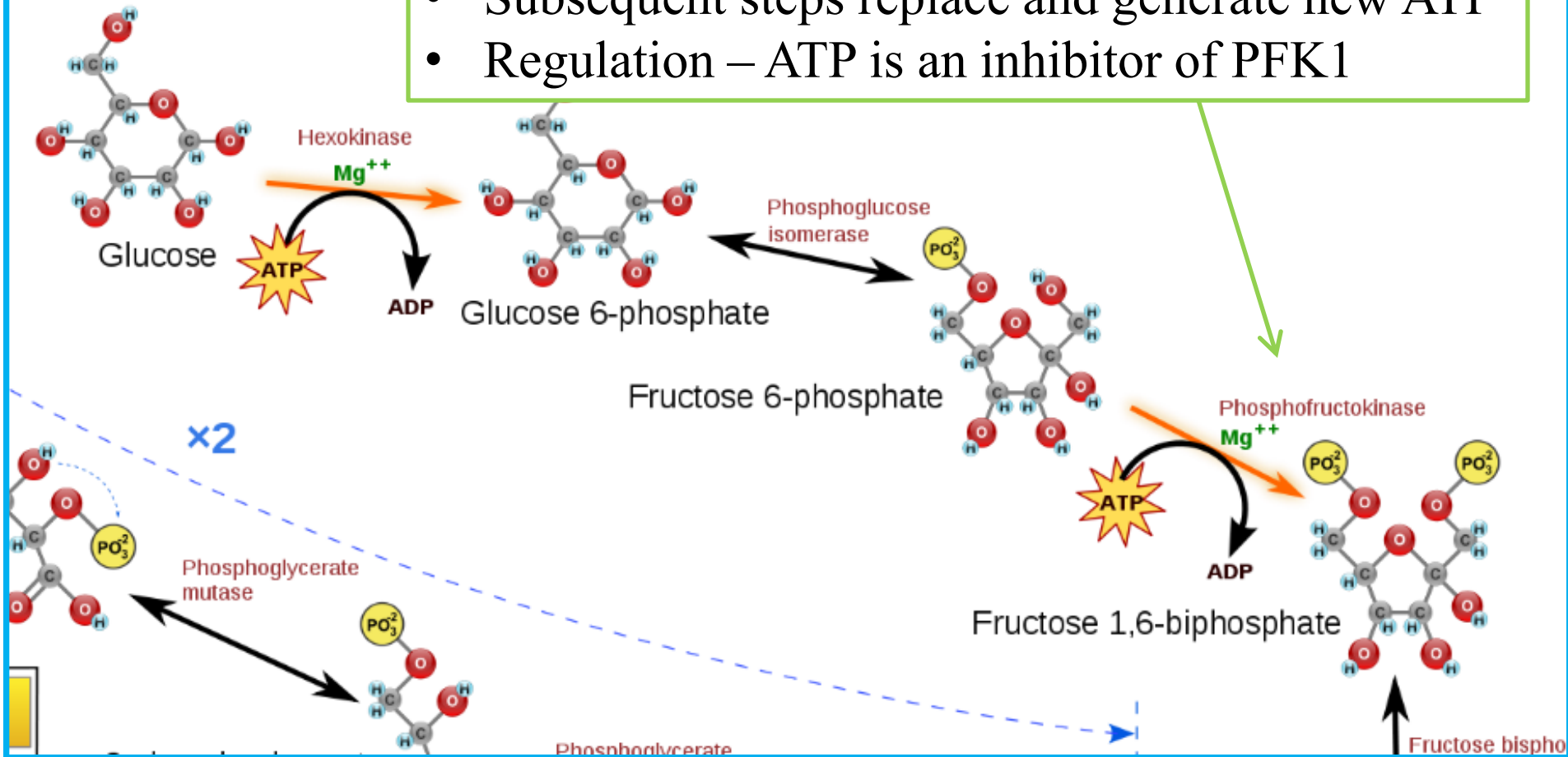
# Threonine synthase



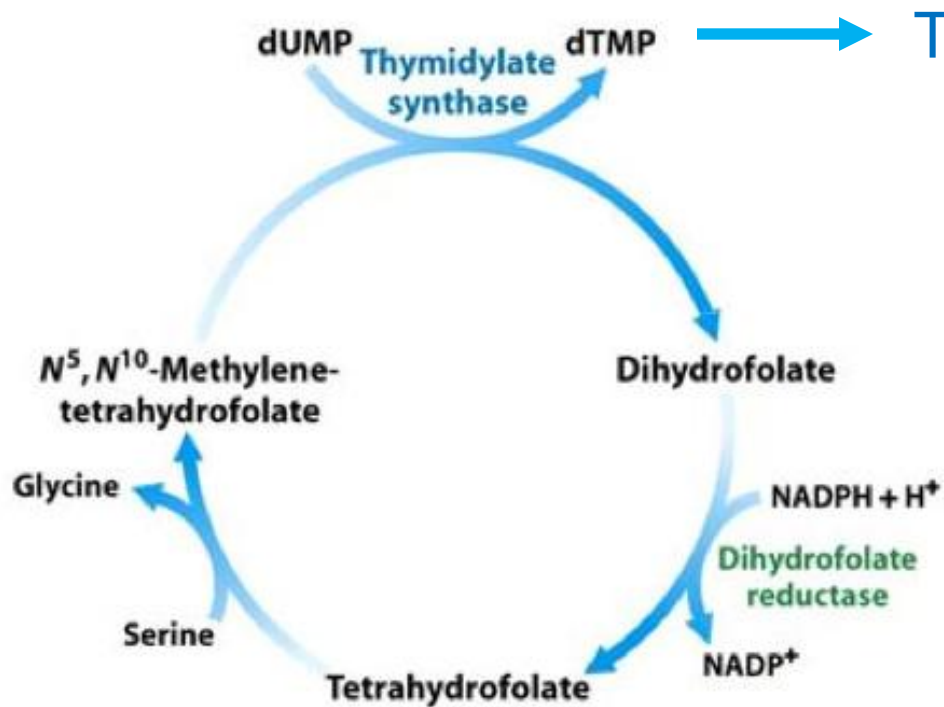


## Phosphofructokinase

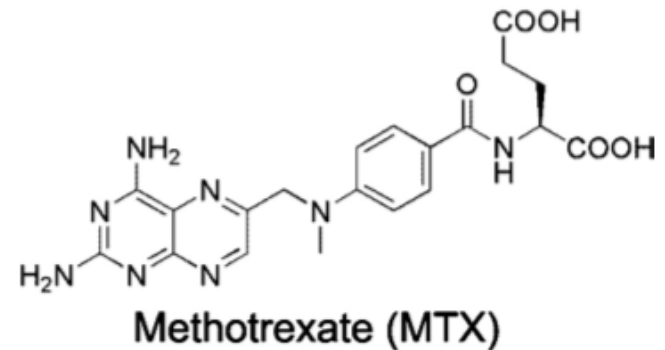
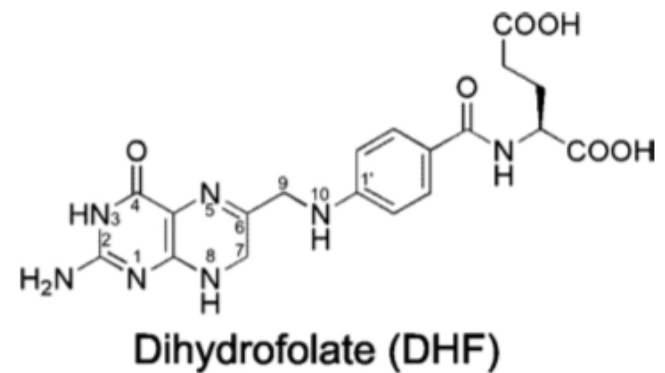
- Adds a second phosphate to F6-P
- Uses ATP to produce F1,6-P.
- Subsequent steps replace and generate new ATP
- Regulation – ATP is an inhibitor of PFK1



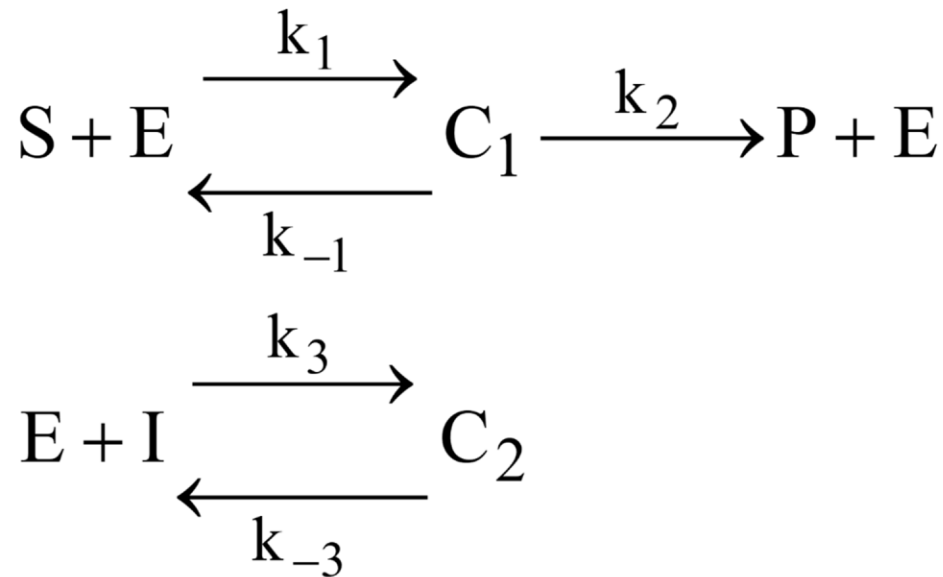
# Competitive inhibition



Thymidine / DNA synthesis



## Competitive inhibition



$$\frac{ds}{dt} = -k_1 se + k_{-1} c_1$$

$$0 \equiv \frac{dc_1}{dt} = k_1 se - (k_{-1} + k_2) c_1$$

$$\frac{di}{dt} = -k_3 ie + k_{-3} c_2$$

$$0 \equiv \frac{dc_2}{dt} = k_3 ie - k_{-3} c_2$$

$$\frac{de}{dt} = -k_1 se + k_{-1} c_1 + k_2 c_1 - k_3 ie + k_{-3} c_2$$

$$\frac{dp}{dt} = k_2 c_1$$

$$e + c_1 + c_2 = e_0$$

## Apply Quasi-steady-state approximation

$C_1$ :

$$k_1 s(e_0 - c_1 - c_2) - (k_{-1} + k_2)c_1 = 0$$

$$\Rightarrow s(e_0 - c_1 - c_2) - K_M c_1 = 0; \quad K_M = \frac{(k_{-1} + k_2)}{k_1}$$

$C_2$ :

$$k_3 i(e_0 - c_1 - c_2) = k_{-3} c_2$$

$$k_3 i(e_0 - c_1) = k_3 i c_2 + k_{-3} c_2$$

$$i(e_0 - c_1) = c_2(i + K_i); \quad K_i = \frac{k_{-3}}{k_3}$$

$$\Rightarrow c_2 = \frac{i(e_0 - c_1)}{i + K_i} = \frac{e_0 - c_1}{(1 + K_i/i)}$$

plug expression for  $C_2$  back into eqn. for  $C_1$

$$se_0 - sc_1 - s \frac{(e_0 - c_1)}{(1 + K_i/i)} - K_M c_1 = 0$$

Multiply by  $(1+K_i/i)$ , change signs

$$-se_0(1 + K_i/i) + se_0 - sc_1 + (s + K_M)(1 + K_i/i)c_1 = 0$$

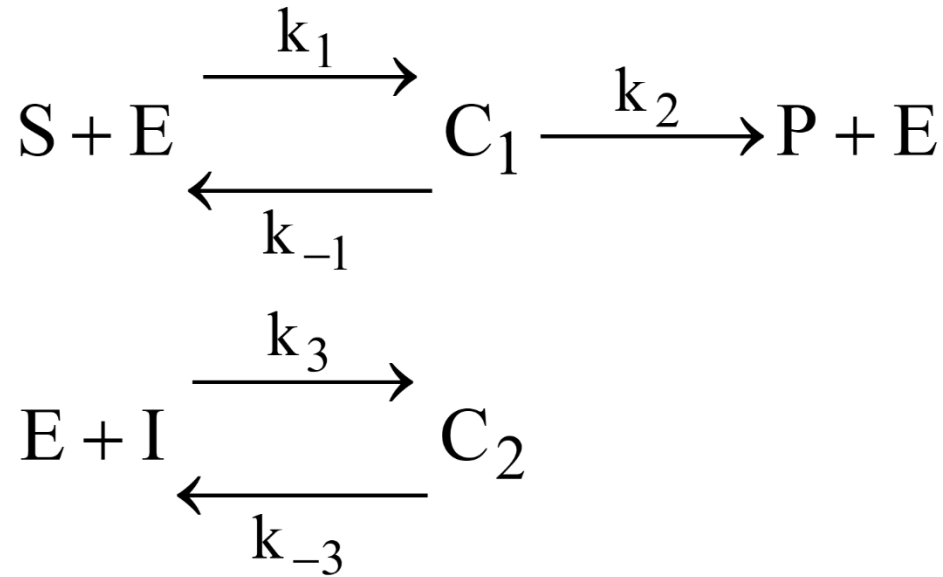
expand, group  $c_1$ 's on left,  $e_0$ 's on right

$$c_1[-s + s + s(K_i/i) + K_M + K_M K_i/i] = se_0(1 + K_i/i - 1)$$

canceling out symbols in bold, solving for  $c_1$  and rearrange into

$$c_1 = \frac{se_0}{s + K_M(1 + i/K_i)}$$

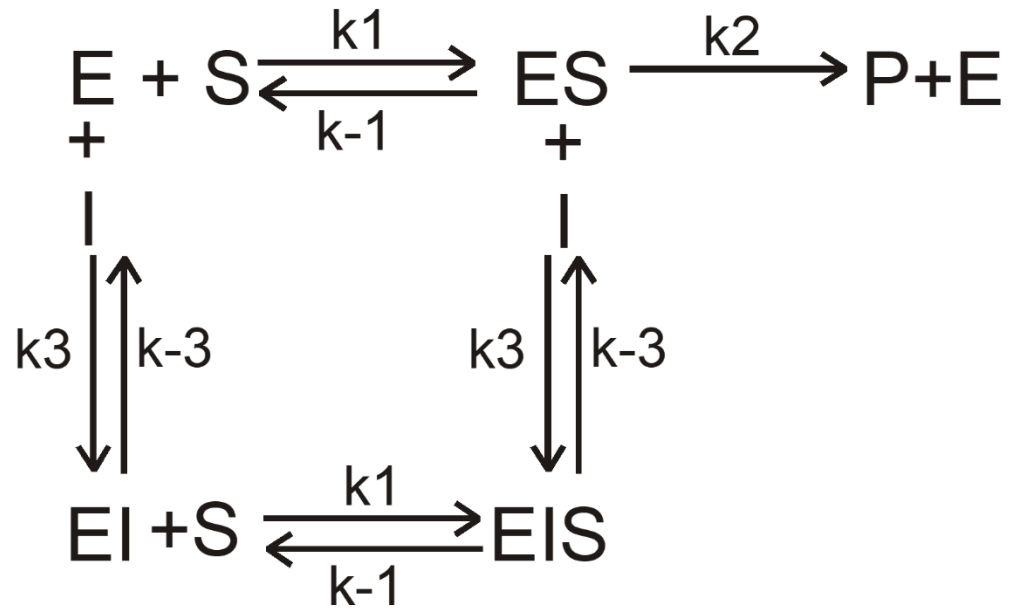
## Competitive inhibition



$$V = k_2 c_1 = k_2 [\text{E}]_0 \frac{[\text{S}]}{K_M (1 + [\text{I}] / K_i) + [\text{S}]} = V_{\max} \frac{[\text{S}]}{K_M (1 + [\text{I}] / K_i) + [\text{S}]}$$

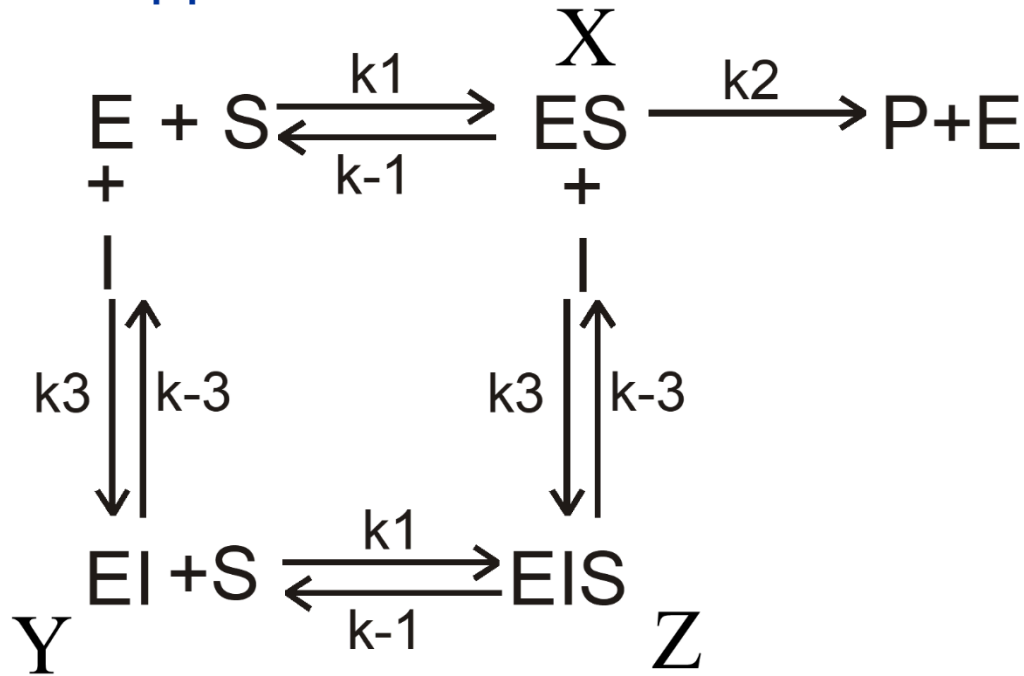
$$K_M = \frac{k_{-1} + k_2}{k_1}; K_i = \frac{k_{-3}}{k_3}$$

## Noncompetitive, allosteric inhibition





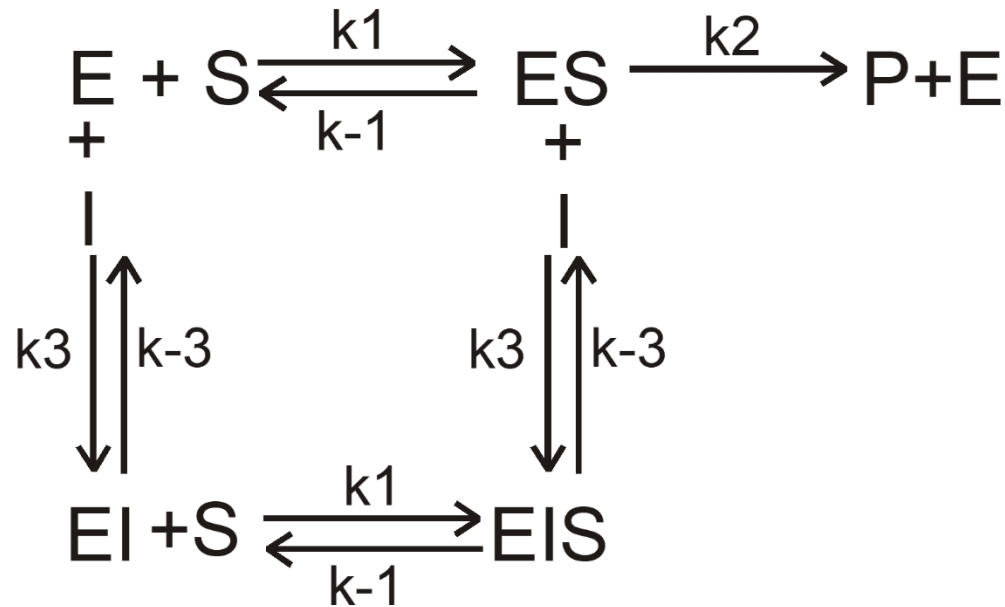
## Apply Equilibrium approximation



1.  $k_1 se = k_{-1} x$
2.  $k_3 ie = k_{-3} y$
3.  $k_1 sy = k_{-1} z$
4.  $k_3 ix = k_{-3} z$

Solve for X (which is ES, why?)

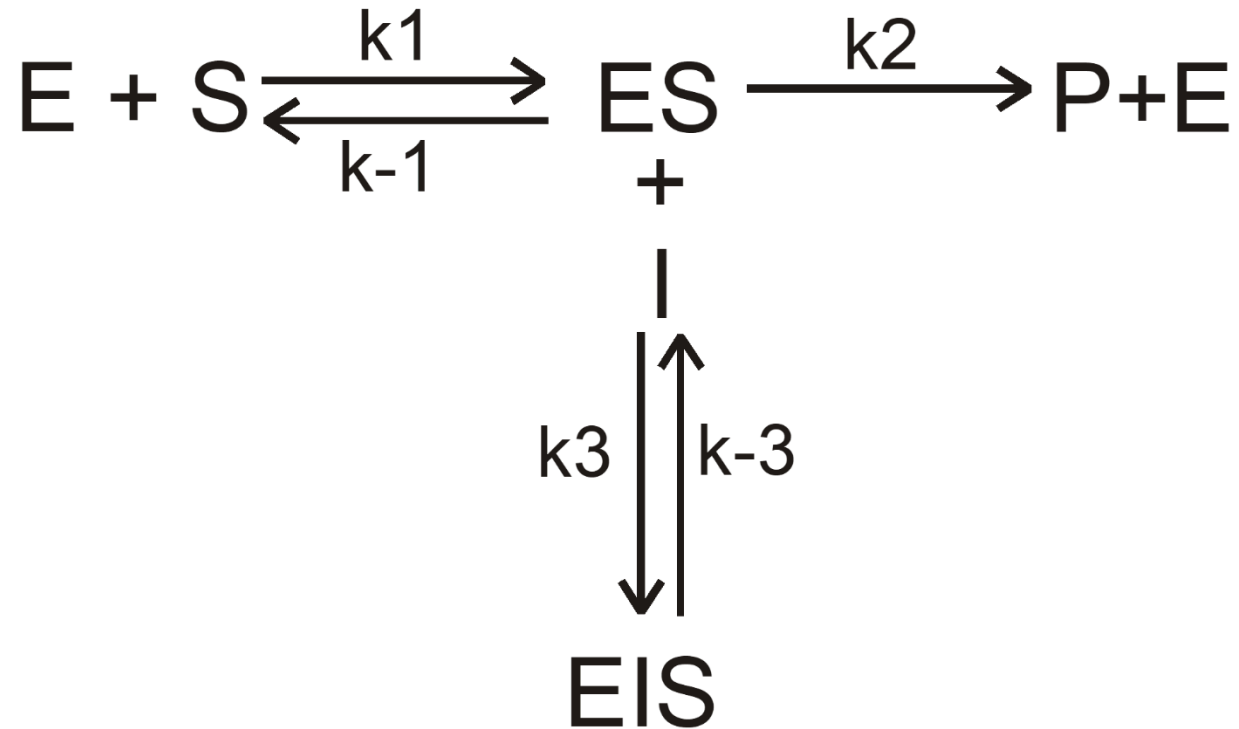
## Noncompetitive, allosteric inhibition



$$x = \frac{se_0 K_i}{(s + K_s)(K_i + i)}; K_i = k_{-3}/k_3 \text{ and } K_s = k_{-1}/k_1$$

$$V = k_2 \frac{se_0 K_i}{(s + K_s)(K_i + i)} = V_{\max} \frac{1}{1 + [I]/K_i} \frac{[S]}{K_s + [S]}$$

## Uncompetitive, allosteric inhibition



$$X=ES$$

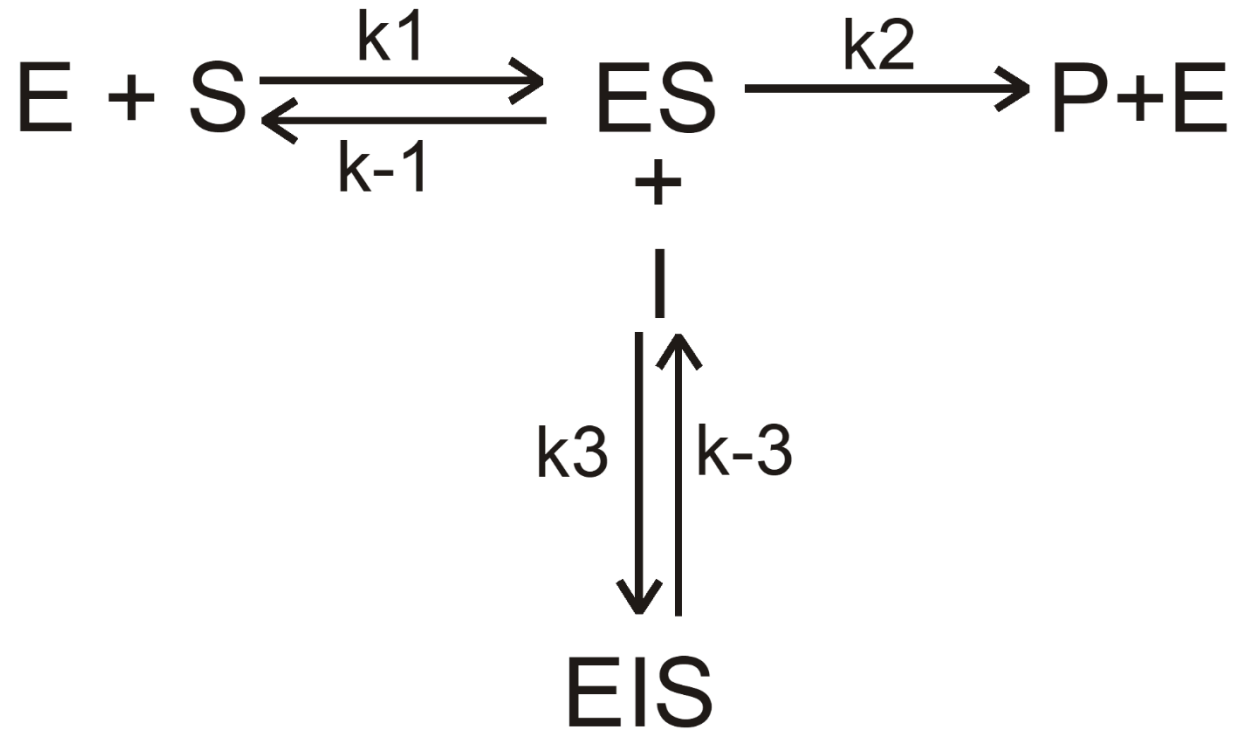
# Y=EIS

1.  $k_1 e s = k_{-1} x$

$$2. \quad k_3 i x = k_{-3} y$$

3.  $e_0 = e + x + y$

## Uncompetitive, allosteric inhibition



$$V = V_{\max} \frac{1}{1 + [I]/K_i} \frac{[S]}{\frac{K_s}{1 + [I]/K_i} + [S]}; K_i = k_{-3}/k_3 \text{ and } K_s = k_{-1}/k_1$$

## Competitive inhibition

$$V = k_2 c_1 = k_2 [E]_0 \frac{[S]}{K_M (1 + [I]/K_i) + [S]} = V_{\text{Max}} \frac{[S]}{K_M (1 + [I]/K_i) + [S]}$$
$$V_{\text{Max}} = k_2 [E]_0; \quad K_M = \frac{k_{-1} + k_2}{k_1}; \quad K_i = \frac{k_{-3}}{k_3}$$

## Noncompetitive, allosteric inhibition

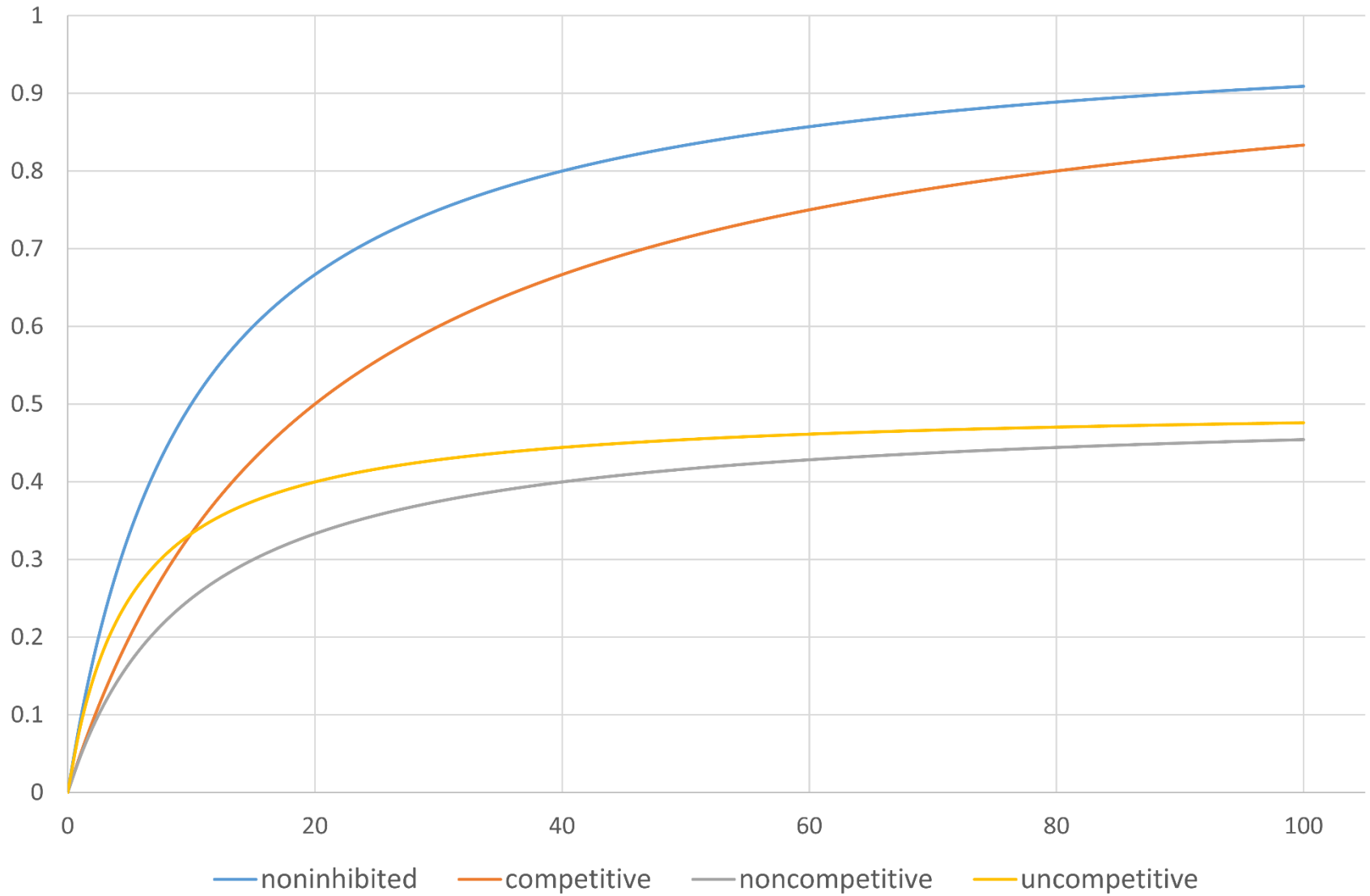
$$V = k_2 \frac{se_0 K_i}{(s + K_s)(K_i + i)} = V_{\text{max}} \frac{1}{1 + [I]/K_i} \frac{[S]}{K_s + [S]}$$

$$K_i = k_{-3}/k_3 \text{ and } K_s = k_{-1}/k_1$$

## Uncompetitive, allosteric inhibition

$$V = V_{\text{max}} \frac{1}{1 + [I]/K_i} \frac{[S]}{\frac{K_s}{1 + [I]/K_i} + [S]}; \quad K_i = k_{-3}/k_3 \text{ and } K_s = k_{-1}/k_1$$

$V/V_{\max}$



# Lineweaver-Burk Plots

*Plot inverse of both sides of expression*

$$V = V_{\max} \frac{[S]}{K_M + [S]} \quad \Rightarrow \quad \frac{1}{V} = \frac{1}{V_{\max}} + \frac{K_M}{V_{\max}} \frac{1}{[S]}$$

