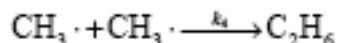
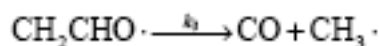


Problem set 10
Old numbers from the First edition.

P37.2) The Rice-Herzfeld mechanism for the thermal decomposition of acetaldehyde (CH_3CHO) is



Using the steady-state approximation, determine the rate of methane (CH_4) formation.

The differential rate expressions for methane and relevant intermediate species are:

$$\frac{d[\text{CH}_4]}{dt} = k_2 [\text{CH}_3\cdot] [\text{CH}_3\text{CHO}]$$

$$\frac{d[\text{CH}_2\text{CHO}\cdot]}{dt} = k_2 [\text{CH}_3\cdot] [\text{CH}_3\text{CHO}] - k_3 [\text{CH}_2\text{CHO}\cdot]$$

$$\frac{d[\text{CH}_3\cdot]}{dt} = k_1 [\text{CH}_3\text{CHO}] - k_2 [\text{CH}_3\cdot] [\text{CH}_3\text{CHO}] + k_3 [\text{CH}_2\text{CHO}\cdot] - 2k_4 [\text{CH}_3\cdot]^2$$

Applying the steady state approximation to the differential rate expressions for the intermediates:

$$\frac{d[\text{CH}_2\text{CHO}\cdot]}{dt} = \frac{d[\text{CH}_3\cdot]}{dt} = 0$$

or

$$0 = k_2 [\text{CH}_3][\text{CH}_3\text{CHO}] - k_3 [\text{CH}_2\text{CHO}]$$

$$0 = k_1 [\text{CH}_3\text{CHO}] - k_2 [\text{CH}_3][\text{CH}_3\text{CHO}] + k_3 [\text{CH}_2\text{CHO}] - 2k_4 [\text{CH}_3]^2$$

Adding the above two equations yields the following expression:

$$2k_4 [\text{CH}_3]^2 = k_1 [\text{CH}_3\text{CHO}]$$

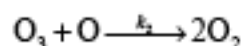
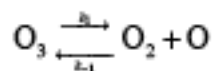
$$[\text{CH}_3] = \sqrt{\frac{k_1}{2k_4}} [\text{CH}_3\text{CHO}]^{1/2}$$

Substitution into the rate expression for $[\text{CH}_4]$ yields

$$\frac{d[\text{CH}_4]}{dt} = k_2 \left[\sqrt{\frac{k_1}{2k_4}} [\text{CH}_3\text{CHO}]^{1/2} \right] [\text{CH}_3\text{CHO}]$$

$$\frac{d[\text{CH}_4]}{dt} = k_{\text{eff}} [\text{CH}_3\text{CHO}]^{3/2} \quad \text{where} \quad k_{\text{eff}} = k_2 \sqrt{\frac{k_1}{2k_4}}$$

P37.3) Consider the following mechanism for ozone thermal decomposition:



- Derive the rate law expression for the loss of O_3 .
- Under what conditions will the rate law expression for O_3 decomposition be first order with respect to O_3 ?

a)

$$\frac{d[\text{O}_3]}{dt} = -k_1 [\text{O}_3] + k_{-1} [\text{O}_2][\text{O}] - k_2 [\text{O}_3][\text{O}]$$

b) Atomic oxygen is the intermediate species, and the differential rate expression for this species is:

$$\frac{d[\text{O}]}{dt} = k_1 [\text{O}_3] - k_{-1} [\text{O}_2][\text{O}] - k_2 [\text{O}_3][\text{O}]$$

Applying the steady-state approximation to the differential rate expression for O yields:

$$\frac{d[\text{O}]}{dt} = 0 = k_1[\text{O}_3] - k_{-1}[\text{O}_2][\text{O}] - k_2[\text{O}_3][\text{O}]$$

$$k_1[\text{O}_3] = k_{-1}[\text{O}_2][\text{O}] + k_2[\text{O}_3][\text{O}]$$

$$\frac{k_1[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} = [\text{O}]$$

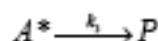
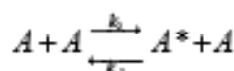
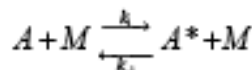
Substituting this result into the differential rate expression for ozone yields:

$$\begin{aligned} \frac{d[\text{O}_3]}{dt} &= -k_1[\text{O}_3] + k_{-1}[\text{O}_2][\text{O}] - k_2[\text{O}_3][\text{O}] \\ &= -k_1[\text{O}_3] + [\text{O}](k_{-1}[\text{O}_2] - k_2[\text{O}_3]) \\ &= -k_1[\text{O}_3] + \left(\frac{k_1[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} \right) (k_{-1}[\text{O}_2] - k_2[\text{O}_3]) \\ &= -k_1[\text{O}_3] + \left(\frac{k_1[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} \right) (k_{-1}[\text{O}_2] - k_2[\text{O}_3]) \\ &= -k_1[\text{O}_3] \left(1 + \frac{-k_{-1}[\text{O}_2] + k_2[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} \right) \\ &= -k_1[\text{O}_3] \left(\frac{k_{-1}[\text{O}_2] + k_2[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} + \frac{-k_{-1}[\text{O}_2] + k_2[\text{O}_3]}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} \right) \\ &= -\frac{2k_1k_2[\text{O}_3]^2}{k_{-1}[\text{O}_2] + k_2[\text{O}_3]} \end{aligned}$$

if $k_2[\text{O}_3] \gg k_{-1}[\text{O}_2]$

$$\frac{d[\text{O}_3]}{dt} = -2k_1[\text{O}_3]$$

P37.10) In the discussion of the Lindemann mechanism, it was assumed that the rate of activation by collision with another reactant molecule, A , was the same as collision with a nonreactant molecule, M , such as a buffer gas. What if the rates of activation for these two processes are different? In this case, the mechanism becomes



a) Demonstrate that the rate law expression for this mechanism is

$$R = \frac{k_3 (k_1 [A][M] + k_2 [A]^2)}{k_{-1}[M] + k_{-2}[A] + k_3}$$

b) Does this rate law reduce to the expected form when $[M] = 0$?

$$a) \frac{d[P]}{dt} = k_3 [A^*]$$

$$\frac{d[A^*]}{dt} = k_1 [A][M] - k_{-1} [A^*][M] + k_2 [A]^2 - k_{-2} [A^*][A] - k_3 [A^*]$$

Applying steady state theory to A^* yields

$$k_3 [A^*] + k_{-1} [A^*][M] + k_{-2} [A^*][A] = k_1 [A][M] + k_2 [A]^2$$

$$[A^*] = \frac{k_1 [A][M] + k_2 [A]^2}{k_{-1}[M] + k_{-2}[A] + k_3}$$

Substituting back into the differential rate expression for the product yields:

$$R = \frac{d[P]}{dt} = \frac{k_3 (k_1 [A][M] + k_2 [A]^2)}{k_{-1}[M] + k_{-2}[A] + k_3}$$

b) If the concentration of M goes to 0, then

$$R = \frac{k_3 (k_2 [A]^2)}{k_{-2}[A] + k_3}$$

which is the Lindemann rate expression.

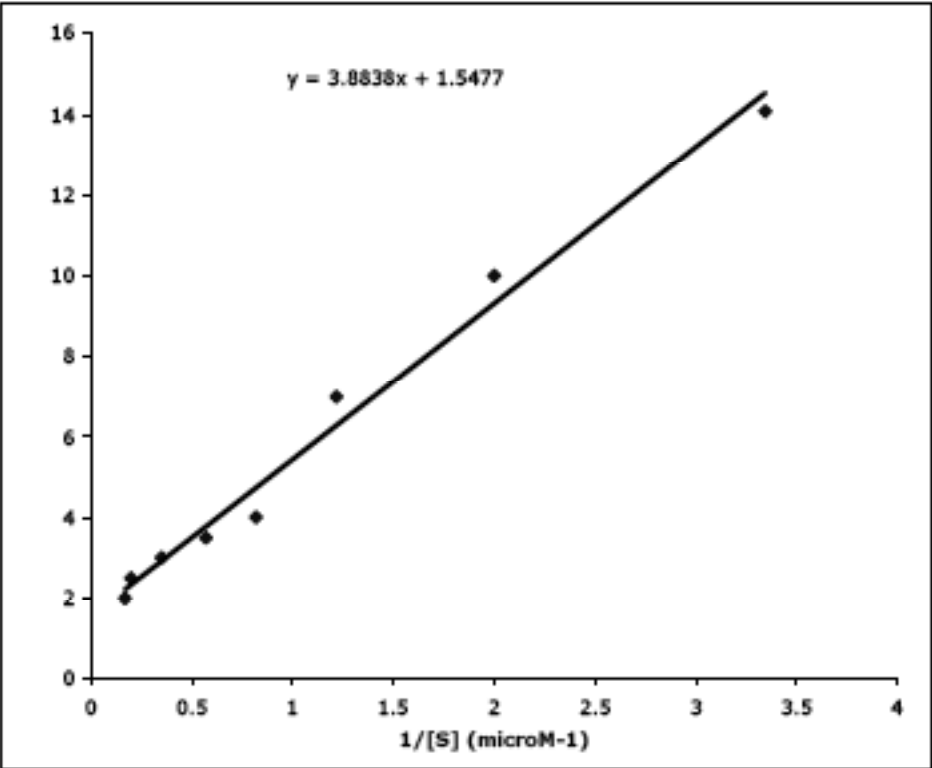
P37.14) Protein tyrosine phosphatases (PTPases) are a general class of enzymes that are involved in a variety of disease processes including diabetes and obesity. In a study by Z.-Y. Zhang and coworkers [*J. Medicinal Chemistry* 43 (2000), 146], computational techniques were used to identify potential competitive inhibitors of a specific PTPase known as PTP1B. The structure of one of the identified potential competitive inhibitors is shown in the text.

The reaction rate was determined in the presence and absence of inhibitor, I , and revealed the following initial reaction rates as a function of substrate concentration:

$[S]$ (μM)	Rate_0 ($\mu\text{M s}^{-1}$), $[I] = 0$	Rate_0 ($\mu\text{M s}^{-1}$) $[I] = 200 \mu\text{M}$
0.299	0.071	0.018
0.500	0.100	0.030
0.820	0.143	0.042
1.22	0.250	0.070
1.75	0.286	0.105
2.85	0.333	0.159
5.00	0.400	0.200
5.88	0.500	0.250

- Determine K_m and rate_{max} for PTP1B.
- Demonstrate that the inhibition is competitive, and determine K_i .

a) Performing a Lineweaver-Burke plot for the uninhibited reaction yields:



Best fit to the data by a straight line yields the following equation:

$$\frac{1}{\text{rate}_0} = 3.88 \times 10^6 \text{ s} \frac{1}{[S]_0} + 1.55 \times 10^6 \text{ M}^{-1} \text{ s}$$

The maximum rate is equal to the inverse of the y-intercept:

$$\text{rate}_{\text{max}} = \frac{1}{y\text{-int}} = \frac{1}{1.55 \times 10^6 \text{ M}^{-1} \text{ s}}$$

$$\text{rate}_{\text{max}} = 6.45 \times 10^{-7} \text{ M s}^{-1}$$

With rate_{max} , the Michaelis constant is determined from the slope:

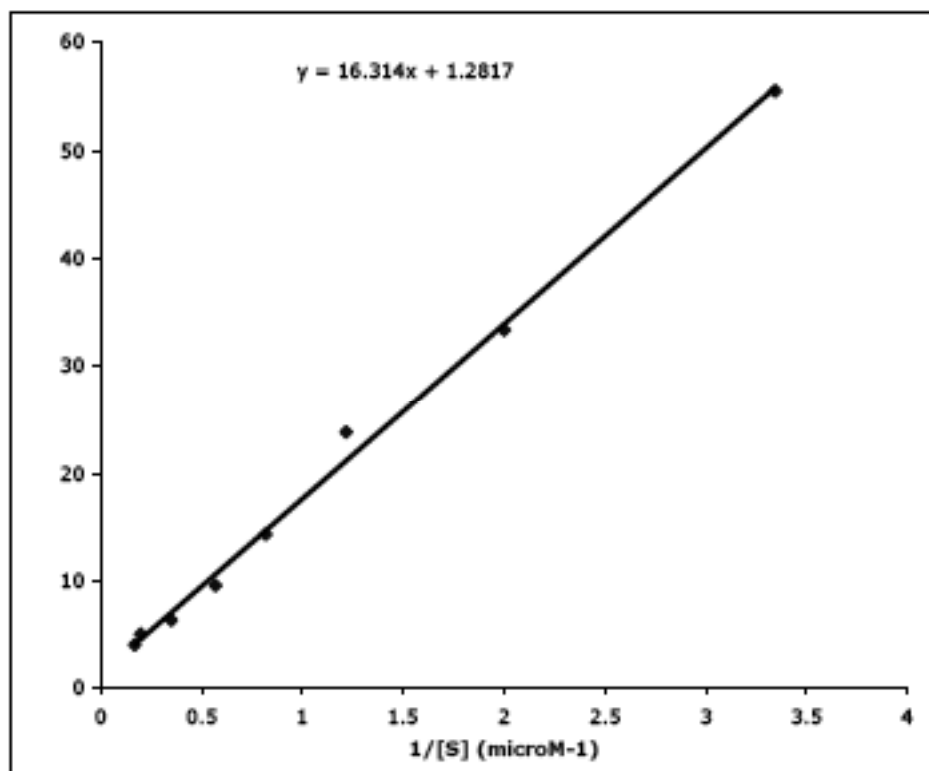
$$K_m = (\text{slope}) (\text{rate}_{\text{max}}) = (3.88 \times 10^6 \text{ s}) (6.45 \times 10^{-7} \text{ M s}^{-1})$$

$$K_m = 2.5 \text{ M}$$

b) With the inhibitor present, the modified Lineweaver-Burke equation is used where:

$$\frac{1}{\text{rate}_0} = \frac{1}{\text{rate}_{\text{max}}} + \frac{K_m^*}{\text{rate}_{\text{max}}} \frac{1}{[S]_0}$$

Again, a plot of the inverse of the initial rate with the inverse of substrate concentration should yield a straight line. The plot is as follows:



Best fit to the data by a straight line yields the following equation:

$$\frac{1}{\text{rate}_0} = 1.63 \times 10^7 \text{ s} \frac{1}{[\text{S}]_0} + 1.28 \times 10^6 \text{ M}^{-1} \text{ s}$$

The maximum rate is given by the inverse of the y-intercept:

$$\text{rate}_{\text{max}} = \frac{1}{y\text{-int}} = \frac{1}{1.26 \times 10^6 \text{ M}^{-1} \text{ s}}$$

$$\text{rate}_{\text{max}} = 7.94 \times 10^{-7} \text{ M s}^{-1}$$

With rate_{max} and the slope of the line the apparent Michaelis constant is:

$$\begin{aligned} K_m^* &= (\text{slope}) (\text{rate}_{\text{max}}) = (1.63 \times 10^7 \text{ s}) (1.28 \times 10^{-6} \text{ M s}^{-1}) \\ &= 20.9 \text{ M} \end{aligned}$$

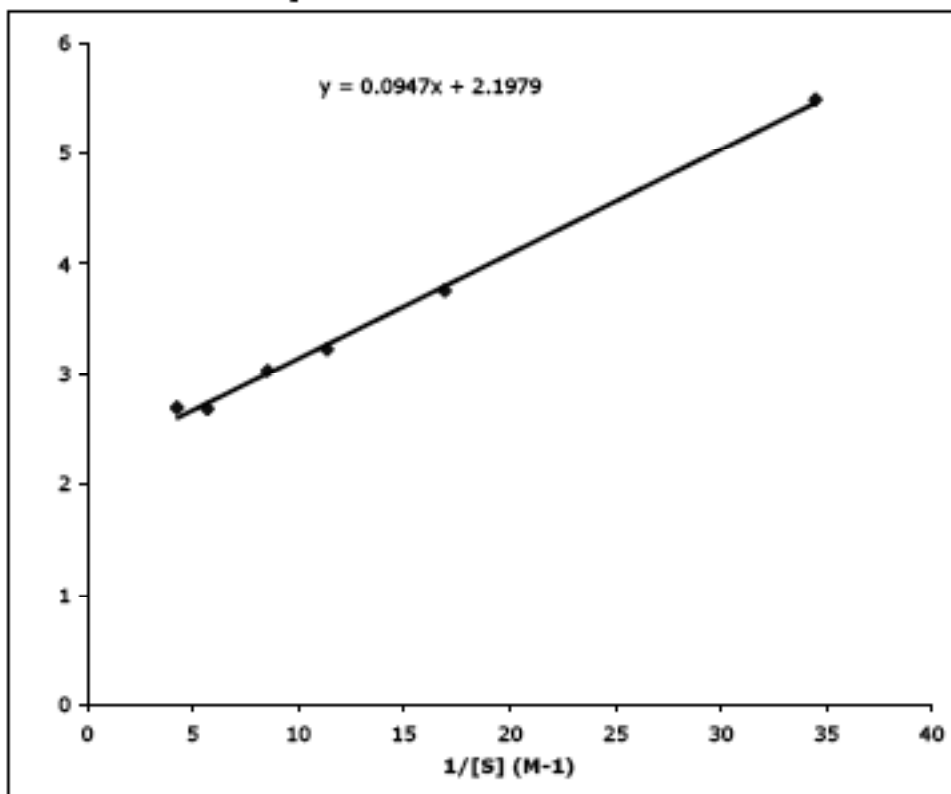
With K_m , K_m^* and $[I]$, K_I is determined as follows:

$$\begin{aligned} K_I &= \frac{[I]}{\frac{K_m^*}{K_m} - 1} \\ &= \frac{200 \times 10^{-6} \text{ M}}{\left(\frac{20.9 \text{ M}}{2.5 \text{ M}}\right) - 1} \\ &= 2.71 \times 10^{-5} \text{ M} \end{aligned}$$

P37.15) The rate of reaction can be determined by measuring the change in optical rotation of the sample as a function of time if a reactant or product is chiral. This technique is especially useful for kinetic studies of enzyme catalysis involving sugars. For example, the enzyme invertase catalyzes the hydrolysis of sucrose, an optically active sugar. The initial reaction rates as a function of sucrose concentration are as follows:

[Sucrose] ₀ (M)	Rate (M s ⁻¹)
0.029	0.182
0.059	0.266
0.088	0.310
0.117	0.330
0.175	0.372
0.234	0.371

Use these data to determine the Michaelis constant for invertase.
The Lineweaver-Burk plot and best fit to the data is as follows:



The equation for the best-fit line is:

$$\frac{1}{\text{rate}_0} = 0.0947 \text{ s} \frac{1}{[\text{S}]_0} + 2.1979 \text{ M}^{-1}\text{s}$$

The maximum rate is equal to the inverse of the y-intercept

$$\text{rate}_{\text{max}} = \frac{1}{\text{int}} = \frac{1}{2.20 \text{ M}^{-1}\text{s}}$$

$$\text{rate}_{\text{max}} = 0.455 \text{ M s}^{-1}$$

The Michaelis constant is equal to the product of rate_{max} and the slope:

$$K_m = \text{slope} \cdot \text{rate}_{\text{max}} = 0.0947 \text{ s} \cdot 0.455 \text{ Ms}^{-1}$$

$$K_m = 0.0431 \text{ M}$$