On the Identifiability of Directed-Cycle Linear Compartment Models

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REU in Algebraic Methods in Computational Biology
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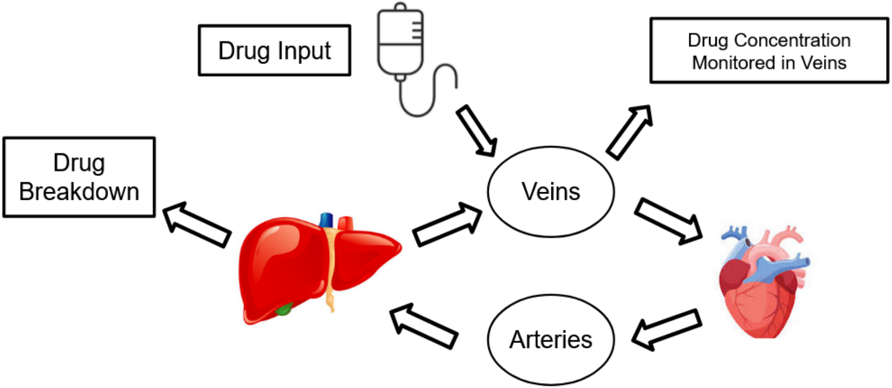
Motivation



Images taken from Google Images

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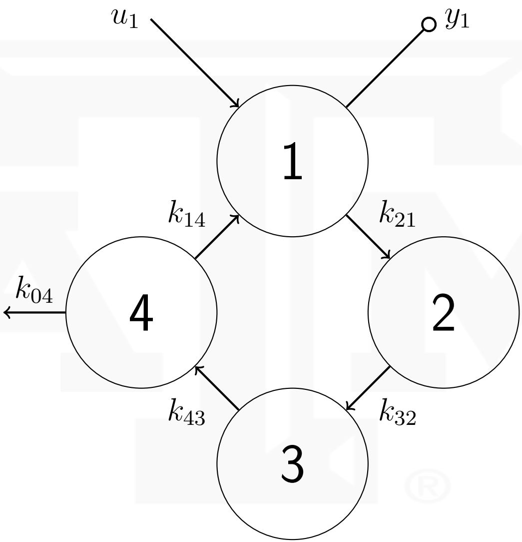

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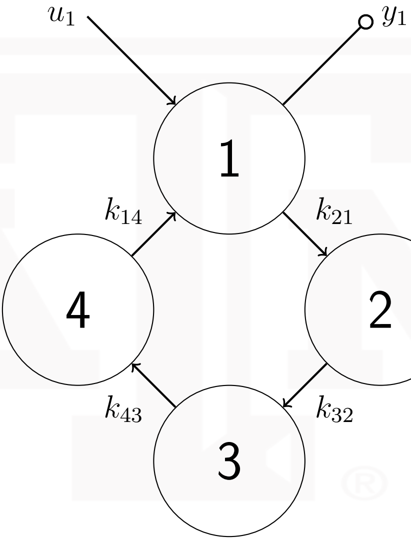

Model Properties

Compartmental Matrix

The **compartmental matrix** of a linear compartmental model $\mathcal{M}$ is given by $A = (a_{ij})$, where

$$a_{ij} := \begin{cases} \text{-}\mathsf{k}_{0i} + \sum_{\{p \mid \exists \ edge: \ i \to p\}} -k_{pi}, \text{ if } i = j \text{ and } i \in Leak \\ \sum_{\{p \mid \exists \ edge: \ i \to p\}} -k_{pi}, \text{ if } i = j \text{ and } i \notin Leak \\ \mathsf{k}_{ij}, \text{ if } i \neq j \text{ and the model contains an edge } j \to i \\ 0, \text{ if } i \neq j \text{ and the model does not contain an edge } j \to i \end{cases}$$

[1, Definition 2.6]

Model Properties

Compartmental Matrix

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[1, Definition 2.6]

$$A = \begin{pmatrix} -k_{21} & 0 & 0 & k_{14} \\ k_{21} & -k_{32} & 0 & 0 \\ 0 & k_{32} & -k_{43} & 0 \\ 0 & 0 & k_{43} & -k_{14} \end{pmatrix}$$

Model Properties

Input-Output Equations [1, Proposition 2.10]

The **input-output equations** for a compartmental matrix A are the system of equations

$$det(\partial I_{n,n} - A)y_j = \sum_{i \in Inputs} (-1)^{i+j} det((\partial I_{n,n} - A)_{i,j})u_i$$

where $j \in Outputs$, ∂ is a derivative operator, $I_{k,\ell}$ is the k by ℓ identity matrix, and $((\partial I_{n,n} - A)_{i,j})$ is the submatrix formed by removing the i^{th} row and j^{th} column from $(\partial I_{n,n} - A)$.

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Rewrite as polynomials in ∂

$$[c_n \partial^n + \cdots + c_1 \partial + c_0] y_j = \sum_{i \in Inputs} [d_{i,n-1} \partial^{n-1} + ... + d_{i,1} \partial + d_{i,0}] u_i$$

where each coefficient c_k and $d_{i,k}$ is a rational function of the rate parameters in the system.

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$$det(\partial I_{n,n} - A)y_j = \sum_{i \in Inputs} (-1)^{i+j} det((\partial I_{n,n} - A)_{i,j})u_i$$

$$(\partial I - A) = \begin{pmatrix} \partial + k_{21} & 0 & 0 & -k_{14} \\ -k_{21} & \partial + k_{32} & 0 & 0 \\ 0 & -k_{32} & \partial + k_{43} & 0 \\ 0 & 0 & -k_{43} & \partial + k_{14} \end{pmatrix}$$

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$$[(\partial+k_{21})(\partial+k_{32})(\partial+k_{43})(\partial+k_{14})-k_{21}k_{32}k_{43}k_{14}]y_1 = [(\partial+k_{32})(\partial+k_{43})(\partial+k_{14})]u_1$$

Elementary Symmetric Polynomials

For a set $S = \{a_1, \dots, a_n\} \subsetneq \mathbb{R}$, we define the k^{th} elementary symmetric polynomial on S as follows:

$e_0(a_1, \dots, a_n) = 1$

$e_k(a_1, \dots, a_n) = \sum_{1 \le i_1 < i_2 < \cdots < i_k \le n} a_{i_1} a_{i_2} \dots a_{i_k}$, where $1 \le k \le n$

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Example

$e_1(x, y, z) = x + y + z$

$e_2(x, y, z) = xy + xz + yz$

$e_3(x, y, z) = xyz$

Elementary Symmetric Polynomials

Property 1

If $S \subsetneq \mathbb{R}$ contains n elements, then

$$\prod_{a \in S}(x-a) = e_0(S)x^n + e_1(S)x^{n-1} + \cdots + e_{n-1}(S)x + e_n(S)$$

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$E = \{k_{21}, k_{32}, k_{43}, k_{14}\}$
$F = \{k_{32}, k_{43}, k_{14}\}$

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$$[(\partial + k_{21})(\partial + k_{32})(\partial + k_{43})(\partial + k_{14}) - k_{21}k_{32}k_{43}k_{14}]y_1 = [(\partial + k_{32})(\partial + k_{43})(\partial + k_{14})]u_1$$

$E = \{k_{21}, k_{32}, k_{43}, k_{14}\}$
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$$[(\partial^4 + e_1(E)\partial^3 + e_2(E)\partial^2 + e_3(E)\partial + e_4(E)) - e_4(E)]y_1 = [\partial^3 + e_1(F)\partial^2 + e_2(F)\partial + e_3(F)]u_1$$

Coefficient Map

$$[\partial^4 + e_1(E)\partial^3 + e_2(E)\partial^2 + e_3(E)\partial]y_1 = [\partial^3 + e_1(F)\partial^2 + e_2(F)\partial + e_3(F)]u_1$$

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Given input-output equations for a model, we define a **coefficient map** $\bar{\boldsymbol{c}} : \mathbb{R}^{L+E} \to \mathbb{R}^m$ mapping the model's set of parameters to the vector

$$(c_n, \quad \ldots, \quad c_0, \quad d_{1,n-1}, \quad \ldots, \quad d_{k,0})$$

where k is the number of inputs.

Coefficient Map

$$[\partial^4 + e_1(E)\partial^3 + e_2(E)\partial^2 + e_3(E)\partial]y_1 = [\partial^3 + e_1(F)\partial^2 + e_2(F)\partial + e_3(F)]u_1$$

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$$\bar{\boldsymbol{c}} : \begin{pmatrix} k_{21} \\ k_{32} \\ k_{43} \\ k_{14} \end{pmatrix} \mapsto \begin{pmatrix} e_1(E) \\ e_2(E) \\ e_3(E) \\ e_1(F) \\ e_2(F) \\ e_3(F) \end{pmatrix}$$

Elementary Symmetric Polynomial Properties

Property 2

Let $X = \{x_1, \ldots, x_n\} \subsetneq \mathbb{R}$ be a set of unknown real numbers. Then, given the values of each elementary symmetric polynomial $\{e_1(X), e_2(X), ..., e_n(X)\}$, there exist n possible values for each variable x_i. Furthermore, there exist $n!$ total possible solutions $(x_1, ..., x_n)$.

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Property 3

Let two sets F and G partition $E \subsetneq \mathbb{R}$.

$$e_i(E) = e_i(F) + e_{i-1}(F)e_1(G) + e_{i-2}(F)e_2(G) + \cdots + e_1(F)e_{i-1}(G) + e_i(G)$$

$$e_1(E) - e_1(F) = k_{21}$$

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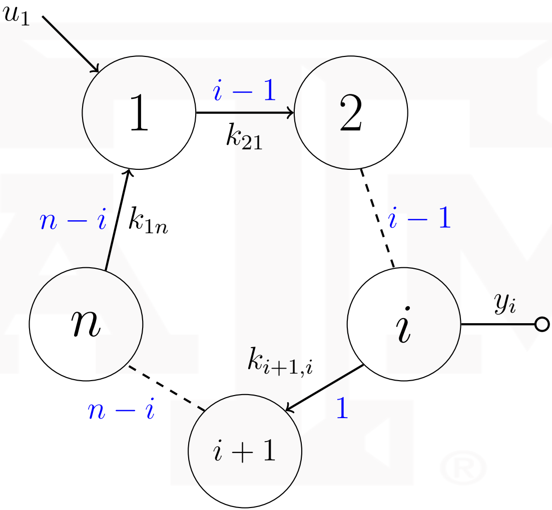
$$e_1(E) - e_1(F) = k_{21}$$

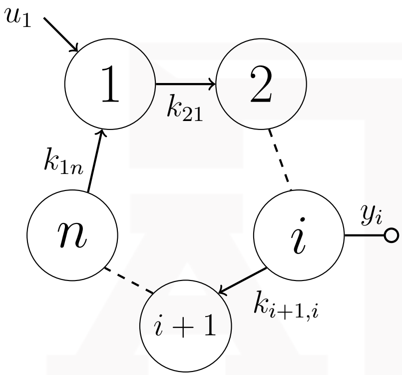
Recall $\{e_1(F), e_2(F), e_3(F)\}$ are known.
By Property 2, k_{32}, k_{43}, k_{14} have 3 solutions (**identifiability degree**).
The model has $3!$ solutions.

Result: Identifiability of Cycle Models ($In = \{1\}, Out = \{i\}, 1 \leq i < n$)



Identifiability degree is $(n-i)!(i-1)!$

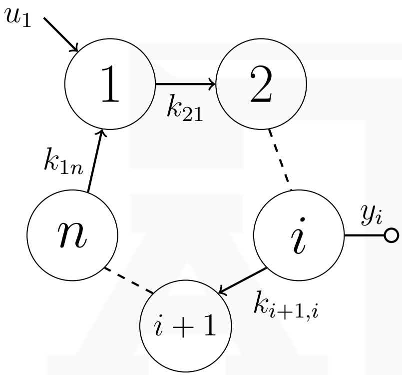
Proof



$$E = \{k_{21}, k_{32}, \ldots, k_{1n}\}$$

$$F = \{k_{i+2,i+1}, \ldots, k_{1n}\}$$

Proof



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Proof

$$\left[\prod_{1\le \ell\le n}(\partial + k_{\ell+1,\ell}) - k_{21}k_{32}\dots k_{1n}\right] y_i =$$

$$(-1)^{i+1}\begin{vmatrix}
-k_{21} & \partial + k_{32} & 0 & \dots & 0 & 0 & \dots & 0 & 0 \\
0 & -k_{32} & \partial + k_{43} & \dots & 0 & 0 & \dots & 0 & 0 \\
0 & 0 & -k_{43} & \ddots & \vdots & \vdots & \dots & \vdots & \vdots \\
0 & 0 & 0 & \ddots & \partial + k_{i,i-1} & 0 & \dots & 0 & 0 \\
0 & 0 & 0 & \dots & -k_{i,i-1} & 0 & \dots & 0 & 0 \\
0 & 0 & 0 & \dots & 0 & \partial + k_{i+2,i+1} & \dots & 0 & 0 \\
\vdots & \vdots & \vdots & \ddots & \vdots & -k_{i+2,i+1} & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \dots & 0 & 0 & \ddots & \partial + k_{n,n-1} & 0 \\
0 & 0 & 0 & \dots & 0 & 0 & \dots & -k_{n,n-1} & \partial + k_{1n}
\end{vmatrix} u_1$$

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\end{vmatrix} u_1$$

$$[\partial^n + e_1(E)\partial^{n-1} + e_2(E)\partial^{n-2} + \cdots + e_{n-1}(E)\partial] y_i =$$

$$k_{21}k_{32}\dots k_{i,i-1}[\partial^{n-i} + e_1(F)\partial^{n-i-1} + \cdots + e_{n-i}(F)] u_1$$

Proof

$$c : \begin{pmatrix} k_{21} \\ k_{32} \\ k_{43} \\ \vdots \\ k_{1n} \end{pmatrix} \mapsto \begin{pmatrix} e_1(E) \\ e_2(E) \\ \vdots \\ e_{n-1}(E) \\ k_{21}k_{32}\dots k_{i,i-1} \\ [k_{21}k_{32}\dots k_{i,i-1}]e_1(F) \\ \vdots \\ [k_{21}k_{32}\dots k_{i,i-1}]e_{n-i}(F) \end{pmatrix}$$

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Use right hand-side coefficients to exactly determine $\{e_1(F), \dots, e_{n-i}(F)\}$

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Use right hand-side coefficients to exactly determine $\{e_1(F), \ldots, e_{n-i}(F)\}$

Elements of $F = \{k_{i+2,i+1}, \ldots, k_{1n}\}$ have $(n-i)$ solutions.

The identifiability degree of F is bounded above by $(n-i)!$

Proof

Use induction to find each of $\{e_1(B), \ldots, e_i(B)\}$, where $B = \{k_{21}, \ldots, k_{i+1,i}\}$

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$$e_i(E) = e_i(F) + e_{i-1}(F)e_1(B) + \cdots + e_i(B)$$

Note $e_i(B) = [k_{21}k_{32} \ldots k_{i,i-1}]k_{i+1,i}$

Reduce as above to find $\{e_1(B \setminus \{k_{i+1,i}\}), \ldots, e_{i-1}(B \setminus \{k_{i+1,i}\})\}$.

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Each of $\{k_{21}, k_{32}, \ldots, k_{i,i-1}\}$ have $(i-1)$ solutions.
Identifiability degree of $B \setminus \{k_{i,i-1}\}$ is bounded above by $(i-1)!$

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$$\vdots$$

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Model identifiability degree is bounded above by $(n-i)!(i-1)!$

Further Results and Problems

Result: Identifiability of directed-cycle models is understood

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- Identifiability degree lower bound

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- Other model classes

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Additional Problems:

- Identifiability degree lower bound
- Other model classes
- Further generalization

Acknowledgements

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References

[1] Saher Ahmed et al. *Identifiability of Catenary and Directed-Cycle Linear Compartmental Models*. 2024. URL: https://arxiv.org/pdf/2412.05283.

Thank You!