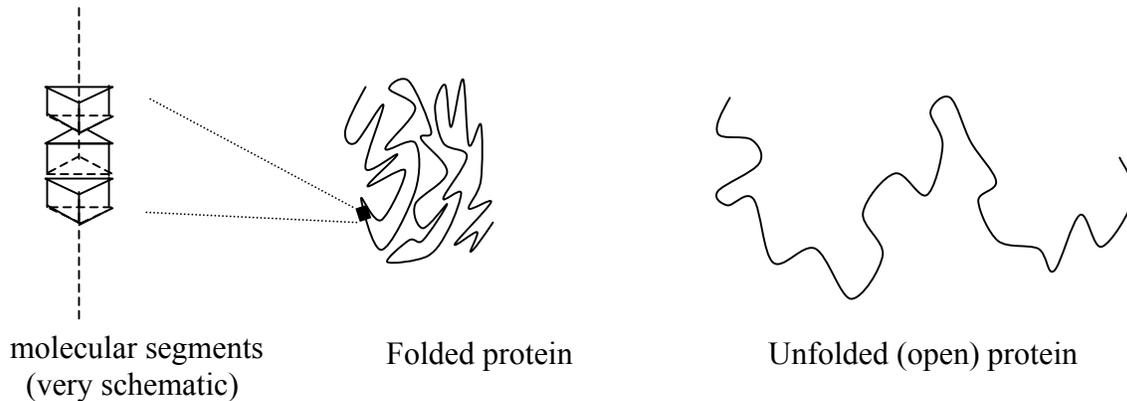


Proteins are long chain molecules. Many of them only function biologically (as enzymes, for example) if they are properly folded up. A simple, very schematic, model consists of  $N$  molecular segments, like the three illustrated schematically below. If the protein is unfolded, each segment can be in one of three possible orientations with respect to its neighbor. If it's folded, each segment must be in one specific orientation.



a) How many configurations are there for the protein to be completely folded ( $\Omega_{\text{folded}}$ ) and to be completely unfolded ( $\Omega_{\text{open}}$ )?

Folded:  $\Omega_F = 1^N = 1$

Unfolded:  $\Omega_U = 3^N$

b) The open molecule has an energy  $\Delta$  higher than in the typical folded state. Recall that the probability of a particular configuration 'c' (open or closed) is given by  $p_c \propto \Omega_c P_c$ , where  $\Omega_c$  is the number of states in that configuration and  $P_c$  is the occupancy probability per state. Complete the following equation in terms of  $N$ ,  $\Delta$  and  $kT$ :

$$R \equiv \frac{\text{Probability}(\text{unfolded})}{\text{Probability}(\text{folded})} = \frac{\Omega_U e^{-E_U/kT}}{\Omega_F e^{-E_F/kT}} = 3^N e^{-\Delta/kT}$$

c) Consider a molecule with  $N = 10$  segments. If  $\Delta = 5 \times 10^{-20}$  J, and the molecule is located in your body ( $T = 310$  K), what is the ratio of the time it spends **open** to the time it spends **folded**?

We just want the ratio of probabilities:  $R = 3^{10} e^{-5 \times 10^{-20} / (1.381 \times 10^{-23} \times 310)} = 0.50$ .

So, the larger number of microstates in the unfolded configuration cancels the Boltzmann factor suppression. The protein spends half of the time folded and unfolded.