Barnase folding process

Barnase is a two-state protein that is denatured in guanidium hydrochloride (GdnHCl). Barnase is 50% unfolded in 3 M GdnHCl, but 99% folded in 0.03 M GdnHCl. If 3 M solution of Barnase is diluted by a factor of 100 (i.e. to 0.03 M) it is observed to reach its new equilibrium in 12 minutes. What is the folding rate constant of this protein?

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Solution: Use microscopic reversibility

$$K = \frac{k_f}{k_u}$$

And the observed rate constant for approach to equilibrium

$$k_{obs} = k_f + k_u = k_f + \frac{k_f}{K} = k_f\left(1 + \frac{1}{K}\right)$$

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Insert the given values to calculate the folding rate constant

$$k_f = \frac{k_{obs}}{\left(1 + \frac{1}{K}\right)} = \frac{1}{\tau_{obs}\left(1 + \frac{fu}{ff}\right)}$$

where fu = fraction unfolded and ff = fraction folded.

$$k_f = \frac{1}{(12\ min.)\left(1 + \frac{1}{99}\right)} = 0.0825\ min^{-1}$$

To put this another way, the folding time (which is the inverse of the folding rate constant) is approximately 12.1 minutes.

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Note on the estimation of the equilibrium constant. The process being considered is a folding equilibrium:

$$u \rightarrow f$$

The equilibrium constant is:

$$K = \frac{[f]}{[u]} = \frac{ff}{fu}$$

We can use the ratio of the fraction in place of the ratio of concentrations.