

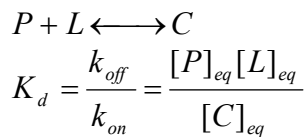
10.37 Exam 2
25 April, 2007
100 points

Problem 1: 35 points

A protein and ligand bind reversibly with $K_d = 10 \text{ nM}$. The association rate constant $k_{on} = 2 \times 10^4 \text{ M}^{-1}\text{s}^{-1}$. The two species are mixed at an initial protein concentration of 3 nM and an initial ligand concentration of 0.2 nM.

- a) At equilibrium, what fraction of the ligand will be complexed with protein? (15 points)
- b) At what time will the fraction of ligand in complex reach 95% of the equilibrium value? (20 points)

Justify any assumptions you make to simplify equations.



Using a batch reactor mole balance and looking at the reaction stoichiometry, it is easy to see that given the initial conditions any unit of complex formed takes away a unit of protein and ligand:

$$[P] + [C] = [P]_0$$

$$[L] + [C] = [L]_0$$

Using these in the equilibrium equation we can get a quadratic equation in $[C]_{eq}$.

$$K_d = \frac{([P]_0 - [C]_{eq})([L]_0 - [C]_{eq})}{[C]_{eq}}$$

$$0 = [C]_{eq}^2 - ([L]_0 + [P]_0 + K_d)[C]_{eq} + [P]_0[L]_0 = 0$$

$$[C]_{eq} = \frac{([L]_0 + [P]_0 + K_d) \pm \sqrt{([L]_0 + [P]_0 + K_d)^2 - 4[P]_0[L]_0}}{2} = 0$$

Reject the positive root, it is too large (larger than the initial amount of ligand and protein).

$$[C]_{eq} = 0.0456 \text{ nM}$$

$$\frac{[C]_{eq}}{[L]_0} = 0.228 = 23\%$$

At this point, it is interesting to look at different approximations to the expression.

Good Approximation: $[P]_0 \gg [C]$

This leads to

$$K_d \approx \frac{([P]_0)([L]_0 - [C]_{eq})}{[C]_{eq}}$$

$$[C]_{eq} = \frac{[L]_0[P]_0}{K_d + [P]_0} = 0.462nM$$

$$\frac{[C]_{eq}}{[L]_0} = 0.231 = 23\%$$

Bad Approximation: $[L]_0 \gg [C]$

$$K_d \approx \frac{([P]_0 - [C]_{eq})([L]_0)}{[C]_{eq}}$$

$$[C]_{eq} = \frac{[L]_0[P]_0}{K_d + [L]_0} = 0.0588$$

$$\frac{[C]_{eq}}{[L]_0} = 0.294 = 29\%$$

The error in $[C]_{eq}$ of the bad approximation is about 30% of the true answer, whereas the good approximation is only off by about 1%.

By noticing that the “good” approximation is a *good* approximation, the dynamic equation becomes easier to solve. (As an aside, an even better approximation would be just to neglect the second order term that is $O([C]_{eq}^2)$.)

Start with the full dynamic equation:

$$\frac{d[C]}{dt} = k_{on}[L][P] - k_{off}[C] = k_{on}([L]_0 - [C])([P]_0 - [C]) - k_{off}[C]$$

Make an appropriate approximation:

$$([P]_0 - [C]) \approx [P]_0$$

$$\frac{d[C]}{dt} \approx k_{on}[L]_0[P]_0 - k_{on}[P]_0[C] - k_{off}[C]$$

Rearrange and solve using the integrating factor:

$$\frac{d[C]}{dt} + [C](k_{on}[P]_0 + k_{off}) = k_{on}[L]_0[P]_0$$

$$\frac{d}{dt}([C] \exp[(k_{on}[P]_0 + k_{off})t]) = k_{on}[L]_0[P]_0 \exp[(k_{on}[P]_0 + k_{off})t]$$

$$([C] \exp[(k_{on}[P]_0 + k_{off})t]) = \frac{k_{on}[L]_0[P]_0 \exp((k_{on}[P]_0 + k_{off})t)}{(k_{on}[P]_0 + k_{off})} + I.C.$$

$$[C] = \frac{[L]_0[P]_0}{([P]_0 + K_d)} + I.C. \exp[-(k_{on}[P]_0 + k_{off})t]$$

Using the initial condition, $[C](t=0) = 0$, we find the integration constant to be:

$$I.C. = -\frac{[L]_0[P]_0}{([P]_0 + K_d)}$$

Hence,

$$[C](t) = \frac{[L]_0[P]_0}{([P]_0 + K_d)} \left\{ 1 - \exp\left[-(k_{on}[P]_0 + k_{off})t\right] \right\}$$

The equilibrium value is clearly the value when t gets large.

$$[C](t) = [C]_{eq} \left\{ 1 - \exp\left[-(k_{on}[P]_0 + k_{off})t\right] \right\}$$

In order to find the point at 95% of the equilibrium value, rearrange and solve for the time when $[C]/[C]_{eq}=0.95$:

$$\frac{[C](t^*)}{[C]_{eq}} = 0.95 = \left\{ 1 - \exp\left[-(k_{on}[P]_0 + k_{off})t^*\right] \right\}$$

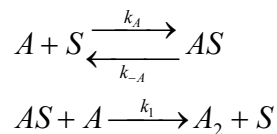
$$0.05 = \exp\left[-(k_{on}[P]_0 + k_{off})t^*\right]$$

$$t^* = \frac{-\ln(0.05)}{(k_{on}[P]_0 + k_{off})} = \frac{-\ln(0.05)}{(k_{on}[P]_0 + k_{on}K_d)} = \frac{3.00}{2 \times 10^{-5} \text{ nM}^{-1} \text{ s}^{-1} [3 \text{ nM} + 10 \text{ nM}]} = 11500 \text{ s}$$

$$t^* = 11500 \text{ s} \approx 3.2 \text{ h}$$

Problem 2: 30 points

A surface-catalyzed reaction follows Rideal-Eley kinetics as follows:



Where A and A_2 are in the gas phase, S is a reactive site on the surface, and AS is a molecule of A adsorbed to a reactive site.

Assuming that:

- adsorption of A is at rapid equilibrium
- reaction of AS with A is rate-limiting
- desorption of A_2 is very rapid

Derive the steady-state rate law for production of A_2 as a function of the concentration of A and the total initial reactive site density S_0 .

$$r_{Ad} = k_A \left(C_A C_v - \frac{C_{AS}}{K_A} \right) \quad \text{where } K_A = \frac{k_A}{k_{-A}}$$

$$r_s = k_1 C_{AS} C_A$$

Adsorption is at rapid equilibrium, so $\frac{r_{Ad}}{k_A} \approx 0$

$$C_A C_v = \frac{C_{AS}}{K_A} \Rightarrow C_{AS} = K_A C_A C_v$$

Overall site balance in terms of S_o :

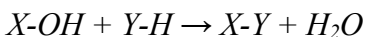
$$S_o = C_v + C_{AS} = C_v + K_A C_A C_v \Rightarrow C_v = \frac{S_o}{1 + K_A C_A}$$

Given that the surface reaction is the rate limiting step, and the stoichiometric coefficient is +1 for A_2 , the rate of production of A_2 is:

$$r'_{A_2} = r_s = k_1 C_{AS} C_A = k_1 K_A C_v C_A^2 = \frac{k_1 K_A S_o C_A^2}{1 + K_A C_A}$$

Problem 3: 35 points

It is desired to make a product X-Y via this reaction:



An equimolar feed of liquid X-OH and Y-H at 25°C are fed to a CSTR. At 25°C, where all 4 material species are liquids, the heat of reaction $\Delta H_{rxn} = -200$ kJ/mole, and the heat capacity of each liquid-phase species is 4 kJ/(kg C°). The molecular weight of X-OH is 150 g/mole, and the molecular weight of Y-H is 100 g/mole. The temperature inside the reactor (T) is controlled by putting the reactor in thermal contact with a fluid flowing over the outside of the reactor at temperature T_a . To a good approximation, the heat transfer rate (Q, in watts) from the fluid flowing over the outside the reactor to the contents of the reactor is given by the linear expression:

$$Q = UA(T_a - T)$$

- a) If the reaction is carried out with the reactor at steady-state at the inlet temperature of 25°C, is T greater than, less than, or equal to T_a ? (5 points)

For an exothermic reaction, to maintain the products at the same temperature as the reactants one must remove heat. So T must be greater than T_a , i.e. T_a must be below room temperature.

- b) When running the reactor at $T = 25^\circ\text{C}$ to 50% conversion, the productivity is unacceptably low. To try to accelerate the reaction, it is decided to increase the steady-state reactor temperature to $T = 105^\circ\text{C}$. At this temperature, all of the H_2O formed evaporates, but the other species are still liquids. The heat of vaporization of H_2O at 105°C is $+40 \text{ kJ/mole}$. When $T=105^\circ\text{C}$, the reaction runs to 50% conversion 10x faster than it did at 25°C , so we increase the flowrates until the reactor is making 10x as much product as it did at 25°C (still at 50% conversion). When we achieve the new steady-state high-productivity operation at 105°C , will the magnitude of Q (i.e. $|Q|$) be larger, smaller, or the same as it was when we were operating at 25°C ? At this steady-state condition, is T greater than, less than, or equal to T_a ? (20 points)

If the reaction ran 100% to completion, it would release $(200 \text{ kJ/mole})(1 \text{ mole}/0.25 \text{ kg entering the reactor})=800\text{kJ/kg entering the reactor}$. Since we only have 50% conversion, the chemical heat release is half as much, 400 kJ/kg . Heating the feed from 25 C to 105 C requires: $(80 \text{ degrees})(4 \text{ kJ/kg}) = 320 \text{ kJ/kg entering the reactor}$. Evaporating the water formed by the reaction requires an additional $(40 \text{ kJ/mole H}_2\text{O})(0.5 \text{ mole H}_2\text{O}/ 0.25 \text{ kg entering reactor}) = 80 \text{ kJ/kg}$. Since the heat release and the heat required to warm up the mixture and evaporate the water balance, $Q=0$ now. In contrast, when we ran the reactor at 298 K , we had to remove heat at a rate of 200 kJ/kg . So the magnitude of Q is much lower now than before, and T should approximately equal T_a .

- c) Since operating hot improved our productivity, but conversion is still pretty low, the operator tries to improve things by cranking up the temperature, preheating the inlet streams to 185°C and increasing T_a . For good measure the operator simultaneously cranks up the reactor pressure from 1 bar to 100 bar; at this high pressure all the species remain as liquids. (The reactor is safe at this condition, and even up $T = 300^\circ\text{C}$.) Curiously, the conversion and productivity of the reactor do not increase under these severe conditions, instead they decrease. Propose an explanation for this experimental observation. (5 points)

It is possible that we are running into equilibrium limitations on the reaction. For exothermic reactions, K_{eq} decreases with increasing temperature. So if we are equilibrium limited at high T, we would expect the conversion to decrease as T increases. (Note that by increasing the pressure so dramatically, the operator prevented most of the H₂O from evaporating, hence the concentration of H₂O in the liquid phase is probably much higher now than it was in the 105 C case where the water evaporated; this contributes to the equilibrium limitation).

- d) Your manager gives the operator who turned up the temperature (without doing any calculations first) a formal reprimand, saying the operator is probably lucky that the conversion went down instead of increasing. Why do you think the manager was happy that conversion was low instead of increasing a lot? (5 points)

Exothermic reactions can “run away” if T goes high enough, i.e. past a certain point, the steady-state conversion will suddenly jump from a low number to a very high conversion, releasing essentially the whole exothermicity, and jumping the T to a temperature above the safety limits of the reaction vessel. In the present case, if the reverse reaction were negligible the reaction would release 800 kJ/kg, enough to increase the temperature inside the reactor by up to 200 degrees, so it could have exceeded the T=300 C safety limit. The results could have been fatal to the operators or anyone else nearby. But fortunately in this case it was lucky that high conversion was not achievable due to the small value of the equilibrium constant.