Immunoglobulin folding kinetics

The maturation of immunoglobulins involves a folding pathway followed by dimerization. The mechanism is:

$$\mathrm{U} \underset{k_{-1}}{\overset{k_1}{\leftrightarrow}} \mathrm{I} \xrightarrow{k_2} \mathrm{N}$$

$$2\mathrm{N} \xrightarrow{k_3} \mathrm{F}_2$$

a.) Write down the rate equations for each of the species in this rate scheme.

b.) Assuming that $k_2 >> k_1$ and $k_3 >> k_2$ determine an expression for the rate of formation of the folded immunoglobulin dimer F_2 as a function of the concentration of the starting unfolded monomer [U].

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a.) Write down the rate equations for each of the species in this rate scheme.

Solution:

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

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

$$\frac{d[N]}{dt} = k_2[I] - k_3[N]^2$$

$$\frac{d[F_2]}{dt} = k_3[N]^2$$

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b.) Assuming that $k_2 >> k_1$ and $k_3 >> k_2$ determine an expression for the rate of formation of the folded immunoglobulin dimer F_2 as a function of the concentration of the starting unfolded monomer [U].

Solution: Apply the steady state approximation to the dimeric intermediate I and N.

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

$$\frac{d[N]}{dt} = k_2[I] - k_3[N]^2 \approx 0$$

$$[I] = \frac{k_1[U]}{k_{-1} + k_2}$$

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b.) Assuming that $k_2 >> k_1$ and $k_3 >> k_2$ determine an expression for the rate of formation of the folded immunoglobulin dimer F_2 as a function of the concentration of the starting unfolded monomer [U].

Complete the substutions to solve for an expression for the final folded immunoglobulin dimer.

$$k_3[N]^2 = k_2[I] = \frac{k_1 k_2[U]}{(k_{-1} + k_2)}$$

$$\frac{d[F_2]}{dt} = \frac{k_1 k_2[U]}{(k_{-1} + k_2)}$$