A Kinetic Study of Domain Swapping in Protein L

For a homodimerization reaction of a protein according to the scheme

\[
M + M \xleftrightarrow{\kappa_{\text{dim}} \kappa_{\text{mon}}} D
\]

\(k_{\text{dim}}\) and \(k_{\text{mon}}\) are the rate constants for dimerization and monomerization, and the
dissociation constant of the homodimer \(D\) is given by

\[
K_d = \frac{k_{\text{mon}}}{k_{\text{dim}}}
\]

The rate equations for the forward and backward reactions are:

\[
\frac{d[M]}{dt} = -k_{\text{dim}} [M]^2 + 2k_{\text{mon}} [D]
\]

\[
\frac{d[D]}{dt} = k_{\text{dim}} [M]^2 - k_{\text{mon}} [D]
\]

where \([M]\) and \([D]\) are the concentrations of the momomeric and the dimeric state.

For a total concentration of protein, \(c_0\), with

\[
c_0 = [M] + 2 \cdot [D]
\]

\([M]\) is given by

\[
[M] = c_0 - 2 \cdot [D]
\]
Using equations (1) and (5) the rate equation (3) can be recast to

\[ \frac{d[D]}{dt} = k_{\text{dim}} \left( c_0 - 2 \cdot [D] \right)^2 - k_{\text{dim}} \cdot K_d \cdot [D] \]

which can be written as

\[ \frac{d[D]}{\left( [D]^2 + [D] \cdot \left( -c_0 - \frac{K_d}{2} \right) + \frac{1}{4} (c_0)^2 \right)} = -4k_{\text{dim}} \cdot dt \]

expansion of the left hand side into partial fractions using

\[ \frac{d[D]}{[D] - \lambda_1 \cdot (D - \lambda_2)} = -4k_{\text{dim}} \cdot dt \]

and

\[ \lambda_{1/2} = \frac{1}{2} \left( \frac{k_{\text{mon}}}{4k_{\text{dim}}} + c_0 \right) \pm \sqrt{\frac{1}{4} \left( \frac{k_{\text{mon}}}{4k_{\text{dim}}} + c_0 \right)^2 - \frac{1}{4} (c_0)^2} \]

yields

\[ \frac{d[D]}{(\lambda_1 - \lambda_2)(D - \lambda_1)} + \frac{d[D]}{(\lambda_1 - \lambda_2)(D - \lambda_2)} = -4k_{\text{dim}} \cdot dt \]

Integration of equation (10) on both sides gives

\[ \frac{1}{(\lambda_1 - \lambda_2)} \cdot \ln \left( \frac{[D] - \lambda_2}{[D] - \lambda_1} \right) = -4k_{\text{dim}} \cdot t + \text{const} \]
Assuming $[D] = 0$ at $t = 0$ (i.e. starting the reaction from the monomer) to calculate

\begin{equation}
\text{const} = \frac{1}{(\lambda_1 - \lambda_2)} \cdot \ln \left( \frac{\lambda_2}{\lambda_1} \right)
\end{equation}

yields the time course of the concentrations of homodimer, $[D(t)]$, and monomer, $[M(t)]$, as

\begin{equation}
[D(t)] = \frac{\lambda_1 \lambda_2 \left(1 - \exp\left(-4k_{\text{dim}}(\lambda_1 - \lambda_2) \cdot t\right)\right)}{\lambda_1 - \lambda_2 \exp\left(-4k_{\text{dim}}(\lambda_1 - \lambda_2) \cdot t\right)}
\end{equation}

\begin{equation}
[M(t)] = c_0 - 2 \frac{\lambda_1 \lambda_2 \left(1 - \exp\left(-4k_{\text{dim}}(\lambda_1 - \lambda_2) \cdot t\right)\right)}{\lambda_1 - \lambda_2 \exp\left(-4k_{\text{dim}}(\lambda_1 - \lambda_2) \cdot t\right)}
\end{equation}

Populations of M and D are obtained by dividing equations (13) and (14) by $c_0$. 

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