Caspase folding kinetics

Caspase-3 has been shown to have a domain-swapped folded form (F_2) and a dimeric intermediate (I_2). The mechanism is:

$$2\,U \underset{k_{-1}}{\overset{k_1}{\leftrightarrows}} I_2 \xrightarrow{k_2} F_2$$

Assuming that $k_2 >> k_1$ determine an expression for the rate of formation of the folded dimer F_2 as a function of the concentration of the starting unfolded polypeptide [U].

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Solution: First we express the mechanistic rate scheme in terms of kinetic equations.

$$\frac{d[U]}{dt} = -k_1[U]^2 + k_{-1}[I_2]$$

$$\frac{d[I_2]}{dt} = -(k_{-1} + k_2)[I_2] + k_1[U]^2$$

$$\frac{d[F_2]}{dt} = k_2[I_2]$$

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Since k_2 >> k_1 we can apply the steady state approximation

$$\frac{d[I_2]}{dt} = -(k_{-1} + k_2)[I_2] + k_1[U]^2 \approx 0$$

We solve the concentration of the intermediate I_2.

$$[I_2] \approx \frac{k_1[U]^2}{k_{-1} + k_2}$$

We substitute that solution into the equation for the appearance of the folded product to obtain an equation interms of the initial unfolded protein U.

$$\frac{d[F_2]}{dt} = k_2[I_2] = \frac{k_1 k_2[U]^2}{k_{-1} + k_2}$$