CHM/COS/MOL/PHY 231/2 Fall 2007

An integrated, quantitative introduction to the natural sciences

Problem Set 4 **Due Friday, 12 October 2007**

Problem 1: The enzyme lysozyme helps to break down complex molecules built out of sugars. As a first step, these molecules (which we will call S) must bind to the enzyme. In the simplest model, this binding occurs in one step, a second order reaction between the enzyme E and the substrate S to form the complex ES:

$$E + S \stackrel{k_+}{\rightarrow} ES, \tag{1}$$

where k_+ is the second order rate constant. The binding is reversible, so there is also a first order process whereby the complex decays into its component parts:

$$ES \stackrel{k_-}{\rightarrow} E + S, \tag{2}$$

where k_- is a first order rate constant. Let's assume that everything else which happens is slow, so we can analyze just this binding/unbinding reaction.

a. Write out the differential equations that describe the concentrations of $[S]$, $[E]$ and $[ES]$. Remember that there are contributions from both reactions (1) and (2).

b. Show that if we start with an initial concentration of enzyme $[E]_0$ and zero concentration of the complex ($[ES]_0 = 0$), then there is a conservation law: $[E] + [ES] = [E]_0$ at all times.

c. Assume that the initial concentration of substrate $[S]_0$ is in vast excess, so that we can always approximate $[S] \approx [S]_0$. Show that there is a steady state at which the concentration of the complex is no longer changing, and that at this steady state

$$[ES]_{\rm ss} = [E]_0 \cdot \frac{[S]}{[S] + K}, \tag{3}$$

where K is a constant. How is K related to the rate constants k_+ and k_-?

d. When the substrate is (N–acetylglucosamine)$_2$, experiments near neutral pH and at body temperature show that the rate constants are $k_+ = 4 \times 10^7\,{\rm M}^{-1}{\rm s}^{-1}$ and $k_- = 1 \times 10^5\,{\rm s}^{-1}$. What is the value of the constant K [in Eq (3)] for this substrate? At a substrate concentration of $[S] = 1\,{\rm mM}$, what fraction of the initial enzyme concentration will be in the the complex $[ES]$ once we reach steady state?

e. Show that the concentration of the complex $[ES]$ approaches its steady state exponentially: $[ES](t) = [ES]_{\rm ss}[1 - \exp(-t/\tau)]$. Remember that we start with $[ES]_0 = 0$. How is the time constant τ related to the rate constants k_+ and k_- and to the substrate concentration $[S]$? For (N–acetylglucosamine)$_2$, what is the *longest* time τ that we will find for the approach to steady state?

Problem 2: Consider the carbon monoxide molecule CO. To a good approximation, the bond between the atoms acts like a Hooke's law spring of stiffness κ and equilibrium length ℓ_0. For the purposes of this problem, neglect rotations of the molecule, so that motion is only in one dimension, parallel to the bond.

a. Write the differential equations corresponding to $F = ma$ for the positions x_C and x_O of the two atoms. Remember that the two atoms have different masses m_C and m_O.

b. Look for solutions of the form

$$
\begin{aligned}
x_C(t) &= x_C^0 + A \exp(-i\omega t) &(4)\\
x_O(t) &= x_O^0 + B \exp(-i\omega t). &(5)
\end{aligned}
$$

where the resting positions x_C^0 and x_O^0 are chosen to match the equilibrium length of the bond. Show that solutions of this form exist, and find the natural frequency ω for these oscillations.