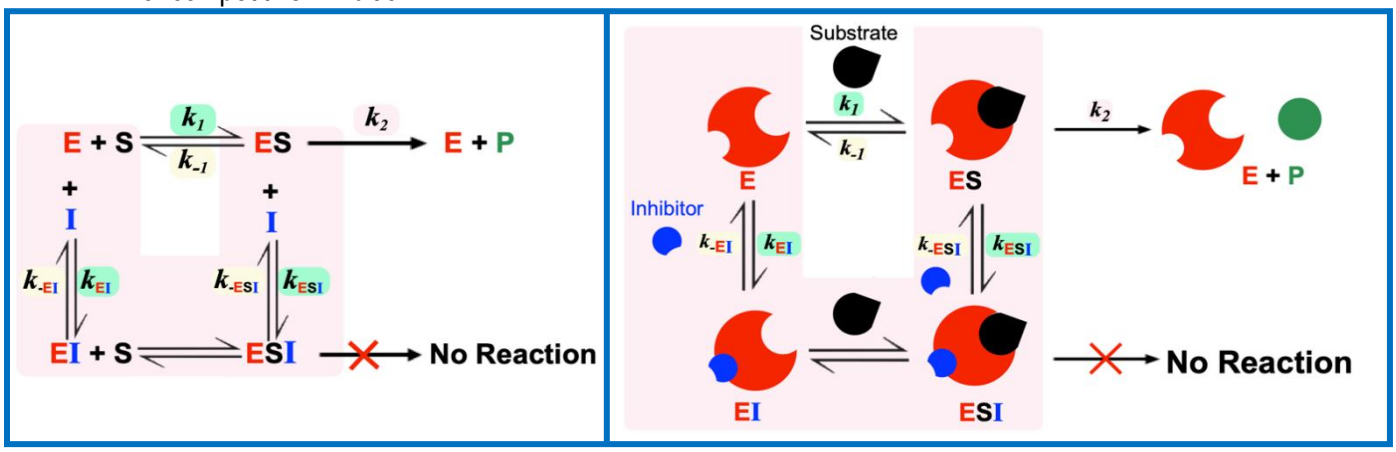
CONCEPT: NONCOMPETITIVE INHIBITION

- ____*ncompetitive inhibitors* are a specific *type* of _____ inhibitor that also do ____t compete with the **S**.
- *Noncompetitive inhibitors*: also bind to allosteric sites on either the _____ enzyme ***OR*** the _____-complex to lower V_0.
  - □ Binding of a *noncompetitive inhibitor* to E or ES-complex ultimately _____ conversion of **S** → **P**.
  - □ Noncompetitive inhibitors bind with the _____ affinity to the *free enzyme* as to the *ES-complex* ($\mathbf{K_I} = \mathbf{K'_I}$).

EXAMPLE: Noncompetitive inhibition.



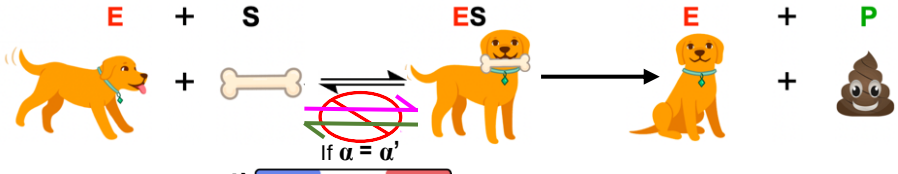
Noncompetitive Inhibitor Effects

- ____ncompetitive inhibitors do ____t affect the K_m^{app}, but do _____ the V_{max}^{app}.

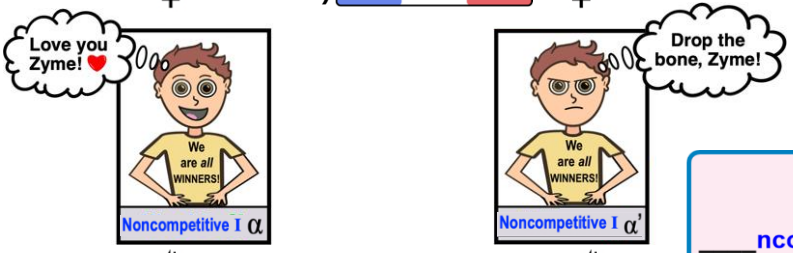
1) By Le Chatelier's Principle, if ____ = ____, then the reaction shifts *cancel* & there is _____ overall reaction shift.

2) **S** *can't* outcompete noncompetitive inhibitors, so effects are *NOT reversed* by ____ [**S**] & V_{max}^{app} is *decreased*.

3) Since noncompetitive inhibitors *decrease* V_{max}^{app}, k_{cat} is also _____.



1) Le Chatelier's Principle



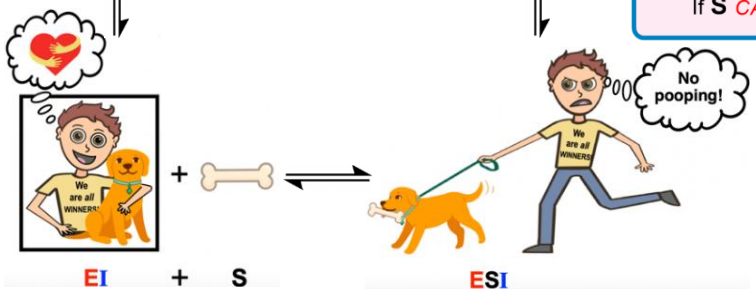
At saturating [**S**]:

2 & 3) $k_{cat} = \frac{\quad}{[\ ]_T}$

α = α'

____ncompetitive Inhibition = NO nKo mpetitive = NO ____ change.

If **S** *CAN'T* **compete,** it *CAN'T* ***keep*** *same* _____ so it's **decreased**.



CONCEPT: NONCOMPETITIVE INHIBITION

Noncompetitive Inhibition & Michaelis-Menten-Plots

●Recall: _____ncompetitive inhibitors are just a specific type of *mixed* inhibitor.

●Noncompetitive inhibitors bind to either *free enzymes* ***OR*** *ES-complexes*, so ____ & α' measures its *degree of inhibition*.

□ A noncompetitive inhibitor is a mixed inhibitor where _____ = _____.

□ Since α = α' with a noncompetitive inhibitor, the K_m^{app} is _____t changed ($K_m^{app} = K_m$).

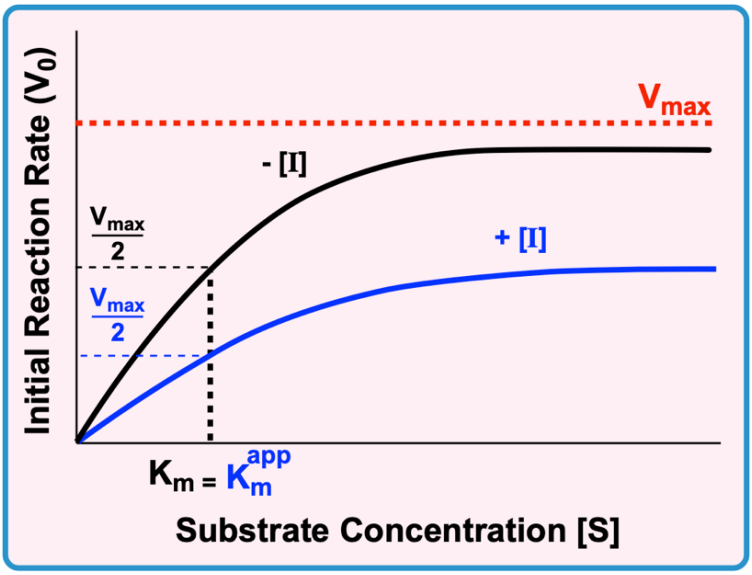
□ α' always _____ V_{max}^{app} (V_{max}/α').

EXAMPLE:

Noncompetitive Inhibitor Michaelis-Menten Equation:

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

$\alpha = \alpha'$



Noncompetitive Inhibition & Lineweaver-Burk-Plots

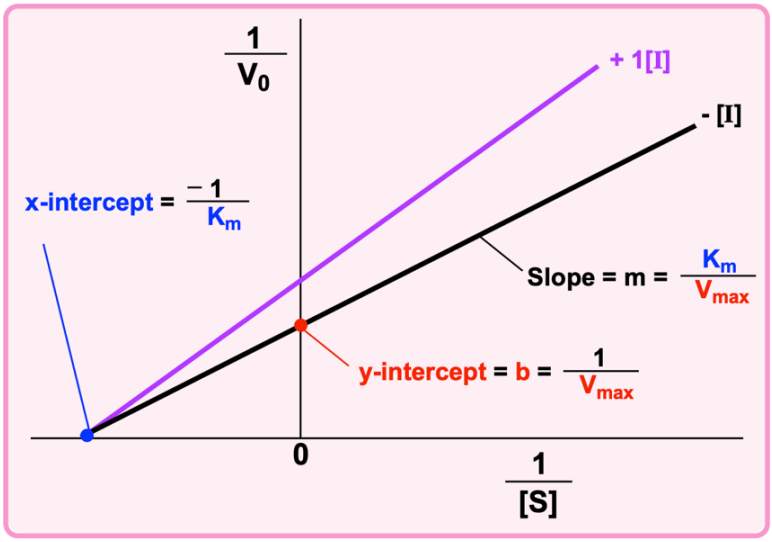
●Slope of the line on a LW-Burk plot (slope = K_m/V_{max}) _____ with more noncompetitive inhibitor.

□ Recall: noncompetitive inhibitors always decrease the V_{max}^{app} but have no effect on the _____.

□ ____-intercept ($1/V_{max}$) on a LW-Burk-Plot always *increases*, but ____-intercept ($-1/K_m$) stays the _____.

Noncompetitive Inhibitor Lineweaver-Burk Equation:

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



CONCEPT: NONCOMPETITIVE INHIBITION

PRACTICE: Indicate with an "x" which of the kinetic parameters would be altered in the presence of the given inhibitor.

K_m	V_{max}	Both	Neither	Factor
				Competitive Inhibitor
				Noncompetitive Inhibitor

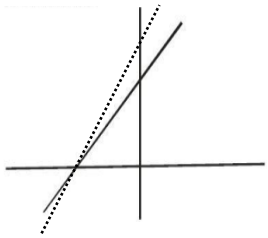
PRACTICE: What can be determined from the following Lineweaver Burk plot?

a) Data collected in the absence (solid line) & presence (dashed line) of a competitive inhibitor.

b) Data collected in the absence (solid line) & presence (dashed line) of a noncompetitive inhibitor.

c) Data collected in the absence (dashed line) & presence (solid line) of a competitive inhibitor.

d) Data collected in the absence (dashed line) & presence (solid line) of a noncompetitive inhibitor.



PRACTICE: How would you expect the line on a Lineweaver-Burk plot to change if the enzyme was treated with a noncompetitive inhibitor?

a) The y-intercept would move up (away from the origin).

b) The x-intercept would move left (away from the origin).

c) The y-intercept would move down (toward the origin).

d) The x-intercept would move right (toward the origin).

PRACTICE: The following values were determined for alcohol dehydrogenase in the absence & presence of acetaldehyde. What kind of inhibitor is acetaldehyde?

	Km (mM)	Vmax (µmol/min)
In the Absence of Acetaldehyde	0.1	750
In the Presence of Acetaldehyde	0.1	500

a) Noncompetitive inhibitor.

b) Uncompetitive inhibitor.

c) Mixed inhibitor.

d) Competitive inhibitor.