A First Course on Kinetics and Reaction Engineering
Unit 9. Homogeneous and Enzymatic Catalysis

Overview

This course is divided into four parts; part II is focused upon modeling the rates of chemical reactions, that is, rate expressions. A mathematical expression for the rate of a non-elementary reaction can be generated from its mechanism, using methods described in the last three units. However, when the reaction mechanism involves charged species, enzymes or homogeneous catalysts, those methods must be modified to account for the conservation of charge or catalyst. This is the subject of Unit 9.

Learning Objectives

Upon completion of this unit, you should be able to define, in words, the following terms:

- homogeneous catalyst
- enzyme
- enzyme inhibitor
- enzyme co-factor

Upon completion of this unit, you should be able to write the defining equation for the following quantities:

- conservation of catalyst or enzyme
- conservation of charge

Upon completion of this unit, you should be able to perform the following specific tasks and be able to recognize when they are needed and apply them correctly in the course of a more complex analysis:

- generate a rate expression for a non-elementary reaction when its mechanism involves charged species, enzymes or homogeneous catalysts, and simplify that expression so that it does not contain concentrations or partial pressures of reactive intermediates
- rearrange the rate expression for simple Michaelis-Menten kinetics to a linear (Lineweaver-Burk) form
- use a Lineweaver-Burk plot to find values for the Michaelis-Menten parameters for an enzymatic reaction

Information

Many reactions are carried out in the presence of an added catalyst (heterogeneous, homogeneous, or enzymatic). Homogeneous catalysts and enzymes are considered in this unit; heterogeneous catalysts are considered in Unit 10. Recall that a catalyst is a material that causes the rate of one or more chemical reactions to increase, but the catalyst itself is not a reactant or product of the overall macroscopically observed reaction. This leads to an additional constraint that can be imposed when extracting an overall rate expression from a postulated mechanism for a homogeneous catalytic or enzymatic reaction. In mechanisms for these kinds of reactions the catalyst or enzyme typically appears in several different chemical forms. That is, some of the catalyst will be free of reactants, products, and intermediates, while some catalyst will be complexed (chemically bound) with reactants, products or other

species. Each of the chemical forms of the catalyst can be treated as a reactive intermediate (they each appear in the reaction mechanism, but not in the overall reaction). The concentrations of the various chemical forms of the catalyst or enzyme typically aren't (or can't easily be) measured, so they are typically eliminated from mechanistic rate expressions using either the steady-state approximation or quasi-equilibrium assumptions.

It's been noted in previous units that for engineering purposes, rate expressions that contain concentrations of reactive intermediates are not desirable because these concentrations are typically unknown and hard to measure. If each of the different non-complexed and complexed forms of a homogeneous catalyst is treated as a reactive intermediate and the Bodenstein steady state approximation is applied, it is found that the resulting equations cannot be solved to obtain expressions for the concentrations of the reactive intermediates as was done in previous units. The reason is that when every non-complexed and complexed form of the catalyst or enzyme is treated as a reactive intermediate, the equations generated using the Bodenstein steady state approximation are no longer mathematically independent.

However, the *total concentration of catalyst or enzyme is usually known* because the amount of catalyst originally added is known, and catalyst is not generated nor consumed by reaction. The sum of the concentrations of all forms of the catalyst (free, reactant-complexed, intermediate-complexed, and product-complexed) must equal the known total concentration of catalyst or catalytic sites. A simple mole balance on the catalyst or enzyme leads to equation (9.1), where C^0_{cat} is the (known) total concentration of the catalyst or enzyme in all of its forms, $C_{cat,free}$ is the concentration of free, non-complexed catalyst or enzyme, $C_{cat,i}$ is the concentration of complexes of the catalyst with species i, and $\nu_{cat,i}$ is the number of catalyst species in the form originally added to the system that are needed to create one complex of the catalyst with species i. In equation (9.1) "catalyst" may refer to either a homogeneous chemical catalyst or to an enzyme (a catalyst originally found within a living organism). If one of the equations resulting from the application of the Bodenstein steady state approximation to each non-complexed and complexed form of the catalyst is replaced by equation (9.1), the resulting set of equations will be mathematically independent. As such that set of equations can be solved to obtain expressions for the concentrations of each reactive intermediate in terms of only rate coefficients, concentrations of stable species and the total concentration of the catalyst in its initial form, C^0_{cat}.

$$C^0_{cat} = C_{cat,free} + \sum_{\substack{i=\text{ all catalyst complexing species}}} \nu_{cat,i} C_{cat,i} \qquad (9.1)$$

A similar complication can arise for either catalytic or non-catalytic reactions if the mechanism involves ionic species while the overall reaction does not. In that case, instead of requiring the total amount of catalyst to be conserved, it is necessary for charge to be conserved. If the reacting solution is uncharged, this means that the sum of the amounts of all positively charged species multiplied by their respective charges must equal the sum of the amounts of all negatively charged species multiplied by their respective charges, as expressed in equation (9.2). In equation (9.2) C denotes concentration, q

denotes charge, p is an index that runs over all species in the system that are positively charged and n is an index that runs over all species in the system that are negatively charged.

$$\sum_{\substack{p=\text{ all}\\ \text{positively}\\ \text{charged}\\ \text{species}}} C_p q_p = \sum_{\substack{n=\text{ all}\\ \text{negatively}\\ \text{charged}\\ \text{species}}} C_n \left|q_n\right| \tag{9.2}$$

Enzyme catalysis and homogeneous chemical catalysis are almost completely analogous, but those who practice enzymatic catalysis typically use a different nomenclature. The “catalyst” is called an “enzyme.” Instead of reactant, the term “substrate” is typically used, and instead of a catalyst poison, one speaks of an enzyme inhibitor. The simplest of enzymatic reactions can be modeled using the mechanism given in equations (9.3) and (9.4) where E is used to denote the non-complexed enzyme, E-S is a complex between the enzyme and the substrate, and P denotes the product. When observed macroscopically, it appears as if the reaction S → P is taking place. If mechanistic step (9.4) is taken to be irreversible (that is, if the rate of the reverse of reaction (9.4) is set equal to zero) and the Bodenstein steady-state approximation is used along with conservation of enzyme, the rate expression given in equation (9.5) results, as shown in Example 9.1. In equation (9.5) C_i denotes the concentration of species i, V_{max} is a constant (maximum reaction velocity) and K_m is another constant often called the Michaelis-Menten constant or just the Michaelis constant. When this rate expression is obeyed, the enzymatic system is said to display *Michaelis-Menten kinetics*, after the scientists who first modeled enzyme kinetics in this way. Other simple enzymatic processes, such as reaction in the presence of an enzyme inhibitor can be modeled in an analogous manner.

$$\text{E + S} \rightleftarrows \text{E-S} \tag{9.3}$$

$$\text{E-S} \rightarrow \text{E + P} \tag{9.4}$$

$$r = \frac{dC_P}{dt} = \frac{V_{\max} C_S}{K_m + C_S} \tag{9.5}$$

If the reciprocal of equation (9.5) is taken, equation (9.6) results. This reciprocal version is useful for the analysis of enzymatic kinetic data. It can be seen from equation (9.6) that when Michaelis-Menten kinetics are obeyed, a plot of the reciprocal of the rate versus the reciprocal of the substrate concentration will yield a straight line. A plot of this type is called a *Lineweaver-Burk plot*. Values for V_{max} and K_m can be found from the slope and intercept of a Lineweaver-Burk plot.

$$\frac{1}{r} = \left(\frac{K_m}{V_{\max}}\right)\frac{1}{C_S} + \frac{1}{V_{\max}} \tag{9.6}$$

As noted above, some enzymes are susceptible to inhibition. Typically an enzyme is a large molecule that has many twists and folds in its structure, and the catalysis associated with the enzyme takes place when the substrate binds to one particular location within the overall structure. Inhibitors are often molecules that also bind to the particular location where the catalysis takes place. When an inhibitor

molecule is bound in this way, the enzyme becomes catalytically inactive until such time that the inhibitor releases from it. In addition to inhibition, some enzymes require co-factor molecules. A co-factor molecule is often an inorganic molecule that has the effect of activating an enzyme when it binds to it. That is, the enzyme alone is not active, but when a co-factor binds to it, it becomes catalytically active.

A typical analysis of an enzymatic reaction mechanism assumes that the conversion of the enzyme-substrate complex is an irreversible reaction while enzyme binding processes (with substrates, inhibitors, cofactors, products, etc.) are reversible. The Bodenstein steady-state approximation is then used along with the assumption of enzyme conservation. Co-factors and inhibitors can also be analyzed using the assumption that they are conserved. This would only be done if it is difficult to measure their free (not complexed) concentration. If it is easy to measure the concentration of non-complexed inhibitor or co-factor, then the presence of their concentrations in the rate expression is acceptable.