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Deficiency Theory in Chemical Reaction Networks: The Analogy of Chemical Kinetics of Models of Infectious Disease Transmission

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Submitted to the School of Mathematics in partial fulfilment for a degree in Master of Science in Applied Mathematics

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Master Thesis

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Abstract

The concept of deficiency theory plays a pivotal role in understanding the dynamics of chemical reaction networks. This research explores the concept of deficiency theory in chemical reaction networks(CRNs) and its analogy with models of infectious disease transmission.

In this study, we begin by introducing the fundamental principles of CRNs and the concept of deficiency, which is a combinatorial parameter that measures the network's potential for complex dynamical behavior. Chemical reaction networks are commonly studied through their reaction rate equations, which are typically described by mass action kinetics. These reactions can be mathematically represented using systems of ordinary differential equations (ODEs), where the deficiency theory characterizes the topological properties of the network. The deficiency, determined by the stoichiometry matrix, provides valuable insights into the network's stability and its capacity to exhibit complex dynamics

Interestingly, infectious disease transmission models, particularly those based on compartmental frameworks e.g. *SIR*, also involve systems of ODEs to describe the interactions between different compartments representing susceptible, infected, and recovered individuals. These models employ parameters that define the transmission and recovery rates, analogous to the reaction rates in chemical kinetics.

This comparative analysis between deficiency theory in chemical reaction networks and infectious disease transmission models offers a fresh perspective on both domains and presents a promising avenue for interdisciplinary research at the interface of mathematics, chemistry, and epidemiology.

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Declaration and Approval

I the undersigned declare that this dissertation is my original work and to the best of my knowledge, it has not been submitted in support of an award of a degree in any other university or institution of learning.

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Date

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In my capacity as a supervisor of the candidate's dissertation, I certify that this dissertation has my approval for submission.

Signature 2nd August 2023
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Dedication

I dedicate this thesis to my beloved family, whose unwavering love, support, and encouragement have been the pillars of my journey. Your belief in my abilities and sacrifices have propelled me forward during the challenging moments.

I also dedicate this work to my mentors and lecturers, whose guidance, expertise, and dedication have shaped my academic growth.

To my dear friends, your companionship and encouragement have made this journey more enjoyable and memorable. Your belief in my abilities has bolstered my confidence during challenging times.

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Bruno Rabson Alex Malipa

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1 Introduction

Deficiency theory is a fundamental concept in the study of chemical reaction networks. It describes how the number of reactions in a network can influence its dynamics and stability. Here, we aim to explore the various aspects of deficiency theory, particularly focusing on complex balancing and the deficiency zero and deficiency one theorems. These theorems provide a powerful framework for analyzing the qualitative behavior of chemical reaction networks. The most significant results are the Deficiency Zero Theorem and the Deficiency One Theorem. All other content here can be considered either as groundwork for the theorem statements or as additional clarification on the theorems themselves.

We explore the elements of reaction network structure, specifically introducing key terminology such as the standard basis, complexes, reaction vectors, rank, linkage classes, deficiency, reversibility, weak reversibility, strong linkage class and terminal strong linkage classes of a reaction network that are significant by defining them and providing examples. Thorough exploration of these elements of reaction network structure, defining them clearly, will provide a solid foundation for understanding the intricate dynamics and behaviors that arise within reaction networks.

Epidemiology is the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the prevention and control of health problems (John, 2001). Epidemiology and CRNs can be linked through the concept of disease transmission. In epidemiology, the spread of diseases within a population is of central importance. This spread can be analogous to chemical reactions occurring within a system. By using CRNs, researchers can model the transmission dynamics of diseases, capturing the interactions between infected and susceptible individuals in a population.

CRNs allow epidemiologists to simulate various scenarios, study the impact of different interventions, and gain insights into the factors influencing disease transmission. This modeling approach helps in understanding how diseases propagate, identifying critical points for intervention, and evaluating the effectiveness of public health measures. Both deficiency theory in chemical reaction networks and epidemiology share the idea of understanding the behavior of complex systems in their underlying structures. By understanding the underlying structure of a chemical reaction network or a disease spread, we can better predict and control their behavior.

The dynamics of disease transmission are then typically modeled with differential equa-

tions that describe the flow of individuals to and from the compartments as the population mixes, the disease is spread/contracted, and infected individuals progress through the stages of the disease(Simon, 2020). Differential equations offer a logical option since we can make sensible assumptions regarding the rates of infection and the progression of individuals through different disease stages. This article emphasizes the connection between compartmental dynamic models of disease transmission in this case the SIR model and chemical reaction kinetics.

1.1 Problem statement

Deficiency theory is a mathematical framework which focus on two important results: complex balancing and the deficiency zero and deficiency one theorems.

Complex balancing refers to the behavior of chemical reaction networks as they approach equilibrium. For a system to exhibit complex balancing, it must meet a series of requirements that guarantee the existence of a singular and stable equilibrium point. The requirements include:

- Detailed balance: The system must satisfy the principle of detailed balance, which requires that for every pair of reversible reactions, the ratio of the forward and reverse reaction rates must be equal to the ratio of the products and reactants' concentrations at equilibrium.
- Deficiency zero: The deficiency of the system must be zero or less than zero. A system with deficiency zero or less than zero has a unique and stable equilibrium point.
- Non-intersecting stoichiometric compatibility classes: The stoichiometric compatibility classes of the network must not intersect, meaning that no two classes share a common non-zero vector. Stoichiometric compatibility classes are sets of reactions that have identical stoichiometric coefficients for all species involved.
- Weak reversibility: The system must satisfy the principle of weak reversibility, which requires that for every pair of reactions, there must exist a reaction pathway that connects the products of one reaction to the reactants of the other reaction. (Horn, 1972)

Our investigation delves into the implications of complex balancing and its significance in the study of chemical reaction networks.

The deficiency zero theorem provides a necessary and sufficient condition for a chemical reaction network to admit a complex balanced equilibrium. The significance of the

deficiency zero theorem and its applications in predicting the behavior of chemical reaction networks is key in this study.(Anderson et al., 2010)

The deficiency zero theorem outlines the criteria for the existence of positive steady states in chemical reaction networks. It is used to determine the existence of positive steady states in such networks. We will explain the Deficiency One Theorem and its relevance to chemical reaction networks.

The Chemical Reaction Network (CRN) is a study on the dynamics of biochemical reactions in a system. In the context of disease transmission, the CRN can be used to model the interactions between pathogens, host cells, and immune responses. By using the CRN, we can analyze the behavior interactions and predict how they might lead to the spread of disease. The Deficiency Theorem in chemical reaction networks will help identify potential bottlenecks or vulnerabilities in the system that could be targeted to prevent or mitigate the spread of disease.

In this work, we offer illustrations and practical implementations of chemical reaction networks by reviewing work in epidemiology. Furthermore, we examine potential developments of deficiency theory and areas for future research.

2 Preliminaries

Our aim in this section is to provide definitions with examples with which reaction network structure and deficiency theory can be discussed. We will introduce terminology in an informal manner, emphasizing examples over strict definitions.

2.1 Reaction Networks

2.1.1 Definition

A chemical reaction network (CRN) is a network of three components $\{\mathscr{S},\mathscr{C},\mathscr{R}\}$ composed of the following;

- Species($\mathscr{S}$) refer to the various chemical substances that participate in a reaction, whether it be as reactants, products, or both. The set of chemical species involved in a given reaction network can be represented as $\mathscr{S} = \{S_1, \cdots, S_n\}$.
- Complexes($\mathscr{C}$) are defined as vectors comprised of non-negative values representing the quantities of each chemical species involved in the reaction. These vectors are derived from linear combinations of the participating species, and together, they form the set of complexes given by $\mathscr{C} = \{y_n\}$. The source vector and the product vector are denoted by y_n and y'_n respectively. (Anderson et al., 2020)
- Reaction ($\mathscr{R}_n$) is defined as a process that results in the transformation of one or more species into one or more different species. It is given by $\mathscr{R}_n = \{y_n \to y'_n\}$ where y_n is the source complex and y'_n is the product complex. A set of all reactions therefore is given by $\mathscr{R}_n = \{y_n \to y'_n | y_n, y'_n \in \mathscr{C}\}$ (Shi, 2020)

For example, consider the following network for the SIR model:

$$S + I \to 2I$$
$$S \to I \to R$$

Then we have

- Species, $\mathscr{S} = \{S, I, R\}$

- Complexes, $\mathscr{C} = \{S+I, 2I, S, I, R\}$
  In the above network where the number of species is $N = 3$ and the number of complexes is $n = 5$, the vectors associated with each complex are as follows;
  For complex S + I, we associate the vector $e_1 + e_2 = [1,1,0]$
  For complex 2I, we associate the vector $2e_2 = [0,2,0]$
  For complex S, we associate the vector $e_1 = [1,0,0]$
  For complex I, we associate the vector $e_2 = [0,1,0]$
  For complex R, we associate the vector $e_3 = [0,0,1]$
  These form a set of complex vectors for the SIR model. In general, for a network with N species and n distinct complexes we obtain a set of n complex vectors in $\mathbb{R}^N$. (Feinberg, 1987).

- Reactions, $\mathscr{R} = \{S+I \to 2I, S \to I, I \to R\}$
  For the reaction $S+I \to 2I$, the corresponding reaction vector in $\mathbb{R}^3$ is $2e_2 - (e_1 + e_2) = e_2 - e_1 = [-1,1,0]$, for the reaction $S \to I$, the corresponding reaction vector is $e_2 - e_1 = [-1,1,0]$ and for the reaction $I \to R$ the corresponding reaction vector is $e_3 - e_2 = [0,-1,1]$. The complete set of reaction vectors for the SIR model network is

$$\{2e_2 - (e_1 + e_2), e_2 - e_1, e_3 - e_2\}$$

The chemical reaction network above is SIR model. It is used to describe the spread of infectious diseases in a population. In a population, we can have; susceptible (S), infected (I), and recovered (R). The model assumes that individuals in the population move between these categories over time, based on their interactions with others in the population. (Rodrigues, 2016)

The disease can spread from infected individuals to susceptible individuals through interactions, such as through physical contact or sharing of objects. The chance of transmission depends on the contagiousness of the disease and the frequency and type of interactions between individuals. With time, some of the susceptible individuals will become infected. This increases the number of infected individuals (I) and decreases the number of susceptible individuals (S).

After a period of time, infected individuals recover and become immune to the disease. Once an individual is in the recovered category, they cannot be infected again hence removed from epidemiological system.

The exact rates of transmission and recovery can be estimated based on data, assumptions about the disease and the population. By simulating the dynamics of the SIR model, estimation of the expected number of people infected can be done, the timing and magnitude of the epidemic peak, and the impact of interventions such as vaccination or social

distancing measures. The model can be used to evaluate control strategies to eliminate the disease in the population.

2.1.2 Reaction network as an embedded graph

Chemical reaction networks can be represented as a graph, where the nodes are the different species involved in the reactions, and the edges are the reactions that connect them. To represent a reaction network as an embedded graph, we need to assign positions to the nodes and edges in a way that reflects the underlying chemical reaction.

A reaction network with n species can be embedded in $\mathbb{Z}^n_{\geq 0}$ in which the directed graph $G = (V, E)$ where $V \subseteq \mathbb{R}^n$ and $E \subseteq V \times V$ and $(y, y) \notin E$ for any $y \in V$. Reactions can be represented by vectors. Since vertices are points in $\mathbb{R}^n$, then an edge can be regarded as a vector in $\mathbb{R}^n$ (Craciun et al., 2020)

For example, the following chemical reaction network with three species and four reactions;

$$\begin{aligned} 2A &\to A + B \\ A + B &\to C \\ C &\to A + B \\ C &\to 2A \end{aligned}$$

can be represented in an embedded graph as follows;

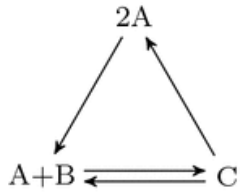


Figure 1. A reaction network represented as an embedded graph

The embedded graph representation can be used to analyze the structure of the reaction network, identifying important nodes or edges, and understanding the overall connectivity and dynamics of the system. It can also be used for further mathematical analysis or simulations to study the behavior of the chemical reaction network.

In epidemiology, reaction networks are used to model the spread of infectious diseases within a population. In this context, the nodes in the network represent individuals within the population, and the edges represent the possible ways that the disease can be transmitted from one individual to another.

2.2 Some key definitions

2.2.1 Standard basis of a reaction network

In the context of chemical reaction networks, the standard basis refers to a set of linearly independent vectors that form a basis for the stoichiometric subspace of the network. The stoichiometric subspace represents all possible combinations of reactants and products that can be formed through the reactions in the network while satisfying the law of mass action.

For example, consider the network for the SIR model above. If N is the number of species in a network under consideration, the in our case $N = 3$. By $\mathbb{R}^N$ we shall mean the usual vector space of N-tuples of real numbers. The standard basis for $\mathbb{R}^N$ will be denoted $\{e_1, e_2, \cdots, e_N\}$, (Feinberg, 1987) where

$$e_1 = [1,0,0]$$
$$e_2 = [0,1,0]$$
$$e_3 = [0,0,1]$$

2.2.2 Stoichiometric coefficient of species within a complex

The stoichiometric coefficient of a species refers to the numerical coefficient that appears in front of the chemical formula of that species.

For example, in the SIR model, the stoichiometric coefficients of species S and I in the complex $S+I$ are each 1, while that for the species R is 0. For the complex $2I$, the stoichiometric coefficient of the species I is 2 while that for the species S and R within this complex are all zero. This implies to all other complexes in the SIR model. It is important to take note that the stoichiometric coefficients of the species within the various complexes are all non-negative numbers. (Feinberg, 1987)

2.2.3 The rank of a reaction network

The rank of a reaction network refers to the number of linearly independent reactions in the network. It represents the maximum number of reactions that can occur independently of each other within the network. That is, the rank of a network is the number of elements in the largest linearly independent set of reaction vectors for the network. (Feinberg, 1987)
The rank of the network is the rank of the stoichiometric matrix of a network which can be computed by standard methods in matrix theory.

2.2.4 Stoichiometric subspace of a reaction network

The linear subspace $S = \text{span}_{\mathbb{R}}(y' - y \mid y \to y' \in G)$ generated by all reaction vectors is called the stoichiometric subspace of the network. Denote $\dim(S) = s$ (Craciun et al., 2020). The stoichiometric subspace, s, for the network is just the line in $\mathbb{R}^N$ that passes through the origin and contains the reaction vectors (Feinberg, 1987). In much simpler terms s is the rank of the stoichiometric matrix of the reaction network.

2.2.5 Compatibility class of reaction network

A compatibility class is a set of reactions that can coexist without violating the conservation laws of the network. Conservation laws refer to the principle of mass conservation in chemical reactions. This principle states that in any chemical reaction, the total amount of each element present in the reactants must be equal to the total amount of that element present in the products. (Pantea & Voitiuk, 2022)
A positive compatibility class is a subset of reactions that can coexist with non-negative concentrations of all species. In other words, if we start with non-negative concentrations of all species in a positive compatibility class, the concentrations will remain non-negative for all time. i.e. from the second definition above if we have any positive vector $x_0 \in \mathbb{R}^n_{\geq 0}$, then $(x_0 + S)_> = (x_0 + S) \cap \mathbb{R}^n_{\geq 0}$ is called the stoichiometric compatibility class of x_0 (Yu & Craciun, 2018)

2.2.6 The linkage classes of a reaction network

Linkage class is grouping together sets of reactions that are connected through shared reactants or products. Specifically, the linkage class is the set of all reactions in the network that share a common reactant or product. A linkage class is a set of complexes of a given reaction in a chemical reaction network.

For example

$$\begin{aligned} 2A &\to A + B \\ A + B &\rightleftharpoons C \\ C &\to 2A \end{aligned}$$

According to Feinberg(1987), the network above is composed of three separate pieces; the first containing complexes $\{2A, A+B\}$, the second containing complexes $\{A+B, C\}$ and the last one containing complexes $\{C, 2A\}$.

Disregarding the directions of reaction arrows, we observe that the complexes within the set $\{2A, A+B\}$ are interconnected with each other, but not with any other complex. Similarly, the complexes in the set $\{A+B, C\}$ are interconnected with each other but not

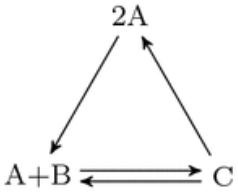
with any other complex. The same applies to the complexes in $\{C, 2A\}$. We designate the sets $\{2A, A+B\}$, $\{A+B, C\}$ and $\{C, 2A\}$ as the linkage classes of the above given network.

The standard reaction diagram of a network provides a quick and easy means of determining both the number of linkage classes and their respective compositions. The count of linkage classes corresponds directly to the number of distinct pieces comprising the diagram. Each individual piece represents a linkage class, which can be associated with the set of complexes present within that specific component. We consider a linkage class as simply a collection of complexes. While the reaction arrows within a given network determine its linkage classes, the linkage classes themselves are solely sets of complexes without any inherent arrow structure.

2.2.7 The strong linkage classes of a reaction network

A strong linkage class is a subset of species in the reaction network that are strongly connected to each other. This means that for any two species within a strong linkage class, there exists a path of reactions that can convert one species into the other.
Two different complexes in a reaction network are strongly linked if there exists a directed arrow pathway pointing from one complex to the other and a directed arrow pathway pointing from the second complex back to the first. Moreover, for reasons that will soon become apparent, we adopt the convention that every complex is strongly linked to itself. (Feinberg, 1987)

To understand the concept of strong linkage, let us consider the reaction network in Figure 1 represented in an embedded graph;



Complex $2A$, is strongly linked to complex C, since there is a directed arrow pathway from $2A$ to C via complex $A+B$ and a directed arrow pathway from C back to $2A$. Similarly, $2A$ is strongly linked to $A+B$. Complexes $A+B$ and C are also linked.

This then means that the strong linkage class for the reaction network is $\{A+B, 2A, C\}$. $\{A+B, C\}$ is not a strong linkage class because although complexes $A+B$ and C, are strongly linked, they are both strongly linked to $2A$ complex that lies outside the set $\{A+B, C\}$.

A set of complexes in a reaction network is considered a strong linkage class if the following conditions hold:

- All pairs of complexes within the set are strongly linked.
- No complex in the set is strongly linked to a complex outside the set.

To identify the strong linkage classes of a given reaction network, one can examine the associated reaction diagram, which allows for the unique determination of these classes.

2.2.8 The terminal strong linkage classes of a reaction network

By a terminal strong linkage class in a reaction network we mean a strong linkage class containing no complex that reacts to a complex in a different strong linkage (Feinberg & Horn, 1977). A strong linkage class is terminal if there is no exit from it along a directed arrow pathway. In simpler terms, we can say that the terminal strong linkage classes refer to sets of species that are mutually linked and cannot participate in any further reactions within the network. These classes represent groups of species that are stuck and cannot be transformed into other species through any sequence of reactions.

The strong linkage class $\{A+B, 2A, C\}$ in the reaction network above is the terminal strong linkage of the network because no member of $\{A+B, 2A, C\}$ react to form any other complex outside $\{A+B, 2A, C\}$.

2.2.9 Rate constants

Rate constants are numerical values that describe the rate of a chemical reaction. They represent the proportionality of the reaction and the concentration of the reactants. Rate constants are usually denoted by k.

3 Reversibility and weak reversibility

Reversibility is a fundamental concept that plays a pivotal role in understanding the dynamics of systems in chemical reaction networks. However, not all reactions exhibit complete reversibility, giving rise to the concept of weak reversibility. In this chapter, we discuss reversibility and weak reversibility in chemical reaction networks.

3.1 Definition

A reversible network refers to a network of reactions where both forward and reverse reactions can occur. In other words, a reversible network involves reactions that can proceed in both directions.
A reaction network $\{\mathscr{S},\mathscr{C},\mathscr{R}\}$ is deemed weakly reversible when every connected component exhibits strong connectivity (Boros, 2019), which means that there can be several reactions from $A+B$ to C if a reaction $C \to A+B$ exists within the network. According to Feinberg(1987), a network is weakly reversible if, whenever there exists a directed arrow pathway (consisting of one or more reaction arrows) pointing from one complex to another, there also exists a directed arrow pathway pointing from the second complex back to the first.
For example, consider the reaction network below with four species and four reactions;

$$\begin{aligned} A+B &\to C \\ C &\to A+B \\ C &\to D \\ D &\to C \end{aligned}$$

The reaction $A+B \to C$ represents the formation of C from A and B, and the reaction $C \to A+B$ represents the breakdown of C into A and B. Similarly, the reactions $C \to D$ and $D \to C$ represent the conversion of C to D and vice versa. We can see from this network that it consists of two connected components: one with species A, B, and C, and one with species C and D. Each connected component exhibits strong connectivity, which means that there is a path from any species to any other species within the component.

It should be clear from the discussion above that every reversible network is also weakly reversible. Thus, any theorem statement about weakly reversible networks applies to reversible networks as a special case. (Feinberg, 1987)

3.2 Weakly reversible system

A weakly reversible system is a chemical reaction network that can be converted into a reversible system by introducing at least one additional reaction in the opposite direction of one or more of the reactions in the original network. In other words, a weakly reversible system can be made reversible by adding at least one new reaction.(Craciun et al., 2020) An example of a weakly reversible system is shown in the following reaction network:

$$A \to B$$
$$B \to C$$
$$C \to D$$

This reaction network is weakly reversible because it can be converted into a reversible system by adding the reaction

$$D \to C$$

which is the reverse of the reaction

$$C \to D$$

Once this additional reaction is introduced, the system becomes reversible and can reach equilibrium. Not all reaction networks can be made reversible by adding just one reaction, some systems may require the addition of multiple reactions to become reversible.

The SIR model is an example of a system which is not weakly reversible system. To make the SIR model weakly reversible, we can add an additional compartment to represent individuals who have recovered from the disease and become susceptible again. This compartment is called the SIRS model. In the SIRS model, individuals who have recovered from the disease and become susceptible again can transition back to the infected compartment upon being infected again.

This can be represented using a diagram as follows:

$$S + I \to 2I$$
$$S \to I \to R$$

From the explanation above, we can make this model weakly reversible by adding the reaction;

$$R \to S$$

This will give us the SIRS model which is weakly reversible.

4 Kinetics and the Corresponding Differential Equations of a Reaction Network

A chemical reaction network, when combined with a specification of reaction rate functions, leads to a system of ordinary differential equations, typically nonlinear. Within this section, we will demonstrate how these equations can be expressed in vector form, enabling certain basic geometric relationships to become clearer, connecting the structure of the reaction network with the characteristics of the equation solutions. Once these connections are grasped, we will be able to ask more precise and penetrating questions.

4.1 Kinetics for a reaction network

Kinetics of a reaction network refers to the study of the rate at which chemical reactions occur. In a reaction network, which consists of multiple interconnected reactions, the kinetics of each individual reaction within the network can be determined. To formulate differential equations that describe how the various species concentrations evolve in time, we must first specify how the instantaneous occurrence rates of the individual reactions in the network depend upon the instantaneous composition state (Feinberg, 1987)

When referring to the kinetics of a reaction network consisting of N species, we define a kinetics assignment for each reaction, denoted as $y \to y'$ of a rate function $k_{y\to y'}(\cdot)$. This assignment involves assigning a rate function to each reaction, which yields non-negative values. In this context, the rate of the reaction $y \to y'$ at composition c is represented by the non-negative number denoted as k.

We will need the following properties from the rate functions of kinetics: For every reaction, $y \to y'$, in the network.

- $k_{y\to y'}(\cdot)$ is continuous and differentiable
  and
- $k_{y\to y'}(c) > 0$ if and only if supp y is contained in supp c.

In the second property above supp y is just the set of species in the reactant complex y and supp c is the set of all species that exist within the system if c represents the current composition state of the mixture. In more general terms, the second property says that reaction $y \to y'$ will exhibit a sluggish rate only when the species comprising the reactant complex y are indeed present within the system.

Note:
By a reaction system we shall mean a reaction network taken together with a kinetics. By a mass action system we shall mean a reaction system for which the kinetics is mass action.(Feinberg, 1987)

4.2 The differential equations for a reaction network system

When considering a reaction network, we often want to describe how the concentrations of the chemical species change over time. This can be achieved by formulating a system of ordinary differential equations (ODEs) that govern the dynamics of the system. The ODEs describe how the concentrations of the species vary as a function of time.

Consider the SIR model

$$S + I \to 2I$$
$$S \to I \to R$$

The molar concentrations of the species are represented as $c_S(t)$, $c_I(t)$ and $c_R(t)$, and we use the composition vector $\mathbf{c}(\mathbf{t})\cdot^*$ to abbreviate this list of numbers.

We aim to formulate the differential equations governing the progression of the three molar concentrations. Given that alterations in composition arise from chemical reactions, comprehending the methodology to construct these differential equations hinges on discerning the respective rates at which multiple reactions take place. The commonly held assumption is that the instantaneous rate of occurrence for each reaction is dependent on the instantaneous mixture composition vector, $\mathbf{c}$, in a unique manner.

For instance, if there exists a non-negative real-valued rate function, denoted as $k_{S+I\to 2I}(\cdot)$, such that $k_{S+I\to 2I}(c)$ represents the instantaneous rate at which reaction $S+I \to 2I$ occurs when the vector c represents the instantaneous mixture composition. Similarly, for the reaction $S \to I$. $k_{S\to I}$ represents the instantaneous rate at which reaction $S \to I$ occurs when the vector c represents the instantaneous mixture composition and for the reaction $I \to R$, $k_{I\to R}$ represents the instantaneous rate at which reaction $I \to R$ occurs when the vector c represents the instantaneous mixture composition.

For the instantaneous change of c_S, we lose S when the reaction $S+I \to 2I$ and $S \to I$ occur and we write

$$\dot{c_S} = -k_{S+I\to 2I}(c)$$

For the instantaneous change of c_I, we gain I when the reaction $S+I \to 2I$ and $S \to I$ occur and lose I when the reaction $I \to R$ and we write

$$\dot{c_I} = k_{S+I\to 2I}(c) + k_{S\to I}(c) - k_{I\to R}(c)$$

For the instantaneous change of c_R, we gain R when the reaction $I \to R$ occur and we write

$$\dot{c_R} = k_{I\to R}(c)$$

The system of differential equation governing the reaction network for the SIR model is as follows:

$$\begin{aligned}
\dot{c_S} &= -k_{S+I\to 2I}(c) \\
\dot{c_I} &= k_{S+I\to 2I}(c) + k_{S\to I}(c) - k_{I\to R}(c) \\
\dot{c_R} &= k_{I\to R}(c)
\end{aligned}$$

Suppose that the instantaneous occurrence rate of $S+I \to 2I$ is proportional to the instantaneous value of c_S and c_I then

$$k_{S+I\to 2I}(c) = \beta c_S c_I$$

Similarly, in the reactions $S \to I$, we have

$$k_{S\to I}(c) = \beta c_S$$

and in the reaction $I \to R$, we have

$$k_{I\to R}(c) = \gamma c_I$$

where β and γ are positive constants.
Therefore, employing mass action kinetics results in rate functions for the network that are expressed as follows:

$$\begin{aligned}
k_{S+I\to 2I}(c) &= \beta c_S c_I \\
k_{S\to I}(c) &= \beta c_S \\
k_{I\to R}(c) &= \gamma c_I
\end{aligned}$$

Assuming mass action kinetics for this network, the corresponding set of differential equations can be expressed as follows:

$$\begin{aligned}
\dot{c_S} &= -\beta c_S c_I \\
\dot{c_I} &= \beta c_S c_I - \gamma c_I \\
\dot{c_R} &= \gamma c_I
\end{aligned}$$

In the preceding chapter, we will solve the above system of differential equations that represents the SIR model, along with the initial conditions. This will allow us to examine the dynamics of the epidemic. We will demonstrate the concept of deficiency theory by analyzing the steady states and stability of the equilibrium points. Furthermore, the solution analysis will incorporate the numbers discussed in the following section.

4.3 The replacement and basic reproduction numbers

The dynamics of the SIR model are characterized and understood by two significant numbers: the replacement number, r, and the basic reproduction number R_0.

The replacement number, $r = r(t)$, is the expected number of individuals directly infected by a typical infectious individual, mixing in the population, over the course of their infectiousness(Simon, 2020). The concentration of susceptible individuals, denoted as $c_S = c_S(t)$ directly affects the rate at which a typical infectious individual comes into contact with a susceptible individual. Consequently, the value of r varies over time. In the SIR model, a typical infectious individual remains infectious for a duration of γ^{-1} and, within this period, generates $\beta c_S(t)$ new infections per unit time (incidence rate per infectious individual). As a result, the replacement number can be expressed as follows:

$$r = r(t) = \frac{\beta}{\gamma} c_S(t)$$

In epidemiology, the basic reproduction number represents the average number of secondary infections caused by a single infected individual in a completely susceptible population. It is a measure of the contagiousness of a disease. R_0 in the SIR model is the replacement number when $c_S \approx 1$:

$$R_0 = \frac{\beta}{\gamma}$$

The relationship between these two number is;

$$r(t) = R_0 c_S(t)$$

If the basic reproduction number R_0 is high or low, the duration of infectivity is prolonged or shortened respectively, the disease transmission is/is not easily facilitated, and/or the interaction between susceptible individuals and infectious individuals is/is not intense.

5 Deficiency Theory

In this chapter, we discuss the deficiency of a chemical reaction network, complex balancing and the most important results contained in this article. These are the Deficiency Zero Theorem and the Deficiency One Theorem. We will provide the statements of the theorems and further elaboration on the theorems themselves.

5.1 Definition of deficiency of a chemical reaction network

The deficiency of a chemical reaction network $\{\mathscr{S},\mathscr{C},\mathscr{R}\}$ is denoted by δ which is defined by;

$$\delta = |\mathscr{C}| - \ell - s$$

where

- $|\mathscr{C}|$ is the number of vertices (complexes)
- ℓ is the number of connected components(linkage classes) and
- s is the dimension of the stoichiometric subspace of the network as defined in the section above. (Anderson et al., 2010)

For example, if we consider the SIR model

$$S + I \to 2I$$
$$S \to I \to R$$

The number of complexes, $|\mathscr{C}|$ is 5, the number of linkage classes, ℓ is 3 and the dimension of the stoichiometric subspace or the rank of the stoichiometric matrix is 2. This means that the deficiency of the SIR model is zero.

The deficiency, δ, of any chemical reaction network satisfies $0 \leq \delta \leq |\mathscr{C}| - \ell - s$, where $|\mathscr{C}|$ is the number of complexes, ℓ is the number of linkage classes and s is the dimension of the stoichiometric subspace. (Gunawardena, 2003). The deficiency of every network is always non-negative.

According to Feinberg(1987), any two reaction networks with the same complexes and the same linkage classes also have the same rank. It follows easily that any two reaction

networks with the same complexes and the same linkage classes also have the same deficiency. (TWO such networks have the same rank; it is obvious that they also have the same number of complexes and the same number of linkage classes.) Thus, the precise nature of the reaction arrows in a network affects the deficiency of the network only insofar as the reaction arrows determine the linkage classes of the network.

Put simply, deficiency measures the number of potential dimensions that are missing from a chemical reaction system due to linear dependence among reactions. A set of chemical reactions is said to be linearly dependent if one or more of the reactions can be expressed as a linear combination of the other reactions in the set. This means that one or more of the reactions can be written as a sum of multiples of the other reactions in the set. Deficiency can also be calculated as the difference between the number of complexes and the sum of the number of linkage classes and the dimension of the stoichiometric subspace, where $|\mathscr{C}|$ represents the maximum dimension and s represents the actual dimension.

5.2 Complex balancing

Complex balancing refers to the process of determining the stoichiometric coefficients of chemical species in a set of chemical reactions such that mass is conserved and the reaction rates are balanced.

A complex balanced equilibrium is a special type of equilibrium state that has some important properties which include being a steady-state solution where the net flux of each chemical species in the network is zero and being stable, meaning that if the system is slightly perturbed from the equilibrium state, it will tend to return to that state. And the equilibrium is called complex because the concentrations of the reactants and products are related in a particular way. The equilibrium is balanced because the rate at which reactants are consumed is exactly balanced by the rate at which products are formed. This means that the total concentration of all chemical species in the system remains constant at the equilibrium state. (Johnston et al., 2013)

The concept of complex balanced equilibrium is used to predict the behavior of chemical reaction networks. If a system has a complex balanced equilibrium, it is more likely to exhibit stable behavior and to resist fluctuations in concentrations of reactants and products.

A chemical reaction network is said to be complex balanced if there exists an equilibrium concentration $x_0 \in \mathbb{R}^n_+$ called the complex-balanced equilibrium satisfying, (Yvinec, 2016)

$$\sum_{y:y\to z\in\mathbb{R}} k_{y\to z} x_0^y = x_0^z \sum_{y':z\to y'\in\mathbb{R}} k_{z\to y'}$$

where x_0 is the equilibrium concentration, k is the vector of rate constants $k_{y\to z}$ and $k_{z\to y'}$ for the inflow and the outflow concentrations respectively and y, y' and z are the complexes in the reaction network.

Not only the species but also the complexes remain constant. (Van der Schaft et al., 2015). This means that the total concentration of a complex remains constant in a chemical reaction network, i.e. the rate of formation of the complex is equal to the rate of breakdown of the complex, so the concentration of the complex does not change over time. This is often referred to as the principle of detailed balance or the steady-state assumption. Detailed balance implies complex balance.

5.3 Principle Theorems

In this section, we will present two theorems that offer prompt and insightful qualitative insights into nonlinear differential equations related to complex reaction systems. These theorems can be effectively utilized by individuals who are familiar with the aspects of reaction network structure we have previously discussed. Specifically, a working knowledge of calculating network rank and deficiency is essential for applying these theorems.

5.3.1 Deficiency Zero

A chemical reaction network (CRN) is said to have deficiency zero if its deficiency is zero as illustrated in the following example;
Consider the following chemical reaction network which has deficiency zero and is not weakly reversible;

$$A + 2B \to C + D$$
$$B + E \to F$$

This network has six species: A, B, C, D, E and F, four complexes and two reactions. To find the deficiency of the network, we need the rank of stoichiometric matrix which can be obtained from the given chemical reaction network using the following steps:

- Write down the balanced chemical equations for all the reactions in the system.
  The equations are as follows

$$A + 2B \to C + D \quad \textbf{(1)}$$
$$B + E \to F \quad \textbf{(2)}$$

- Identify all the reactants and products involved in each reaction.
  In reaction (1), the reactants are A and B and the products are C and D.
  In reaction (2), the reactants are B and E and the product is F.

- Write down a row for each chemical species, with each column representing a reaction in the system.

Chemical Species	Reaction (1)	Reaction (2)
A		
B		
C		
D		
E		
F		

Table 1. Stoichiometric matrix format

- Fill in the entries of the matrix by putting the stoichiometric coefficients of each species in the appropriate column for the reaction it is involved in.

Chemical Species	Reaction (1)	Reaction (2)
A	1	0
B	2	1
C	1	0
D	1	0
E	0	1
F	0	1

Table 2. Putting stoichiometric coefficients in appropriate columns

- If a species is a reactant in a particular reaction, the stoichiometric coefficient will be negative. If it is a product, the coefficient will be positive.

Chemical Species	Reaction (1)	Reaction (2)
A	-1	0
B	-2	-1
C	1	0
D	1	0
E	0	-1
F	0	1

Table 3. Assigning appropriate signs to the stoichiometric coefficients

The stoichiometric matrix for this network is:

$$\begin{bmatrix} -1 & 0 \\ -2 & -1 \\ 1 & 0 \\ 1 & 0 \\ 0 & -1 \\ 0 & 1 \end{bmatrix}$$

In this matrix, the rows represent the chemical species A, B, C, D, E and F, and the columns represent the two reactions in the system resulting into a 6×2 matrix. The entries in the matrix show the stoichiometric coefficients of each species in each reaction. For example, in the first reaction, A has a coefficient of -1, B has a coefficient of -2, C has a coefficient of 1, D has a coefficient of 1 and there is no E and F, hence the entries of the first column. And the second column is generated in a similar way using the second reaction.

The rank of the above matrix is 2, the number of complexes is 4 and the number of independent reactions is also 2.
This then means that $|\mathscr{C}| = 4$, $\ell = 2$, and $s = 2$
Therefore, the deficiency of this network is:

$$\delta = |\mathscr{C}| - \ell - s = 4 - 2 - 2 = 0$$

Theorem 5.3.1. ***(The deficiency zero)***
If a chemical reaction network is weakly reversible and has deficiency zero and the rate constants are positive then, the rate equations will have precisely one fixed point in each positive stoichiometric compatibility class (Anderson et al., 2010).

(i) The theorem states that the solution is complex balanced, and any solution within the same stoichiometric compatibility class, which is sufficiently close to the initial solution, will eventually approach the equilibrium over time. Furthermore, there are no other positive periodic solutions.

(ii) For any choice of rate constants, if a network has deficiency zero, is not weakly reversible, and the rate constants are positive, then the equation does not admit a positive solution or a positive periodic solution.

(iii) For any parameter values, deficiency zero predicts the presence of distinct fixed points and factorized steady states..

From parts (i) and (ii) of the theorem we can quickly conclude that, no matter what the rate constants might be, the differential equations for the corresponding mass action system cannot admit a positive steady state, nor can they admit a cyclic composition trajectory along which all species concentrations are positive. (Feinberg, 1987) To demonstrate the application of the Deficiency Zero Theorem, we will provide an illustrative example. Initially, we will review the SIR model and assume, for the purpose of discussion, that the network operates under mass action kinetics. As a consequence, the resulting mass action system can be described by a set of three interrelated polynomial differential equations, representing the concentrations of three different species in the system. A key inquiry arises: Does this system possess a positive steady state or a cyclic composition trajectory in which all species concentrations remain positive?

We will answer these questions by solving the differential equations corresponding to the SIR model and analysing the behaviour of the system at the stationary points subject to the following initial conditions:

$$\begin{aligned} c_S(0) &= (c_S)_0 \\ c_I(0) &= (c_I)_0 \\ c_R(0) &= 0, \end{aligned}$$

with $c_S(0) + c_I(0) = 1$, $c_S(0), c_I(0) > 0$, and $c_I(0) << 0$

MATLAB will be used to come up with the solution curves and phase portrait for different values of the parameters β and γ where β is the infection rate and γ is the recovery rate.

Solution Curves for the SIR model

Using two sets of values of β and γ, we obtain the following diagrams for the solution curves for the SIR model;

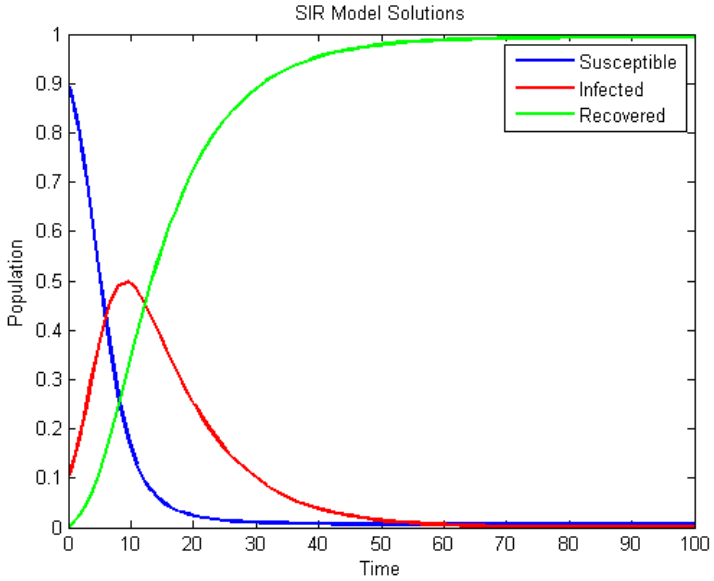


Figure 2. Solution curve for the SIR model for $\beta = 0.5$ and $\gamma = 0.1$

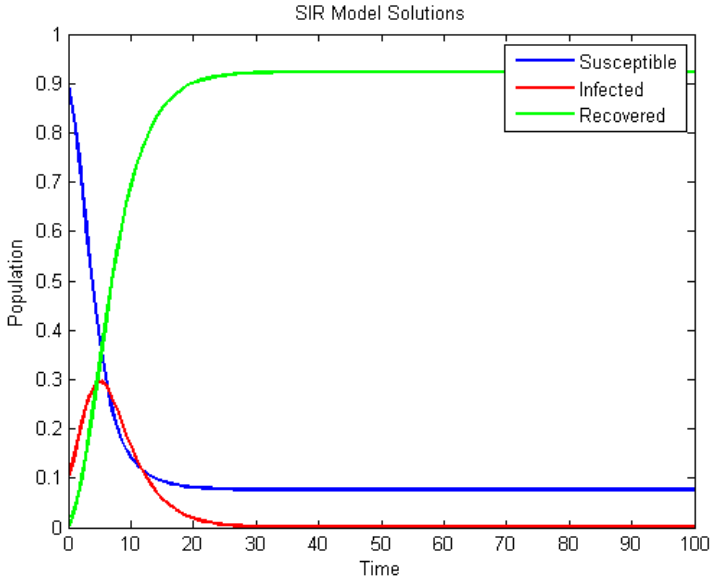


Figure 3. Solution curve for the SIR model for $\beta = 0.8$ and $\gamma = 0.3$

The curve representing the susceptible population shows the number of individuals who are susceptible to the disease at each point in time. Initially, the susceptible population is high, but as the infection spreads, the number of susceptible individuals decreases. The curve will typically exhibit a decreasing trend until it reaches a minimum value.

The curve representing the infected population shows the number of individuals currently infected with the disease at each point in time. Initially, the infected population is low, but it starts to increase as the disease spreads. The curve will typically show an increasing trend until it reaches a peak, representing the maximum number of infected individuals. After reaching the peak, the curve will start to decline as individuals recover from the disease.

The curve representing the recovered population shows the number of individuals who have recovered from the disease and gained immunity at each point in time. Initially, the recovered population is 0, but it starts to increase as individuals recover from the disease. The curve will continue to rise until it reaches a plateau, indicating that most of the population has recovered and gained immunity.

By analyzing the shape and behavior of these solution curves, you can gain insights into the progression of the epidemic. For example:

- The peak of the infected population curve represents the maximum number of individuals infected at any given time, indicating the severity of the outbreak.
- The point at which the infected population curve starts to decline signifies the beginning of the recovery phase and the decline of new infections.
- The point at which the susceptible population curve reaches a minimum indicates a potential turning point, where the majority of individuals have been infected or gained immunity.

We can also compare different sets of parameter values (such as different values of β and γ) to observe their effects on the shape and dynamics of the solution curves. This analysis can help in understanding the impact of various factors on the spread and control of the epidemic.

Orbits and phase portrait of the SIR system

The orbit of a differential equation refers to the trajectory followed by a solution in phase space.

The orbits of the SIR system can be determined using a calculus-based technique we are familiar with. To accomplish this, we rewrite the SIR system as follows:

$$\frac{dS}{dt} = -\beta SI$$
$$\frac{dI}{dt} = \beta SI - \gamma I$$

By dividing the first equation into the second equation, we obtain a differential equation that describes the orbits in SI-space traced by the solutions. Thus, we have:

$$\frac{dI}{dS} = -1 + \frac{\gamma}{\beta S}$$

Integrating, we get the following;

$$I = -S + \frac{\gamma}{\beta}\ln S + C$$

The maximum value for all these curves will be at $S = \frac{\gamma}{\beta}$. The figure below shows one of such curves when $R_0 > 1$.

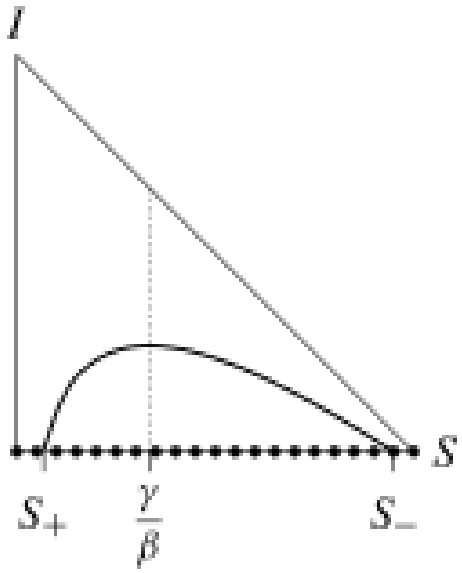
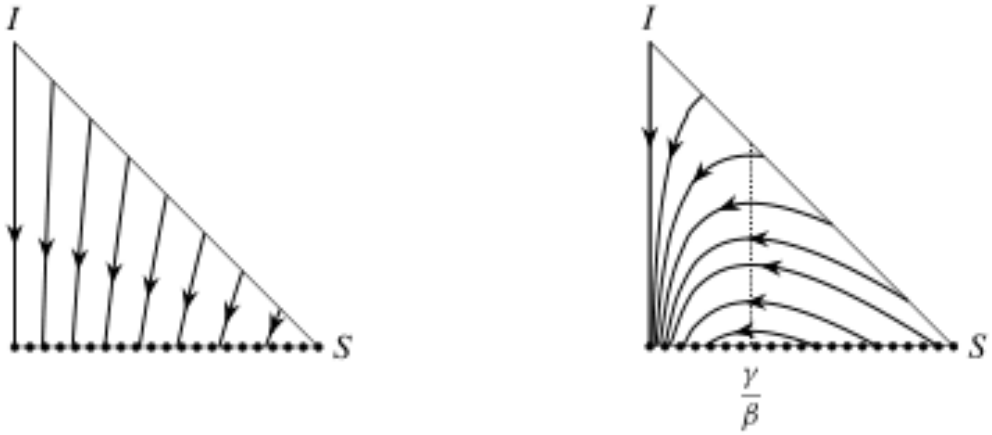


Figure 4. One orbit of the SIR system

In the figure above, we have one orbit of the SIR system with $R_0 = \frac{\beta}{\gamma} = 3$, which means that $\frac{\gamma}{\beta} = \frac{1}{3}$.

A phase portrait of $\dot{x} = f(x)$ is a sketch of phase space that shows all unusual orbits and examples of typical orbits, together with arrows on the orbits that indicate the direction of movement(López-Flores et al., 2021).

The SIR system exhibits unconventional equilibria along the S-axis and a distinct vertical orbit along the I-axis, which can be considered atypical. Conversely, the curves described by the equation for I are regarded as typical. Notably, the phase portrait of the SIR system is solely influenced by the ratio $\frac{\gamma}{\beta}$ or, equivalently, by $R_0 = \frac{\beta}{\gamma}$.



(a) $R_0 = 1/3$ ($\beta = 0.1, \gamma = 0.3$). (b) $R_0 = 3$ ($\beta = 0.3, \gamma = 0.1$).

Figure 5. Phase Portrait for the SIR system

The figure above illustrates the phase portrait of the SIR system for two scenarios: $R_0 < 1$ and $R_0 > 1$. In (b), $\frac{\gamma}{\beta} = \frac{1}{3}$

Orbital interpretation

If $R_0 > 1$, many orbits of the SIR system resemble the one depicted in first Figure above. These orbits connect an equilibrium

$$(S,I) = (S_-,0), \qquad \frac{\gamma}{\beta} < S_- \leq 1$$

to an equilibrium

$$(S,I) = (S_+,0), \qquad 0 < S_+ < \frac{\gamma}{\beta}$$

This type of orbit can be interpreted as follows:
Initially, an epidemic begins with a population state near $(S,I) = (S_-,0)$ with $\frac{\gamma}{\beta} < S_- \leq 1$, where the population fraction S_- is susceptible and no one is infected yet. The remaining fraction of the population, $R_- = 1 - S_-$, is not susceptible. When the disease is introduced and the number of infectives (I) becomes slightly positive, the number of infected individuals increases, causing a decline in the number of susceptibles. Eventually, the number of susceptibles falls below $\frac{\gamma}{\beta}$, and the number of infectives begins to decrease, leading to

the extinction of the disease.

Hence, it is important to look at the computation of S_+ when S_- is given. This can be accomplished using the following method:

If the curve $I = -S + \frac{\gamma}{\beta}\ln S + C$ intersects the point $(S_-, 0)$, then

$$0 = -S_- + \frac{\gamma}{\beta}\ln S_- + C \;\Rightarrow\; C = S_- - \frac{\gamma}{\beta}\ln S_-$$

And if it again intersects the point $(S_+, 0)$, we get

$$0 = -S_+ + \frac{\gamma}{\beta}\ln S_+ + C = -S_+ + \frac{\gamma}{\beta}\ln S_+ + S_- - \frac{\gamma}{\beta}\ln S_-$$

This implies that

$$-(S_+ - S_-) + \frac{\gamma}{\beta}(\ln S_+ - \ln S_-) = 0$$

We can find S_+ given S_- by

$$F(S) = -(S - S_-) + \frac{\gamma}{\beta}(\ln S - \ln S_-) = 0$$

and obtaining the value of S through numerical computation.

The value of particular interest is S_+ when $S_- = 1$, which represents the scenario where the entire population is initially susceptible to the disease. In this case, $1 - S_+$ indicates the fraction of the population that becomes infected during the epidemic.

The SIR model has deficiency zero, but is not weakly reversible. According to the Theorem for general kinetics there are no positive equilibria or positive nontrivial periodic orbits.

5.3.2 Deficiency One

Deficiency one in chemical reaction networks refers to a property of a network of chemical reactions, where there is exactly one linearly independent conservation law. The conservation law in this case is a mathematical expression that describes a quantity that remains constant throughout a chemical reaction network. e.g. the total number of atoms of each element must remain constant in a closed system. If a reaction network has a deficiency of one, it means that there is exactly one linear combination of the stoichiometric vectors that is non-negative and can be written as a linear combination of the conservation laws.

The Deficiency One Theorem extends the information provided by the Deficiency Zero Theorem, but it does not offer any dynamical insight. Its focus is solely on issues related to the existence and uniqueness of positive steady states(Farinas et al., 2020). However, it applies to a more diverse set of networks than the Deficiency Zero Theorem. The following is the statement of the Deficiency One Theorem, and further examples and applications will be explored in subsequent sections of this work.

Theorem 5.3.2. ***(The deficiency one)***
Consider a mass action system for which the underlying reaction network has ℓ linkage classes, each containing just one terminal strong linkage class. Suppose that the deficiency of the network and the deficiencies of the individual linkage classes satisfy the following conditions:

i. $\delta_\theta \leq 1, \quad \theta = 1, 2, \cdots, \ell$

ii. $\sum_{\theta=1}^{\ell} \delta_\theta = \theta.$

Then, no matter what positive values the rate constants take, the corresponding differential equations can allow no more than one steady state within a positive stoichiometric compatibility class. If the network is weakly reversible, the differential equations allow precisely one steady state in each positive stoichiometric compatibility class.

For networks having just one linkage class condition ii. is satisfied trivially leading to the following corollary.

Corollary: A mass action system for which the underlying reaction network has just one linkage class can admit multiple steady states within a positive stoichiometric compatibility class only if the deficiency of the network or the number of its terminal strong

linkage classes exceeds one.(Feinberg, 1987)

Consider the following mass action system which is an example of a system with deficiency one and weakly reversible:

$$\mathrm{A} \underset{\mathrm{k_2}}{\overset{\mathrm{k_1}}{\rightleftharpoons}} 2\,\mathrm{A}$$
$$\mathrm{A}+\mathrm{B} \underset{\mathrm{k_4}}{\overset{\mathrm{k_3}}{\rightleftharpoons}} \mathrm{C} \underset{\mathrm{k_6}}{\overset{\mathrm{k_5}}{\rightleftharpoons}} \mathrm{B}$$

To confirm the assumption above we compute the deficiency of the system as follows where the stoichiometric matrix for this given system is:

$$\begin{bmatrix} 1 & -1 & -1 & 1 & 0 & 0 \\ 0 & 0 & -1 & 1 & 1 & -1 \\ 0 & 0 & 1 & -1 & -1 & 1 \end{bmatrix}$$

Where, the number of rows is the number of species and the number of columns is the number of reactions in the system. The rank of this matrix is 2. The number of linkage classes and complexes are 2 and 5 respectively. Therefore, the deficiency of this network is:

$$\delta = |\mathscr{C}| - \ell - s = 5 - 2 - 2 = 1$$

To explain the concept of deficiency, we need to search for the equalibria and whether they are complex balanced or not. We solve the differential equations corresponding to the system and plot the solution curves to analyse the behaviour of the mass action system. The system of differential equations are:

$$\begin{aligned} \dot{c_A} &= k_1 c_A - k_2 c_A^2 - k_3 c_A c_B + k_4 c_C \\ \dot{c_B} &= -k_3 c_A c_B + k_4 c_C + k_5 c_C - k_6 c_B \\ \dot{c_C} &= k_3 c_A c_B + k_6 c_B - (k_4 + k_5) c_C \end{aligned}$$

At equilibrium points, we have $\dot{c_A} = 0$, $\dot{c_A} = 0$ and $\dot{c_A} = 0$. This implies that

$$\begin{aligned} k_1 c_A - k_2 c_A^2 - k_3 c_A c_B + k_4 c_C &= 0 \\ -k_3 c_A c_B + (k_4 + k_5) c_C - k_6 c_B &= 0 \\ k_3 c_A c_B + k_6 c_B - (k_4 + k_5) c_C &= 0 \end{aligned}$$

From the third equation above, we get

$$c_C = \frac{k_3 c_A c_B + k_6 c_B}{k_4 + k_5}$$

Substituting in the first equation, we have

$$\begin{aligned} k_1 c_A - k_2 c_A^2 - k_3 c_A c_B + k_4 \frac{k_3 c_A c_B + k_6 c_B}{k_4 + k_5} &= 0 \\ k_1 c_A - k_2 c_A^2 - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A c_B + \frac{k_4 k_6}{k_4 + k_5} c_B &= 0 \\ c_B \left(\frac{k_4 k_6}{k_4 + k_5} - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A \right) &= -k_1 c_A + k_2 c_A^2 \\ c_B &= \frac{-k_1 c_A + k_2 c_A^2}{\frac{k_4 k_6}{k_4 + k_5} - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A} \end{aligned}$$

Plugging c_B in c_C to get c_C in terms of one variable c_A only gives

$$c_C = \frac{k_3 c_A + k_6}{k_4 + k_5} \cdot \frac{-k_1 c_A + k_2 c_A^2}{\frac{k_4 k_6}{k_4 + k_5} - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A}$$

Therefore, the equilibria for the system above is given by the points;

$$\left(c_A, \frac{-k_1 c_A + k_2 c_A^2}{\frac{k_4 k_6}{k_4 + k_5} - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A}, \frac{k_3 c_A + k_6}{k_4 + k_5} \cdot \frac{-k_1 c_A + k_2 c_A^2}{\frac{k_4 k_6}{k_4 + k_5} - \left(k_3 - \frac{k_3 k_4}{k_4 + k_5} \right) c_A} \right) = (0, 0, 0)$$

if we set $c_A = 0$

It should turn out that there is one equation that the rate constants need to satisfy to get complex balancing. We use this fact to obtain the equilibria in terms of the rate constants. Consider $A \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 2A$ which gives us the following;

$$\begin{aligned} k_1 c_A &= k_2 c_A^2 \\ (k_1 - 2k_2 c_A) c_A &= 0 \end{aligned}$$

This implies that

$$c_A = 0 \quad \text{OR} \quad c_A = \frac{k_1}{2k_2}$$

It follows that

$$\left(c_A, \frac{-k_1c_A+k_2c_A^2}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)c_A}, \frac{k_3c_A+k_6}{k_4+k_5}\cdot\frac{-k_1c_A+k_2c_A^2}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)c_A}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{-k_1\left(\frac{k_1}{2k_2}\right)+k_2\left(\frac{k_1}{2k_2}\right)^2}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)\left(\frac{k_1}{2k_2}\right)}, \frac{k_3\left(\frac{k_1}{2k_2}\right)+k_6}{k_4+k_5}\cdot\frac{-k_1\left(\frac{k_1}{2k_2}\right)+k_2\left(\frac{k_1}{2k_2}\right)^2}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)\left(\frac{k_1}{2k_2}\right)}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{\frac{-k_1^2}{2k_2}+\frac{k_1^2}{4k_2}}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)\left(\frac{k_1}{2k_2}\right)}, \frac{k_3\left(\frac{k_1}{2k_2}\right)+k_6}{k_4+k_5}\cdot\frac{\frac{-k_1^2}{2k_2}+\frac{k_1^2}{4k_2}}{\frac{k_4k_6}{k_4+k_5}-\left(k_3-\frac{k_3k_4}{k_4+k_5}\right)\left(\frac{k_1}{2k_2}\right)}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{\frac{-k_1^2}{4k_2}}{\frac{k_4k_6}{k_4+k_5}-\frac{k_1k_3k_4}{2k_2(k_4+k_5)}}, \frac{\frac{-k_1^3k_3-2k_1^2k_2k_6}{8k_2^2}}{k_4k_6-\frac{k_1k_3k_5}{2k_2}}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{\frac{-k_1^2}{4k_2}}{\frac{k_4k_6}{k_4+k_5}-\frac{k_1k_3k_4}{2k_2(k_4+k_5)}}, \frac{\frac{-k_1^3k_3-2k_1^2k_2k_6}{8k_2^2}}{k_4k_6-\frac{k_1k_3k_5}{2k_2}}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{\frac{-k_1^2}{4k_2}}{\frac{2k_2k_4k_6-k_1k_3k_5}{2k_2(k_4+k_5)}}, \frac{\frac{-k_1^3k_3-2k_1^2k_2k_6}{8k_2^2}}{\frac{2k_2k_4k_6-k_1k_3k_5}{2k_2}}\right)$$

$$= \left(\frac{k_1}{2k_2}, \frac{-k_1^2(k_4+k_5)}{4k_2k_4k_6-2k_1k_3k_5}, \frac{-k_1^3k_3-2k_1^2k_2k_6}{4k_2(2k_2k_4k_6-k_1k_3k_5)}\right)$$

For all positive values of the rate constants the set of equilibrium points will be represented by;

$$\left(\frac{k_1}{2k_2}, \frac{-k_1^2(k_4+k_5)}{4k_2k_4k_6-2k_1k_3k_5}, \frac{-k_1^3k_3-2k_1^2k_2k_6}{4k_2(2k_2k_4k_6-k_1k_3k_5)}\right)$$

Using Python, we can solve the system of differential equations by setting the initial conditions

$$c_A(0)=0.1,\ \ c_B(0)=0.1 \quad \text{and} \quad c_C(0)=0.1$$

and assigning random positive values to the rate constants as follows:

$$k_1=1,\ \ k_2=0.5,\ \ k_3=0.2,\ \ k_4=0.3,\ \ k_5=0.4 \ \text{ and } \ k_6=0.1$$

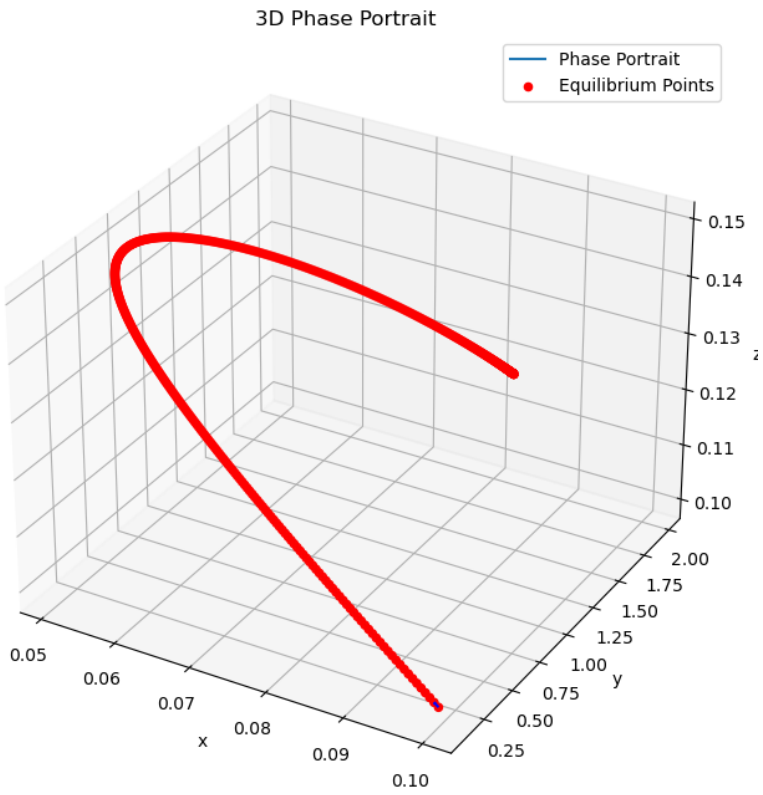


Figure 6. Phase Portrait showing equilibrium points

The 3D phase portrait shows how the concentrations of the three chemical species A, B, and C change with respect to each other over time. Each point in the 3D plot represents a state of the system at a specific time, with the x-coordinate representing the concentration of A, the y-coordinate representing the concentration of B, and the z-coordinate representing the concentration of z.

The trajectory of the system in the 3D phase portrait indicates how the concentrations evolve over time, depending on the initial conditions and the parameters of the reaction network. The equilibrium points of the system, where the concentrations remain constant over time, are represented by red line in the plot and it is clear that there are infinitely many such points.

The system fails condition $i.$ of the deficiency one theory because the phase portrait shows that there exists a choice of physical kinetics such that the system has multiple positive equilibria on some stoichiometry class. This means that there exists a subset of its constituent species that can produce another non-empty set of species in a single step. This situation can lead to cycles and multi-stationarity in the system. As a result, the system may have multiple steady states, and it becomes challenging to predict the behavior of the system accurately.

By mass action kinetics: there exists a choice of rate constants and inflows and outflows such that the system fails condition *ii*.. This indicates that the network structure may not support a unique positive steady-state concentration vector. The system could have multiple positive steady states, making it more complex to analyze its behavior and predict its dynamics.

6 Conclusion

We have provided definitions and brief discussions of key concepts related to reaction networks, including weakly reversible system, complex balancing, deficiency zero and deficiency one theorems. The SIR model has been used to explain some of these concepts to show how chemical reaction networks can be used in epidemiology.

This research has also shown that the application of deficiency theory, originally developed for chemical reaction networks, can offer valuable insights into the dynamics of infectious disease transmission models. Through the examination of the parallels between chemical kinetics and disease transmission, the research underscores the shared principles underlying complex systems with interacting components. Deficiency theory, which characterizes the ability of a system to exhibit multiple equilibria, turns out to be applicable to both chemical reactions and disease spread dynamics. The analysis reveals that the deficiency of a network can provide meaningful information about the potential for stability in both chemical and epidemiological contexts.

This research establishes a strong connection between deficiency theory in chemical reaction networks and models of infectious disease transmission. It demonstrates that deficiency theory's application can uncover deep insights into the stability, bifurcation, and equilibria behavior of both systems. This convergence of concepts and the fact that the analysis is always difficult for systems which are not weakly reversible enriches the theoretical framework for understanding complex systems and invites further exploration into how we can make systems which are not weakly reversible to be weakly reversible by using network translation.

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Appendix A: MATLAB Code for the Solution Curves and Phase Portrait of the SIR model

```
% SIR model parameters
beta = 0.3;    % Infection rate
gamma = 0.8;    % Recovery rate

% Time span for simulation
tspan = [0 100];

% Initial conditions
S0 = 0.9;     % Initial susceptible population
I0 = 0.1;     % Initial infected population
R0 = 0;      % Initial recovered population

% Define the SIR model differential equations
sirODEs = @(t, y) [-beta*y(1)*y(2); beta*y(1)*y(2) - gamma*y(2); gamma*y(2)];

% Solve the differential equations
[t,y] =ode45(sirODEs, tspan, [S0, I0, R0]);

% Extract solution components
S = y(:, 1);
I = y(:, 2);
R = y(:, 3);

% Plot the solutions
figure;
plot(t, S, 'b', 'LineWidth', 2);
hold on;
plot(t, I, 'r', 'LineWidth', 2);
plot(t, R, 'g', 'LineWidth', 2);
xlabel('Time');
ylabel('Population');
legend('Susceptible', 'Infected', 'Recovered');
title('SIR Model Solutions');

% Generate the phase portrait figure;
```

```
plot(S, I, 'b', 'LineWidth', 2);
xlabel('Susceptible');
ylabel('Infected');
title('Phase Portrait of SIR Model');
```

Appendix B: Python Code for Solving a System of Differential Equations

```
import numpy as np
import matplotlib.pyplot as plt
from scipy.integrate import odeint

def differential_equations(y, t, alpha, beta, gamma, epsilon, theta, eta):

# Define the differential equations here
dydt = alpha*y[0] - beta*y[0]**2 - gamma*y[0]*y[1] + epsilon*y[2]
dzdt = -gamma*y[0]*y[1] + epsilon*y[2] + theta*y[2] - eta*y[1]
dxdt = gamma*y[0]*y[1] + eta*y[1] - epsilon*y[2] - theta*y[2]
return np.array([dydt, dzdt, dxdt])

# Define time points to integrate over
t = np.linspace(0, 10, 1000)

# Define initial conditions
initial_conditions = [0.1, 0.1, 0.1]

# Define parameter values
alpha = 1.0
beta = 0.5
gamma = 0.2
epsilon = 0.3
theta = 0.4
eta = 0.1

# Solve the differential equations
solution = odeint(differential_equations, initial_conditions, t, args=(alpha, beta, gamma,
epsilon, theta, eta))

# Extract the variables from the solution
y_values = solution[:, 0]
z_values = solution[:, 1]
x_values = solution[:, 2]
```

```
# Plot the 2D phase portrait with arrows
plt.figure(figsize=(8, 6))
plt.plot(y_values, z_values, x_values, label='Phase Portrait')
plt.scatter(y_values, z_values, x_values, color='red', label='Equilibrium Points')

# Add arrows to indicate the direction of flow
for i in range(0, len(t), len(t) // 20):
plt.arrow(y_values[i], z_values[i], x_values[i], (y_values[i+1] - y_values[i])*0.1, (z_values[i+1]
- z_values[i])*0.1, (x_values[i+1] - x_values[i])*0.1,
head_width=0.05, head_length=0.01, fc='blue', ec='blue')

plt.xlabel('y')
plt.ylabel('z')
plt.legend()
plt.title('2D Phase Portrait')
plt.grid()
plt.show()
```