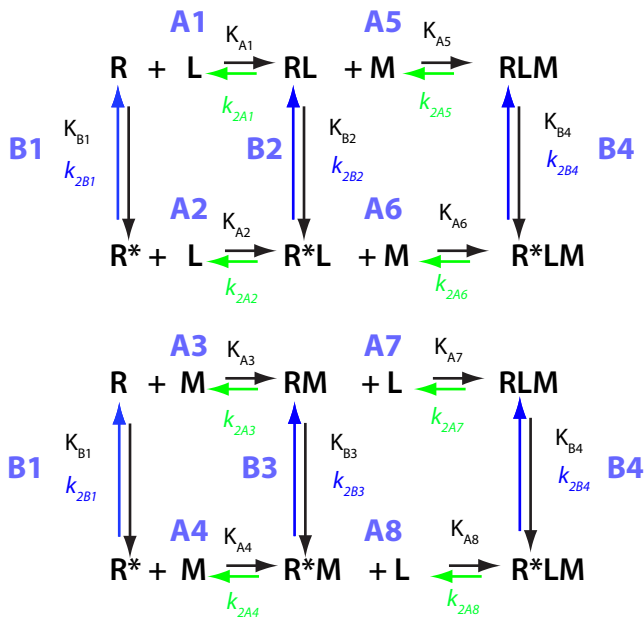


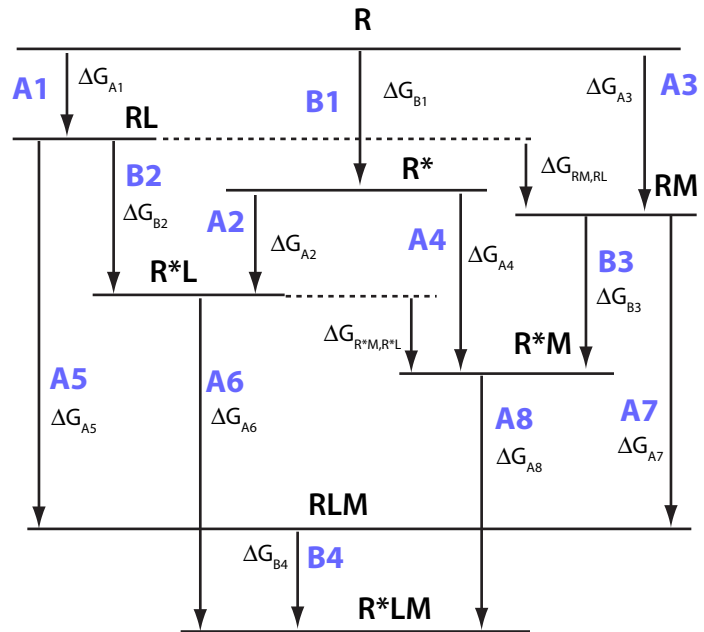
U-R-RL-RM-RLM

Binding of two ligands at *non-mutually exclusive* binding sites coupled with intramolecular isomerization of the receptor (*allosterically linked* binding sites).

Reaction scheme



Free-energy diagram
(positions of energy levels are chosen for easy viewing)



Thermodynamic cycles

$$\Delta G_{B1}^{\circ} + \Delta G_{A2}^{\circ} = \Delta G_{A1}^{\circ} + \Delta G_{B2}^{\circ}, \quad K_{B1} K_{A2} = K_{A1} K_{B2}$$

$$\Delta G_{B1}^{\circ} + \Delta G_{A4}^{\circ} = \Delta G_{A3}^{\circ} + \Delta G_{B3}^{\circ}, \quad K_{B1} K_{A4} = K_{A3} K_{B3}$$

$$\Delta G_{A1}^{\circ} + \Delta G_{A5}^{\circ} = \Delta G_{A3}^{\circ} + \Delta G_{A7}^{\circ}, \quad K_{A1} K_{A5} = K_{A3} K_{A7}$$

$$\Delta G_{A1}^{\circ} + \Delta G_{B2}^{\circ} + \Delta G_{A6}^{\circ} = \Delta G_{A3}^{\circ} + \Delta G_{B3}^{\circ} + \Delta G_{A8}^{\circ}, \quad K_{A1} K_{B2} K_{A6} = K_{A3} K_{B3} K_{A8}$$

For calculations I will assume that I know equilibrium constants for B1, B2, B3, B4, A1, A3, A5 and A7. Dependent constants then correspond to A2, A4, A6, A7 and A8. :

$$\begin{aligned}
 K_{A2} &= K_{A1} K_{B2} / K_{B1} \\
 K_{A4} &= K_{A3} K_{B3} / K_{B1} \\
 K_{A6} &= K_{A5} K_{B4} / K_{B2} \\
 K_{A7} &= K_{A1} K_{A5} / K_{A3} \\
 K_{A8} &= K_{A7} K_{B4} / K_{B3}
 \end{aligned}$$

Additional equilibrium constants between alternative forms of R and R* may be determined as:

Relationship between concentrations of bound forms of R:

$$\begin{aligned}
 K_{\text{RM,RL}} &= [\text{RM}][\text{L}] / \{[\text{RL}][\text{M}]\} \\
 \Delta G_{A3}^{\circ} - \Delta G_{A1}^{\circ} &= \Delta G_{\text{RM,RL}}^{\circ} \\
 K_{\text{RM,RL}} &= K_{A3} / K_{A1}
 \end{aligned}$$

Relationship between concentrations of bound forms of R*:

$$\begin{aligned}
 K_{\text{R}^*\text{M,R}^*\text{L}} &= [\text{R}^*\text{M}][\text{L}] / \{[\text{R}^*\text{L}][\text{M}]\} \\
 \Delta G_{A3}^{\circ} + \Delta G_{B3}^{\circ} - \Delta G_{A1}^{\circ} - \Delta G_{B2}^{\circ} &= \Delta G_{\text{R}^*\text{M,R}^*\text{L}}^{\circ} \\
 K_{\text{R}^*\text{M,R}^*\text{L}} &= K_{A3} K_{B3} / (K_{A1} K_{B2})
 \end{aligned}$$