CONCEPT: COMPETITIVE INHIBITION

●Competitive inhibitors are the *most common* in biochemistry and tend to be *substrate* ___________.

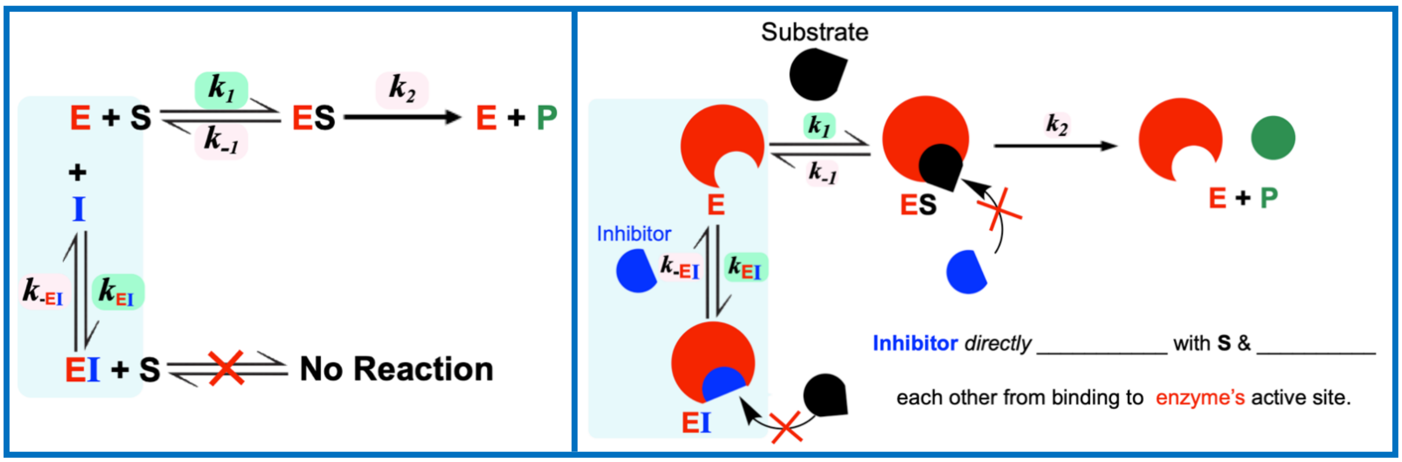
□ *Substrate analogs*: compounds that are structurally ___________ to substrates.

●________________ *inhibitors*: *compete* with the substrate for a position in the *free* enzyme's ___________ site to ____ V_0.

□ Only bind to *empty* active sites of _________ enzymes that have *not yet bound* to their substrates.

□ __________ active sites: substrates cannot bind to an enzyme already bound to the competitive inhibitor (EI).

EXAMPLE: Competitive inhibition.



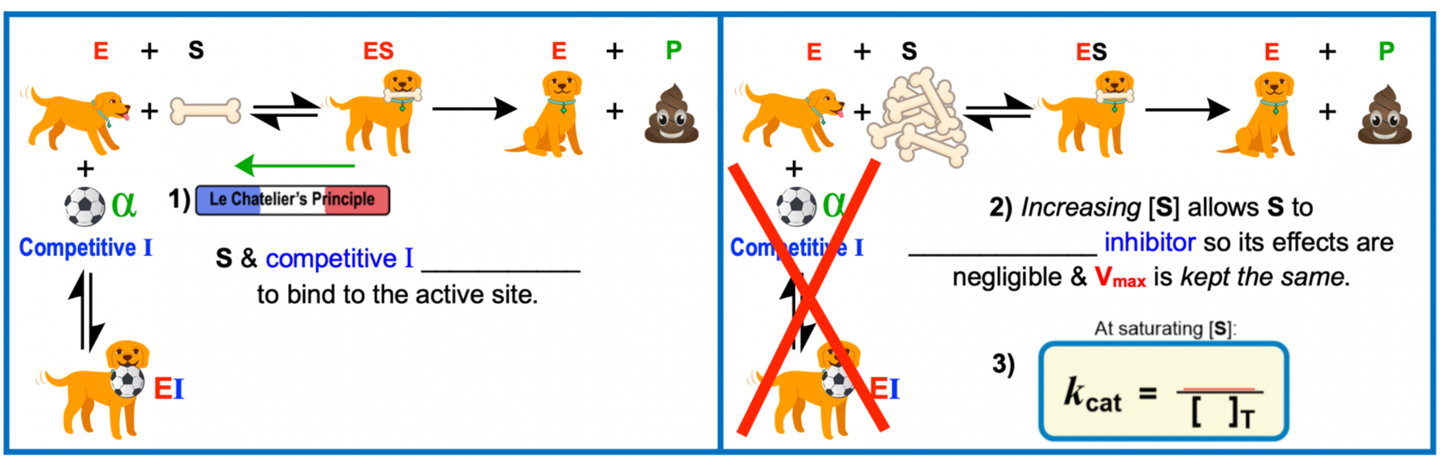
Competitive Inhibitor Effects

●Recall: competitive inhibitors _____________ the K_m^{app} but do ______ affect the V_{max}^{app} of an enzyme; BUT how/why?

1) Competitive inhibitors *decrease* [E], causing the k_{-1} reaction to shift ________, weakening ES affinity & ___ K_m^{app}.

2) Competitive inhibitors do *not* change V_{max}^{app} because a sufficient *increase* in [S] will _______________ the inhibitor.

3) Since V_{max}^{app} is not affected, _______ is also not affected.



____________ Inhibition = KoMpetitive INhibition = ______ ________

If S can compete, it can keep *SAME* _____.

CONCEPT: COMPETITIVE INHIBITION

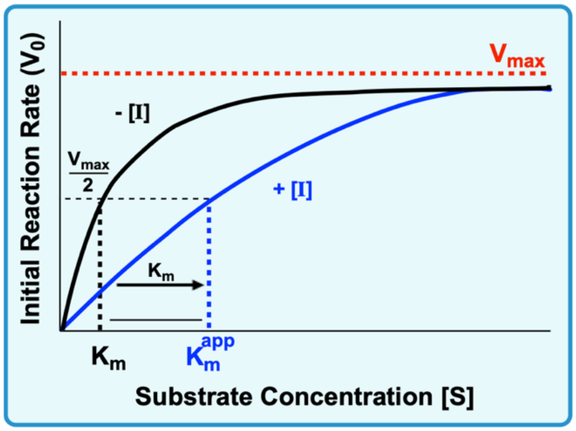
Competitive Inhibition & Michaelis-Menten-Plots

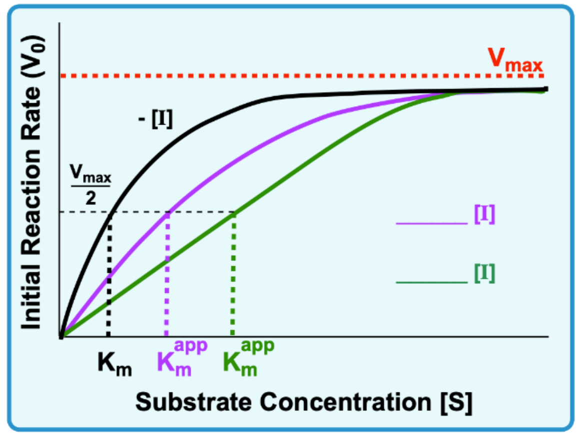
- Recall: All inhibitors, including competitive inhibitors, _____________ V_0 of an enzyme-catalyzed-reaction.
- Recall: Competitive inhibitors bind to ________ enzymes, so ____ measures its *degree of inhibition* on the free enzyme.
  - □ α of a competitive inhibitor only *increases* K_m^{app} ($K_m^{app} = \alpha K_m$); but there is ____ change to V_{max}^{app} ($V_{max}^{app} = V_{max}$).

$$V_0 = \frac{V_{max}[S]}{K_m + [S]}$$

Competitive Inhibitor Michaelis-Menten Equation:

$$V_0 = \frac{V_{max}[S]}{\alpha K_m + [S]}$$





Competitive Inhibition & Lineweaver-Burk-Plots

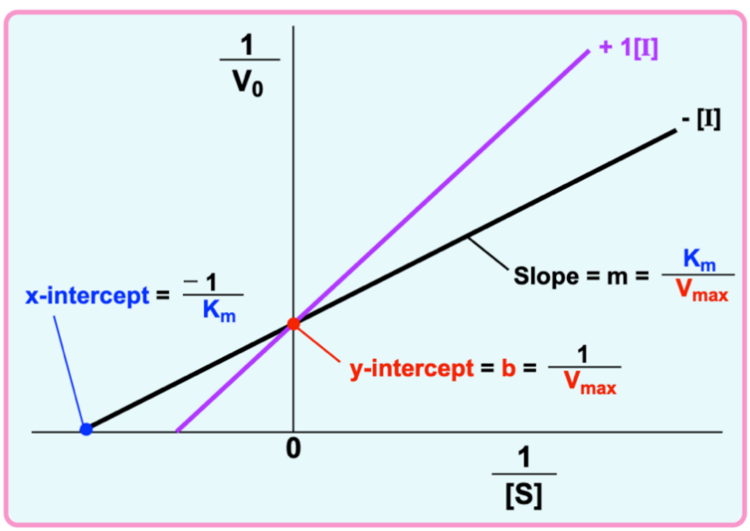
- Slope of the line on a LW-Burk plot (slope = K_m/V_{max}) ______________ with *more* competitive inhibitor
  - □ The *more* competitive inhibitor, the ______________ the line becomes.
  - □ ____-intercept ($1/V_{max}$) magnitude is *not changed* since V_{max} stays the __________.
  - □ ____-*intercept* ($-1/K_m$) magnitude is *decreased*, but the K_m itself is ________________.

EXAMPLE: Draw the representative line for the enzyme's activity if the concentration of competitive inhibitor was doubled.

$$y = mX + b \quad \vdots \quad \frac{1}{V_0} = \frac{K_m}{V_{max}}\left(\frac{1}{[S]}\right) + \frac{1}{V_{max}}$$

Competitive Inhibitor Lineweaver-Burk Equation:

$$\frac{1}{V_0} = \frac{\alpha K_m}{V_{max}}\left(\frac{1}{[S]}\right) + \frac{1}{V_{max}}$$



CONCEPT: COMPETITIVE INHIBITION

PRACTICE: Which of the following would be altered on a Lineweaver-Burk plot in the presence of a competitive inhibitor?

a) Slope of the line on the plot.
b) Intercept on the 1/[S] axis.
c) Intercept on the $1/V_0$ axis.
d) V_{max}.
e) a and b only.
f) a, b, c and d.

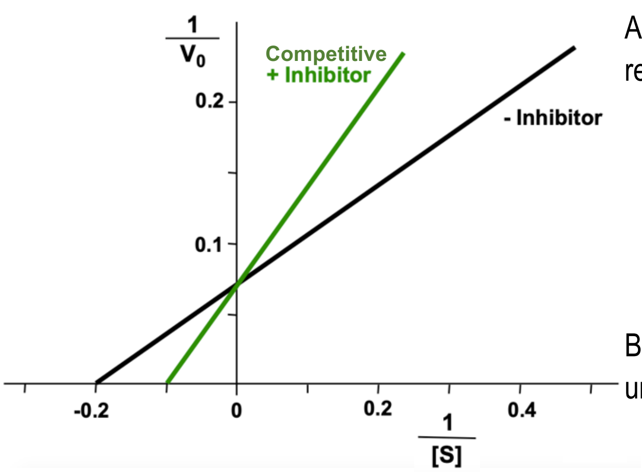
PRACTICE: N-hydroxy-L-arginine (an intermediate in nitric oxide biosynthesis) can bind to the active site of arginase making its manganese reactive metal center unavailable for catalysis. How would an increased concentration of this intermediate be expected to affect the kinetic parameters of this enzyme?

a) The apparent V_{max} will decrease.
b) The apparent K_m for arginine will decrease.
c) The apparent V_{max} will increase.
d) The apparent K_m for arginine will increase.

PRACTICE: An enzyme has a K_m of 8 μM in the absence of a competitive inhibitor and a $\mathbf{K_m^{app}}$ of 12 μM in the presence of 3 μM of the inhibitor. Calculate the K_I.

a) 1/6
b) 1.5
c) 3
d) 6

PRACTICE: Use the Lineweaver-Burk plot below to answer the following questions. Units of [S] are in nM.



A) Estimate the values of $\mathbf{K_m}$ & $\mathbf{V_{max}}$ as well as the K_m^{app} & V_{max}^{app} for the reactions in the **absence** and **presence** of the competitive inhibitor.

B) Would you expect the competitive inhibitor to be more effective under conditions of high or low [S]? Why?

C) If [I] = 10 nM, calculate the inhibition constant (K_I).