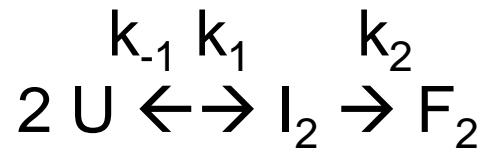


Caspase folding kinetics

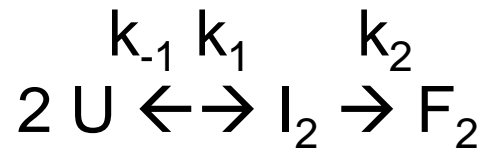
Caspase-3 has been shown to have a domain-swapped folded form (F_2) and a dimeric intermediate (I_2). The mechanism is:



Assuming that $k_2 \gg k_1$ 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 $[U]$.

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:



Assuming that $k_2 \gg k_1$ 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 $[U]$.

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

$$\begin{aligned}\frac{d[U]}{dt} &= -k_1[U]^2 + k_{-1}[I_2] \\ \frac{d[I_2]}{dt} &= -(k_{-1} + k_2)[I_2] + k_1[U]^2 \\ \frac{d[F_2]}{dt} &= k_2[I_2]\end{aligned}$$

Caspase folding kinetics

Since $k_2 \gg k_1$ 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 in terms of the initial unfolded protein U .

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