CONCEPT: PROTEIN-LIGAND EQUILIBRIUM CONSTANTS

Protein-Ligand Association Constant (K_a)

●Recall: equilibrium constant (_____) is the ratio of [Product] over [Reactant] at equilibrium.

●*Association constant* (_____): *equilibrium constant* for the ___________________ of the protein & ligand into a complex.

- □ *Don't confuse* the protein-ligand-association constant (**K_a**) with the acid-dissociation constant (which is also "K_a").

●**K_a** and protein-affinity for ligand are ____________ proportional.

- □ Therefore, the ___________ the **K_a** value, the *stronger* the affinity a protein has for that ligand.
- □ **K_a** has units of ______ and is the ________________ of the dissociation constant _____ (**K_a** = 1/K_d).

$$P + L \underset{k_d}{\overset{k_a}{\rightleftharpoons}} PL$$

Association Constant:

$$K_a = \frac{[\quad]}{[\quad][\quad]} = \frac{\quad}{\quad} = \frac{1}{\quad}$$

K_a Units: ______

Protein-Ligand Dissociation Constant (K_d)

●Dissociation constant (_____): *equilibrium constant* for __________________ of protein-ligand-complex back into P + L.

- □ Recall: **K_d** and K_a are ________________ of each other, so **K_d** has units of ______.
- □ **K_d** is used __________ often than K_a to express the protein-affinity for a ligand.

$$P + L \underset{k_d}{\overset{k_a}{\rightleftharpoons}} PL$$

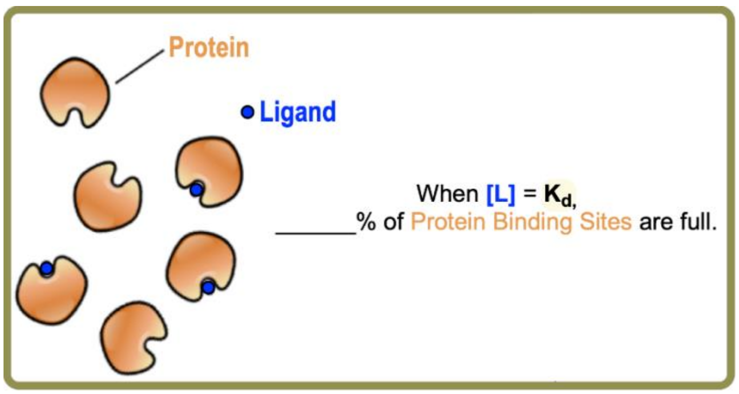
Dissociation Constant:

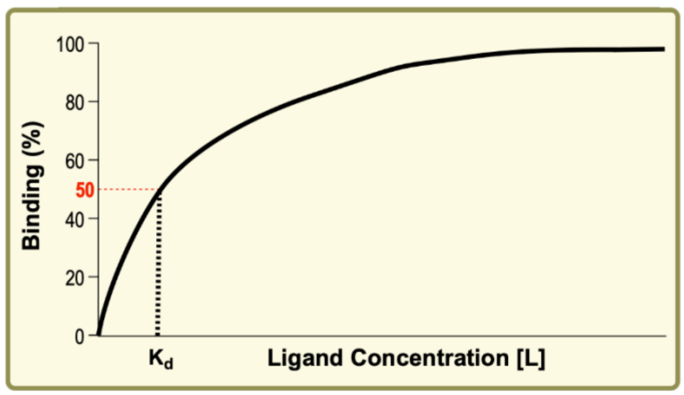
$$K_d = \frac{[\quad][\quad]}{[\quad]} = \frac{\quad}{\quad} = \frac{1}{\quad}$$

K_d Units: ______

●The ______ &______ are very similar to each other (ex. **K_d** & protein-affinity for ligand are _____________ proportional).

- □ Therefore, the ___________ the K_d value, the *stronger* the affinity a protein has for that ligand.
- □ Similar to how **K_m** = [**S**] that allows **V_0** = ½**V_{max}**, **K_d** = [___] that allows _____ *L-binding-sites* to be *occupied*.





CONCEPT: PROTEIN-LIGAND EQUILIBRIUM CONSTANTS

PRACTICE: Protein A has a binding site for ligand X with a K_d of 54 mM. Protein B has a binding site for ligand X with a K_d of 58 mM. Answer the following questions based on this information:

A) Which protein has a stronger affinity for ligand X?

a) Protein A. b) Protein B.

B) Convert the K_d to K_a for both proteins.

K_a for Protein A: __________ K_a for Protein B: __________

PRACTICE: You prepare a solution of protein and its ligand where the initial concentrations are [P] = 10 mM and [L] = 10 mM. At equilibrium you measure the concentration of the complex [PL] = 5 mM. If the protein-ligand reaction can be represented by $P + L \rightleftharpoons PL$, what is the K_d of the reaction under these conditions?

a) 0.05 mM.
b) 20 nM.
c) 5 mM.
d) 25 μM.
e) 20 mM.
f) 25 mM.