ABSTRACT

BORTNER, CASHOUS WILLIAM. Identifiability Analysis of Two Families of ODE Models. (Under the direction of Seth Sullivant).

Ordinary differential equations have been used to model natural phenomena in various scientific disciplines for hundreds of years. A natural question stemming from these models is whether we can recover unknown information from within the model using known or measured information. From this question formed the study of identifiability of ODE models. In this thesis, we focus on the identifiability of two families of ODE models, both of which have a corresponding graphical structure.

The first family we consider is LCR circuit systems consisting of parallel and series combinations of inductors, capacitors, and resistors. We first derive a method of constructing the defining constitutive equation corresponding to an LCR circuit system. Using this constitutive equation construction along with previous identifiability results on related viscoelastic models, we completely classify identifiability of all two base element type LCR circuit systems based on the structure of the corresponding graph. We also state several results on general LCR circuit systems and their corresponding constitutive equations, and construct a classification of LCR circuit systems we believe could be useful in future identifiability study.

The second family of ODE models we consider is linear compartmental models which have an underlying structure visualized by a directed graph. First, we consider models which we know are unidentifiable, and consider a reparametrization based on the structure of the corresponding directed graph. We classify models for which this reparametrization results in an identifiable model as identifiable path-cycle models. We then explore the relationship between identifiable path-cycle models and identifiable models. We also consider the identifiability of another subclass of models called linear compartmental tree models. In this study, we state a novel characterization of the defining input-output equation of a linear compartmental model. We then use this characterization to completely classify the identifiability of linear compartmental tree models solely on the structure of the corresponding graph.

Identifiability Analysis of Two Families of ODE Models

by
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DEDICATION

To my wife, without whom none of this would have been possible.

BIOGRAPHY

Cashous "Cash" Bortner grew up in McCook, Nebraska, where he attended McCook Senior High School. He graduated from the University of Nebraska-Lincoln in May 2017 with a major in Mathematics. Cash began his graduate work in mathematics at North Carolina State University in August 2017. He will continue his academic career as a tenure-track faculty member of California State University - Stanislaus.

In his spare time, Cash loves to cheer for the Huskers and the New York Yankees, spend time with his wife, two dogs, and two cats, cook/bake, and help undergraduate and graduate math students in any way he can.

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INTRODUCTION

In this chapter, we present background material related to the topics of this thesis. Section 1.1 is an introduction to the study of identifiability and some of the tools we will use in this thesis. Section 1.2 is an introduction to the graph theoretic background needed in this thesis. Section 1.3 is an introduction to the tools from algebraic geometry that we need in this thesis, including ideals, varieties and projective geometry. Section 1.4 introduces LCR circuit systems, which will be the main focus of Chapter 2. Section 1.5 introduces linear compartmental models, the focus of Chapters 3 and 4. Finally, Section 1.6 gives a summary of the main results from this thesis.

1.1 Identifiability

Modeling the physical world using ordinary differential equations (ODEs) has long been of interests in several academic fields ranging from physics to biology and epidemiology (Berman and Schoenfield 1956; Stefano 2014; Mulholland and Keener 1974; Wagner 1981). These models consist of known input and output variables, and unknown parameters and state variables. A natural question in the study of ODE models is whether or not we can recover the unknown parameters from the known input and output variables. This question is the basis for the study of *identifiability*.

The study of identifiability has been split into two subcategories called *structural* and *practical* identifiability. Structural identifiability, the focus of this thesis, is the question of recovering parameters of an ODE system *a priori*. In essence, analysis of the structural identifiability of a model asks whether under perfect conditions with no noise or error in measurements, we can recover the parameters of a model. This is a key first step in evaluating, and perhaps even adjusting an ODE model.

On the other hand, the study of practical identifiability asks the same question with the addition of noise, i.e. practical identifiability is the study of actually recovering parameters from measured data. Structural and practical identifiability are intimately connected in that structural identifiability is a prerequisite for practical identifiability. In practice, structural identifiability is done in the preliminary stages of model analysis to determine the viability of practical identifiability, and to potentially find reparametrizations of the model which yields an identifiable model.

The ODE models that are considered in this thesis have the form

$$\Sigma = \begin{cases} \dot{\mathbf{x}} & = \mathbf{f}(\mathbf{x}, \mathbf{a}, \mathbf{u}) \\ \mathbf{y} & = \mathbf{g}(\mathbf{x}, \mathbf{a}, \mathbf{u}) \end{cases}$$

where $\mathbf{x}$ is a vector of state variables, $\mathbf{u}$ and $\mathbf{y}$ are vectors of the input and output variables respectively, and $\mathbf{a}$ is the vector of model parameters. Define an *input-output equation* corresponding to a model to be an ODE in the known input and output variables and their derivatives, with coefficients in the unknown parameters. In this thesis we consider the case where the input-output equation is a polynomial function F satisfying $F(y, \dot{y}, \ddot{y}, \ldots, u, \dot{u}, \ddot{u}, \ldots, a_1, a_2, \ldots) = 0$ and analyze identifiability of functions of parameters via this input-output equation. There are several other methods for studying structural identifiability, including the Taylor series approach, the generating series approach, identifiability tableaus, and similarity transformation approach among others (Chis et al. 2011). The input-output equation[s] corresponding to an ODE model is the minimal set of defining ODEs of the model in the measurable variables, with coefficients consisting of functions of parameters.

Example 1.1.1. Consider the model with known input u_1, known output y_2, and unknown parameter a_{21}, and state variables x_1 and x_2 defined by the following system of ODEs:

$$\begin{aligned}\dot{x}_1 &= -a_{21}x_1 + u_1\\ \dot{x}_2 &= a_{21}x_1\\ y_2 &= x_2.\end{aligned}$$

An input-output equation for this systems would be a differential equation consisting of only y_2 and u_1 and their derivatives, along with a_{21}. This can be quickly constructed via substitution resulting in the input-output equation:

$$\ddot{y}_2 + a_{21}\dot{y}_2 = a_{21}u_1. \tag{1.1}$$

As we assume $\ddot{y}_2$, $\dot{y}_2$, and u_1 are known, then we can solve for the unknown parameter a_{21} via Equation 1.1 as

$$a_{21} = \frac{\ddot{y}_2}{u_1 - \dot{y}_2}.$$

Note that several other assumptions must be made in order to actually recover a_{21}, including $u_1 \neq \dot{y}_2$ and that y_2 has nontrivial first and second derivatives.

The method for recovering the parameter in Example 1.1.1 of solving for the parameter directly in terms of the input and output variables is not the standard method used in the study of identifiability, particularly because it is not possible for more complex models. In this thesis, we use the differential algebra approach and consider identifiability by the input-output equation, and more specifically by the map from the parameter space to the space of coefficients of the input-output equation.

Definition 1.1.2. Consider a model with parameters $\mathbf{a}$, input variables $\mathbf{u}$, output variables $\mathbf{y}$, and input-output equations

$$\begin{aligned}f_1(\mathbf{u},\mathbf{y}) &= 0\\ f_2(\mathbf{u},\mathbf{y}) &= 0\\ &\vdots\\ f_k(\mathbf{u},\mathbf{y}) &= 0\end{aligned}$$

Here, each f_i is an ODE in $\mathbf{u}$ and $\mathbf{y}$ and their derivatives with coefficients consisting of functions of parameters $\mathbf{a}$. Define the *coefficient map* $\mathbf{c}\colon \Theta \to \mathbb{R}^{\nu}$ to be the map from the space of parameters to the space of coefficients. Similarly, we can define a coefficient map for each $f_i(\mathbf{u},\mathbf{y})$ as $c_i : \Theta \to \mathbb{R}^{\nu_i}$ which maps from the parameter space to the coefficients of $f_i(\mathbf{u},\mathbf{y})$.

Remark 1.1.3. In this thesis, we analyze structural identifiability of models by their input-output equations, and specifically by considering the injectivity of the coefficient map. The fact that we can study the identifiability of these models using the input-output equation is not trivial, and in general not necessarily true. Specifically, it could be impossible to recover the coefficients from a set of input-output equations.

In order to recover the coefficients from the input-output equations $f_1,\ldots,f_n$, we need to make assumptions about $\mathbf{u}$ and $\mathbf{y}$ and their relationship with their respective derivatives. Namely, we need that each $c_i(\mathbf{a})$ is uniquely determined by the input-output variables. Specifically, we assume that if

$$f_i(\mathbf{u},\mathbf{y}) = g_{i1}(\mathbf{u},\mathbf{y}) + \sum_{j=2}^{\nu_i} c_{ij}(\mathbf{a}) g_{ij}(\mathbf{u},\mathbf{y}) = 0 \tag{1.2}$$

where $g_{ij}(\mathbf{u},\mathbf{y})$ is the jth monomial term in $f_i(\mathbf{u},\mathbf{y})$, then there exists some N and $t_1,\ldots,t_N \in \mathbb{R}$ such that the system of rN equations obtained by evaluating each of the r input-output equations 1.2 at the $t_1,\ldots,t_N$ has a solution in the unknowns $c_{ij}(\mathbf{a})$.

In practice, the existence of N and $t_1,\ldots,t_N$ is not guaranteed, particularly in the case when there is more than one output variable. Theorem 1 of Ovchinnikov et al. (2021a) states that we are able to consider identifiability of a model by considering the injectivity of the coefficient map, what they call input-output identifiability, in the case when there is exactly one output. In this thesis, we restrict our study of identifiability to models with a single output. We do make statements about input-output equations for models with multiple outputs, particularly in Chapter 4, for the sake of future study in this area.

Our investigation of identifiability in this thesis is split into a two part problem. First, we need to determine a method of generating the input-output equation of a model, and second we determine the injectivity of the input-output equation. We place a heavy emphasis on generating the input-output equations using combinatorial methods in the hope that we can make deductions about the identifiability using only a surface study of the structure of the model and input-output equations. Specifically, in Chapter 2 we use the number of parameters as compared to the number of coefficients to completely classify identifiability a subset of LCR models. In Chapter 4, we generate the coefficients of the input-output equations via the graphical structure of the model, resulting in several identifiability results based solely on the underlying graph structure of the model.

Example 1.1.4. Consider the model with parameters a_1, a_2, a_3, a_4 and input-output equation

$$a_1 \ddot{y} + \frac{a_1 a_2}{a_4} \dot{y} = \ddot{u} + \left(\frac{a_1}{a_3} + \frac{a_1}{a_4} + \frac{a_2}{a_4} \right) \dot{u} + \frac{a_1 a_2}{a_3 a_4} u.$$

Then, the coefficient map corresponding to this model is

$$\mathbf{c}\colon (a_1, a_2, a_3, a_4) \mapsto \left(a_1, \frac{a_1 a_2}{a_4}, \frac{a_1}{a_3} + \frac{a_1}{a_4} + \frac{a_2}{a_4}, \frac{a_1 a_2}{a_3 a_4}. \right)$$

Note that we omit the monic coefficient of $\ddot{u}$ from the coefficient map, as it will not have an effect on the injectivity of the map $\mathbf{c}$. Also, this map is only well defined when a_2, a_3 and a_4 are nonzero. In general, throughout this thesis we will assume we are away from regions in the parameter space that make the coefficient map undefined.

Now we define structural identifiability more formally, and make distinctions between different types of structural identifiability. Also, as we only discuss structural identifiability from this point forward, we drop the “structural.”

Definition 1.1.5. Let $\mathbf{c}\colon \Theta \to \mathbb{R}^n$ be the coefficient map of a model from a parameter space $\Theta \subseteq \mathbb{R}^k$. Then, we say the model is

- *globally identifiable* if $\mathbf{c}^{-1}(\mathbf{c}(\mathbf{a})) = \mathbf{a}$ for all $\mathbf{a} \in \Theta$;
- *locally identifiable* if $|\mathbf{c}^{-1}(\mathbf{c}(\mathbf{a}))| < \infty$ for almost all $\mathbf{a} \in \Theta$;
- *unidentifiable* if $|\mathbf{c}^{-1}(\mathbf{c}(\mathbf{a}))| = \infty$ for almost all $\mathbf{a} \in \Theta$.

We now introduce one of the main tools we use for identifiability analysis, which gives insight as to why so many of the results in this thesis relate to local identifiability.

Definition 1.1.6. For a polynomial map

$$\begin{aligned} f : \mathbb{R}^n &\to \mathbb{R}^m \\ (a_1, a_2, \ldots, a_n) &\mapsto \big(f_1(a_1, \ldots, a_n), \ldots, f_m(a_1, \ldots, a_n) \big) \end{aligned}$$

the *Jacobian matrix* associated to f, sometimes called the differential, is the m by n matrix where each row corresponds to one of the f_i, and each column is the partial derivative of that f_i with respect to one of the variables a_j

$$J_f(a_1, a_2, \ldots, a_n) = \begin{pmatrix} \frac{\partial f_1}{\partial a_1} & \frac{\partial f_1}{\partial a_2} & \cdots & \frac{\partial f_1}{\partial a_n} \\ \frac{\partial f_2}{\partial a_1} & \frac{\partial f_2}{\partial a_2} & \cdots & \frac{\partial f_2}{\partial a_n} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\partial f_m}{\partial a_1} & \frac{\partial f_m}{\partial a_2} & \cdots & \frac{\partial f_m}{\partial a_n} \end{pmatrix}$$

The Jacobian matrix is of interest because of its relationship with the local injectivity of its corresponding function, as outlined in the Inverse Function Theorem (Chern et al. 2006, Theorem 3.1).

Theorem 1.1.7 (Inverse Function Theorem)**.** *Suppose W is an open subset of $\mathbb{R}^n$ and $f : W \longrightarrow \mathbb{R}^n$ is a smooth map. If at a point $x_0 \in W$ the determinant of the Jacobian matrix is nonzero, i.e.* $\det(J_f(x_0)) \neq 0$*, then there exists a neighborhood $U \subset W$ of x_0 in $\mathbb{R}^n$ such that $V = f(U)$ is a neighborhood of $f(x_0)$ in $\mathbb{R}^n$, and f has a smooth inverse on V.*

The Inverse Function Theorem, and specifically the Jacobian matrix, will be one of our main tools in the identifiability analysis of a coefficient map. As a result, many of the results in this thesis are *local* identifiability results, since the Inverse Function Theorem only gives us local information about injectivity.

Example 1.1.8. We saw that we could recover the single parameter a_{21} in the model in Example 1.1.1 directly from the input and output variables. We can come to this conclusion via the input-output equation, since in this case the input-output equation is $\mathbf{c}: (a_{21}) \mapsto (a_{21}, a_{21})$. This map is certainly injective for all $a_{21} \in \mathbb{R}$, thus we find that this model is globally identifiable.

Consider the model with input-output equation

$$\ddot{y} + \frac{bc + ad}{cd}\dot{y} + \frac{ab}{cd}y = \frac{ab(c+d)}{cd}\dot{u} + (a+b)u$$

hence coefficient map

$$\mathbf{c}: (a, b, c, d) \mapsto \Bigg(\underbrace{\frac{bc + ad}{cd}}_{f_1}, \underbrace{\frac{ab}{cd}}_{f_2}, \underbrace{\frac{ab(c+d)}{cd}}_{f_3}, \underbrace{a+b}_{f_4}\Bigg).$$

Now a quick Jacobian calculation yields

$$J_{\mathbf{c}}(a,b,c,d) = \begin{array}{c c} & \begin{array}{cccc} a & b & c & d \end{array} \\ \begin{array}{c} f_1 \\ f_2 \\ f_3 \\ f_4 \end{array} & \begin{pmatrix} \frac{1}{c} & \frac{1}{d} & \frac{b}{cd} - \frac{bc+ad}{c^2 d} & \frac{a}{cd} - \frac{bc+ad}{cd^2} \\ \frac{b}{cd} & \frac{a}{cd} & -\frac{ab}{c^2 d} & -\frac{ab}{cd^2} \\ \frac{b(c+d)}{cd} & \frac{a(c+d)}{cd} & \frac{ab}{cd} - \frac{ab(c+d)}{c^2 d} & \frac{ab}{cd} - \frac{ab(c+d)}{cd^2} \\ 1 & 1 & 0 & 0 \end{pmatrix} \end{array}.$$

The determinant of this Jacobian is

$$\det(J_{\mathbf{c}}(a,b,c,d)) = \frac{-c^2ab^3 + 2a^2b^2cd - a^3bd^2}{c^4d^4}.$$

Thus, for generic entries of (a,b,c,d), this determinant is nonzero meaning $\mathbf{c}$ is locally injective by the Inverse Function Theorem, hence the model is locally identifiable.

This model is not globally identifiable as the two points (a,b,c,d) and (b,a,d,c) have the same image for all positive a, b, c, and d.

Finally, if we consider any model with fewer coefficients in the input-output equation than parameters, for example a model with coefficient map

$$\mathbf{c}: (a,b,c,d) \mapsto (abc, ab+ac+bd, a+b+c+d),$$

then the result is an unidentifiable model, as a map from a larger dimensional space to a smaller dimensional space cannot possibly be injective.

Remark 1.1.9. When the coefficient map maps from a space of some dimension to a space of smaller dimension, we immediately can determine that the map is not injective, hence the model is unidentifiable. This fact will actually be the focus of many of our results on unidentifiability, though to use it we must first determine the number of nontrivial coefficients in the input-output equation of a model.

Much of this thesis will focus on local identifiability results, as one of the main tools we use in identifiability analysis is the Jacobian matrix, with which we can only determine local injectivity as outlined in the Inverse Function Theorem (Theorem 1.1.7).

Often we want to show that each individual parameter is identifiable. In cases when we immediately know that each parameter cannot be identifiable, we are interested is finding identifiable functions, also called identifiable combinations, of parameters for the sake of possible reparametrization. Ovchinnikov et al. (2021a,b) note that this notion of identifiability is not necessarily the same as the analytic definition of identifiability. In the case of the models that we consider in this thesis, the analytic notion of identifiability does align with the “input-output identifiability” that we have introduced via the three main results from Ovchinnikov et al. (2021a).

In the case that a model is not identifiable, we are often interested in reparametrizing the model into one which *is* identifiable. To do this, we first need to define an identifiable function of parameters.

Definition 1.1.10. Let $\mathbf{c}$ be a function $\mathbf{c} : \Theta \subseteq \mathbb{R}^n \to \mathbb{R}^k$. A function $f : \mathbb{R}^n \to \mathbb{R}$ is *globally identifiable* from $\mathbf{c}$ if there exists a function $\Phi : \mathbb{R}^k \to \mathbb{R}$ such that $\Phi \circ \mathbf{c} = f$. The function f is *locally identifiable* if there is a finitely multi-valued function $\Phi : \mathbb{R}^k \to \mathbb{R}$ such that $\Phi \circ \mathbf{c} = f$.

Working with unidentifiable models to find identifiable reparametrizations is the focus of Chapter 3. Consider the following example.

Example 1.1.11. Consider the functions

$$\mathbf{c} \colon (a, b, c) \mapsto (a, ab + bc)$$
$$f : (a, b, c) \mapsto b + c.$$

The function f is globally identifiable from $\mathbf{c}$ since if we let

$$\Phi \colon (c_1, c_2) \mapsto \frac{c_2}{c_1},$$

then we have that $\Phi \circ \mathbf{c} = f$.

In Chapter 3, we consider models which are immediately unidentifiable due to the input-output equation having fewer coefficients than there are parameters, however we reparametrize these models using graph structures to get identifiable models.

1.2 Graph Theory

In this section, we discuss graph theoretic concepts that are necessary for the rest of this thesis. Standard references for this material can be found in Biggs (1993) and Diestel (2006).

Definition 1.2.1. A *undirected graph* $G = (V, E)$ is defined by the set of *vertices* $V = \{v_1, \ldots, v_n\}$ and the set of *edges* $E \subseteq \{\{i, j\} \colon i, j \in V\}$. We define *directed graphs* similarly as $H = (V, E')$, where the edges now consist of ordered pairs $E' \subseteq \{(i, j) \colon i, j \in V\}$

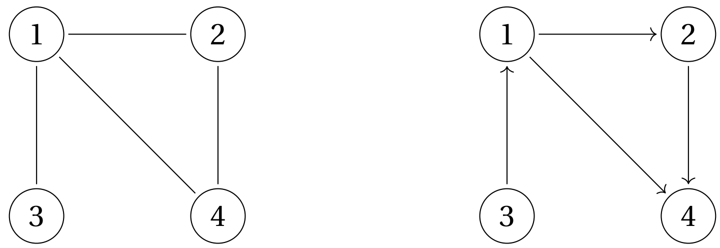

Figure 1.1: Undirected and directed graphs G and H respectively described in Example 1.2.2.

Undirected graphs can be visualized with vertices corresponding to points in the plane and edges corresponding to line segments between vertices. Directed graphs on the other hand can be visualized with the same vertex points in the plane, but with directed arrows between these points.

Example 1.2.2. Figure 1.1 gives visual representations of an undirected and directed graph respectively both over the set of vertices $V = \{1,2,3,4\}$. The undirected graph $G = (V,E)$ has edge set $E = \{\{1,2\},\{1,4\},\{2,4\},\{3,1\}\}$, while the directed graph $H = (V,E')$ has nearly the same edge set, but with *ordered* pairs $E' = \{(1,2),(1,4),(2,4),(3,1)\}$. In this case, we say that the undirected graph is the *underlying undirected graph* of the directed graph. These graphs are examples of *simple graphs* meaning they have at most one edge between each pair of vertices, and no self-loops, i.e. edges from a vertex to itself.

Define a *subgraph* of a graph $G = (V,E)$ as $H = (W,F)$ such that $V \subseteq W$ and $F \subseteq \{\{i,j\} \in E : i,j \in W\}$. An *induced subgraph* of a graph $G = (V,E)$ is defined by some $W \subseteq V$ as

$$G_W = (W, \{\{i,j\} \subseteq E : i,j \in W\}).$$

Example 1.2.3. The induced subgraph on the undirected graph defined in Example 1.2.2 by the set $\{1,2,3\}$ is

$$G_{\{1,2,3\}} = (\{1,2,3\},\ \{\{1,2\},\{3,1\}\}).$$

A *path* is a non-empty graph $P_k = (V,E)$ of the form

$$V = \{v_0, v_1, \ldots, v_k\} \quad \text{and} \quad E = \{\{v_0,v_1\},\{v_1,v_2\},\ldots,\{v_{k-1},v_k\}\} \tag{1.3}$$

where all v_i are distinct. A *directed path* is defined accordingly with a directed edge set as $E = \{(v_0,v_1),(v_1,v_2),\ldots(v_{k-1},v_k)\}$. We often consider paths found within other graphs, that is paths which are subgraphs of other graphs. For example, we define the distance between two vertices in a graph as the number of edges on the shortest path between the two vertices. The distance between two vertices i and j is denoted dist(i, j). Similarly, for directed graphs, we define dist(i, j) as the length of the shortest directed path from i to j.

We say an undirected graph is *connected* if there is a path from every vertex to every other vertex within the graph. Similarly, we say a directed graph is *strongly connected* if there is a directed path from every vertex to every other vertex. A directed graph is said to be *inductively strongly connected with respect to vertex 1* if there exists an ordering of the vertices $1, 2, \ldots, n$ such that the induced subgraphs $G_{\{1,\ldots,i\}}$ are strongly connected for each $i \in \{1, \ldots, n\}$.

For an undirected path $P_k = (V, E)$ as defined in 1.3, define a *cycle* to be the graph $C_k = (V, E \cup \{k, 1\})$, i.e. the path on k vertices with an additional edge connecting one end of the path to the other. Similarly, we define a directed cycle as a directed path with the addition of the directed edge from the last vertex in the path to the first vertex. Again, we are often interested in finding cycles within other graphs, i.e. as subgraphs of other graphs.

A undirected graph is said to be a *forest* if there are no underlying cycles (subgraphs which are cycles), and a *tree* if the graph is a connected forest. In fact, a defining property of a tree is that there is exactly one path between any two vertices.

Example 1.2.4. Consider the graphs G and H in Figure 1.2. Note that both graphs are strongly connected, as in both graphs there is a directed path from any vertex to any other vertex. In fact, note that G is a subgraph of H, and is the directed cycle graph on four vertices. Note that the graph G is **not** inductively strongly connected, as the removal of any vertex yields a graph which is not strongly connected. The graph H on the other hand **is** inductively strongly connected with respect to the vertex 1 and the ordering $1, 2, 3, 4$, since the induced subgraphs $G_{\{1\}}, G_{\{1,2\}}$, and $G_{\{1,2,3\}}$ are all strongly connected, and as discussed $G = G_{\{1,2,3,4\}}$ is strongly connected.

These graph structures are a main element of this thesis, as all of the models considered in later chapters can be visualized with a graph. This is especially evident in Chapters 3 and 4, as linear compartmental models are defined partially by a directed graph. One of the main goals of our study of identifiability, particularly with respect to linear compartmental models, is to classify identifiability strictly by the structure of the corresponding directed graph.

Definition 1.2.5. Define the *Laplacian matrix* L of a directed graph $G = (V, E)$ with weights

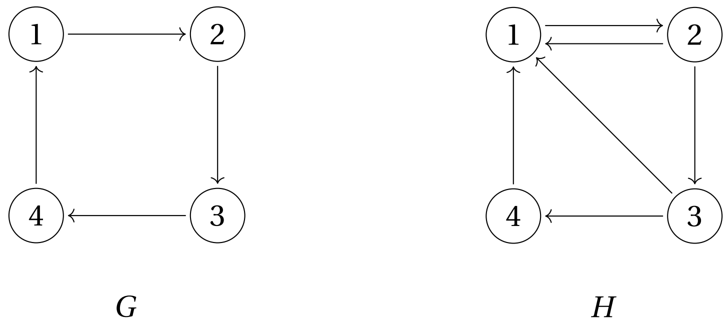

Figure 1.2: Directed graphs G and H, with G strongly connected but not inductively strongly connected, and H inductively strongly connected.

a_{ij} for the edge $j \to i \in E$ is defined as

$$L_{ij} = \begin{cases} \sum_{j \to k \in E} a_{kj} & \text{if } i = j \\ -a_{ij} & \text{if } j \to i \in E \\ 0 & \text{otherwise.} \end{cases} \tag{1.4}$$

There is also a standard definition for the Laplacian matrix of undirected and unweighted graphs, though we will not need this definition in this thesis, so it is omitted (Biggs 1993, Chapter 4).

Example 1.2.6. The Laplacian Matrix associated to the directed graph G in Figure 1.3 with weights a_{ji} for each edge $j \to i$ has the form:

$$L = \begin{pmatrix} a_{21} + a_{41} & 0 & -a_{13} & 0 \\ -a_{21} & a_{42} & 0 & 0 \\ 0 & 0 & a_{13} & 0 \\ -a_{41} & -a_{42} & 0 & 0 \end{pmatrix} \tag{1.5}$$

We now consider a specific type of graph called an incoming forest which will play a key role in one of our main theorems relating to input-output equations in Chapter 4.

Definition 1.2.7. A directed graph is an *incoming forest* if no vertex has more than one outgoing edge, and its underlying undirected graph is a forest.

We introduce the following notation for a directed graph H:

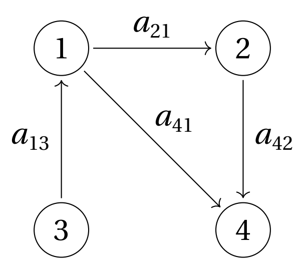

Figure 1.3: A weighted graph discussed in Example 1.2.6.

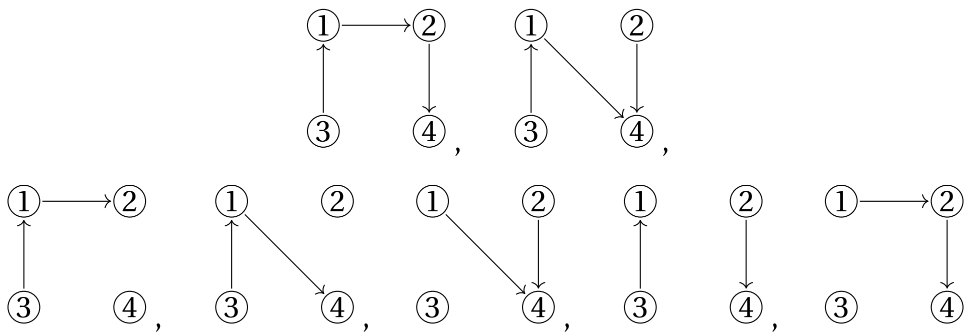

Figure 1.4: All seven incoming forest subgraphs of the directed graph from Example 1.2.2 containing more than one edge.

- $\mathscr{F}_j(H)$ is the set of all incoming forests of H with exactly j edges, and
- $\mathscr{F}_j^{k,\ell}(H)$ is the set of all incoming forests of H with exactly j edges, such that some connected component (of the underlying undirected graph) contains both of the vertices k and ℓ.

Example 1.2.8 (Continuation of Example 1.2.2)**.** The directed graph G given in Example 1.2.2 is not an incoming forest, as the underlying undirected graph, also seen in Example 1.2.2 contains the cycle $1 \to 2 \to 4 \to 1$. With that being said, this graph does have several subgraphs which are incoming forest, all of which can be seen in Figure 1.4. There are two incoming forests in G containing three edges i.e. $|\mathscr{F}_3(G)| = 2$, and five incoming forests in G containing two edges which are incoming forests i.e. $|\mathscr{F}_2(G)| = 5$. Also, note that by definition, any subgraph contain one or zero edges is an incoming forest.

The following version of the well-known Matrix Tree Theorem connects the ideas of the Laplacian matrix and its characteristic polynomial, with incoming forests found within the corresponding graph. This will be a key element of the proof of one of the main theorems of Chapter 4.

Proposition 1.2.9 (All Minors Matrix Tree Theorem, Buslov (2016))**.** *Let*

$$\det(\lambda I - L) = \sum_{k=0}^{N} c_k \lambda^k \tag{1.6}$$

be the characteristic polynomial of the weighted Laplacian of an N-vertex directed graph G without loops and with edge weights a_{ji}. Then

$$c_k = (-1)^{N-k}\left(\sum_{F\in\mathscr{F}_k(G)} \pi_F\right) \quad \textit{where} \quad \pi_F = \prod_{(i,j)\in E_F} a_{ji}.$$

For a weighted graph G, the π_G defined in Proposition 1.2.9 is called the *productivity* of G. Following the usual convention, we define $\pi_H = 1$ for graphs H having no edges.

Example 1.2.10 (Continuation of Example 1.2.2)**.** The characteristic polynomial of the weighted Laplacian matrix from Example 1.2.6 associated to the directed graph in Example 1.2.2 is

$$\begin{aligned}\det(\lambda I - L) &= \det\begin{pmatrix} \lambda - a_{21} - a_{41} & 0 & a_{13} & 0 \\ a_{21} & \lambda - a_{42} & 0 & 0 \\ 0 & 0 & \lambda - a_{13} & 0 \\ a_{41} & a_{42} & 0 & \lambda \end{pmatrix} \\ &= \lambda^4 - (a_{13}+a_{21}+a_{41}+a_{42})\lambda^3 + (a_{13}a_{21}+a_{13}a_{41}+a_{41}a_{42}+a_{13}a_{42}+a_{21}a_{42})\lambda^2 \\ &\quad - (a_{13}a_{21}a_{42}+a_{13}a_{41}a_{42})\lambda \end{aligned} \tag{1.7}$$

If we label the coefficient of λ^i as c_i, then each c_i in Equation 1.7 corresponds exactly to the sum of the productivities of the incoming forests of G containing i edges, as in Proposition 1.2.9. The coefficient of λ^3 is of the sum of each of the edge weights in the graph, as any single edge constitutes an incoming forest. The seven incoming forests corresponding to the coefficients of λ and λ^2 can be seen in Example 1.2.8.

Also note that the λ^0 coefficient is zero. This is due to the constant in the characteristic polynomial being the determinant of L, which in the case of the Laplacian is a singular matrix. The singularity of the Laplacian matrix comes from the fact that by definition, the sum of all of the rows of the Laplacian is the zero vector.

The Laplacian matrix is connected to the compartmental matrix of a linear compartmental model. We use this fact coupled with the All Minors Matrix Tree Theorem to find a combinatorial characterization of the input-output equation of linear compartmental models in terms of incoming forests of graphs closely related to the model in Theorem 4.2.1.

1.3 Algebraic Geometry

In this section, we focus on the study of polynomials, and specifically their roots and coefficients and the relationship between them. Standard introductory references for this material can be found in Cox et al. (2005).

1.3.1 Ideals, Varieties, and Projective Geometry

If $\mathbb{K}$ is a field, let $\mathbb{K}[x_1, x_2, \ldots, x_n]$ be the set of polynomials in $x_1, x_2, \ldots, x_n$ with coefficients in $\mathbb{K}$.

Definition 1.3.1. An *ideal* $I \subseteq \mathbb{K}[x_1, \ldots, x_n]$ is a set of polynomials such that

- $0 \in I$,
- if $f, g \in I$ then $f + g \in I$, and
- if $f \in I$ and $g \in \mathbb{K}[x_1, \ldots, x_n]$, then $fg \in I$.

We can now define ideals generated by the polynomials $f_1, \ldots, f_m$ as

$$\langle f_1, \ldots, f_m \rangle = \left\{ \sum_{i=1}^{m} h_i f_i \; : \; h_1, \ldots h_m \in \mathbb{K}[x_1, \ldots, x_n] \right\}$$

In this case, we say that $f_1, \ldots, f_m$ are the generating set for this ideal. A major result of commutative algebra called the *Hilbert Basis Theorem*, states that every polynomial ideal $I \subseteq \mathbb{K}[x_1, \ldots, x_n]$ has a finite generating set, i.e. there exists some $g_1, \ldots, g_m \in \mathbb{K}[x_1, \ldots, x_n]$ with m finite such that $\langle g_1, \ldots, g_m \rangle = I$.

We now define another set determined by a finite set of polynomials.

Definition 1.3.2. For a set of polynomials $f_1, \ldots, f_m \in \mathbb{K}[x_1, \ldots, x_n]$, let

$$V(f_1, \ldots, f_m) = \{(a_1, \ldots, a_n) \in \mathbb{K}^n : f_i(a_1, \ldots, a_n) = 0 \text{ for all } 1 \le i \le m\}.$$

We call this $V(f_1, \ldots f_m)$ the *affine variety* defined by $f_1, \ldots, f_m$.

Thus, an affine variety is the set of shared roots for all of the polynomials over which it is defined.

Example 1.3.3. Consider the polynomials $f = x^2 + y^2 - 1$ and $g = y - x - 1$ both in $\mathbb{R}[x, y]$. The affine variety defined by f alone is

$$V(f) = \{(x, y) \in \mathbb{R}^2 \colon x^2 + y^2 = 1\},$$

i.e. the unit circle in the plane.

The affine variety defined by f and g, i.e.

$$V(f, g) = \{(x, y) \in \mathbb{R}^2 \colon x^2 + y^2 = 1 \text{ and } y = x + 1\}.$$

Thus, $V(f, g) = \{(0, 1), (-1, 0)\}$, as these are the only two pairs of real numbers which satisfy both equations.

Note that a natural relationship exists between an ideal generated by a set of polynomials, and the affine variety determined by the same set of polynomials. Suppose $\mathbf{a} = (a_1, \ldots, a_n) \in V(f_1, \ldots, f_m)$ is an element of the affine variety determined by $f_1, \ldots, f_m$. Note then that if $g \in \langle f_1, \ldots, f_m \rangle$ is an element of the ideal generated by $f_1, \ldots, f_m$, then by definition $g = h_1 f_1 + \cdots + h_m f_m$ for some $h_1, \ldots, h_m \in \mathbb{K}[x_1, \ldots, x_n]$. Also, since $\mathbf{a} \in V(f_1, \ldots, f_m)$, then $f_1(\mathbf{a}) = f_2(\mathbf{a}) = \cdots = f_m(\mathbf{a}) = 0$, thus $g(\mathbf{a}) = 0$. In fact, we can define an affine variety of a polynomial ideal $I \subseteq \mathbb{K}[x_1, \ldots, x_n]$ as

$$V(I) = \left\{(a_1, \ldots, a_n) \in \mathbb{K}^n \colon f(a_1, \ldots, a_n) = 0 \text{ for all } f \in I\right\}.$$

This relationship between ideals and varieties generated by a set of polynomials culminates in the following proposition thanks to the Hilbert Basis Theorem:

Proposition 1.3.4. *If $I = \langle f_1, \ldots, f_m \rangle$, then $V(I) = V(f_1 \ldots, f_m)$.*

We now define *Projective n-space* $\mathbb{PK}^n$ to be the set of all lines in affine space containing the origin, i.e. $\overline{0} \in \ell \subseteq \mathbb{K}^{n+1}$. Note then that each of these lines takes the form

$$\mathrm{span}(\mathrm{a}_0, \mathrm{a}_1, \ldots, \mathrm{a}_\mathrm{n}) = \lambda(\mathrm{a}_0, \mathrm{a}_1, \ldots, \mathrm{a}_\mathrm{n})$$

for $\lambda \in \mathbb{K}$ and $(a_0, a_1, \ldots, a_n) \in \mathbb{K}^{n+1} - \{0\}$.

The projective space can be thought of as the following equivalence class

$$\mathbb{PK}^n = (\mathbb{K}^{n+1} - \{0\}) / \sim$$

with the equivalence relation

$$(a_0', \dots, a_n') \sim (a_0, \dots, a_n) \quad \text{if} \quad (a_0', \dots, a_n') = \lambda(a_0, \dots, a_n)$$

for some $\lambda \in \mathbb{K} - \{0\}$.

The *degree of a monomial* $x_1^{\alpha_1} x_2^{\alpha_2} \cdots x_n^{\alpha_n}$ is defined as the sum of the powers of each variable in the monomial, i.e.

$$\deg\left(x_1^{\alpha_1} x_2^{\alpha_2} \cdots x_n^{\alpha_n}\right) = \alpha_1 + \alpha_2 + \cdots + \alpha_n.$$

From this notion, we can define the *degree of a polynomial* as the maximal degree of each monomial in the polynomial, i.e. if f is a polynomial consisting of a sum of m monomial terms

$$f = \sum_{k=1}^{m} x_1^{\alpha_{1,k}} x_2^{\alpha_{2,k}} \cdots x_n^{\alpha_{n,k}}$$

then

$$\deg(f) = \max_{k \in \{1,\dots,m\}} (\alpha_{1,k} + \alpha_{2,k} + \cdots + \alpha_{n,k}).$$

Now define a polynomial to be *homogeneous of total degree k* if every monomial term in the sum generating the polynomial has the same degree, namely k. In the language above, this means that

$$\begin{aligned}
k = \deg(f) &= \max_{k \in \{1,\dots,m\}} (\alpha_{1,k} + \alpha_{2,k} + \cdots + \alpha_{n,k}) \\
&= \alpha_{1,1} + \alpha_{2,1} + \cdots + \alpha_{n,1} \\
&= \alpha_{1,2} + \alpha_{2,2} + \cdots + \alpha_{n,2} \\
&\ \ \vdots \\
&= \alpha_{1,m} + \alpha_{2,m} + \cdots + \alpha_{n,m}.
\end{aligned}$$

For a given polynomial $f \in \mathbb{K}[x_1, \dots, x_n]$, we can *homogenize* f in the polynomial ring $\mathbb{K}[x_0, x_1, \dots, x_n]$ as follows: Let $f \in \mathbb{K}[x_1, \dots, x_n]$ with degree d and let $f = \sum_{i=0}^{d} f_i$ where f_i

consists of every monomial in f of degree i. Now define

$$f^h = \sum_{i=0}^{d} f_i x_0^{d-i}.$$

Note that $f^h \in \mathbb{K}[x_0, \ldots, x_n]$ has degree d, and also that f^h is now homogeneous in $x_0, \ldots, x_n$, since $\deg(f_i x_0^{d-i}) = \deg(f_i) + \deg(x_0^{d-i}) = i + d = d$.

Using this homogenization, given an variety $V(f_1, \ldots, f_m) \subseteq \mathbb{K}^n$, we can generate a projective variety $V(f_1^h, \ldots, f_m^h) \subseteq \mathbb{PK}^n$. We say that an ideal $I \subseteq \mathbb{K}[x_0, x_1, \ldots, x_n]$ is *homogeneous* if it admits a collection of homogeneous generators, i.e. $\langle f_1, \ldots, f_m \rangle = I$ with each f_i homogeneous in the same degree. Homogeneous polynomials and homogeneous ideals are of interest because of their natural relationship with projective varieties and the study of projective geometry which provide us with unique tools not available in the affine point of view.

1.3.2 Resultants

Definition 1.3.5. Consider the following two polynomials in one variable of positive degree:

$$f = a_n x^m + a_{n-1} x^{n-1} + \cdots + a_0$$
$$g = b_m x^n + b_{m-1} x^{m-1} + \cdots + b_0.$$

The *Sylvester matrix* associated to f and g is the $n+m$ by $n+m$ matrix that has m columns of the coefficients of f and n columns of the coefficients of b in the following way

$$\mathrm{Syl}(f,g) = \underbrace{\left(\begin{array}{cccc} a_n & 0 & \cdots & 0 \\ \vdots & a_n & \cdots & 0 \\ a_0 & \vdots & \cdots & \vdots \\ 0 & a_0 & \cdots & 0 \\ \vdots & 0 & \cdots & a_n \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & a_0 \end{array}\right.}_{m}\underbrace{\left.\begin{array}{cccc} b_m & 0 & \cdots & 0 \\ \vdots & b_m & \cdots & 0 \\ b_0 & \vdots & \cdots & \vdots \\ 0 & b_0 & \cdots & 0 \\ \vdots & 0 & \cdots & b_m \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & b_0 \end{array}\right)}_{n}$$

Silvester matrices are of interest because they can tell us when two polynomials share a root, even if we do not know what the roots of the polynomial are.

Theorem 1.3.6. *Two nonconstant polynomials $f, g \in k[x]$ have a common factor if and only if* $\det(\mathrm{Syl(f,g)}) = 0$. *This determinant is called the resultant of f and g.*

Example 1.3.7. Consider the following three polynomials

$$\begin{aligned} f &= (x-4)(x+2)^2 = x^3 - 12x - 16 \\ g &= (x-4)(x+3)(x-1) = x^3 - 2x^2 - 11x + 12 \\ h &= (x+8)(x-6)(x-2) = x^3 - 52x + 96 \end{aligned}$$

The Sylvester matrices for f and g and f and h are

$$\mathrm{Syl(f,g)} = \begin{pmatrix} 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & -2 & 1 & 0 \\ -12 & 0 & 1 & -11 & -2 & 1 \\ -16 & -12 & 0 & 12 & -11 & -2 \\ 0 & -16 & -12 & 0 & 12 & -11 \\ 0 & 0 & -16 & 0 & 0 & 12 \end{pmatrix},$$

$$\mathrm{Syl(f,h)} = \begin{pmatrix} 1 & 0 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 0 & 1 & 0 \\ -12 & 0 & 1 & -52 & 0 & 1 \\ -16 & -12 & 0 & 96 & -52 & 0 \\ 0 & -16 & -12 & 0 & 96 & -52 \\ 0 & 0 & -16 & 0 & 0 & 96 \end{pmatrix}.$$

Note that $\det(\mathrm{Syl(f,g)}) = 0$, which we would expect by Theorem 1.3.6 since f and g share a root at $x = 4$. On the other hand, $\det(\mathrm{Syl(f,h)}) = -1769472$, i.e. nonzero as expected by Theorem 1.3.6 since f and h share no roots.

We will consider a Silvester matrix of two generic polynomials in the proof of one of the main results of Chapter 2, using the following Corollary.

Corollary 1.3.8. *The Sylvester matrix of two generic polynomials is invertible.*

1.4 LCR Circuit Systems

LCR circuits, also referred to as LCR systems or models, are electrical circuits consisting of networks of inductors, capacitors, and resistors, which we call *base elements*. These circuits have a wide array of applications, most notably in communications systems, such as filters and tuners used in television and radio tuning (Wang 2010). Also of interest are the circuits generated by two base element types, for example simple LR circuits can be made into high-pass (or low-pass) filters which pass high frequencies through the circuit with minimal dampening, while low frequencies are not able to pass as a result of strong dampening (Felix 2014).

Each of the base elements in an LCR system has a defining parameter which are referred to as the inductance (L), capacitance (C), and resistance (R) respectively. The system as a whole also has measurable state variables called the voltage (V) and the current (I). A natural question emerging from the study of LCR systems is whether or not we can determine the parameter values of each of the base elements given the measurements of the voltage and current over time over the whole system, and in particular if we can do so uniquely.

The ideal resistor follows Ohm's law which describes a relationship between the voltage (V) across the resistor, and the current (I). In the case of the resistor, the voltage and current are proportional with constant of proportionality R which is referred to as the *resistance*, which we write as:

$$V = RI. \tag{1.8}$$

Similarly, the ideal inductor exhibits the following relationship between the voltage and the derivative with respect to time of the current:

$$V = L\dot{I} \tag{1.9}$$

where L is called the *inductance*. The ideal capacitor is often considered the dual of the inductor, where the relationship between the time derivative of the voltage and current is described by

$$\dot{V} = CI \tag{1.10}$$

where C is the *inverse capacitance*. Note that we use $\dot{V} = CI$ instead of the more familiar $C\dot{V} = I$ for mathematical convenience. For this reason, C in this chapter is the inverse of the capacitance. This change will not affect results of identifiability.

We call these equations relating the voltage and current of LCR systems *constitutive equations*. We can relate these to general input-output equations described in Section 1.1 by thinking of the voltage as the input, and the measured current as the output. In this case, the individual resistances of resistors, inductance of inductors, and capacitance of

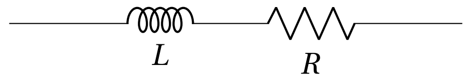

Figure 1.5: Series combination of a resistor and an inductor.

capacitors within the model are the unknown parameters we wish to identify. In general, we can use Kirchhoff's Current and Voltage Laws to generate a single constitutive equation of circuits consisting of parallel and series combinations of these three base elements.

Theorem 1.4.1 (Kirchhoff's Current Law)**.** *The algebraic sum of the currents entering any node is zero, i.e. the net current flowing into and out of any node must be zero.*

Theorem 1.4.2 (Kirchhoff's Voltage Law)**.** *The algebraic sum of the voltages around any loop is zero.*

Remark 1.4.3. When drawn, we generally assume that the left and right-hand sides of the circuit are connected. For example, in Figure 1.5 we assume that the right side of the resister element is connected to the left side of the inductor element. We visualize this with dashed lines in Figures 1.7 and 1.8, but omit this dashed line for the other figures of LCR circuits in this thesis.

Example 1.4.4. Consider the series combination of a resistor and an inductor shown in Figure 1.5. By Kirchhoff's Voltage Law, we get that the voltage over the whole system V must be the sum of the voltages over each element in the system, i.e.

$$V = V_L + V_R = L\dot{I}_L + RI_R.$$

Also, by Kirchhoff's Current Law, we know that the net current of the system must be equal to the current of each element, i.e. $I_L = I_R = I$. Therefore, we get that the constitutive equation describing this circuit is

$$V = L\dot{I} + RI.$$

Example 1.4.5. Now consider a parallel combination of a resistor and an inductor shown in Figure 1.6. By Kirchhoff's voltage law, the sum of the voltage around the parallel loop must be zero, hence $V_L = V_R = V$. Also, by Kirchhoff's current law, the current of the system is the sum of each of the currents, i.e. $I = I_R + I_L$.

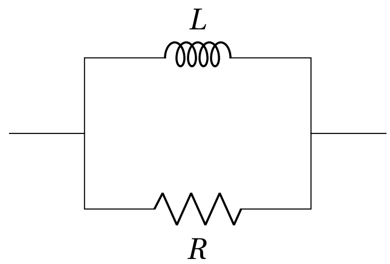

Figure 1.6: Parallel combination of a resistor and an inductor.

Taking the time based derivative of this current sum, along with the time based derivative of the resistor constitutive equation, we get

$$\dot{I} = \dot{I}_R + \dot{I}_L = \frac{1}{R}\dot{V}_R + \frac{1}{L}V_L.$$

Thus, the constitutive equation the system is

$$\dot{I} = \frac{1}{R}\dot{V} + \frac{1}{L}V.$$

A natural question to ask is how we can generate these constitutive equations for more complex systems. Suppose S_1 and S_2 represent two circuits with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ where f_i are all linear differential operators with constant coefficients. We can write these differential operators as

$$\begin{aligned} f_1 &= a_{n_1}\frac{d^{n_1}}{dt^{n_1}} + \cdots + a_{m_1}\frac{d^{m_1}}{dt^{m_1}} \\ f_2 &= b_{n_2}\frac{d^{n_2}}{dt^{n_2}} + \cdots + b_{m_2}\frac{d^{m_2}}{dt^{m_2}} \\ f_3 &= c_{n_3}\frac{d^{n_3}}{dt^{n_3}} + \cdots + c_{m_3}\frac{d^{m_3}}{dt^{m_3}} \\ f_4 &= d_{n_4}\frac{d^{n_4}}{dt^{n_4}} + \cdots + d_{m_4}\frac{d^{m_4}}{dt^{m_4}} \end{aligned} \tag{1.11}$$

Now we will consider parallel and series combination of the systems S_1 and S_2, and derive the resulting constitutive equation from those of S_1 and S_2.

Proposition 1.4.6 (Series Combination)**.** *The series combination of two LCR systems S_1 and*

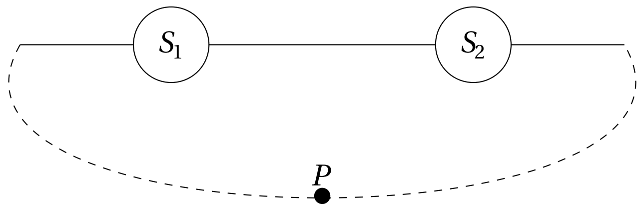

Figure 1.7: Series combination of system S_1 and S_2 with node P between the systems.

S_2 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ has constitutive equation

$$f_1 f_3 V = (f_1 f_4 + f_2 f_3) I.$$

Proof. Let T be the series combination of two LCR systems S_1 and S_2 seen in Figure 1.7 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$.

Note that by Kirchhoff's Current Law, the node P between the two systems must have a net zero incoming current. Therefore, the current of either system must be the same and this current will also be the current of the new system T, i.e. $I_1 = I_2 = I$. Similarly, by Kirchhoff's Voltage Law, the voltage on the loop, which in this case is the whole system, must sum to the voltage of the system, i.e. $V = V_1 + V_2$. If f_1 and f_3 are relatively prime, then we get

$$\begin{aligned} V &= V_1 + V_2 \\ V &= \frac{f_2}{f_1} I_1 + \frac{f_4}{f_3} I_2 \\ (f_1 f_3) V &= (f_1 f_4 + f_2 f_3) I \end{aligned} \tag{1.12}$$

Thus, the series combination of the two systems S_1 and S_2 has constitutive equation of the form in Equation 1.12. □

Proposition 1.4.7 (Parallel Combination)**.** *The parallel combination of two LCR systems S_1 and S_2 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ has constitutive equation*

$$(f_1 f_4 + f_2 f_3) V = f_2 f_4 I$$

Proof. Let T be the parallel combination of two LCR systems S_1 and S_2 seen in Figure 1.8 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$.

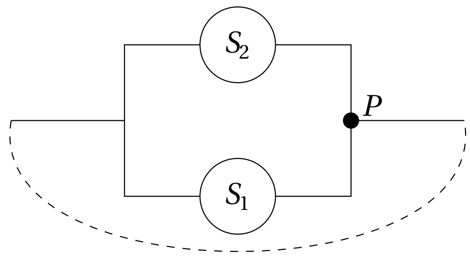

Figure 1.8: Parallel combination of systems S_1 and S_2 with node P between the systems.

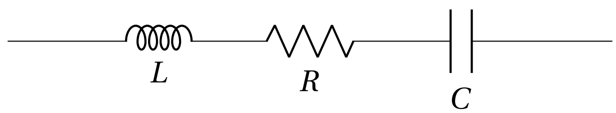

Figure 1.9: Series combination of an inductor, resistor, and capacitor.

Again, by Kirchhoff's Voltage Law, we get that the total voltage around the parallel combination loop must be net zero, i.e. $V_1 - V_2 = 0$. Also the voltage around the entire system must be net zero, thus $V = V_1 = V_2$. Kirchhoff's Current Law states that the node P must have a net zero incoming current, i.e. $I - I_1 - I_2 = 0$, hence $I = I_1 + I_2$. Thus, we get that the parallel combination of two systems S_1 and S_2 has constitutive equation

$$(f_1 f_4 + f_2 f_3)V = (f_2 f_4)I. \tag{1.13}$$

□

Example 1.4.8. Consider the series combination of each of the three base elements of an LCR system as seen in Figure 1.9. Let the resistor have resistance R, the capacitor have inverse capacitance C, and the inductor have inductance L.

The constitutive equation for this model is

$$\dot{V} = L\ddot{I} + R\dot{I} + CI. \tag{1.14}$$

Note that the coefficient map of this constitutive equation is

$$\mathbf{c}\colon (L, R, C) \mapsto (L, R, C).$$

This map is injective, hence the model consisting of a series combination of an inductor, resistor, and capacitor is globally identifiable.

Remark 1.4.9. The special structure of series-parallel networks means that it is possible to use notation purely in equations to represent a series-parallel LCR circuit, rather than necessarily using a figure. Specifically, we can use the notation $M \vee N$ to denote the parallel combination of networks M and N, and $M \wedge N$ to denote the series combination. The base elements can be written using the symbols for their respective parameters. For example, the network in Example 1.4.8 can be represented as

$$L \wedge R \wedge C.$$

Note that the $\wedge$ and $\vee$ operations are commutative and associative in terms of their relations for producing new networks, but they do not satisfy a distributive law.

1.5 Linear Compartmental Models

Compartmental models are commonly used in fields such as pharmocokinetics, ecology, and epidemiology to understand interacting groups, or compartments (Godfrey 1983). In pharmocokinetics, the compartments may represent tissue or tissue groups (DiPiro 2010; Hedaya 2012; Tozer 1981; Wagner 1981); in ecology, the compartments may represent habitat zones or role in a population (e.g., forager bee and nurse bee) (Gydesen 1984; Khoury et al. 2011; Knisley et al. 2011; Mulholland and Keener 1974); while in epidemiology, the compartments may represent groups of infected, susceptible, and recovered individuals (Blackwood and Childs 2018; Tang et al. 2020). Interactions, exchanges, or flows between compartments are represented by edges between compartments, resulting in a directed graph, with distinguished nodes representing inputs, outputs, and leaks from the system. *Linear compartmental models*, which are the topic of this section as well as Chapters 3 and 4, are commonly used compartmental models described by a parameterized system of *linear* ordinary differential equations.

A *linear compartmental model* $\mathcal{M} = (G, In, Out, Leak)$ consists of a directed graph $G = (V_G, E_G)$ without multi-edges and sets $In, Out, Leak \subseteq V_G$, which are called the *input*, *output*, and *leak* compartments, respectively. An edge $j \to i \in E_G$ is labeled by the parameter a_{ij}. We always assume that Out is nonempty, because models with no outputs are not identifiable. Finally, a model $\mathcal{M} = (G, In, Out, Leak)$ is *strongly connected* if G is strongly connected.

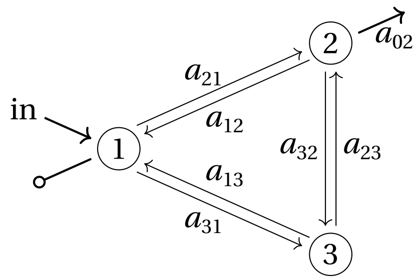

Figure 1.10: A linear compartmental model.

A linear compartmental model is depicted by its graph G, plus leaks indicated by outgoing edges, input compartments labeled by "in," and output compartments marked by this symbol: $\circ\!\!\!\!\diagup$.

For a linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ with n compartments (so, $n = |V_G|$), the *compartmental matrix* A is the $n \times n$ matrix defined by:

$$A_{i,j} = \begin{cases} -a_{0i} - \sum_{k:\, i \to k \in E_G} a_{ki} & i = j,\ i \in Leak, \\ -\sum_{k:\, i \to k \in E_G} a_{ki} & i = j,\ i \notin Leak, \\ a_{ij} & i \neq j,\ (j,i) \in E_G, \\ 0 & i \neq j,\ (j,i) \notin E_G. \end{cases} \tag{1.15}$$

Note that this definition is similar to that of the Laplacian matrix of a weighted directed graph described in Section 1.2, with the addition of the leak parameters a_{0i} in the diagonal entries corresponding to nodes in the $Leak$ set from the model.

Next, the model $\mathcal{M}$ defines the following ODE system (1.16), where $u_i(t)$ and $y_i(t)$ denote the concentrations of input and output compartments, respectively, at time t, and $x(t) = (x_1(t), x_2(t), \ldots, x_n(t))$ is the vector of concentrations of all compartments:

$$\begin{aligned} \frac{dx}{dt} &= Ax(t) + u(t), \\ y_i(t) &= x_i(t) \qquad \text{for all } i \in Out\,, \end{aligned} \tag{1.16}$$

where $u_i(t) \equiv 0$ for $i \notin In$.

Example 1.5.1. Consider the 3-compartment model $\mathcal{M} = (G, In, Out, Leak)$ shown in

Figure 1.10, $In = Out = \{1\}$, and $Leak = \{2\}$. The defining ODEs of this model are

$$\begin{aligned}
\dot{x}_1 &= (-a_{21} - a_{31})x_1 + a_{12}x_2 + a_{13}x_3 + u_1 \\
\dot{x}_2 &= a_{21}x_1 + (-a_{02} - a_{12} - a_{32})x_2 + a_{23}x_3 \\
\dot{x}_3 &= a_{31}x_1 + a_{32}x_2 + (-a_{13} - a_{23})x_3 \\
y_1 &= x_1.
\end{aligned}$$

As in Equation 1.16, we can characterize this system of ODEs utilizing the compartmental matrix

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{pmatrix} = \begin{pmatrix} -a_{21} - a_{31} & a_{12} & a_{13} \\ a_{21} & -a_{02} - a_{12} - a_{32} & a_{23} \\ a_{31} & a_{32} & -a_{13} - a_{23} \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} + \begin{pmatrix} u_1 \\ 0 \\ 0 \end{pmatrix}.$$

This matrix characterization of the defining ODEs will be instrumental in constructing the input-output equation for linear compartmental models in both Chapters 3 and 4.

1.6 Summary of Results

The contents of Chapter 2 of this thesis was published in the Journal of Symbolic Computation (Bortner and Sullivant 2022). In Chapter 2, we consider series-parallel LCR circuit systems, their constitutive equations, and the identifiability of these systems from their constitutive equations. In the cases where there is a series-parallel LCR network that only involves two types of components (i.e., inductor-resistor systems, capacitor-resistor systems, or inductor-capacitor systems) we give a complete characterization of when these models are identifiable. In particular, we have the following theorem.

Theorem (Corollaries 2.3.2 and 2.3.3 and Theorem 2.4.12)**.** *Let $\mathcal{N}$ be a series-parallel LCR network that involves only two types of components. Then the network is locally identifiable if and only if the constitutive equation of the model has as many non-monic coefficients as there are parameters.*

We also give explicit combinatorial conditions on the series-parallel constructions that guarantee local identifiability in two component type LCR models, which are summarized in certain “multiplication tables”.

We close Chapter 2 by beginning the study of general series-parallel LCR circuits. These turn out to be much more complicated because there are LCR systems where the number of non-monic coefficients is larger than the number of parameters. As a result, in addition to the identifiability problem, there are also interesting questions about the constraints on the coefficients that arise. Our analysis of the structure of the constitutive equations shows that for general series-parallel LCR systems, there are 22 different types of constitutive equations.

The contents of Chapter 3 has been accepted for publication in the Bulletin of Mathematical Biology (Bortner and Meshkat 2022). In Chapter 3, we discuss a class of linear compartmental models which are known to be unidentifiable, namely path-cycle models. Though it is not possible to recover each individual parameter from these models, it is possible to recover combinations of parameters, information potentially useful in reparametrizing an unidentifiable model. Specifically, we consider identifiable path-cycle models with every independent path and cycle identifiable. Our first main result describes sufficient conditions for a model to be an identifiable path/cycle model based solely on the corresponding graph structure.

Theorem (Theorem 3.2.27)**.** *For a linear compartmental model $\mathscr{M} = (G, In, Out, Leak)$ with a single input, single output, which is strongly input-output connected with $|E| = 2|V| - (\mathrm{dist(i,j)} + 2)$, then if $\mathscr{M}$ becomes strongly connected with the addition of an edge from the output to the input, $\mathscr{M}$ is an identifiable path cycle model.*

We also derive several results relating identifiable path/cycle models with identifiable linear compartmental models, specifically by constructing the identifiable models by removing leaks from the identifiable path/cycle models.

In Chapter 4, we discuss linear compartmental models, and specifically linear compartmental tree models. The main tool we use in understanding the input-output equation of linear compartmental models comes in the form of a novel combinatorial generation of the input-output equation of a general linear compartmental model dependent only on the graph of the model.

Using this characterization of the input-output equation coefficients of linear compartmental models, we are able to state necessary and sufficient conditions for linear compartmental models to be identifiable. On top of this, we completely classify the identifiability of a large class of linear compartmental models called tree models.

Theorem (Theorem 4.4.2)**.** *A tree model with one input and one output is generically locally identifiable if and only if the distance between the input and output is at most one and the model has either no leaks or a single leak.*

CHAPTER

2

STRUCTURAL IDENTIFIABILITY OF SERIES-PARALLEL LCR SYSTEMS

In this chapter, we study the structural identifiability of LCR circuits where the underlying network of components is a series-parallel graph.

The organization of this chapter is as follows: Section 2.1 gives a quick background on the motivation behind this study. Section 2.2 discusses the perspective of projective geometry for studying circuit models, and uses this to prove a duality result. Section 2.3 describes results of the two-element systems containing only resistors and inductors, as well as the two-element systems containing only resistors and capacitors. Finally, Section 2.4 presents results for the two-element systems containing only inductors and capacitors. Section 2.5 describes results of the general LCR systems. Section 2.6 introduces the problem of studying the equations that define the vanishing ideal of an LCR circuit model.

2.1 Preliminaries

Part of our motivation for pursuing this project comes from past work of Mahdi et al. (2014), which characterized the identifiability of series-parallel viscoelastic systems whose elements consists of springs and dashpots. The *electromechanical analogy*, sometimes called the impedance analogy, allows us to extend identifiability results of spring-dashpot systems to RL systems, and due to certain duality results, RC systems. We then considered the final two base element type subsystems of LCR systems, namely the LC systems where we lose the ability to apply the electromechanical analogy directly to the spring-dashpot systems, and must derive a similar identifiability condition from scratch.

2.2 Projective Geometry and Circuit Duality

In this section, we introduce a perspective based on projective geometry. This provides us a useful framework for discussing identifiability that avoids the use of non-monic coefficients. It also allows for a straightforward duality results about the interchange of capacitors and inductors.

In this chapter, we consider linear differential equations. To this end, the set of all differential equations with a given shape is naturally considered as a projective space. Indeed, if $L_1 V = L_2 I$ is a differential equation coming from a particular LCR circuit, and λ is any nonzero constant, then $\lambda L_1 V = \lambda L_2 V$ describes the same dynamics. In particular, it is only possible to recover the underlying constitutive equation up to a constant. The typical way that this is dealt with is to talk about non-monic coefficients in the constitutive equation– essentially, picking one term to be the leading term and dividing through so the coefficient of that term is equal to one. This is a satisfactory approach in most situations. We find the perspective from projective geometry can also be useful.

To start with, we consider the constitutive equations of the three basic elements:

$$V = RI, \qquad V = L\dot{I}, \qquad \dot{V} = CI.$$

Thinking about these projectively, we would have the basic constitutive equations:

$$R_0 V = R_1 I, \qquad L_0 V = L_1 \dot{I}, \qquad C_0 \dot{V} = C_1 I. \tag{2.1}$$

So in projective geometry language, our parameter space for an LCR model, goes from an

$\mathbb{R}^k$ (in the case that there are k basic elements), to a $(\mathbb{PR}^1)^k$.

Example 2.2.1. Consider the LCR circuit system from Example 1.4.8, which has three components. Using the projective version of the parameters from (2.1) we get the constitutive equation

$$R_0 L_0 C_0 \dot{V} = R_0 L_1 C_0 \ddot{I} + R_1 L_0 C_0 \dot{I} + R_0 L_0 C_1 I.$$

This shows that the coefficient map is a map from $(\mathbb{P}^1)^3$ into $\mathbb{P}^3$, defined by

$$([R_0 : R_1], [L_0 : L_1], [C_0 : C_1]) \mapsto (R_0 L_0 C_0 : R_0 L_1 C_0 : R_1 L_0 C_0 : R_0 L_0 C_1).$$

We arrive at the usual constitutive equation by dehomogenizing this one: specifically by the substitution

$$R_0 = 1,\ R_1 = R,\ L_0 = 1,\ L_1 = L,\ C_0 = 1,\ C_1 = C.$$

One useful application of the projective perspective is that it makes it possible to derive a duality result for identifiability of LCR systems. The idea of duality of these systems and those like it date back to the work of Alexander Russell in 1904 with inspiration from reciprocals found in geometry, and the goal of finding "convenient methods of making measurements or even suggest novel instruments or machines of value in electro-technics" (Russell 1904).

Definition 2.2.2. Let M be a series-parallel LCR circuit model, expressed as a formula in terms of resistors $R_1, R_2, \ldots$, capacitors $C_1, C_2, \ldots$, and inductors $L_1, L_2, \ldots$, using the series and parallel operations $\wedge$ and $\vee$. Define the *dual system* $\overline{M}$, to be expressed as a formula in terms of $\overline{R}_1, \overline{R}_2, \ldots, \overline{C}_1, \overline{C}_2, \ldots$, and $\overline{L}_1, \overline{L}_2, \ldots$ by the following rules:

1. Swap each $\wedge$ with a $\vee$ and vice versa
2. Each R_i is replaced with a $\overline{R}_i$
3. Each C_i is replaced with a $\overline{L}_i$, and
4. Each L_i is replaced with a $\overline{C}_i$.

Example 2.2.3. Consider the series-parallel network model $M = (R_1 \wedge C_1) \vee (R_2 \wedge L_1)$. The dual network is $\overline{M} = (\overline{R}_1 \vee \overline{L}_1) \wedge (\overline{R}_2 \vee \overline{C}_1)$. The example is illustrated in Figure 2.1.

There is no formal difference between components of the original system M and the dual system $\overline{M}$, e.g. a resistor R_1 and $\overline{R}_1$ are the same from a modeling standpoint. However,

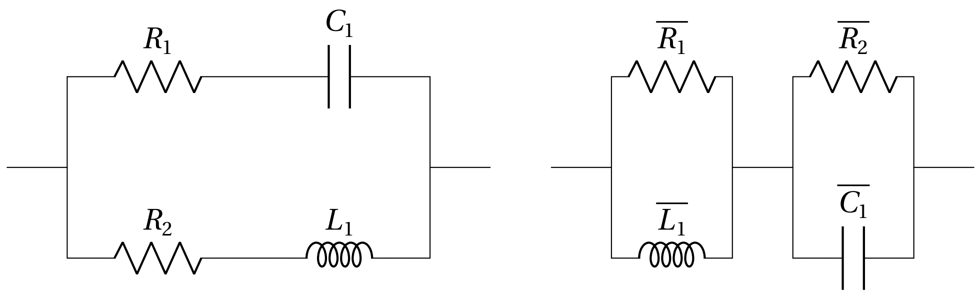

Figure 2.1: A series-parallel LCR network and its dual network.

when we want to talk about the identifiability of these systems, it is useful to distinguish between the components of the original system and that of the dual system.

Theorem 2.2.4. *Suppose that M is a series-parallel LCR system and let $\overline{M}$ be the dual LCR system. Then M is (generically, locally) identifiable if and only if $\overline{M}$ is.*

To prove this, we make direct use of the projective representation of the network. To each basic component, denoted R_i, L_i, C_i, we associated a projective constitutive equation

$$R_{0,i} V = R_i I, \quad L_{0,i} V = L_i \dot{I}, \quad C_{0,i} \dot{V} = C_i I.$$

Then on the projective representation, the duality has the effect of swapping V and I and L and C. So the dual basic constitutive equation in the projective representation becomes

$$R_i V = R_{0,i} I, \quad C_i V = C_{0,i} \dot{I}, \quad L_i \dot{V} = L_{0,i} I.$$

Note that affinely this corresponds to $\overline{R}_i = 1/R_i$, $\overline{L}_i = 1/C_i$ and $\overline{C}_i = 1/L_i$.

Proposition 2.2.5. *Suppose that M is a series-parallel LCR system with corresponding projective parameters $\mathbf{R} = (R_1, \ldots, R_r, R_{0,1}, \ldots, R_{0,r})$, $\mathbf{L} = (L_1, \ldots, L_s, L_{0,1}, \ldots, L_{0,s})$, and $\mathbf{C} = (C_1, \ldots, C_t, C_{0,1}, \ldots, C_{0,t})$. Let $\overline{M}$ be the dual LCR system with corresponding dual projective parameters $\overline{\mathbf{R}} = (R_{0,1}, \ldots, R_{0,r}, R_1, \ldots, R_r)$, $\overline{\mathbf{L}} = (L_{0,1}, \ldots, L_{0,s}, L_1, \ldots, L_s)$, and $\overline{\mathbf{C}} = (C_{0,1}, \ldots, C_{0,t}, C_1, \ldots, C_t)$. Let*

$$f_1(\mathbf{R}, \mathbf{C}, \mathbf{L}, \tfrac{d}{dt})V = f_2(\mathbf{R}, \mathbf{C}, \mathbf{L}, \tfrac{d}{dt})I$$

be the constitutive equation of M. Then

$$f_2(\overline{\mathbf{R}}, \overline{\mathbf{L}}, \overline{\mathbf{C}}, \tfrac{d}{dt})V = f_1(\overline{\mathbf{R}}, \overline{\mathbf{L}}, \overline{\mathbf{C}}, \tfrac{d}{dt})I$$

is the constitutive equation of $\overline{M}$.

Proof. The proof is by induction on the number of components. The statement is clearly true if there is only one component by the definition of the duality operations.

Suppose that M has more than one component. That means it can be broken up as either a series or parallel combination of two other components. We handle the case of a series combination, the case of a parallel combination being analogous. So suppose that $M = M_1 \wedge M_2$. The corresponding dual LCR system is $\overline{M} = \overline{M}_1 \vee \overline{M}_2$. Let

$$f_1(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})V_1 = f_2(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})I_1$$

$$f_3(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})V_2 = f_4(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})I_2$$

be the constitutive equations of M_1 and M_2 respectively. Thus the constitutive equation of M is

$$(f_1 f_3)(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})V = (f_1 f_4 + f_2 f_3)(\mathbf{R},\mathbf{C},\mathbf{L},\tfrac{d}{dt})I$$

By induction, the constitutive equations of $\overline{M}_1$ and $\overline{M_2}$ are

$$f_2(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})V_1 = f_1(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})I_1$$

$$f_4(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})V_2 = f_3(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})I_2$$

Since $\overline{M}$ is a parallel combination of $\overline{M}_1$ and $\overline{M}_2$ its constitutive equation is

$$(f_1 f_4 + f_2 f_3)(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})V = (f_1 f_3)(\overline{\mathbf{R}},\overline{\mathbf{L}},\overline{\mathbf{C}},\tfrac{d}{dt})I.$$

This is clearly the desired correct form. This proves the result for series combinations, and the proof for a parallel combination is similar. □

Proof of Theorem 2.2.4. By Proposition 2.2.5 the coefficient map for M and $\overline{M}$ is the same except for relabeling parameters and swapping the order of some of the coefficients. The coefficient maps clearly have the same behavior in both cases in terms of being one-to-one, generically one-to-one, finite-to-one, etc. □

2.3 RL/RC System Analysis

In this section, we consider the identifiability of series-parallel circuits consisting of only two types of base elements: either resistor-inductor (RL) networks or resistor-capacitor (RC) networks. The electromechanical analogy establishes a bijection between identifiability problems for RL-networks and identifiability problems for viscoelastic mechanical systems consisting of springs and dashpots. The results of (Mahdi et al. 2014) will be used to deduce the main identifiability result for RL series-parallel networks. Then we use Theorem 2.2.4 to deduce the analogous identifiability result for RC series-parallel networks.

First, consider the case of the two-element system generated by parallel and series combinations of inductors and resistors. The electromechanical analogy, specifically the Maxwell or impedance analogy, yields that a system comprised of series and parallel combinations of resistors and inductors is analogous to a mechanical system consisting of series and parallel combinations of springs and dashpots (Stephens and Bate 1966). The spring-dashpot system is commonly referred to as the *viscoelastic model*, and has many applications, including modeling various biological systems. The problem of identifiability of the spring-dashpot system is well studied, with the problem of determining local identifiability reduced down to counting the number of elements in the system, i.e. parameters, and comparing that to the number of coefficients (Mahdi et al. 2014).

Recall that in determining identifiability, an immediate indication that a model is unidentifiable by the constitutive equation is to see that there are fewer coefficients than parameters, meaning a necessary condition for identifiability is that there are at least as many coefficients as parameters. In the case of the viscoelastic system, it was shown by Mahdi et al. (2014) that the number of coefficients is bounded above by the number of parameters, thus the previous necessary condition for identifiability becomes that there must be exactly the same number of parameters as coefficients. It is then shown that this equality of the number of coefficients and parameters is in fact a sufficient condition for local identifiability via the following theorem.

Theorem 2.3.1 (Theorem 2, Mahdi et al. (2014))**.** *A viscoelastic model represented by a spring-dashpot network is locally identifiable if and only if the number of non-monic, non-trivial coefficients of the corresponding constitutive equation equals the total number of its parameters.*

Due to the electromechanical analogy, we can deduce the following equivalent statement in terms of RL systems:

Corollary 2.3.2. *An RL system is locally identifiable if and only if the number of non-monic, nontrivial coefficients of the corresponding constitutive equation equals the total number of its parameters.*

Via the duality of Theorem 2.2.4, we also get the following corollary.

Corollary 2.3.3. *An RC system is locally identifiable if and only if the number of non-monic, nontrivial coefficients of the corresponding constitutive equation equals the total number of its parameters.*

Proof. The duality operation turns an RL system into an RC system and vice versa. Theorem 2.2.4, shows that the RL system is identifiable if and only if the dual RC system is identifiable. Since the duality preserves the number of coefficients, this follows from Corollary 2.3.2. □

In general, the problem of identifiability of a model is much more difficult to answer than it is for the RC and RL systems. We will see in Section 2.5 that in the case of LCR systems, we no longer have a bound on the coefficients by the number of parameters, making finding identifiability criterion considerably more difficult.

In addition to these results on identifiability and relation to the number of coefficients in the RC/RL models, it is also possible to import from Mahdi et al. (2014) precise rules for identifiability of series and parallel combinations of identifiable models. These are encapsulated in the identifiability multiplications for the types of combinations of constitutive equations of different shapes. We do not reproduce the identifiability multiplication tables from Mahdi et al. (2014) here, but we will see analogous results for LC systems in the next section.

2.4 LC System Analysis

Now we consider the two-element systems which contain parallel and series combinations of inductors and capacitors, i.e. LC systems. To analyze the identifiability of these LC systems we first will classify these systems into four *types* dependent upon the structure of their constitutive equations. Since the LC systems are specific cases of LCR systems, we can state several general propositions about the structure of their constitutive equations, which we prove in the next section. First, we recognize an upper bound on the number of coefficients on either side of the constitutive equation of an LCR, and thus an LC system.

Proposition 2.5.1. *The maximum order of either side of the constitutive equation of an LCR system is bounded above by the number of parameters, i.e. base elements, in the model.*

Note that the previous proposition yields that the maximum number of non-monic, nonzero coefficients in the constitutive equation of an LCR system is $2n+1$, where n is the number of parameters. We can also make a statement relating the lowest and highest orders of the left-hand and right-hand sides of the constitutive equation of an LCR system.

Proposition 2.5.2. *In an LCR system, the largest orders on either side of the constitutive equation must be within one of each other. Similarly, the smallest orders on either side of the constitutive equation must be within one of each other.*

In the case of LC systems, we can actually make a slightly stronger statement.

Corollary 2.4.1. *In an LC system, the absolute difference of the largest order of either side of the constitutive equation is **exactly** one. Similarly, the absolute difference of the smallest order of either side of the constitutive equation of an LC system is **exactly** one.*

Proof. This is true by the exact same argument in the proof of Proposition 2.5.2, where the base cases are only the single inductor and single capacitor systems, and replacing any "less than or equal to" statements with "equal to" statements. □

Now we make a statement about how many of the coefficients on either side of a constitutive equation of an LC system must be zero. We also introduce the idea of a constitutive equation *alternating*, that is, every coefficient of even or odd order in the equation having a value of zero.

Definition 2.4.2. We say that a polynomial *alternates* if all odd degree or all even degree coefficients are zero. We say a polynomial is *saturated* if every coefficient between the smallest and largest degree is nonzero.

Remark 2.4.3. Note the difference between describing a polynomial as "not alternating" and "saturated." In the case of a polynomial not alternating, we could possibly still have coefficients of zero between the largest and smallest degree, we just do not have that every other coefficient is zero.

Note that the product of two polynomials, both of which have this alternation property, also must alternate. With this in mind, if both sides of two LC systems' constitutive equations alternate, we must have that one side of their series or parallel combination also alternates, namely the side with a single product of two previous differential operators by Propositions 1.4.6 and 1.4.7. With that being said, it is not immediately clear that the side which consists of a sum of two products of the previous differential operators also alternates. This is because although each of the products in the sum must alternate, it is possible that the powers in either alternating product have different parity, so when summed together the result does not alternate. In the case of LC systems, we show that this parity mismatch cannot occur.

Proposition 2.4.4. *An LC system must have both sides of its constitutive equation alternate.*

Proof. We proceed by induction. Note that by our definition of alternating, the base elements inductor and capacitor are inherently alternating, since one side of either constitutive equation has a single odd power, and the other has a single even power in either case.

Suppose two LC systems N_1 and N_2 have the alternating property on either side of their constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ respectively. From Corollary 2.4.1, we know that f_1 and f_2 have difference of highest order of one, hence have different parity, and similarly f_3 and f_4 have different parity. Note that because of the remark before the statement of this proposition, to show that both sides of the constitutive equation of a combination of two LC systems alternate, we need only show that $f_1 f_4$ and $f_2 f_3$ do not have different parity. However, we know that f_1 and f_2 have different parity and f_3 and f_4 have different parity. Then $f_1 f_2 f_3 f_4$ has to have even parity, so $f_1 f_4$ and $f_2 f_3$ must have the same parity. Thus, by induction, both sides of the constitutive equation corresponding to an LC system, must alternate. □

Now we can place an upper bound on the number of nonzero coefficients in an LC system, similar to the bound in the RC and RL systems.

Theorem 2.4.5. *The number of non-monic, nontrivial coefficients of an LC system constitutive equation is bounded above by the number of base elements.*

Proof. First, note that by Proposition 2.5.1, the maximum order of either side of the constitutive equation of an LC system with n base elements is n. Also, by Corollary 2.4.1, the maximum order of the other side of constitutive equation of an LC system is $n-1$. By Proposition 2.4.4, we know that every other coefficient on either side of the constitutive equation of an LC system must be zero, i.e. if the maximum order on one side is n, then at most $\lceil \frac{n+1}{2} \rceil$ coefficients must be nonzero. Thus, if both sides of a constitutive equation have their maximal orders n and $n-1$, then the total number of nonzero coefficients is bounded above by

$$\left\lceil \frac{n+1}{2} \right\rceil + \left\lceil \frac{n}{2} \right\rceil = n+1.$$

Thus, after normalizing, there are at most n non-monic, nontrivial coefficients in the constitutive equation of an LC system. □

Remark 2.4.6. Note that to recover all n parameters from an LC system with n base elements, we need the constitutive equation defining the system to have at least n nontrivial coefficients. This, coupled with Theorem 2.4.5 implies that, as in the case of RL and RC systems, a necessary condition for identifiability of an LC system with n parameters is that the constitutive equation has n non-monic, nontrivial coefficients. We spend the rest of this section showing that, in fact, this is also a sufficient condition.

Now we can classify identifiable LC systems into four different “types” depending on the difference in the largest orders and smallest orders of the left and right-hand sides of their constitutive equations. We will define the type of the LC system with constitutive equation $f_1 V = f_2 I$ where

$$f_1 = a_{n_1} d^{n_1}/dt^{n_1} + \cdots + a_{m_1} d^{m_1}/dt^{m_1}$$
$$f_2 = b_{n_2} d^{n_2}/dt^{n_2} + \cdots + b_{m_2} d^{m_2}/dt^{m_2}$$

by the ordered pair $(m_1 - m_2,\ n_1 - n_2)$. Note that by Corollary 2.4.1, we know that there are only four possible such pairs, which we define as the following types:

$$A := (-1,-1), \quad B := (-1,1), \quad C := (1,-1), \quad D := (1,1).$$

We now consider how to build identifiable LC systems from identifiable LC systems. We do this by considering the *shape* of each of the differential operators of an identifiable LC system which we define as the ordered pair $[a, b]$ representing the smallest and largest order respectively of the differential operator. Note that depending on the parity of the number of parameters n of an LC system, certain types cannot be identifiable. For example, consider an LC system of type A, then for the constitutive equation to have enough coefficients to potentially be identifiable, the shape in V must be $[0, n-1]$ and the shape in I must be $[1, n]$, so we know that n must be odd by Proposition 2.4.4. Similarly, LC systems of type D must have an odd number of parameters to potentially be identifiable, while LC systems of types B and C must have an even number of parameters to potentially be identifiable.

Tables 2.1 and 2.2 give the identifiability results of the series and parallel combinations of all of the identifiable LC system types, with a count of the number of non-monic, nontrivial coefficients, as well as the resulting type. Note that in the column labeled “Identifiable?", if there is a “no" we already can see that this model is unidentifiable, as there are not enough coefficients as compared to the number of parameters. On the other hand, we still need to

Table 2.1: All identifiable **series** combinations of the four types of LC systems, with resulting shapes, number of coefficients, identifiability, and type.

Type	Shape in V	Shape in I	Non-monic coeff.	Identifiable?	Type
(A,A)	$[0,n_1+n_2-2]$	$[1,n_1+n_2-1]$	n_1+n_2-1	No	A
(A,B)	$[0,n_1+n_2-1]$	$[1,n_1+n_2]$	n_1+n_2	Yes	A
(A,C)	$[1,n_1+n_2-2]$	$[0,n_1+n_2-1]$	n_1+n_2-1	No	C
(A,D)	$[1,n_1+n_2-1]$	$[0,n_1+n_2]$	n_1+n_2	Yes	C
(B,B)	$[0,n_1+n_2]$	$[1,n_1+n_2-1]$	n_1+n_2	Yes	B
(B,C)	$[1,n_1+n_2-1]$	$[0,n_1+n_2]$	n_1+n_2	Yes	C
(B,D)	$[1,n_1+n_2]$	$[0,n_1+n_2-1]$	n_1+n_2	Yes	D
(C,C)	$[2,n_1+n_2-2]$	$[1,n_1+n_2-1]$	n_1+n_2-2	No	C
(C,D)	$[2,n_1+n_2-1]$	$[1,n_1+n_2]$	n_1+n_2-1	No	C
(D,D)	$[2,n_1+n_2]$	$[1,n_1+n_2-1]$	n_1+n_2-1	No	D

prove that the "yes" entries are actually identifiable. Proving that this is the case will occupy the rest of the section and complete the proof of Theorem 2.4.12, which is the main result of this section.

Remark 2.4.7. Checking for identifiability of a parallel or series combination of LC systems can be done in polynomial time via Tables 2.1 and 2.2. Similarly, checking for identifiability of a series or parallel combination of RL, and thus RC, systems can be done in polynomial time via tables found in Mahdi et al. (2014).

2.4.1 The Alternating Shape Factorization Problem

We now define the alternating shape factorization problem, which is analogous to the shape factorization problem as defined in Mahdi et al. (2014), though this time for alternating polynomials.

Definition 2.4.8. The *alternating shape factorization problem* for a quadruple of shapes

$$Q=([m_1,n_1],[m_2,n_2],[m_3,n_3],[m_4,n_4])$$

is defined as follows: for a generic pair of alternating polynomials (f,g) with f monic such that $\text{shape}(f)=[m_1+m_3,n_1+n_3]$ and $\text{shape}(g)=[\min(m_1+m_4,m_2+m_3),\max(n_1+n_4,n_2+n_3)]$, do there exist finitely many quadruples of alternating polynomials (f_1,f_2,f_3,f_4) with shape $f_i=[m_i,n_i]$ and f_1,f_3 monic, such that $f=f_1f_3$ and $g=f_1f_4+f_2f_3$? A quadruple of

Table 2.2: All identifiable **parallel** combinations of the four types of LC systems, with resulting shapes, number of coefficients, identifiability, and type.

Type	Shape in V	Shape in I	Non-monic coeff.	Identifiable?	Type
(A,A)	$[0,n_1+n_2-1]$	$[2,n_1+n_2]$	n_1+n_2-1	No	A
(A,B)	$[1,n_1+n_2]$	$[2,n_1+n_2-1]$	n_1+n_2-1	No	B
(A,C)	$[0,n_1+n_2-1]$	$[1,n_1+n_2]$	n_1+n_2	Yes	A
(A,D)	$[0,n_1+n_2]$	$[1,n_1+n_2-1]$	n_1+n_2	Yes	B
(B,B)	$[1,n_1+n_2-1]$	$[2,n_1+n_2-2]$	n_1+n_2-2	No	B
(B,C)	$[0,n_1+n_2]$	$[1,n_1+n_2-1]$	n_1+n_2	Yes	B
(B,D)	$[0,n_1+n_2-1]$	$[1,n_1+n_2-2]$	n_1+n_2-1	No	B
(C,C)	$[1,n_1+n_2-1]$	$[0,n_1+n_2]$	n_1+n_2	Yes	C
(C,D)	$[1,n_1+n_2]$	$[0,n_1+n_2-1]$	n_1+n_2	Yes	D
(D,D)	$[1,n_1+n_2-1]$	$[0,n_1+n_2-2]$	n_1+n_2-2	No	D

shapes Q is said to be *alternating good* if the alternating shape factorization problem for that quadruple has a positive solution.

Proposition 2.4.9. *Let M be the series combination of two LC systems N_1 and N_2 with respective constitutive equation $f_1V_1 = f_2I_1$ and $f_3V_2 = f_4I_2$ and let f_i have shape $[m_i, n_i]$. Then the LC system M is locally identifiable if and only if*

(i) N_1 and N_2 are locally identifiable, and

(ii) $([m_1,n_1],[m_2,n_2],[m_3,n_3],[m_4,n_4])$ is an alternating good quadruple.

We now work toward necessary and sufficient conditions for the series combination of two LCR models to yield a good alternating quadruple, inspired by the work done following Proposition 10 in Mahdi et al. (2014) for the viscoelastic case.

Let h and g be two alternating polynomials, and note that for fixed shapes $[m_1,n_1]$ and $[m_3,n_3]$, there are at most finitely many factorization $h = f_1f_3$, with alternating f_1 and f_3 having shapes $[m_1,n_1]$ and $[m_3,n_3]$ respectively. Thus, in fixing one of these finitely many choices of f_1 and f_3, the equation $g = f_1f_4 + f_3f_2$ is a linear system in the unknown coefficients of alternating f_2 and f_4.

For a particular polynomial $f = j_nx^n + \cdots + j_mx^m$ with shape $[m,n]$, we can denote the coefficients of f in an $n-m+1$ dimensional vector as

$$[f] := \begin{pmatrix} j_n \\ \vdots \\ j_m \end{pmatrix}.$$

Again, if the f_i have respective shape $[m_i, n_i]$, then the vector of coefficients of $f_1 f_4$ and $f_2 f_3$ can be written as the following matrix products:

$$[f_1 f_4] = \begin{pmatrix} a_{n_1} & 0 & \cdots & 0 \\ \vdots & a_{n_1} & \cdots & 0 \\ a_{m_1} & \vdots & \cdots & \vdots \\ 0 & a_{m_1} & \cdots & 0 \\ \vdots & 0 & \cdots & a_{n_1} \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & a_{m_1} \end{pmatrix} \begin{pmatrix} d_{n_4} \\ \vdots \\ d_{m_4} \end{pmatrix}, \quad [f_3 f_2] = \begin{pmatrix} c_{n_3} & 0 & \cdots & 0 \\ \vdots & c_{n_3} & \cdots & 0 \\ c_{m_3} & \vdots & \cdots & \vdots \\ 0 & c_{m_3} & \cdots & 0 \\ \vdots & 0 & \cdots & c_{n_3} \\ \vdots & \vdots & \cdots & \vdots \\ 0 & 0 & \cdots & c_{m_3} \end{pmatrix} \begin{pmatrix} b_{n_2} \\ \vdots \\ b_{m_2} \end{pmatrix}.$$

We refer to the matrix containing the coefficients of f_1 as G'' and the matrix containing the coefficients of f_3 as H'', hence the above matrix products can be represented by $G''[f_4]$ and $H''[f_2]$ respectively. Note that this matrix G'' has dimension $n_1 + n_4 - m_1 - m_4 + 1$ by $n_4 - m_4 + 1$, while H'' has dimension $n_2 + n_3 - m_2 - m_3 + 1$ by $n_2 - m_2 + 1$.

We can nearly represent the coefficients of g by adding these two products, however there could be a difference in the dimension of the largest and smallest orders of $f_1 f_4$ and $f_2 f_3$. Note however that this difference is well understood, as by Corollary 2.4.1, the difference in the largest and smallest orders of f_1 and f_2 must be at exactly one, and likewise for f_3 and f_4. Thus, either the largest order of $f_1 f_4$ is the same as the largest order of $f_2 f_3$, or it is exactly two larger or smaller. The same is also true for the smallest orders of $f_1 f_4$ and $f_2 f_3$.

Thus, we will let G' and H' represent the matrices G'' and H'' where either has an additional two rows of zeros added to the top or bottom of their respective matrix, if necessary. Therefore, we can now represent the coefficients of g as

$$[g] = [f_1 f_4 + f_2 f_3] = G'[f_4] + H'[f_2] = (G' \; H') \begin{pmatrix} [f_4] \\ [f_2] \end{pmatrix}$$

Note then that this matrix $(G' \; H')$ has dimension

$$\max\{n_1 + n_4, n_2 + n_3\} - \min\{m_1 + m_4, m_2 + m_3\} + 1 \text{ by } n_2 - m_2 + n_4 - m_4 + 2.$$

Now, note that since both f_2 and f_4 alternate, many of the entries of $\begin{pmatrix} [f_4] \\ [f_2] \end{pmatrix}$ are zero. In fact, every other entry of $[f_2]$ and $[f_4]$ are zero, hence we can eliminate both these $(n_2 - m_2 +$

$n_4 - m_4)/2$ rows in the vector and the corresponding columns in the matrix $(G'\ H')$, yielding the same information. The resulting matrix which we now call $(\overline{G}\ \overline{H})$ has dimension

$$\max\{n_1+n_4, n_2+n_3\} - \min\{m_1+m_4, m_2+m_3\} + 1 \text{ by } \frac{n_2 - m_2 + n_4 - m_4}{2} + 2.$$

Note that every other row of the $(\overline{G}\ \overline{H})$ matrix will consist of only zeros, since the alternation property of the polynomials f_1 and f_3 yield every other diagonal of $(G'\ H')$ consists of only zeros. Thus, we can eliminate $(\max\{n_1+n_4, n_2+n_3\} - \min\{m_1+m_4, m_2+m_3\})/2$ rows of $(\overline{G}\ \overline{H})$ and retain the same information. We define this final reduced matrix to be $(G\ H)$, and note that it has dimension:

$$\frac{\max\{n_1+n_4, n_2+n_3\} - \min\{m_1+m_4, m_2+m_3\}}{2} + 1 \text{ by } \frac{n_2 - m_2 + n_4 - m_4}{2} + 2. \tag{2.2}$$

We now determine when the alternating shape factorization problem has finitely many solutions.

Proposition 2.4.10. *The quadruple* $([m_1, n_1], [m_2, n_2], [m_3, n_3], [m_4, n_4])$ *for the four alternating polynomials is alternating good if and only the matrix* $(G\ H)$ *is invertible.*

Proof. We can write the shape factorization problem of $([m_1, n_1], [m_2, n_2], [m_3, n_3], [m_4, n_4])$ in the matrix factored form $G'[f_4] + H'[f_2] = [g]$, where every other coefficient will be zero. Thus, we can actually reduce this factored form to $G\overline{[f_4]} + H\overline{[f_2]} = \overline{[g]}$ where $\overline{[f]}$ is the coefficient vector of the alternating function f with the zeros removed, that is

$$(G\ H)\begin{pmatrix}\overline{[f_4]}\\ \overline{[f_2]}\end{pmatrix} = \overline{[g]}.$$

This system has a unique solution if and only if $(G\ H)$ is invertible for a generic choice of parameter values, i.e. generically invertible. □

Note that for the matrix $(G\ H)$ to be generically invertible, it needs to be square and have full rank. Recall from Theorem 1.3.6 that the determinant of the Sylvester matrix of two polynomials is zero if and only if the two polynomials have a common root. Thus for generic polynomials f and g, the Sylvester matrix is invertible.

Note that in the case of $(G\ H)$, this matrix is nearly the Sylvester matrix of two polynomials, though not exactly f_1 and f_3, but it possibly contains extra rows and columns.

The following proposition and proof mirror that of Proposition 13 of (Mahdi et al. 2014).

Proposition 2.4.11. *If the matrix $(G\ H)$ is square, then it is generically invertible.*

Proof. Suppose $(G\ H)$ is square. We claim that the columns of $(G\ H)$ can be ordered in such a way that the block form of the matrix is

$$\begin{pmatrix} S' & 0 & 0 \\ X & S & Y \\ 0 & 0 & S'' \end{pmatrix}$$

where S is the Sylvester matrix of $\hat{f}_1$ and $\hat{f}_3$ where $\hat{f}$ for an alternating polynomial f is the polynomial with lowest degree zero and coefficient vector $\overline{[f]}$. That is, $\hat{f}$ is a polynomial which does not alternate, with the same coefficients as f (associated to different powers).

We will show that either $(G\ H)$ is exactly the Sylvester matrix of generic polynomials $\hat{f}_1$ and $\hat{f}_3$, hence has full rank, or that one or both of S' and S'' are 1 by 1 matrices with nonzero entry, and S is the same Sylvester matrix, meaning that $(G\ H)$ continues to have full rank. Note that the Sylvester matrix S of these two polynomials $\hat{f}_1$ and $\hat{f}_3$ will have dimension $(n_1-m_1+n_3-m_3)/2$ by $(n_1-m_1+n_3-m_3)/2$. Recall from Equation 2.2 that $(G\ H)$ is a matrix of dimension

$$\frac{\max\{n_1+n_4, n_2+n_3\}-\min\{m_1+m_4, m_2+m_3\}}{2}+1 \text{ by } \frac{n_2-m_2+n_4-m_4}{2}+2. \tag{2.3}$$

Without loss of generality, we assume that $\max\{n_1+n_4, n_2+n_3\} = n_1+n_4$. This occurs in one of three ways by Corollary 2.4.1:

(i) $n_1 = n_2+1$ and $n_4 = n_3-1$, (in which case the two sums are equivalent)

(ii) $n_1 = n_2-1$ and $n_4 = n_3+1$, (in which case the two sums are equivalent) or

(iii) $n_1 = n_2+1$ and $n_4 = n_3+1$.

In the first two cases, we do not add any zero rows above either G'' or H'' (described above) in making the matrices G' and H'. In either of these cases, we remove the row and column involving S' from the block matrix.

In the last case, we add exactly two rows of zeros above the H'' matrix to make the matrix H', and add no rows of zeros above G'' to make G', hence we will have that S' will be a 1 by 1 matrix with nonzero entry a_{n_1}, and X is the remaining coefficients of $\hat{f}_1$ followed by zeros.

Now we consider the two possible cases of $\min\{m_1+m_4, m_2+m_3\}$.

First, suppose $\min\{m_1+m_4, m_2+m_3\} = m_1+m_4$. This implies that the dimension of the $(G\ H)$ matrix is $(n_1+n_4-m_1-m_4)/2+1$ by $(n_2+n_4-m_2-m_4)/2+2$.

This can occur one of three ways by Corollary 2.4.1:

(a) $m_1 = m_2+1$ and $m_4 = m_3-1$, (in which case the two sums are equivalent)

(b) $m_1 = m_2-1$ and $m_4 = m_3+1$, (in which case the two sums are equivalent) or

(c) $m_1 = m_2-1$ and $m_4 = m_3-1$.

In the first two cases, we do not add any zero rows below either G'' or H'' in making the matrices G' and H'. In either of these cases, we remove the row and column involving S'' from the block matrix above.

In the last case, we add exactly two rows of zeros below the H'' matrix to make the matrix H', and add no rows of zeros below G'' to make G'. Thus, we will have that S'' will be a 1 by 1 matrix with nonzero entry a_{m_1}, and Y will continue with the other coefficients of $\hat{f}_1$ with zeros above.

Similarly, consider the case when $\min\{m_1+m_4, m_2+m_3\} = m_2+m_3$. Here, we have that the dimension of $(G\ H)$ is $(n_1+n_4-m_2-m_3)/2+1$ by $(n_2+n_4-m_2-m_4)/2+2$. This can occur one of three ways by Corollary 2.4.1:

(A) $m_1 = m_2+1$ and $m_4 = m_3-1$, (in which case the two sums are equivalent)

(B) $m_1 = m_2-1$ and $m_4 = m_3+1$, (in which case the two sums are equivalent) or

(C) $m_1 = m_2+1$ and $m_4 = m_3+1$.

In the first two cases, we do not add any zero rows below either G'' or H'' in making the matrices G' and H'. In either of these cases, we remove the row and column involving S'' from the block matrix above.

In the last case, we add exactly two rows of zeros below the G'' matrix to make the matrix G', and add no rows of zeros below H'' to make H'. Thus, we will have that S'' will be a 1 by 1 matrix with nonzero entry c_{m_3}, and Y will continue with the other coefficients of $\hat{f}_3$ with zeros above.

In any case, we have that S is the Sylvester matrix of two polynomials with generic coefficients, namely $\hat{f}_1$ and $\hat{f}_3$, hence has full rank, and if S' or S'' are in the block matrix, then they are 1 by 1 matrices with nonzero entries, hence have full rank. Thus the matrix $(G\ H)$ has generic full rank, i.e. is generically invertible. $\square$

Theorem 2.4.12. *An LC system is locally identifiable if and only if the number of non-monic, nontrivial coefficients in the constitutive equation is equal to the number of parameters.*

Proof. Here, we show that if the number of parameters equals the number of non-monic, nontrivial coefficients, then the $(G\ H)$ matrix is square, hence by Propositions 2.4.9, 2.4.10, and 2.4.11 the model is locally identifiable.

Suppose $\mathscr{M}$ is an LC system which consists of a series combination of two smaller LC systems N_1 and N_2 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ where f_1 and f_3 are monic. Also, suppose f_i has shape $[m_i, n_i]$. By induction, we suppose that the number of parameters equals the number of nontrivial, non-monic coefficients in both systems N_1 and N_2. This implies that N_1 has $(n_1 + n_2 - m_1 - m_2)/2 + 1$ parameters, and N_2 has $(n_3 + n_4 - m_3 - m_4)/2 + 1$ parameters.

Assume the number of parameters equals the number of coefficients in the whole system, i.e.

$$\begin{aligned}&\frac{n_1+n_2+n_3+n_4-m_1-m_2-m_3-m_4}{2}+2\\ &=\frac{\max\{n_1+n_4, n_2+n_3\}-\min\{m_1+m_4, m_2+m_3\}+n_1+n_3-m_1-m_3}{2}+1\end{aligned}$$

Subtracting $(n_1 + n_3 - m_1 - m_3)/2$ from both sides, we get

$$\frac{n_2+n_4-m_2-m_4}{2}+2=\frac{\max\{n_1+n_4, n_2+n_3\}-\min\{m_1+m_4, m_2+m_3\}}{2}+1$$

This occurs exactly when the matrix $(G\ H)$ is square via Equation 2.2. The argument for a parallel combination is identical, and omitted. □

2.5 LCR System Analysis

Now we consider the systems containing series and parallel combinations of all three base elements, that is LCR systems. We are not able to derive a complete classification of identifiability of these models, and there already seem to be some significant challenges to generalizing the results for two element systems to arbitrary LCR. For example, there are general series-parallel LCR systems where there are more coefficients than the number of parameters. Thus, there can be nontrivial relations between the coefficients in a general series-parallel LCR system. We will explore those equations in Section 2.6. In this section, we look at basic properties of the general LCR systems, including the number of types of systems in terms of the structure of the constitutive equation. We will show that there are 22 different types.

To begin our study of general LCR systems, we first consider several bounds on the orders of the constitutive equation.

Proposition 2.5.1. *The maximum order of either side of the constitutive equation of an LCR system is bounded above by the number of parameters, i.e. base elements, in the model.*

Proof. We will prove this statement inductively. As the base case, note that the statement is true for each of our one element systems containing either a resistor, capacitor, or inductor.

Suppose that for LCR systems with less than k base elements, the resulting constitutive equation has largest power less than or equal to the number of base elements.

Now consider some LCR system $\mathscr{M}$ with k base elements, which is a series combination of two smaller (in number of base elements) models which have m and n parameters respectively where $m+n=k$. By the inductive hypothesis, we know that the largest order of either side of the constitutive equations of the two smaller models are m and n respectively, i.e. if $f_1V_1 = f_2I_1$ and $f_3V_2 = f_4I_2$ are the constitutive equations of the two models respectively, then $\deg(f_1), \deg(f_2) \leq n$ and $\deg(f_3), \deg(f_4) \leq m$.

Recall by Proposition 1.4.6 that the series combination of two systems with constitutive equations $f_1V_1 = f_2I_1$ and $f_3V_2 = f_4I_2$ yields constitutive equation:

$$f_1f_3V = (f_1f_4 + f_2f_3)I.$$

Therefore, the largest power of either side of the constitutive equation is $n+m=k$. By duality, we also have the result when $\mathscr{M}$ is a parallel combination. $\square$

Proposition 2.5.2. *In an LCR system, the largest orders on either side of the constitutive equation must be within one of each other. Similarly, the smallest orders on either side of the constitutive equation must be within one of each other.*

Proof. We prove the proposition using induction on the number of base elements in the system. As the base case, note that in both the inductor, and the capacitor base element, the difference in the largest power between the two sides of the constitutive equation is one. Similarly, since the smallest power is the largest power, that difference is also one. In the case of a single resistor, both sides have a single element of order zero.

Suppose then that the statement of the proposition is true for LCR systems with less than k base elements. Then suppose that M is an LCR system with k elements which is generated by, without loss of generality, a series combination of two strictly smaller (in terms of number of base elements) systems N_1 and N_2. Suppose that N_1 and N_2 have respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ where each f_i is defined just as in Equation 1.11.

By the inductive hypothesis, since N_1 andN_2 have less than k base elements, then we know that $|n_1 - n_2| \leq 1$, $|m_1 - m_2| \leq 1$, $|n_3 - n_4| \leq 1$, and $|m_3 - m_4| \leq 1$. Note that by Equation 1.12, the constitutive equation of the system M generated by combining N_1 and N_2 in series is

$$f_1 f_3 V = (f_1 f_4 + f_2 f_3) I. \tag{2.4}$$

Thus, we have that the maximal order of the left-hand side of the Equation 2.4 is $n_1 + n_3$, while the maximal order of the right-hand side is $\max\{n_1 + n_4, n_2 + n_3\}$. Therefore, the difference in the largest order of either side of the constitutive equation of M is

$$\begin{aligned} |n_1 + n_3 - \max\{n_1 + n_4, n_2 + n_3\}| &= |\min\{n_1 + n_3 - n_1 - n_4,\ n_1 + n_3 - n_2 - n_3\}| \\ &= |\min\{n_3 - n_4,\ n_1 - n_2\}| \end{aligned}$$

Note that in either case, we have that $|n_1 - n_2| \leq 1$ and $|n_3 - n_4| \leq 1$, thus the difference of the maximal order of either side of the constitutive equation of M is at most one.

The bound for the minimal order is similar (with maximums and minimums swapped) and is omitted. The bounds also follow for parallel combinations by circuit duality.

Thus, by induction, LCR systems have the difference of the largest order of either side of their constitutive equations at most one, and the difference of the smallest order of either side of their constitutive equations at most one. □

Remark 2.5.3. The main difference between all of the two base element systems and the general three base element system is that we no longer have a bound on the number of coefficients of the constitutive equation by the number of parameters. In fact, by the previous two propositions, we can have up to $2n+1$ nonzero, non-monic coefficients in the constitutive equation of an LCR system with n base elements. As a result of this lack of a bound, we could have systems with more coefficients than base elements which are locally identifiable. This is not entirely surprising, however the existence of systems with more base elements than coefficients which are **not** locally identifiable leads us to believe that to find a sufficient condition for the identifiability of an LCR system, we need to look beyond comparing the number of coefficients to the number of parameters.

Example 2.5.4. Consider the LCR system depicted in Figure 2.2. This system has constitutive

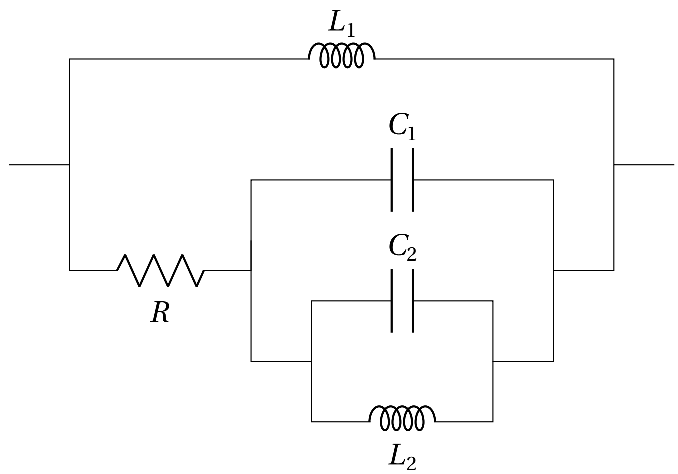

Figure 2.2: An LCR system $L_1 \vee (R \wedge (C_1 \vee (L_2 \vee C_2)))$.

equation:

$$\begin{aligned}(C_1L_1L_2 + C_2L_1L_2)V^{(3)} + (C_1L_2R + C_2L_2R)\ddot{V} + (C_1C_2L_1 + C_1C_2L_2)\dot{V} + C_1C_2RV \\ = (C_1L_1L_2R + C_2L_1L_2R)I^{(3)} + C_1C_2L_1L_2\ddot{I} + C_1C_2L_1R\dot{I}.\end{aligned}$$

Note that this LCR system has five parameters and after normalization has six non-monic, nonzero coefficients in its constitutive equation. If we consider the Jacobian matrix of the map from the space of parameters to the space of coefficients of the constitutive equation corresponding to this example, we see that the rank of the Jacobian is non-maximal, meaning the system is not identifiable. This example first shows that the number of coefficients in a constitutive equation of an LCR system is not bounded by the number of parameters, and moreover having at least as many coefficients as parameters in an LCR system is not a sufficient condition for local identifiability.

We now introduce a similar notion of types as in the LC systems to more general LCR systems.

Definition 2.5.5. Let $\mathcal{M}$ be an LCR system with constitutive equation $f_1V = f_2I$ where $f_1 = a_{n_1}x^{n_1} + \cdots + a_{m_1}x^{m_1}$ and $f_2 = b_{n_2}x^{n_2} + \cdots + b_{m_2}x^{m_2}$. Then we define the *type* of $\mathcal{M}$ as the quadruple $(m_1 - m_2,\ n_1 - n_2,\ c,\ d)$ where $c, d = 1$ if f_1 and f_2 have the alternating property respectively, and are 0 otherwise.

Example 2.5.6. The three base elements can be characterized by type, where because there is only a single nonzero coefficient on either side of the constitutive equation, each side of all three constitutive equations are defined as alternating. More explicitly, by Equations 1.8, 1.9, and 1.10, we have that the resistor, inductor, and capacitor have respective types $(0,0,1,1)$, $(-1,-1,1,1)$ and $(1,1,1,1)$.

Remark 2.5.7. The four types, A, B, C, D of LC systems described in Section 2.4 can be generalized as $A=(-1,-1,1,1)$, $B=(-1,1,1,1)$, $C=(1,-1,1,1)$ and $D=(1,1,1,1)$ as LCR types.

Note that there are certain restrictions on what this type quadruple can look like. For example we know that because of Proposition 2.5.2, the first two entries of the type must both be in the set $\{-1,0,1\}$. We have not yet shown that for an LCR system that the left and right-hand sides of the constitutive equation must strictly have the alternating property or the saturated property. More precisely, it is not obvious that a differential operator in the constitutive equation of an LCR system cannot skip an order without having the alternating property, i.e. have an order with zero coefficient, but not have the remaining even or odd orders also have zero coefficients. We now prove that this is in fact the case, and conclude that all LCR systems fall into one of these types. To do this, we first need the following Lemma.

Lemma 2.5.8. *No LCR system can have constitutive equation of type* $(*,-1,0,1)$ *for any entry of* $*$.

Proof. Suppose $\mathscr{M}$ is an n base element LCR system with type of the form $(*,-1,0,1)$, and constitutive equation $f_1 V = f_2 I$. Note that f_2 must alternate since the fourth entry of the type quadruple is 1, and also f_2 must have largest order one larger than f_1 since the second entry of the type quadruple is -1. Similarly, f_1 must not alternate since the third entry of the quadruple is 0.

Recall that the three base elements, the resistor, inductor, and capacitor, have respective types $(0,0,1,1)$, $(-1,-1,1,1)$ and $(1,1,1,1)$, hence $\mathscr{M}$ cannot be a base element, i.e. $n \geq 1$. Therefore, $\mathscr{M}$ must be made of some series or parallel combination of two systems with strictly fewer elements, say A_1 and A_2. Let A_1 and A_2 have constitutive equations $g_1 V_1 = g_2 I_1$ and $g_3 V_2 = g_4 I_2$ respectively.

First, if we suppose $\mathscr{M}$ is a series combination of A_1 and A_2, then we have that $f_1 = g_1 g_3$ and $f_2 = g_1 g_4 + g_2 g_3$. Note that since f_2 must alternate, then all four of g_1, g_2, g_3 and g_4 must alternate (and have some parity conditions), however f_1 must not alternate meaning that at least one of g_1 or g_3 cannot alternate, a contradiction. Thus, an LCR system of type $(*, -1, 0, 1)$ cannot be constructed via a series combination of other systems with fewer elements.

Now suppose $\mathscr{M}$ is a parallel combination of A_1 and A_2. In this case, we have that $f_1 = g_1 g_4 + g_2 g_3$ and $f_2 = g_2 g_4$. Since f_2 must have one higher largest order than f_1, we must have that $\deg(g_1) < \deg(g_2)$ and $\deg(g_3) < \deg(g_4)$. Thus, by Proposition 2.5.2, we have that $\deg(g_2) = \deg(g_1) + 1$ and $\deg(g_4) = \deg(g_3) + 1$, meaning that A_1 and A_2 have respective types with second entry both being -1.

Given that f_2 is alternating, we must have that both g_2 and g_4 are alternating, i.e. both A_1 and A_2 have a 1 in the last entry of their types. Similarly, given that f_1 is not alternating, we must have either g_1 or g_3 not alternating, or that $g_1 g_4$ and $g_2 g_3$ have opposite parity. Note though that $g_1 g_4$ and $g_2 g_3$ must have the same parity, since the pairs g_1, g_2 and g_3, g_4 must have different parity (because their maximal orders have a difference of exactly one from above), meaning $g_1 g_4$ has even (odd) parity if and only if $g_2 g_3$ has even (odd) parity. Thus, A_1 and A_2 must have types of the form $(*, -1, r_1, 1)$ and $(*, -1, r_2, 1)$ where at least one of r_1 or r_2 is equal to 0.

Therefore, the only way to generate a system of type $(*, -1, 0, 1)$ is by a parallel combination of two systems, one of which has type $(*, -1, 0, 1)$, but since none of the base elements have this type, then this type must not exist.

$\square$

Proposition 2.5.9 (Skipping but not alternating)**.** *Let M be a series-parallel LCR system. Then each side of the constitutive equation must either be alternating or saturated.*

Proof. We prove this statement by induction on the number of base elements in the system. As the base case, note that in each of the one-element systems, the statement is certainly true, as each side only has a single nonzero coefficient.

Now, suppose the statement is true for LCR systems with less than k base elements, that is, either side of the constitutive equation for LCR systems with less than k base elements cannot skip an order without having that side alternate. Also, suppose $\mathscr{M}$ is an LCR system with k base elements, which is generated by a series combination of two smaller systems N_1 and N_2 with strictly less than k base elements. Let N_1 and N_2 have constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$ respectively, and note by the inductive hypothesis, f_1, f_2, f_3 and f_4 cannot skip a coefficient without alternating. Therefore, each of N_1 and N_2 can be characterized by a type as described in Definition 2.5.5. Let us define each polynomial f_1, f_2, f_3 and f_4 as in Equation 1.11.

By Proposition 2.5.2, we know that the first two entries of each N_i system's type is either $-1, 0$ or 1.

Also, we have that the constitutive equation of $\mathscr{M}$ is $f_1 f_3 V = (f_1 f_4 + f_2 f_3)I$. Note that for each of the three products of two f_i, if both polynomials in the product alternate, then the resulting product alternates. Also, if at least one of the polynomials in the product is saturated, then by Lemma 2.5.10, we know that the resulting product is saturated. Thus, we immediately have that the left-hand side of the constitutive equation, i.e. the product $f_1 f_3$, cannot skip without alternating. We also know that each element of the sum of the right-hand side cannot skip without alternating, hence to finish the proof we need only show that their sum cannot skip without alternating.

Note that by Proposition 2.5.2, we know that the absolute difference in the largest orders, and the absolute difference of the smallest orders of $f_1 f_4$ and $f_2 f_3$ are both at most two.

Thus, the only way that the right-hand side of the constitutive equation for $\mathscr{M}$ could skip an order without alternating is if one of the elements of the sum had maximal (or minimal) order two larger (smaller) than the other, and the one with larger maximal order alternates while the other is saturated. This would result in skipping the second largest (smallest) order of the sum, but the rest of the sum having nonzero coefficients.

Suppose without loss of generality that $f_1 f_4$ has largest order two larger than $f_2 f_3$ and suppose f_1 and f_4 alternate, while at least one of f_2 and f_3 is saturated. Thus, the third entry of the type of N_1 and the fourth entry of the type of N_2 must be 1. Also, either the fourth entry of the type of N_1 or the third entry of the type of N_2 must be zero. Without loss of generality we suppose that it is f_3 that is saturated. Note that for $f_1 f_4$ to have largest order two larger than $f_2 f_3$, we must have that $n_1 = n_2 + 1$ and $n_4 = n_3 + 1$, i.e. f_1 and f_4 have largest order one larger than f_2 and f_3 respectively by Proposition 2.5.2. Thus, the second entry in the type of N_1 must be a 1, while the second entry in the type of N_2 must be a -1. Therefore, N_1 must have type $(*, 1, 1, *)$ and N_2 must have type $(*, -1, 0, 1)$ where the $*$ represents any possible entry.

Since the only way to have a constitutive equation which skips but does not alternate is to have an element of type $(*, -1, 0, 1)$ which does not exist by Lemma 2.5.8, then there cannot be a constitutive equation which skips but does not alternate with k base elements. Thus, by induction, no LCR system can skip but not alternate.

The case of a parallel combination follows from circuit duality. □

Lemma 2.5.10. *If f and g are polynomials with non-negative coefficients such that f is saturated and g is alternating, then the product fg is saturated.*

Proof. Suppose f is saturated, and g is alternating, such that they have form

$$f = a_n x^n + a_{n-1} x^{n-1} + \cdots + a_{m+1} x^{m+1} + a_m x^m$$
$$g = b_v x^v + b_{v-2} x^{v-2} + \cdots + b_{u+2} x^{u+2} + b_u x^u$$

Note that the product of f and g has form

$$fg = \sum_{k=m+u}^{n+v} \left(\sum_{i+j=k} a_i b_j \right) x^k.$$

Thus, to show the statement of the Lemma is true, we need only show that for each k, there is some nonzero combination of coefficients from g and f with corresponding degree adding to k. Given that g alternates and f is saturated, and all coefficients are non-negative, this problem equates to the following: Given the sets of non-negative integers $\mathscr{F} = \{n, n-1, \ldots, m+1, m\}$ and $\mathscr{G} = \{v, v-2, \ldots, u+2, u\}$, for every integer k with $m + u \leq k \leq n + v$, can we find a sum of an element $i \in \mathscr{F}$ and an element $j \in \mathscr{G}$ such that $i + j = k$? The answer to this question is yes, as we can generate every natural number from $m + u$ to $n + v$ as

$$m+u, (m+1)+u, m+(u+2), (m+1)+(u+2), \ldots, (n-1)+(v-2), n+(v-2), (n-1)+v, n+v.$$

Thus, for each k there is some a_i and b_j such that $a_i b_j \neq 0$ and $i + j = k$, hence fg is saturated, as desired. □

Corollary 2.5.11. *Every LCR system has one of the types as defined in Definition 2.5.5.*

Proof. The only way that we could not classify an LCR system with a type would be if it had a constitutive equation which did not alternate, but also was not saturated by our definition, i.e. that skipped without alternating. By Proposition 2.5.9, this cannot happen. Thus, every LCR system can be characterized by a type. □

We can now make several more statements about the type characterization we propose for LCR systems.

Proposition 2.5.12. *We can characterize the type of a series combination of two LCR systems of types (a, b, c, d) and (e, f, g, h) respectively as*

$$(a, b, c, d) \odot (e, f, g, h) = \big(\max\{a, e\},\ \min\{b, f\},\ cg,\ cdgh(1 - ||a| - |e||)\big). \tag{2.5}$$

Proof. Suppose $\mathscr{M}$ is generated by a series combination of two smaller LCR systems N_1 and N_2 with respective constitutive equations $f_1 V_1 = f_2 I_1$ and $f_3 V_2 = f_4 I_2$. Note then that the constitutive equation of $\mathscr{M}$ is $f_1 f_3 V = (f_1 f_4 + f_2 f_3) I$.

Let us define each polynomial f_1, f_2, f_3, and f_4 just as in Equation 1.11.

Note that the first entry in the type of $\mathscr{M}$ is the difference in the smallest orders of both sides of its constitutive equation, i.e.

$$\begin{aligned}(m_1+m_3)-\min\{m_1+m_4,\ m_2+m_3\} &= \max\{m_1+m_3-m_1-m_4,\ m_1+m_3-m_2-m_3\}\\ &= \max\{m_3-m_4,\ m_1-m_2\}\\ &= \max\{e,a\}.\end{aligned}$$

Similarly, the second entry in the type of $\mathscr{M}$ is the difference in the largest orders of both sides of its constitutive equation, i.e.

$$\begin{aligned}(n_1+n_3)-\max\{n_1+n_4,\ n_2+n_3\} &= \min\{n_1+n_3-n_1-n_4,\ n_1+n_3-n_2-n_3\}\\ &= \min\{n_3-n_4,\ n_1-n_2\}\\ &= \min\{f,b\}.\end{aligned}$$

Also, $f_1 f_3$ alternates if and only if f_1 and f_3 both alternate, i.e. the third entry of the type of $\mathscr{M}$ is 1 if and only if both third entries of the types of N_1 and N_2 are 1. This is true exactly when $c = g = 1$, equivalently if and only if $cg = 1$.

Finally, the right hand side of the constitutive equation of $\mathscr{M}$ alternates if and only if all four of the f_i alternate, and $f_1 f_4$ has the same parity as $f_2 f_3$. Note that these two products have the same parity if and only if either all f_i have the same parity, or if f_1 and f_2 have different parity and f_3 and f_4 have different parity. More explicitly, we can consider the smallest order of all of the alternating f_i and note that these two products have the same parity if and only if either each of $a = e = 0$, or $|a| = |e| = 1$. Thus, the fourth entry of the type of $\mathscr{M}$ is 1 if and only if all of the third and fourth entries of N_1 and N_2 are 1 and $||a|-|e|| = 0$, i.e. $1-||a|-|e|| = 1$. □

By circuit duality, we also get a similar formula for parallel combinations.

Proposition 2.5.13. *We can characterize the type of a parallel combination of two LCR systems of types (a,b,c,d) and (e,f,g,h) respectively as*

$$(a,b,c,d)\oplus(e,f,g,h) = \big(\min\{a,e\},\ \max\{b,f\},\ cdgh(1-||a|-|e||),\ dh\big). \tag{2.6}$$

Given our type characterization and the restrictions imposed on the type by Propositions 2.5.2 and 2.5.9, there are 36 possible types of the form $(\{-1,0,1\}, \{-1,0,1\}, \{0,1\}, \{0,1\})$. Note however that not all 36 of these quadruples correspond to types of LCR systems which are generated by series and parallel combinations of the three base elements, as evident by Lemma 2.5.8. We can generate all possible types by implementing a recursive algorithm starting with a generating set consisting of the three base element types $(0,0,1,1)$, $(-1,-1,1,1)$, and $(1,1,1,1)$, generating every possible combination of these types, and adding these combinations to the generating set. Repeating this process until no new quadruples are added to the generating set, we then have all possible types.

Proposition 2.5.14. *The following* 22 *quadruples are the only possible LCR types:*

$$
\begin{array}{cccccc}
(1,0,0,0), & (-1,0,0,0), & (0,0,1,1), & (1,-1,1,0), & (0,1,0,1), & (0,-1,0,0), \\
(1,1,0,0), & (-1,1,1,1), & (1,1,1,1), & (0,0,0,1), & (0,0,1,0), & (-1,-1,0,0), \\
(1,-1,0,0), & (0,1,0,0), & (-1,1,0,1), & (0,-1,1,0), & (0,0,0,0), & (-1,-1,1,1), \\
 & (1,-1,1,1), & (1,0,1,0), & (-1,0,0,1), & (-1,1,0,0). &
\end{array}
$$

Remark 2.5.15. One could also prove Proposition 2.5.14 algebraically showing that each of the 14 non-possible types cannot be generated via series and parallel combinations of the base elements, similar to the argument done for Lemma 2.5.8.

To conclude this section, we give an example that shows that type analysis, as was performed to analyze the two component systems, is not sufficient to characterize the identifiability of general series-parallel LCR systems.

Example 2.5.16. Consider the model $M = (R_1 \vee C) \wedge (R_2 \vee L)$. This model has constitutive equation

$$R_1 L\ddot{V} + (CL + R_1R_2)\dot{V} + CR_2V = LR_1R_2\ddot{I} + (LCR_1 + LCR_2)\dot{I} + CR_1R_2I.$$

This model is saturated on both sides, and the shapes of the differential operators are $[0,2]$ and $[0,2]$. Since the constitutive equation has the same highest and lowest order on both sides, this model has type $(0,0,0,0)$.

Now consider the model $N = M \wedge R_3$ obtained by joining M in series to a new resistor R_3. The model of a single resistor has type $(0,0,1,1)$, so the model N will also have type $(0,0,0,0) \odot (0,0,1,1) = (0,0,0,0)$, and the differential operators also have shapes $[0,2]$ and $[0,2]$. In this case there are five parameters and five non-monic coefficients, and a direct calculation shows that the model is locally identifiable.

Finally, consider the new model $N' = N \wedge R_4$ obtained by joining N in series to a new resistor R_4. Again this model N' will have type $(0,0,0,0) \odot (0,0,1,1) = (0,0,0,0)$ and the differential operators also have shapes $[0,2]$ and $[0,2]$. But now the model cannot be identifiable because there are six parameters and there continue to be only five non-monic coefficients. This shows that the combinations of types $(0,0,0,0) \odot (0,0,1,1)$ may or may not be identifiable depending on the structure of the underlying model.

2.6 Equations Defining LCR Models

General LCR models can have more non-monic coefficients than the number of parameters. Hence, the set of constitutive equations consistent with a particular model M will be a subset of all possible differential equations of a given type. Understanding the algebra and geometry of these sets of constitutive equations is an interesting problem, and might be useful for addressing identifiability questions for general LCR circuit systems.

Example 2.6.1. Consider the LCR system $M = (R \vee C) \wedge L$. The constitutive equation in this case is

$$R\dot{V} + V = RL\ddot{I} + L\dot{I} + RCI.$$

Note that there are three parameters and four non-monic coefficients. Hence, not every constitutive equation of shape

$$c_1\dot{V} + c_0V = d_2\ddot{I} + d_1\dot{I} + d_0I$$

with positive coefficients can arise from some choice of R, C, L. To describe the relations that arise, we find it useful to work in the projective representation, as this will produce homogeneous equations. In this case, the projective version of the constitutive equation is

$$L_0C_0R_1\dot{V} + L_0C_0R_0V = L_1C_0R_1\ddot{I} + L_1C_0R_0\dot{I} + L_0C_1R_1I.$$

Note that these coefficients satisfy the relation: $c_1d_1 = c_0d_2$.

Example 2.6.2. Consider the four element model $M = (R_1 \wedge C) \vee (R_2 \wedge L)$. The constitutive equation is

$$R_1L\ddot{V} + (CL + R_1R_2)\dot{V} + CR_2V = R_1R_2L\ddot{I} + (CR_2L + CR_1L)\dot{I} + R_1R_2CI.$$

There are six coefficients and four parameters. In the projective version, we expect a single homogeneous equation that defines the relations on the coefficients. It is

$$c_0^2 d_2^2 - c_1 c_0 d_2 d_1 + c_2 c_0 d_1^2 + \underline{2 c_2 c_0 d_2 d_0} - c_2 c_1 d_1 d_0 + c_2^2 d_0^2 = 0.$$

This polynomial is remarkably similar looking to the resultant of the two quadratic polynomials $c_2 x^2 + c_1 x + c_0$ and $d_2 x^2 + d_1 x + d_0$. However, the sign of the underlined term is wrong. It is unclear if this polynomial can be expressed as the resultant of related polynomials. We also do not know if every 6-tuple $(c_2, c_1, c_0, d_2, d_1, d_0)$ of positive numbers that satisfies this equation can come from some choice of positive values for C, L, R_1, and R_2.

Examples 2.6.1 and 2.6.2 just give a small taste of the types of equations that can arise. We do not have a general theory of what those equations should look like, but we can try to derive properties of the ideals in the hopes of understanding their structure.

In general, associated to any series-parallel model M is a homogeneous ideal

$$I_M \subseteq \mathbb{R}[\mathbf{c}, \mathbf{d}] = \mathbb{R}[c_0, c_1, \ldots, c_m, d_0, d_1, \ldots, d_m].$$

For example, in Example 2.6.1, we get that $I_M = \langle c_1 d_1 - c_0 d_2 \rangle$. In fact, beyond being just an ordinary homogeneous ideal, I_M satisfies some other homogeneities as well.

Call a polynomial $p(c, d) \in \mathbb{R}[\mathbf{c}, \mathbf{d}]$ bihomogeneous, if it is homogeneous in each set of variables, that is $p(\lambda c, \delta d) = \lambda^m \delta^n p(c, d)$ for some m and n. The pair (m, n) is called the bidegree of p. An ideal $I \in \mathbb{R}[\mathbf{c}, \mathbf{d}]$ is bihomogeneous if it has a generating set consisting of bihomogeneous polynomials. The notion of bihomogeneity of ideals also can be interpreted naturally in terms of the corresponding variety, at least when I is radical. Let $V = V(I) \subseteq \mathbb{R}^{2n+2}$ be the corresponding variety of pairs $(\mathbf{c}, \mathbf{d})$ coming from the model. Bihomogeneity of the radical ideal $I \subseteq \mathbb{R}[\mathbf{c}, \mathbf{d}]$ is equivalent to the following condition on the variety $V = V(I)$: for any pair $(\mathbf{c}, \mathbf{d}) \in V$ and any nonzero $\lambda, \delta \in \mathbb{C}$, $(\lambda \mathbf{c}, \delta \mathbf{d})$ is also in V.

Proposition 2.6.3. *For any series-parallel circuit network M, the vanishing ideal I_M is bihomogeneous in* $\mathbf{c}$ *and* $\mathbf{d}$.

Proof. We proceed by induction on the number of components in the network. The statement is clearly true if the networks have just one component, since the vanishing ideal is the zero ideal in that case.

By symmetry, we can suppose that the model is a series combination $M = M_1 \wedge M_2$. By induction, we can suppose that M_1 and M_2 satisfy the bihomogeneity assumption. For two sequences $\mathbf{c} = (c_0, c_1, c_2, \ldots)$ and $\mathbf{d} = (d_0, d_1, d_2, \ldots)$ let $\mathbf{c} * \mathbf{d}$ denote the convolution

$$\mathbf{c} * \mathbf{d} = (c_0 d_0, c_1 d_0 + c_0 d_1, c_2 d_0 + c_1 d_1 + c_0 d_2, \ldots).$$

Then, with this operation defined, we have that

$$M = \{(\mathbf{c} * \mathbf{c}', \mathbf{c} * \mathbf{d}' + \mathbf{c}' * \mathbf{d}) : (\mathbf{c}, \mathbf{d}) \in M_1, (\mathbf{c}', \mathbf{d}') \in M_2\}.$$

So, we need to show that if $(\mathbf{c}*\mathbf{c}', \mathbf{c}*\mathbf{d}'+\mathbf{c}'*\mathbf{d}) \in M$ and if $\lambda, \delta \in \mathbb{C}^*$ then $(\lambda(\mathbf{c}*\mathbf{c}'), \delta(\mathbf{c}*\mathbf{d}'+\mathbf{c}'*\mathbf{d})) \in M$. But by the inductive hypothesis, we know that if $(\mathbf{c}, \mathbf{d}) \in M_1$, $(\mathbf{c}', \mathbf{d}') \in M_2$, and $\lambda, \delta, \lambda', \delta'$ are nonzero then

$$(\lambda\lambda' \mathbf{c} * \mathbf{c}', \lambda\delta' \mathbf{c} * \mathbf{d}' + \lambda'\delta \mathbf{c}' * \mathbf{d}) \in M.$$

Taking $\lambda = \lambda$, $\lambda' = 1$, $\delta = \delta$ and $\delta' = \delta/\lambda$ gives the desired result. □

A second type of homogeneity also holds for the vanishing ideals of circuit models. We introduce a grading on the polynomial ring $\mathbb{R}[\mathbf{c}, \mathbf{d}]$ by setting $\deg(c_i) = \deg(d_i) = i$. The degree of a monomial $\deg(c^\alpha d^\beta)$ is the sum of the degrees of all variables in the monomial, counted with multiplicity. So, for example,

$$\deg(c_1^2 c_3 d_0 d_4) = 1 + 1 + 3 + 0 + 4 = 9.$$

A polynomial in $\mathbb{R}[\mathbf{c}, \mathbf{d}]$ in the degree grading is called homogeneous if every monomial appearing has the same degree. An ideal I_M is degree homogeneous if it has a generating set consisting of degree homogeneous polynomials. The notion of degree homogeneity can also be interpreted in terms of the corresponding variety, at least when the ideal is radical. Degree homogeneity of the radical ideal $I \subseteq \mathbb{R}[\mathbf{c}, \mathbf{d}]$ is equivalent to the following condition on the variety $V = V(I)$: for any pair $(\mathbf{c}, \mathbf{d}) \in V$ and any nonzero $\lambda \in \mathbb{C}$, $(\lambda^0 c_0, \lambda^1 c_1, \lambda^2 c_2, \ldots, \lambda^0 d_0, \lambda^1 d_1, \lambda^2 d_2,)$ is also in V. Denote the operation of applying λ to $(\mathbf{c}, \mathbf{d})$ in this way by $\lambda \cdot (\mathbf{c}, \mathbf{d}) = (\lambda \cdot \mathbf{c}, \lambda \cdot \mathbf{d})$.

Proposition 2.6.4. *For any series-parallel circuit network M, the vanishing ideal I_M is degree homogeneous in* $\mathbf{c}$ *and* $\mathbf{d}$.

Proof. We proceed by induction on the number of components in the network. The statement is clearly true if the networks have just one component, since the vanishing ideal is the zero ideal in that case.

By symmetry, we can suppose that the model is a series combination $M = M_1 \wedge M_2$. By induction, we can suppose that M_1 and M_2 satisfy the degree homogeneity assumption. As in the proof of Proposition 2.6.3, we need to show that if $(\mathbf{c}*\mathbf{c}', \mathbf{c}*\mathbf{d}' + \mathbf{c}'*\mathbf{d}) \in M$ and $\lambda \in \mathbb{C}^*$ then $(\lambda \cdot (\mathbf{c}*\mathbf{c}'), \lambda \cdot (\mathbf{c}*\mathbf{d}' + \mathbf{c}'*\mathbf{d}) \in M$. Note that $\cdot$ and $*$ interact in the following way:

$$(\lambda \cdot \mathbf{c}) * (\lambda \cdot \mathbf{c}') = \lambda \cdot (\mathbf{c} * \mathbf{c}')$$

with similar expressions holding for other combinations of $\mathbf{c}, \mathbf{d}, \mathbf{c}', \mathbf{d}'$. Since $\lambda \cdot (\mathbf{c}, \mathbf{d}) = (\lambda \cdot \mathbf{c}, \lambda \cdot \mathbf{d}) \in M_1$ and $\lambda \cdot (\mathbf{c}', \mathbf{d}') = (\lambda \cdot \mathbf{c}', \lambda \cdot \mathbf{d}') \in M_2$ we get that

$$((\lambda \cdot \mathbf{c}) * (\lambda \cdot \mathbf{c}'), (\lambda \cdot \mathbf{c}) * (\lambda \cdot \mathbf{d}') + (\lambda \cdot \mathbf{c}') * (\lambda \cdot \mathbf{d})) = (\lambda \cdot (\mathbf{c} * \mathbf{c}'), \lambda \cdot (\mathbf{c} * \mathbf{d}' + \mathbf{c}' * \mathbf{d}) \in M$$

which is the desired result. $\square$

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CHAPTER

3

IDENTIFIABLE PATHS AND CYCLES IN LINEAR COMPARTMENTAL MODELS

In this chapter, we expand upon the results in Meshkat and Sullivant (2014) and Meshkat et al. (2015) in the following ways. First, we consider the case of inputs and outputs not necessarily in the same compartment and define the analogous *identifiable path/cycle model* (Definition 3.2.4), which is a model where all the monomial functions associated to the directed cycles and paths from input to output are identifiable. Just as in Meshkat and Sullivant (2014), this occurs when the model has a coefficient map whose image has maximal dimension (Theorem 3.2.16). We then take these identifiable path/cycle models and remove leaks from all compartments except input/output compartments to achieve identifiable models (Theorem 3.2.23). A similar result was demonstrated in Meshkat et al. (2015), but in that version, the intersection of input and output compartments was nonempty, whereas in the present work the input and output compartments need not coincide. We then show that these identifiable path/cycle models yield the *only* identifiable models with certain conditions on their graph structure (Theorem 3.3.1). We thus provide necessary and sufficient conditions for identifiable models with certain graph properties (Corollary 3.3.4). We also give a sufficient condition for a model to be an identifiable path/cycle model which can be tested simply by examining the graph itself (Theorem 3.2.27). In addition, we weaken the conditions on the graph structure to obtain some necessary and sufficient conditions for identifiability (Corollary 3.4.11). We also give some necessary conditions for identifiability in terms of the structure of the graph (Theorems 3.5.1, 3.5.3, 3.5.4). Finally, we give a construction of identifiable models using results from Baaijens and Draisma (2016) (Algorithm 3.8.4).

Our results apply to a large class of linear compartmental models which arise in many real-world applications. Path models of the form in Proposition 3.2.34 arise in physiological models involving metabolism, biliary, or excretory pathways (DiStefano 2015) and models of neuronal dendritic trees (Bressloff and Taylor 1993). Path models also arise when modeling the delayed response to input and are called *time-delay models* (DiStefano 2015). One such example is Example 4.13 from DiStefano (2015) on oral dosing losses and delays in the gastrointestinal tract. Some other path models are considered in Section 3.6. More generally, we consider models that are *strongly input-output connected*. Mammillary and catenary models (DiStefano 2015) fall into this category, as well as a variation of mammillary and catenary models where input and output are in distinct neighboring compartments but the edge from output to input is missing (see Figure 3.1). More generally, our results apply to models that can be thought of as path models combined with catenary models and are considered in Section 3.6. Such a model could, for example, represent a time-delay model coupled with a catenary model.

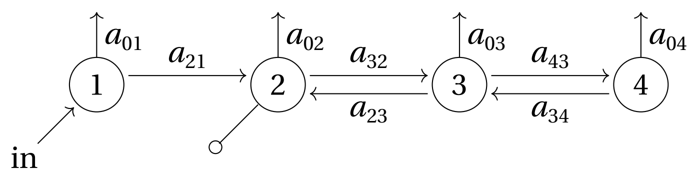
The organization of the chapter is as follows. Section 3.1 gives the necessary background. Section 3.2 gives the definition of an identifiable path/cycle model and how to obtain one. Section 3.3 gives a classification of all identifiable models with certain graph properties. Section 3.4 examines weaker conditions on the graph structure for necessary and sufficient conditions for identifiability. Section 3.5 gives necessary conditions for identifiability in terms of the graph structure of the model. Section 3.6 demonstrates our results on some real-world examples. Section 3.7 gives computations on the number of models with maximal dimension with a certain number of inputs and outputs. Finally, Section 3.8 gives a construction of identifiable models.

3.1 Preliminaries

First, we consider an example.

Table 3.1: Summary of main results of Chapter 3.

Result	**Explanation**
Corollary 3.3.4	Gives necessary and sufficient conditions for a strongly input-output connected model to be an identifiable path/cycle model
Theorem 3.2.27	Gives a sufficient condition to be an identifiable path/cycle model based on graph structure
Corollary 3.4.11	Gives necessary and sufficient conditions for an output connectable model to be an identifiable path/cycle model



$\mathscr{M}$

Figure 3.1: Graph for Example 3.1.1.

Example 3.1.1. The model $\mathscr{M} = (G, \{1\}, \{2\}, V)$ with G given in Figure 3.1 is a linear compartmental model with equations given by:

$$\begin{pmatrix} x_1' \\ x_2' \\ x_3' \\ x_4' \end{pmatrix} = \begin{pmatrix} -a_{01}-a_{21} & 0 & 0 & 0 \\ a_{21} & -a_{02}-a_{32} & a_{23} & 0 \\ 0 & a_{32} & -a_{03}-a_{23}-a_{43} & a_{34} \\ 0 & 0 & a_{43} & -a_{04}-a_{34} \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} + \begin{pmatrix} u_1 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \tag{3.1}$$

with output equation $y_2 = x_2$.

For a model $(G, In, Out, Leak)$ where there is a leak in every compartment (i.e. $Leak = V$), it can greatly simplify the representation to use the fact that the diagonal entries of A are the only places where the parameters a_{0i} appear. Since these are algebraically independent parameters, we can introduce a new algebraically independent parameter a_{ii} for the diagonal entries (i.e. we make the substitution $a_{ii} = -a_{0i} - \sum_{k:i\to k\in E} a_{ki}$) to get generic parameter values along the diagonal. Identifiability questions in such a model are equivalent

Table 3.2: Summary of which new results in this chapter generalize the prior results from Meshkat and Sullivant (2014) and Meshkat et al. (2015).

Prior Result	**New Result**	**Explanation**
Theorem 1.2 from Meshkat and Sullivant (2014)	Theorem 3.2.16	Generalizes conditions for identifiable cycle model to identifiable path/cycle model
Theorem 5 from Meshkat et al. (2015)	Theorem 3.2.23	Generalizes removing leaks to obtain identifiability
Theorem 5.13 from Meshkat and Sullivant (2014)	Theorem 3.2.27	Generalizes inductively strongly connected to almost inductively strongly connected
Proposition 5.4 from Meshkat and Sullivant (2014)	Proposition 3.2.34	Generalizes identifiable cycle to identifiable path
Proposition 5.5 from Meshkat and Sullivant (2014)	Proposition 3.2.35	Generalizes adding a new vertex
Proposition 5.3 from Meshkat and Sullivant (2014)	Theorem 3.5.3 Theorem 3.5.4	Generalizes necessary condition of having an exchange to having a path

to identifiability questions in the model with this reparametrized matrix.

We now define the path/cycle map for a model $\mathcal{M} = (G, In, Out, V)$:

Definition 3.1.2. Let $\mathscr{P} = \mathscr{P}(G)$ be the set of all directed cycles and paths from input to output vertices in the graph G. Define the *path/cycle* map by:

$$\pi : \mathbb{R}^{|E|+|V|} \to \mathbb{R}^{|\mathscr{P}|}, \mathscr{A} \mapsto (a^C)_{C \in \mathscr{P}} \tag{3.2}$$

Example 3.1.3 (Continuation of Example 3.1.1)**.** Consider the model $\mathcal{M} = (G, \{1\}, \{2\}, V)$ as described in Example 3.1.1. The path/cycle map for this model is

$$\pi : \mathbb{R}^9 \to \mathbb{R}^7$$
$$(a_{11}, a_{22}, a_{33}, a_{44}, a_{21}, a_{23}, a_{32}, a_{34}, a_{43}) \mapsto (a_{21}, a_{11}, a_{22}, a_{33}, a_{44}, a_{23}a_{32}, a_{34}a_{43})$$

Now we give some definitions from Gross et al. (2019) regarding an important subgraph to this work:

Definition 3.1.4. For a linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$, let $i \in Out$. The *output-reachable subgraph to i* (or *to y_i*) is the induced subgraph of G containing all vertices j for which there is a directed path in G from j to i. A linear compartmental model is *output connectable* if every compartment has a directed path leading from it to an output compartment.

We add the following definition:

Definition 3.1.5. A linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ is *output connectable to every output* if every compartment has a directed path leading from it to every output compartment.

We now state Theorem 3.8 from Gross et al. (2019) with input i and output j, which gives the input-output equation in y_j in terms of the output-reachable subgraph to y_j.

Theorem 3.1.6. *Let $\mathcal{M} = (G, In, Out, Leak)$ be a linear compartmental model with at least one input. Let $j \in Out$, and assume that there exists a directed path from some input compartment to compartment-j. Let H denote the output-reachable subgraph to y_j, let A_H denote the compartmental matrix for the restriction $\mathcal{M}_H$, and let ∂I be the the product of the differential operator d/dt and the $|V_G| \times |V_G|$ identity matrix. Then the following is an input-output equation for $\mathcal{M}$ involving y_j:*

$$\det(\partial I - A_H) y_j = \sum_{i \in In \cap V_H} (-1)^{i+j} \det(\partial I - A_H)_{ij} \, u_i \, , \tag{3.3}$$

where $(\partial I - A_H)_{ij}$ denotes the matrix obtained from $(\partial I - A_H)$ by removing the row corresponding to compartment-i and the column corresponding to compartment-j. Thus, this input-output equation (3.3) *involves only the output-reachable subgraph to y_j.*

Example 3.1.7 (Continuation of Example 3.1.1)**.** The model $\mathcal{M} = (G, \{1\}, \{2\}, V)$ with G given by the graph $\{\ 1 \to 2, 2 \to 3, 3 \to 2, 3 \to 4, 4 \to 3\ \}$ has leaks from every compartment, thus writing the diagonal elements as a_{ii}, we have the following input-output equation:

$$\begin{aligned}
& y_2^{(4)} + (-a_{11} - a_{22} - a_{33} - a_{44}) y_2^{(3)} \\
& \quad + (a_{11}a_{22} - a_{23}a_{32} + a_{11}a_{33} + a_{22}a_{33} - a_{34}a_{43} + a_{11}a_{44} + a_{22}a_{44} + a_{33}a_{44}) y_2'' \\
& \quad + (a_{11}a_{23}a_{32} - a_{11}a_{22}a_{33} + a_{11}a_{34}a_{43} + a_{22}a_{34}a_{43} - a_{11}a_{22}a_{44} + a_{23}a_{32}a_{44} - a_{11}a_{33}a_{44} - a_{22}a_{33}a_{44}) y_2' \\
& \quad + (-a_{11}a_{22}a_{34}a_{43} - a_{11}a_{23}a_{32}a_{44} + a_{11}a_{22}a_{33}a_{44}) y_2 \\
& = (a_{21}) u_1'' \\
& \quad + (-a_{21}a_{33} - a_{21}a_{44}) u_1' \\
& \quad + (a_{21}a_{33}a_{44} - a_{21}a_{34}a_{43}) u_1 \, .
\end{aligned}$$

3.1.1 Strongly input-output connected

In order to consider identifiable path/cycle models, we will be considering graphs G that have the special property of being connected and every edge is contained in a cycle or path from input to output. We call this *strongly input-output connected*:

Definition 3.1.8. We say a graph G is *strongly input-output connected* if it is connected and every edge is contained in a cycle or path from input to output.

We first show that, in the case of a single output, being strongly input-output connected implies being output connectable, so if we assume the former we get output connectable and can use Theorem 3.1.6 with the whole matrix A. Likewise, for the case of multiple outputs, we show that being strongly connected implies being output connectable to every output.

Proposition 3.1.9. *(1) Consider a model $\mathscr{M} = (G, In, \{j\}, Leak)$. Assume G is strongly input-output connected. Then G is output connectable. (2) Now consider a model $\mathscr{M} = (G, In, Out, Leak)$. Assume G is strongly connected. Then G is output connectable to every output.*

Proof. Let $\mathscr{M} = (G, In, \{j\}, Leak)$. Assume G is strongly input-output connected, i.e. it is connected and every edge is contained in a cycle or path from input to output. Since every edge contained in a path from input to output is connected to the output, we need only consider the edges in cycles. If a vertex in a cycle coincides with a vertex on a path from input to output, then we are done. Thus, assume that there exists a cycle whose vertices do not intersect with the vertices on paths from input to output. Since the graph is connected, the cycle must be attached via a directed edge from either the cycle to a path from input to output or vice versa. But the attaching edge must also be on a path from input to output. Thus for any edge from the path to the cycle, there must be a corresponding edge from the cycle to the path. Thus the graph is output connectable.

If $\mathscr{M} = (G, In, Out, Leak)$ and G is strongly connected, then since there is a path from each vertex to every other vertex, then G is output connectable to every output. □

Remark 3.1.10. Note that in Proposition 3.1.9, G must be strongly connected as opposed to strongly input-output connected when $\mathscr{M} = (G, \{i\}, Out, Leak)$, or else not every vertex may connect to *every* output.

Remark 3.1.11. A model that is strongly input-output connected in the case of a single output or strongly connected in the case of multiple outputs is always *structurally observable*

(Godfrey and Chapman 1990), as it is output connectable to every output by Proposition 3.1.9.

We now show that the property of being strongly input-output connected is *almost* strongly connected, in the sense that the graph becomes strongly connected once an edge is added (if not already there) from the output to every input if $\mathscr{M} = (G, In, \{j\}, Leak)$ or an edge is added from every output to the input if $\mathscr{M} = (G, \{i\}, Out, Leak)$.

Proposition 3.1.12. *(1) Consider a model $\mathscr{M} = (G, In, \{j\}, Leak)$. The model $\mathscr{M}$ is strongly connected if an edge is added from output j to every input if and only if it is strongly input-output connected. (2) Now consider a model $\mathscr{M} = (G, \{i\}, Out, Leak)$. The model $\mathscr{M}$ is strongly connected if an edge is added from every output to input i if and only if it is strongly input-output connected. Strongly connected implies strongly input-output connected.*

Proof. A model $\mathscr{M} = (G, In, \{j\}, Leak)$ is strongly connected if and only if it is connected and every edge is contained in a cycle. Thus a model $\mathscr{M} = (G, In, \{j\}, Leak)$ is strongly connected if a path from output j to every input is added if and only if it is connected and every edge is contained in a cycle or path from input to output, i.e. strongly input-output connected. Likewise, a model $\mathscr{M} = (G, \{i\}, Out, Leak)$ is strongly connected if a path from every output to input i is added if and only if it is connected and every edge is contained in a cycle or path from input to output, i.e. strongly input-output connected. Additionally, if a model is strongly connected, then it is strongly input-output connected, as every edge is contained in a cycle. □

We can also examine the *minimum* number of edges in order to be either strongly connected or strongly input-output connected:

Proposition 3.1.13. *If G is strongly connected, the minimum number of edges is $|V|$. If G is strongly input-output connected for input i and output j, the minimum number of edges is $|V|-1$.*

Proof. For G to be strongly connected, each vertex must have at least one incoming and one outgoing edge. Thus the minimum number of edges is $|V|$. If a graph is strongly input-output connected for input i and output j, then this means it becomes strongly connected if an edge is added from output j to input i (if not already there). This means the minimum number of edges is $|V|-1$. □

3.1.2 Expected number of coefficients

We first give a result from Meshkat et al. (2015), which we have reworded to agree with the new terminology in this work and have split into two parts: Proposition 3.1.14 shows that the coefficient map factors through, i.e. can be written purely in terms of, cycles, self-cycles and paths, and Lemma 3.1.18 gives the degree of the highest-order term on the right hand side of the input-output equation.

Proposition 3.1.14 (Proposition 5 from Meshkat et al. (2015))**.** *Let $\mathcal{M} = (G, In, \{j\}, V)$ represent a linear compartmental model that is output connectable. The coefficient map c factors through cycles, self-cycles, and paths from input to output.*

Proof. Let $\mathscr{C}(G)$ be the set of all cycles in G, corresponding to a matrix A. Recall that the coefficients of the characteristic polynomial of A can be written as

$$c_i = (-1)^i \sum_{C_1,\dots,C_k \in \mathscr{C}(G)} \prod_{j=1}^{k} \operatorname{sign}(C_j) a^{C_j},$$

where the sum is over all collections of vertex disjoint cycles involving exactly i edges of G, and $\operatorname{sign}(C) = 1$ if C is odd length and $\operatorname{sign}(C) = -1$ if C is even length. This means for every i, all cycles of length i appear as monomial terms in c_i, and for $j > i$, these cycles of length i appear as monomial products with other cycles in c_j.

By Theorem 3.1.6 and the fact that G is output connectable, meaning that the output-reachable subgraph of G is all of G, the input-output equation for y_j is given by:

$$\det(\partial I - A) y_j = \sum_{i \in In} (-1)^{i+j} \det(\partial I - A)_{ij} u_i. \tag{3.4}$$

This means the coefficients on the left hand side factor through the cycles in G.

Let us now examine these coefficients of the u_i terms in Equation (3.4). For $i = j$, the term $\det(\partial I - A)_{ii}$ gives the coefficients of the characteristic polynomial for the matrix A_{ii} with row i and column i removed, thus these coefficients factor through cycles of the induced subgraph removing vertex i.

Now assume $i \neq j$. The characteristic polynomial of A can be determined by expanding $\det(\partial I - A)$ along the i^{th} row. Let $\tilde{A}$ be the matrix A with the entry a_{ij} nonzero. Then for $i \neq j$, taking the partial derivative of the characteristic polynomial of $\tilde{A}$ with respect to a_{ij} precisely gives the polynomial $\det(\partial I - A)_{ij}$, up to a minus sign. Since the coefficients of the characteristic polynomial of $\tilde{A}$ factor through the cycles, then taking the derivative of these coefficients with respect to a_{ij} has the effect of removing all monomial terms not involving a_{ij} and setting a_{ij} to one in the monomial terms that do involve a_{ij}. This effectively transforms all cycles involving a_{ij} to paths from the i^{th} vertex to the j^{th} vertex. Thus, each of the monomial terms are products of paths from the i^{th} vertex to the j^{th} vertex, cycles, and self-cycles. In other words, coefficients are of the form:

$$c_m = (-1)^m \sum_{P_1,\dots,P_n \in \mathscr{P}(G)} \prod_{l=1}^{n} \operatorname{sign}(P_l) a^{P_l},$$

where the sum is over all collections of vertex disjoint cycles and paths from i to j involving exactly m edges of G, and $\operatorname{sign}(P) = 1$ if P is odd length and $\operatorname{sign}(P) = -1$ if P is even length.

Thus the coefficients can be factored over cycles, self-cycles, and paths from input to output. In other words, there is a polynomial map

$$\psi : \mathbb{R}^{|\mathscr{P}|} \to \mathbb{R}^k$$

which we will refer to as the path/cycle to coefficient map where k is the number of coefficients, such that $c = \psi \circ \pi$ where π is the path/cycle map from Equation 3.2. $\square$

Definition 3.1.15. Let the polynomial map ψ from the path/cycle space $\mathbb{R}^{|\mathscr{P}|}$ of an output connectable model $\mathscr{M}$ to its corresponding input-output equation coefficient space $\mathbb{R}^k$ be defined as the *path/cycle to coefficient map*.

Example 3.1.16 (Continuation of Example 3.1.1)**.** Consider the model $\mathscr{M} = (G, \{1\}, \{2\}, V)$ as described in Example 3.1.1. The path/cycle to coefficient map for this model is

$$\begin{aligned} \psi : \mathbb{R}^7 &\to \mathbb{R}^7 \\ (p_1, p_2, p_3, p_4, p_5, p_6, p_7) &\mapsto \begin{pmatrix} -p_2 - p_3 - p_4 - p_5 \\ p_2p_3 - p_6 + p_2p_4 + p_3p_4 - p_7 + p_2p_5 + p_3p_5 + p_4p_5 \\ p_2p_6 - p_2p_3p_4 + p_2p_7 + p_3p_7 - p_2p_3p_5 + p_5p_6 - p_2p_4p_5 - p_3p_4p_5 \\ -p_2p_3p_7 - p_2p_5p_6 + p_2p_3p_4p_5 \\ p_1 \\ -p_1p_4 - p_1p_5 \\ p_1p_4p_5 - p_1p_7 \end{pmatrix}^{\mathsf{T}} \end{aligned}$$

Note that the composition of the path/cycle map π in Example 3.1.3 and the path/cycle to coefficient map ψ in Example 3.1.16 yields the coefficients of the input-output equation for $\mathscr{M}$ as shown in Example 3.1.7.

We will be writing the number of coefficients in terms of the minimal distance between an input and output compartment. We define this now:

Definition 3.1.17. Let i be an input compartment and let j be an output compartment, $i \neq j$. Let $\mathscr{P}(i,j)$ be the set of all paths from vertex i to vertex j. Let $l(P)$ denote the length of a path $P \in \mathscr{P}$. Then we can define the minimum length of all paths from vertex i to vertex j as $\mathrm{dist(i,j)} = \min_{\mathrm{P}\in\mathscr{P}(\mathrm{i,j})} l(P)$.

Lemma 3.1.18 (Proposition 5 from Meshkat et al. (2015))**.** *Let $\mathscr{M} = (G, In, \{j\}, V)$ represent a linear compartmental model with $\mathscr{M}$ output connectable. The highest-order term in u_i where $i \in In$ on the right hand side of the input-output equation, Equation (3.4), is of degree $|V| - 1 - \mathrm{dist(i,j)}$.*

Proof. Let $\tilde{A}$ be the matrix A with the entry a_{ij} nonzero. Let $\mathscr{C}(\tilde{G})$ be the set of all cycles in $\tilde{G}$, corresponding to a matrix $\tilde{A}$. To determine the coefficient of the highest-order term in u_i, recall that the coefficients of the characteristic polynomial of $\tilde{A}$ can be written as

$$c_m = (-1)^m \sum_{C_1,\ldots,C_k \in \mathscr{C}(\tilde{G})} \prod_{l=1}^{k} \mathrm{sign}(C_l) a^{C_l},$$

where the sum is over all collections of vertex disjoint cycles involving exactly i edges of $\tilde{G}$, and $\mathrm{sign}(C) = 1$ if C is odd length and $\mathrm{sign}(C) = -1$ if C is even length. This means for every m, all cycles of length m appear as monomial terms in c_m, and for $l > m$, these cycles of length m appear as monomial products with other cycles in c_l.

We now determine the highest-order term in u_i. Since $\det(\partial I - A)_{ij}$ is just the partial derivative of the characteristic polynomial of $\tilde{A}$ with respect to a_{ij}, up to a minus sign, then the right-hand side of the input-output equation for output y_j is of the form, where $n = |V|$:

$$\sum_{i\in In} (-1)^{i+j} \left(\frac{\partial c_1}{\partial a_{ij}} u_i^{(n-1)} + \frac{\partial c_2}{\partial a_{ij}} u_i^{(n-2)} + \frac{\partial c_3}{\partial a_{ij}} u_i^{(n-3)} + \cdots + \frac{\partial c_n}{\partial a_{ij}} u_i \right)$$

We note that not all of these coefficients $\frac{\partial c_k}{\partial a_{ij}}$ for $k = 1, \ldots, n$ are nonzero and thus we must determine the first nonzero coefficient.

Recall Definition 3.1.17 for the minimal distance between i and j. Let the length of the shortest cycle involving a_{ij} be of length $\mathrm{dist(i,j)} + 1$, so that the length of the shortest path from i to j is of length $\mathrm{dist(i,j)}$. Then the coefficient of the highest-order term in u_i is $\partial c_{\mathrm{dist(i,j)}+1} / \partial a_{ij}$, which is a sum of the shortest paths (of length $\mathrm{dist(i,j)}$) from i to j. Thus it is of the form $\sum_{P\in\mathscr{P}(i,j):l(P)=\text{dist(i,j)}} a^P$. This means the highest-order term in u_i is of degree $|V|-(\text{dist(i,j)}+1)=\text{|V|}-1-\text{dist(i,j)}$. $\square$

We now give a formula for the number of coefficients of the input-output equation in the case of either single input or single output.

Theorem 3.1.19 (Number of nonzero coefficients)**.** *Let $\mathscr{M}=(G,\{i_1,i_2,...,i_{|In|}\},\{j\},L)$ represent a linear compartmental model with G output connectable with at least $|In\cup Out|$ leaks with $In\cup Out\subseteq L$. There are $|V|+n|V|-\sum_k \text{dist(i}_\text{k}\text{, j)}+\text{m(|V|}-1)$ nonzero coefficients where $n=|In-Out|$ and $m=|In\cap Out|$. Now let $\mathscr{M}=(G,\{i\},\{j_1,j_2,...,j_{|Out|}\},L)$ represent a linear compartmental model with G output connectable to every output with at least $|In\cup Out|$ leaks with $In\cup Out\subseteq L$. There are $|V|+n|V|-\sum_k \text{dist(i, j}_\text{k}))+\text{m(|V|}-1)$ nonzero coefficients where $n=|Out-In|$ and $m=|In\cap Out|$.*

Proof. Assume $\mathscr{M}=(G,\{i_1,i_2,...,i_{|In|}\},\{j\},L)$ is a linear compartmental model with G output connectable with at least $|In\cup Out|$ leaks with $In\cup Out\subseteq L$. By Equation (3.4), the highest degree term is $|V|$ on the left hand side. For the right hand side, $|In\cap Out|$ is either 1 or 0. If $|In\cap Out|=1$, then the highest-order term in u_j is of degree $|V|-1$ on the right hand side. The highest-order term in u_j is monic, so there are $|V|-1$ coefficients of terms in u_j. For each $i\in In-Out$, the highest degree term in u_i is of order $|V|-1-\text{dist(i,j)}$ on the right hand side by Lemma 3.1.18. In this case, the highest-order term in u_i is not monic, so there are $|V|-1-\text{dist(i,j)}+1=\text{|V|}-\text{dist(i,j)}$ coefficients of terms in u_i when $i\neq j$. Altogether, there are $|V|+n|V|-\sum_k \text{dist(i}_\text{k}\text{, j))}+\text{m(|V|}-1)$ nonzero coefficients where $n=|In-Out|$ and $m=|In\cap Out|$.

For the case with multiple outputs, let $\mathscr{M}=(G,\{i\},\{j_1,j_2,...,j_{|Out|}\},L)$ represent a linear compartmental model with G output connectable to every output with at least $|In\cup Out|$ leaks with $In\cup Out\subseteq L$. By applying the formula for the case of single output above for each input-output equation, we obtain that there are $|V|+n|V|-\sum_k \text{dist(i, j}_\text{k}))+\text{m(|V|}-1)$ nonzero coefficients where $n=|Out-In|$ and $m=|In\cap Out|$.

We need only show that the coefficients are nonzero (for a generic choice of parameters).

If there are leaks from every compartment, Proposition 3.1.14 shows that the coefficients factor through cycles, self-cycles, and paths from input to output.

Now consider the case of removing leaks. We will be substituting a_{ii} as the negative sum of all outgoing edges when $i\notin L$, but if $i\in L$ then a_{ii} stays the same. Since $In\cup Out\subseteq L$, we have that every compartment has an outgoing edge or leak, as every vertex has an outgoing edge except for possibly the output vertex by the output connectable assumption. This means the substitution a_{ii} as the negative sum of all outgoing edges and leaks retains the (i,i) entry of A to be nonzero.

Recall by Proposition 3.1.14, these coefficients can be factored over cycles, self-cycles, and paths when $L = V$. Each coefficient, except for the highest order coefficient in u_{i_k} when $i_k \neq j$ (which is a sum of paths from i_k to j), must have a term involving a self-cycle. If the self-cycles in every coefficient are only from leak compartments, we are done. Otherwise, consider a coefficient that has terms involving self-cycles from non-leak compartments which we must substitute into for the case $L \subset V$. We want to show that the substitution of the non-leak diagonal terms as the negative sum of all outgoing edges does not cancel every term in that coefficient, so that the coefficients remain nonzero after substitution. We claim that the substitution of a_{kk} as the negative sum of all outgoing edges for $k \notin L$ cannot create only terms that are products of cycles and paths from input to output. Since the graph must be output connectable, any cycle formed from the non-leak vertices must connect to the output. In other words, for a chain of vertices in a cycle $k_1, k_2, ..., k_l$, one of these vertices must connect to the output via a path from that vertex to the output. Without loss of generality, assume it is vertex k_1. Thus the substitution of the non-leaks $a_{k_1k_1}$, $a_{k_2k_2}$, ...,$a_{k_lk_l}$ cannot create a single monomial term of the form $\pm a_{k_1k_2}a_{k_2k_3}\cdots a_{k_lk_1}$, but must also create a monomial $\pm a_{k_1k_2}a_{k_2k_3}\cdots a_{rk_1}$ where we have substituted $a_{k_1k_1}$ as $-a_{k_lk_1} - a_{rk_1}$ for some vertex r that connects via a path to the output.

This monomial $a_{k_1k_2}a_{k_2k_3}\cdots a_{rk_1}$ cannot itself be a path from input to output, as the input and output vertices have leaks and thus the corresponding diagonal terms do not get substituted. Thus, it is not a path from input to output, and thus cannot cancel with any other terms in that coefficient. □

Remark 3.1.20. We note that the assumption of at least $|In \cup Out|$ leaks with $In \cup Out \subseteq L$ and G to be output connectable is to prevent the situation where there are no outgoing edges or leaks from a non-leak vertex and thus upon substitution of the diagonal element a_{ii} as the negative sum of all outgoing edges and leaks, it becomes zero.

Definition 3.1.21 (Expected number of coefficients)**.** We say a model $\mathcal{M} = (G, \{i_1, i_2, ..., i_{|In|}\}, \{j\}, L)$ with $In \cup Out \subseteq L$ has the *expected number of coefficients* if there are $|V| + n|V| - \sum_k \mathrm{dist(i_k, j)} + \mathrm{m(|V| - 1)}$ nonzero coefficients in the input-output equations (3.3) where $n = |In - Out|$ and $m = |In \cap Out|$. We say $\mathcal{M} = (G, \{i\}, \{j_1, j_2, ..., j_{|Out|}\}, L)$ with $In \cup Out \subseteq L$ has the *expected number of coefficients* if there are $|V| + n|V| - \sum_k \mathrm{dist(i, j_k)} + \mathrm{m(|V| - 1)}$ nonzero coefficients in the input-output equations (3.3) where $n = |Out - In|$ and $m = |In \cap Out|$.

3.2 Identifiable path/cycle models

Definition 3.2.1. We say a model $\mathscr{M} = (G, In, Out, V)$ has a coefficient map with *expected dimension* if the dimension of the image of the coefficient map is maximal.

We will be examining a special class of models we call *identifiable path/cycle models*. This class of models is a generalization of *identifiable cycle models* as defined in Meshkat et al. (2015):

Definition 3.2.2 (Identifiable Cycle Models)**.** We say a model $\mathscr{M} = (G, \{i\}, \{i\}, V)$ with G strongly connected is an *identifiable cycle model* if all of the independent monomial cycles in the model are locally identifiable.

Example 3.2.3. The models $(G, \{1\}, \{1\}, V)$ and $(H, \{1\}, \{1\}, V)$ where G corresponds to a chain of exchanges $1 \longleftrightarrow 2, 2 \longleftrightarrow 3$, etc, and H correspond to a central compartment given by compartment 1 and exchanges $1 \longleftrightarrow 2, 1 \longleftrightarrow 3$, etc, are identifiable cycle models due to Theorem 5.13 of Meshkat and Sullivant (2014). The first model is commonly called a *catenary* model and the second model is called a *mammillary* model (DiStefano 2015).

It was shown in Meshkat and Sullivant (2014) that a sufficient condition for a model to be an identifiable cycle model is that the dimension of the image of the coefficient map is $|E|+1$. We now define the main object of interest in this chapter, *identifiable path/cycle models* and spend the rest of this section forming analogous sufficient conditions on the dimension of the image of the coefficient map.

Definition 3.2.4 (Identifiable Path/Cycle Models)**.** We say a model $\mathscr{M} = (G, In, Out, V)$ is an *identifiable path/cycle model* if all of the independent monomial cycles and monomial paths from input to output in the model are locally identifiable and each parameter is contained in such a cycle or path.

Remark 3.2.5. As identifiable path/cycle models require all of the cycles and paths from input to output in the model to be identifiable, it only makes sense to consider models that are *connected and every edge is contained in a cycle or path from input to output*, i.e. strongly input-output connected. Otherwise, an edge that is not contained in a cycle or path from input to output will not appear in the coefficient map.

Example 3.2.6 (Continuation of Example 3.1.1)**.** The model $\mathscr{M} = (G, \{1\}, \{2\}, V)$ with G given by the graph $\{\ 1 \to 2, 2 \to 3, 3 \to 2, 3 \to 4, 4 \to 3\ \}$ is an identifiable path/cycle model, with identifiable paths and cycles given by $a_{11}, a_{22}, a_{33}, a_{44}, a_{21}, a_{23}a_{32}, a_{34}a_{43}$. This can be demonstrated by writing each path and cycle as a function of the coefficients c_i, e.g. using Groebner Bases. Further justification will come from Theorem 3.2.16.

For models with leaks from every compartment, the dimension of the image of the coefficient map is bounded above by the number of independent paths and cycles in the graph from Proposition 3.1.14. We now determine what this number is. We first show that when G is output connectable for the case of single output, there are $|E|+|In \cup Out|$ independent directed paths and undirected cycles. We then examine the case where G is strongly input-output connected so that the indicator vectors for the independent directed paths and directed cycles in the graph correspond to 0/1 vectors. We show that this number of independent paths and cycles is equal to $|E|+|In \cup Out|$.

We define the $|V|$ by $|E|$ *incidence matrix* $E(G)$ as:

$$E(G)_{i,(j,k)} = \begin{cases} 1 & \text{if } i=j \\ -1 & \text{if } i=k \\ 0 & \text{otherwise.} \end{cases} \tag{3.5}$$

In other words, $E(G)$ has column vectors corresponding to the edges $j \to k \in E$ with a 1 in the jth row, -1 in the kth row, and 0 otherwise. We define the *indicator vector* of a directed cycle C as the vector $(x_s)_{s\in E}$ such that $x_s = 1$ if $s \in E_C$ and $x_s = 0$ if $s \notin E_C$, where E_C is the set of edges associated to the directed cycle C.

We can also define the *indicator vector* of an undirected cycle C' with associated directed cycle C (reversing arrows to all point in the same direction) as the vector $(x_s)_{s\in E}$ such that $x_s = 1$ if $s \in E_C$, $x_s = -1$ if $-s \in E_C$, and $x_s = 0$ if $s \notin E_C$, where E_C is the set of edges associated to the directed cycle C and $-s$ corresponds to an edge s going in the opposite direction. In other words, if s corresponds to $i \to j$, then $-s$ corresponds to $j \to i$.

The rank of the directed incidence matrix is well-known:

Proposition 3.2.7 (Proposition 4.3 of Biggs (1993))**.** *Let G be a graph with $|V|$ vertices, $|E|$ edges, and l connected components. Then the rank of $E(G)$ is $|V|-l$. Thus, the dimension of the kernel of $E(G)$ is $|E|-|V|+l$.*

We state one final result from Meshkat et al. (2015), which shows that the kernel of $E(G)$ can be written in terms of $|E|-|V|+1$ directed cycles when G is strongly connected, thus the indicator vectors are 0/1 vectors:

Proposition 3.2.8. *[Proposition 4 of Meshkat et al. (2015)] Let G be a strongly connected graph. Then a set of $|E|-|V|+1$ linearly independent indicator vectors of directed cycles form a basis for the kernel of $E(G)$.*

In other words, this proposition shows that the space of all undirected cycles can be generated by the space of all directed cycles when G is strongly connected. We now prove a similar result in terms of cycles and paths from input to output when G is strongly input-output connected.

Proposition 3.2.9. *Let $\mathcal{M} = (G, In, Out, V)$ represent a linear compartmental model with G strongly input-output connected. Then the space of all directed paths and undirected cycles can be generated by the space of all directed paths and directed cycles and vice versa.*

Proof. Let B have as its columns the indicator vectors of all directed paths and undirected cycles. We show that, for every undirected cycle, we can add a positive integer multiple of a directed path vector or directed cycle vector to obtain either a directed cycle or directed path from input to output. Since G is strongly input-output connected, every edge is in either a cycle or path from input to output. For every edge with a negative entry in the indicator vector of an undirected cycle, that edge either belongs to a cycle or path from input to output. If it belongs to a path from input to output, one can add a positive multiple of the path to the undirected cycle to achieve only non-negative entries corresponding to a closed path or path from input to output. If it does not belong to a path from input to output, then it belongs to a directed cycle. Thus one can add a positive multiple of the directed cycle to the undirected cycle to achieve only non-negative entries corresponding to a closed path or path from input to output. In either case, this corresponds to a multigraph with the property that the indegree of each vertex equals the outdegree of each vertex except possibly at input and output vertices. Cycles can be removed so that the result is a cycle or a path from input to output. □

Lemma 3.2.10. *Let $\mathcal{M} = (G, In, Out, V)$ represent a linear compartmental model with G output connectable if $|Out| = 1$ or G strongly input-output connected otherwise. Then the number of independent undirected cycles and directed paths from input to output is $|E| + |In \cup Out|$.*

Proof. Let the matrix B have as columns the indicator vectors of the *undirected* cycles and directed paths from input to output vertices. Since G is either output connectable in the single output case or strongly input-output connected, then G is certainly connected, and thus there are $|E| - |V| + 1$ undirected cycles that form a basis for the kernel of $E(G)$ and there must be at least one path from input to output, so B is certainly not the zero matrix. Form the product $E(G)B$. If column k of B corresponds to a cycle, then column k of $E(G)B$

will be zero, and if column k of B corresponds to a path from input in i and output in j, then column k of $E(G)B$ will have a 1 in row i and a -1 in row j.

Remove the zero columns and duplicate columns (which occur when there is more than one path from an input to an output) and zero rows from this matrix $E(G)B$ and call the resulting matrix M. We claim M is the incidence matrix of the graph where there are $|In \cup Out|$ vertices corresponding to each input/output compartment and there is a directed edge from an input compartment to an output compartment if and only if there is a path from the corresponding input to the corresponding output in the graph G. Call this graph G_M. Note that there are only $|In \cup Out|$ vertices in G_M because we deleted zero rows from the matrix $E(G)B$ to obtain the matrix M, thus deleting vertices that do not correspond to inputs or outputs. This graph G_M must be connected because we assumed G is output connectable in the single output case and strongly input-output connected otherwise. Since the rank of the incidence matrix for a connected graph is the number of vertices minus one, this means the rank of $E(G)B$ is $|In \cup Out| - 1$.

Since the rank of $E(G)B$ is equal to the rank of B minus the dimension of the column space of B intersected with the kernel of $E(G)$, which is exactly $|E| - |V| + 1$ because B is generated by paths and undirected cycles and a basis for the kernel of $E(G)$ is given by undirected cycles, then this means the rank of B is exactly $|E| - |V| + 1 + |In \cup Out| - 1 = |E| - |V| + |In \cup Out|$. Adding the $|V|$ self-cycles, we obtain that the dimension of the path/cycle map is $|V| + |E| - |V| + |In \cup Out| = |E| + |In \cup Out|$. □

Corollary 3.2.11. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model with G strongly input-output connected. Then the number of independent directed cycles and directed paths from input to output is $|E| + |In \cup Out|$.*

Proof. If $|Out| = 1$, strongly input-output connected implies output connectable and if $|Out| > 1$, we have strongly input-output connected. The statement follows from Lemma 3.2.10 and Proposition 3.2.9 to achieve a set of $|E| + |In \cup Out|$ independent directed cycles and directed paths from input to output. □

We now show that the dimension of the image of the coefficient map is bounded above by the number of independent paths and cycles. We will add the important assumption of either $|In| = 1$ or $|Out| = 1$ so that the number of distinct input-output pairs equals $|In \cup Out| - 1$, described in the Remark below. For $|Out| = 1$ we can assume G is strongly input-output connected as stated in Corollary 3.2.11, but for the case of $|In| = 1$ we will assume G is strongly connected in order to ensure the input-output equations are irreducible as

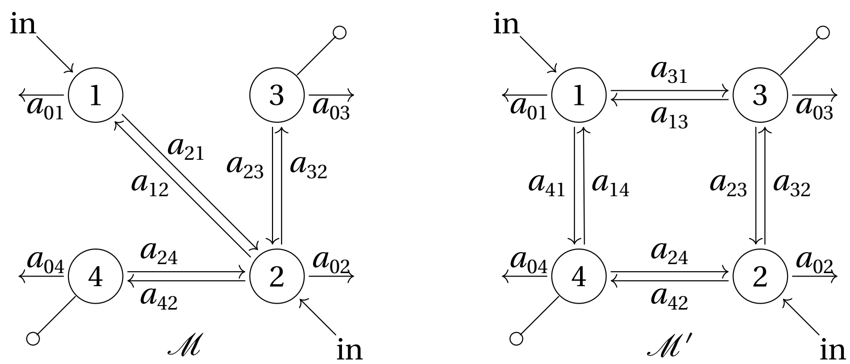


Figure 3.2: The models $\mathscr{M}$ and $\mathscr{M}'$ from Example 3.2.14.

shown in Section 2. For the special case where $|In| = |Out| = 1$ and $In = Out$, we note that strongly input-output connected reduces to strongly connected. For the special case where $|In| = |Out| = 1$ and $In \neq Out$, then strongly input-output connected is sufficient in what follows, i.e. we can take the weaker of the two conditions strongly input-output connected and strongly connected.

Lemma 3.2.12. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model. Assume that either G is strongly input-output connected and $|Out| = 1$ or G is strongly connected and $|In| = 1$. The dimension of the image of the coefficient map is bounded above by $|E| + |In \cup Out|$.*

Proof. The coefficient map factors through the cycles, self-cycles, and paths from input to output from Proposition 3.1.14. By Corollary 3.2.11, the number of independent paths and cycles is $|E| + |In \cup Out|$. Thus the dimension of the image of the coefficient map is bounded above by $|E| + |In \cup Out|$. $\square$

Remark 3.2.13. We require $|In| = 1$ or $|Out| = 1$ so that there are either $|Out| - |In \cap Out|$ or $|In| - |In \cap Out|$ distinct input-output pairs, respectively, which equals $|In \cup Out| - 1$, the rank of $E(G)B$ in the proof of Lemma 3.2.10. Example 3.2.14 demonstrates this.

Example 3.2.14. The model $\mathscr{M} = (G, \{1,2\}, \{3,4\}, V)$ seen in Figure 3.2. Note that $\mathscr{M}$ has $|E| + |In \cup Out| = 10$ independent paths and cycles but the coefficient map factors over 11 paths and cycles given by $a_{12}a_{21}$, $a_{23}a_{32}$, $a_{24}a_{42}$, a_{32}, a_{42}, $a_{21}a_{32}$, $a_{21}a_{42}$, a_{11}, a_{22}, a_{33}, a_{44}. The problem here is that there are only 10 parameters, but we are attempting to factor over 11 paths and cycles. This is why we require $|In| = 1$ or $|Out| = 1$. However, this is a sufficient condition but not a necessary condition, as the model $\mathscr{M}' = (G', \{1,2\}, \{3,4\}, V)$ seen in Figure 3.2 has $|E|+|In \cup Out| = 12$ independent paths and cycles given by a_{31}, a_{41}, a_{32}, a_{42}, $a_{13}a_{31}$, $a_{14}a_{41}$, $a_{23}a_{32}$, $a_{24}a_{42}$, a_{11}, a_{22}, a_{33}, a_{44} and the coefficient map factors over these as well.

Remark 3.2.15. Notice that in Lemma 3.2.12, we assume that G is either strongly input-output connected or strongly connected. We have just shown that the expected dimension in this case is $|E|+|In \cup Out|$. But a natural question that arises is, what if we do not assume this connectedness condition on G? Clearly, we still have that the coefficient map factors through cycles and paths. In this case there will be *at most* $|E|+|In \cup Out|$ independent cycles and paths that appear in the coefficient map, i.e. the coefficient map may factor over fewer than $|E|+|In \cup Out|$ independent paths and cycles. See Section 3.4.

This gives us the following theorem:

Theorem 3.2.16. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model with either G strongly input-output connected and $|Out| = 1$ or G strongly connected and $|In| = 1$. If the image of the coefficient map has dimension $|E|+|In \cup Out|$, then the model is an identifiable path/cycle model.*

Proof. By Lemma 3.2.12, the dimension of the image of the coefficient map is bounded above by $|E|+|In \cup Out|$, which is also the number of independent paths and cycles. Recall a function f is locally identifiable if there is a finitely multivalued function ϕ : $\mathbb{R}^{|E|+|In \cup Out|} \to \mathbb{R}$ such that $\phi \circ c = f$. Let $\pi : \mathbb{R}^{|E|+|V|} \to \mathbb{R}^{|E|+|In \cup Out|}$ be the path/cycle map from Equation 3.2. Since $c : \mathbb{R}^{|E|+|V|} \to \mathbb{R}^{|E|+|In \cup Out|}$ factors over paths and cycles, then there exists a function $\psi : \mathbb{R}^{|E|+|In \cup Out|} \to \mathbb{R}^{|E|+|In \cup Out|}$ as defined in Definition 3.1.15 such that $c = \psi \circ \pi$. If the dimension of the image of the coefficient map is precisely $|E|+|In \cup Out|$, then this function ψ is locally invertible with $\psi^{-1} = \phi$ and thus $\pi = \phi \circ c$. Thus the paths and cycles are identifiable. □

Example 3.2.17 (Continuation of Example 3.1.1)**.** The model $\mathscr{M} = (G, \{1\}, \{2\}, V)$ from Example 3.1.1 can be shown to have dimension of the image of the coefficient map equal to $|E|+|In \cup Out| = 5+2 = 7$. Thus there are 7 identifiable paths and cycles given by the monomials $a_{11}, a_{22}, a_{33}, a_{44}, a_{21}, a_{23}a_{32}, a_{34}a_{43}$.

3.2.1 Necessary condition for number of edges and the edge inequality

Proposition 3.2.18. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model with either G strongly input-output connected and $|Out| = 1$ or G strongly connected and*

$|In| = 1$. *If $\mathcal{M} = (G, In, Out, V)$ is an identifiable path/cycle model, then $|E| + |In \cup Out| \leq$ the expected number of coefficients.*

Proof. We have that the dimension of the image of the coefficient map is bounded above by the expected number of coefficients, as it cannot exceed the number of coefficients. Thus $|E| + |In \cup Out| \leq$ the expected number of coefficients. $\square$

Definition 3.2.19 (Edge inequality)**.** We say that a model has a number of edges given by the *edge inequality* if the number of edges $|E|$ satisfies $|E| + |In \cup Out| \leq$ the expected number of coefficients.

We can also show that the property of being strongly input-output connected is a necessary condition for having expected dimension in the case of maximal number of edges.

Proposition 3.2.20. *Let $\mathcal{M} = (G, In, Out, V)$ with G output connectable and $|Out| = 1$ represent a linear compartmental model for which the edge inequality is an equality with expected dimension $|E| + |In \cup Out|$. Then the graph must be strongly input-output connected.*

Proof. Assume the coefficient map has expected dimension $|E| + |In \cup Out|$ with the maximal number of edges. This means the expected dimension is the number of coefficients. If the graph is not connected with every edge in a cycle or path from input to output, then there are parameters that do not appear in the coefficient map, and thus the coefficient map factors over fewer than $|E| + |In \cup Out|$ independent paths and cycles. But this contradicts having expected dimension $|E| + |In \cup Out|$. $\square$

Remark 3.2.21. If there are fewer edges, we can still achieve expected dimension without this condition of strongly input-output connected. In other words, being strongly input-output connected is a sufficient but not necessary condition to achieve $|E| + |In \cup Out|$ independent cycles and paths in the coefficient map. See Section 3.4.

3.2.2 Obtaining identifiability by removing leaks

In this section, we show that removing all leaks except leaks from input/output compartments results in identifiability, much like the results in Meshkat et al. (2015). We will follow the same proof. Recall that for an identifiable path/cycle model, we have the coefficient map $c : \mathbb{R}^{|V|+|E|} \to \mathbb{R}^k$. Let $\pi : \mathbb{R}^{|V|+|E|} \to \mathbb{R}^{|E|+|In \cup Out|}$ be the path/cycle map from Equation

3.2, that is $\pi(A(G)) = (a^P : P$ is a cycle or path from input to output of $G)$. Then Proposition 3.1.14 tells us that c factors through π without loss of dimension. Thus $c = \psi \circ \pi$ where ψ is defined as in Definition 3.1.15 and the dimension of the image of c equals the dimension of the image of π.

Passing from a model (G, In, Out, V) to a model $(G, In, Out, Leak)$ such that $|Leak| = |In \cup Out|$ amounts to restricting the parameter space $\mathbb{R}^{|V|+|E|}$ to a linear subspace $\Lambda \subseteq \mathbb{R}^{|V|+|E|}$ of dimension $|E|+|Leak|$ and we would like the image of Λ under the coefficient map c to have dimension $|E|+|Leak|$. Since c factors through the path/cycle map π it suffices to prove that the image of Λ under π has dimension $|E|+|Leak|$.

Lemma 3.2.22. *Let $G = (V, E)$ be a directed graph with corresponding identifiable path/cycle model (G, In, Out, V). Assume that either G is strongly input-output connected and $|Out| = 1$ or G is strongly connected and $|In| = 1$. Consider a model (G, In, Out, L) where $In \cup Out \subseteq L$. Let $\pi : \mathbb{R}^{|V|+|E|} \to \mathbb{R}^{|E|+|In \cup Out|}$ denote the path/cycle map. Let $\Lambda \subseteq \mathbb{R}^{|V|+|E|}$ be the linear space satisfying*

$$\Lambda = \{\mathscr{A} \in \mathbb{R}^{|V|+|E|} : a_{ii} = -\sum_{j, j \neq i} a_{ji} \text{ for all } i \notin L\}.$$

Then the dimension of the image of Λ under the map π is $|E|+|In \cup Out|$.

Proof. Since Λ is a linear space, we just consider the natural map from $\mathbb{R}^{|E|+|L|} \to \mathbb{R}^{|E|+|In \cup Out|}$ which maps to the path/cycle space. To show that the dimension of the image of this map is correct, we consider the Jacobian of this map and show that it has full rank.

Note that the rows corresponding to the $|L|$ self-cycles are linearly independent so we focus on the $|E|+|In \cup Out|-|L|$ by $|E|$ submatrix ignoring those rows and columns, which we will call J. Arrange the matrix so that the first $|E|-|V|+|In \cup Out|$ rows correspond to the paths and cycles of G and the last $|V|-|L|$ rows correspond to the non-leak diagonal elements. Let the first $|E|-|V|+|In \cup Out|$ rows be called A and the last $|V|-|L|$ rows be called B. Clearly the rows of A are linearly independent by Lemma 3.2.12. The rows of B are linearly independent since they are in triangular form since each involves distinct parameters. To show that the full set of $|E|+|In \cup Out|-|L|$ rows are linearly independent, we need only show that the row space of A and the row space of B intersect only in the origin.

To prove that J generically has maximal possible rank, it is enough to show that there is some point where the evaluation of J at said point yields the maximal rank. We choose the point where we set all the edge parameters $a_{ij} = 1$ for all $j \to i \in E$. This specialization yields that the row space of A is exactly the path/cycle space of the graph G, i.e. all of the weightings on the edges of the graph where the indegree equals the outdegree of every vertex in a cycle and every vertex except the first and last in a path from input to output. Also, we have that the matrix B which has dimension $(|V|-|L|)\times(|E|)$, which consists of the rows corresponding to the vertices in $V \setminus L$, and the (negated) row corresponding to vertex i has a one for an edge $i' \to j'$ if and only if $i = i'$, with all other entries zero.

Since A spans the path/cycle space of G, each element in the row space of A corresponds to a weighting on the edges of G where the total weight of all incoming edges at a vertex i equals the total weight of all outgoing edges at vertex i except at input or output vertices $In \cup Out$. On the other hand, we claim that the only vector in the row span of B with the same property is the zero vector. To show this, let b_i be the row vector associated to some vertex i. Note that a vector in the row span of B will have zero weight on any of the outgoing edges of vertices in $In \cup Out$.

In order for the indegree to equal the outdegree, we would need to include a b_j with an edge pointing toward vertex i. Continuing in this way, we can only stop when we have included an input or output vertex since the indegree need not equal the outdegree for those vertices. However, this contradicts the fact that a vector in the row span of B will have zero weight on any of the outgoing edges of vertices in $In \cup Out$. □

Theorem 3.2.23 (Removing Leaks)**.** *Let $\mathcal{M} = (G, In, Out, V)$ represent a linear compartmental model. Assume that either G is strongly input-output connected and $|Out| = 1$ or G is strongly connected and $|In| = 1$. Assume it is an identifiable path/cycle model. Then, the corresponding model $\widetilde{\mathcal{M}} = (G, In, Out, L)$ where $In \cup Out \subseteq L$ for any such L has expected dimension. In particular, if $L = In \cup Out$, then $\widetilde{\mathcal{M}}$ is locally identifiable.*

Proof. By Lemma 3.2.22 and the comments preceding it we know that the image of the restricted parameter space under the path/cycle map π has dimension $|E|+|In \cup Out|$, which is equal to the dimension of the image of the full parameter space under the path/cycle map. Since, for an identifiable path/cycle model, the dimension of the image of the coefficient map c is $|E|+|In \cup Out|$, this must be the same for the restricted model. In particular, if $|L| = |In \cup Out|$, then the model has $|E|+|In \cup Out|$ parameters, hence it is locally identifiable. □

Example 3.2.24 (Continuation of Example 3.1.1)**.** The model $\widetilde{\mathcal{M}} = (G, \{1\}, \{2\}, \{1, 2\})$ seen in Figure 3.3 obtained from the model in Example 3.1.1 by removing two leaks and leaving the leaks in the input and output compartments is locally identifiable.

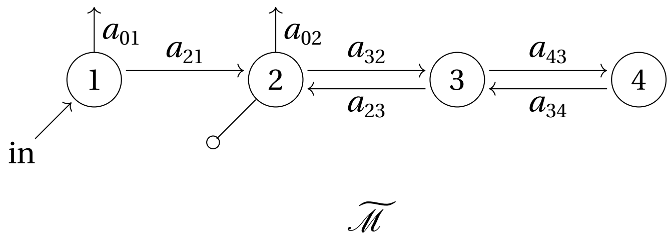


Figure 3.3: Graph for model corresponding to $\widetilde{\mathscr{M}}$ in Example 3.2.24.

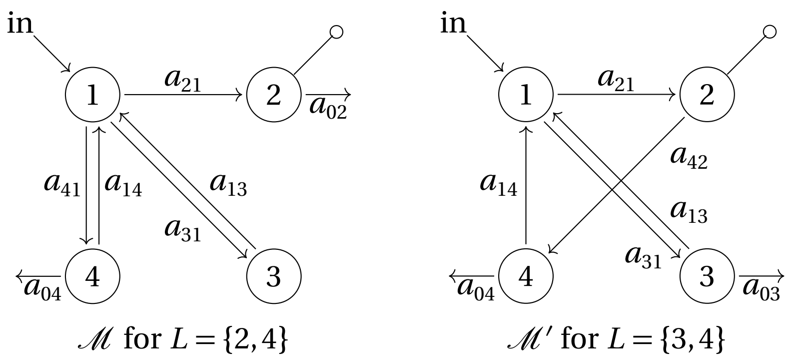


Figure 3.4: On the left is the graph corresponding to $\mathscr{M}$ with leak set $L = \{2,4\}$, and on the right is the graph corresponding to $\mathscr{M}'$ with leak set $L = \{3,4\}$ from Example 3.2.26.

Remark 3.2.25. We note that, while $L = In \cup Out$ is sufficient in Theorem 3.2.23, it is certainly not necessary, as there are other possible configurations of $|L| = |In \cup Out|$ leaks that also result in identifiability. The next example demonstrates this.

Example 3.2.26. Consider the model $\mathscr{M} = (G, \{1\}, \{2\}, L)$ see in Figure 3.4 where $|L| = |In \cup Out| = 2$ and G is given by the edges $\{\ 1 \to 2, 1 \to 3, 3 \to 1, 1 \to 4, 4 \to 1\ \}$. The identifiable models are the ones where $L = \{2,4\}, \{2,3\}, \{1,2\}$ and the unidentifiable models have $L = \{3,4\}, \{1,4\}, \{1,3\}$.

We note that while $2 \in L$ appears to be sufficient for identifiability in this model, we can consider another model given by $\mathscr{M}' = (G', \{1\}, \{2\}, L)$ also seen in Figure 3.4 where $|L| = |In \cup Out| = 2$ and G' is given by the edges $\{\ 1 \to 2, 3 \to 1, 4 \to 1, 1 \to 3, 2 \to 4\ \}$. The identifiable models are the ones where $L = \{3,4\}, \{2,3\}, \{1,4\}, \{1,2\}$ and the unidentifiable models have $L = \{2,4\}, \{1,3\}$. This shows the pattern of identifiability depends on the graph structure itself and not just the placement of inputs and outputs.

3.2.3 Sufficient condition for identifiable path/cycle model

We now give a sufficient condition for a model to be an identifiable path/cycle model with 1 input and 1 output. This sufficient condition is analogous to the sufficient condition from Meshkat and Sullivant (2014) of inductively strongly connected for models with input and output in the same compartment. In fact, Theorem 3.2.27 reduces to Theorem 5.13 of Meshkat and Sullivant (2014) if the input and output compartments are the same.

Theorem 3.2.27. *Let $\mathcal{M} = (G, \{i\}, \{j\}, V)$ represent a linear compartmental model with G strongly input-output connected and $|E| = 2|V| - (\mathrm{dist(i,j)} + 2)$. If $\mathcal{M} = (G, \{i\}, \{j\}, V)$ has no path from compartment j to compartment i but becomes inductively strongly connected if an edge from compartment j to compartment i is added, then $\mathcal{M}$ is an identifiable path/cycle model.*

Before we prove Theorem 3.2.27, we define a graph structure which will be useful in the proof.

Definition 3.2.28 (Definition 5.6 from Meshkat and Sullivant (2014))**.** A *chain of cycles* is a graph H which consists of a sequence of directed cycles that are attached to each other in a chain by joining at the vertices.

Theorem 3.2.29. *Suppose $\mathcal{M}' = (G', \{i\}, \{j\}, V)$ represents a linear compartmental model with G' strongly input-output connected and $|E| = 2|V| - (\mathrm{dist(i,j)} + 2)$. Suppose too that $\mathcal{M}'$ has expected dimension and also that $\mathcal{M}'$ has no path from j to i and becomes inductively strongly connected if the edge from j to i is added. Then, if G is a new graph obtained from G' by adding a vertex n and two edges $k \to n$ and $n \to l$ such that G has a chain of cycles containing either i and n or j and n, then the model $\mathcal{M} = (G, \{i\}, \{j\}, V \cup \{n\})$ has expected dimension.*

Recall that we can induce a *weight order* on a polynomial ring $\mathbb{K}[x_1, \ldots, x_n]$ for some weight vector $\omega \in \mathbb{Q}^n$ where the weight of a monomial $x_1^{\alpha_1} \cdots x_n^{\alpha_n}$ is $\omega \cdot \alpha$ where $\alpha = (\alpha_1, \ldots, \alpha_n)$. We can then define the *initial forms* of a polynomial f as $\mathrm{in}_\omega(\mathrm{f})$ to be the sum of all terms of f whose monomial has the highest weight with respect to said ω.

Now, if we define the coefficient map associated to the graph G as $\phi_G : \mathbb{R}^{|V|+|E|} \longrightarrow \mathbb{R}^k$, then we can also consider the pull-back of said map defined as $\phi_G^* : \mathbb{K}[c, d] \to \mathbb{K}[a]$ where c, d correspond to the coefficients of the left and right-hand side of the input-output equation respectively, and a corresponds to the parameters found in compartmental matrix A. Now define $\phi_{G,\omega}$ to be the initial parameterization defined as the parameterization with pullback $\phi_{G,\omega}^*$ where $\phi_{G,\omega}^*(f) = \mathrm{in}_\omega(\mathrm{f})$ for a given weight ω.

Lemma 3.2.30 (Corollary 5.9, Meshkat and Sullivant (2014))**.** *Let $\phi^*\colon \mathbb{K}[x] \to \mathbb{K}[y]$ be a $\mathbb{K}$-algebra homomorphism and $\omega \in \mathbb{Q}^m$ a weight vector, then*

$$\dim(\mathrm{im}\phi_\omega) \leq \dim(\mathrm{im}\phi).$$

We will use Lemma 3.2.30 in the following way. We want to compute the dimension of the image of a polynomial parametrization ϕ. We know for other reasons an upper bound d on this dimension. We have a weight vector ω where we can compute the dimension of the image of the polynomial parametrization ϕ_ω, and we show it is equal to d. Then, by Lemma 3.2.30, we know that the dimension of the image of ϕ must be d.

Proof of Theorem 3.2.29. Suppose $\mathcal{M}' = (G', \{i\}, \{j\}, V)$ is a linear compartmental model with expected dimension such that G' is strongly input-output connected, $|E| = 2|V| - (\text{dist(i, j)} + 2)$. Also suppose that if we add the edge from j to i, the new graph becomes inductively strongly connected. Note that by Theorem 3.1.19, the input-output equation of the model $\mathcal{M}'$ has $2|V| - \text{dist(i, j)}$ nonzero, non-monic coefficients. Let $|V| = n-1$ and $m = |E|$.

Define $\phi_G\colon \mathbb{R}^{|V|+|E|} \to \mathbb{R}^{2|V|-\text{dist(i,j)}}$, to be the coefficient map associated to a graph G as above with corresponding pull-back ϕ_G^*. Choose weight ω as follows:

$$\omega_{uv} = \begin{cases} 0 & \text{if } (u,v) = (n,n) \\ \frac{1}{2} & \text{if } (u,v) = (n,k) \text{ or } (l,n) \\ 1 & \text{otherwise.} \end{cases}$$

Recall that for each coefficient, the corresponding polynomial function is homogeneous in terms of the parameters. Also, recall that the left-hand side coefficients are generated by cycles of the corresponding graph, while the right-hand side coefficients are generated by products of cycles of the corresponding graph along with paths from the input to output.

Applying this weight to the polynomial coefficients has the effect of removing any monomial containing a cycle which is incident to compartment n, in all coefficients except for the lowest order terms in both c and d. Note that in the case of c_n and d_{n-1}, each of the monomials in the sum will have a cycle incident to n, meaning that each of them has the same weight.

More explicitly, in terms of the pull-back maps we have in all cases that

$$
\begin{aligned}
\phi^*_{G,\omega}(c_i) &= \phi^*_{G'}(c_i) \quad i = 1,\dots,n-1\\
\phi^*_{G,\omega}(d_i) &= \phi^*_{G'}(d_i) \quad i = \mathrm{dist(i,j)},\dots,\mathrm{n}-2\\
\phi^*_{G,\omega}(c_n) &= \phi^*_{G}(c_n)\\
\phi^*_{G,\omega}(d_{n-1}) &= \phi^*_{G}(d_{n-1}).
\end{aligned}
$$

Thus, $\phi_{G,\omega}$ agrees with $\phi_{G'}$ everywhere except for the highest order coefficients on either side of the input-output equation, in which case $\phi_{G,\omega}$ matches ϕ_G. This implies that the Jacobian matrix corresponding to $\phi_{G,\omega}$ defined as $J(\phi_{G,\omega})$ (whose generic rank yields the dimension of the image of the map), has the form

$$
J(\phi_{G,\omega}) = \begin{pmatrix} J(\phi_{G'}) & 0 \\ * & C \end{pmatrix}
$$

where $J(\phi_{G'})$ is the $(2n-(\mathrm{dist(i,j)}+2))\times(\mathrm{n+m}-3)$ Jacobian matrix of $\phi_{G'}$ and C is the 2×3 matrix

$$
C = \begin{pmatrix} \frac{\partial c_n}{\partial a_{nn}} & \frac{\partial c_n}{\partial a_{ln}} & \frac{\partial c_n}{\partial a_{nk}} \\ \frac{\partial d_{n-1}}{\partial a_{nn}} & \frac{\partial d_{n-1}}{\partial a_{ln}} & \frac{\partial d_{n-1}}{\partial a_{nk}} \end{pmatrix}
$$

where l and k are the nodes to which the added node n has an edge to and from respectively.

Note that we assume that the model corresponding to G' has expected dimension, hence $J(\phi_{G'})$ has rank $2(n-1)-\mathrm{dist(i,j)}$. Since $J(\phi_G)$ is lower block triangular, to show that it has rank $2n-\mathrm{dist(i,j)}$, we need only show that C has generic rank 2.

Let H be a chain of cycles in G defined as $s_2,\dots,s_t$ in order such that s_2 is a cycle containing either the input or the output and s_t is the cycle containing the node n. Also, define s_1 to be one of the shortest paths from i to j.

Now we will choose entries for the matrix A such that the matrix C has rank 2. First, let all diagonal elements of A be 1, i.e. $a_{kk}=1$ for all $k=1,\dots,n$. Also, let $a_{uv}=0$ for all edges $v\to u\notin H$. For all edges in H, for each cycle s_i, choose the edge weights so that the product of edges' weights is equal to $(-1)^{\ell(s_i)-1}$, that is so that the product of the edges in the cycle is equivalent to the sign of the cycle. For s_1, choose edge weights so that the product of the edges' weights is also equal to $(-1)^{\ell(s_i)-1}$.

First, consider the entry $\frac{\partial c_n}{\partial a_{nn}}$. The only nonzero monomials appearing here will arise from taking products of the cycles $s_2,\dots,s_{t-1}$, since the cycle s_t cannot be involved, as we only consider the elements of the sum of c_n with a_{nn} as a factor. Also, s_1 is not a cycle, hence cannot be part of any of the c_i. Since each cycle touches its two neighboring cycles, and no other cycles, and in the expansion we expand over all products of nontouching cycles that cover all n vertices, we get that the number of monomials will equal the number of subsets of $\{2,\ldots,t-1\}$ with no adjacent elements. By Lemma 3.2.31, this is exactly F_t.

Now consider the entry $\frac{\partial d_{n-1}}{\partial a_{nn}}$, which will arise from taking products of $s_1, s_3, \ldots, s_{t-1}$, since we must have s_1, hence cannot have s_2, and by similar reasoning above cannot have s_t. Thus, we get that the number of monomials are the number of nonadjacent subsets of $\{s_3,\ldots,s_{t-1}\}$, hence we get the Fibonacci number F_{t-1}.

In the case of the entry $\frac{\partial c_n}{\partial a_{ln}}$ or equivalently $\frac{\partial c_n}{\partial a_{nk}}$, we must use the cycle s_t prohibiting us from using s_{t-1}, and again must not use s_1. This yields that the number of monomials is the number of nonadjacent subsets of $s_2,\ldots,s_{t-2}$, i.e. the Fibonacci number F_{t-1}.

Finally, when considering entry $\frac{\partial d_{n-1}}{\partial a_{ln}}$ or equivalently $\frac{\partial d_{n-1}}{\partial a_{nk}}$, we must use s_1 and cycles s_t, hence cannot use cycles s_2 or s_{t-1}. This means that the number of monomials will be the number of nonadjacent subsets of $s_3,\ldots,s_{t-2}$, i.e. the Fibonacci number F_{t-2}.

Thus, the submatrix C will have the form

$$C = \begin{pmatrix} F_t & F_{t-1} & F_{t-1} \\ F_{t-1} & F_{t-2} & F_{t-2} \end{pmatrix}.$$

The classical identity of Fibonacci number $F_t F_{t-2} - F_{t-1}^2 = (-1)^{t-1}$ yields that this matrix has full rank. hence, the Jacobian of $\phi^*_{G,\omega}$ has full rank.

Note that the upper bound for the number of coefficients of the input-output equation, i.e. the upper bound on the dimension of the image of the coefficient map is $2n - \text{dist(i, j)}$ via Theorem 3.1.19. Thus, because $\dim(\text{im}(\phi^*_{\mathrm{G},\omega})) \leq \dim(\text{im}(\phi^*_{\mathrm{G}}))$ by Lemma 3.2.30, and $\dim(\text{im}(\phi^*_{\mathrm{G}}))$ is bounded above by $2n - \text{dist(i, j)}$, we have that $\dim(\text{im}(\phi^*_{\mathrm{G}})) = 2\text{n} - \text{dist(i, j)}$ as desired. □

Lemma 3.2.31. *The number of subsets S of $\{1,2,\ldots,n\}$ such that S contains no pair of adjacent numbers is the $n+2$-nd Fibonacci number, F_{n+2} which satisfies the recurrence $F_0 = 0$, $F_1 = 1$, and $F_{n+1} = F_n + F_{n-1}$.*

We can now prove Theorem 3.2.27.

Proof of Theorem 3.2.27. By Theorem 3.2.29 and the inductive nature of inductively strongly connected graphs, it suffices to show that every inductively strongly connected graph beginning with a cycle between i and j has a chain of cycles containing the vertices i and n (or, analogously, a chain of cycles containing the vertices j and n).

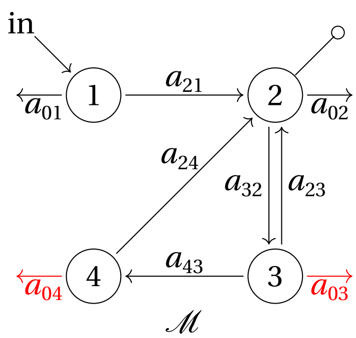


Figure 3.5: The model $\mathscr{M}$ corresponds to the above graph with all four leaks, while the graph $\mathscr{M}'$ has the same graph with only the black leaks, that is leaks in compartments 1 and 2, all from Example 3.2.33.

We prove this by induction on n. Since G is inductively strongly connected if the edge from j to i is added, there is a nontrivial cycle c that passes through the vertex n. If c contains i, we are done. Otherwise, let q be the smallest vertex appearing in c, and let G' be the induced subgraph on $\{i, j, \ldots, q\}$. By induction, G' has a chain of cycles containing i and q. Attaching c to H gives a chain of cycles in G containing i and n. A similar argument can be applied to give a chain of cycles in G containing j and n. □

Theorem 3.2.27 is not only useful as a sufficient condition for an identifiable path/cycle model, but it is also useful as a means to start with an identifiable path/cycle model and then remove leaks to obtain identifiability:

Corollary 3.2.32. *Let $\mathscr{M} = (G, \{i\}, \{j\}, V)$ represent a linear compartmental model with G strongly input-output connected and $|E| = 2|V| - (\mathrm{dist(i,j)} + 2)$. If $\mathscr{M} = (G, \{i\}, \{j\}, V)$ has no path from compartment j to compartment i but becomes inductively strongly connected if the edge from compartment j to compartment i is added, then $\mathscr{M}' = (G, \{i\}, \{j\}, \{i, j\})$ is locally identifiable, i.e. removing all but two leaks in the input/output compartments.*

Proof. This follows from Theorem 3.2.27 and Theorem 3.2.23. □

Example 3.2.33. The model $\mathscr{M} = (G, \{1\}, \{2\}, V)$ seen in Figure 3.5 with G given by the edges $\{1 \to 2, 2 \to 3, 3 \to 4, 4 \to 2, 3 \to 2\}$ is an identifiable path/cycle model by Theorem 3.2.27. Thus, the model $\mathscr{M}' = (G, \{1\}, \{2\}, \{1, 2\})$ where we remove all but two leaks from the input/output compartments is locally identifiable.

We also note that, as cycles with input/output in the same compartment were shown to have expected dimension in Meshkat and Sullivant (2014) (see Proposition 5.4), paths from input to output can be shown to have expected dimension as well.

Proposition 3.2.34. *Let $\mathcal{M} = (G, \{1\}, \{|V|\}, V)$ be a linear compartmental model with G given by a path from input 1 to output $|V|$ with $|V|-1$ edges. Then $\mathcal{M}$ is an identifiable path/cycle model and the model $\widetilde{\mathcal{M}} = (G, \{1\}, \{|V|\}, \{1, |V|\})$ is locally identifiable.*

Proof. Let $n = |V|$. Assume $\mathcal{M} = (G, \{1\}, \{n\}, V)$ is a linear compartmental model with G given by a path from input 1 to output n with $n-1$ edges. Recall the coefficients on the left hand side of the input-output equation are given by the characteristic polynomial of A, which is:

$$(\lambda - a_{11})(\lambda - a_{22}) \cdots (\lambda - a_{nn})$$

Since the roots of a polynomial can be determined from its coeffiicents, then all of $a_{11}, a_{22}, \ldots, a_{nn}$ are locally identifiable. Since the degree of the highest-order term on the right hand side of the input-output equation is n—1—dist(1, n) by Lemma 3.1.18, this reduces to zero so the right hand side is $a_{n,n-1} \cdots a_{32} a_{21} u_n$. Thus the monomial path $a_{n,n-1} \cdots a_{32} a_{21}$ is identifiable. This means the dimension of the image of the coefficient map is $|E| + |In \cup Out| = n - 1 + 2 = n + 1$ which is the number of paths and cycles, thus the model is an identifiable path/cycle model. By Theorem 3.2.23, the model $\widetilde{\mathcal{M}} = (G, \{1\}, \{n\}, \{1, n\})$ is locally identifiable. □

In Meshkat and Sullivant (2014), it was shown in Proposition 5.5 that if a model $\mathcal{M} = (G, \{1\}, \{1\}, V)$ has expected dimension, then the model $\mathcal{M} = (G', \{1'\}, \{1'\}, V)$ also has expected dimension, where G' is the new graph obtained from G by adding a new vertex $1'$ and an exchange $1 \to 1', 1' \to 1$ and making $1'$ the new input-output node. We show an analogous result now:

Proposition 3.2.35. *Let $\mathcal{M} = (G, \{1\}, \{j\}, V)$ be a linear compartmental model that has expected dimension where $|V| = n$ and $j \neq 1$. Let G' be a new graph obtained from G by adding a set of new vertices $n+1, n+2, \ldots, n+k$ and a set of edges $n+1 \to 1, n+2 \to n+1, \ldots, n+k \to n+(k-1)$ and making $n+k$ the new input node. Then the model $\widetilde{\mathcal{M}} = (G', \{n+k\}, \{j\}, V \cup \{n+1, n+2, \ldots, n+k\})$ also has expected dimension.*

Proof. Let A be the full matrix associated to the graph G' where the first k rows and k columns correspond to the added path from compartment $n+k$ to compartment 1, A_k

be the matrix where the first k rows and first k columns have been deleted (and, hence associated to the graph G), and let E_G be the edges of the graph G. We assume that the dimension of the image of the map c associated to the model $\mathcal{M} = (G, \{1\}, \{j\}, V)$ is $|E_G| + |In \cup Out| = |E_G| + 2$, and we want to show that for the model $\widetilde{\mathcal{M}} = (G', \{n+k\}, \{j\}, V \cup \{n+1, n+2, \ldots, n+k\})$ we get $|E_{G'}| + 2 = |E_G| + k + 2$, as we are adding k new edges.

The input-output equation for the model $\widetilde{\mathcal{M}} = (G', \{n+k\}, \{j\}, V \cup \{n+1, n+2, \ldots, n+k\})$ is:

$$\det(\partial I - A) y_j = \det(\partial I - A)_{1,j+k} u_{n+k}$$

where $\det(\partial I - A) = (\partial - a_{n+1,n+1}) \cdots (\partial - a_{n+k,n+k}) \det(\partial I - A_k)$ and $\det(\partial I - A)_{1,j+k} = a_{1,n+1} a_{n+2,n+1} \cdots a_{n+k,n+k-1} \det(\partial I - A_k)_{1j}$. The input-output equation for the model $\mathcal{M} = (G, \{1\}, \{j\}, V)$ is:

$$\det(\partial I - A_k) y_j = \det(\partial I - A_k)_{1j} u_1$$

For notational ease, we write ∂ as λ, $|V| = n$, $p = (a_{n+1,n+1}, \ldots, a_{n+k,n+k})$, and $q = a_{1,n+1} a_{n+2,n+1} \cdots a_{n+k,n+k-1}$. Note that p is the vector of new self-cycles and q can be interpreted as the added monomial path from compartment $n+k$ to compartment 1. We can write $\det(\lambda I - A_k)$ as:

$$\lambda^n + c_1 \lambda^{n-1} + \ldots + c_{n-1} \lambda + c_n$$

and we can write $\det(\lambda I - A_k)_{1j}$ as

$$d_1 \lambda^{n-1} + d_2 \lambda^{n-2} + \ldots + d_{n-1} \lambda + d_n.$$

Thus $\det(\lambda I - A) = (\lambda - a_{n+1,n+1}) \cdots (\lambda - a_{n+k,n+k}) \det(\lambda I - A_k)$ can be written as (up to a minus sign):

$$\begin{aligned}\lambda^{n+k} &+ (c_1 - S_1(p))\lambda^{n+k-1} + (c_2 - c_1 S_1(p) + S_2(p))\lambda^{n+k-2} + (c_3 - c_2 S_1(p) + c_1 S_2(p) - S_3(p))\lambda^{n+k-3} \\ &+ \ldots + (c_k - c_{k-1} S_1(p) + c_{k-2} S_2(p) - \ldots - S_k(p))\lambda^n \\ &+ \ldots + (c_n - c_{n-1} S_1(p) + c_{n-2} S_2(p) - \ldots - c_{n-k} S_k(p))\lambda^k \\ &+ (-c_n S_1(p) + \ldots + c_{n-k+2} S_{k-1}(p) - c_{n-k+1} S_k(p))\lambda^{k-1} \\ &+ \ldots + (-c_n S_{k-2}(p) + c_{n-1} S_{k-1}(p) - c_{n-2} S_k(p))\lambda^2 + (c_n S_{k-1}(p) - c_{n-1} S_k(p))\lambda - c_n S_k(p) \quad (3.6)\end{aligned}$$

where $S_1(p), \ldots, S_k(p)$ are the k elementary symmetric polynomials in the parameter vector

p. Here we assumed $n > k$, but an analogous formula follows for the case of $n \leq k$.

We will refer to the non-constant coefficients of $\det(\lambda I - A)$ as $C_1, \ldots, C_{n+k}$. Note that these are by assumption identifiable. Likewise,

$$\det(\lambda I - A)_{1,j+k} = q d_1 \lambda^{n-1} + q d_2 \lambda^{n-2} + \ldots + q d_{n-1}\lambda + q d_n. \tag{3.7}$$

We will refer to the coefficients of $\det(\lambda I - A)_{1,j+k}$ as $D_1, \ldots, D_n$. Note that these are by assumption identifiable. We must now show that if the mapping given by $(c_1, \ldots, c_n, d_1, \ldots, d_n)$ has expected dimension, then the new mapping $(C_1, \ldots, C_{n+k}, D_1, \ldots, D_n)$ also has expected dimension. Since the parameters in p are roots of the polynomial $\det(\lambda I - A)$, then this means these parameters can be written in terms of the coefficients $(C_1, \ldots, C_{n+k})$, which are identifiable, and thus the parameters in p are identifiable. This means each of the elementary symmetric polynomials $S_1(p), \ldots, S_k(p)$ are identifiable. Since C_1 and $S_1(p)$ are identifiable from Equation 3.6, then c_1 can be recovered from the first coefficient from Equation 3.6. Likewise, since C_2, c_1, $S_1(p)$, and $S_2(p)$ are identifiable, then c_2 can be recovered from the second coefficient of Equation 3.6. Continuing in this fashion, we can recover $c_1, \ldots, c_n$, i.e. $c_1, \ldots, c_n$ are identifiable. This means the dimension of the image of $(C_1, \ldots, C_{n+k})$ is k more than the dimension of the image of $(c_1, \ldots, c_n)$. Since the coefficients of Equation 3.7 are just the coefficients $d_1, \ldots, d_n$ scaled by q, which contains disjoint parameters from the parameters in the coefficients $c_1, \ldots, c_n, d_1, \ldots, d_n$, then the dimension of the image of $(D_1, \ldots, D_n)$ is the same as the dimension of the image of $(d_1, \ldots, d_n)$. The parameters in p do not appear in $(D_1, \ldots, D_n)$, thus combining the maps $(C_1, \ldots, C_{n+k})$ and $(D_1, \ldots, D_n)$ we have that the dimension of the image of the new map $(C_1, \ldots, C_{n+k}, D_1, \ldots, D_n)$ must be k more than the dimension of the image of $(c_1, \ldots, c_n, d_1, \ldots, d_n)$ due to the identifiability of the parameters in p. Thus the model $\widetilde{\mathcal{M}} = (G', \{n+k\}, \{j\}, V \cup \{n+1, n+2, \ldots, n+k\})$ has dimension of the image of the coefficient map equal to $|E_G| + k + 2$, i.e. k more than $\mathcal{M} = (G, \{1\}, \{j\}, V)$.

□

3.3 Classification of all identifiable models that are strongly input-output connected with 1 output or strongly connected with 1 input and leaks in input/output compartments

The following Theorem 3.3.1 gives necessary conditions for strongly input-output connected models with 1 output or strongly connected models with 1 input with leaks in input/output compartments to be identifiable, namely that they must be identifiable path/cycle models when all the leaks are added to the model.

3.3.1 Necessary conditions for identifiability

Theorem 3.3.1 (Adding Leaks)**.** *Let $\mathcal{M} = (G, In, Out, L)$ represent a linear compartmental model with $|L| = |In \cup Out|$ and either G strongly input-output connected and $|Out| = 1$ or G strongly connected and $|In| = 1$ which we assume has expected dimension, i.e. has dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$. Then, the corresponding model with an additional leak $\widetilde{\mathcal{M}} = (G, In, Out, L \cup \{k\})$ also has expected dimension. Thus the model $\widetilde{\mathcal{M}} = (G, In, Out, Leak)$ where $L \subseteq Leak$ and $|Leak| \leq |V|$ also has expected dimension.*

Proof. Suppose $\mathcal{M} = (G, In, Out, L)$ is a linear compartmental model with either G strongly input-output connected and $|Out| = 1$ or G strongly conencted and $|In| = 1$ and $|L| = |In \cup Out|$ which we assume has expected dimension, i.e. has dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$.

Note that because we assume that $\mathcal{M}$ has expected dimension and $|L|$ leaks, this implies that the Jacobian of the coefficient map has the expected number of coefficients as the number of rows and $(|E| + |In \cup Out|)$ columns with full rank $|E| + |In \cup Out|$. Note too that the addition of the $|V| - |L|$ parameters from the leaks being added to the model $\mathcal{M}$ will not increase the number of coefficients in the resulting input-output equation, as the number of coefficients is the maximal amount by Theorem 3.1.19.

Therefore, the Jacobian of the coefficient map of the model $\widetilde{\mathcal{M}} = (G, In, Out, V)$ generated by forcing every compartment in $\mathcal{M}$ to have a leak, has the same number of rows but now $(|E| + |V|)$ columns. The dimension of the image of the coefficient map is bounded above by the number of cycles and paths when there are $|V|$ leaks, which is $|E| + |In \cup Out|$.

Thus adding $|V|-|L|$ leaks to a $|L|$-leak model cannot increase the dimension of the image of the coefficient map above $|E|+|In \cup Out|$ if it has already achieved that dimension with $|L|$ leaks.

Note then that if we consider the specialization generated by substituting zero for every added leak, and consider the submatrix of said Jacobian with expected number of coefficients as the number of rows and $(|E|+|In \cup Out|)$ columns generated by the $(|E|+|In \cup Out|)$ columns corresponding to the edges and leaks in L, we have exactly the Jacobian of the coefficient map of $\mathcal{M}$, which we know is full rank. Therefore, we have that the Jacobian of the coefficient map of $\widetilde{\mathcal{M}}$ is also full rank, implying that the model has expected dimension.

The same argument applies for adding any number of leaks up to $|V|$ total leaks. □

Remark 3.3.2. We note that while Theorem 3.2.23 and Theorem 3.3.1 assume opposite operations of adding or subtracting leaks, we have the condition in Theorem 3.2.23 that $In \cup Out \subseteq Leak$, while in Theorem 3.3.1 only $|Leak| = |In \cup Out|$ is assumed, i.e. only the number and not the placement of leaks matters.

3.3.2 Necessary and sufficient conditions for identifiability

Combining Theorem 3.3.1 with Theorem 3.2.23, we now come to the main result of this section and obtain the following necessary and sufficient conditions for identifiable models:

Corollary 3.3.3. *Let $\mathcal{M} = (G, \{i\}, \{i\}, \{k\})$ represent a linear compartmental model with G strongly connected and let $\widetilde{\mathcal{M}} = (G, \{i\}, \{i\}, V)$ be the corresponding model with a leak in every compartment. $\mathcal{M}$ is locally identifiable if and only if $\widetilde{\mathcal{M}}$ is an identifiable cycle model.*

Proof. This follows from combining Theorem 3.3.1 and Theorem 1 of Meshkat et al. (2015) (also written as Theorem 3.8.3). □

Corollary 3.3.4. *Let $\mathcal{M} = (G, In, Out, L)$ represent a linear compartmental model with and $L = In \cup Out$ and assume that either G is strongly input-output connected and $|Out| = 1$ or G is strongly connected and $|In| = 1$. Let $\widetilde{\mathcal{M}} = (G, In, Out, V)$ be the corresponding model with a leak in every compartment. $\mathcal{M}$ is locally identifiable if and only if $\widetilde{\mathcal{M}}$ is an identifiable path/cycle model.*

Proof. This follow from combining Theorem 3.3.1 and Theorem 3.2.23. □

Remark 3.3.5. Corollary 3.3.4 gives us a complete classification of all identifiable models that are strongly input-output connected with 1 output or strongly connected with 1 input and leaks in input/output compartments. We note that this class of models has the very special property of being *dimension-preserving* when leaks are added or subtracted from non-input/output compartments, up to a point. To demonstrate that this special dimension-preserving property when removing leaks is not always the case, we revisit Example 3.2.26.

Example 3.3.6. Recall Example 3.2.26 where we had the model $\mathscr{M} = (G, \{1\}, \{2\}, L)$ where $|L| = |In \cup Out| = 2$ and G is given by the edges $\{1 \to 2, 1 \to 3, 3 \to 1, 1 \to 4, 4 \to 1\}$. The identifiable models are the ones where $L = \{2,4\}, \{2,3\}, \{1,2\}$ and the unidentifiable models have $L = \{3,4\}, \{1,4\}, \{1,3\}$, so removing leaks from output compartments is not dimension-preserving for this example.

In the next section, we give a conjecture about removing leaks from non-input/output compartments in the general output connectable case for models with one output.

3.4 Other expected dimension results

We first show that there are at most $|E|+|In \cup Out|$ independent paths and cycles appearing in the coefficient map c if we relax the condition of strongly input-output connected to *output connectable* instead:

Proposition 3.4.1. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model with G output connectable. Assume that $|Out| = 1$. Then there are at most $|E| + |In \cup Out|$ independent paths and cycles in the coefficient map c.*

Proof. If G is strongly input-output connected (or strongly connected) then we have already shown in Lemma 3.2.12 that the coefficient map factors through $|E| + |In \cup Out|$ independent paths and cycles. If G is output connectable but not strongly input-output connected, then there may be fewer than $|E| + |In \cup Out|$ independent directed paths and directed cycles because there are $|E| - |V| + |In \cup Out|$ independent directed paths and undirected cycles by Lemma 3.2.10. Since the coefficient map factors over the directed paths and directed cycles, then there are at most $|E| + |In \cup Out|$ independent paths and cycles in the coefficient map c. □

This means the expected dimension is now the number of independent directed paths and directed cycles, which may be less than $|E| + |In \cup Out|$.

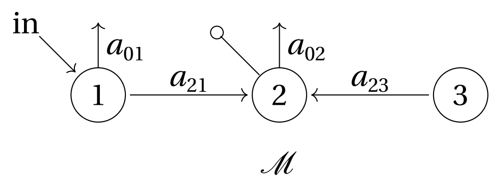


Figure 3.6: The graph corresponding to model $\mathscr{M}$ from Example 3.4.3.

We can relax the connectedness conditions in Theorem 3.3.1 to *output connectable* instead and still obtain statements about expected dimension, although now the models with a full set of leaks are **not** identifiable path/cycle models.

Theorem 3.4.2. *Let $\mathscr{M} = (G, In, Out, L)$ represent a linear compartmental model with G output connectable and $|L| = |In \cup Out|$ and $|Out| = 1$ which we assume has dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$. Then, the corresponding model with a leak in every compartment $\widetilde{\mathscr{M}} = (G, In, Out, V)$ also has dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$.*

Proof. The proofs mirrors the one in Theorem 3.3.1. □

Example 3.4.3. The model $\mathscr{M} = (G, \{1\}, \{2\}, \{1, 2\})$ seen in Figure 3.6 where G is the graph given by $\{1 \to 2, 3 \to 2\}$ is output connectable and has dimension of the image of the coefficient map equal to $|E| + 2 = 4$, thus it is locally identifiable. By Theorem 3.4.2, the model $\widetilde{\mathscr{M}} = (G, \{1\}, \{2\}, V)$ also has dimension of the image of the coefficient map equal to $|E| + 2 = 4$. Thus the identifiable functions are $a_{11}, a_{22}, a_{33}, a_{21}$. Note that it is *not* an identifiable path/cycle model because the parameter a_{23} does not appear in the coefficient map (as it is not strongly input-output connected).

This result shows that if a model has its dimension of the image of the coefficient map is equal to $|E| + |In \cup Out|$, then adding leaks alone maintains the dimension of the image of the coefficient map. This result is perhaps more useful for its contrapositive, i.e. if a model with leaks from every compartment does not have dimension $|E| + |In \cup Out|$ for c, then no amount of removing leaks up to a certain point ($|L| = |In \cup Out|$) can attain identifiability.

Corollary 3.4.4. *Let $\widetilde{\mathscr{M}} = (G, In, Out, V)$ represent a linear compartmental model with G output connectable and $|Out| = 1$ which does **not** have the dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$. Then, the corresponding model $\mathscr{M} = (G, In, Out, L)$ with $|L| = |In \cup Out|$ is **not** locally identifiable.*

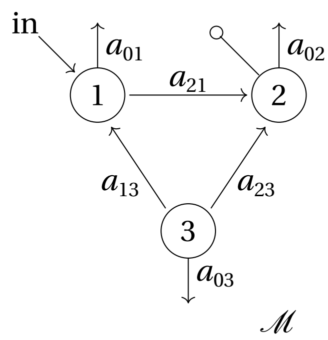


Figure 3.7: The graph corresponding to model $\mathcal{M}$ from Example 3.4.5.

Example 3.4.5. The model $\mathcal{M} = (G, \{1\}, \{2\}, V)$ seen in Figure 3.7 where G is the graph given by $\{1 \to 2, 3 \to 2, 3 \to 1\}$ is output connectable and has dimension of the image of the coefficient map *not* equal to $|E| + 2 = 5$, but equal to 4 instead. By Corollary 3.4.4, the model $\widetilde{\mathcal{M}} = (G, \{1\}, \{2\}, L)$ where $|L| = 2$ is thus *not* locally identifiable.

These results also give us insight into models that have dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$ but are not strongly input-output connected. We can show that the self-cycles are always identifiable:

Theorem 3.4.6. *Let $\mathcal{M} = (G, In, Out, V)$ represent a linear compartmental model with G output connectable and $|Out| = 1$. If $\mathcal{M}$ has dimension of the image of the coefficient map equal to $|E| + |In \cup Out|$, then the self-cycles $a_{11}, ..., a_{nn}$ are locally identifiable.*

Proof. Since the coefficient map always factors over $a_{11}, ..., a_{nn}$, this means the self-cycles are locally identifiable. □

Finally, we give a conjecture on removing leaks from non-input/output compartments for output connectable models and prove this conjecture in a special case:

Conjecture 3.4.7. Let $\mathcal{M} = (G, In, Out, V)$ represent a linear compartmental model. Assume that G is output connectable and $|Out| = 1$. Assume the dimension of the image of the coefficient map is k. Then, the corresponding model $\widetilde{\mathcal{M}} = (G, In, Out, L)$ where $In \cup Out \subseteq L$ also has dimension of the image of its coefficient map as k.

In other words, we conjecture that this property of being dimension-preserving applies to all output connectable models. However, if the dimension to begin with is not maximal, the dimension-preserving property will not lead to identifiability. We give a proof of this conjecture in the special case where the dimension of the image of the coefficient map is $|E|+|In \cup Out|$:

Theorem 3.4.8. *Let $\mathscr{M} = (G, In, Out, V)$ represent a linear compartmental model with G output connectable and $|Out| = 1$. If $\mathscr{M}$ has dimension of the image of the coefficient map equal to $|E|+|In \cup Out|$, then the the corresponding model $\widetilde{\mathscr{M}} = (G, In, Out, L)$ where $In \cup Out \subseteq L$ also has dimension of the image of its coefficient map as $|E|+|In \cup Out|$. In particular, if $L = In \cup Out$, then $\widetilde{\mathscr{M}}$ is locally identifiable.*

To prove Theorem 3.4.8, we give a variation of Lemma 3.2.22 and then a variation of the proof of Theorem 3.2.23.

Lemma 3.4.9. *Let $G = (V, E)$ be a directed graph with corresponding model (G, In, Out, V). Assume that G is output connectable and $|Out| = 1$. Consider a model (G, In, Out, L) where $In \cup Out \subseteq L$. Let $\pi : \mathbb{R}^{|V|+|E|} \to \mathbb{R}^{|E|+|In \cup Out|}$ denote the path/cycle map. Let $\Lambda \subseteq \mathbb{R}^{|V|+|E|}$ be the linear space satisfying*

$$\Lambda = \{\mathscr{A} \in \mathbb{R}^{|V|+|E|} : a_{ii} = -\sum_{j, j \neq i} a_{ji} \text{ for all } i \notin L\}.$$

If the dimension of the image of π is $|E|+|In \cup Out|$, then the dimension of the image of Λ under the map π is $|E|+|In \cup Out|$.

Proof. Removing the assumption of strongly input-output connected from Lemma 3.2.22 means that we cannot guarantee there are $|E|+|In \cup Out|$ independent directed paths and directed cycles. However, if we assume the dimension of the image of π is $|E|+|In \cup Out|$, then the rest of the proof follows that of Lemma 3.2.22. □

Proof of Theorem 3.4.8. By Lemma 3.4.9 we know that the image of the restricted parameter space under the path/cycle map π has dimension $|E|+|In \cup Out|$, which is equal to the dimension of the image of the full parameter space under the path/cycle map. Since the dimension of the image of the coefficient map c is $|E|+|In \cup Out|$, this must be the same for the restricted model. In particular, if $|L| = |In \cup Out|$, then the model has $|E|+|In \cup Out|$ parameters, hence it is locally identifiable. □

Example 3.4.10 (Example 3.4.3 revisited)**.** The model $\widetilde{\mathscr{M}} = (G, \{1\}, \{2\}, V)$ where G is the graph given by $\{1 \to 2, 3 \to 2\}$ is output connectable and has dimension of the image of the coefficient map equal to $|E|+2 = 4$, thus the model given by $\mathscr{M} = (G, \{1\}, \{2\}, \{1, 2\})$ is locally identifiable.

Combining Theorem 3.4.2 and Theorem 3.4.8, we get the following necessary and sufficient conditions:

Corollary 3.4.11. *Let $\mathcal{M} = (G, In, Out, L)$ represent a linear compartmental model with and $L = In \cup Out$ and assume that G is output connectable and $|Out| = 1$. Let $\widetilde{\mathcal{M}} = (G, In, Out, V)$ be the corresponding model with a leak in every compartment. $\mathcal{M}$ is locally identifiable if and only if $\widetilde{\mathcal{M}}$ has dimension of the image of the coeffiicent map as $|E| + |In \cup Out|$.*

Remark 3.4.12. Corollary 3.4.11 shows that this dimension-preserving property when adding or removing leaks from non-input/output compartments also holds in the output connectable case when the dimension of the image of the coefficient map is $|E|+|In\cup Out|$.

3.5 Necessary conditions for identifiable models based on model structure

Outside of checking the conditions in Theorem 3.2.27, i.e. if a model is an inductively strongly connected model if edges from output to input are added, checking if a model is an identifiable path/cycle model amounts to checking the dimension of the image of the coefficient map, and thus cannot be ascertained by simply examining the graph of the model. However, it is possible to provide necessary conditions for identifiable models and identifiable path/cycle models based on the graph itself, and thus can be used to rule out identifiability.

Theorem 3.5.1. *Let $\mathcal{M} = (G, In, Out, L)$ represent a linear compartmental model with either G strongly input-output connected and $|Out| = 1$ or G strongly connected and $|In| = 1$. If $|L| > |In \cup Out|$, then $\mathcal{M}$ is unidentifiable.*

Proof. If the number of parameters $|E| + |L| > |E| + |In \cup Out|$, where $|E| + |In \cup Out|$ is the maximal dimension by Lemma 3.2.12, then the model is unidentifiable. This reduces to $|L| > |In \cup Out|$. □

We can now make some statements about necessary conditions in the case of the maximal amount of edges.

Theorem 3.5.2. *Let $\mathcal{M} = (G, \{i\}, \{i\}, \{k\})$ represent a linear compartmental model with G strongly connected and $2|V| - 2$ edges. If $\mathcal{M}$ is locally identifiable (or equivalently, $\widetilde{\mathcal{M}} = (G, \{i\}, \{i\}, V)$ is an identifiable cycle model), it must have an exchange.*

Proof. From Proposition 5.3 of Meshkat and Sullivant (2014), we know that G must have an exchange in order for $\widetilde{\mathcal{M}} = (G, \{i\}, \{i\}, V)$ to be an identifiable cycle model. Thus, if G does not have an exchange, $\widetilde{\mathcal{M}}$ is not an identifiable cycle model and thus $\mathcal{M} = (G, \{i\}, \{i\}, \{k\})$ is not an identifiable model. $\square$

Theorem 3.5.3. *Let $\mathcal{M} = (G, \{i\}, \{j\}, L)$ represent a linear compartmental model with G strongly input-output connected,* $\mathrm{dist(i,j)} = 1$*, and* $2|V| - (\mathrm{dist(i,j)} + 2)$ *edges and* $|L| = |In \cup Out|$*. If $\mathcal{M}$ is locally identifiable (or equivalently, $\widetilde{\mathcal{M}} = (G, \{i\}, \{j\}, V)$ is an identifiable path/cycle model), it must have an edge from i to j (i.e. a path of length* $\mathrm{dist(i,j)}$*).*

Proof. If there is no path from i to j, then the coefficient of the highest-order term on the right hand side of the input-output equation is zero and there would be fewer than $2|V| - \mathrm{dist(i,j)}$ coefficients. But there are $2|V| - (\mathrm{dist(i,j)} + 2)$ edges, so if $\mathcal{M}$ is locally identifiable, then it has expected dimension $|E| + 2 = 2|V| - \mathrm{dist(i,j)}$, which is impossible if there are fewer than $2|V| - \mathrm{dist(i,j)}$ coefficients. $\square$

We can also have an analogous necessary condition in the case of fewer than $2|V| - (\mathrm{dist(i,j)} + 2)$ edges.

Theorem 3.5.4. *Let $\mathcal{M} = (G, \{i\}, \{j\}, L)$ with $i \neq j$ represent a linear compartmental model with G strongly input-output connected and $2|V| - (k+2)$ edges where $k \geq 1$ and $|L| = |In \cup Out|$. If $\mathcal{M}$ is locally identifiable (or equivalently, $\widetilde{\mathcal{M}} = (G, \{i\}, \{j\}, V)$ is an identifiable path/cycle model), it must have a path from i to j of length at most k.*

Proof. The coefficient of the highest-order term on the right hand side of the input-output equation is a sum of shortest paths from input to output of length $\mathrm{dist(i,j)}$ and this must be nonzero for $\mathcal{M}$ to have expected dimension. Since there are $2|V| - \mathrm{dist(i,j)}$ nonzero coefficients and expected dimension is $|E| + 2$, this means k is at least $\mathrm{dist(i,j)}$. So there must be a path from i to j of length at most k. $\square$

3.6 Examples

We now provide some real world examples that fall into the categories of models considered in this chapter. In particular, we obtain identifiability or unidentifiability results in Example 3.6.1 and Example 3.6.2 without any symbolic computation, i.e. purely based on the graph structure alone.

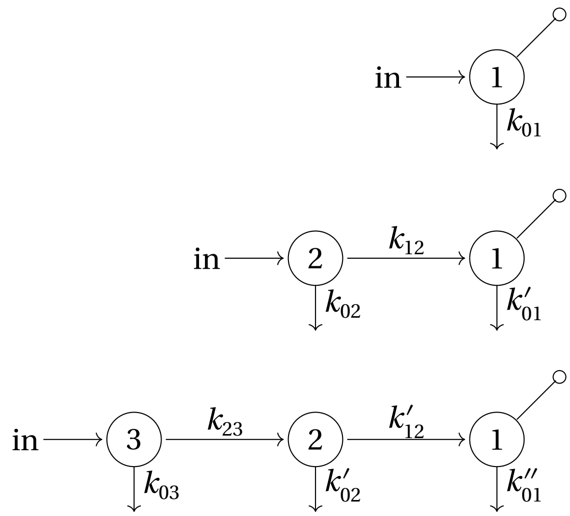


Figure 3.8: Example 13.6 from DiStefano (2015) on HIV vaccine development (Part 1).

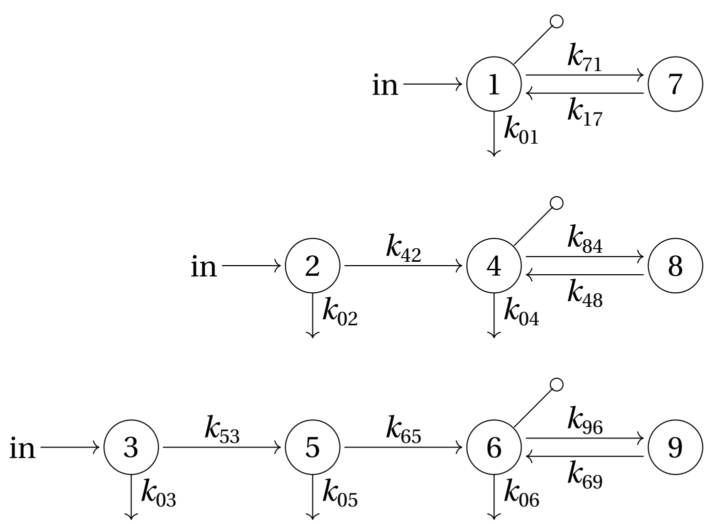


Figure 3.9: Example 13.16 from DiStefano (2015) on HIV vaccine development (Part 3).

Example 3.6.1. Consider Example 13.6 from DiStefano (2015) on HIV vaccine development (Part 1). Three models are considered that fall into the category of path models with leaks from every compartment as in Proposition 3.2.34, shown in Figure 3.8. The top model corresponds to Experiment 1, the middle model corresponds to Experiment 2, and the bottom model corresponds to Experiment 3. It is clear that the Experiment 1 model is identifiable. Using Proposition 3.2.34, we can easily obtain that the Experiment 2 model is identifiable. By Proposition 3.2.34, the Experiment 3 model has expected dimension and is thus unidentifiable with identifiable functions given by the paths and cycles (where the "self-cycles" have been expanded out): $k_{23}k'_{12}, -k_{03}-k_{23}, -k'_{02}-k'_{12}, -k''_{01}$.

Example 3.6.2. Consider Example 13.16 from DiStefano (2015) on HIV vaccine development (Part 3). The models from Example 3.6.1 are amended by adding on exchanges to the output compartments, shown in Figure 3.9, and the numbering scheme has changed to agree with DiStefano (2015). The Experiment 1 model is identifiable by Theorem 3.2.23 as it is an identifiable cycle model (it is inductively strongly connected) with a single leak in the input/output compartment. The Experiment 2 model is almost inductively strongly connected and thus is identifiable by Corollary 3.2.32. A variation on the Experiment 3 model with leaks from all compartments can be shown to be an identifiable path/cycle model by a direct calculation, thus removing the leak from compartment 9 retains the dimension by Theorem 3.2.23, which means the model in Experiment 3 is unidentifiable. Alternatively, one can apply Proposition 3.2.35 to a variation on the model in Experiment 2 with leaks from every compartment (which has expected dimension) and thus obtain that the variation on the model in Experiment 3 with leaks from every compartment also has expected dimension. Now removing the leak from compartment 9 retains the dimension by Theorem 3.2.23, and thus the model in Experiment 3 is unidentifiable. The identifiable functions are given by the paths and cycles (where the "self-cycles" have been expanded out): $k_{53}k_{65}, k_{69}k_{96}, -k_{03}-k_{53}, -k_{05}-k_{65}, -k_{06}-k_{96}, -k_{69},$.

3.7 Computations

In Table 3.3 we outline the number of graphs with n vertices and m edges that have the expected dimension with input in i and output in j, assuming leaks from every compartment.

The number of strongly connected graphs and the number of strongly input-output connected graphs with different input/output configurations is noted.

Table 3.3: The number of graphs with n vertices and m edges that have the expected dimension with input in i and output in j, assuming leaks from every compartment.

(n,m)	Total	Strongly Connected	$i=1$, $j=1$	$i=1$, $j=2,3$	Strongly input-output connected $i=1$, $j=2$	$i=1$, $j=2$	Strongly input-output connected $i=1,3$, $j=2$	$i=1,3$, $j=2$
(3,2)	15	NA	NA	NA	1	1	3	3
(3,3)	20	2	2	2	7	4	10	8
(3,4)	15	9	7	3	11	NA	12	4
(4,3)	220	NA	NA	NA	2	2	7	7
(4,4)	495	6	6	6	37	25	72	59
(4,5)	792	84	54	62	193	70	267	167
(4,6)	924	316	166	118	445	NA	518	184
(4,7)	792	492	NA	86	565	NA	603	96
(5,4)	4845	NA	NA	NA	6	6	24	24
(5,5)	15,504	24	24	24	222	162	518	432
(5,6)	38,760	720	576	600	2470	1288	4130	1110
(5,7)	77,520	6440	4052	4030	13,004	3154	17,708	1552
(5,8)	125,970	26,875	9565	10,336	40,126	NA	48,277	17,113
(5,9)	167,960	65,280	NA	15,984	82,159	NA	91,658	20,272
(5,10)	184,756	105,566	NA	9841	120,202	NA	128,003	10,689

We then computed the number of models with expected dimension for 4 notable cases: the case of identical single input and single output with a strongly connected graph G (as in Meshkat and Sullivant (2014)), the case of single input but multiple outputs with a strongly connected graph G, the case of distinct single input and single output with a strongly input-output connected graph G, and the case of single output but multiple inputs with a strongly input-output connected graph G. Due to restrictions on the number of edges, not all cases are possible, and those are labeled “NA”.

3.8 Construction of Identifiable Models

In this section, we consider the special case of single input and single output in the same compartment with G strongly connected and $Leak = V$, as in Meshkat and Sullivant (2014), i.e. $\mathcal{M} = (G, \{i\}, \{i\}, V)$ with G strongly connected. Since $Leak$ is assumed to be V and input/output are assumed to be the same vertex, we can just discuss the graph G in what follows.

In Meshkat and Sullivant (2014), Theorem 5.7 gives a way of constructing a new model with expected dimension from a smaller model with expected dimension by adding an incoming and outgoing edge to a chain of cycles (See Definition 3.2.28):

Theorem 3.8.1 (Theorem 5.7 of Meshkat and Sullivant (2014))**.** *Let G' be a graph that has the expected dimension with $n-1$ vertices. Let G be a new graph obtained from G' by adding a new vertex and two edges $k \to n$ and $n \to l$ and such that G has a chain of cycles containing both 1 and n. Then G has the expected dimension.*

In Baaijens and Draisma (2016), the authors strengthened this result to allow for adding loops of any length, not just length two:

Proposition 3.8.2. *[Proposition 4.14 of Baaijens and Draisma (2016)] Let $G = (V, E)$ on $n-1$ vertices be a graph with the expected dimension. Construct G' from G by adding new vertices $n_1, ..., n_s$ and edges $k \to n_1$, $n_s \to l$, and $n_i \to n_{i+1}$ for $i = 1, ..., s-1$ where $k, l \in V$ are vertices of G. Then G' has the expected dimension.*

We will use Proposition 4.14 from Baaijens and Draisma (2016) combined with Theorem 1 of Meshkat et al. (2015) to form identifiable models. In other words, we will use Proposition 4.14 to construct identifiable cycle models and then use Theorem 1 to eliminate all but one leak to form an identifiable model. We state Theorem 1 here:

Theorem 3.8.3 (Theorem 1 from Meshkat et al. (2015))**.** *Let M be an identifiable cycle model. If the model is changed to have exactly one leak, then the resulting model is locally identifiable.*

Algorithm 3.8.4 (Construction of identifiable models with $In = Out = \{1\}$ and one leak $|L| = 1$)**.**

1. Begin with $(G, \{1\}, \{1\}, \{1\})$ where $V = \{1\}$ and $E = \emptyset$.

2. Construct G' from G by adding new vertices $n_1, ..., n_s$ and edges $1 \to n_1$, $n_s \to 1$, and $n_i \to n_{i+1}$ for $i = 1, ..., s-1$ where $k, l \in V$ are vertices of G and adding leaks from every new vertex.

3. Repeat Step 2 by starting a some vertex n_i and ending at some vertex n_j for $n_i, n_j \in \{1, n_1, ..., n_s\}$ and adding leaks from every new vertex.

4. Continue adding edges, vertices, and leaks as described in Steps 2 and 3.

5. Remove all leaks except one leak.

Theorem 3.8.5. *Let $\mathscr{M} = (G, \{1\}, \{1\}, \{k\})$ be a model constructed from Algorithm 3.8.4. The model $\mathscr{M}$ is identifiable.*

Proof. By Proposition 3.8.2 the model $\mathscr{M}$ is an identifiable cycle model and by Theorem 3.8.3 the model with only one leak is identifiable. □

Example 3.8.6. The model $\mathscr{M} = (G, \{1\}, \{1\}, V)$ seen in Figure 3.10 where G is given by the edges $\{1 \to 2, 2 \to 3, 3 \to 1, 2 \to 4, 4 \to 5, 5 \to 3\}$ is an identifiable cycle model by Proposition 3.8.2. Thus we can remove all leaks except one, e.g. $\widetilde{\mathscr{M}} = (G, \{1\}, \{1\}, \{5\})$ and the resulting model is identifiable. We note that this model is *not* inductively strongly connected, thus Proposition 3.8.2 does expand upon the results in Meshkat et al. (2015) to construct identifiable models.

Note that the authors in Baaijens and Draisma (2016) only considered *identifiable cycle models*. We suspect there may be a similar result to Proposition 3.8.2 for the case of identifiable path/cycle models.

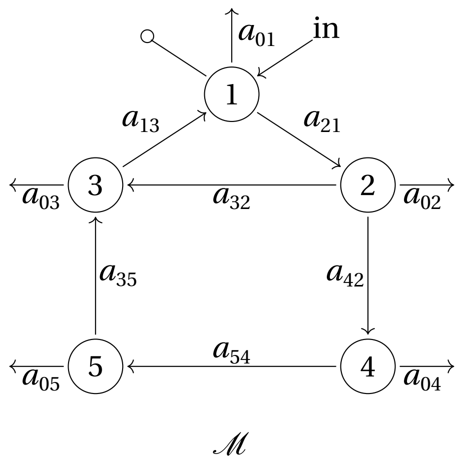


Figure 3.10: The graph corresponding to $\mathscr{M}$ from Example 3.8.6.

Acknowledgments

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CHAPTER

4

IDENTIFIABILITY OF LINEAR COMPARTMENTAL TREE MODELS

In this chapter, we study the input-output equations and structural identifiability of linear compartmental models, with an emphasis on tree models.

The organization of this chapter is as follows. Section 4.1 discusses relevant tree model background and preliminary results. Our formula for the coefficients of input-output equations is proven in Section 4.2. Section 4.3 contains our results on operations that preserve identifiability. In Section 4.4, we classify identifiable tree models.

4.1 Preliminaries

4.1.1 Graphs associated to linear compartmental models

We define several auxiliary graphs arising from a linear compartmental model

$$\mathcal{M} = (G, In, Out, Leak).$$

- Recall that the *leak-augmented graph* (Gross et al. 2017), denoted by $\widetilde{G}$, is obtained from G by adding (1) a new node, labeled by 0 and referred to as the *leak node*, and (2) for every $j \in Leak$, an edge $j \to 0$ with label a_{0j}.

- We introduce the graph $\widetilde{G}_i^*$ (where i is some compartment), which is obtained from $\widetilde{G}$ by removing all outgoing edges from node i. We also define a related matrix, denoted by A_i^*, which is obtained from the compartmental matrix A of G by replacing the column corresponding to compartment-i with zeros.

- The graph $\widetilde{G}_i$ is obtained from $\widetilde{G}_i^*$ by (1) replacing every edge $j \to i$ (labeled by a_{ij}) by the edge $j \to 0$ labeled a_{ij}, and then (2) deleting node i.

Remark 4.1.1. Among the graphs defined above, only the graph $\widetilde{G}_i$ may have multi-edges (more than one edge with the same source and target). Specifically, such edges may appear from a compartment to the leak node (for instance, see the graph $\widetilde{G}_1$ in Figure 4.1).

Remark 4.1.2. Our definition of $\widetilde{G}_i$ differs slightly from that in Gross et al. (2017). Here, we use multi-edges (e.g., a_{02} and a_{12} in $\widetilde{G}_1$ in Figure 4.1), while the corresponding graph in (Gross et al. 2017) uses a single edge with the sum of the labels (e.g., $a_{02} + a_{12}$). Using multi-edges here is more convenient. Moreover, in the result from (Gross et al. 2017) that we use and improve (Proposition 4.1.6 below), it is straightforward to check that our definition of $\widetilde{G}_i$ yields the same sum of productivities. Thus, both Proposition 4.1.6 and the result in (Gross et al. 2017) are correct, even with our updated definition of $\widetilde{G}_i$.

Example 4.1.3. For the model in Figure 1.10, the corresponding graphs $G, \widetilde{G}, \widetilde{G}_1$, and $\widetilde{G}_1^*$ are shown in Figure 4.1. The corresponding matrices are as follows:

$$A = \begin{bmatrix} -(a_{21}+a_{31}) & a_{12} & a_{13} \\ a_{21} & -(a_{02}+a_{12}+a_{32}) & a_{23} \\ a_{31} & a_{32} & -(a_{13}+a_{23}) \end{bmatrix},\ A_1^* = \begin{bmatrix} 0 & a_{12} & a_{13} \\ 0 & -(a_{02}+a_{12}+a_{32}) & a_{23} \\ 0 & a_{32} & -(a_{13}+a_{23}) \end{bmatrix}$$

The ODE system (1.16) for this model is as follows:

$$\begin{pmatrix} \dot{x}_1 \\ \dot{x}_2 \\ \dot{x}_3 \end{pmatrix} = A \begin{pmatrix} x_1 \\ x_2 \\ x_3 \end{pmatrix} + \begin{pmatrix} u_1 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} -(a_{21}+a_{31})x_1 + a_{12}x_2 + a_{13}x_3 + u_1 \\ a_{21}x_1 + -(a_{02}+a_{12}+a_{32})x_2 + a_{23}x_3 \\ a_{31}x_1 + a_{32}x_2 + -(a_{13}+a_{23})x_3 \end{pmatrix},$$

with $y_1 = x_1$.

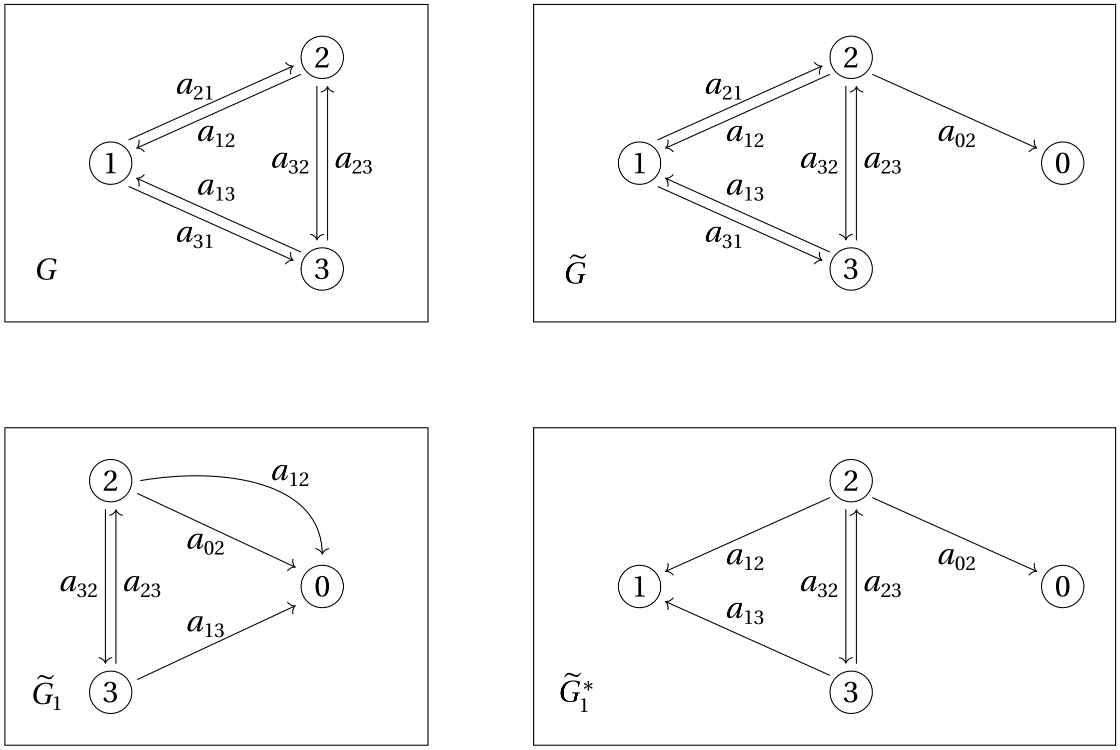

Figure 4.1: Graphs arising from the linear compartmental model in Figure 1.10.

4.1.2 Input-output equations

In what follows, we use the following notation. For a matrix B, we let $B^{i,j}$ denote the matrix obtained from B by removing row i and column j. Similarly, $B^{\{i,j\},\{k,\ell\}}$ denotes the matrix obtained from B by removing rows i and j and columns k and ℓ.

For a linear compartmental model, an *input-output equation* is an equation that holds along all solutions of the ODEs (1.16), and involves only the parameters a_{ij}, input variables u_i, output variables y_i, and their derivatives. One way to obtain such equations is given in the following result, which is due to Meshkat, Sullivant, and Eisenberg (Meshkat et al. 2015, Theorem 2) (see also (Gross et al. 2019, Proposition 2.3 and Remark 2.7)):

Proposition 4.1.4 (Input-output equations)**.** *Let $\mathcal{M} = (G, In, Out, Leak)$ be a linear compartmental model with n compartments and at least one input. Define ∂I to be the $n \times n$ matrix in which every diagonal entry is the differential operator d/dt and every off-diagonal entry is 0. Let A be the compartmental matrix. Then, the following equations are input-output* *equations of $\mathcal{M}$:*

$$\det(\partial I - A) y_i \;=\; \sum_{j \in In} (-1)^{i+j} \det(\partial I - A)^{j,i}\, u_j \qquad \text{for } i \in Out\ . \tag{4.1}$$

Example 4.1.5 (Example 4.1.3, continued)**.** Returning to the model in Figure 1.10, the input-output equation (4.1) is as follows:

$$\begin{aligned} & y_1^{(3)} + (a_{02}+a_{12}+a_{13}+a_{21}+a_{23}+a_{31}+a_{32})\ddot{y}_1 + (a_{02}a_{13}+a_{12}a_{13}+a_{02}a_{21}+a_{13}a_{21}+a_{02}a_{23}+a_{12}a_{23} \\ & \quad + a_{21}a_{23}+a_{02}a_{31}+a_{12}a_{31}+a_{23}a_{31}+a_{13}a_{32}+a_{21}a_{32}+a_{31}a_{32})\dot{y}_1 + (a_{02}a_{13}a_{21}+a_{02}a_{21}a_{23}+a_{02}a_{23}a_{31})y_1 \\ & = \ddot{u}_1 + (a_{02}+a_{12}+a_{13}+a_{23}+a_{32})\dot{u}_1 + (a_{02}a_{13}+a_{12}a_{13}+a_{02}a_{23}+a_{12}a_{23}+a_{13}a_{32})u_1 . \end{aligned}$$

The following result is Theorem 4.5 of Gross et al. (2017).

Proposition 4.1.6 (Coefficients when input equals output)**.** *Consider a linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ with $In = Out = \{1\}$. Let n denote the number of compartments, and let A be the compartmental matrix. Write the input-output equation* (4.1) *as:*

$$y_1^{(n)} + c_{n-1} y_1^{(n-1)} + \cdots + c_1 y_1' + c_0 y_1 \;=\; u_1^{(n-1)} + d_{n-2} u_1^{(n-2)} + \cdots + d_1 u_1' + d_0 u_1\ . \tag{4.2}$$

Then the coefficients of this input-output equation are as follows:

$$\begin{aligned} c_i &= \sum_{F \in \mathscr{F}_{n-i}(\widetilde{G})} \pi_F \quad \textit{for } i = 0, 1, \ldots, n-1\ , \ \textit{and} \\ d_i &= \sum_{F \in \mathscr{F}_{n-i-1}(\widetilde{G}_1)} \pi_F \quad \textit{for } i = 0, 1, \ldots, n-2\ . \end{aligned}$$

One of the aims of Chapter 4 is to generalize Proposition 4.1.6 to allow for the input and output to be in distinct compartments and for more inputs and outputs (see Theorem 4.2.1).

Next, we introduce the coefficient maps arising from input-output equations. We begin by regarding the input-output equations (4.1) as polynomials in the y_j's and u_i's and their derivatives. Thus, each coefficient of the equation is a polynomial in the parameters ($a_{\ell m}$ for edges $m \to \ell$, and a_{0p} for leaks $p \in Leak$).

Definition 4.1.7. Let $\mathcal{M} = (G, In, Out, Leak)$ be a linear compartmental model.

(i) The *coefficient map* $\mathbf{c} : \mathbb{R}^{|E_G|+|Leak|} \to \mathbb{R}^m$ sends the vector of parameters to the vector of all non-constant coefficients of all input-output equations of the form (4.1). Here,

m denotes the number of such coefficients.

(ii) $\mathscr{M}$ has *expected dimension* if the dimension of the image of its coefficient map $\mathbf{c} : \mathbb{R}^{|E_G|+|Leak|} \to \mathbb{R}^m$ equals the minimum of $|E_G| + |Leak|$ and m.

Remark 4.1.8. Having expected dimension is useful for proving a model has an identifiable reparameterization (Meshkat and Sullivant 2014). For example, a strongly connected model with at most $2|V_G|-2$ edges, input and output in the same compartment, and leaks from every compartment has an identifiable scaling reparameterization if and only if the model has expected dimension, which in this case is the number of independent cycles of the graph (Meshkat and Sullivant 2014, Theorem 1.2).

Definition 4.1.9. A *tree model* or bidirectional tree model is a linear compartmental model with underlying directed graph a bidirectional tree.

Tree models appear often in applications. Indeed, (Meshkat et al. 2015, Example 7) discusses the importance of tree models in applications, using diffusion models along rivers and streams (Gydesen 1984) and models of neuronal dendritic trees (Bressloff and Taylor 1993) as motivating applications. As another example, (Meshkat et al. 2015, Example 6) considers a 11-compartment tree model, obtained by modifying a compartmental model of manganese pharmacokinetics in rats (Douglas et al. 2010).

Two families of tree models appearing often in applications are catenary and mammillary models. For catenary (respectively, mammillary) models, the underlying directed graph is a path (respectively, a star). As corollaries to the main theorem, we give a full classification of when catenary and mammillary models are generically locally identifiable in the case of a single input and output (Corollaries 4.4.3 and 4.4.4) .

Combinatorial conditions for identifiability that can be visually verified, as in the main theorem, are desired because compartmental models are described using a graphical structure and are often used in settings with few compartments. Prior results in this direction were given by Cobelli et al. (1979), who showed that mammillary and catenary models are identifiable when the models have a single input and output in the same compartment (specific to the respective models) and have at most one leak. Another known result asserts that models with inductively strongly connected graphs, a single input and output in a certain compartment, and at most one leak are identifiable (Gross et al. 2019; Meshkat and Sullivant 2014; Meshkat et al. 2015). Other related results are due to Boukhobza et al. (2014), who gave graph-theoretic criterion for identifiability, Chau (1985a,b), who explored properties of catenary and mammillary models, Delforge (1984) and Delforge et al. (1985), who described necessary conditions for identifiability and posed conjectures on global identifiability, and Vajda (1984), who gave a condition for global identifiability based on the submodels obtained by deleting one edge at a time.

Establishing structural identifiability of a model can be achieved by using differential algebra techniques to translate the problem to a linear algebra question (Ljung and Glad 1994; Meshkat et al. 2015). In particular, the question of whether a given linear compartmental model is generically locally identifiable is equivalent to asking whether the Jacobian matrix of a certain coefficient map (arising from certain input-output equations) is generically full rank. Our second significant result, Theorem 4.2.1, gives a general formula for the coefficients of these equations in terms of the combinatorics of the underlying directed graph associated to the model. Previous formulas appear in Gross et al. (2017) and Meshkat and Sullivant (2014), but only apply to models that satisfy certain conditions. For example, the results in Gross et al. (2017) requires the input and output to be in the same compartment. In comparison, the only condition of Theorem 4.2.1 is the existence of at least one input.

A general formula for coefficients allows us then to explore the effect of adding edges and moving inputs and outputs as we work towards an understanding of tree models. Indeed, Theorem 4.2.1 implies that if the input and output are too far apart then the model is unidentifiable (Corollary 4.2.5). This result places immediate constraints on how inputs and outputs can be moved if identifiability is to be preserved, which we can glimpse in the main theorem, Theorem 4.4.2, stated above. Our third set of results, which we summarize in Table 4.1, concern operations involving moving inputs and outputs and adding leaf edges, and establish situations where such operations preserve identifiability. These results therefore contribute to a recent body of work aimed at understanding the effect on identifiability of adding, deleting, or moving an input, output, leak, or edge (Chan et al. 2021; Gerberding et al. 2020; Gross et al. 2019).

Table 4.1: Summary of results on operations preserving identifiability. For an identifiable, strongly connected, linear compartmental model $\mathscr{M}$ with one input, one output, and no leaks, if $\mathscr{M}'$ is obtained from $\mathscr{M}$ by the specified operation, then $\mathscr{M}'$ is identifiable.

Model	**Operation**	**Result**
Any	Add leaf edge	Theorem 4.3.2
Model with $In = Out = \{i\}$	Add leaf edge at i, and move input or output to the new compartment	Theorem 4.3.3

The following three results, which pertain to spanning incoming forests, will be used to prove the main result in Section 4.2.

Lemma 4.1.10. *Every connected component of a spanning incoming forest contains exactly one sink node, i.e., exactly one node with no outgoing edges.*

Proof. Let C be a connected component of a spanning incoming forest H of a (finite) graph G. To see that a sink node exists in C, we start from some node in C and follow outgoing arrows; eventually (as H is finite and cycle-free) we must reach a sink node.

Now assume for contradiction that C has two sink nodes v and v'. The underlying undirected graph of C is a tree, so it contains a unique undirected path P from v to v'. In the directed version of this path, each edge points in the direction of either v or v'. Both v and v' have only incoming edges, so some node on the path P has two outgoing edges – one pointing toward v and one toward v'. This contradicts the fact that nodes in an incoming forest have no more than one outgoing edge. □

Lemma 4.1.11. *Let $(G, In, Out, Leak)$ be a linear compartmental model. Let k and ℓ be distinct compartments, and let j be a positive integer. Then every forest $F \in \mathscr{F}_j^{k,\ell}(\widetilde{G}_\ell^*)$ contains a directed path from k to ℓ.*

Proof. Let $F \in \mathscr{F}_j^{k,\ell}(\widetilde{G}_\ell^*)$. By definition, some connected component C of F contains k and ℓ. By construction, the node ℓ has no outgoing edges in $\widetilde{G}_\ell^*$. So, by Lemma 4.1.10 and its proof, ℓ is the unique sink node of C, and there is a directed path in F from k to ℓ. □

The following lemma views spanning forests with a path from k to ℓ as a union, over edges of the form $k \to i$, of forests with paths from i to ℓ.

Lemma 4.1.12. *Let $H = (V_H, E_H)$ be a (directed) graph. Consider vertices $k, \ell \in V_H$ with $k \neq \ell$, and let j be a positive integer. Assume that H has no edges outgoing from ℓ. Let K be the graph obtained from H by removing all edges outgoing from k. Then the following equality holds:*

$$\mathscr{F}_j^{k,\ell}(H) = \bigcup_{i:(k\to i)\in E_H} \left\{(V_H,\ E_F \cup \{k \to i\}) \mid F \in \mathscr{F}_{j-1}^{i,\ell}(K)\right\} .$$

Proof. We first prove "⊆". Let $F^* \in \mathscr{F}_j^{k,\ell}(H)$. Then, k and ℓ are in the same connected component C of F^*. Also, by assumption, ℓ has no outgoing edges and so, by Lemma 4.1.10, ℓ is the unique sink node of C. Thus, k is a non-sink node, and so there is an edge $k \to i$ in F^*. Moreover, this is the unique such edge (as F^* is a spanning incoming forest).

It follows that $F := (V_H,\ E_{F^*} \smallsetminus \{k \to i\})$ is a $(j-1)$-edge, spanning subgraph of K. Moreover, F has no cycles and each node has at most 1 outgoing edge (because F^* has the same properties). Finally, i and ℓ are in the same connected component of F because (as we saw in the proof of Lemma 4.1.10) by following edges in F^* we must eventually reach ℓ, and the edge $k \to i$ is not encountered here, because otherwise F^* would contain a cycle. We conclude that $F^* = (V_H,\ E_F \cup \{k \to i\})$, with $F \in \mathscr{F}_{j-1}^{i,\ell}(K)$, as desired.

We prove "$\supseteq$." Assume that $k \to i$ is an edge of H, and let $F \in \mathscr{F}_{j-1}^{i,\ell}(K)$. We must show that after adding the edge $k \to i$, the new graph $F^* := (V_H,\ E_F \cup \{k \to i\})$ is in $\mathscr{F}_j^{k,\ell}(H)$. By construction, F^* is a j-edge spanning subgraph of H. Also, each node of F^* has at most 1 outgoing edge (this property was true for F, and F – as a subgraph of K – had no outgoing edges from k). Next, k and ℓ are in the same connected component of F^*, due to the edge $k \to i$ and the fact that i and ℓ are in the same component of F.

Finally, we must show that F^* has no cycles. In K (and thus also in F), both k and ℓ have no outgoing edges and hence are sink nodes. Thus, by Lemma 4.1.10, k and ℓ are in distinct connected components of F. Adding the edge $k \to i$ therefore joins these two components, but does not introduce any cycles. This completes the proof. □

4.1.3 Previous Identifiability Results

Next, we recall the following useful criteria for identifiability Meshkat et al. (2015) and expected dimension from Chapter 3.

Proposition 4.1.13. *A linear compartmental model $\mathscr{M} = (G, In, Out, Leak)$ is generically locally identifiable (respectively, has expected dimension) if and only if the rank of the Jacobian matrix of its coefficient map, $\mathbf{c} : \mathbb{R}^{|E_G|+|Leak|} \to \mathbb{R}^m$, when evaluated at a generic point, equals $|E_G| + |Leak|$ (respectively, equals the minimum of $|E_G| + |Leak|$ and m).*

Next, we recall from Meshkat and Sullivant (2014) and Meshkat et al. (2015) a class of identifiable models $\mathscr{M} = (G, In, Out, Leak)$ for which the graph G is inductively strongly connected.

The following result combines results from Gross et al. (2019) and Meshkat et al. (2015).

Proposition 4.1.14 (Inductively strongly connected models)**.** *Let $\mathscr{M} = (G, In, Out, Leak)$ be a linear compartmental model such that $In = Out = \{1\}$, $|Leak| \leq 1$, and G is inductively strongly connected with respect to vertex 1. Then $\mathscr{M}$ is generically locally identifiable.*

Proof. The model $\mathscr{M}$ with $|Leak| = 1$ is generically locally identifiable due to (Meshkat et al. 2015, Theorem 1) and (Meshkat et al. 2015, Remark 1), and the model $\mathscr{M}$ with $|Leak| = 0$ is still generically locally identifiable by (Gross et al. 2019, Proposition 4.6) (or by definition if G has no edges). $\square$

Finally, we recall two additional results on adding or removing leaks (Gross et al. 2019, Proposition 4.6 and Theorem 4.3), which we summarize in the following proposition.

Proposition 4.1.15 (Add or remove leak)**.** *Let $\mathcal{M}$ be a linear compartmental model that is strongly connected and has at least one input. Assume that one of the following holds:*

1. *$\mathcal{M}$ has no leaks, and $\widetilde{\mathcal{M}}$ is a model obtained from $\mathcal{M}$ by adding one leak; or*
2. *$\mathcal{M}$ has an input, an output, and a leak in a single compartment (and no other inputs, outputs, or leaks), and $\widetilde{\mathcal{M}}$ is obtained from $\mathcal{M}$ by removing the leak.*

If $\mathcal{M}$ is generically locally identifiable, then so is $\widetilde{\mathcal{M}}$.

4.2 Results on coefficients of input-output equations

The main result of this section is a combinatorial formula for the coefficients of input-output equations (Theorem 4.2.1). This result generalizes Proposition 4.1.6, which was the case of input and output in the same compartment.

4.2.1 Main results

This subsection features our formula for the coefficients of input-output equations (Theorem 4.2.1), which we use to evaluate the number of non-constant coefficients of the input-output equation for strongly connected models with one input and one output (Corollary 4.2.4). As a consequence, we obtain a criterion for unidentifiability which arises when a model has more parameters than coefficients (Corollary 4.2.5).

Theorem 4.2.1 (Coefficients of input-output equations)**.** *Consider a linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ with at least one input. Let n denote the number of compartments. Write the input-output equation* (4.1) *(for some $i \in Out$) as follows:*

$$y_i^{(n)} + c_{n-1} y_i^{(n-1)} + \cdots + c_1 y_i' + c_0 y_i \;=\; \sum_{j \in In} (-1)^{i+j} \left(d_{j,n-1} u_j^{(n-1)} + \cdots + d_{j1} u_j' + d_{j0} u_j \right). \quad (4.3)$$

Then the coefficients of the input-output equation (4.3) *are as follows:*

$$c_k = \sum_{F \in \mathscr{F}_{n-k}(\widetilde{G})} \pi_F \qquad \text{for } k = 0, 1, \ldots, n-1, \quad \text{and}$$
$$d_{j,k} = \sum_{F \in \mathscr{F}^{ji}_{n-k-1}(\widetilde{G}^*_i)} \pi_F \qquad \text{for } j \in In \text{ and } k = 0, 1, \ldots, n-1 .$$

The proof of Theorem 4.2.1 is given in Section 4.2.2.

From Theorem 4.2.1, we can determine the non-constant coefficients in the input-output equations. We state this result in the case of strongly connected models with one input and one output, as follows.

Corollary 4.2.2 (Non-constant coefficients)**.** *Consider a strongly connected linear compartmental model* $\mathscr{M} = (G, In, Out, Leak)$ *with* $In = \{j\}$ *and* $Out = \{i\}$. *Let* n *be the number of compartments. Write the input-output equation* (4.1) *as follows:*

$$y_i^{(n)} + c_{n-1} y_i^{(n-1)} + \cdots + c_1 y_i' + c_0 y_i = (-1)^{i+j} \left(d_{n-1} u_j^{(n-1)} + \cdots + d_1 u_j' + d_0 u_j \right) . \tag{4.4}$$

The coefficients on the left-hand side of (4.4) *that are non-constant are as follows:*

$$\begin{cases} c_0, c_1, \ldots, c_{n-1} & \text{if } Leak \neq \emptyset \\ c_1, c_2, \ldots, c_{n-1} & \text{if } Leak = \emptyset . \end{cases}$$

The coefficients on the right-hand side of (4.4) *that are non-constant are as follows:*

$$\begin{cases} d_0, d_1, \ldots, d_{n-2} & \text{if } In = Out \\ d_0, d_1, \ldots, d_{n-L-1} & \text{if } In \neq Out , \end{cases}$$

where L *is the length of the shortest (directed) path from the input* j *to the output* i.

Proof. We first analyze the left-hand side of (4.4). By equation (4.1), the coefficient c_0 equals, up to sign, $\det A$. This determinant is 0 if $Leak = \emptyset$ (as A in this case is the negative Laplacian of a strongly connected graph). If, on the other hand, $Leak \neq \emptyset$, then $\det A$ is a nonzero polynomial (Meshkat et al. 2015, Proposition 1) of degree n in the $a_{k\ell}$'s.

Thus, it suffices to show that $c_1, c_2, \ldots, c_{n-1}$ are nonzero (they are non-constant, as their degrees are $n-1, n-2, \ldots, 1$). As G is strongly connected, there exists a spanning tree T of G that is directed toward compartment i (which necessarily has $(n-1)$ edges and no vertex with more than one outgoing edge). Let $\widetilde{T}$ be the corresponding subtree (with the same edges) of $\widetilde{G}$. Then, $\pi_{\widetilde{T}}$ is a summand of c_1 by Theorem 4.2.1. Similarly, a summand of c_2 (respectively, $c_3, c_4, \ldots, c_{n-1}$) is obtained by removing 1 edge (respectively, $2, 3, \ldots, n-2$ edges) from $\widetilde{T}$. This completes the analysis of the left-hand side.

For the right-hand side of (4.4), we consider two cases. Consider first the case when $In = Out$ (i.e., $i = j$). By Theorem 4.2.1, the summands of (respectively) $d_{n-1}, d_{n-2}, \ldots, d_0$ correspond to the spanning incoming forests of $\widetilde{G}_i^*$ that have (respectively) $0, 1, \ldots, n-1$ edges. There is a unique such forest with no edges, so $d_{n-1} = 1$. Next, by construction, the tree T from earlier in the proof has no edges outgoing from i, so we can consider the corresponding subtree (with the same edges) $\widetilde{T}_i^*$ of $\widetilde{G}_i^*$. So, by removing (respectively) $0, 1, \ldots, n-2$ edges from $\widetilde{T}_i^*$, we obtain a forest corresponding to a summand of (respectively) $d_0, d_1, \ldots, d_{n-2}$. Hence, $d_0, d_1, \ldots, d_{n-2}$ are nonzero polynomials of degree (respectively) $n-1, n-2, \ldots, 1$.

We now consider the remaining case, when $In \neq Out$ (i.e., $i \neq j$). First, we claim that $d_{n-1} = d_{n-2} = \cdots = d_{n-L} = 0$. Indeed, by Theorem 4.2.1 and Lemma 4.1.11, these d_k's are sums over certain subgraphs of G, with $0, 1, \ldots, L-1$ (respectively) edges, containing a path from the input compartment j to output i; but no such subgraphs exist (by definition of L). On the other hand, spanning incoming forests of $\widetilde{G}_i^*$ having $L, L+1, \ldots, n-1$ edges and a directed path from the input j to output i do exist. We construct such forests as follows. Start with a spanning incoming forest F of $\widetilde{G}_i^*$ with $n-1$ edges (so the underlying undirected graph is a tree) such that F contains a directed path P of length L from input to output (it is straightforward to show that such a forest exists, using the fact that G is strongly connected). Next, to obtain an appropriate forest with (respectively) $L, L+1, \ldots, n-1$ edges, remove (respectively) $n-L-1, n-L-2, \ldots, 0$ non-P edges from F. Thus, as desired, the coefficients $d_{n-L-1}, d_{n-L-2}, \ldots, d_0$ are non-constant. □

Remark 4.2.3 (Constant coefficients)**.** From the proof of Corollary 4.2.2, we know the values of the constant coefficients in the input-output equation (4.4):

$$\begin{cases} c_0 = 0 & \text{if } Leak = \emptyset \\ d_{n-1} = 1 & \text{if } In = Out \\ d_{n-L} = d_{n-L+1} = \cdots = d_{n-1} = 0 & \text{if } In \neq Out\ . \end{cases}$$

In particular, in the right-hand side of (4.4), the highest derivative $u_j^{(d)}$ (with nonzero coefficient) in that sum is when $d = n-1-L$, where L is the length of the shortest (directed) path from the unique input to the unique output.

Corollary 4.2.2 immediately yields the next result, which answers the question posed in (Gerberding et al. 2020, §2.2) of how read off the number of coefficients directly from a model. That is, we give a formula for the number D where $\mathbf{c}\mathbb{R}^{|E|+|Leak|} \to \mathbb{R}^D$ is the coefficient map.

Corollary 4.2.4 (Number of coefficients)**.** *Consider a strongly connected linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ with $|In| = |Out| = 1$. Let n be the number of compartments and L the length of the shortest (directed) path in G from the (unique) input compartment to the (unique) output. Then the numbers of non-constant coefficients on the left-hand and right-hand sides of* (4.4) *are as follows:*

$$\#\text{ on LHS} = \begin{cases} n & \text{if } Leak \neq \emptyset \\ n-1 & \text{if } Leak = \emptyset \end{cases} \qquad \text{and} \qquad \#\text{ on RHS} = \begin{cases} n-1 & \text{if } In = Out \\ n-L & \text{if } In \neq Out. \end{cases}$$

In the next section, we use Corollary 4.2.4 to prove that identifiability is preserved when a linear compartmental model is enlarged in certain ways (see Theorems 4.3.2 and 4.3.3). In Chan et al. (2021), Corollary 4.2.4 is used to partially resolve some conjectures on identifiability.

Finally, we obtain an easy-to-check condition that guarantees that a model is unidentifiable due to having more parameters than coefficients.

Corollary 4.2.5 (Criterion for unidentifiability)**.** *Consider a strongly connected linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$, where $G = (V, E)$. Assume $|In| = |Out| = 1$. Let n be the number of compartments, and let L be the length of the shortest (directed) path in G from the (unique) input compartment to the (unique) output. If one of the following conditions holds:*

1. *$Leak \neq \emptyset$, $In = Out$, and $|E| + |Leak| > 2n-1$,*
2. *$Leak \neq \emptyset$, $In \neq Out$, and $|E| + |Leak| > 2n-L$,*
3. *$Leak = \emptyset$, $In = Out$, and $|E| > 2n-2$, or*
4. *$Leak = \emptyset$, $In \neq Out$, and $|E| > 2n-L-1$,*

then $\mathcal{M}$ is unidentifiable.

Proof. First consider the case of no parameters (i.e., $|E|+|Leak|=0$). Then, $|E|=0 \leq 2n-2$ and (if $In \neq Out$) $|E|=0 \leq 2n-L-1$, so none of the four conditions hold.

Now assume that $|E|+|Leak| \geq 1$. Let $\mathbf{c}\mathbb{R}^{|E|+|Leak|} \to \mathbb{R}^D$ denote the coefficient map arising from the input-output equation (4.1). Corollary 4.2.4 implies that $|E|+|Leak| > D$, and so, c is infinite-to-one. Hence, $\mathscr{M}$ is unidentifiable. □

Remark 4.2.6. Corollary 4.2.5 is complementary to Theorem 3.5.1, a special case of which asserts that a strongly connected linear compartmental model with $|In|=|Out|=1$ and $|Leak| > |In \cup Out|$, is unidentifiable.

Example 4.2.7 (Example 4.1.5, continued)**.** For the model in Figure 1.10, the input-output equation was shown in Example 4.1.5. The resulting coefficient map $\mathbf{c}\mathbb{R}^7 \to \mathbb{R}^5$ is:

$$
\begin{aligned}
&(a_{02}, a_{12}, a_{13}, a_{21}, a_{23}, a_{31}, a_{32}) \mapsto \\
&\qquad (a_{02}+a_{12}+a_{13}+a_{21}+a_{23}+a_{31}+a_{32}, \ldots, a_{02}a_{13}+a_{12}a_{13}+a_{02}a_{23}+a_{12}a_{23}+a_{13}a_{32})\,.
\end{aligned}
$$

There are more parameters than coefficients, so c is generically infinite-to-one, hence unidentifiable.

Also, note that this model has $n=3$ compartments, $Leak=\emptyset$, $In=Out=\{1\}$, and $|E|+|Leak|=6+17>2n-1=5$. So, Corollary 4.2.4 confirms what we just found, i.e. the model is unidentifiable.

Example 4.2.8 (Bidirectional cycle models)**.** Let $n \geq 3$. Let G_n be the bidirectional cycle graph with n vertices (so the edges are $1 \leftrightarrows 2 \leftrightarrows \cdots \leftrightarrows n \leftrightarrows 1$). This graph has $2n$ edges, so Corollary 4.2.5 implies that every linear compartmental model $\mathscr{M}=(G_n, In, Out, Leak)$ with $|In|=|Out|=1$ – such as the model in Figure 1.10 – is unidentifiable.

The next example shows that, in general, the converse of Corollary 4.2.5 does not hold.

Example 4.2.9. The model displayed in Figure 4.2 has $n=3$ compartments, $In=Out$, $Leak=\emptyset$, and $|E|=4=2n-2$. Thus, Corollary 4.2.5 does not apply. Nevertheless, it is straightforward to check that the model is unidentifiable.

4.2.2 Proof of Theorem 4.2.1

To prove Theorem 4.2.1, we need several preliminary results.

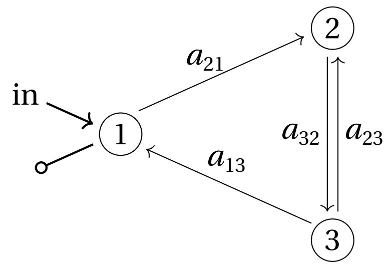

Figure 4.2: A linear compartmental model described in Example 4.2.9

Lemma 4.2.10. *Consider a linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ with compartmental matrix A. Let i and j be distinct compartments with $i \neq 1$ and $j \neq 1$. Then:*

$$\det\big((\lambda I - A)^{\{1,i\},\{1,j\}}\big) \;=\; \lambda^{-1} \det\big((\lambda I - A_1^*)^{i,j}\big).$$

Proof. Recall that A_1^* is obtained from A by replacing the first column by a column of 0's. Thus, the first column of $(\lambda I - A_1^*)^{i,j}$ is $(\lambda, 0, \ldots, 0)^T$ (we are also using $1 \neq i, j$ here), and so Laplace expansion along that column yields the following equality:

$$\begin{aligned} \det\big((\lambda I - A_1^*)^{i,j}\big) \;&=\; \lambda \det\big((\lambda I - A_1^*)^{\{1,i\},\{1,j\}}\big) \\ &=\; \lambda \det\big((\lambda I - A)^{\{1,i\},\{1,j\}}\big), \end{aligned} \tag{4.5}$$

and the second equality comes from the fact that, after removing column-1, the matrices A and A_1^* (and thus also $\lambda I - A$ and $\lambda I - A_1^*$) are equal. The equalities (4.5) now imply the desired equality. □

Lemma 4.2.11. *Consider a linear compartmental model $\mathcal{M} = \{G, In, Out, Leak\}$ with $In = Out = \{1\}$. Then, for every positive integer j, the following equality holds:*

$$\sum_{F^* \in \mathscr{F}_j^{1,1}(\widetilde{G}_1^*)} \pi_{F^*} \;=\; \sum_{F \in \mathscr{F}_j(\widetilde{G}_1)} \pi_F \;.$$

Proof. First, for any graph H, note that $\mathscr{F}_j^{i,i}(H)$, i.e., the j-edge, spanning, incoming forests of H containing a path from i to i, is the same as $\mathscr{F}_j(H)$, i.e., the j-edge, spanning, incoming forests of H. Hence, to complete the proof, it suffices to find a bijection of the following form that preserves productivity (that is, $\pi_{\phi(F^*)} = \pi_{F^*}$):

$$\phi : \mathscr{F}_j(\widetilde{G}_1^*) \to \mathscr{F}_j(\widetilde{G}_1) . \tag{4.6}$$

We first explain informally what this map ϕ will be. Recall that $\widetilde{G}_1$ is obtained from $\widetilde{G}_1^*$ by "flipping" all edges pointing toward compartment-1 (e.g., $2 \to 1$ and $3 \to 1$ in the lower-right of Figure 4.1) so that they point toward compartment-0 (e.g., $2 \to 0$ and $3 \to 0$ in the lower-left of Figure 4.1), while keeping the same edge labels. Accordingly, we will define ϕ to do the same edge-flipping in spanning forests F^* of $\widetilde{G}_1^*$ in order to obtain (as we will show) spanning forests of $\widetilde{G}_1$.

We define ϕ precisely, as follows. Let $\mathscr{L}$ denote the set of edge labels of $\widetilde{G}_1$ (which is also the set of edge labels of $\widetilde{G}_1^*$). A spanning subgraph (of any graph) is uniquely determined by its set of edges, so every size-j subset of labels $S \subseteq \mathscr{L}$ defines (i) a unique j-edge subgraph of $\widetilde{G}_1$, which we denote by F_S, and also (ii) a unique j-edge subgraph of $\widetilde{G}_1^*$, which we denote by F_S^*. By construction, F_S and F_S^* have the same productivity (for any $S \subseteq \mathscr{L}$). Hence, we define ϕ by $\phi : F_S^* \mapsto F_S$, and then to show that this map gives the desired bijection (4.6), we need only prove the following two claims:

Claim 1: If $F_S^* \in \mathscr{F}_j(\widetilde{G}_1^*)$, then each node of F_S has at most 1 outgoing edge and there is no cycle in the underlying undirected graph of F_S .

Claim 2: If $F_S \in \mathscr{F}_j(\widetilde{G}_1)$, then each node of F_S^* has at most 1 outgoing edge and there is no cycle in the underlying undirected graph of F_S^* .

The condition on the outgoing edges in Claims 1 and 2 is easy to verify. Indeed, the edge-flip procedure preserves the source node of each edge and so the number of outgoing edges of each node is the same in F_S and F_S^* (or, in the case of node 1, there are no outgoing edges in F_S^* while the node simply does not exist in F_S).

We prove the rest of Claims 1 and 2 by contrapositive, as follows. Assume that F_S is a subgraph of $\widetilde{G}_1$ such that (i) each node has at most 1 outgoing edge and (ii) the underlying undirected graph contains a cycle. It follows that this cycle must in fact form a directed cycle, and so must not involve node-0. Hence, the edges of the cycle are not affected by edge-flipping, and so F_S^* contains the same cycle. Similarly, if F_S^* is a subgraph of $\widetilde{G}_1^*$ with each node having at most 1 outgoing edge and containing a cycle, then this must be a directed cycle which therefore avoids nodes 0 and 1, and so is present in F_S.

Hence, Claims 1 and 2 hold, and so we have the required bijection ϕ as in (4.6). □

Proposition 4.2.12. *Let $\mathscr{M} = (G, In, Out, Leak)$ be a linear compartmental model with n compartments and compartmental matrix A. Let q and r be compartments. Then, in the* *following equation:*

$$\det((\lambda I - A)^{r,q}) = c_{n-1}\lambda^{n-1} + c_{n-2}\lambda^{n-2} + \cdots + c_0 \ , \tag{4.7}$$

the coefficients are given by

$$c_k \ = \ (-1)^{q+r} \sum_{F \in \mathscr{F}^{r,q}_{n-k-1}(\widetilde{G}^*_q)} \pi_F \quad \text{for } k = 0, 1, \ldots, n-1. \tag{4.8}$$

Proof. For convenience, we rename $out := q$. Next, we claim that it suffices to consider the case of $r = 1$. Indeed, if $r \neq 1$, then switching (relabeling) compartments 1 and r (without relabeling edges) yields a model for which the compartmental matrix, which we denote by B, is obtained from A by switching rows 1 and r and columns 1 and r, and so $(\lambda I - A)^{r,out}$ and $(\lambda I - B)^{1,out}$ have the same determinant. Thus, the $r \neq 1$ case reduces to the $r = 1$ case, and so we assume $r = 1$ for the rest of the proof.

We first analyze the case when $out = 1$. Then, by Proposition 4.1.6, the coefficients c_k in (4.7) (for $k = 0, 1, \ldots, n-1$) are given by the first equality here:

$$c_k \quad = \quad (-1)^{1+1} \sum_{F \in \mathscr{F}_{n-k-1}(\widetilde{G}_1)} \pi_F \quad = \quad \sum_{F \in \mathscr{F}^{1,1}_{n-k-1}(\widetilde{G}^*_1)} \pi_F \ ,$$

and the second equality comes from Lemma 4.2.11. This completes the case of $out = 1$.

Now suppose that $out \neq 1$. We proceed by strong induction on the number of edges of G. For the base case, suppose that G has no edges. Then the only edges of $\widetilde{G}^*_{out}$ (if any) are leak edges ($\ell \to 0$ for $\ell \in Leak$). Thus, there are no spanning incoming forests on $\widetilde{G}^*_{out}$ in which out and 1 are in the same connected component (recall that $1 \neq out$). The formula in equation (4.8) therefore yields $c_0 = c_1 = \cdots = c_{n-1} = 0$.

Thus, it suffices (for the base case) to show that $\det(\lambda I - A)^{1,out} = 0$. To see this, note that the only nonzero entries of A (if any) are leak terms on the diagonal. Therefore $(\lambda I - A)$ is also a diagonal matrix. Hence, in the matrix $(\lambda I - A)^{1,out}$, the column corresponding to 1 (which exists because $1 \neq out$) consists of 0's, and so the determinant of $(\lambda I - A)^{1,out}$ is 0. This completes the base case.

Now suppose that the theorem holds for all models $\mathscr{N} = (H, In_{\mathscr{N}}, Out_{\mathscr{N}}, Leak_{\mathscr{N}})$ with $|E_H| \leq p - 1$ (for some $p \geq 1$). Consider a model $\mathscr{M} = (G, In, Out, Leak)$ with $|E_G| = p$.

We first consider the special case when G has no edges of the form $1 \to i$, that is, outgoing from compartment-1. Essentially the same argument we made in the earlier base case applies, as follows. In the compartmental matrix A, the first column consists of 0's, and so $\det\big((\lambda I - A)^{1,out}\big) = 0$. Also, there are no spanning incoming forests on $\widetilde{G}^*_{out}$ in which out and 1 are in the same connected component (recall Lemma 4.1.11 and our assumption that $1 \neq out$). So, equation (4.8) yields $c_0 = c_1 = \cdots = c_{n-1} = 0$. The theorem therefore holds in the case when G has no edges outgoing from 1.

Assume now that G has at least one edge of the form $1 \to i$. Our first step in evaluating $\det\big((\lambda I - A)^{1,out}\big)$ is to perform a Laplacian expansion along the first column. In this column, the nonzero entries are precisely the $-a_{i,1}$'s, for those $2 \leq i \leq n$ for which $1 \to i$ is an edge (because row-1 of the matrix $(\lambda I - A)$ was deleted). Laplace expansion along this column therefore yields the first equality here:

$$\begin{aligned}
\det\big((\lambda I - A)^{1,out}\big) &= \sum_{i:\,(1\to i)\in E_G} (-1)^i(-a_{i1})\det\big((\lambda I - A)^{\{1,i\},\{1,out\}}\big) \\
&= \sum_{i:\,(1\to i)\in E_G} (-1)^{i+1} a_{i1}\lambda^{-1}\det\big((\lambda I - A_1^*)^{i,out}\big)\ ,
\end{aligned} \tag{4.9}$$

and the second equality follows from Lemma 4.2.10 (and simplifying).

Our next step is to evaluate the determinant that appears in the right-hand side of equation (4.9). Accordingly, we claim that the following equality holds:

$$\det\big((\lambda I - A_1^*)^{i,out}\big) = (-1)^{i+out}\sum_{j=0}^{n-1}\left(\sum_{F\in\mathscr{F}^{i,out}_{n-j-1}(\widetilde{\mathfrak{G}}^*_{out})}\pi_F\right)\lambda^j\ , \tag{4.10}$$

where $\mathfrak{G}$ is the graph obtained from G by removing all edges outgoing from compartment 1.

We will prove the claimed equality (4.10) by interpreting the matrix A_1^* as the compartmental matrix of a model having fewer edges than $\mathscr{M}$, and so the inductive hypothesis will apply. To this end, notice that A_1^* is the compartmental matrix of the following model:

$$\mathscr{M}_1^* := (\mathfrak{G},\ In,\ Out,\ Leak \smallsetminus In)\,.$$

We consider two subcases, based on whether $i = out$. The subcase when $i = out$ was proven already at the beginning of the proof (applied to the model $\mathscr{M}_1^*$):

$$\det\big((\lambda I - A_1^*)^{out,out}\big) = \sum_{j=0}^{n-1}\left(\sum_{F\in\mathscr{F}^{out,out}_{n-j-1}(\widetilde{\mathfrak{G}}^*_{out})}\pi_F\right)\lambda^j\ .$$

Now consider the remaining subcase, when $i \neq out$. By construction and our assumption that G has an edge of the form $1 \to i$, the graph $\mathfrak{G}$ has fewer edges than G. The inductive hypothesis therefore holds for $\mathscr{M}_1^*$ and yields precisely the equality (4.10), and so our claim is proven.

Next, we substitute the expression in (4.10) into the right-hand side of equation (4.9), simplify, rearrange the order of summation, apply Lemma 4.1.12 (where $H = \widetilde{G}^*_{out}$, $K = \widetilde{\mathfrak{G}}^*_{out}$, $k = 1$, and $\ell = out$), and then apply the change of variables $k = j - 1$:

$$\begin{aligned}
\det\big((\lambda I - A)^{1,out}\big) &= \sum_{i\,:\,(1\to i)\in E_G} (-1)^{i+1} a_{i1} \lambda^{-1} (-1)^{i+out} \sum_{j=0}^{n-1} \left(\sum_{F \in \mathscr{F}^{i,out}_{n-j-1}\left(\widetilde{\mathfrak{G}}^*_{out}\right)} \pi_F \right) \lambda^j \\
&= (-1)^{out+1} \sum_{j=0}^{n-1} \left(\sum_{i\,:\,(1\to i)\in E_G} \; \sum_{F \in \mathscr{F}^{i,out}_{n-j-1}\left(\widetilde{\mathfrak{G}}^*_{out}\right)} a_{i1} \pi_F \right) \lambda^{j-1} \\
&= (-1)^{out+1} \sum_{j=0}^{n-1} \left(\sum_{F^* \in \mathscr{F}^{1,out}_{n-j}\left(\widetilde{G}^*_{out}\right)} \pi_{F^*} \right) \lambda^{j-1} \\
&= (-1)^{out+1} \sum_{k=-1}^{n-2} \left(\sum_{F \in \mathscr{F}^{1,out}_{n-k-1}\left(\widetilde{G}^*_{out}\right)} \pi_F \right) \lambda^{k} .
\end{aligned}$$

Comparing the above expression with the desired coefficients in (4.7) and (4.8), it suffices to show that, when $k = -1$ or $k = n-1$, the following coefficient is 0:

$$c_k \;=\; \sum_{F \in \mathscr{F}^{1,out}_{n-k-1}\left(\widetilde{G}^*_{out}\right)} \pi_F \; .$$

We first consider $k = -1$. The graph $\widetilde{G}^*_{out}$ has $n+1$ nodes, and both out and 0 (the leak compartment) have no outgoing edges. Therefore, every incoming spanning forest of $\widetilde{G}^*_{out}$ has at least two sink nodes and so (by Lemma 4.1.10) at least two connected components. Such a forest therefore has no more than $n-1$ edges. We conclude that $\mathscr{F}^{1,out}_{n-k-1}(\widetilde{G}^*_{out}) = \mathscr{F}^{1,out}_{n}(\widetilde{G}^*_{out}) = \emptyset$, and so $c_{-1} = 0$, as desired.

Similarly, for $k = n-1$, we have $\mathscr{F}^{1,out}_{n-k-1}(\widetilde{G}^*_{out}) = \mathscr{F}^{1,out}_{0}(\widetilde{G}^*_{out}) = \emptyset$, because the graph with no edges lacks a path from 1 to out (recall that we have assumed $1 \neq out$). So, $c_{n-1} = 0$. This completes the case of $1 \neq out$, and thus our proof is complete. □

We can now prove Theorem 4.2.1.

Proof of Theorem 4.2.1. The left-hand side of the input-output equation (4.1) is $\det(\partial I - A)y_i$, and the formula for the coefficients of this expression was previously shown in Proposition 4.1.6. As for the right-hand side, the formula for these coefficients follows easily from Propositions 4.1.4 and 4.2.12. $\square$

4.3 Results on adding an edge

In this section, we introduce a new operation on linear compartmental models: we add a bidirected edge from an existing compartment to a new compartment (Definition 4.3.1). For instance, in Figure 4.3, the bidirected edge $1 \leftrightarrows 4$ is added to $\mathscr{M}$ to obtain the models $\mathscr{M}'$ and $\mathscr{M}''$ (in $\mathscr{M}'$, the output is also moved). We prove that identifiability is preserved when the original model has input and output in a single compartment, the new edge involves that compartment, and the input or output is moved to the new compartment (Theorem 4.3.3). Similarly, we prove that identifiability is preserved when the input and output, which may be in distinct compartments, are not moved (Theorem 4.3.2).

Definition 4.3.1. Let $G = (V_G, E_G)$ be a graph with vertex set $V_G = \{1, 2, \ldots, n-1\}$ (for some $n \geq 2$). Let $i \in V_G$. The *graph obtained from G by adding a leaf edge at i* is the graph $H = (V_H, E_H)$ with vertex set $V_H := \{1, 2, \ldots, n\}$ and edge set $E_H := E_G \cup \{i \longleftrightarrow n\}$.

Theorem 4.3.2 (Add leaf edge)**.** *Assume $n \geq 3$. Consider a strongly connected linear compartmental model with $n-1$ compartments, one input, one output, and no leaks, $\mathscr{M} = (G, \{in\}, \{out\}, \emptyset)$. Let H be the graph obtained from G by adding a leaf edge at compartment $n-1$, and consider the linear compartmental model $\mathscr{M}' = (H, \{in\}, \{out\}, \emptyset)$. If $\mathscr{M}$ has expected dimension (or, respectively, is generically locally identifiable), then $\mathscr{M}'$ also has expected dimension (respectively, is generically locally identifiable).*

We prove Theorem 4.3.2 in Section 4.3.1.

Theorem 4.3.3 (Add leaf edge and move input or output)**.** *Assume $n \geq 3$. Let $\mathscr{M} = (G, In, Out, Leak)$ be a strongly connected linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$ and $Leak = \emptyset$. Let H be the graph obtained from G by adding a leaf edge at compartment 1. Consider a linear compartmental model $\mathscr{M}' = (H, In', Out', Leak')$ with $Leak' = \emptyset$ and either $(In', Out') = (\{1\}, \{n\})$ or $(In', Out') = (\{n\}, \{1\})$. Then $\mathscr{M}$ has expected dimension (or, respectively, is generically locally identifiable) if and only if $\mathscr{M}'$ has expected dimension (respectively, is generically locally identifiable).*

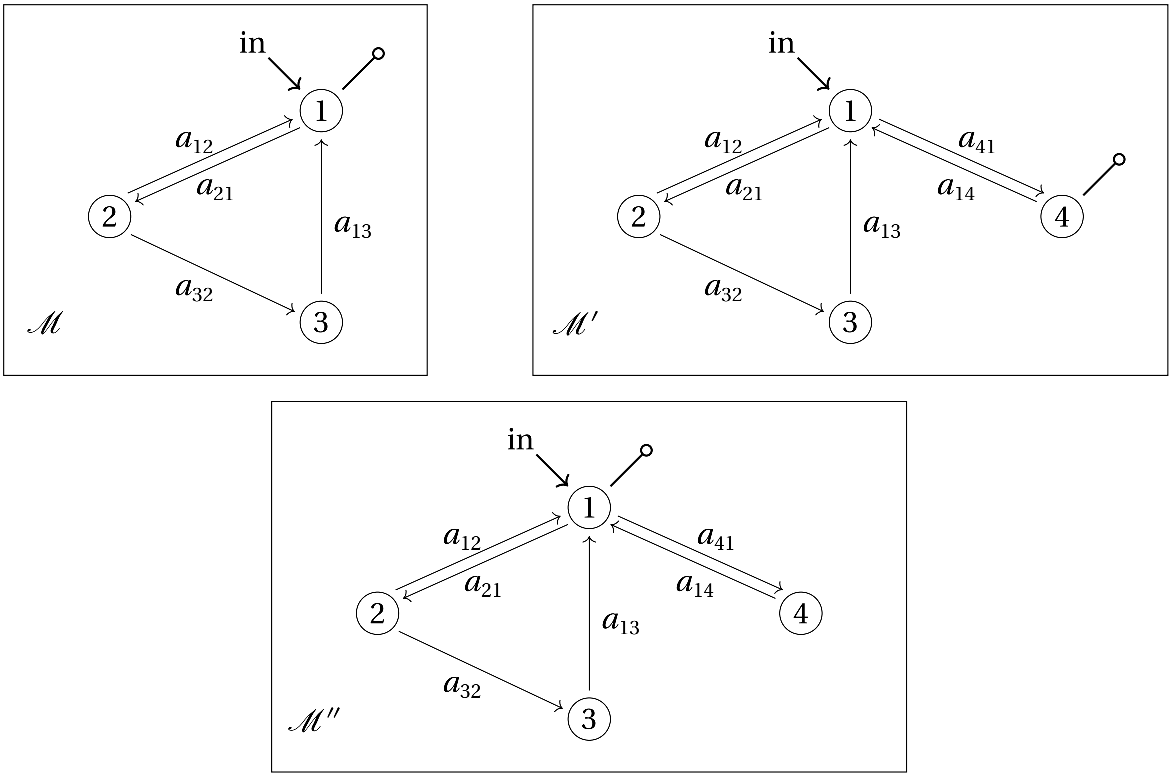

Figure 4.3: Depicted are three models, $\mathscr{M} = (G, \{1\}, \{1\}, \emptyset)$, $\mathscr{M}' = \{G', \{1\}, \{4\}, \emptyset\}$, and $\mathscr{M}'' = \{G', \{1\}, \{1\}, \emptyset\}$, where G' is the graph obtained from G by adding a leaf edge at compartment 1 (to a new compartment 4). See Example 4.3.9.

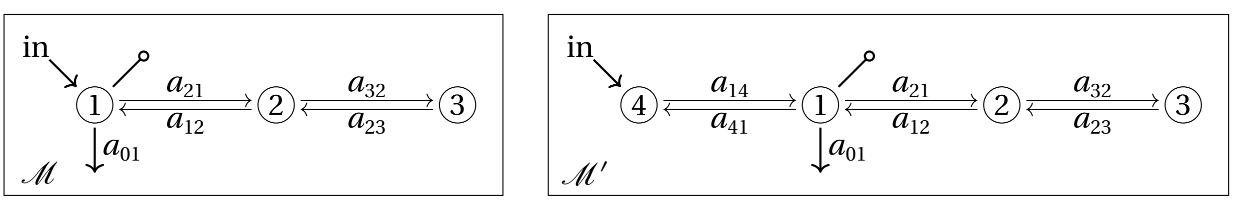

Figure 4.4: Two (catenary) models, $\mathscr{M} = (G, \{1\}, \{1\}, \{1\})$ and $\mathscr{M}' = (G', \{4\}, \{1\}, \{1\})$, where the graph G' is obtained from G by adding a leaf edge at compartment 1.

We prove Theorem 4.3.3 in Section 4.3.4. An immediate corollary, which comes from applying Proposition 4.1.15(1), pertains to models with one leak, as follows.

Corollary 4.3.4. *Assume $n \geq 3$. Let $\mathscr{M} = (G, In, Out, Leak)$ be a strongly connected linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$ and $Leak = \emptyset$. Let H be the graph obtained from G by adding a leaf edge at compartment 1. Consider a linear compartmental model $\mathscr{M}' = (H, In', Out', Leak')$ with $|Leak'| = 1$ and either $(In', Out') = (\{1\}, \{n\})$ or $(In', Out') = (\{n\}, \{1\})$. If $\mathscr{M}$ is identifiable, then $\mathscr{M}'$ is also identifiable.*

Next, we reveal a new class of identifiable models, namely, inductively strongly connected models in which the input and output compartments form a leaf edge, as follows.

Corollary 4.3.5 (Add a leaf and move input/output in inductively strongly connected models)**.** *Assume $n \geq 3$. Let $\mathscr{M} = (G, In, Out, Leak)$ be a linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$, $Leak = \emptyset$, and G is inductively strongly connected with respect to vertex 1. Let H be the graph obtained from G by adding a leaf edge at compartment 1. Consider a model $\mathscr{M}' = (H, In', Out', Leak')$ with $|Leak'| \leq 1$ and either $(In', Out') = (\{1\}, \{n\})$ or $(In', Out') = (\{n\}, \{1\})$. Then $\mathscr{M}'$ is generically locally identifiable.*

Proof. This result follows from Proposition 4.1.14, Theorem 4.3.3, and Corollary 4.3.4. □

Remark 4.3.6. The assumption of $n \geq 3$ in Theorems 4.3.2 and 4.3.3 and other results in this section is simply to avoid cases of models we are not interested in, namely, those with no compartments or no parameters.

Remark 4.3.7. The effect of moving the input or output *without* adding new compartments or edges was considered for cycle models in Gerberding et al. (2020).

Remark 4.3.8. Baaijens and Draisma considered operations that preserve expected dimension in models with input and output in the same compartment and leaks in all compartments (Baaijens and Draisma 2016).

Example 4.3.9. Consider the models shown in Figure 4.3. The model $\mathscr{M}$ is identifiable by Proposition 4.1.14. So, by Theorems 4.3.2 and 4.3.3, $\mathscr{M}''$ and $\mathscr{M}'$ are also identifiable. Another way to see that $\mathscr{M}'$ is identifiable, is by applying Corollary 4.3.5 to $\mathscr{M}$.

Example 4.3.10. Consider the models in Figure 4.4. The model $\mathscr{M}$ is identifiable, by Proposition 4.1.14. Thus, the model obtained from $\mathscr{M}$ by removing the leak, which we denote by $\mathscr{M}_0$, is also identifiable, by Proposition 4.1.15(2). Applying Corollary 4.3.4 to the model $\mathscr{M}_0$, we obtain that $\mathscr{M}'$ is also identifiable.

Theorems 4.3.2 and 4.3.3 are both used in the next section to classify identifiable models in which the underlying graph is a bidirected tree. In particular, for catenary models (that is, when the graph is a path), we saw in Example 4.3.10 that a corollary of Theorem 4.3.3 applies to some models with an input or output in a leaf compartment (e.g., compartments 1 and 3 of the model $\mathscr{M}$ in Figure 4.4), but we will need Theorem 4.3.2 to handle models in which both the input and output are in non-leaf compartments.

The rest of this section is dedicated to proving Theorems 4.3.2 and 4.3.3. We first prove Theorem 4.3.2 (Section 4.3.1). Next, we analyze moving the output (Section 4.3.2) and the input (Section 4.3.3), and then combine those results to prove Theorem 4.3.3 (Section 4.3.4).

4.3.1 Proof of Theorem 4.3.2

To prove Theorem 4.3.2, we need a result from Meshkat and Sullivant (2014). To state that result, we must first recall how a weight vector ω defines initial forms of polynomials. Consider a polynomial $g \in \mathbb{K}[x_1, x_2, \ldots, x_r]$, where $\mathbb{K}$ is a field. Let $\omega \in \mathbb{Q}^r$. Then ω defines a weight of a monomial x^α (where $\alpha \in \mathbb{Z}^r_{\geq 0}$), namely, $\langle \omega, \alpha \rangle$. Now the *initial-form polynomial* (with respect to ω) of g, denoted by g_ω, is the sum of all terms of g for which the monomial has highest weight. We can now state the following lemma, which is (Meshkat and Sullivant 2014, Corollary 5.9).

Lemma 4.3.11. *Let $\mathbb{K}$ be a field. Consider a map $\phi : \mathbb{K}^r \to \mathbb{K}^s$ given by polynomials $f_1, f_2, \ldots, f_s \in \mathbb{K}[x_1, x_2, \ldots, x_r]$. Let $\omega \in \mathbb{Q}^r$. Define $\phi_\omega : \mathbb{K}^r \to \mathbb{K}^s$ to be the map given by the inital-form polynomials $(f_1)_\omega, (f_2)_\omega, \ldots, (f_s)_\omega$. Then*

$$\dim(\text{image } \phi_\omega) \leq \dim(\text{image } \phi)\,.$$

The following proof closely follows that of (Meshkat and Sullivant 2014, Theorem 5.7).

Proof of Theorem 4.3.2. If $in = out$, we define $D := 1$. If $in \neq out$, we define D to be the length of the shortest (directed) path in G from in to out. By construction, if $in \neq out$, then D is also the length of the shortest (directed) path from in to out in H.

Let $\phi_{\mathscr{M}}$ and $\phi_{\mathscr{M}'}$ denote, respectively, the coefficient maps for $\mathscr{M}$ and $\mathscr{M}'$. By Corollary 4.2.4, the number of coefficients of $\phi_{\mathscr{M}}$ is $(n-2)+(n-1-D) = 2n-3-D$. Similarly, the number of coefficients of $\phi_{\mathscr{M}'}$ is $2n-1-D$. Also, by construction, $\mathscr{M}$ has $|E_G|$ parameters; and $\mathscr{M}'$ has $|E_G|+2$ parameters. Therefore, the assumption that $\mathscr{M}$ has expected dimension is the following equality:

$$\dim(\text{image } \phi_{\mathscr{M}}) = \min\{|E_G|,\ 2n-3-D\}\ , \tag{4.11}$$

in which case our goal is to prove the following equality:

$$\dim(\text{image } \phi_{\mathscr{M}'}) = \min\{|E_G|+2,\ 2n-1-D\}\ . \tag{4.12}$$

Similarly, the assumption that $\mathscr{M}$ is identifiable is the following equality:

$$\dim(\text{image } \phi_{\mathscr{M}}) = |E_G|\ , \tag{4.13}$$

in which case our goal is to prove the following equality:

$$\dim(\text{image } \phi_{\mathscr{M}'}) = |E_G|+2\ . \tag{4.14}$$

The inequalities "$\leq$" in (4.12) and (4.14) always hold, so we need only prove "$\geq$". Moreover, in light of the equalities (4.11) and (4.13), it suffices (for either case) to prove that

$$\dim(\text{image } \phi_{\mathscr{M}'}) \geq 2+\dim(\text{image } \phi_{\mathscr{M}})\ . \tag{4.15}$$

With an eye toward applying Lemma 4.3.11, define the weight vector $\omega : \{a_{ij} \mid (j,i) \in E_H\} \to \mathbb{R}$ as follows:

$$\omega(a_{ij}) := \begin{cases} 0 & \text{if } (i,j) \in \{(n-1,n),\ (n,n-1)\} \\ 1 & \text{otherwise.} \end{cases}$$

We will analyze the pullback maps $\phi^*_{\mathscr{M}} : \mathbb{Q}[c_1, c_2, \ldots, c_{n-2},\ d_0, d_1, \ldots, d_{n-2-D}] \to \mathbb{Q}[a_{ij} \mid (j,i) \in E_G]$ and $\phi^*_{\mathscr{M}'} : \mathbb{Q}[c_1, c_2, \ldots, c_{n-1},\ d_0, d_1, \ldots, d_{n-1-D}] \to \mathbb{Q}[a_{ij} \mid (j,i) \in E_H]$. Recall that $\phi^*_{\mathscr{M}}$ (respectively, $\phi^*_{\mathscr{M}'}$) sends each c_k or d_k to the corresponding polynomial in the a_{ij}'s for the model $\mathscr{M}$ (respectively, $\mathscr{M}'$), as given in Theorem 4.2.1.

By Theorem 4.2.1, all the polynomials $\phi^*_{\mathscr{M}}(c_i)$, $\phi^*_{\mathscr{M}}(d_i)$, $\phi^*_{\mathscr{M}'}(c_i)$, and $\phi^*_{\mathscr{M}'}(d_i)$ are homogeneous in the parameters $a_{j\ell}$. Hence, the corresponding initial-form polynomials $\phi^*_{\mathscr{M},\omega}(c_i)$, $\phi^*_{\mathscr{M},\omega}(d_i)$, $\phi^*_{\mathscr{M}',\omega}(c_i)$, and $\phi^*_{\mathscr{M}',\omega}(d_i)$ are obtained by removing all terms involving $a_{n-1,n}$ or $a_{n,n-1}$ – as long as there exist other terms in the polynomial. These other terms, by Theorem 4.2.1, correspond to spanning incoming forests of H that do not involve the edges

$(n-1) \leftrightarrows n$ (there are no leaks, so we need not leak-augment the graph), or, equivalently, spanning incoming forests of G. In particular, there exist such forests of G with $1, 2, \ldots, n-2$ edges, and so we obtain:

$$\phi^*_{\mathscr{M}',\omega}(c_i) = \phi^*_{\mathscr{M}}(c_{i-1}) \quad \text{for } i = 2, 3, \ldots, n-1 \,. \tag{4.16}$$

(The shift in the index, from i to $i-1$, comes from the fact that H has n compartments, while G has $n-1$.) Similarly, there are spanning incoming forests of G with in and out in the same component and $D, D+1, \ldots, n-2$ edges. Thus, we have:

$$\phi^*_{\mathscr{M}',\omega}(d_i) = \phi^*_{\mathscr{M}}(d_{i-1}) \quad \text{for } i = 1, 2, \ldots, n-1-D \,. \tag{4.17}$$

There are two more coefficients of $\mathscr{M}'$ to consider: c_1 and d_0. By Theorem 4.2.1, c_1 and d_0 (or, more precisely, $\phi^*_{\mathscr{M}',\omega}(c_1)$ and $\phi^*_{\mathscr{M}',\omega}(d_0)$) are both sums of productivities of $(n-1)$-edge spanning incoming forests on H (which has n vertices). Hence, each such forest must use exactly one edge from the edges $(n-1) \leftrightarrows n$. We conclude that each term in $\phi^*_{\mathscr{M}',\omega}(c_1)$ (respectively, in $\phi^*_{\mathscr{M}',\omega}(d_0)$) contains exactly one of $a_{n-1,n}$ or $a_{n,n-1}$. This implies that the respective initial-form polynomials agree with the two original polynomials:

$$\widetilde{c}_1 := \phi^*_{\mathscr{M}',\omega}(c_1) = \phi^*_{\mathscr{M}'}(c_1) \qquad \text{and} \qquad \widetilde{d}_0 := \phi^*_{\mathscr{M}',\omega}(d_0) = \phi^*_{\mathscr{M}'}(d_0) \,. \tag{4.18}$$

We can say more about the polynomials $\widetilde{c}_1$ and $\widetilde{d}_0$ in (4.18). First, $\widetilde{d}_0$ does not involve the parameter $a_{n,n-1}$, as $\widetilde{d}_0$ is a sum over $(n-1)$-edge spanning incoming forests of H in which out is the only sink (by Theorem 4.2.1 and Lemma 4.1.10) and such forests do not contain the edge $(n-1) \to n$ (as this would make compartment-n a sink). Moreover, it is straightforward to check that these forests are exactly those obtained by adding the edge $n \to (n-1)$ to an $(n-2)$-edge spanning incoming forest of G in which out is the only sink.

Similarly, the $(n-1)$-edge spanning incoming forests of H (with no condition on the location of the sink) that involve the edge $n \to (n-1)$ are obtained by attaching that edge to an $(n-2)$-edge spanning incoming forest of G. We summarize the above analysis as follows:

$$\begin{aligned} \widetilde{c}_1 &= a_{n-1,n}\phi^*_{\mathscr{M}}(c_1) + (\text{terms involving } a_{n,n-1} \text{ but not } a_{n-1,n}) \,, \\ \widetilde{d}_0 &= a_{n-1,n}\phi^*_{\mathscr{M}}(d_0) \,. \end{aligned} \tag{4.19}$$

Let $J_{\mathscr{M}}$ and $J_{\mathscr{M}',\omega}$ (respectively) denote the Jacobian matrices of $\phi_{\mathscr{M}}$ and $\phi_{\mathscr{M}',\omega}$, where the last two rows of $J_{\mathscr{M}',\omega}$ correspond to $\widetilde{c}_1$ and $\widetilde{d}_0$, and the last two columns correspond to the parameters $a_{n-1,n}$ and $a_{n,n-1}$. We use equations (4.16–4.19) to relate the two Jacobian matrices as follows:

$$J_{\mathcal{M}',\omega} = \left(\begin{array}{ccc|cc} & & & 0 & 0 \\ & J_{\mathcal{M}} & & \vdots & \vdots \\ & & & 0 & 0 \\ \hline * & \cdots & * & \frac{\partial \tilde{c}_1}{\partial a_{n-1,n}} & \frac{\partial \tilde{c}_1}{\partial a_{n,n-1}} \\ * & \cdots & * & \frac{\partial \tilde{d}_0}{\partial a_{n-1,n}} & \frac{\partial \tilde{d}_0}{\partial a_{n,n-1}} \end{array}\right) = \left(\begin{array}{ccc|cc} & & & 0 & 0 \\ & J_{\mathcal{M}} & & \vdots & \vdots \\ & & & 0 & 0 \\ \hline * & \cdots & * & * & \phi^*_{\mathcal{M}}(c_1) \\ * & \cdots & * & \phi^*_{\mathcal{M}}(d_0) & 0 \end{array}\right). \tag{4.20}$$

Both $\phi^*_{\mathcal{M}}(c_1)$ and $\phi^*_{\mathcal{M}}(d_0)$ are nonzero (by Corollary 4.2.2), so equation (4.20) implies that $\mathrm{rank}(J_{\mathcal{M}',\omega}) = 2 + \mathrm{rank}(J_{\mathcal{M}})$. Hence, we obtain the equality below (and the inequality comes from Lemma 4.3.11):

$$\dim(\text{image } \phi_{\mathcal{M}'}) \geq \dim(\text{image } \phi_{\mathcal{M}',\omega}) = 2 + \dim(\text{image } \phi_{\mathcal{M}}).$$

Thus, our desired inequality (4.15) holds, and this completes the proof. □

Remark 4.3.12 (Add leak)**.** Let $\mathcal{M}$ be a strongly connected model with one input, one output, and no leaks. Theorem 4.3.2 shows that expected dimension is preserved when a leaf edge is added to $\mathcal{M}$. The same is true when, instead of a leaf edge, a leak is added to $\mathcal{M}$. This result can be proven in an analogous way to the proof of Theorem 4.3.2, using a weight vector ω that is 0 on the new leak parameter, and 1 on all other parameters. Another approach to proving this result is given in the proof of (Gross et al. 2019, Theorem 4.3).

4.3.2 Moving the output

In this subsection, we examine what happens to a model when a leaf edge is added and the output is moved to the new compartment (see Proposition 4.3.14). The key lemma we need is as follows.

Lemma 4.3.13. *Assume $n \geq 3$. Let $\mathcal{M} = (G, In, Out, Leak)$ be a linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$ and $Leak = \emptyset$. Let H be the graph obtained from G by adding a leaf edge at compartment 1, and let $\mathcal{M}' = (H, In', Out', Leak')$ be a linear compartmental model with $Leak' = \emptyset$. Let A and A^* (respectively) denote the compartmental matrices of $\mathcal{M}$ and $\mathcal{M}'$. Then:*

1. $\det(\lambda I - A^*) = \lambda \det(\lambda I - A) + a_{1n} \det(\lambda I - A) + a_{n1} \lambda \det\big((\lambda I - A)^{1,1}\big)$,

2. $\det\big((\lambda I - A^*)^{1,n}\big) = (-1)^{n-1} a_{n1} \det\big((\lambda I - A)^{1,1}\big)$, *and*

3. $\det\big((\lambda I - A^*)^{n,1}\big) = (-1)^{n-1} a_{1n} \det\big((\lambda I - A)^{1,1}\big)$.

Proof. Letting B denote the matrix obtained by removing the first row from $\lambda I - A$, we have the following:

$$\lambda I - A = \left(\begin{array}{ccccc} \lambda + \sum_{(1\to j)\in E_G} a_{j1} & -a_{12} & -a_{13} & \cdots & -a_{1(n-1)} \\ \hline & & & & \\ & & B & & \\ & & & & \end{array}\right), \text{ and}$$

$$\lambda I - A^* = \left(\begin{array}{ccccc|c} \lambda + a_{n1} + \sum_{(1\to j)\in E_G} a_{j1} & -a_{12} & -a_{13} & \cdots & -a_{1(n-1)} & -a_{1n} \\ \hline & & & & & 0 \\ & & B & & & \vdots \\ & & & & & 0 \\ \hline -a_{n1} & 0 & 0 & \cdots & 0 & \lambda + a_{1n} \end{array}\right), \tag{4.21}$$

where, for non-edges $k \to 1$, we define $a_{1k} := 0$. Next, letting $B^{\emptyset,1}$ denote the matrix obtained by removing the first column of B, we have $B^{\emptyset,1} = (\lambda I - A)^{1,1}$. We will use this equality several times in the rest of the proof.

Applying a Laplace expansion along the last row of the matrix $(\lambda I - A^*)^{1,n}$ (see (4.21)), we obtain Lemma 4.3.13(2):

$$\det\big((\lambda I - A^*)^{1,n}\big) = (-1)^{n-2}(-a_{n1})\det(B^{\emptyset,1}) = (-1)^{n-1} a_{n1} \det\big((\lambda I - A)^{1,1}\big)\,.$$

Similarly, a Laplacian expansion along the last column yields Lemma 4.3.13(3):

$$\det\big((\lambda I - A^*)^{n,1}\big) = (-1)^{n-2}(-a_{1n})\det(B^{\emptyset,1}) = (-1)^{n-1} a_{1n} \det\big((\lambda I - A)^{1,1}\big)\,.$$

Finally, we prove Lemma 4.3.13(1) by expanding along the last column in (4.21) and using the linearity of the determinant:

$$\begin{aligned}\det(\lambda I - A^*) \;=\; & (-1)^{n-1}(-a_{1n})(-1)^{n-2}(-a_{n1})\det(B^{\emptyset,1}) \\ & + (\lambda + a_{1n})\left(\det(\lambda I - A) + \det\left(\begin{array}{cccc} a_{n1} & 0 & \cdots & 0 \\ \hline & & & \\ & B & & \\ & & & \end{array}\right)\right) \\ =\; & -a_{1n}a_{n1}\det(B^{\emptyset,1}) + (\lambda + a_{1n})(\det(\lambda I - A) + a_{n1}\det(B^{\emptyset,1})) \\ =\; & \lambda \det(\lambda I - A) + a_{1n}\det(\lambda I - A) + a_{n1}\lambda \det\left((\lambda I - A)^{1,1}\right) .\end{aligned}$$

□

Proposition 4.3.14 (Move output). *Assume $n \geq 3$. Let $\mathcal{M} = (G, In, Out, Leak)$ be a strongly connected linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$ and $Leak = \emptyset$. Let H be the graph obtained from G by adding a leaf edge at compartment 1, and let $\mathcal{M}' = (H, In', Out', Leak')$ be the linear compartmental model with $In' = \{1\}$, $Out' = \{n\}$, and $Leak' = \emptyset$. Write the input-output equation (4.1) for $\mathcal{M}$ as:*

$$y_1^{(n-1)} + c_{n-2}y_1^{(n-2)} + \cdots + c_1 y_1' + c_0 y_1 \;=\; u_1^{(n-2)} + d_{n-3}u_1^{(n-3)} + \cdots + d_1 u_1' + d_0 u_1 \;,$$

and define $c_{n-1} := 1$ and $d_{n-2} := 1$. Similarly, write the input-output equation for $\mathcal{M}^*$ as:

$$y_1^{(n)} + c_{n-1}^* y_1^{(n-1)} + \cdots + c_1^* y_1' + c_0^* y_1 \;=\; d_{n-2}^* u_1^{(n-2)} + \cdots + d_1^* u_1' + d_0^* u_1 \;.$$

Then:

1. *the coefficients of $\mathcal{M}$ and $\mathcal{M}^*$ are related as follows:*

$$\begin{array}{lll} \text{(i)} & d_i^* = (-1)^{n-1} a_{n1} d_i & \textit{for } i \in \{0, 1, \ldots, n-2\}, \\ \text{(ii)} & c_i^* = c_{i-1} + a_{1n} c_i + a_{n1} d_{i-1} & \textit{for } i \in \{1, 2, \ldots, n-1\}, \\ \text{(iii)} & c_0^* = c_0 = 0 \,. & \end{array}$$

2. *letting $c_{\mathcal{M}}$ and $c_{\mathcal{M}^*}$ (respectively) denote the coefficient maps of $\mathcal{M}$ and $\mathcal{M}^*$, the ranks of the resulting Jacobian matrices are related by:*

$$\operatorname{rank}(\operatorname{Jac}(c_{\mathcal{M}^*})) \;=\; \operatorname{rank}(\operatorname{Jac}(c_{\mathcal{M}})) + 2 \;.$$

Proof. The input-output equations (4.1) for $\mathcal{M}$ and $\mathcal{M}^*$ are, respectively, as follows:

$$\det(\lambda I - A) y_1 = \det\big((\lambda I - A)^{1,1}\big)\, u_1 \,, \quad \text{and} \quad \det(\lambda I - A^*) y_n \quad = \det\big((\lambda I - A^*)^{1,n}\big)\, u_1 \,.$$

Now Proposition 4.3.14(1)(i–ii) follows easily from Lemma 4.3.13(1–2). Also, Proposition 4.3.14(1)(iii) comes from the fact that the models $\mathcal{M}$ and $\mathcal{M}^*$ have no leaks (cf. (Gerberding et al. 2020, Remark 2.10)).

Now we prove part (2) of the proposition. Using part (1) of the proposition, plus $c_{n-1} := 1$ and $d_{n-2} := 1$, we obtain the following the Jacobian matrix of the coefficient map of $\mathcal{M}^*$, which we denote by J^*:

$$J^* = \begin{array}{c} \\ d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-2} \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} \begin{array}{c} \begin{array}{ccc} a_{n1} & a_{1n} & \text{Parameters } a_{kj} \text{ for all } (j,k) \in E_G \end{array} \\ \left(\begin{array}{cc|c} (-1)^{n-1} & 0 & 0 \ \cdots \ 0 \\ d_0 & c_1 & \left(a_{1n}\frac{\partial c_1}{\partial a_{kj}} + a_{n1}\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline d_1 & c_2 & \left(\frac{\partial c_1}{\partial a_{kj}} + a_{1n}\frac{\partial c_2}{\partial a_{kj}} + a_{n1}\frac{\partial d_1}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \vdots & \vdots & \vdots \\ d_{n-3} & c_{n-2} & \left(\frac{\partial c_{n-3}}{\partial a_{kj}} + a_{1n}\frac{\partial c_{n-2}}{\partial a_{kj}} + a_{n1}\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline 1 & 1 & \left(\frac{\partial c_{n-2}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline (-1)^{n-1} d_0 & 0 & \left((-1)^{n-1} a_{n1}\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \vdots & \vdots & \vdots \\ (-1)^{n-1} d_{n-3} & 0 & \left((-1)^{n-1} a_{n1}\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \end{array}\right) \end{array}.$$

Next, we perform the following row operations to J^*, where R_k denotes the row of J^* corresponding to the coefficient k:

- for all $i \in \{0,2,\dots n-2\}$, replace row $R_{d^*_i}$ by $(-1)^{n-1} R_{d^*_i}$,
- for all $i \in \{1,2,\dots n-2\}$, replace row $R_{c^*_i}$ by $(R_{c^*_i} - R_{d^*_{i-1}})$,
- iteratively from $i = n-2$ down to $i = 1$, replace row $R_{c^*_i}$ by $(R_{c^*_i} - a_{1n} R_{c^*_{i+1}})$,
- for all $i \in \{0,1,\dots n-3\}$. replace row $R_{d^*_i}$ by $\frac{1}{a_{n1}} R_{d^*_i}$.

The resulting matrix, which has the same rank as J^*, has the following form:

$$
\begin{array}{cc}
 & \begin{array}{ccc} a_{n1} & a_{1n} & \phantom{\left(\frac{\partial c_1}{\partial a_{kj}}\right)_{(j,k)\in E_G}} \end{array} \\
\begin{array}{c} d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} &
\left(\begin{array}{cc|c}
1 & 0 & 0\cdots 0 \\
0 & \chi & 0\cdots 0 \\ \hline
0 & * & \left(\frac{\partial c_1}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
0 & * & \left(\frac{\partial c_{n-2}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline
\frac{1}{a_{n1}} d_0 & 0 & \left(\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
\frac{1}{a_{n1}} d_{n-3} & 0 & \left(\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G}
\end{array}\right)
\end{array}
=
\begin{array}{cc}
 & \begin{array}{ccc} a_{n1} & a_{1n} & \end{array} \\
\begin{array}{c} d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} &
\left(\begin{array}{cc|c}
1 & 0 & 0\cdots 0 \\
0 & \chi & 0\cdots 0 \\ \hline
0 & * & \\
\vdots & \vdots & \\
0 & * & J \\
\frac{1}{a_{n1}} d_0 & 0 & \\
\vdots & \vdots & \\
\frac{1}{a_{n1}} d_{n-3} & 0 &
\end{array}\right)
\end{array}, \tag{4.22}
$$

where

$$
\chi \;=\; c_1 - a_{1n}(c_2 - a_{1n}(\cdots - a_{1n}(c_{n-2} - a_{1n}))) \;=\; (-1)^n (a_{1n})^{n-2} + \sum_{i=1}^{n-2} (-a_{1n})^{i-1} c_i \,.
$$

By construction, each c_i only involves parameters a_{kj} for edges (j,k) in G, and so:

$$
\chi|_{a_{kj}=0 \text{ for all } (j,k)\in E_G} \;=\; (-1)^n (a_{1n})^{n-2}.
$$

We conclude that χ is a nonzero polynomial.

The fact that χ is nonzero, together with the lower block diagonal structure of the matrix on the right-hand side of (4.22), imply that $\text{rank}(J^*) = 2 + \text{rank}(J)$, as desired. □

4.3.3 Moving the input

In the previous subsection, we analyzed moving the output when a leaf edge is added; now we consider moving the input. The following result is the analogous result to Proposition 4.3.14, and their proofs are very similar.

Proposition 4.3.15 (Move input)**.** *Assume $n \geq 3$. Let $\mathcal{M} = (G, In, Out, Leak)$ be a strongly connected linear compartmental model with $n-1$ compartments such that $In = Out = \{1\}$ and $Leak = \emptyset$. Let H be the graph obtained from G by adding a leaf edge at compartment 1, and let $\mathcal{M}' = (H, In', Out', Leak')$ be the linear compartmental model with $In' = \{1\}$,*

$Out' = \{n\}$, and $Leak' = \emptyset$. Write the input-output equation (4.1) *for $\mathcal{M}$ as:*

$$y_1^{(n-1)} + c_{n-2} y_1^{(n-2)} + \cdots + c_1 y_1' + c_0 y_1 \ = \ u_1^{(n-2)} + d_{n-3} u_1^{(n-3)} + \cdots + d_1 u_1' + d_0 u_1 \ ,$$

and define $c_{n-1} := 1$ and $d_{n-2} := 1$. Similarly, write the input-output equation for $\mathcal{M}^*$ as:

$$y_1^{(n)} + c_{n-1}^* y_1^{(n-1)} + \cdots + c_1^* y_1' + c_0^* y_1 \ = \ d_{n-2}^* u_1^{(n-2)} + \cdots + d_1^* u_1' + d_0^* u_1 \ .$$

Then:

1. *the coefficients of $\mathcal{M}$ and $\mathcal{M}^*$ are related as follows:*

$$\begin{array}{llll} \text{(i)} & d_i^* & = (-1)^{n-1} a_{1n} d_i & \textit{for } i \in \{0, \ldots, n-2\} \\ \text{(ii)} & c_i^* & = c_{i-1} + a_{1n} c_i + a_{n1} d_{i-1} & \textit{for } i \in \{1, \ldots, n-1\} \\ \text{(iii)} & c_0^* & = c_0 = 0 \ . & \end{array}$$

2. *letting $c_{\mathcal{M}}$ and $c_{\mathcal{M}^*}$ (respectively) denote the coefficient maps of $\mathcal{M}$ and $\mathcal{M}^*$, the ranks of the resulting Jacobian matrices are related by:*

$$\mathrm{rank}(\mathrm{Jac}(c_{\mathcal{M}^*})) \ = \ 2 + \mathrm{rank}(\mathrm{Jac}(c_{\mathcal{M}})) \ .$$

Proof. The input-output equations (4.1) for $\mathcal{M}$ and $\mathcal{M}^*$ are, respectively, as follows:

$$\det(\lambda I - A) y_1 = \det\left((\lambda I - A)^{1,1}\right) u_1 \ , \quad \text{and} \quad \det(\lambda I - A^*) y_1 \quad = \det\left((\lambda I - A^*)^{n,1}\right) u_n \ .$$

Now Proposition 4.3.15(1) follows easily from Lemma 4.3.13(1) and Lemma 4.3.13(3) (and, as in the proof of Proposition 4.3.14, the fact that the models $\mathcal{M}$ and $\mathcal{M}^*$ have no leaks).

We use part (1) of the proposition, plus $c_{n-1} := 1$ and $d_{n-2} := 1$, to obtain the Jacobian matrix of the coefficient map of $\mathscr{M}^*$, denoted by J^*:

$$
J^* = \begin{array}{rc}
 & \begin{array}{ccc} a_{1n} & \qquad a_{n1} & \qquad \text{Parameters } a_{kj} \text{ for all } (j,k)\in E_G \end{array} \\
\begin{array}{r} d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-2} \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} &
\left(\begin{array}{cc|c}
(-1)^{n-1} & 0 & 0 \quad \cdots \quad 0 \\
c_1 & d_0 & \left((-1)^{n-1} a_{1n}\frac{\partial c_1}{\partial a_{kj}} + a_{n1}\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline
c_2 & d_1 & \left(\frac{\partial c_1}{\partial a_{kj}} + a_{1n}\frac{\partial c_2}{\partial a_{kj}} + a_{n1}\frac{\partial d_1}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
c_{n-2} & d_{n-3} & \left(\frac{\partial c_{n-3}}{\partial a_{kj}} + a_{1n}\frac{\partial c_{n-2}}{\partial a_{kj}} + a_{n1}\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline
1 & 1 & \left(\frac{\partial c_{n-2}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline
(-1)^{n-1} d_0 & 0 & \left((-1)^{n-1} a_{1n}\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
(-1)^{n-1} d_{n-3} & 0 & \left((-1)^{n-1} a_{1n}\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G}
\end{array}\right)
\end{array}.
$$

We perform row operations on J^*, where R_k denotes the row of J^* corresponding to the coefficient k:

- for all $i \in \{0,2,\dots n-2\}$, replace row $R_{d_i^*}$ by $(-1)^{n-1}R_{d_i^*}$,
- for all $i \in \{1,2,\dots n-2\}$, replace row $R_{c_i^*}$ by $(R_{c_i^*} - (a_{n1}/a_{1n})R_{d^*_{i-1}})$,
- iteratively from $i = n-2$ down to $i = 1$, replace row $R_{c_i^*}$ by $(R_{c_i^*} - a_{1n}R_{c^*_{i+1}})$,
- for all $i \in \{0,1,\dots n-3\}$, replace row $R_{d_i^*}$ by $\frac{1}{a_{n1}}R_{d_i^*}$.

The resulting matrix, which has the same rank as J^*, has the following form:

$$
\begin{array}{rc}
 & \begin{array}{cc} a_{1n} & \quad a_{n1} \end{array} \\
\begin{array}{r} d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} &
\left(\begin{array}{cc|c}
1 & 0 & 0\cdots 0 \\
* & x & 0\cdots 0 \\ \hline
* & * & \left(\frac{\partial c_1}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
* & * & \left(\frac{\partial c_{n-2}}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\ \hline
\frac{1}{a_{1n}} d_0 & 0 & \left(\frac{\partial d_0}{\partial a_{kj}}\right)_{(j,k)\in E_G} \\
\vdots & \vdots & \vdots \\
\frac{1}{a_{1n}} d_{n-3} & 0 & \left(\frac{\partial d_{n-3}}{\partial a_{kj}}\right)_{(j,k)\in E_G}
\end{array}\right)
\end{array}
=
\begin{array}{rc}
 & \begin{array}{cc} a_{1n} & \quad a_{n1} \end{array} \\
\begin{array}{r} d^*_{n-2} \\ c^*_1 \\ c^*_2 \\ \vdots \\ c^*_{n-1} \\ d^*_0 \\ \vdots \\ d^*_{n-3} \end{array} &
\left(\begin{array}{cc|c}
1 & 0 & 0\cdots 0 \\
* & x & 0\cdots 0 \\ \hline
* & * & \\
\vdots & \vdots & \\
* & * & J \\
\frac{1}{a_{1n}} d_0 & 0 & \\
\vdots & \vdots & \\
\frac{1}{a_{1n}} d_{n-3} & 0 &
\end{array}\right)
\end{array},
\tag{4.23}
$$

where

$$\chi \;=\; d_0 - a_{1n}(d_2 - a_{1n}(\cdots - a_{1n}(d_{n-3} - a_{1n}))) \;=\; (-1)^n (a_{1n})^{n-2} + \sum_{i=1}^{n-2} (-a_{1n})^{i-1} d_i \;.$$

For the same reason as in the proof of Proposition 4.3.14, χ is a nonzero polynomial. Thus, from the lower block diagonal structure of the matrix on the right-hand side of (4.23), we obtain the desired equality: $\text{rank}(J^*) = 2 + \text{rank}(J)$. □

4.3.4 Proof of Theorem 4.3.3

We now apply Propositions 4.3.14 and 4.3.15 to prove our result on adding a leaf edge and moving the input or output.

Proof of Theorem 4.3.3. For models $\mathscr{M}$ and $\mathscr{M}^*$, let J and J^* denote the Jacobian matrices of the respective coefficient maps. We first examine identifiability. By definition, $\mathscr{M}$ is identifiable if and only if $\text{rank}(J) = |E_G|$ (recall that $\mathscr{M}$ has no leaks). Similarly, $\mathscr{M}^*$ is identifiable if and only if $\text{rank}(J^*) = |E_H|$. Now the identifiability result follows from Propositions 4.3.14–4.3.15 and the fact that (by construction) $|E_H| = 2 + |E_G|$.

As for expected dimension, we first compute the number of non-constant coefficients in the coefficient map of $\mathscr{M}$ (respectively, $\mathscr{M}^*$), which we denote by $N_{\mathscr{M}}$ (respectively, $N_{\mathscr{M}^*}$. These numbers, by a straightforward application of Corollary 4.2.4 (in particular, we use the fact that there is an edge in $\mathscr{M}^*$ from input to output, and so the length of the shortest path from input to output is 1), are as follows:

$$N_{\mathscr{M}} \;=\; 2n-4 \qquad \text{and} \qquad N_{\mathscr{M}^*} \;=\; 2n-2\,. \tag{4.24}$$

Next, by Proposition 4.1.13, $\mathscr{M}$ has expected dimension if and only if $\text{rank}(J) = \min\{|E_G|, N_{\mathscr{M}}\}$. Similarly, $\mathscr{M}^*$ has expected dimension if and only if $\text{rank}(J^*) = \min\{|E_H|, N_{\mathscr{M}^*}\}$. Now, the desired result follows from Propositions 4.3.14–4.3.15 and the equalities (4.24). □

4.4 Tree Models

In this section, we introduce bidirectional tree models, and completely characterize which of these models with one input and one output are identifiable (Theorem 4.4.2). As a consequence, we determine which catenary and mammillary models with one input and

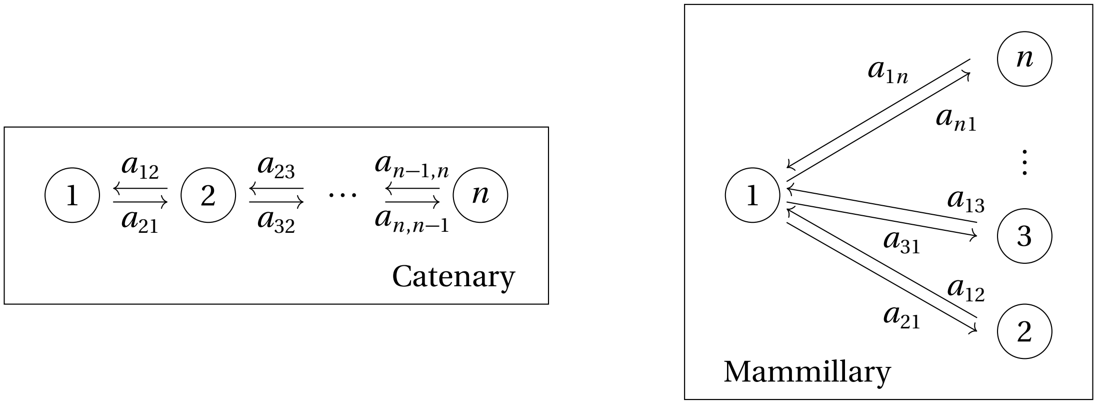

Figure 4.5: Two bidirected graphs with n compartments (cf. (Gross et al. 2017, Figures 1–2)). Left: **Catenary** (path), denoted by Cat_n. Right: **Mammillary** (star), denoted by Mam_n.

one output are identifiable (Corollary 4.4.3 and 4.4.4). Our results therefore extend those of Cobelli et al. (1979), which concerned the case when the input and output are in the same compartment.

Definition 4.4.1. A *bidirectional tree graph* is a graph G that is obtained from an undirected tree graph by making every edge bidirected (that is, $(i \to j) \in E_G$ implies that $(i \leftrightarrows j) \in E_G$). A linear compartmental model $\mathcal{M} = (G, In, Out, Leak)$ is a *bidirectional tree model* (or, to be succinct, a *tree model*) if the graph G is a bidirectional tree graph.

In the following theorem, which is the main result of the section, we use the notation $\mathrm{dist_G(i,j)}$ to denote the length of shortest (directed) path in G from vertex i to vertex j.

Theorem 4.4.2 (Classification of identifiable tree models)**.** *A tree model with exactly one input and one output* $\mathcal{M} = (G, \{in\}, \{out\}, Leak)$ *is generically locally identifiable if and only if* $\mathrm{dist_G(in, out)} \leq 1$ *and* $|Leak| \leq 1$.

The proof of Theorem 4.4.2 appears in Section 4.4.1.

As an easy consequence of Theorem 4.4.2, we obtain results on catenary and mammillary models (that is, models in which the underlying graph is, respectively, a path or a star graph, as in Figure 4.5). These results form a substantial improvement over prior results, which largely concerned the case when input and output are equal (see Lemma 4.4.5).

Corollary 4.4.3 (Classification of identifiable catenary models)**.** *Let* $n \geq 2$*, and let* Cat_n *denote the* n*-compartment catenary graph depicted in Figure 4.5. Then a model* $(\mathrm{Cat}_n, In, Out, Leak)$

with $|In| = |Out| = 1$ *is generically locally identifiable if and only if* $|Leak| \leq 1$ *and either (1)* $In = Out$ *or (2) the input and output compartments are adjacent.*

Corollary 4.4.4 (Classification of identifiable mammillary models)**.** *Let* $n \geq 2$*, and let* Mam_n *denote the* n*-compartment mammillary graph depicted in Figure 4.5. Then a model* $(\mathrm{Mam}_n, In, Out, Leak)$ *with* $|In| = |Out| = 1$ *is generically locally identifiable if and only if* $|Leak| \leq 1$ *and (at least) one of the following hold: (1)* $In = Out$*, (2)* $In = \{1\}$*, or (3)* $Out = \{1\}$.

4.4.1 Proof of Theorem 4.4.2

To prove Theorem 4.4.2, we need two lemmas. The first pertains to tree models whose identifiability is known from prior results.

Lemma 4.4.5. *If* $\mathcal{M} = (G, In, Out, Leak)$ *is a tree model with* $|Leak| \leq 1$ *and input and output in a single compartment (*$In = Out = \{i\}$*), then* $\mathcal{M}$ *is generically locally identifiable.*

Proof. Let n be the number of compartments. Since $In = Out = \{i\}$, $|Leak| \leq 1$, and G is inductively strongly connected with respect to i, the lemma follows from Proposition 4.1.14. □

The next result, which follows easily from a result in a prior section, pertains to when tree models are unidentifiable due to having more parameters than coefficients.

Lemma 4.4.6 (Unidentifiable tree models)**.** *Let* $n \geq 1$*. Consider a tree model with* n *compartments, one input, and one output,* $\mathcal{M} = (G, \{in\}, \{out\}, Leak)$*. If* $\mathrm{dist}_G(\mathrm{in}, \mathrm{out}) \geq 2$ *or* $|Leak| \geq 2$*, then* $\mathcal{M}$ *is unidentifiable.*

Proof. As G is a bidirectional tree with n vertices, it has $|E_G| = 2n - 2$ edges. We consider first the case when $|Leak| \geq 2$. Then $|E_G| + |Leak| \geq (2n-2) + 2 = 2n > 2n - 1$. So, by Corollary 4.2.5, $\mathcal{M}$ is unidentifiable.

In the other case, we have $L := \mathrm{dist}_G(\mathrm{in}, \mathrm{out}) \geq 2$. There are two subcases. If $Leak \neq \emptyset$, then $|E_G| + |Leak| \geq (2n-2) + 1 > 2n-2 \geq 2n-L$. If $Leak = \emptyset$, then $|E_G| = 2n-2 > 2n-2-1 \geq 2n-L-1$. In either subcase, by Corollary 4.2.5, $\mathcal{M}$ is unidentifiable. □

We now prove Theorem 4.4.2, which we recall states that the implication in Lemma 4.4.6 is in fact an equivalence.

Proof of Theorem 4.4.2. The forward direction ($\Rightarrow$) is Lemma 4.4.6.

To prove the backward direction ($\Leftarrow$), we first consider the case when $|Leak| = 0$. If $\text{dist}_G(\text{in}, \text{out}) = 0$, then Lemma 4.4.5 implies that $\mathscr{M}$ is identifiable.

Now assume that $\text{dist}_G(\text{in}, \text{out}) = 1$ (i.e., $in \leftrightarrows out$ are edges in G). We will build the bidirectional tree graph G by starting with a subtree G' and then successively adding leaf edges. The subtree G' comes from removing the edges $in \leftrightarrows out$, which disconnects G, and taking the component containing in. More precisely, G' is the subgraph induced by all $i \in V_G$ such that $\text{dist}_G(\text{in}, \text{i}) < \text{dist}_G(\text{out}, \text{i})$. It follows that $in \in V_{G'}$ and G' is a bidirectional tree. So, by Lemma 4.4.5, the model $\mathscr{M}' = (G', \{in\}, \{in\}, \emptyset)$ is identifiable.

Next, let G'' be obtained from G' by adding a leaf edge at the input compartment and labeling the new compartment by out (so the new pair of edges is $in \leftrightarrows out$). By construction, G'' is a bidirectional tree and an induced subgraph of G. Now Proposition 4.3.14 implies that the model $\mathscr{M}'' = (G'', \{in\}, \{out\}, \emptyset)$ is identifiable (because $\mathscr{M}'$ is). If $G'' = G$, we are done. If not, we finish building G from G'' by adding one leaf edge at a time. At each step, the graph is a bidirectional tree and an induced subgraph of G; and also (by Theorem 4.3.2) the resulting model with $In = \{in\}$, $Out = \{out\}$, and $Leak = \emptyset$ is identifiable. So, as desired, $\mathscr{M} = (G, \{in\}, \{out\}, \emptyset)$ is identifiable.

Finally, consider the case when $|Leak| = 1$. We already showed that models with $\text{dist}_G(\text{in}, \text{out}) \leq 1$ and $|Leak| = 0$ are identifiable, and now Proposition 4.1.15 implies that adding a leak to such models preserves identifiability. This completes the proof. □

4.4.2 Expected dimension of tree models

Tree models with more than one leak are unidentifiable by Lemma 4.4.6, but they have expected dimension for any number of leaks, as long as the input and output are equal or adjacent.

Proposition 4.4.7. *Consider a tree model with exactly one input and one output, $\mathscr{M} = (G, \{in\}, \{out\}, Leak)$. If $\text{dist}_G(\text{in}, \text{out}) \leq 1$, then $\mathscr{M}$ has expected dimension.*

Proof. Let n be the number of compartments. First assume $|Leak| \leq 1$. By Theorem 4.4.2, $\mathscr{M}$ is generically locally identifiable and so has expected dimension (by Proposition 4.1.13). In particular, for the model $\overline{\mathscr{M}} := (G, \{in\}, \{out\}, \{i\})$, the coefficient map, which has the form $\bar{\mathbf{c}} : \mathbb{R}^{|E_G|+1} = \mathbb{R}^{2n-1} \to \mathbb{R}^{2n-1}$ by Corollary 4.2.4, has image with dimension equal to $2n-1$.

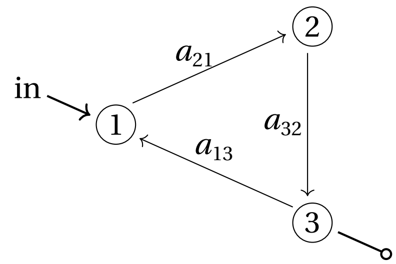

Figure 4.6: Figure described in Example 4.4.9

Now assume $|Leak| \geq 2$. By Corollary 4.2.4, the coefficient map of $\mathscr{M}$ has the form $\mathbf{c} : \mathbb{R}^{|E|+|Leak|} \to \mathbb{R}^{2n-1}$ and (by Theorem 4.2.1) is an extension of $\bar{\mathbf{c}}$ when $i \in Leak$. Thus, the image of $\mathbf{c}$ has dimension equal to $2n-1$, and so $\mathscr{M}$ has expected dimension. $\square$

4.4.3 Beyond tree models

Recall that Theorem 4.4.2 states that a tree model $\mathscr{M} = (G, \{in\}, \{out\}, Leak)$ is identifiable if and only if $\text{dist}_G(\text{in}, \text{out}) \leq 1$ and $|Leak| \leq 1$. It is natural to ask whether any part of this theorem generalizes to strongly connected models. Unfortunately, this is not the case, as the following examples show.

Example 4.4.8 (Unidentifiable, but $\text{dist}_G(\text{in}, \text{out}) = 0$ and $|Leak| = 0$)**.** Recall that in the model from Example 4.2.9, the input and output are equal, and there are no leaks. Nonetheless, the model is unidentifiable.

Example 4.4.9 (Identifiable, but $\text{dist}_G(\text{in}, \text{out}) = 2$)**.** In the model depicted in Figure 4.6, the distance of the shortest path from input to output is 2, and (Gerberding et al. 2020, Theorem 3.5) implies that the model is generically locally identifiable.

Example 4.4.10 (Identifiable, but $|Leak| = 2$)**.** In the model depicted in Figure 4.7, there are 2 leaks and Corollary 3.2.32 implies that the model is generically locally identifiable.

In spite of the above examples, we recall from Remark 4.2.6 that strongly connected models (with one input and one output) with $|Leak| \geq 3$ (or, if input equals output, $|Leak| \geq 2$) are unidentifiable.

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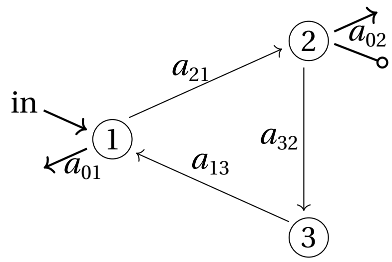

Figure 4.7: Figure described in Example 4.4.10.

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