Indistinguishability of Linear Compartmental Models

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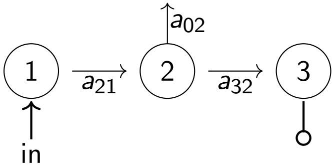
7/10/2025

Motivating Example



Linear Compartmental Model

$$\mathcal{M} = (G, In, Out, Leak)$$
$$= (\overrightarrow{P}_3, \{1\}, \{3\}, \{2\}).$$

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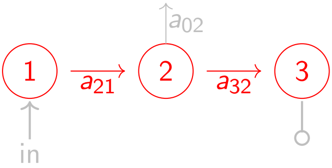

Directed Graph: $G = \overrightarrow{P}_3$

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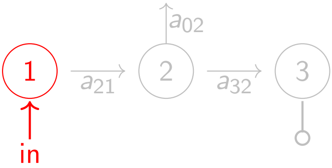

Input Compartment: $In = \{1\}$

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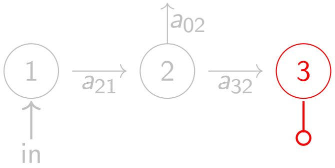

Output Compartment: $Out = \{3\}$

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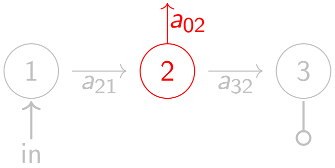
Motivating Example



Leak Compartment: $Leak = \{2\}$

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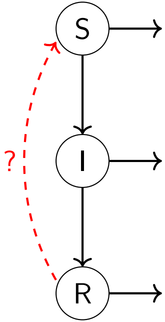
Compartmental Models in the Wild

- SIR Model for spread of a virus in Epidemiology (non-linear)
- SIV Model for vaccine efficiency in Epidemiology
- Modeling Pharmacokinetics for absorption, distribution, metabolism, and excretion in the blood
- Modeling different biological systems



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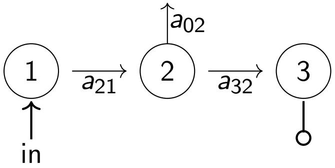

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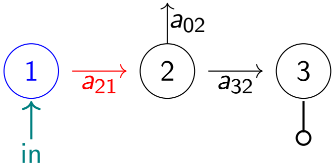


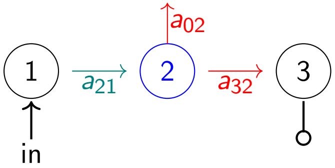
Linear Compartmental Model

$$\mathcal{M} = (G, In, Out, Leak) = (\overrightarrow{P}_3, \{1\}, \{3\}, \{2\}).$$

ODEs in terms of concentrations $x_i(t)$, input $u_1(t)$, and output $y_3(t)$:

$$\dot{x}_1(t) = -a_{21}x_1(t) \qquad + u_1(t)$$

Motivating Example



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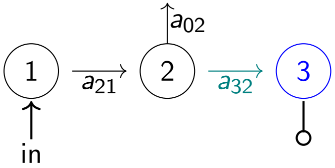

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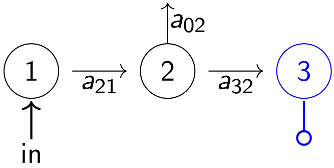

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with

$$y_3(t) = x_3(t).$$

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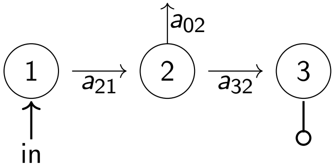

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$$\begin{pmatrix} \dot{x}_1(t) \\ \dot{x}_2(t) \\ \dot{x}_3(t) \end{pmatrix} = \underbrace{\begin{pmatrix} -a_{21} & 0 & 0 \\ a_{21} & -a_{02} - a_{32} & 0 \\ 0 & a_{32} & 0 \end{pmatrix}}_{\text{compartmental matrix A}} \begin{pmatrix} x_1(t) \\ x_2(t) \\ x_3(t) \end{pmatrix} + \begin{pmatrix} u_1(t) \\ 0 \\ 0 \end{pmatrix}$$

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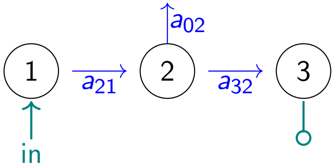
Motivating Example: Input/Output Equation



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Via an application of Cramer's Rule:

$$\det(\partial I - A)y_3 = \overbrace{\det(\partial I - A)^{1,3}}^{\text{remove row 1, col. 3}} u_1$$

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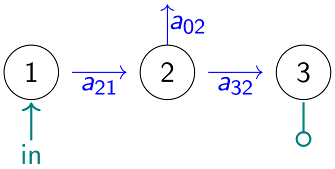

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an ODE in only the measurable variables and the parameters:

Input/Output Equation

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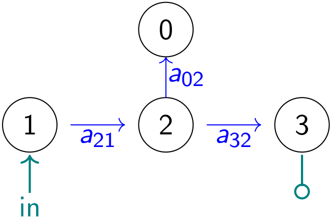

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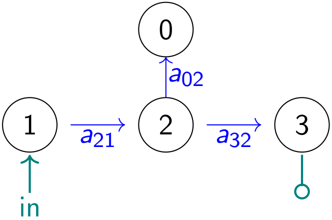

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Theorem ($, Gross, Meshkat, Shiu, Sullivant [2023])

The coefficients of the input-output equation of a LCM $(G, In, Out, Leak)$ can be generated by *incoming forests* on graphs related to G.

- *incoming*: no vertex has more than **one** outgoing edge
- *forest*: no cycles

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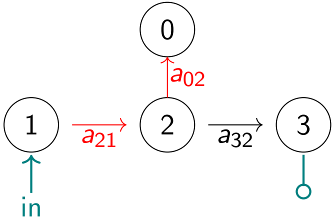

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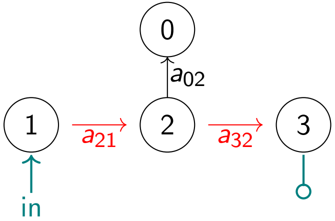

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Indistinguishability

Motivating Question

How do we know if the model structure we chose which seems to represent the data well is **unique**?

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Two LCMs are *indistinguishable* if for any choice of parameters in the first model, there is a choice of parameters in the second model that will yield the same *dynamics* in both models.

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How do we know if the model structure we chose which seems to represent the data well is **unique**?

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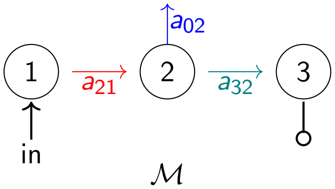
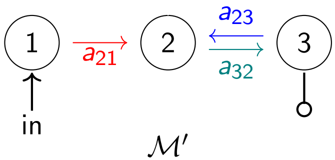
What does "same dynamics" mean?

Motivating Example: Indistinguishability





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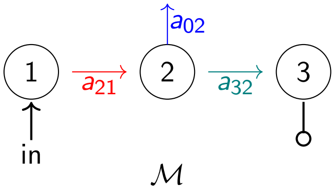

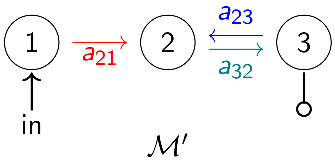

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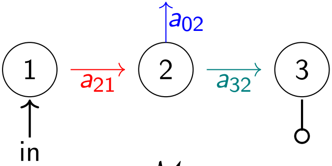
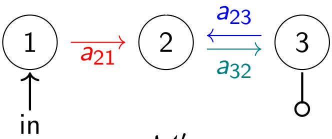
Remark

From the perspective of the input-output equations, we can not *distinguish* between these two very structurally different models.

Motivating Example: Indistinguishability



$\mathcal{M}$



$\mathcal{M}'$

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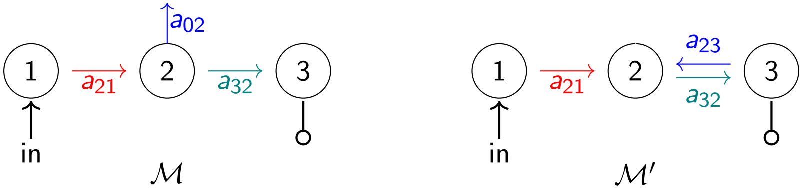
Working Definition

Two models are *permutation indistinguishable* if they have the same input-output equations up to renaming the parameters.

Motivating Example: Indistinguishability



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$$\text{renaming: } \begin{pmatrix} a_{21} \\ a_{02} \\ a_{32} \end{pmatrix} \mapsto \begin{pmatrix} a_{21} \\ a_{23} \\ a_{32} \end{pmatrix}$$

Motivating Example: Indistinguishability

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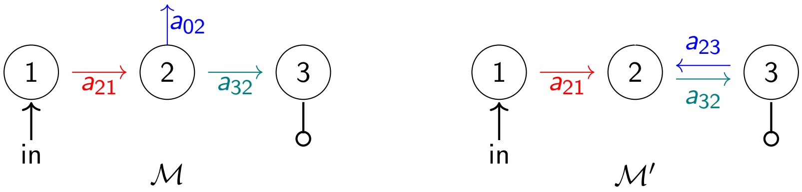
Remark

Permuation indistinguishability is an *equivalence relation*!

Motivating Example: Indistinguishability



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Permuation indistinguishability is an *equivalence relation*!
Question: What is the *equivalence class* of a model?

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Remark

Permuation indistinguishability is an *equivalence relation*!

Question: What is the *equivalence class* of a model? (Size 1?)

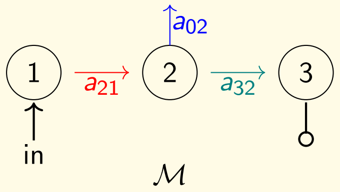
Previous Work: Necessary Conditions for Indist.

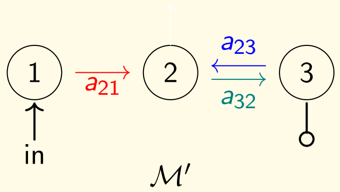
Theorem (Godfrey & Chapman [1990])

Two indistinguishable models must preserve the following:

1. The length of the shortest path from the input to the output
2. The number of compartments with a path to any output compartment
3. The number of compartments that can be reached from an input
4. The number of traps*

Example





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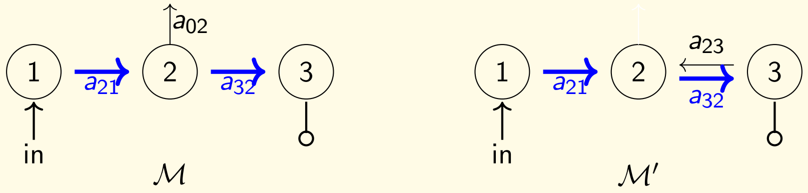
Example (1. $\text{Dist}(1,3) = 2$ in both!)



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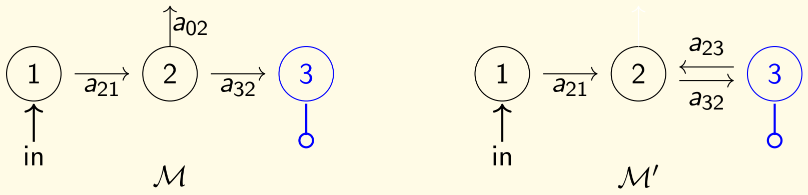
Example (2. **Two** compartments with a path to the output!)



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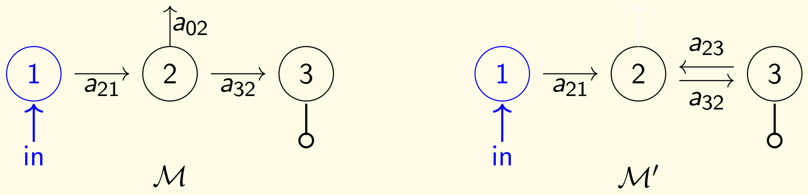
Example (3. Two compartments with a path from the input!)



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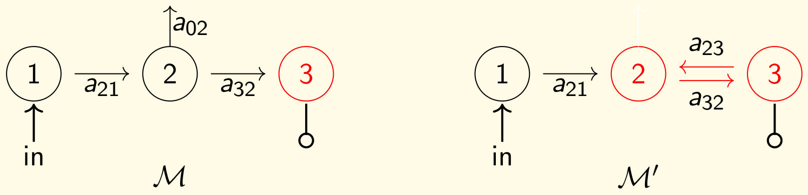
Example (4. Each model has one trap!)



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Goal:

Find *sufficient* conditions for permutation indistinguishability of two models based on their graph structures.

Skeletal Path Models

Definition

A *skeletal path model* is an LCM whose graph contains the directed path $\overrightarrow{P_n}$, i.e $1 \to 2 \to \ldots \to n$, with $In = \{1\}$ and $Out = \{n\}$.

Example

Skeletal Path Moves: Walking the Leak

Question

What *moves* can you perform on a basic skeletal path model resulting in an indistinguishable model?

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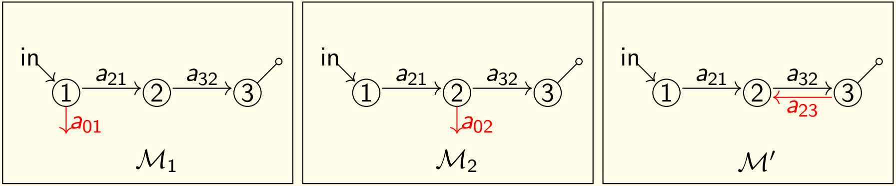
Theorem ($ & Meshkat [2024]; $, Gilliana, Patel, & Tamras [2025*])

The following skeletal path models are indistinguishable:

- $\mathcal{M}_i = (\overrightarrow{P_n}, \{1\}, \{n\}, \{i\})$ for any $i \in \{1, 2, 3, \ldots, n-1\}$
- $\mathcal{M}' = (\overrightarrow{P_n} \cup \{n \to n-1\}, \{1\}, \{n\}, \emptyset)$.

Example



Proof idea

Theorem ($ & Meshkat [2024]; $, Gilliana, Patel, & Tamras [2025*])

The following skeletal path models are indistinguishable:

- $\mathcal{M}_i = (\overrightarrow{P_n}, \{1\}, \{n\}, \{i\})$ for any $i \in \{1, 2, 3, \dots, n-1\}$
- $\mathcal{M}' = (\overrightarrow{P_n} \cup \{n \to n-1\}, \{1\}, \{n\}, \emptyset)$.

Proof idea 1: Left-hand side of the input/output equation of $\mathcal{M}_i$ given by:

$$\det(\partial I - A_i) y_n = \det \begin{pmatrix} \partial + a_{21} & 0 & \cdots & \cdots & 0 & 0 \\ -a_{21} & \ddots & \ddots & \ddots & \vdots & \vdots \\ 0 & \ddots & \partial + a_{0i} + a_{i(i-1)} & \ddots & \vdots & \vdots \\ \vdots & \ddots & -a_{i(i-1)} & \ddots & 0 & 0 \\ 0 & \cdots & \ddots & \ddots & \partial + a_{n(n-1)} & 0 \\ 0 & \cdots & \cdots & 0 & -a_{n(n-1)} & \partial \end{pmatrix} y_n$$

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Proof idea 2:

- Under a renaming of the parameters, the incoming forests of each $\mathcal{M}_i$ are exactly the same as the incoming forests of each $\mathcal{M}_j$ (and $\mathcal{M}'$).

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Proof idea 2:

- Under a renaming of the parameters, the incoming forests of each $\mathcal{M}_i$ are exactly the same as the incoming forests of each $\mathcal{M}_j$ (and $\mathcal{M}'$).
- Thus, each of the coefficients of the respective input/output equations are indistinguishable.

Detour Models

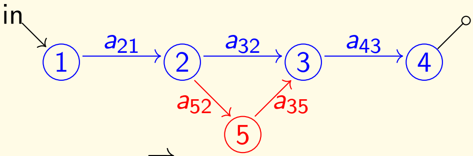
Definition

A *detour model* is given by

$$\mathcal{M} = (\overrightarrow{P_n} \cup D^*_{i,j}, \{1\}, \{n\}, Leak)$$

where D is some connected directed graph, and $D^*_{i,j}$ includes one edge from node i and to node j in the skeletal path.

Example



$$\mathcal{M} = (\overrightarrow{P}_4 \cup D^*_{2,3}, \{1\}, \{4\}, \emptyset)$$

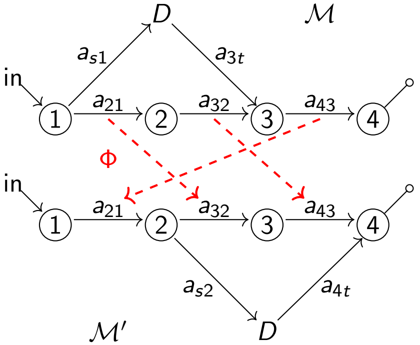
Detour Models

Theorem ($ & Meshkat [2024])

The following two detour models are indistinguishable:

- $\mathcal{M} = (\overrightarrow{P_n} \cup D^*_{i,j}, \{1\}, \{n\}, Leak)$
- $\mathcal{M}' = (\overrightarrow{P_n} \cup D^*_{i+1,j+1}, \{1\}, \{n\}, Leak)$

Proof idea:



- Break the A matrices into blocks, and show equivalent determinants under Φ

Detour Models

Theorem ($ & Meshkat [2024])

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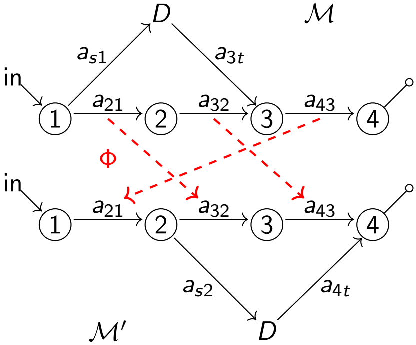
Proof idea:



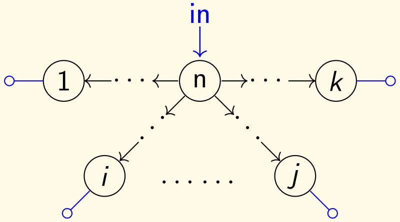
- Break the A matrices into blocks, and show equivalent determinants under Φ
- Or, the incoming forests under the renaming Φ are the same, so the coefficients are the same!

Source and Sink Models

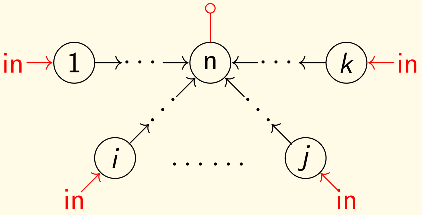
Corollary ($ & Meshkat [2024]

We can extend results from detour models to *source* and *sink* models.

Example



Basic Source Model



Basic Sink Model

Future Work

- These are very specific families of LCMs, but this is a proof of concept moving forward!
- More implementation of graph theory in showing sufficient conditions for other families of models
  - Cycle Models (undergraduate research project)
  - Tree Models
- Look into more general indistinguishability from a graph perspective
- Help biologists determine if the model they are using is the **only** model which yield the same dynamics

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This Presentation!