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Controllability conditions for chemical and microbiological systems

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ABSTRACT

To solve (bio)chemical problems, often required to control the processes. However, the investigated system is not controllable at every state–space point. It is necessary to know what conditions must be provided for controllability. In this paper, we determine conditions for the controllability of chemical and microbiological reactions in isothermal and non-isothermal cases. In two examples, we show how can be applied the results in the study of different processes.

1. Introduction

The controllability of chemical and microbiological systems is an important issue in engineering practice. The amount of (harmful) by-products can be minimized, and the amount of required products can be maximized by controlling reactions. The controllability conditions depend on the kinetics of the reaction, the type of the reactor, the temperature dependence of the process, Etc. In order to control the processes, the conditions for controllability must be known.

The investigation of controllability is a wide area of researches. Several papers deal with the investigation of the controllability of (bio)chemical systems. A sufficient condition of local controllability of chemical reactions controlled by the reaction rate constants is shown in [1]. The global controllability of chemical reactions controlled by the reaction rate constants is investigated in [2]. A sufficient condition of global controllability for chemical reactions with temperature input is presented in [3]. The stability and controllability analysis of chemical processes are studied in [4]. The authors deal with the assessment of process controllability in [5]. An example for a flatness-based analysis of chemical reaction is shown in [6]. Controllability aspects of microbial growth processes based on the biomass age distribution are studied in [7].

In industrial processes, the reactions usually take place in a reactor. The type of the applied reactor influences the transport dynamics of the process; therefore, it must also be considered for controllability investigations. The local controllability of stirred tank reactors is investigated in [8]. Necessary conditions for controllability in a continuous stirred tank reactor are presented in [9].

In this paper, we study controllability conditions for chemical and microbiological systems. The rank condition from the control theory gives a necessary and sufficient condition for controllability in the case of nonlinear systems. In this work, we investigate, how to specify the condition of the rank theorem for chemical and microbiological systems in special cases. In addition to the form of the reaction, the type of the reactor is also considered in the investigations. The controllability of the reactions is studied in both isothermal and non-isothermal cases. The application of the results is shown in two examples (yeast growth, oximation reaction).

2. Mathematical description of reaction systems

In this section, the mathematical model of the investigated systems is shown. First, we describe the model for microbiological and chemical systems; then, we show the types of the applied reactors.

2.1. Microbiological systems

To describe the microbiological system, we will use the following state–space model [10]. Suppose that the system contains N components and M reactions. The general dynamical model of bioreactors reads

$$\frac{d\xi}{dt} = K\varphi(\xi, t) - D\xi - Q(\xi) + F. \tag{1}$$

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The state vector ξ has the form $\xi = (\xi_1, \xi_2, \dots, \xi_N)^T$, where $\xi_i,\ i = 1, 2, \dots, N$, are the concentrations of the components. The concentration changing over time is determined by the kinetics of the reaction and the transport processes between the system and the outside environment. At the right-hand side of Eq. (1), $K\varphi(\xi, t)$ represents the kinetics of the reaction, and $-D\xi - Q(\xi) + F$ models the transport dynamics of the components. In the part of the kinetics of Eq. (1), matrix $K = [K_{ij}]_{N\times M}$ contains the yield coefficients. The element K_{ij} reads

$$K_{ij} = \begin{cases} \pm k_{ij}, & \text{if the } j\text{th reaction step contains the} \\ & \xi_i \text{ component} \\ 0, & \text{else} \end{cases} \tag{2}$$

for all $i \in \{1, 2 \dots N\}$, and $j \in \{1, 2 \dots M\}$. The sign of the yield coefficient k_{ij} is positive if component ξ_i is a product and negative if component ξ_i is a reactant. The vector field $\varphi = (\varphi_1, \varphi_2, \dots, \varphi_M)^T$ contains the reaction rates for the reaction steps.

In the part of the transport dynamics of Eq. (1) D denotes the rate of the influent flow rate F_{in} and the volume of the reactor V,

$$D = \frac{F_{in}}{V}. \tag{3}$$

The change of the volume V in time can be written by the expression

$$\frac{dV}{dt} = F_{in} - F_{out}, \tag{4}$$

where F_{out} is the effluent flow rate. In the following, we will study batch and CSTR type systems. In the case of these reactor types $F_{in} = F_{out}$, therefore the volume V can be considered constant. The vector field Q has the form $Q = (Q_1, Q_2, \dots, Q_N)^T$, where Q_i is the rate of mass outflow for the component ξ_i for all $i \in \{1, 2, \dots, N\}$. The vector field $F = (F_1, F_2, \dots, F_N)^T$ contains the mass feed rates. The element F_i reads

$$F_i(t) = \begin{cases} \text{the mass feed rate of the component } \xi_i, \\ \text{if } \xi_i \text{ is an external substrate} \\ 0, \quad \text{otherwise} \end{cases} \tag{5}$$

for all $i \in \{1, 2 \dots N\}$.

2.2. Chemical systems

The general model of chemical systems can be described with a similar method to the model of biological systems. The change in concentrations over time is determined by the kinetics of the reactions and the transport processes. The part of the transport dynamics can be modeled in an analogous way to biological systems; however, the kinetics model is slightly different [10].

For modeling chemical systems, we will also denote by N the number of the components and M for the number of the reactions. The general dynamical model of a chemical system reads

$$\frac{dx}{dt} = \gamma r(x, t) - Dx - Q(x) + F. \tag{6}$$

In Eq. (6), x denotes the vector field of the concentrations. It has the form $x = (x_1, x_2, \dots, x_N)^T$, where x_i denotes the concentration of component X_i for all $i \in \{1, 2, \dots, N\}$. In the kinetics part, γ denotes the stoichiometric matrix, and $r(x, t)$ represents the reaction rate.

In the case of biological systems, the kinetics part can be determined only empirically. In contrast, in the case of chemical reactions, the stoichiometric matrix and the reaction rate can be given by knowing the reaction equation, the concentrations, and the reaction rate coefficients [10,11]. Consider a chemical reaction of general form,

$$\sum_{i=1}^{N} \alpha_{ij} X_i \xrightarrow{k_j} \sum_{i=1}^{N} \beta_{ij} X_i, \qquad j = 1, 2, \dots, M. \tag{7}$$

In Eq. (7), $X_i,\ i \in \{1, 2, \dots, N\}$ denote the components. The components at the left-hand side are called reactants, and the components at the right-hand side are called products. The stoichiometric coefficients in the jth reaction step are denoted by α_{ij} for the X_i reactant and β_{ij} for the X_i product. With these notations, the elements of the stoichiometric matrix $\gamma = [\gamma_{ij}]_{N\times M}$ can be specified; $\gamma_{ij} = \beta_{ij} - \alpha_{ij}$ for all $i \in \{1, 2, \dots, N\}$, and $j \in \{1, 2, \dots, M\}$.

The reaction rate $r(x, t)$ can be given by the mass action law. The elements of the vector field $r(x, t) = (r_1(x, t), r_2(x, t), \dots, r_M(x, t))^T$ are then $r_j(x, t) = k_j \prod_{i=1}^{N} x_i^{\alpha(i,j)}$, where k_j is the reaction rate coefficient for the jth reaction step for all $j \in \{1, 2, \dots, M\}$.

Note that for catalytic reactions or biological reactions, other expressions for the reaction rates can be considered, like the Langmuir–Hinshelwood expression for catalytic reactions, or Monod, Contois or Haldane models for biological reactions (see e.g. [10]). Yet in the examples considered below, simple kinetic models that follow the above basic kinetic rule of being equal to zero in the absence of any reactant/substrate (and of the autocatalyst X in biological reactions) involved in the reaction. This has been done to keep a tractable controllability analysis while being consistent with the fundamental kinetic rules.

In microbiological processes, only a small change in temperature is allowed because the microorganisms cannot tolerate the major changes in their environment. A significant temperature change destroys them. Thus, biological processes can generally be considered isothermal. In contrast, significant temperature changes can occur during chemical reactions. If the reaction is non-isothermal, the equation describing the temperature change must also be considered in the modeling [9]. The completed system reads

$$\frac{dx}{dt} = \gamma r(x, t) - Dx + u, \tag{8}$$

$$\frac{dT}{dt} = \sum_{j=1}^{M} h_j r_j(x, T) - D_T T + u_T, \tag{9}$$

where h_j represents the heat of the jth reaction step for all $j \in \{1, 2, \dots, M\}$, $T \in \mathbb{R}_0^+$ denotes the temperature, and D_T is the heat flow per unit volume. In Eq. (8), u is the concentration changing input, and u_T denotes the input of the temperature changing in Eq. (9). This model does not consider the rate of mass outflow for the components.

2.3. Reactor types

In the case of chemical and biological processes, in addition to the form of the reaction, the type of reactor also influences the processes that take place. Therefore, the type of the used reactor must also be considered. The CSTR (Continuous Stirred Tank Reactor) and batch reactors are two particular reactor types that are often used in practice [10,8,12].

- Batch reactor
  A reactor is called a batch reactor, if $F_{in} = F_{out} = 0$, i.e., if neither inflow nor outflow during the reaction. In batch case, the part of the transport dynamics of the dynamical models (1) and (6) is equal with 0; therefore, the dynamics have the following forms; in the case of biological systems

$$\frac{d\xi}{dt} = K\varphi(\xi, t), \tag{10}$$

in the case of chemical systems

$$\frac{dx}{dt} = \gamma r(x, t). \tag{11}$$

- CSTR
  A reactor is called a continuous stirred tank reactor if $F_{in} = F_{out}$, i.e., if the inflow is equal with the outflow. In the CSTR case, the dynamical models (1) and (6) describe the system.

3. Investigation of controllability

We investigate the conditions of controllability for biological and chemical systems in the case of batch and CSTR reactors. Biological processes are considered isothermal. In the case of chemical reactions, in both isothermal and non-isothermal cases, we investigate how the conditions of controllability can be specified.

Consider a nonlinear system given by the following differential equation

$$\dot{\xi} = f(\xi) + g(\xi)u, \quad \xi(0) = \xi^* \in \mathbb{R}^n, \tag{12}$$

where $f, g \in \mathbb{C}^\infty(\mathbb{R}^n, \mathbb{R}^n)$ are smooth vector fields, and $u \in \mathbb{R}$ is the control input variable [13–15,3].

Definition 1. Define the $R(x^*, T)$ reachability set: $R(x^*, T) = \{x(T)|$ the set of the states of the system (12) at time T if the initial condition is $x(0) = x^*$ with all of the possible bounded input u provided that the solution is defined on $[0, T]\}$.

The system described with differential equation (12) is called strongly reachable from point x^* if the set $R(x^*, T)$ has an interior point for all $T > 0$.

Definition 2. Suppose that $f \in \mathbb{C}^\infty(\mathbb{R}^n, \mathbb{R}^n)$ and $g \in \mathbb{C}^\infty(\mathbb{R}^n, \mathbb{R}^n)$ vector fields. The Lie bracket of the vector fields f and g reads

$$[f, g] = Dg \cdot f - Df \cdot g. \tag{13}$$

Definition 3. The operator assigns a linear subspace of $\mathbb{R}^N$ to each $x \in \mathbb{R}^N$ point is called a distribution. Distributions are denoted by Δ.

Definition 4. The controllability distribution Δ_c of (12) is the smallest distribution which satisfies the following conditions,

- $g \in \Delta_c$,
- for all $\eta \in \Delta_c$ Lie bracket $[\eta, f] \in \Delta_c$,
- for all $\eta_1, \eta_2 \in \Delta_c$ Lie bracket $[\eta_1, \eta_2] \in \Delta_c$.

To investigate controllability, we can use a rank condition known from control theory [13].

Theorem 1. *Consider the controllability distribution Δ_c of (12). The System (12) is strongly reachable at point $\xi^* \in \mathbb{R}^n$ if and only if $\dim \Delta_c(\xi^*) = n$.*

In Theorem 1, n denotes the number of the linearly independent equations. If the differential equations describing the system are all independent, n is equal to the number of equations, i.e., $n = N$. However, in the case of biological and chemical systems, the differential equations are usually not all independent.

Example 1. Consider a simple isomerization reaction in a batch system,

$$X_1 \xrightarrow{k_1} X_2. \tag{14}$$

The differential equations describing the system reads

$$\dot{x}_1 = -k_1 x_1, \tag{15}$$

$$\dot{x}_2 = k_1 x_1. \tag{16}$$

It is easy to see that the two equations are not linearly independent.

For linearly dependent systems, the largest independent subsystem can be determined using the following algorithm [10]. Consider a biological reaction in the form (1)

$$\frac{d\xi}{dt} = K\varphi(\xi, t) - D\xi - Q(\xi) + F. \tag{17}$$

Denote p the rank of matrix K. Let be K_a $(p \times N)$ an arbitrary full rank submatrix of K, and K_b is the remaining submatrix of K. Denote (ξ_a, ξ_b), (Q_a, Q_b), and (F_a, F_b) the appropriate partitions of ξ, Q, and F. Then the dynamic model (17) can be written in

$$\frac{d\xi_a}{dt} = K_a\varphi(\xi_a, t) - D\xi_a - Q_a(\xi_a) + F_a, \tag{18}$$

$$\frac{d\xi_b}{dt} = K_b\varphi(\xi_b, t) - D\xi_b - Q_b(\xi_b) + F_b \tag{19}$$

form. The state transformation $Z = A_0\xi_a + \xi_b$ can be used to determine the linearly independent subsystem, where A_0 $((N - p) \times p)$ represents the unique solution of the matrix equation $A_0K_a + K_b = 0$. Then the linearly independent system equivalent to Eq. (17) is

$$\frac{d\xi_a}{dt} = K_a\varphi(\xi_a, t) - D\xi_a - Q_a + F_a, \tag{20}$$

$$\frac{dZ}{dt} = -DZ + A_0(F_a - Q_a) + (F_b - Q_b). \tag{21}$$

In the following, we investigate how can be expressed the number of the linearly independent equations n in special cases using the parameters in the general dynamic model.

3.1. Batch systems

First, we will determine the form of n for batch systems. The dynamics of (isothermal) biological systems in a batch reactor can be described by Eq. (10),

$$\frac{d\xi}{dt} = K\varphi(\xi, t). \tag{22}$$

Suppose the reactions describe model (1) are independent. The system (22) is linearly independent if and only if the elements of $\varphi(\xi, t)$ can be uniquely specified by the elements of K and $d\xi/dt$. The problem can be considered if the solvability of an "$Ax = b$" forms linear equation system should be determined. The system (22) is linearly independent if and only if it has a unique solution like a linear equation system. System (22), like a linear equation system, has a unique solution if and only if matrix K has full rank. In other words, the number of the independent equations must be equal to the rank of the largest full rank submatrix in K. Therefore, for (isothermal) biological systems in a batch reactor, $n = \mathrm{rank}(K)$.

The number of linearly independent equations can be determined similarly for isothermal chemical reactions in a batch reactor. The dynamics of the isothermal chemical system can be described by Eq. (11),

$$\frac{dx}{dt} = \gamma r(x, t). \tag{23}$$

The problem can also be treated as investigating the solvability of a linear system of equations. In this case, the number of linearly independent equations must be equal to the rank of the largest full rank submatrix from γ. Therefore, in the case of isothermal chemical reactions in a batch reactor $n = \mathrm{rank}(\gamma)$.

For non-isothermal chemical reactions in a batch reactor, the system can be described by Eqs. (8)–(9)

$$\frac{dx}{dt} = \gamma r(x,t), \tag{24}$$

$$\frac{dT}{dt} = \sum_{j=1}^{M} h_j r_j(x,T) + u_T. \tag{25}$$

The system of Eqs. (24)–(25) can be written in "$Ax = b$" form,

$$\begin{pmatrix} \frac{dx}{dt} \\ \frac{dT}{dt} \end{pmatrix} = \begin{pmatrix} \gamma & 0 \\ h & 1 \end{pmatrix} \begin{pmatrix} r(x,t) \\ u_T \end{pmatrix}, \tag{26}$$

where h denotes the vector field $h = (h_1, h_2, \dots, h_M)$. In Eq. (26), matrix γ is $N \times M$ times, vector field h is $1 \times M$ times, vector field 0 is $N \times 1$ times, and 1 is an 1×1 times constant. Based on an argument similar to isothermal biological systems

$$n = \operatorname{rank}\begin{pmatrix} \gamma & 0 \\ h & 1 \end{pmatrix}. \tag{27}$$

The last row of the matrix is linearly independent of the others, therefore leaving the last row, the rank of the matrix decreases by 1. So the Condition (27) can be written in a more simple form; for non-isothermal chemical reactions in a batch reactor $n = \operatorname{rank}(\gamma) + 1$.

3.2. Continuous stirred tank reactors

In the following, we determine the expression for the number of independent equations n in the case of CSTR. The dynamics of (isothermal) biological systems in a CSTR reactor can be described by Eq. (1),

$$\frac{d\xi}{dt} = K\varphi(\xi,t) - D\xi - Q(\xi) + F. \tag{28}$$

Similar to the batch case, Eq. (28) describing the dynamics can be transformed to "$Ax = b$" form,

$$\frac{d\xi}{dt} + D\xi + Q = \begin{pmatrix} K & I_F \end{pmatrix} \begin{pmatrix} \varphi(\xi,t) \\ F \end{pmatrix}, \tag{29}$$

where the elements of the matrix $I_F = [I_F\ ij]_{N\times N}$ are the follows,

$$I_F\ ij = \begin{cases} 1, & \text{if } i = j, \text{ and } F_i \neq 0 \\ 0, & \text{else.} \end{cases} \tag{30}$$

Eq. (29) can be written in another form,

$$\frac{d\xi}{dt} + D\xi + Q = \begin{pmatrix} K & g \end{pmatrix} \begin{pmatrix} \varphi(\xi,t) \\ u \end{pmatrix}, \tag{31}$$

where $g = I_F$ is the control vector field, and $u = F$ is the input of the system. System (31), like a linear equation system, has a unique solution if and only if the matrix $(K|g)$ has full rank and $\varphi(\xi,t)$ and u are linearly independent. The number of the linearly independent equations is equal to the rank of the matrix $(K|g)$, i.e. $n = \operatorname{rank}(K|g)$.

In the case of isothermal chemical systems, the system can be written in (6) form,

$$\frac{dx}{dt} = \gamma r(x,t) - Dx - Q(x) + F. \tag{32}$$

With a similar argument to the biological case, the expression of n for the isothermal chemical reactions in CSTR is $n = \operatorname{rank}(\gamma|g)$.

The following condition is known for determining the value of n for CSTR reactors [9].

Theorem 2. *Two simple necessary conditions for a continuous stirred tank reactor to be controllable are:*

- $q + \operatorname{rank}(K) \geq n$,
- $\operatorname{rank}(g, K) = n$,

where q is the number of inputs.

Remark 1. The first condition of Theorem 2 is a consequence of the second condition.

The rank of a block matrix is always less than or equal to the sum of the rank of the blocks, so

$$\operatorname{rank}(g, K) \leq \operatorname{rank}(g) + \operatorname{rank}(K). \tag{33}$$

The number of column vectors of the matrix g is equal to the number of inputs, therefore

$$\operatorname{rank}(g) \leq q. \tag{34}$$

It can be seen from (33) and (34) that

$$\operatorname{rank}(g, K) \leq q + \operatorname{rank}(K). \tag{35}$$

The first condition is derived from (35) using the second condition of the theorem.

3.3. The modification of the rank theorem

Based on the results obtained for the batch and CSTR systems, Theorem 1 can be modified as follows:

Consider the following nonlinear dynamical system, given by the differential equation

$$\dot{\xi} = f(\xi) + g(\xi)u, \quad \xi(0) = \xi^* \in \mathbb{R}^n, \tag{36}$$

where $f, g \in \mathbb{C}^\infty(\mathbb{R}^n, \mathbb{R}^n)$ are smooth vector fields, and $u \in \mathbb{R}$ is the control input variable.

Theorem 3. *Denote by Δ_c the controllability distribution for (36). The System (36) is strongly reachable at point $\xi^* \in \mathbb{R}^n$ if and only if $\dim \Delta_c(\xi^*) = n$, where n can be written in the following form*

Table 1
Expressions for the number of the linearly independent vector fields n.

Reaction	Reactor type	n
Isothermal biological system	batch	$\operatorname{rank}(K)$
Isothermal chemical system	batch	$\operatorname{rank}(\gamma)$
Non-isothermal chemical system	batch	$\operatorname{rank}(\gamma) + 1$
Isothermal biological system	CSTR	$\operatorname{rank}(K\|g)$
Isothermal chemical system	CSTR	$\operatorname{rank}(\gamma\|g)$

In other words, the necessary and sufficient condition to have strong reachability is that the full rank condition if verified for the matrix given in Table 1.

Remark 2. In the above cases, n can be written in the form $n = \operatorname{rank}(K^*|g)$, where

$$K^* = \begin{cases} K, & \text{for isothermal biological system} \\ \gamma, & \text{for isothermal chemical system} \\ \begin{pmatrix} \gamma_{N\times M} \\ h_{1\times M} \end{pmatrix}, & \text{for non-isothermal chemical system} \end{cases}. \tag{37}$$

For isothermal batch systems, the vector field g equals 0, so we get the expressions in the first two rows of Table 1. In the case of non-isothermal chemical systems in a batch reactor, we got the result that n has the form of (27), i.e.

$$n = \operatorname{rank}\begin{pmatrix} \gamma & 0 \\ h & 1 \end{pmatrix}. \tag{38}$$

Expression (38) is written in another form

$$n = \operatorname{rank}\begin{pmatrix} \gamma & \\ h & g \end{pmatrix}. \tag{39}$$

4. Applications

In the following, we will show two examples for an application of Theorem 3. First, in the case of a biological system (yeast growth), we examine when the system is controllable, and then in the case of a chemical example (oximation reaction), we determine the conditions of controllability. In the case of yeast growth, we suppose that the process works in a CSTR, and we consider the system isothermal. In the case of oximation reaction, a batch reactor is supposed, and the process is non-isothermal.

4.1. Yeast growth

As a biological example, we study the growth process of yeast [10]. It is assumed that the process takes place in a CSTR reactor. The following equations can describe the reaction

$$S + C \xrightarrow{\varphi_1 \curvearrowleft} X + P \tag{40}$$

$$S \xrightarrow{\varphi_2 \curvearrowleft} X + E + P \tag{41}$$

$$E + C \xrightarrow{\varphi_3 \curvearrowleft} X + P. \tag{42}$$

Eq. (40) is the respiratory growth on glucose, equation (41) is the fermentative growth on glucose, and Eq. (42) describes the respiratory growth on ethanol. In Eqs. (40)–(42)

S is the glucose concentration,
C is the dissolved oxygen concentration,
E is the ethanol concentration,
X is the yeast concentration, and
P is the dissolved carbon dioxide concentration.

The reaction rates for each processes are denoted by $\varphi_1, \varphi_2, \varphi_3$. Differential equations describing the system reads

$$\begin{pmatrix} \frac{dX}{dt} \\ \frac{dS}{dt} \\ \frac{dE}{dt} \\ \frac{dC}{dt} \\ \frac{dP}{dt} \end{pmatrix} = \begin{pmatrix} 1 & 1 & 1 \\ -k_1 & -k_2 & 0 \\ 0 & k_4 & -k_3 \\ -k_5 & 0 & -k_6 \\ k_7 & k_8 & -k_9 \end{pmatrix} \cdot \begin{pmatrix} SCX & 0 & 0 \\ 0 & SX & 0 \\ 0 & 0 & ECX \end{pmatrix} \cdot \begin{pmatrix} \alpha_1 \\ \alpha_2 \\ \alpha_3 \end{pmatrix} - D \begin{pmatrix} X \\ S \\ E \\ C \\ P \end{pmatrix} + \begin{pmatrix} 0 \\ DS_{in} \\ 0 \\ Q_{in} \\ 0 \end{pmatrix} - \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ Q_i \end{pmatrix}. \tag{43}$$

The dissolved carbon dioxide concentration, P, does not appear in the reactant side, and it can leave the liquid phase, therefore leaving the last equation from system (43) the system remains well described. The remaining equation system reads

$$\begin{pmatrix} \frac{dX}{dt} \\ \frac{dS}{dt} \\ \frac{dE}{dt} \\ \frac{dC}{dt} \end{pmatrix} = \begin{pmatrix} SCX\alpha_1 + SX\alpha_2 + ECX\alpha_3 \\ -k_1 SCX\alpha_1 - k_2 SX\alpha_2 \\ k_4 SX\alpha_2 - k_3 ECX\alpha_3 \\ -k_5 SCX\alpha_1 - k_6 ECX\alpha_3 \end{pmatrix} - D \begin{pmatrix} X \\ S - S_{in} \\ E \\ C \end{pmatrix} + Q_{in} \begin{pmatrix} 0 \\ 0 \\ 0 \\ 1 \end{pmatrix}. \tag{44}$$

The variable ξ generally has the form $\xi = (X, S, E, C)^T$, however in this case $\xi = (X, S - S_{in}, E, C)^T$. The vector field f and the control vector fields g_1, g_2 for system (44) are

$$f = \begin{pmatrix} SCX\alpha_1 + SX\alpha_2 + ECX\alpha_3 \\ -k_1 SCX\alpha_1 - k_2 SX\alpha_2 \\ k_4 SX\alpha_2 - k_3 ECX\alpha_3 \\ -k_5 SCX\alpha_1 - k_6 ECX\alpha_3 \end{pmatrix}, \tag{45}$$

$$g_1 = - \begin{pmatrix} X \\ S - S_{in} \\ E \\ C \end{pmatrix}, \quad g_2 = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 1 \end{pmatrix}. \tag{46}$$

Controllability can be investigated using Theorem 3. In the case of isothermal biological systems in CSTR, Theorem 3 tells that the system is strongly reachable if and only if $\dim \Delta_c(\xi^*) = \operatorname{rank}(K|g)$. For system (44), the form of the matrix (Kg) is

$$(Kg) = \left(\begin{array}{ccc|cc} 1 & 1 & 1 & X & 0 \\ -k_1 & -k_2 & 0 & S - S_{in} & 0 \\ 0 & k_4 & -k_3 & E & 0 \\ -k_5 & 0 & -k_6 & C & 1 \end{array}\right). \tag{47}$$

The rank of matrix (Kg) is almost everywhere $n = 4$. The matrix has singularities at the points $k_2 k_3 - k_1 k_4 - k_1 k_3 = 0$. First we suppose that $k_2 k_3 - k_1 k_4 - k_1 k_3 \neq 0$. Thus the system is strongly reachable if and only if the dimension of the controllability distribution is 4. The system contains two control vector fields, g_1 and g_2, so two linearly independent Lie brackets must be found, linearly independent of each other and from g_1 and g_2. Lie brackets $[f, g_2]$ and $[[f, g_2], g_1]$ has the forms

$$[f, g_2] = \begin{pmatrix} SX\alpha_1 + EX\alpha_3 \\ -k_1 SX\alpha_1 \\ -k_3 EX\alpha_3 \\ -k_5 SX\alpha_1 - k_6 EX\alpha_3 \end{pmatrix}, \tag{48}$$

$$[[f, g_2], g_1] = \begin{pmatrix} (S - S_{in})X\alpha_1 + EX\alpha_3 \\ -k_1 (S - S_{in})X\alpha_1 \\ -k_3 EX\alpha_3 \\ -k_5 (S - S_{in})\alpha_1 - k_6 EX\alpha_3 \end{pmatrix}. \tag{49}$$

To determine the linear independence of the vector fields g_1, g_2, $[f, g_2]$ and $[[f, g_2], g_1]$, we can form the following matrix from the vector fields,

$$\Theta = (g_1, g_2, [f, g_2], [[f, g_2], g_1]). \tag{50}$$

The determinant of matrix Θ is $\det(\Theta) = S_{in} X^2 E \alpha_1 \alpha_3 (k_1 k_3 X + k_3 (S - S_{in}) + k_1 E)$. Matrix Θ has full rank if $X \neq 0$, $E \neq 0$, and $S_{in} \notin \{0, k_1 X + S + \frac{k_1}{k_3} E\}$. Therefore, based on Theorem 1, the system is strongly reachable if $X \neq 0$, $E \neq 0$, and $S_{in} \notin \{0, k_1 X + S + \frac{k_1}{k_3} E\}$.

Consider the $k_2 k_3 - k_1 k_4 - k_1 k_3 = 0$ singularity points. The rank of the matrix in the singularity points is $n = 3$, so the system is strongly reachable in these points if and only if the dimension of the controllability distribution is $n = 3$. Consider the matrix formed from the vector fields g_1, g_2, and $[f, g_2]$,

$$\Theta_{singularity} = (g_1, g_2, [f, g_2]). \tag{51}$$

The last row of the matrix $\Theta_{singularity}$ is linearly independent of the other rows, so leaving it out of the matrix, the rank decreases by 1. The second column of the remaining matrix is a zero vector. Leaving the second column out of the matrix does not reduce the rank. Then the remaining matrix can be transformed with equivalent transformations to

$$\tilde{\Theta}_{singularity} = \begin{pmatrix} X + \frac{S - S_{in}}{k_1} + \frac{E}{k_3} & 0 \\ \frac{S - S_{in}}{k_1} & -k_1 SX\alpha_1 \\ \frac{E}{k_3} & -k_3 EX\alpha_3 \end{pmatrix} \tag{52}$$

form. Matrix $\tilde{\Theta}_{singularity}$ has full rank if it has a 2×2 times submatrix, whose determinant is not zero, i.e., if $-SX\alpha_1(X + (S -$

$\mathrm{S_{in}}/k_1 + \mathrm{E}/k_3)) \neq 0$, or $-\mathrm{EX}\alpha_1(\mathrm{X} + (\mathrm{S} - \mathrm{S_{in}}/k_1 + \mathrm{E}/k_3)) \neq 0$, or $\mathrm{EX}\alpha_3/(\mathrm{S} - \mathrm{S_{in}})k_1 - \mathrm{SX}\alpha_1(\mathrm{E}/k_3) \neq 0$. Simplifying the terms, the condition of the controllability is the follows. The system is strongly reachable at the singularity points $k_2k_3 - k_1k_4 - k_1k_3 = 0$ if $\mathrm{X} \neq 0$ and one of the following conditions are satisfied:

- $\alpha_1 \neq 0,\ \mathrm{X} + \frac{\mathrm{S}-\mathrm{S_{in}}}{k_1} + \frac{\mathrm{E}}{k_3} \neq 0$, and $S \neq 0$ or $\mathrm{E} \neq 0$
- $\mathrm{E} \neq 0$ and $\alpha_3 \frac{\mathrm{S}-\mathrm{S_{in}}}{k_1} - \alpha_1 \frac{\mathrm{S}}{k_3} \neq 0$.

4.2. Oximation reaction

As a chemical example, an oximation reaction in a batch system is investigated [16]. It is studied in the case of an acidic medium. The following equations can describe the reaction,

$$\mathrm{X_1} + \mathrm{X_2} \xrightarrow{k_1} \mathrm{X_3} \tag{53}$$

$$\mathrm{X_3} + \mathrm{X_4} \xrightarrow{k_2} \mathrm{X_5} + \mathrm{X_6}. \tag{54}$$

Eq. (53) shows the formation of hydroxylamine hydrochloride from hydroxylamine and hydrochloric acid, and Eq. (54) describes the formation of acetoxime hydrochloride from hydroxylamine hydrochloride and acetone. In Eqs. (53)–(54)

$\mathrm{X_1}$ is the hydroxylamine,
$\mathrm{X_2}$ is the hydrochloric acid,
$\mathrm{X_3}$ is the hydroxylamine hydrochloride,
$\mathrm{X_4}$ is the acetone,
$\mathrm{X_5}$ is the acetoxime hydrochloride, and
$\mathrm{X_6}$ is the water.

The reaction rate coefficients for the corresponding reactions are k_1 and k_2. The reaction is non-isothermal, so the equation for temperature changing must be considered in the investigations. The input of the system is $\dot{T}$.

The system of differential equations describing system (53)–(54) is

$$\begin{pmatrix} \frac{dx_1}{dt} \\ \frac{dx_2}{dt} \\ \frac{dx_3}{dt} \\ \frac{dx_4}{dt} \\ \frac{dx_5}{dt} \\ \frac{dx_6}{dt} \end{pmatrix} = \begin{pmatrix} -1 & 0 \\ -1 & 0 \\ 1 & -1 \\ 0 & -1 \\ 0 & 1 \\ 0 & 1 \end{pmatrix} \cdot \begin{pmatrix} k_1x_1x_2 \\ k_2x_3x_4 \end{pmatrix}, \tag{55}$$

$$\frac{dT}{dt} = \frac{k_1}{\beta}x_1x_2 + \frac{k_2}{\beta}x_3x_4 + u_T. \tag{56}$$

The vector field f and the control vector field g for the system (55) reads

$$f = \begin{pmatrix} -k_1x_1x_2 \\ -k_1x_1x_2 \\ k_1x_1x_2 - k_2x_3x_4 \\ -k_2x_3x_4 \\ k_2x_3x_4 \\ k_2x_3x_4 \\ \frac{k_1}{\beta}x_1x_2 + \frac{k_2}{\beta}x_3x_4 \end{pmatrix}, g = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{pmatrix}. \tag{57}$$

Theorem 3 can be used to study controllability. In the case of non-isothermal chemical reactions in a batch reactor, the system is strongly reachable if and only if $\dim \Delta_c = \mathrm{rank}(\gamma) + 1$. The rank of the stoichiometric matrix is $\mathrm{rank}(\gamma) = 2$, so the system is strongly reachable if and only if the dimension of the controllability distribution is 3. To determine the conditions of controllability, the linear independence of the Lie brackets formed from the vector fields f and g must be studied. The Lie brackets $[f, g]$, and $[[f, g], g]$ reads

$$[f, g] = \begin{pmatrix} -\frac{dk_1}{dT}x_1x_2 \\ -\frac{dk_1}{dT}x_1x_2 \\ \frac{dk_1}{dT}x_1x_2 - \frac{dk_2}{dT}x_3x_4 \\ -\frac{dk_2}{dT}x_3x_4 \\ \frac{dk_2}{dT}x_3x_4 \\ \frac{dk_2}{dT}x_3x_4 \\ \frac{1}{\beta}\frac{dk_1}{dT}x_1x_2 + \frac{1}{\beta}\frac{dk_2}{dT}x_3x_4 \end{pmatrix}, \tag{58}$$

$$[[f, g], g] = \begin{pmatrix} -\frac{d^2k_1}{dT^2}x_1x_2 \\ -\frac{d^2k_1}{dT^2}x_1x_2 \\ \frac{d^2k_1}{dT^2}x_1x_2 - \frac{d^2k_2}{dT^2}x_3x_4 \\ -\frac{d^2k_2}{dT^2}x_3x_4 \\ \frac{d^2k_2}{dT^2}x_3x_4 \\ \frac{d^2k_2}{dT^2}x_3x_4 \\ \frac{1}{\beta}\frac{d^2k_1}{dT^2}x_1x_2 + \frac{1}{\beta}\frac{d^2k_2}{dT^2}x_3x_4 \end{pmatrix}. \tag{59}$$

The matrix Θ can be formed from the vector fields g, $[f, g]$ and $[[f, g], g]$,

$$\Theta = \begin{pmatrix} g & [f, g] & [[f, g], g] \end{pmatrix}. \tag{60}$$

The last row of matrix Θ is linearly independent of the other row vectors, so leaving it from the matrix, the rank decreases by 1. The first column of the remaining matrix is a zero vector, so leaving it out of the matrix, the rank does not decrease. The row vectors of the given matrix are produced as a linear combination of the first and last rows, so leaving the other row vectors out of the matrix, the rank does not decrease. Denote the remaining matrix by $\tilde{\Theta}$,

$$\tilde{\Theta} = \begin{pmatrix} -\frac{dk_1}{dT}x_1x_2 & -\frac{d^2k_1}{dT^2}x_1x_2 \\ \frac{dk_2}{dT}x_3x_4 & \frac{d^2k_2}{dT^2}x_3x_4 \end{pmatrix}. \tag{61}$$

The determinant of matrix $\tilde{\Theta}$ is $\det \tilde{\Theta} = (\frac{dk_1}{dT}\frac{d^2k_2}{dT^2} - \frac{dk_2}{dT}\frac{d^2k_1}{dT^2})x_1x_2 x_3x_4$. Matrix $\tilde{\Theta}$ has full rank if $x_1 > 0$, $x_2 > 0$, $x_3 > 0$, $x_4 > 0$ and $\frac{dk_1}{dT}/\frac{d^2k_1}{dT^2} \neq \frac{dk_2}{dT}/\frac{d^2k_2}{dT^2}$. So the system is strongly reachable if x_1, x_2, x_3, x_4 are all positive, and the ratio of the first and second temperature derivatives of the reaction rate coefficients k_1 and k_2 are equal.

5. Conclusion

In this work, the controllability of reaction systems has been investigated. We determined the controllability conditions for chemical and microbiological processes in batch reactor and CSTR. The biological systems were considered isothermal because the microorganisms cannot tolerate the major temperature changes. In the case of chemical systems, isothermal and non-isothermal processes were also investigated. The application of the results has been shown in two examples; an isothermal biological system in CSTR (yeast growth) and a non-isothermal chemical system in a batch reactor (oximation reaction).

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