

General Rate Equations and Their Applications for Cyclic Reaction Networks: Single-Cycle Systems

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The network reduction technique and the Bodenstein approximation of quasi-stationary behavior of reaction intermediates were systematically applied to derive general rate equations for reaction networks in homogeneous catalysis with and without inhibition. Single-cycle reaction networks with and without branches were considered. The general rate equations derived in this study are applicable for most enzymatic reactions and for some heterogeneous catalytic reactions involving first-order reactions with respect to the intermediates, but not applicable for the heterogeneous catalytic reactions involving bimolecular surface reaction, dissociative adsorption, or associative desorption. Examples of a simple reaction with inhibition were used to illustrate the application of the general rate equations for network elucidation.

Introduction

Because many chemical reactions of industrial importance involve complex reaction pathways and networks and the determination of the reaction rate laws is very difficult and time-consuming, power-law type reaction rate equations are usually used to correlate kinetic data. These power-law type rate equations are empirical in nature and cannot be used confidently in scale-up and optimization of chemical reactors. Scale-up of chemical reactors by large factors is highly desirable in today's industrial practice. To be safe, such scale-up should be based on kinetic modeling that correctly reflects reaction pathways and networks. Christiansen¹ was the first to derive a general equation for multistep catalytic cycles of steps (called "closed sequences" by him, the "closed" indicating that the catalyst circulated through the steps). The rates of reactant consumption and product formation, which were not explicitly given by Christiansen, are readily derived from his formula. Christiansen did not specifically discuss heterogeneous catalysis, to which his approach turns out to be applicable, but only if no more than one of the reactants is adsorbed before reacting. Also, his formula becomes very lengthy for reactions with more than two or three steps, a fact that has discouraged its use.

A graphic method was proposed by King and Altman² to derive the rate laws for enzyme-catalyzed reactions. The method is basically the same as Christiansen's approach. King and Altman expressed the concentration of each intermediate (enzyme complex) as a quotient of two summations of terms, each term being the products of rate coefficients and the appropriate concentrations of reactants or products. The net rate of production of a product was then expressed in terms of the intermediate concentrations, not directly in terms of the rate coefficients and the concentrations of reactants or products. Although the method is useful for single-cycle networks without branches, it is very difficult to use for the networks involving branches, multiple pathways, and

multiple cycles. To deal with the multicycle networks, King and Altman's method was modified^{3,4} by assuming that most steps were at equilibrium.

In modeling of reactions of heterogeneous catalysis, an important step was taken by Boudart⁵ with the introduction of the concept of the most abundant surface intermediate (masi). He showed that many terms in Christiansen's formula become negligible if most of the catalyst surface is covered by a single reaction intermediate. Combining the concept of masi and rate determining step (rds) he was able to obtain rate equations simple enough to be practical even for rather complex reactions such as ammonia synthesis.

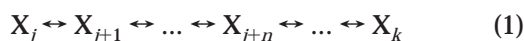
Helfferich⁶ proposed a systematic approach to elucidation of multistep reaction networks; the rate equations for specific reaction networks are recovered by simple substitutions, cancellations, and collection of terms. Chern and Helfferich⁷ used the technique of network reduction to obtain the general equations for rates and yield ratios of homogeneous reactions with an arbitrary number of steps and location of nodes and coreactant entries. This paper extends the previous approach to homogeneous catalytic reactions involving cyclic reaction networks such as enzymatic reactions. The network reduction technique and systematic use of the Bodenstein approximation for intermediates will be applied to homogeneous catalytic reactions with the purpose of obtaining simple, yet acceptably accurate, equations for rates that can be used for pathway or network elucidation and effective mathematical modeling. Only the so-called "rake mechanism" or simple networks whose intermediates are at trace level and for which there is no step of higher than first order in intermediates will be considered here. With respect to details of the method, familiarity with the two previous publications^{6,7} will be taken for granted.

Method

As shown in the previous papers,^{6,7} the Bodenstein approximation of quasi-stationary behavior of intermediates permits any "simple" network (that is, with all intermediates at trace level and no steps of higher order in intermediates) to be reduced to one with only pseudo-

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single steps between nodes and end points. Specifically, the net rate contribution of a multistep, reversible simple network segment between nodes X_j and X_k



(coreactants and coproducts not shown) is

$$r_{j \rightarrow k} = \Lambda_{jk}[X_j] - \Lambda_{kj}[X_k] \quad (2)$$

where the "segment coefficients" Λ are given by

$$\Lambda_{jk} = \frac{\prod_{i=j}^{k-1} \lambda_{i,i+1}}{D_{jk}} \quad \text{and} \quad \Lambda_{kj} = \frac{\prod_{i=k}^{j-1} \lambda_{i+1,i}}{D_{jk}} \quad (3)$$

with

$$D_{jk} = \sum_{i=j+1}^k \left(\prod_{m=j+1}^{i-1} \lambda_{m,m-1} \prod_{m=i}^{k-1} \lambda_{m,m+1} \right) \quad (4)$$

(products $\Pi = 1$ if the lower index exceeds the upper). More easily, D_{jk} is generated as the sum of the products of the rows of the square matrix of order n with elements 1 along the diagonal, with rate coefficients of the m th step in the m th column, and with forward rate coefficients above and reverse rate coefficients below the diagonal:

$$\begin{bmatrix} 1 & \lambda_{j+1,j+2} & \lambda_{j+2,j+3} & \dots & \lambda_{k-2,k-1} & \lambda_{k-1,k} \\ \lambda_{j+1,j} & 1 & \lambda_{j+2,j+3} & \dots & \lambda_{k-2,k-1} & \lambda_{k-1,k} \\ \lambda_{j+1,j} & \lambda_{j+2,j+1} & 1 & \dots & \lambda_{k-2,k-1} & \lambda_{k-1,k} \\ \dots & \dots & \dots & \dots & \dots & \dots \\ \lambda_{j+1,j} & \lambda_{j+2,j+1} & \lambda_{j+3,j+2} & \dots & 1 & \lambda_{k-1,k} \\ \lambda_{j+1,j} & \lambda_{j+2,j+1} & \lambda_{j+3,j+2} & \dots & \lambda_{k-1,k-2} & 1 \end{bmatrix} \quad (5)$$

For example, for $j = 0$ and $k = 4$ (three intermediates):

$$D_{04} = \lambda_{12}\lambda_{23}\lambda_{34} + \lambda_{10}\lambda_{23}\lambda_{34} + \lambda_{10}\lambda_{21}\lambda_{34} + \lambda_{10}\lambda_{21}\lambda_{32} \quad (6)$$

The λ coefficients are pseudo-first-order rate coefficients of quasi-single molecular steps and are the products of the actual rate coefficients and the concentrations of any coreactants of the respective steps. For example, for the step $X_0 + A \rightarrow X_1$, $\lambda_{01} = k_{01}[A]$.

Single-Cycle Networks. For a given overall reaction, the combination of all the elementary steps is called a reaction network. Consider a homogeneous catalytic reaction with the network shown in Figure 1. The steady-state rate through the cycle is

$$r = \frac{\left(\prod_{i=0}^n \lambda_{i,i+1} - \prod_{i=0}^n \lambda_{i+1,i} \right) [X_T]}{\sum_{i=0}^n D_{ii}} \quad (7)$$

(taking index $n + 1 = 0$)

where the generalized rate coefficient $\lambda_{i,i+1}$ is the product of the forward rate constant ($k_{i,i+1}$) and coreactant concentration, and D_{ii} can be obtained from a square matrix of order n by n by tearing the closed network into a linear one with the intermediate X_i on both ends.

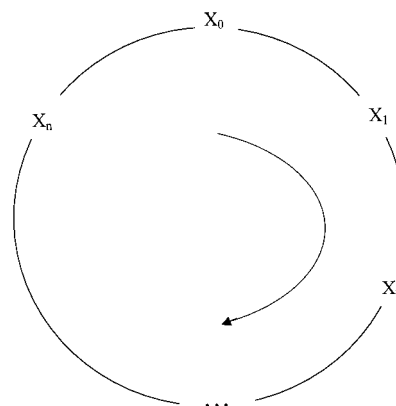


Figure 1. Single loop reaction network with an arbitrary number of intermediates (coreactants and coproducts not shown).

Equation 7 can be derived from the application of the Bodenstein approximation to the intermediates X_i , $i = 0, 1, \dots, n$, and the total catalyst or enzyme balance. According to eq 7, the steady-state rate through the reaction cycle is proportional to the total catalyst or enzyme concentration, $[X_T]$. Equation 7 is the general rate equation for a single-cycle network with an arbitrary number of intermediates. The denominator in eq 7 contains $(n + 1)^2$ terms. If the cycle contains at least one irreversible step, the general equation can be reduced to

$$r = \frac{\prod_{i=0}^n \lambda_{i,i+1} [X_T]}{\sum_{i=0}^n D_{ii}} \quad (8)$$

Note that some terms in the denominator of eq 7 can be canceled because all terms involving λ_{ji} are equal to zero if $X_i \rightarrow X_j$ is an irreversible step.

If intermediate X_i is the *masi* of the single-cycle network, i.e., $[X_i] \approx [X_T]$ and $[X_j] \approx 0$ for all $j \neq i$, all the D_{ij} ($j \neq i$) terms in eqs 7 and 8 can be neglected compared to D_{ii} and the rate equations can be greatly simplified.

Single-Cycle Networks with Occupied Sites. In some enzymatic or heterogeneous catalytic reactions some active sites may be occupied by the adsorption of nonreactive substrates. This adsorption of the nonreactive substrates will definitely reduce the steady-state rate through the cycle. If the adsorption of the nonreactive substrate is irreversible, the steady-state rate becomes zero and the enzyme or catalyst is said to be poisoned.

Consider a single-cycle network with one site occupied by a nonreactive species as shown in Figure 2. Applying the Bodenstein approximation to the intermediates in the cycle, X_0 to X_n , leads to

$$\begin{bmatrix} \lambda_{01}[X_0] - \lambda_{10}[X_1] = r \\ \lambda_{12}[X_1] - \lambda_{21}[X_2] = r \\ \dots \\ \lambda_{n0}[X_n] - \lambda_{0n}[X_0] = r \end{bmatrix} \quad (9)$$

The total catalyst or enzyme balance is

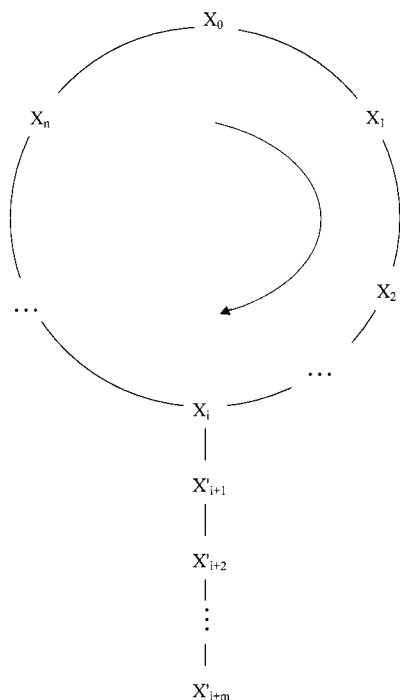


Figure 2. Single loop reaction network with single-branch deactivated intermediates from a single site (coreactants and coproducts not shown).

$$[X_T] = \sum_{j=0}^n [X_j] + \sum_{k=i+1}^{i+m} [X'_k] \quad (10)$$

Applying the Bodenstein approximation to the intermediates in the branch, X'_{i+1} to X'_{i+m} , leads to the fact that all the reaction steps in the branch are at equilibrium or there is no net rate through the branch. The intermediate concentrations in the branch can be expressed by the following equation:

$$[X'_k] = \frac{\prod_{j=1}^{k-1} \lambda'_{j,j+1}}{\prod_{j=1}^{k-1} \lambda'_{j+1,j}} [X_i] = K'_{ik} [X_i] \quad (11)$$

Combining eqs 9–11 leads to

$$r = \frac{(\prod_{i=0}^n \lambda_{i,i+1} - \prod_{i=0}^n \lambda_{i+1,i}) [X_T]}{\sum_{i=0}^n D_{ii} + D_{ir} S_{i,i+m}} \quad (12)$$

where

$$S_{i,i+m} = \sum_{k=i+1}^{i+m} K'_{ik} \quad (13)$$

With this S' notation, the linear branch leading to X'_{i+m} can be replaced by a single step: $X_i \leftrightarrow X'_{i+m}$.

Comparing eqs 7 and 12, one can find that the denominator in eq 12 contains m more terms that result from the site X_i occupied by a nonreactive species with m inactivated intermediates. These additional terms

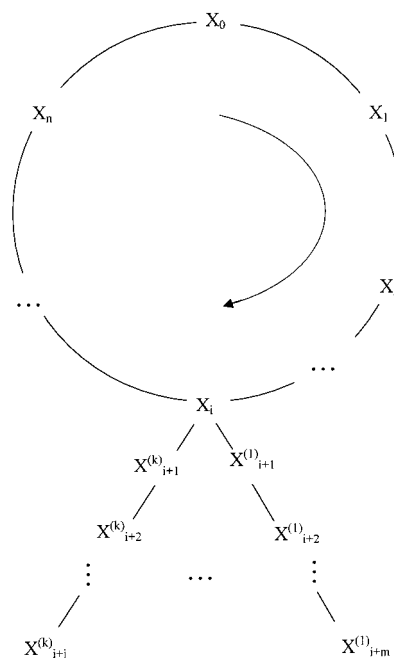


Figure 3. Single loop reaction network with multibranch deactivated intermediates from a single site (coreactants and coproducts not shown).

obviously decrease the steady-state rate through the cycle. If the adsorption of the nonreactive species contains at least one irreversible step, say, $\lambda'_{i+j,i+j-1} = 0$ for some j , then $K'_{ij} = \infty$ and the steady-state rate through the cycle becomes zero, according to eq 12. This means that an irreversible adsorption of a nonreactive species poisons the catalyst or enzyme.

Equation 12 can be easily extended to the case with multiple branches from the same site as shown in Figure 3. With the S' notation, all the branches can be reduced to single steps and the steady-state rate through the cycle is

$$r = \frac{(\prod_{i=0}^n \lambda_{i,i+1} - \prod_{i=0}^n \lambda_{i+1,i}) [X_T]}{\sum_{i=0}^n D_{ii} + D_{ir} \sum_{j=1}^m S_{i,i+k_j}} \quad (14)$$

Equation 12 can also be further extended to the case with multiple branches resulted from different sites, as shown in Figure 4. With the S' notation, all the branches can be reduced to single steps and the steady-state rate through the cycle is

$$r = \frac{(\prod_{i=0}^n \lambda_{i,i+1} - \prod_{i=0}^n \lambda_{i+1,i}) [X_T]}{\sum_{i=0}^n D_{ii} + \sum_i (D_{ii} \sum_{j=1}^m S_{i,i+k_j})} \quad (15)$$

Applications. As an example illustrating the application of the general rate equations, consider a simple reaction $A \leftrightarrow P$ with a nonreactive species occupying an active site (or an inhibitor complexing with the enzyme). Table 1 shows three different reaction mechanisms proposed and Figure 5 shows the corresponding reaction networks. The steady-state rate through the

Table 1. Hypothetical Mechanisms of Overall Reaction $A \leftrightarrow P$ with Inhibition

Mechanism I	Mechanism II	Mechanism III
$X_0 + A \xrightleftharpoons[k_{10}]{k_{01}} X_1$ $X_1 \xrightleftharpoons[k_{21}]{k_{12}} X_2$ $X_2 \xrightleftharpoons[k_{02}]{k_{20}} X_0 + P$ $X_0 + I \xrightleftharpoons[k'_{10}]{k'_{01}} X'_0$	$X_0 + A \xrightleftharpoons[k_{10}]{k_{01}} X_1$ $X_1 \xrightleftharpoons[k_{21}]{k_{12}} X_2$ $X_2 \xrightleftharpoons[k_{02}]{k_{20}} X_0 + P$ $X_1 + I \xrightleftharpoons[k'_{21}]{k'_{12}} X'_1$	$X_0 + A \xrightleftharpoons[k_{10}]{k_{01}} X_1$ $X_1 \xrightleftharpoons[k_{21}]{k_{12}} X_2$ $X_2 \xrightleftharpoons[k_{02}]{k_{20}} X_0 + P$ $X_2 + I \xrightleftharpoons[k'_{02}]{k'_{20}} X'_2$

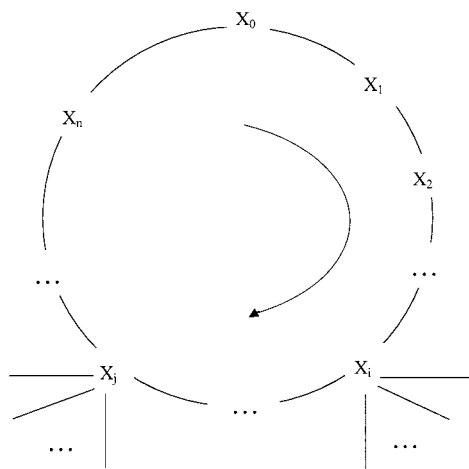


Figure 4. Single loop reaction network with multibranch deactivated intermediates from multiple sites (coreactants and coproducts not shown).

cycle for each mechanism can be easily obtained from eq 12. Substituting all the D_{ij} and S' into eq 12 and grouping the rate coefficients lead to the rate equations shown in Table 2.

As is clearly shown in Table 2, mechanisms I and II result in rate equations with different mathematical forms while mechanisms II and III result in mathematically indistinguishable rate equations. The initial rates in the absence of the product P are also shown in Table 2. Since there is no net rate in the branch, the inhibitor concentration remains unchanged during the reaction. Initial rate data are easier for use to discriminate mechanisms I and II. The initial rates for mechanisms I and II can be rewritten into the following linear forms:

$$\left[\begin{aligned} \frac{[A]}{r_0} &= \frac{1 + K_4[I]}{K_1} + \frac{K_2}{K_1}[A] && \text{for mechanism I} \\ \frac{[A]}{r_0} &= \frac{1}{K_1} + \frac{K_2 + K_4[I]}{K_1}[A] && \text{for mechanism II} \end{aligned} \right] \quad (16)$$

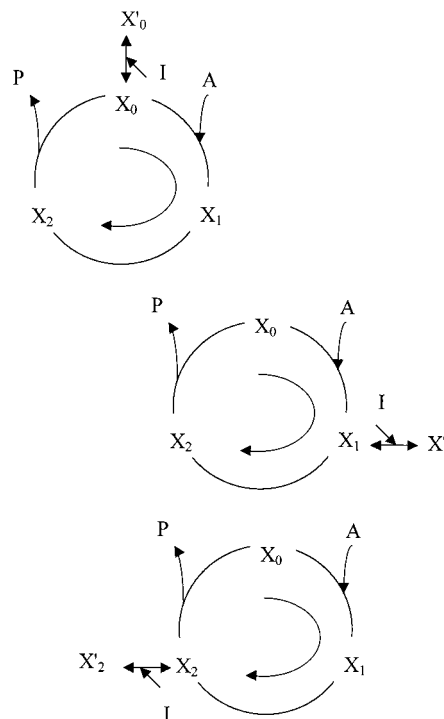


Figure 5. A single-cycle network with active site occupied by an inhibitor: a for mechanism I, b for mechanism II, c for mechanism III.

According to eq 16, a linearized plot of $[A]/r_0$ versus $[A]$ can be used to discriminate mechanisms I and II. For mechanism I, the slope is independent of the inhibitor concentration, $[I]$, while the intercept increases linearly with $[I]$, for mechanism II, the slope increases linearly with $[I]$ while the intercept is independent of $[I]$. The difference of the linearized plots can be seen more clearly in Figure 6.

In the rate equations, the equilibrium constant, K_{eq} , can be experimentally determined from the equilibrium concentrations of A and P or theoretically calculated from the free energy change of the reaction and is not

Table 2. Rate Equations of A \leftrightarrow P Corresponding to Different Mechanisms

Mechanism	Rate equation	Parameters
I	$r = \frac{K_1 \left([A] - \frac{[P]}{K_{eq}} \right)}{1 + K_2[A] + K_3[P] + K_4[I]}$ <p>initial rate:</p> $r_0 = \frac{K_1[A]}{1 + K_2[A] + K_4[I]}$	$K_{eq} = \frac{k_{01}k_{12}k_{20}}{k_{10}k_{21}k_{02}}$ $K_1 = \frac{k_{01}k_{12}k_{20}[X_T]}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_2 = \frac{k_{01}(k_{12} + k_{21} + k_{20})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_3 = \frac{k_{02}(k_{12} + k_{21} + k_{10})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_4 = \frac{k'_{01}}{k'_{10}}$
II	$r = \frac{K_1 \left([A] - \frac{[P]}{K_{eq}} \right)}{1 + K_2[A] + K_3[P] + K_4[A][I] + K_5[P][I]}$ <p>initial rate:</p> $r_0 = \frac{K_1[A]}{1 + K_2[A] + K_4[A][I]}$	$K_{eq} = \frac{k_{01}k_{12}k_{20}}{k_{10}k_{21}k_{02}}$ $K_1 = \frac{k_{01}k_{12}k_{20}[X_T]}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_2 = \frac{k_{01}(k_{12} + k_{21} + k_{20})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_3 = \frac{k_{02}(k_{12} + k_{21} + k_{10})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_4 = \frac{k_{01}(k_{20} + k_{21})k'_{12}}{k'_{21}(k_{12}k_{20} + k_{10}k_{21} + k_{10}k_{20})}$ $K_5 = \frac{k_{21}k_{02}k'_{12}}{k'_{21}(k_{12}k_{20} + k_{10}k_{21} + k_{10}k_{20})}$
III	$r = \frac{K_1 \left([A] - \frac{[P]}{K_{eq}} \right)}{1 + K_2[A] + K_3[P] + K_4[A][I] + K_5[P][I]}$ <p>initial rate:</p> $r_0 = \frac{K_1[A]}{1 + K_2[A] + K_4[A][I]}$	$K_{eq} = \frac{k_{01}k_{12}k_{20}}{k_{10}k_{21}k_{02}}$ $K_1 = \frac{k_{01}k_{12}k_{20}[X_T]}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_2 = \frac{k_{01}(k_{12} + k_{21} + k_{20})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_3 = \frac{k_{02}(k_{12} + k_{21} + k_{10})}{k_{12}k_{20} + k_{10}k_{20} + k_{10}k_{21}}$ $K_4 = \frac{k_{01}k_{12}k'_{20}}{k'_{02}(k_{12}k_{20} + k_{10}k_{21} + k_{10}k_{20})}$ $K_5 = \frac{k_{02}(k_{12} + k_{10})k'_{20}}{k'_{02}(k_{12}k_{20} + k_{10}k_{21} + k_{10}k_{20})}$

an adjustable parameter to fit the experimental data to the kinetic model. The other lumped coefficients, K_1 to K_5 , are usually treated as adjustable parameters to fit the experimental data to the kinetic model or obtained from various linearized plots. The data fitting or parameter determination, which is not the primary

objective of this paper, can be found in many chemical reaction engineering textbooks.

Conclusions

Explicit rate equations for single-cycle networks with and without branches have been derived by using the

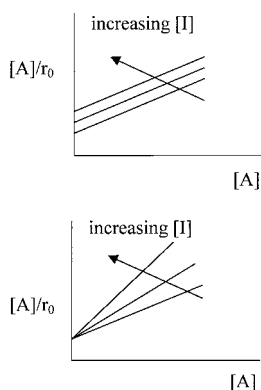


Figure 6. Linearized plots of initial rate equations: a for mechanism I, b for mechanism II or III.

network reduction technique systematically. These rate equations can be used to facilitate reaction pathway and network elucidation. For most homogeneous catalytic reactions involving first-order reactions with respect to the enzyme complexes, the general rate equations are applicable. The general rate equations are also applicable for the heterogeneous catalytic reactions with first-order steps in intermediates. However, for the heterogeneous catalytic reactions involving bimolecular surface reaction, dissociative adsorption, or associative desorption, the general rate equations are not applicable. The general rate equations and methodology developed in this study can facilitate practical engineers

to establish kinetic models that correctly reflect reaction pathways and networks for scale-up and optimization.

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