

1.) a) From class...

$$\text{free surface receptor: } \frac{dR_s}{dt} = -k_f L R_s + k_r R_s^* - k_e R_s + V_s \quad (1)$$

$$\text{bound surface receptor: } \frac{dR_s^*}{dt} = k_f L R_s - k_r R_s^* - k_e^* R_s^* \quad (2)$$

$$\text{total internal receptor: } \frac{dR_i^T}{dt} = k_e R_s + k_e^* R_s^* - k_{deg} R_i^T \quad (3)$$

$$R_i^T = R_i^s + R_i^*$$

when recycled, both have k_{rec}

w/ recycling...

$$\text{free surface receptor: } \frac{dR_s}{dt} = -k_f L R_s + k_r R_s^* - k_e R_s + V_s + k_{rec} R_i \quad (4)$$

$$\text{bound surface receptor: } \frac{dR_s^*}{dt} = k_f L R_s - k_r R_s^* - k_e^* R_s^* + k_{rec} R_i^* \quad (5)$$

$$\text{free endosome receptor: } \frac{dR_i}{dt} = k_e R_s - k_{deg} R_i - k_{rec} R_i \quad (6)$$

$$\text{bound endosome receptor: } \frac{dR_i^*}{dt} = k_e^* R_s^* - k_{deg} R_i^* - k_{rec} R_i^* \quad (7)$$

Total $[R_s^*]$:

$$\begin{aligned} \text{a) S.S. (4)} \quad 0 &= -k_f L R_s + k_r R_s^* - k_e R_s + V_s + k_{rec} R_i \\ (k_f L + k_e) R_s &= k_r R_s^* + V_s + k_{rec} R_i \\ R_s &= \frac{k_r R_s^* + V_s + k_{rec} R_i}{k_f L + k_e} \end{aligned}$$

$$\begin{aligned} \text{(5)} \quad 0 &= k_f L R_s - k_r R_s^* - k_e^* R_s^* + k_{rec} R_i^* \\ R_s &= \frac{(k_r + k_e^*) R_s^* - k_{rec} R_i^*}{k_f L} \end{aligned}$$

$$(4)-(5) \Rightarrow \frac{K_r R_s^* + V_s + K_{rec} R_i}{(K_{eL} + K_e)} = \frac{(K_r + K_e) R_s^* - K_{rec} R_i}{K_{eL}}$$

$$(K_{eL} + K_e)(K_r + K_e) R_s^* - (K_{eL} + K_e) K_{rec} R_i = K_{eL} K_r R_s^* + K_{eL} V_s + K_{eL} K_{rec} R_i$$

$$(K_{eL} + K_e)(K_r + K_e) R_s^* - (K_{eL} + K_e) K_{rec} R_i = K_{eL} K_r R_s^* + K_{eL} V_s + K_{eL} K_{rec} R_i$$

$$(K_e^* K_{eL} + K_{eL} K_r + K_e K_e^*) R_s^* = K_{eL} V_s + (K_{eL} + K_e) K_{rec} R_i + K_{eL} K_{rec} R_i$$

divide
by K_{eL}

$$\left(K_e^* + \frac{K_{eL} K_r}{K_{eL}} + \frac{K_e K_e^*}{K_{eL}} \right) R_s^* = V_s + \left(1 + \frac{K_e}{K_{eL}} \right) K_{rec} R_i + K_{rec} R_i$$

$$R_s^* = V_s \frac{1}{K_e^* + \frac{K_{eL} K_r}{K_{eL}} + \frac{K_e K_e^*}{K_{eL}}} + \frac{(1 + \frac{K_e}{K_{eL}}) K_{rec} R_i + K_{rec} R_i}{K_e + \frac{K_{eL} K_r}{K_{eL}} + \frac{K_e K_e^*}{K_{eL}}}$$

$$R_s^* = V_s \frac{K_{eL}}{K_e^* K_{eL} + K_{eL} K_r + K_e K_e^*} + \frac{(K_{eL} + K_e) K_{rec} R_i + K_{eL} K_{rec} R_i}{K_e^* K_{eL} + K_{eL} K_r + K_e K_e^*}$$

$$R_s^* = \frac{V_s}{K_e^*} \frac{K_{eL}}{K_e^* K_{eL} + K_e(K_r + K_e^*)} + \frac{((K_e^* K_{eL} + K_e^* K_e) K_{rec} R_i + K_{eL} K_{eL} K_{rec} R_i)}{K_e^* K_{eL} + K_e(K_r + K_e^*)}$$

$$\text{let } K_{ss} = \frac{K_e^* K_{eL}}{K_e(K_r + K_e^*)}$$

$$R_s^* = \frac{V_s}{K_e^*} \frac{K_{ss} L}{K_{ss} L + 1} + \frac{(K_{ss} L + K_{ss} \frac{K_e}{K_e^*}) K_{rec} R_i + K_{ss} L K_{rec} R_i}{K_{ss} L + 1} \frac{1}{K_e^*}$$

$$R_s^* = \left(\frac{V_s}{K_e^*} \right) \frac{K_{ss} L}{K_{ss} L + 1} + \left(\frac{K_{rec}}{K_e^*} \right) \frac{K_{ss} L (R_i^* + R_i)}{K_{ss} L + 1} + \frac{K_{ss} \frac{K_e}{K_e^*} R_i^*}{K_{ss} L + 1}$$

@ SS. (7) $\theta = K_e^* R_s^* - K_{deg} R_i^* - K_{rec} R_i^*$

(9) $R_i^* = \frac{K_e^* R_s^*}{(K_{deg} + K_{rec})}$

continued
simplification...

expression for total concentration of active receptor

$$(7) \quad R_i^* = \frac{k_e^* R_s^*}{(k_{deg} + k_{rec})}$$

$$(8) \quad R_s^* = \frac{K_{ss}}{K_{ss}L + 1} \left[\frac{V_s}{K_e^*} L + \frac{k_{rec}}{k_e^*} \left(R_i^T L + \frac{k_e}{k_f} R_i^* \right) \right]$$

$$R_T^* = R_s^* + R_i^* \quad (8) + (9)$$

→ to get maximum total concentration of active receptor,
 $\frac{K_{ss}L}{K_{ss}L + 1} = 1$ (ranges 0 to 1) $\therefore L$ should be very large

So when L is large...

$$R_s^* = \frac{K_{ss}}{K_{ss}L + 1} \left[\frac{V_s}{K_e^*} L + \frac{k_{rec}}{k_e^*} \left(R_i^T L + \frac{k_e}{k_f} R_i^* \right) \right]$$

$$R_s^* = \frac{K_{ss}L}{K_{ss}L + 1} \left(\frac{V_s}{K_e^*} + \frac{k_{rec}}{k_e^*} R_i^T \right)$$

$$R_s^* = \frac{V_s}{K_e^*} + \frac{k_{rec}}{k_e^*} R_i^T$$

$$R_T^* = R_s^* + R_i^* = \frac{V_s}{K_e^*} + \frac{k_{rec}}{k_e^*} R_i^T + \frac{k_e^*}{(k_{deg} + k_{rec})} \left(\frac{V_s}{K_e^*} + \frac{k_{rec}}{k_e^*} R_i^T \right)$$

$$R_{T,m}^* = \left(\frac{1}{K_e^*} + \frac{1}{(k_{deg} + k_{rec})} \right) (V_s + k_{rec} R_i^T)$$

By including the recycling process, the surface receptor balance equations now rely on internal receptors as well. So, the maximum concentration of active receptors now relies on the total internal receptors and the k_{rec} term. More specifically, k_{rec} act as if it is a resistor in series with k_{deg} , which then is parallel to k_e ; within the first quantity representing resistance to reaching $R_{T,m}^*$. Then

the second quantity is just the synthesis & recycling of the receptors.