Dynamics and Kinetics. Exercises 5: Solutions

Problem 1

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} E + P$$

a) Steady state for *ES*:

$$0 \approx \frac{d[ES]}{dt} = k_1[E][S] + k_{-2}[E][P] - (k_{-1} + k_2)[ES]$$

$$[ES] = \frac{k_1[S] + k_{-2}[P]}{k_{-1} + k_2}[E] = \left(\frac{[S]}{K_S} + \frac{[P]}{K_P}\right)[E] = x[E],$$

where we de ned:

$$x := \frac{[S]}{K_S} + \frac{[P]}{K_P}$$

Rate of reaction:

$$v = \frac{d[P]}{dt} = k_2[ES] - k_{-2}[E][P] = \left(\frac{k_2}{K_S}[S] + \frac{k_2 k_{-2} - k_{-2}(k_{-1} + k_2)}{k_{\ 1} + k_2}[P]\right)[E]$$

$$= \left(\frac{k_2[S]}{K_S} - \frac{k_{-1}[P]}{K_P}\right)[E]$$

Total enzyme: $[E]_0 = [E] + [ES] = [E](1 + x)$

$$v = \left(\frac{k_2[S]}{K_S} - \frac{k_{-1}[P]}{K_P}\right)\frac{[E]_0}{1 + x}$$

b) At short times: $[P] \longrightarrow 0$ (no product formed yet)

$$v = \left(\frac{\frac{k_2[S]}{K_S}}{1 + \frac{[S]}{K_S}}\right)[E]_0 = \frac{k_2[E]_0}{1 + \frac{K_S}{[S]}}$$

which corresponds to the Michaelis-Menten equation with $K_M = K_S$ and $v_{max} = k_2[E]_0$

c) Competitive inhibition

Add a reaction: $$E + I \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} EI$$

Steady state approximation:

$$0 \approx \frac{d[EI]}{dt} = k_3[E][I] - k_{-3}[EI] \qquad \Rightarrow \qquad [EI] = \frac{k_3}{k_{-3}}[E][I]$$

Total enzyme:

$$[E]_0 = [E] + [ES] + [EI] = [E](1 + x + y)$$

where we defined:

$$y := \frac{k_3}{k_{-3}}[I]$$

As in a)

$$\text{Rate } v = \frac{d[P]}{dt} = \left(\frac{k_2[S]}{K_S} - \frac{k_{-1}[P]}{K_P}\right)[E]$$
$$= \frac{\frac{k_2[S]}{K_S} - \frac{k_{-1}[P]}{K_P}}{1+x+y}[E]_0$$

For short times ($[P] \to 0$):

$$v = \frac{k_2[S][E]_0}{K_S + [S] + \frac{k_3}{k_{-3}}K_S[I]}$$

d) Short times ⇒ we can consider only the simplified mechanisms for short times [either the Michaelis-Menten in part (b) or the Michaelis-Menten with inhibition in second part of part (c)]

Use: Lineweaver-Burk plots $\left(\frac{1}{v} \text{ vs. } \frac{1}{[S]}\right)$

Recall from lecture:

i) Competitive inhibition → changes slope,

ii) Incompetitive inhibition → changes *y* intercept.

Results from linear regression:

Without inhibitor: $\frac{1}{v} = a_0\frac{1}{[S]} + b_0 \qquad a_0 = 4.0\text{s}, \quad b_0 = 5000\text{M}^{-1}\text{s}$

With inhibitor: $\frac{1}{v} = a\frac{1}{[S]} + b \qquad a = 11.5\text{s}, \quad b = 4800 \approx 5000\text{M}^{-1}$

Slope changes ⇒ **Competitive inhibition**

$$\frac{1}{v} = \frac{K_S}{k_2[E]_0}\left(1 + \frac{k_3}{k_{\ 3}}[I]\right)\frac{1}{[S]} + \frac{1}{k_2[E]_0}$$

where

Ratio of the slopes:

$$a = \frac{K_S}{k_2[E]_0}\left(1 + \frac{k_3}{k_{-3}}[I]\right)$$
$$b = \frac{1}{k_2[E]_0}$$

$$\frac{11.5}{4.0} = \frac{a}{a_0} = 1 + \frac{k_3}{k_{-3}}[I] \qquad \Rightarrow \qquad \frac{k_3}{k_{-3}} = \frac{\frac{11.5}{4} - 1}{[I]} = 9400\text{M}^{-1}$$

y intercept:

$$b_0 = \frac{1}{k_2[E]_0} \qquad \Rightarrow \qquad k_2 = \frac{1}{b_0[E]_0} = \frac{1}{5000 \times 10^{-5}} \mathrm{s}^{-1} = 20\mathrm{s}^{-1}$$

Slope:

$$a_0 = \frac{K_S}{k_2[E]_0} \qquad \Rightarrow \qquad K_S = K_M = \frac{a_0}{b_0} = \frac{4.0}{5000} \mathrm{M} = 8 \times 10^{-4} \mathrm{M}$$

Problem 2

The recombination of iodine atoms in the presence of argon is a third order reaction, that has been extensively studied using techniques such as flash photolysis.

$$\mathrm{I} + \mathrm{I} + \mathrm{Ar} \xrightarrow{k} \mathrm{I}_2 + \mathrm{Ar}$$

a) In an experiment, the concentration of argon is 1*10^{-2} mol/l, and the initial concentration of iodine atoms is 6*10^{-5} mol/l. At a temperature of 298 K, the half-life of the iodine atoms is 238 μs. Calculate the rate constant.

The rate equation is

$$v = -\frac{1}{2}\frac{d[\mathrm{I}]}{dt} = k\,[\mathrm{I}]^2\,[\mathrm{Ar}]$$

which we can integrate ($[\mathrm{Ar}] = const$)

$$\int_{[\mathrm{I}]_0}^{[\mathrm{I}]} \frac{d[\mathrm{I}]}{[\mathrm{I}]^2} = -2k[\mathrm{Ar}] \int_0^t dt$$

to obtain

$$t = \frac{\frac{1}{[\mathrm{I}]} - \frac{1}{[\mathrm{I}]_0}}{2k[\mathrm{Ar}]}$$

With

$$[\mathrm{I}]\left(t = t_{\frac{1}{2}}\right) = \frac{1}{2}\,[\mathrm{I}]_0$$

we find

$$t_{\frac{1}{2}} = \frac{1}{2k[\mathrm{Ar}][\mathrm{I}]_0}$$

With [Ar] = 1*10^{-2} mol/l, $[\mathrm{I}]_0$ = 6*10^{-5} mol/l and $t_{\frac{1}{2},298\ \mathrm{K}}$ = 238 µs, we obtain a rate constant

$$k_{298\ \mathrm{K}} = \frac{1}{2t_{\frac{1}{2},298\ \mathrm{K}}[\mathrm{Ar}][\mathrm{I}]_0} = 3.50 \cdot 10^9 \frac{l^2}{mol^2 s}$$

b) At a temperature of 350 K, but otherwise identical initial conditions as in a), the half-life of the iodine atoms is 342 µs. Calculate the activation energy of the reaction.

For $t_{\frac{1}{2},350\ \mathrm{K}}$ = 342 µs, the rate constant is

$$k_{350\ \mathrm{K}} = \frac{1}{2t_{\frac{1}{2},350\ \mathrm{K}}[\mathrm{Ar}][\mathrm{I}]_0} = 2.44 \frac{l^2}{mol^2 s}$$

With the Arrhenius equation

$$k = A\, e^{-\frac{E_A}{RT}}$$

it follows that

$$E_A = \frac{\ln(\frac{k_{350\ \mathrm{K}}}{k_{298\ \mathrm{K}}})\ R}{\frac{1}{298\ \mathrm{K}} - \frac{1}{350\ \mathrm{K}}} = -6.05 \frac{kJ}{mol}$$

c) The following reaction mechanism has been suggested for the recombination of iodine atoms. First, the van-der-Waals complex IAr is formed in a weakly exothermic reaction that is reversible.

$$\mathrm{I} + \mathrm{Ar} \underset{k_{-1}}{\overset{k_1}{\rightleftarrows}} \mathrm{IAr}$$

In a second step, collision with another iodine atom leads to the formation of I_2.

$$\mathrm{IAr} + \mathrm{I} \xrightarrow{k_2} \mathrm{I_2} + \mathrm{Ar}$$

The activation energy for this second step is zero. Since this second step is rate limiting, a pre-equilibrium exists for the formation of the complex IAr in the first step.

Write down the rate equation for the formation of I_2 under the assumption of a pre-equilibrium for the complex IAr and explain why the recombination of iodine atoms has a negative activation energy. Hint: Consider the temperature dependence of the effective rate constant.

The rate equation for the pre-equilibrium is

$$v = \frac{d[\mathrm{I}_2]}{dt} = k_2 K [\mathrm{I}]^2 [\mathrm{Ar}]$$

with

$$K = \frac{k_1}{k_{-1}}$$

We thus obtain an effective rate constant for the reaction

$$k_{\mathrm{effective}} = k_2 K$$

The temperature dependence of $k_2 = Ae^{-\frac{E_a}{RT}} = A$ is small. In contrast, the equilibrium is increasingly shifted to the reactant side with increasing temperature since $K = e^{-\frac{\Delta \mathrm{G}^0}{RT}}$ and $\Delta \mathrm{G}^0$ is negative. This leads to a negative activation energy.

$$E_a = RT^2 \frac{d\, lnk}{dT} \approx \Delta \mathrm{G}^0$$