

Control of DNA Strand Displacement Kinetics using Toehold Exchange

Addendum

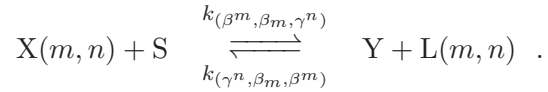
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Addendum: Derivation of BM rate constants with reverse reaction.

In the derivation of the BM rate constant in text S1, we ignored the reverse reaction $Y + L(m, n) \rightarrow X(m, n) + S$ for simplicity of derivation and because it reflected experimental conditions. Here, we show that the BM rate constants derived in the analysis of the full reaction model including that reverse reaction is actually identical to that derived earlier. Recall that the net toehold exchange reaction can be expressed as:



The expressions for the forward and reverse BM rate constants $k_{(\beta^m, \beta_m, \gamma^n)}$ and $k_{(\gamma^n, \beta_m, \beta^m)}$ must capture the kinetics of the overall reaction:

$$\frac{d[Y]}{dt} = \frac{d[L(m, n)]}{dt} = k_{(\beta^m, \beta_m, \gamma^n)}[X(m, n)][S] - k_{(\gamma^n, \beta_m, \beta^m)}[Y][L(m, n)] \quad (1)$$

$$\frac{d[X(m, n)]}{dt} = \frac{d[S]}{dt} = k_{(\gamma^n, \beta_m, \beta^m)}[Y][L(m, n)] - k_{(\beta^m, \beta_m, \gamma^n)}[X(m, n)][S] . \quad (2)$$

From the three-step model, the rates of production of Y and S are expressed as:

$$\frac{d[Y]}{dt} = k_r(\beta^m)[J] - k_f[Y][L(m, n)] \quad (3)$$

$$\frac{d[S]}{dt} = k_r(\beta^n)[I] - k_f[X(m, n)][S] . \quad (4)$$

We use QSS to analyze the production rate of Y and S from the three-step model. Under QSS, the steady state conditions on intermediates I and J are:

$$\frac{d[I]}{dt} = k_f[X(m, n)][S] + k_b[J] - k_b[I] - k_r(\gamma^n)[I] \approx 0 \quad (5)$$

$$\frac{d[J]}{dt} = k_b[I] + k_f[Y][L(m, n)] - k_b[J] - k_r(\beta^m)[J] \approx 0 . \quad (6)$$

Rearranging eq. (6),

$$[I] = \frac{k_b[J] + k_r(\beta^m)[J] - k_f[Y][L(m, n)]}{k_b}$$

Substituting this expression for [I] back into equation (5),

$$\begin{aligned}
0 &= k_f[X(m, n)][S] + k_b[J] - \left(k_b[J] + k_{r(\beta^m)}[J] - k_f[Y][L(m, n)] \right) \frac{k_b + k_{r(\gamma^n)}}{k_b} \\
0 &= k_f[X(m, n)][S] + \left(k_f + \frac{k_f k_{r(\gamma^n)}}{k_b} \right) [Y][L(m, n)] - \left(k_{r(\beta^m)} + k_{r(\gamma^n)} + \frac{k_{r(\beta^m)} k_{r(\gamma^n)}}{k_b} \right) [J] \\
[J] &= \frac{k_f k_b [X(m, n)][S] + (k_f k_b + k_f k_{r(\gamma^n)}) [Y][L(m, n)]}{k_b k_{r(\beta^m)} + k_b k_{r(\gamma^n)} + k_{r(\gamma^n)} k_{r(\beta^m)}} .
\end{aligned}$$

Substituting this expression for [J] into equation (3),

$$\begin{aligned}
\frac{d[Y]}{dt} &= k_{r(\beta^m)}[J] - k_f[Y][L(m, n)] \\
&= \frac{k_f k_b k_{r(\beta^m)} [X(m, n)][S] + (k_f k_b k_{r(\beta^m)} + k_f k_{r(\gamma^n)} k_{r(\beta^m)}) [Y][L(m, n)]}{k_b k_{r(\beta^m)} + k_b k_{r(\gamma^n)} + k_{r(\gamma^n)} k_{r(\beta^m)}} - k_f [Y][L(m, n)] \\
&= \frac{k_{r(\beta^m)} k_f k_b}{k_{r(\gamma^n)} k_{r(\beta^m)} + k_{r(\gamma^n)} k_b + k_{r(\beta^m)} k_b} [X(m, n)][S] - \frac{k_{r(\gamma^n)} k_f k_b}{k_{r(\gamma^n)} k_{r(\beta^m)} + k_{r(\gamma^n)} k_b + k_{r(\beta^m)} k_b} [Y][L(m, n)] .
\end{aligned}$$

Combining this result with equation (1), we derive the BM rate constants $k_{(\beta^m, \beta_m, \gamma^n)}$ and $k_{(\gamma^n, \beta_m, \beta^m)}$:

$$\begin{aligned}
k_{(\beta^m, \beta_m, \gamma^n)} &= \frac{k_{r(\beta^m)} k_f k_b}{k_{r(\gamma^n)} k_{r(\beta^m)} + k_{r(\gamma^n)} k_b + k_{r(\beta^m)} k_b} \\
k_{(\gamma^n, \beta_m, \beta^m)} &= \frac{k_{r(\gamma^n)} k_f k_b}{k_{r(\gamma^n)} k_{r(\beta^m)} + k_{r(\gamma^n)} k_b + k_{r(\beta^m)} k_b} .
\end{aligned}$$

Solving for steady state [I] and substituting into equation (4) yields the same rate constant expressions.