Identifiability of Directed-Cycle Compartmental Models

Paul Dessauer, Tanisha Grimsley, Jose Lopez

University of Texas at El Paso, Juniata College, California State University - Fresno

MSRI-UP 2022

July 22, 2022

What are Linear Compartmental Models? Why are they useful?

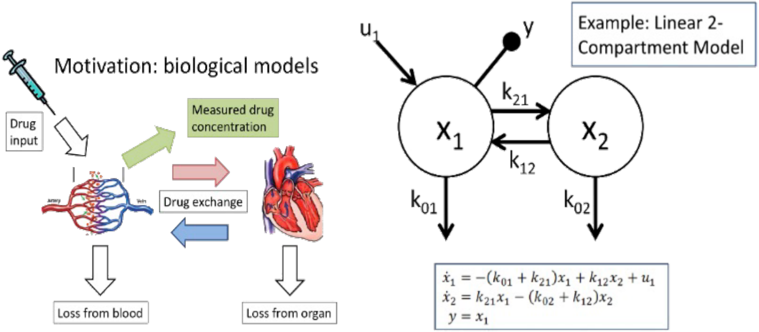
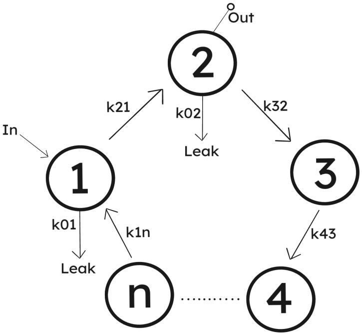


Figure: Credit: Nicolette Meshkat

Defining Our Models

Definition 1

A **directed-cycle model** is a directed graph G that is described by a set of inputs, outputs, and leaks, denoted $(G, In, Out, Leak)$, such that $G = \{(v_1, \ldots, v_n), (e_1, \ldots, e_n)\}$, where $e_i = (v_i, v_{i+1})$ for $i < n$, and $e_n = (v_n, v_1)$.
Each edge $j \to i$ is denoted by a parameter k_{ij}. The leaks are denoted by k_{0j} where j is the compartment corresponding to that leak.



Defining Identifiability

Definition 2

A mathematical model is **identifiable** if its parameters, k_{ij} can be recovered from data.

Proposition 1 (Meshkat, Sullivant, Eisenberg, 2015)

A linear compartmental model $(G, In, Out, Leak)$*, with* $G = (V, E)$*, is generically locally identifiable if and only if the rank of the Jacobian matrix of its coefficient map c , when evaluated at a generic point, is equal to* $|E| + |Leak|$.

Question

Can we determine identifiability based on the structure of the model?

Coefficient Map Formula

Proposition 2 (Gerberding, Obatake, Shiu, 2020)

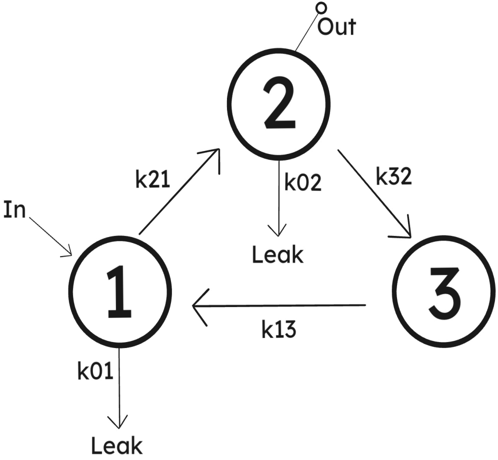
Assume $n \geq 3$. Let M be an n-compartment cycle model with $In = \{1\}$, $Out = \{p\}$ (for some $1 \leq p \leq n$), and $Leak = \{i_1, i_2, \ldots, i_t\} \neq \emptyset$. Then the coefficient map $c : \mathbb{R}^{n+t} \mapsto \mathbb{R}^{2n-p+1}$ is given by

$$(k_{21}, k_{32}, \ldots, k_{1,n}, k_{0,i_1}, k_{0,i_2}, \ldots, k_{0,i_t}) \mapsto$$

$$(e_1, e_2, \ldots, e_{n-1}, e_n - \prod_{i=1}^{n} k_{i+1,i}, \kappa, e_1^* \kappa, \ldots e_{n-p}^* \kappa)$$

where $\kappa := \prod_{i=2}^{p} k_{i,i-1}$, and e_j and e_j^* denote the j^{th} elementary symmertric polynomial on the sets $E = \{k_{\ell+1,\ell} \mid \ell \notin Leak\} \cup \{k_{\ell+1,\ell} + k_{0,\ell} \mid \ell \in Leak\}$ and $E^* = \{k_{\ell+1,\ell} \mid p+1 \leq \ell \leq n, \ \ell \notin Leak\} \cup \{k_{\ell+1,\ell} + k_{0,\ell} \mid p+1 \leq \ell \leq n, \ \ell \in Leak\}$, respectively.

Coefficient Map Example



Coefficient Map Example

Using the Proposition, we obtain the following coefficient map:

$$(k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3 - k_{21}k_{32}k_{13}, \kappa, e_1^* \kappa)$$

Coefficient Map Example

Using the Proposition, we obtain the following coefficient map:

$$(k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3 - k_{21}k_{32}k_{13}, \kappa, e_1^* \kappa)$$

First, we compute $\kappa = \prod_{i=2}^{p} k_{i,i-1} = \prod_{i=2}^{2} k_{i,i-1} = k_{21}$.

Coefficient Map Example

Coefficient Map:

$$(k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3 - k_{21}k_{32}k_{13}, k_{21}, e_1^* k_{21})$$

Now, we want to find the following sets for our Model:

$$E = \{k_{\ell+1,\ell} | \ell \notin Leak\} \cup \{k_{\ell+1,\ell} + k_{0,\ell} | \ell \in Leak\} \rightarrow \{k_{13}\} \cup \{k_{21} + k_{01}, k_{32} + k_{02}\}$$

$$E^* = \{k_{\ell+1,\ell} | \ell = 3, \ell \notin Leak\} \cup \{k_{\ell+1,\ell} + k_{0,\ell} | \ell = 3, \ell \in Leak\} \rightarrow \{k_{13}\}$$

Coefficient Map Example

Now we want to find the elementary symmetric polynomials e_1, e_2, e_3, and e_1^* on the following sets:

$$E = \{k_{13}, k_{21} + k_{01}, k_{32} + k_{02}\}$$

$$E^* = \{k_{13}\}$$

Coefficient Map Example

Now we want to find the elementary symmetric polynomials e_1, e_2, e_3, and e_1^* on the following sets:

$$E = \{k_{13}, k_{21} + k_{01}, k_{32} + k_{02}\}$$

$$E^* = \{k_{13}\}$$

$$\begin{aligned}
e_1 &= k_{13} + k_{21} + k_{01} + k_{32} + k_{02} \\
e_2 &= k_{13}(k_{21} + k_{01}) + k_{13}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02}) \\
e_3 &= k_{13}(k_{21} + k_{01})(k_{32} + k_{02})
\end{aligned}$$

$$e_1^* = k_{13}$$

Coefficient Map Example

Finally, for the model with $N = 3$, $In = \{1\}$, $Out = \{2\}$, $Leak = \{1, 2\}$, we have the following Coefficient Map

$$(k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3 - k_{21}k_{32}k_{13}, k_{21}, e_1^* k_{21})$$

$$\begin{aligned} e_1 &= k_{13} + k_{21} + k_{01} + k_{32} + k_{02} \\ e_2 &= k_{13}(k_{21} + k_{01}) + k_{13}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02}) \\ e_3 &= k_{13}(k_{21} + k_{01})(k_{32} + k_{02}) \end{aligned}$$

$$e_1^* = k_{13}$$

$$\begin{aligned} (k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (&\underbrace{k_{21} + k_{32} + k_{13} + k_{01} + k_{02}}_{e_1}, \\ &\underbrace{k_{21}k_{13} + k_{01}k_{13} + k_{21}k_{32} + k_{01}k_{32} + k_{13}k_{32} + k_{21}k_{02} + k_{13}k_{02} + k_{01}k_{02}}_{e_2}, \\ &\underbrace{k_{01}k_{13}k_{32} + k_{21}k_{13}k_{02} + k_{01}k_{13}k_{02}}_{e_3 - k_{21}k_{32}k_{13}}, \underbrace{k_{21}}_{\kappa}, \underbrace{k_{21}k_{13}}_{e_1^* \kappa}) \end{aligned}$$

Jacobian Matrix

From the definition of the coefficient map we get the following general form of the Jacobian matrix with two leaks:

Let $r = \prod_{i=1}^{n} k_{i+1,i}$

$$
\begin{array}{ccccccc|c}
\mathbf{k_{21}} & \mathbf{k_{32}} & \dots & \mathbf{k_{n,n-1}} & \mathbf{k_{1,n}} & \mathbf{k_{0i}} & \mathbf{k_{0j}} & \\
1 & 1 & \dots & 1 & 1 & 1 & 1 & \mathbf{e_1} \\
e_2^{(k_{21})} & e_2^{(k_{32})} & \dots & e_2^{(k_{n,n-1})} & e_2^{(k_{1,n})} & e_2^{(k_{0i})} & e_2^{(k_{0j})} & \mathbf{e_2} \\
\vdots & \vdots & \ddots & \vdots & \vdots & \vdots & \vdots & \vdots \\
e_{n-1}^{(k_{21})} & e_{n-1}^{(k_{32})} & \dots & e_{n-1}^{(k_{n,n-1})} & e_{n-1}^{(k_{1,n})} & e_{n-1}^{(k_{0i})} & e_{n-1}^{(k_{0j})} & \mathbf{e_{n-1}} \\
(e_n - r)^{(k_{21})} & (e_n - r)^{(k_{32})} & \dots & (e_n - r)^{(k_{n,n-1})} & (e_n - r)^{(k_{1,n})} & e_n^{(k_{0i})} & e_n^{(k_{0j})} & \mathbf{e_n - r} \\
\kappa^{(k_{21})} & \kappa^{(k_{32})} & \dots & 0 & 0 & 0 & 0 & \kappa \\
(e_1^*\kappa)^{(k_{21})} & (e_1^*\kappa)^{(k_{32})} & \dots & (e_1^*\kappa)^{(k_{n,n-1})} & (e_1^*\kappa)^{(k_{1n})} & (e_1^*\kappa)^{(k_{0i})} & (e_1^*\kappa)^{(k_{oj})} & \mathbf{e_1^*}\kappa \\
\vdots & \vdots & \dots & \vdots & \vdots & \vdots & \vdots & \vdots \\
(e_{n-p}^*)\kappa^{(k_{21})} & (e_{n-p}^*)\kappa^{(k_{32})} & \dots & (e_{n-p}^*)\kappa^{(k_{n,n-1})} & (e_{n-p}^*)\kappa^{(k_{1n})} & (e_{n-p}^*)\kappa^{(k_{0i})} & (e_{n-p}^*)\kappa^{(k_{oj})} & \mathbf{e_{n-p}^*}\kappa
\end{array}
$$

Jacobian Matrix Example

From the coefficient map, we get the following Jacobian matrix

$$\begin{bmatrix} 1 & 1 & 1 & 1 & 1 \\ k_{02}+k_{13}+k_{32} & k_{01}+k_{13}+k_{21} & k_{01}+k_{02}+k_{21}+k_{32} & k_{02}+k_{13}+k_{32} & k_{01}+k_{13}+k_{21} \\ (k_{02}+k_{32})k_{13}-k_{13}k_{32} & (k_{01}+k_{21})k_{13}-k_{13}k_{21} & (k_{01}+k_{21})(k_{02}+k_{32})-k_{21}k_{32} & (k_{02}+k_{32})k_{13} & (k_{01}+k_{21})k_{13} \\ 1 & 0 & 0 & 0 & 0 \\ k_{13} & 0 & k_{21} & 0 & 0 \end{bmatrix}$$

Recall that to be generically locally identifiable, the rank needs to equal #Edges + #Leaks.

We have three edges, two leaks, and the rank of the Jacobian matrix is 5. Thus, the model is generically locally identifiable.

Definition 3

A directed-cycle model with n compartments is a **minimal model** if it satisfies any of the following: $n = 3$, there is a leak in the n^{th} compartment, or the output is in the n^{th} compartment.

Definitions

Definition 3

A directed-cycle model with n compartments is a **minimal model** if it satisfies any of the following: $n = 3$, there is a leak in the n^{th} compartment, or the output is in the n^{th} compartment.

Definition 4

Let G_n be a directed-cycle compartmental model with n compartments, $In = \{1\}$, $Out = \{p\}$, and $Leak = \{i_1, \ldots, i_t\}$ s.t. $i_t < n$. Then $G'_{n,m}$ is the m compartment **sub-model** of G_n s.t. $3 \leq m < n$, and the input, output and leak locations are the same as in G_n.

Definitions

Definition 3

A directed-cycle model with n compartments is a **minimal model** if it satisfies any of the following: $n = 3$, there is a leak in the n^{th} compartment, or the output is in the n^{th} compartment.

Definition 4

Let G_n be a directed-cycle compartmental model with n compartments, $In = \{1\}$, $Out = \{p\}$, and $Leak = \{i_1, \ldots, i_t\}$ s.t. $i_t < n$. Then $G'_{n,m}$ is the m compartment **sub-model** of G_n s.t. $3 \leq m < n$, and the input, output and leak locations are the same as in G_n.

Remark

If G is minimal, then it has no sub-models.

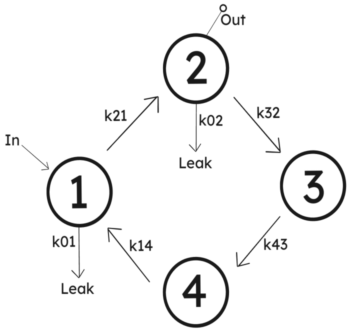
Theorem

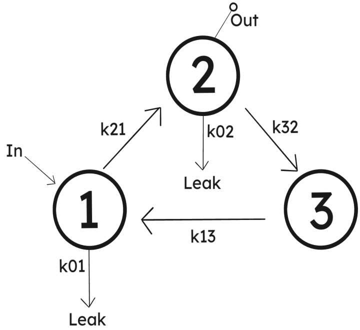
Theorem 1 (Dessauer, Grimsley, Lopez 2022)

Let G_n be a non-minimal directed-cycle compartmental model and let $G'_{n,n-1}$ be the $n-1$ compartment sub-model of G_n. Then the coefficient map of $G'_{n,n-1}$ can be derived from the coefficient map of G_n through the following transformations:

$$\begin{aligned} k_{1,n} &\mapsto 0 \\ k_{n,n-1} &\mapsto k_{1,n-1} \\ k_{0,l} &\mapsto k_{0,l} \\ k_{l+1,l} &\mapsto k_{l+1,l} \qquad \textit{for } l < n-1 \end{aligned}$$

Theorem Example





Theorem Example

$$(k_{21}, k_{32}, k_{43}, k_{14}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3, e_4 - k_{21}k_{32}k_{43}k_{14}, k_{21}, e_1^* k_{21}, e_2^* k_{21})$$

$e_1 = k_{43} + k_{14} + k_{21} + k_{01} + k_{32} + k_{02}$

$e_2 = k_{43}k_{14} + k_{43}(k_{21} + k_{01}) + k_{43}(k_{32} + k_{02}) + k_{14}(k_{21} + k_{01}) + k_{14}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02})$

$e_3 = k_{43}k_{14}(k_{21} + k_{01}) + k_{43}k_{14}(k_{32} + k_{02}) + k_{43}(k_{21} + k_{01})(k_{32} + k_{02}) + k_{14}(k_{21} + k_{01})(k_{32} + k_{02})$

$e_4 = k_{43}k_{14}(k_{21} + k_{01})(k_{32} + k_{02})$

$\kappa = k_{21}$

$e_1^* = (k_{43} + k_{14})$

$e_2^* = k_{43}k_{14}$

Theorem Example

$e_1 = \mathbf{k_{13}} + \mathbf{0} + k_{21} + k_{01} + k_{32} + k_{02}$

$e_2 = \mathbf{k_{13}}\mathbf{0} + \mathbf{k_{13}}(k_{21} + k_{01}) + \mathbf{k_{13}}(k_{32} + k_{02}) + \mathbf{0}(k_{21} + k_{01}) + \mathbf{0}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02})$

$e_3 = \mathbf{k_{13}}\mathbf{0}(k_{21}+k_{01})+\mathbf{k_{13}}\mathbf{0}(k_{32}+k_{02})+\mathbf{k_{13}}(k_{21}+k_{01})(k_{32}+k_{02})+\mathbf{0}(k_{21}+k_{01})(k_{32}+k_{02})$

$e_4 = \mathbf{k_{13}}\mathbf{0}(k_{21} + k_{01})(k_{32} + k_{02})$

$\kappa = k_{21}$

$e_1^* = (\mathbf{k_{13}} + \mathbf{0})$

$e_2^* = \mathbf{k_{13}}\mathbf{0}$

Theorem Example

$$e_1 = k_{13} + k_{01} + k_{32} + k_{02}$$

$$e_2 = k_{13}(k_{21} + k_{01}) + k_{13}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02})$$

$$e_3 = k_{13}(k_{21} + k_{01})(k_{32} + k_{02})$$

$$\kappa = k_{21}$$

$$e_1^* = k_{13}$$

Theorem Example

$$e_1 = k_{13} + k_{01} + k_{32} + k_{02}$$

$$e_2 = k_{13}(k_{21} + k_{01}) + k_{13}(k_{32} + k_{02}) + (k_{21} + k_{01})(k_{32} + k_{02})$$

$$e_3 = k_{13}(k_{21} + k_{01})(k_{32} + k_{02})$$

$$\kappa = k_{21}$$

$$e_1^* = k_{13}$$

Plug in these values into the coefficient map and we get the following map:

$$(k_{21}, k_{32}, k_{13}, k_{01}, k_{02}) \mapsto (\underbrace{k_{21} + k_{32} + k_{13} + k_{01} + k_{02}}_{e_1},$$
$$\underbrace{k_{21}k_{13} + k_{01}k_{13} + k_{21}k_{32} + k_{01}k_{32} + k_{13}k_{32} + k_{21}k_{02} + k_{13}k_{02} + k_{01}k_{02}}_{e_2},$$
$$\underbrace{k_{01}k_{13}k_{32} + k_{21}k_{13}k_{02} + k_{01}k_{13}k_{02}}_{e_3 - k_{21}k_{32}k_{13}}, \underbrace{k_{21}}_{\kappa}, \underbrace{k_{21}k_{13}}_{e_1^*\kappa})$$

Corollary 1

Let G_n be a non-minimal directed-cycle compartmental model and let $G'_{n,m}$ be the m compartment sub-model of G_n. Then the coefficient map of $G'_{n,m}$ can be derived from the coefficient map of G_n by doing the following transformations:

$$
\begin{aligned}
k_{m+1,m} &\mapsto k_{1,m} \\
k_{0,l} &\mapsto k_{0,l} \\
k_{l+1,l} &\mapsto 0 \qquad \text{for } n \geq l > m \\
k_{l+1,l} &\mapsto k_{l+1,l} \qquad \text{for } l < m
\end{aligned}
$$

Corollary 2

The mapping on the G_n coefficient map $\mapsto G'_{n,n-1}$ coefficient map from Theorem 1 is equivalent to the following mapping on the $Jac(G_n) \mapsto Jac(G'_{n,n-1})$:

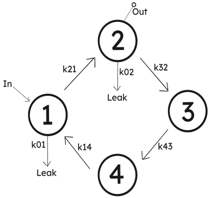
1. *Remove the n^{th} column, the n^{th} row, and the last row of the Jacobian G_n.*
2. *Perform the transformation from Theorem 1.*
3. *Subtract $\frac{\partial}{\partial k_l}\left(\prod_{i=1}^{n-1} k_{i+1,i}\right)$ from the $(n-1)^{th}$ row, where k_l is the parameter corresponding to column l.*

Corollary 2

The mapping on the G_n coefficient map $\mapsto G'_{n,n-1}$ coefficient map from Theorem 1 is equivalent to the following mapping on the $Jac(G_n) \mapsto Jac(G'_{n,n-1})$:

1. *Remove the n^{th} column, the n^{th} row, and the last row of the Jacobian G_n.*
2. *Perform the transformation from Theorem 1.*
3. *Subtract $\frac{\partial}{\partial k_l}\left(\prod_{i=1}^{n-1} k_{i+1,i}\right)$ from the $(n-1)^{th}$ row, where k_l is the parameter corresponding to column l.*

$$(k_{21}, k_{32}, k_{43}, k_{14}, k_{01}, k_{02}) \mapsto (e_1, e_2, e_3, e_4 - k_{21}k_{32}k_{43}k_{14}, k_{21}, e_1^* k_{21}, e_2^* k_{21})$$



Database

We constructed a database that classifies the identifiability of all models for $n = 3, 4, 5$. Here is a subset of our database.

	locally identifiable?	Globally Identifiable	Locally Identifiable	Not Identifiable
n = 3				
$p = 2$, L$= 1, 2$	Yes, SIAN	$k_{13}, k_{21}, k_{32}, x_2(0), x_3(0)$	$k_{01}, k_{02}, x_1(0)$	
$p = 2$, L$= 1, 3$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{03}, k_{13}, k_{32}, x_1(0), x_3(0)$	
n = 4				
$p = 2$, L$= 1, 2$	Yes, SIAN	$k_{21}, k_{32}, x_2(0)$	$k_{01}, k_{02}, k_{14}, k_{43}, x_1(0), x_3(0), x_4(0)$	
$p = 2$, L$= 1, 3$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{03}, k_{14}, k_{32}, k_{43}, x_1(0), x_3(0), x_4(0)$	
$p = 2$, L$= 1, 4$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{04}, k_{14}, k_{32}, k_{43}, x_1(0), x_3(0), x_4(0)$	
$p = 3$, L$= 1, 3$	Yes, SIAN	$k_{14}, k_{43}, x_3(0), x_4(0)$	$k_{01}, k_{03}, k_{21}, k_{32}, x_1(0), x_2(0)$	
$p = 3$, L$= 1, 4$	Yes, SIAN	$x_3(0)$	$k_{01}, k_{04}, k_{14}, k_{21}, k_{32}, k_{43}, x_10, x_2(0), x_4(0)$	
$p = 3$, L$= 2, 3$	Yes, SIAN	$k_{14}, k_{43}, x_3(0), x_4(0)$	$k_{02}, k_{03}, k_{21}, k_{32}, x_1(0), x_2(0)$	
$p = 3$, L$= 2, 4$	Yes, SIAN	$x_3(0)$	$k_{02}, k_{04}, k_{14}, k_{21}, k_{32}, k_{43}, x_10, x_2(0), x_4(0)$	
n = 5				
$p = 2$, L$= 1, 2$	Yes, SIAN	$k_{21}, k_{32}, x_2(0)$	$k_{01}, k_{02}, k_{15}, k_{43}, k_{54}, x_1(0), x_3(0), x_4(0), x_5(0)$	
$p = 2$, L$= 1, 3$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{03}, k_{15}, k_{32}, k_{43}, k_{54}, x_1(0), x_3(0), x_4(0), x_5(0)$	
$p = 2$, L$= 1, 4$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{04}, k_{15}, k_{32}, k_{43}, k_{54}, x_1(0), x_3(0), x_4(0), x_5(0)$	
$p = 2$, L$= 1, 5$	Yes, SIAN	$k_{21}, x_2(0)$	$k_{01}, k_{05}, k_{15}, k_{32}, k_{43}, k_{54}, x_1(0), x_3(0), x_4(0), x_5(0)$	
$p = 3$, L$= 1, 3$	Yes, SIAN	$k_{43}, x_3(0)$	$k_{01}, k_{03}, k_{15}, k_{21}, k_{32}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 3$, L$= 1, 4$	Yes, SIAN	$x_3(0)$	$k_{01}, k_{04}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 3$, L$= 1, 5$	Yes, SIAN	$x_3(0)$	$k_{01}, k_{05}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 3$, L$= 2, 3$	Yes, SIAN	$k_{43}, x_3(0)$	$k_{02}, k_{03}, k_{15}, k_{21}, k_{32}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 3$, L$= 2, 4$	Yes, SIAN	$x_3(0)$	$k_{02}, k_{04}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 3$, L$= 2, 5$	Yes, SIAN	$x_3(0)$	$k_{02}, k_{05}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_4(0), x_5(0)$	
$p = 4$, L$= 1, 4$	Yes, SIAN	$k_{15}, k_{54}, x_4(0), x_5(0)$	$k_{01}, k_{04}, k_{21}, k_{32}, k_{43}, x_1(0), x_2(0), x_3(0)$	
$p = 4$, L$= 1, 5$	Yes, SIAN	$x_4(0)$	$k_{01}, k_{05}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_3(0), x_5(0)$	
$p = 4$, L$= 2, 4$	Yes, SIAN	$k_{15}, k_{54}, x_4(0), x_5(0)$	$k_{02}, k_{04}, k_{21}, k_{32}, k_{43}, x_1(0), x_2(0), x_3(0)$	
$p = 4$, L$= 2, 5$	Yes, SIAN	$x_4(0)$	$k_{02}, k_{05}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_3(0), x_5(0)$	
$p = 4$, L$= 3, 4$	Yes, SIAN	$k_{15}, k_{54}, x_4(0), x_5(0)$	$k_{02}, k_{03}, k_{21}, k_{32}, k_{43}, x_1(0), x_2(0), x_3(0)$	
$p = 4$, L$= 3, 5$	Yes, SIAN	$x_4(0)$	$k_{03}, k_{05}, k_{15}, k_{21}, k_{32}, k_{43}, k_{54}, x_1(0), x_2(0), x_3(0), x_5(0)$	

Conjecture 1

Conjecture 1

Let G_n be a non-minimal directed-cycle compartmental model and let $G'_{n,m}$ be the m compartment sub-model of G_n. If G_n is identifiable, then so is $G'_{n,m}$.

Conjecture 1

Let G_n be a non-minimal directed-cycle compartmental model and let $G'_{n,m}$ be the m compartment sub-model of G_n. If G_n is identifiable, then so is $G'_{n,m}$.

$n=3$	$n=4$	$n=5$
$p=2$, L$=1,2$	$p=2$, L$=1,2$	$p=2$, L$=1,2$
$p=2$, L$=1,3$	$p=2$, L$=1,3$	$p=2$, L$=1,3$
	$p=2$, L$=1,4$	$p=2$, L$=1,4$
	$p=3$, L$=1,3$	$p=3$, L$=1,3$
	$p=3$, L$=1,4$	$p=3$, L$=1,4$
	$p=3$, L$=2,3$	$p=3$, L$=2,3$
	$p=3$, L$=2,4$	$p=3$, L$=2,4$

Conjecture 1

Let G_n be a non-minimal directed-cycle compartmental model and let $G'_{n,m}$ be the m compartment sub-model of G_n. If G_n is identifiable, then so is $G'_{n,m}$.

$n = 3$	$n = 4$	$n = 5$
$p = 2$, L$= 1, 2$	$p = 2$, L$= 1, 2$	$p = 2$, L$= 1, 2$
$p = 2$, L$= 1, 3$	$p = 2$, L$= 1, 3$	$p = 2$, L$= 1, 3$
	$p = 2$, L$= 1, 4$	$p = 2$, L$= 1, 4$
	$p = 3$, L$= 1, 3$	$p = 3$, L$= 1, 3$
	$p = 3$, L$= 1, 4$	$p = 3$, L$= 1, 4$
	$p = 3$, L$= 2, 3$	$p = 3$, L$= 2, 3$
	$p = 3$, L$= 2, 4$	$p = 3$, L$= 2, 4$

Conjecture 2

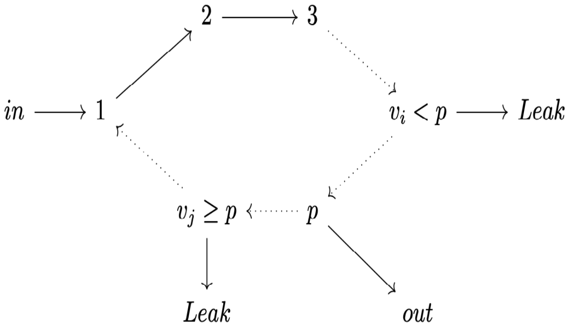
Conjecture 2

Let G_n be a directed-cycle model with $In = \{1\}$, $Out = \{p\}$ s.t. $1 < p < n$, $Leak = \{i, j\}$. Then G_n is generically locally identifiable if and only if $i < p \leq j$.

Conjecture 2

Conjecture 2

Let G_n be a directed-cycle model with $In = \{1\}$, $Out = \{p\}$ s.t. $1 < p < n$, $Leak = \{i, j\}$. Then G_n is generically locally identifiable if and only if $i < p \leq j$.



Future Research

- Prove both conjectures
- Extend the database
- Investigate if the reduction that results from Theorem 1 preserves the identifiability of the subsets of parameters

Identifiable:	Globally	Locally
$n = 3$		
$p = 2,\ L = 1, 2$	k_{13}, k_{21}, k_{32}	k_{01}, k_{02}
$p = 2,\ L = 1, 3$	k_{21}	$k_{01}, k_{03}, k_{13}, k_{32}$
$n = 4$		
$p = 2,\ L = 1, 2$	k_{21}, k_{32}	$k_{01}, k_{02}, k_{14}, k_{43}$
$p = 2,\ L = 1, 3$	k_{21}	$k_{01}, k_{03}, k_{14}, k_{32}, k_{43}$
$p = 2,\ L = 1, 4$	k_{21}	$k_{01}, k_{04}, k_{14}, k_{32}, k_{43}$
$n = 5$		
$p = 2,\ L = 1, 2$	k_{21}, k_{32}	$k_{01}, k_{02}, k_{15}, k_{43}, k_{54}$
$p = 3,\ L = 1, 3$	k_{43}	$k_{01}, k_{03}, k_{15}, k_{21}, k_{32}, k_{54}$
$p = 4,\ L = 1, 4$	k_{15}, k_{54}	$k_{01}, k_{04}, k_{21}, k_{32}, k_{43}$

Acknowledgements

The research was initiated and conducted as part of the MSRI-UP REU, which is funded by the Alfred P. Sloan Foundation and the National Science Foundation (DMS-2149642). We want to thank the following MSRI-UP 2022 team: Dr. Federico Ardila for being the on-site director, Dr. Anne Shiu for being the Research director, and Natasha Crepeau for being our RA. They all provided invaluable help and support throughout the REU, as well as resources that enabled us to conduct our research.

References

Seth Gerberding, Nida Obatake, and Anne Shiu.
Identifiability of Linear Compartmental Models: The Effect of Moving Inputs, Outputs, and Leaks.
arXiv 1910.13549, 2020.

Hoon Hong, Alexey Ovchinnikov, Gleb Pogudin, and Chee Yap.
SIAN: Software for Structural Identifiability Analysis of ODE Models.
Bioinformatics, 35(16):2873–2874, 2019.

Nicolette Meshkat, Seth Sullivant, and Marisa Eisenberg.
Identifiability Results for Several Classes of Linear Compartment Models.
Bulletin of Mathematical Biology, 77:1620–1651, 2015.