Receptor Thermodynamic to Kinematic Conversion

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We have the following concentrations for the three constituent elements:

- Receptor domain 1: $[R_1]$
- Receptor domain 2: $[R_2]$
- Ligand: $[L]$

Now we have the following configurational states:

State/Concentration	Configuration	Energy
$[R_1]$	Unbound receptor	ϵ_0
$[C_{off}] = [R_1 - R_2]$	Bound receptor w/o ligand	$\epsilon_0 + \Delta\epsilon_b - k_b T \ln[R_2]$
$[C_{on}] = [R_1 - R_2 - L]$	Bound receptor w/ ligand	$\epsilon_0 + \Delta\epsilon_b - k_b T \ln[R_2] + \Delta\epsilon_L - k_b T \ln[L]$

The probability of the unbound state is

$$p(R_1) = \frac{[R_1]}{[R_1] + [R_1 - R_2] + [R_1 - R_2 - L]} = \frac{e^{-\beta\epsilon_0}}{e^{-\beta\epsilon_0} + e^{-\beta(\epsilon_0 + \Delta\epsilon_b - k_b T \ln[R_2])} + e^{-\beta(\epsilon_0 + \Delta\epsilon_b - k_b T \ln[R_2] + \Delta\epsilon_L - k_b T \ln[L])}} \tag{1}$$

$$= \frac{1}{1 + [R_2]e^{-\beta\Delta\epsilon_b} + [R_2][L]e^{-\beta(\Delta\epsilon_B + \Delta\epsilon_L)}} \tag{2}$$

Similarly, the probabilities of the other two states are

$$p(C_{off}) = \frac{[R_1 - R_2]}{[R_1] + [R_1 - R_2] + [R_1 - R_2 - L]} = \frac{[R_2]e^{-\beta\Delta\epsilon_b}}{1 + [R_2]e^{-\beta\Delta\epsilon_b} + [R_2][L]e^{-\beta(\Delta\epsilon_B + \Delta\epsilon_L)}} \tag{3}$$

$$p(C_{on}) = \frac{[R_1 - R_2 - L]}{[R_1] + [R_1 - R_2] + [R_1 - R_2 - L]} = \frac{[R_2][L]e^{-\beta(\Delta\epsilon_B + \Delta\epsilon_L)}}{1 + [R_2]e^{-\beta\Delta\epsilon_b} + [R_2][L]e^{-\beta(\Delta\epsilon_B + \Delta\epsilon_L)}} \tag{4}$$

$$\tag{5}$$

Now we can convert to kinetic coefficients. There are three transitions we can consider, each related to a ratio of probabilities. First the transitions from unbound to off

$$k^+_{R_1 \to off}[R_1][R_2] = k^-_{R_1 \to off}[C_{off}] \tag{6}$$

From this, we see that the kinetic coefficients are given by,

$$\frac{k^+_{R_1 \to off}}{k^-_{R_1 \to off}} = \frac{[C_{off}]}{[R_1][R_2]} = \frac{p(C_{off})}{p(R_1)[R_2]} = e^{-\beta\Delta\epsilon_b} \tag{7}$$

Next, the transition from off to on,

$$k^+_{off \to on}[C_{off}][L] = k^-_{off \to on}[C_{on}] \tag{8}$$

which gives us

$$\frac{k^+_{off \to on}}{k^-_{off \to on}} = \frac{[C_{on}]}{[C_{off}][L]} = \frac{p(C_{on})}{p(C_{off})[L]} = e^{-\beta\Delta\epsilon_L} \tag{9}$$

Finally, the transition from on to unbound,

$$k^+_{on \to R_1}[C_{on}] = k^-_{on \to R_1}[R_1][R_2][L] \tag{10}$$

which gives us

$$\frac{k^+_{on\to R_1}}{k^-_{on\to R_1}} = \frac{[R_1][R_2][L]}{[C_{on}]} = \frac{p(R_1)[R_2][L]}{p(C_{on})} = \frac{1}{e^{-\beta(\Delta\epsilon_B+\Delta\epsilon_L)}} \tag{11}$$

Note that the kinetic coefficients are related such that

$$\frac{k^+_{R_1\to off}}{k^-_{R_1\to off}}\frac{k^+_{off\to on}}{k^-_{off\to on}}\frac{k^+_{on\to R_1}}{k^-_{on\to R_1}} = 1 \tag{12}$$

Finally, we want the combined concentration of $[C_{off}]$ and $[C_{on}]$,

$$\frac{[C_{tot}]}{[R_1]+[C_{off}]+[C_{on}]} = p(C_{off}) + p(C_{on}) \tag{13}$$

$$= \frac{e^{-\beta\Delta\epsilon_b} + [R_2][L]e^{-\beta(\Delta\epsilon_B+\Delta\epsilon_L)}}{1+[R_2]e^{-\beta\Delta\epsilon_b} + [R_2][L]e^{-\beta(\Delta\epsilon_B+\Delta\epsilon_L)}} \tag{14}$$

$$= p(R_1)[R_2]e^{-\beta\Delta\epsilon_b}\left(1+[L]e^{-\beta\Delta\epsilon_L}\right) \tag{15}$$

$$= \frac{[R_1]}{[R_1]+[C_{off}]+[C_{on}]}[R_2]\frac{k^+_{R_1\to off}}{k^-_{R_1\to off}}\left(1+[L]\frac{k^+_{off\to on}}{k^-_{off\to on}}\right) \tag{16}$$

Multiplying both sides by the total concentration,

$$[C_{tot}] = [R_1][R_2]\frac{k^+_{R_1\to off}}{k^-_{R_1\to off}}\left(1+[L]\frac{k^+_{off\to on}}{k^-_{off\to on}}\right) \tag{17}$$