Estimate reaction rate parameters via linear regression. (Problem 3.3 of Shuler & Kargi)
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$$E + S \underset{k_i}{\overset{k_1}{\longleftrightarrow}} ES \xrightarrow{k_2} E + P$$

Given kinetic constants: $k_1 := 10^9 \ M^{-1} \cdot s^{-1}$ $\quad k_i := 4.4 \cdot 10^4 \ s^{-1}$ $\quad k_2 := 10^3 \ s^{-1}$

Find Michaelis-Menten constant: $K_m := \dfrac{k_i + k_2}{k_1}$ $\quad K_m = 4.5 \cdot 10^{-5} \ M$

Given initial enzyme conc: $E_0 := 10^{-6} M$

Find maximum reaction rate: $v_m := k_2 \cdot E_0$ $\quad v_m = 0.001 M \cdot s^{-1}$ $\quad v(s) := \dfrac{v_m \cdot s}{K_m + s}$

Given initial substrate conc. $s_0 := 10^{-3} \ M$

Find initial reaction rate: $v_0 := v(s_0)$ $\quad v_0 = 9.569 \cdot 10^{-4} \ M \cdot s^{-1}$

When K_m is small, the reaction rate is approximately 0th order wrt s. $\quad v_0 := v_m \quad v_0 = 0.001 \ M \cdot s^{-1}$

Beyond the Initial Rate.

Integrating $\dfrac{ds}{dt} = -v(s) = -\dfrac{v_m \cdot s}{K_m + s}$ gives $s_0 - s - K_m \cdot \ln\left(\dfrac{s}{s_0}\right) = v_m \cdot t$

An analytical expression of s(t) does not exist.
The numerical solution starting with an initial guess of $s := s_0$

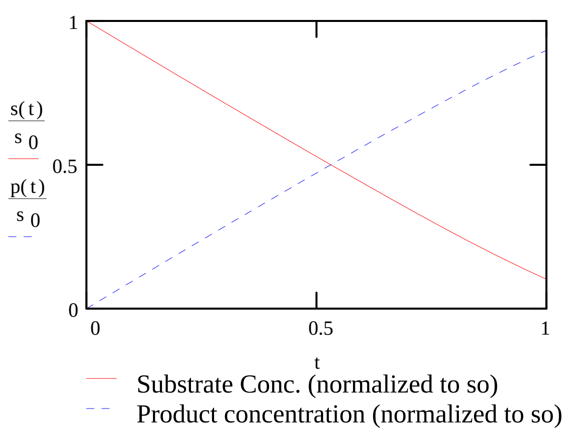
Given $\quad s_0 - s - K_m \cdot \ln\left(\dfrac{s}{s_0}\right) = v_m \cdot t \qquad s(t) := \text{Find}(s) \qquad$ Example. $\quad s(1) = 1.025 \cdot 10^{-4}$

When K_m is small, the reaction rate is approximately 0th order, and the above expression is:

$$s_0 - s = v_m \cdot t$$

The product concentration is $p(t) := s_0 - s(t)$

$t := 0, 0.01 .. 1$



Since K_m<<s_0, straight lines describe the changes of s and p with time quite well.

Substrate Half-Life. The length of time it takes for s to drop from s=s_0 to $s = \frac{s_0}{2}$

(Copy s_0/2 into memory, mark s in the following eqn, choose |Symbolic|Substitute for Variable|)

$$s_0 - s - K_m \cdot \ln\left(\frac{s}{s_0}\right) = v_m \cdot t$$ Doing so gives: $$\frac{1}{2} \cdot s_0 + K_m \cdot \ln(2) = v_m \cdot t_{half}$$

Thus, $t_{half} := \frac{s_0 + 2 \cdot K_m \cdot \ln(2)}{2 \cdot v_m}$ $t_{half} = 0.531$ s

When K_m is small, the half life is approximately: $t_{half} = \frac{s_0}{2 \cdot v_m}$

Enzyme Deactivation.

With 1st-order enzyme deactivation, we have $\frac{ds}{dt} = -v(s) = -\frac{v_m \cdot \exp(-k_d \cdot t) \cdot s}{K_m + s}$

Integrating $$-\int_{s_0}^{s} \frac{K_m + S}{S} dS = \int_0^t v_m \cdot \exp(-k_d \cdot T)\, dT$$ gives

$$s_0 - s - K_m \cdot \ln\left(\frac{s}{s_0}\right) = \frac{v_m}{k_d} \cdot (1 - \exp(-k_d \cdot t))$$

Again, an analytical expression of s(t) does not exist. The following defines how s changes with time in the presence of enzyme deactivation.

$$s := s_0 \quad \text{Given} \quad s_0 - s - K_m \cdot \ln\left(\frac{s}{s_0}\right) = \frac{v_m}{k_d} \cdot (1 - \exp(-k_d \cdot t)) \quad s_d(t, k_d) := \text{Find}(s)$$

Half-life: $\frac{1}{2} \cdot s_0 + K_m \cdot \ln(2) = \frac{v_m}{k_d} \cdot (1 - \exp(-k_d \cdot t_{halfd}))$

With enzyme deactivation, it now takes twice as long to reduce the substrate level to one half of the initial value, compared to that without enzyme deactivation. Find the deactivation time constant τ_d=1/k_d.

We first substitute into the above half-life expression $t_{halfd} = 2 \cdot t_{half} = \frac{s_0 + 2 \cdot K_m \cdot \ln(2)}{v_m}$

$$\frac{1}{2} \cdot s_0 + K_m \cdot \ln(2) = \frac{v_m}{k_d} \cdot \left(1 - \exp\left(-k_d \cdot \frac{s_0 + 2 \cdot K_m \cdot \ln(2)}{v_m}\right)\right)$$ $\longrightarrow$ solve for k_d.

Alternatively, take the ratio of the half-life expression /wo enzyme deactivation and that /w enzyme deactivation. Doing so gives:

$$t_{half} = \frac{1}{k_d} \cdot (1 - \exp(-k_d \cdot t_{halfd})) \longrightarrow \quad k_d \cdot t_{half} = 1 - \exp(-2 \cdot k_d \cdot t_{half}) \quad \longrightarrow$$ Let $x = k_d \cdot t_{half}$

$$x := 1 \quad \text{Given} \quad x = 1 - \exp(-2 \cdot x) \quad x := \text{Find}(x) \quad k_d := \frac{x}{t_{half}} \quad \tau_d := \frac{1}{k_d} \quad \tau_d = 0.667 \text{ s}$$

With an enzyme that follows the Michaelis-Menten kinetics and deactivates, complete conversion of the substrate is **not** possible. At t→∞, we have:

$s_{limit} := s_0$ Given $s_0 - s_{limit} - K_m \cdot \ln\left(\frac{s_{limit}}{s_0}\right) = \frac{v_m}{k_d}$ $s_{limit} := \mathrm{Find}(s_{limit})$ $s_{limit} = 0.377 \cdot s_0$

$t := 0, 0.01 .. 5$