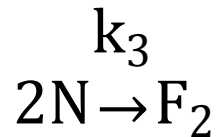
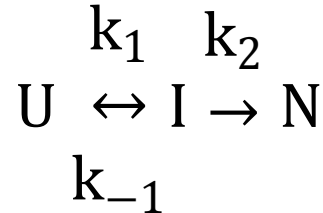


# Immunoglobulin folding kinetics

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



- a.)** Write down the rate equations for each of the species in this rate scheme.
- b.)** Assuming that  $k_2 \gg k_1$  and  $k_3 \gg k_2$  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  $[U]$ .

# Immunoglobulin folding kinetics

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

Solution:

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

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

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

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

# Immunoglobulin folding kinetics

**b.)** Assuming that  $k_2 \gg k_1$  and  $k_3 \gg k_2$  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  $N$ .

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

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

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

# Immunoglobulin folding kinetics

**b.)** Assuming that  $k_2 \gg k_1$  and  $k_3 \gg k_2$  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 substitutions to solve for an expression for the final folded immunoglobulin dimer.

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

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