Parameter Identifiability of Catenary Models

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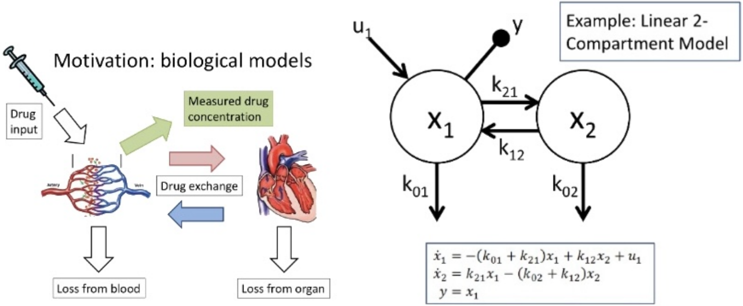
Presentation Overview

1. Motivation
2. Definitions
3. Statement of Purpose
4. Results
5. Future Directions

Motivation



[1]

[1] Photo credit: Nicolette Meshkat

Definitions

Definition (Parameter)

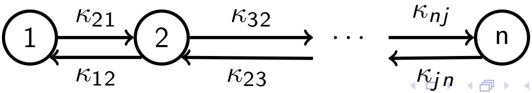
Rate at which a substance enters and exits a compartment

Definition (Identifiability)

- **Globally**: can determine a specific value for a parameter
- **Locally**: can determine a finite set of values for a parameter
- **Unidentifiable**: cannot determine a specific/set of values for a parameter

Definition (Catenary)

A type of bidirected tree model that consists of paths



Statement of Purpose

We focus on catenary models with 1 input, 1 output, and a variation of leaks and develop a systematic method of determining the identifiability of individual parameters. Biologically, the information derived can indicate how substances move throughout the body.

Results

Previous Theorem(s)

Proposition (Bortner, et al.)

A bidirected tree model with 1 input and 1 output is generically locally identifiable $\iff \begin{cases} dist_G(in, out) \leq 1 \\ \#leaks \leq 1 \end{cases}$

Question: What is the identifiability of each individual parameter in the model?

Results
Our Approach

Our approach: Deal with the proposition in 3 cases

3 Cases:

1. $dist_G(in, out) = 0$ and $\#$ leaks ≤ 1
2. $dist_G(in, out) = 1$ and $\#$ leaks $= 1$
3. $dist_G(in, out) = 1$ and $\#$ leaks $= 0$

Results

Theorem 1

Theorem 1 (Edozie, Garcia-Lopez, Neri 2022)

Given a 3-compartment catenary model G with 1 input and 1 output where {Input}=j and {Output}=i. If $dist_G(i,j) = 0$ and # leaks ≤ 1, then all the parameters are globally identifiable[2]

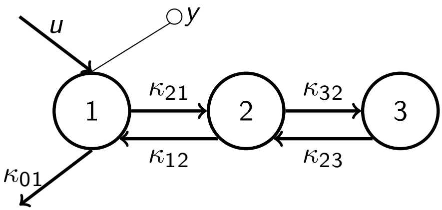
[2] Special case: If $i = j = 2$, all the parameters are locally identifiable. If a leak is (not) in the center, it is globally (locally) identifiable

Results

Theorem 1 Example

Theorem 1 (Edozie, Garcia-Lopez, Neri 2022)

If $dist_G(i, j) = 0$ and # leaks ≤ 1, then all the parameters are globally identifiable.



Results

Theorem 1 Example

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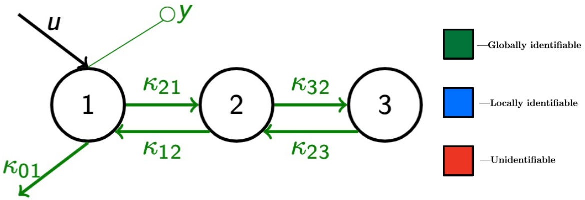


Results

Theorem 2

Theorem 2 (Edozie, Garcia-Lopez, Neri 2022)

Given a 3 compartment catenary model G with 1 input and 1 output where {Input}=j and {Output}=i. If $dist_G(i,j) = 1$ and # leaks = 1 where {Leak}=l.

- If $dist_G(j,l) < dist_G(i,l)$: k_{0l} is locally identifiable. Otherwise, it is globally identifiable.
- If $dist_G(i,l) = 2$: k_{ij} is globally identifiable. The rest of the edge parameters are locally identifiable.
- If $dist_G(i,l) \leq 1$: k_{ij} and k_{23} are globally identifiable. The rest of the edge parameters are locally identifiable[3]

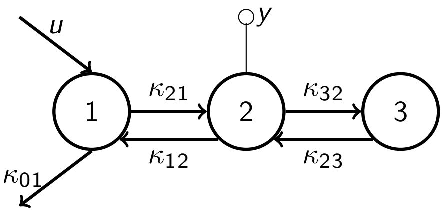
[3] If $i = 2$ and $l \neq j$, the rest of the edge parameters are globally identifiable

Results

Theorem 2 Example

Theorem 2 (Edozie, Garcia-Lopez, Neri 2022)

If $dist_G(j,l) < dist_G(i,l)$: k_{0l} is locally identifiable. Otherwise, it is globally identifiable.



Results

Theorem 2 Example

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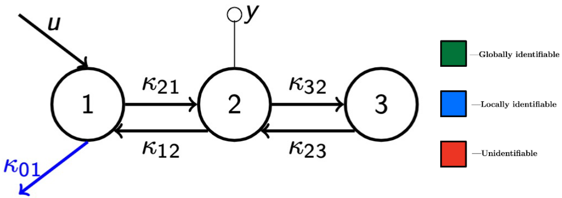
If $dist_G(j, l) < dist_G(i, l)$: k_{0l} is locally identifiable. Otherwise, it is globally identifiable.

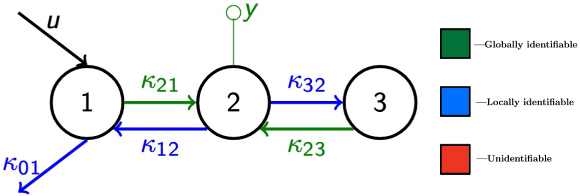


Results

Theorem 2 Example

Theorem 2 (Edozie, Garcia-Lopez, Neri 2022)

If $dist_G(i,l) \leq 1$: k_{ij} and k_{23} are globally identifiable. The rest of the edge parameters are locally identifiable, unless $i = 2$ and $l \neq j$ (in which case, the rest of the edge parameters are globally identifiable).



Results

Theorem 3

Theorem 3 (Edozie, Garcia-Lopez, Neri 2022)

Given a 3 compartment catenary model with 1 input and 1 output where {Input}=j and {Output}=i. If $dist_G(i,j) = 1$ and # leaks=0, then all the parameters are globally identifiable[4]

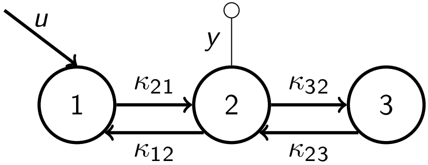
[4]Special case: If $i \in \{1,3\}$, then k_{21} and k_{32} are locally identifiable and the rest are globally identifiable

Results

Theorem 3 Example

Theorem 3 (Edozie, Garcia-Lopez, Neri 2022)

If $dist_G(i, j) = 1$ and $\#$ leaks $= 0$, then all the parameters are globally identifiable.



Results

Theorem 3 Example

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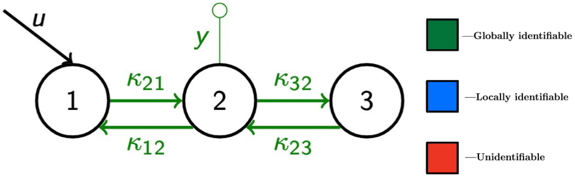
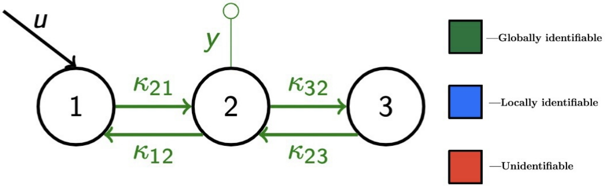


Results

Theorem 3 Example

Model:



A-Matrix:

$$A(G) = \begin{pmatrix} x_1' \\ x_2' \\ x_3' \end{pmatrix} = \begin{pmatrix} -k_{21} & k_{12} & 0 \\ k_{21} & -k_{12} - k_{32} & k_{23} \\ 0 & k_{32} & -k_{23} \end{pmatrix}$$

Results

Input-Output Equation

Input-Output Equation

$$\det(\partial I - A)y_i = \sum_{j \in In} (-1)^{i+j} \det(\partial I - A)^{j,i} u_j \quad \text{for } i \in Out,\ j \in In.$$

LHS:

$$det(\partial I - A)y_2 = det \begin{pmatrix} \frac{d}{dt} + k_{21} & -k_{12} & 0 \\ -k_{21} & \frac{d}{dt} + k_{12} + k_{32} & -k_{23} \\ 0 & -k_{32} & \frac{d}{dt} + k_{23} \end{pmatrix} y_2$$

RHS:

$$det(\partial I - A)^{1,2} u_1 = (-1)^{1+2} det \begin{pmatrix} -k_{21} & -k_{23} \\ 0 & \frac{d}{dt} + k_{23} \end{pmatrix} u_1$$

Input-Output Equation:

$$y_2^{(3)} + (k_{21} + k_{12} + k_{32} + k_{23})y_2^{(2)} + (k_{21}k_{32} + k_{12}k_{23} + k_{21}k_{23})y_2^{(1)} = (k_{21})u_1^{(1)} + (k_{21}k_{23})u_1$$

Coefficient Equations:

$$c_1 = k_{21} + k_{12} + k_{32} + k_{23}$$

$$c_2 = k_{21}k_{32} + k_{12}k_{23} + k_{21}k_{23}$$

$$c_3 = k_{21}$$

$$c_4 = k_{21}k_{23}$$

Results

Coefficient Mapping

Theorem 4 (Ahmed, Edozie, Garcia-Lopez, Neri 2022)

G is an n compartment catenary model with $|Inputs| = |Outputs| = 1$ ({Input}=j, {Output}=i) and any # of leaks. The coefficient map is given by:

$$c : \mathbb{R}^{3n-2} \to \mathbb{R}^{2n-1}$$

$$(k_{12}, k_{21}, ..., k_{n(n-1)}, k_{(n-1)n}, k_{01}, ..., k_{0n}) \mapsto (c_1, c_2, ..., c_n, d_1, d_2, ..., d_{n-1})$$

- E = {All parameters}
- $c_i = e_i(E) - \sigma_i$
- $d_z = \begin{cases} \mathrm{e}_z(E) - \sigma''_z], & \text{if } dist(i,j) = 0 \\ \mathrm{k}_{ij}[e_{z-1}(E) - \sigma''_{z-1}], & \text{if } dist(i,j) = 1 \end{cases}$ for $z \in \{1, ..., n-1\}$

Results

Coefficient Mapping

Define elementary symmetric polynomials $e_1 \ldots e_n$:

$$e_1 = \sum_{1 \le j \le n} X_j$$

$$e_2 = \sum_{1 \le j < k \le n} X_j X_k$$

$$e_3 = \sum_{1 \le j < k < i \le n} X_j X_k X_i$$

$$e_n = \ldots$$

Results

Coefficient Mapping

Define ideals: $\langle k_i \rangle$

$$I = \langle k_{ij} k_{mj} \rangle$$

$$I' = \langle k_{ij} k_{ji} \rangle$$

$$I'' = \langle k_{ij} \mid j \in (In \cup Out) \rangle$$

Results

Coefficient Mapping

Define ideals: $\langle k_i \rangle$

$$I = \langle k_{ij} k_{mj} \rangle$$

$$I' = \langle k_{ij} k_{ji} \rangle$$

$$I'' = \langle k_{ij} \mid j \in (In \cup Out) \rangle$$

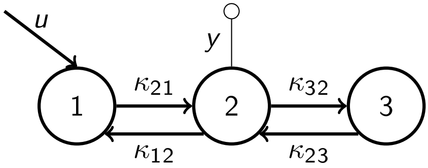
Important summations:

$$\sigma_i = \sum_{x \in (I \cup I')_i} x$$

$$\sigma''_i = \sum_{x \in (I \cup I' \cup I'')_i} x$$

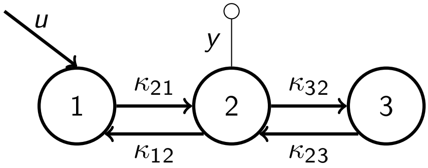
Results

Coefficient Mapping Example



Results

Coefficient Mapping Example



$\mathrm{E} = \{k_{21}, k_{12}, k_{32}, k_{23}\}$

Results

Coefficient Mapping Example

$$E = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$c_i = e_i(E) - \sigma_i$$

Results

Coefficient Mapping Example

$$\mathrm{E} = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$c_i = e_i(E) - \sigma_i$$

$$\begin{aligned} c_1 &= e_1(E) - \sigma_1 \\ &= k_{21} + k_{12} + k_{32} + k_{23} \end{aligned}$$

Results

Coefficient Mapping Example

$$\text{E} = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$c_i = e_i(E) - \sigma_i$$

$$\begin{aligned} c_1 &= e_1(E) - \sigma_1 \\ &= k_{21} + k_{12} + k_{32} + k_{23} \end{aligned}$$

$$\begin{aligned} c_2 &= e_2(E) - \sigma_2 \\ &= k_{21}k_{12} + k_{21}k_{32} + k_{21}k_{23} + k_{12}k_{32} + k_{12}k_{23} + k_{32}k_{23} \\ &\qquad -(k_{21}k_{12} + k_{12}k_{32} + k_{32}k_{23}) \\ &= k_{21}k_{32} + k_{21}k_{23} + k_{12}k_{23} \end{aligned}$$

Results

Coefficient Mapping Example

$$E = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

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no c_3 coefficient

Results

Coefficient Mapping Example

$$\text{E} = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$d_z = k_{ij}[e_{z-1}(E) - \sigma''_{z-1}] \text{ for } z \in \{1, ..., n-1\}$$

Results

Coefficient Mapping Example

$$\mathrm{E} = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$d_z = k_{ij}[e_{z-1}(E) - \sigma''_{z-1}] \text{ for } z \in \{1, ..., n-1\}$$

$$\begin{aligned} d_1 &= k_{21}[e_0(E) - \sigma''_0] \\ &= k_{21} \end{aligned}$$

Results

Coefficient Mapping Example

$$E = \{k_{21}, k_{12}, k_{32}, k_{23}\}$$

$$d_z = k_{ij}[e_{z-1}(E) - \sigma''_{z-1}] \text{ for } z \in \{1, ..., n-1\}$$

$$\begin{aligned} d_1 &= k_{21}[e_0(E) - \sigma''_0] \\ &= k_{21} \end{aligned}$$

$$\begin{aligned} d_2 &= k_{21}[e_1(E) - \sigma''_1] \\ &= k_{21}[(k_{21} + k_{12} + k_{32} + k_{23}) - (k_{21} + k_{12} + k_{32})] \\ &= k_{21}(k_{23}) \\ &= k_{21}k_{23} \end{aligned}$$

Results

Coefficient Mapping Example

Using the coefficients, we can:

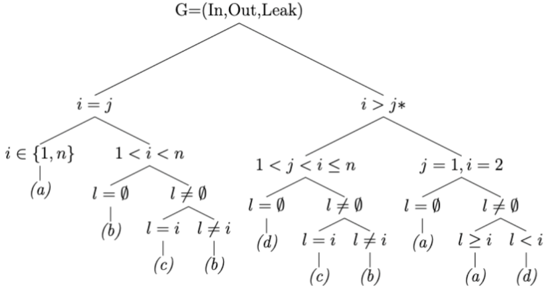
- Solve the system of coefficient equations
- Determine if the individual parameters are globally, locally, not identifiable
  - Globally identifiable: parameter has unique solution
  - Locally identifiable: parameter has finite number of solutions
  - Not identifiable: parameter solution can not be determined

Results

Iterative Process of Classifying Parameter Identifiability

Conjecture 1 (Edozie, Garcia-Lopez, Neri 2022)

Let G be an n compartment catenary model with $|Inputs| = |Outputs| = 1$, where {Input}=j, {Output}=i, $dist(i,j) \leq 1$, and $\#$ leaks ≤ 1 (if $\exists$ leak, {Leak}=l). The following tree can be used to classify the individual parameters of G.



Results

Iterative Process of Classifying Parameter Identifiability

(a): All parameters are globally identifiable.

(b): All parameters are locally identifiable. For $n = 3$: if $i > j$ and $l = j$, then κ_{j1} is globally identifiable.

(c): κ_{0l} is globally identifiable and all other parameters are locally identifiable. For $n = 3$: if $i > j$, then κ_{j1} is globally identifiable.

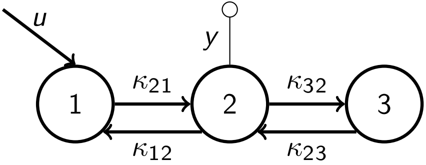
(d): All parameters are locally identifiable. For $n = 3$: κ_{21} if $i = n$ and κ_{23} if $i = 2$ is globally identifiable.

$*\kappa_{ij}$ is a globally identifiable parameter for all cases stemming from this node

Results

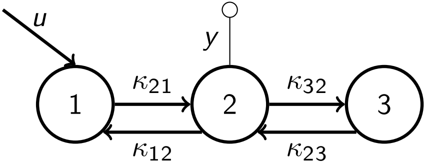
Iterative Process of Classifying Parameter Identifiability Example

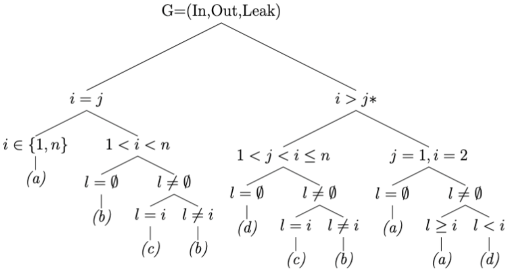
In the model below, the $dist(i,j) = 1$, $input = j = 1$ and $output = i = 2$, and $I = \emptyset$. We can use the iterative process as a means of classifying all the parameters.



Results

Iterative Process of Classifying Parameter Identifiability Example





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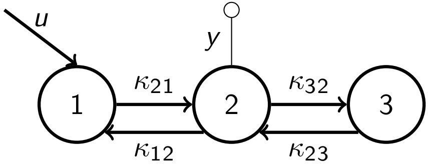

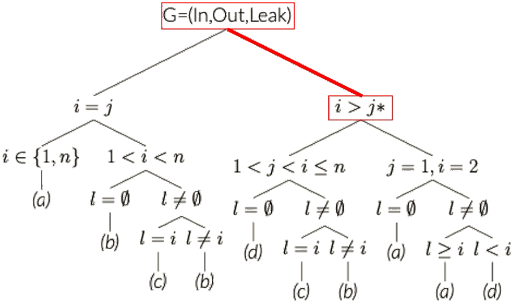

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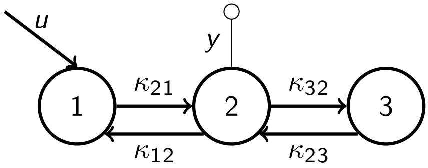

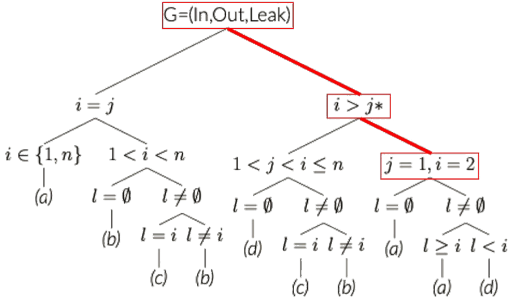

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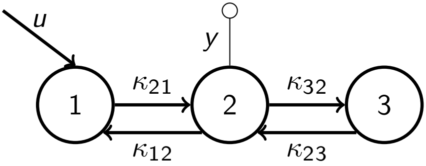

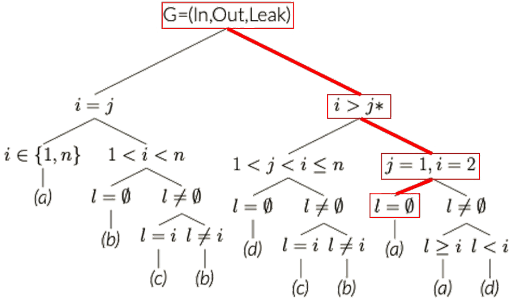

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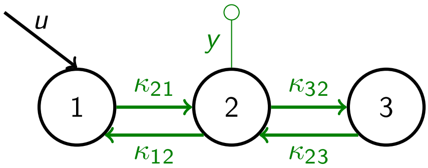
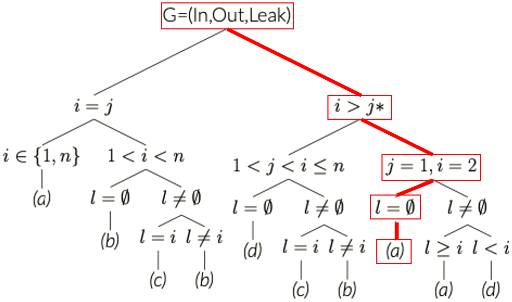
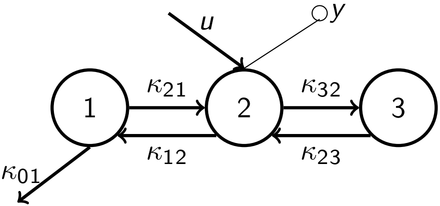


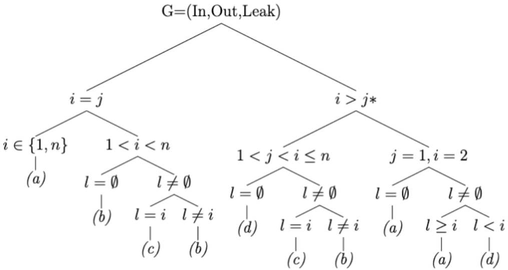


(a): all parameters are globally identifiable

Results

Iterative Process of Classifying Parameter Identifiability Example





Results

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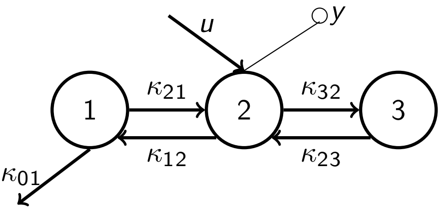

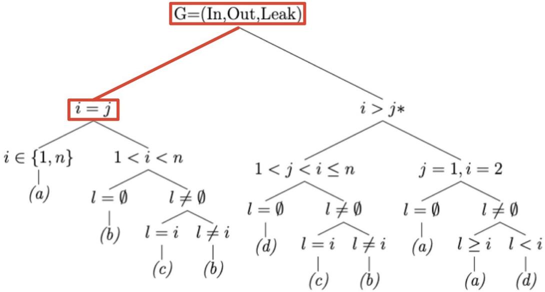

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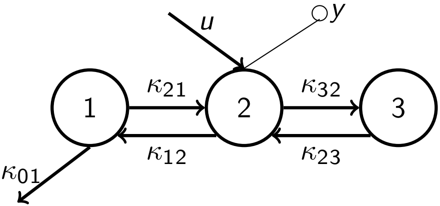

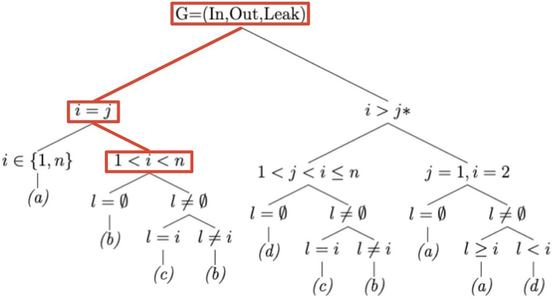

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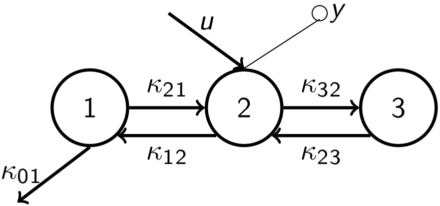

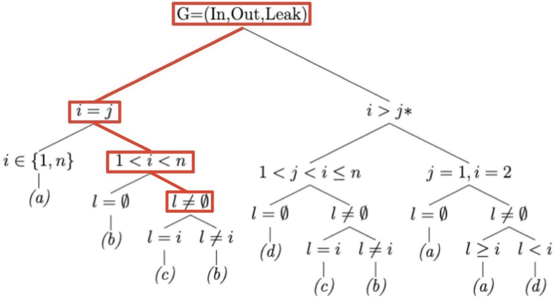

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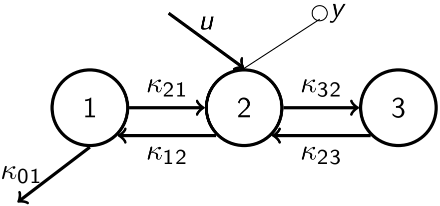

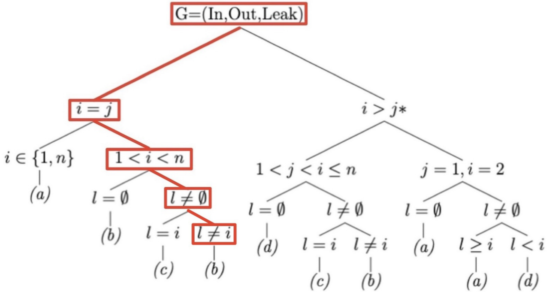

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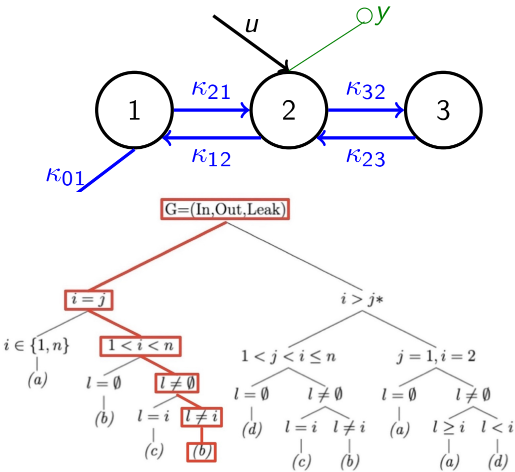

(b): all parameters are locally identifiable. For n=3: if $i > j$ and $l = j$, then k_{j1} is globally identifiable.

Future Directions

- Increase the number of inputs, outputs, and leaks
- Increase the distance between input and output
- Examine other types of bidirected tree models (i.e. mammillary)

Acknowledgements

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References

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