CONCEPT: SEQUENTIAL MODEL
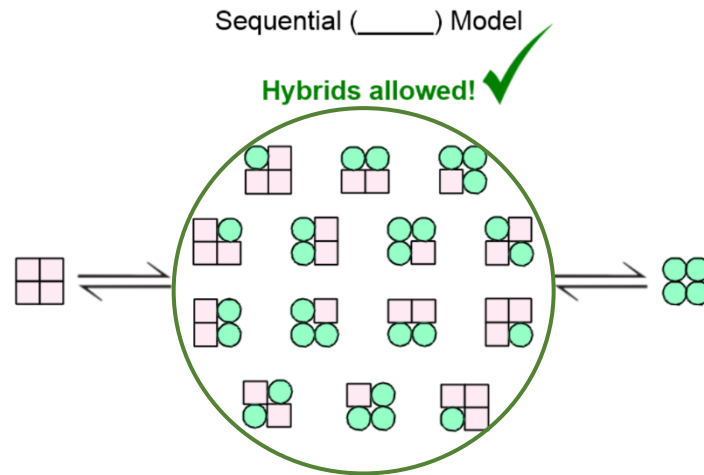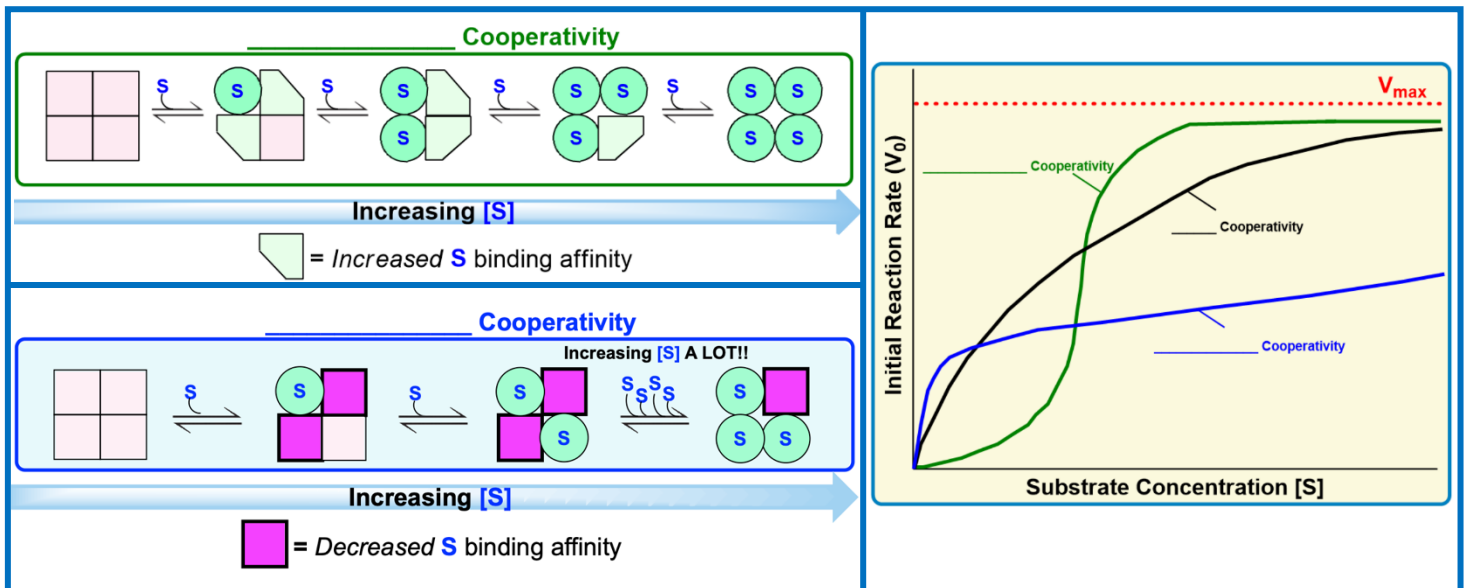
● *Sequential* (*KNF*) *Model*: an allosteric enzyme's *subunits* undergo _____ T & R State changes (via **S** *induced-fit*).

　□ Subunits of the same allosteric enzyme can be present in different states (_____ are allowed).

　□ In other words, T State to R State transitions do _____ necessarily encompass the *entire* allosteric enzyme.

Sequential (_____) Model

Hybrids allowed! ✔

Positive & Negative Cooperativity of Sequential Model

● Unlike the concerted model, the sequential model allows for both *positive* & _____ cooperativity.

　□ **S** binding to one subunit _____ likelihood of *neighboring* subunits to take on *either* a T or R state.

　□ *Positive Cooperativity*: binding of **S** on a subunit promotes neighboring subunits to take on the ____ state.

　□ *Negative Cooperativity*: binding of **S** on a subunit promotes neighboring subunits to take on the ____ state.

EXAMPLE: Positive & Negative Cooperativity of the Sequential Model.

PRACTICE: True or False: Most allosteric enzymes behave according to the concerted model, not the sequential model.

　　　a) True.　　　　　　　b) False.

Concerted Model vs. Sequential Model

●Most allosteric enzymes behave according to some _____ of the *concerted* & *sequential* models.

Concerted (MWC) Model

All subunits *always* in _____ state.

No *substrate* needed for T⇌R conversion
&
No hybrids allowed!

Concerted (_____) Model	*Sequential* (_____) Model
T/R state conversions occur _____ in *all* subunits.	T/R state conversions occur _____ in each subunit.
T/R state conversions do _____ require *substrate*.	T/R state conversions occur via *substrate* binding (_____-Fit).
_____ hybrids allowed.	Hybrids allowed.
Only allows _____ cooperativity.	Allows both *positive* & _____ cooperativity.

Sequential (KNF) Model

Hybrids allowed! ✔

PRACTICE: Which of the following is not a difference between the Concerted & Sequential models of allosteric enzymes?

a) The sequential model considers the induced-fit model of substrate binding whereas the concerted model focuses on perturbing the equilibrium between the T and R states.

b) Positive cooperativity can be explained by the sequential model but not by the concerted model.

c) The sequential model allows for subunits to be in different conformations while the concerted model does not.

d) Negative cooperativity can be explained by the sequential model but not by the concerted model.

e) Both models can have one or multiple subunits bound to a single enzyme for proper function.

f) All the above are true.

PRACTICE: The Sequential model for allosteric enzyme behavior:

a) Cannot account for the reactions that display negative cooperativity.

b) Postulates binding of substrates & inhibitors by the induced-fit model.

c) Requires that the conformation of all subunits change simultaneously.

d) Is conceptually and mathematically simpler than the concerted model.

PRACTICE: Which of the following best describes negative cooperativity?

a) Binding of one substrate molecule stimulates binding of a second substrate.

b) Binding of one substrate molecule inhibits binding of a second substrate.

c) Binding of one substrate molecule leads to negative reaction rates.

d) Binding of one substrate molecule causes a negative effect/result in the cell.